

OPTIMIZATION OF GEL-BASED NANOEMULSION OF TURMERIC ESSENTIAL OIL WITH QUALITY BY DESIGN: CHARACTERISTICS AND ANTIOXIDANT EFFECTS

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Background & Objectives

One of the newest research strategies is applying natural products to develop effective formulations with minimal drawbacks and maximum therapeutic effect⁽¹⁻²⁾. Turmeric essential oil (TEO) is one of the essential oils that have the potential as a natural antioxidant⁽³⁻⁴⁾. This study aimed to observe the effect of emulsifier concentration and gelling agent in producing nanoemulgel (NEG) and its antioxidant effect from TEO. This study is the first development of a formulation using TEO NE-loaded into a gel base proposed for topical use.

Method

Initially, various TEO-loaded NEG formulations were prepared using high-speed homogenization. The formulation design used the Central Composite of the Response Surface Method (CCD-RSM) to obtain the optimal TEO-loaded NEG formula. The optimization variables of the TEO-loaded NEG formula include the concentration of SpanTM 80-Tween 80 (X_1) and Carbopol[®] 980 NF (X_2) with particle size response (PZ) (Y_1), polydispersity index (PDI) (Y_2), zeta potential (ZP) (Y_3), and IC_{50} (Y_4). The evaluation result of the responses of the actual TEO-loaded NEG was compared with the predicted CCD-RSM.

Results

The optimal TEO-loaded NEG developed was made with a 5.13% of emulsifier and 1.14% of gelling agent. The evaluation results showed the optimal nano-metric size of TEO-loaded NEG (178.8 ± 5.3 nm) with PDI (0.430 ± 0.017), zeta potential (-26.29 ± 4.69 mV), and medium potency IC_{50} (124.84 ± 2.96 mg/mL).

Statistical analysis results on CCD-RSM showed that the interaction between gelling and emulsifier affected particle size. At the same time, the factors that influence the IC_{50} are the concentrations of the two types of excipients and the interactions between gelling molecules.

Conclusion

The optimal formulation showed unfavourable characteristics in the PDI and zeta potential values, so it was necessary to re-observe other factors to obtain a potential delivery system for topical administration.

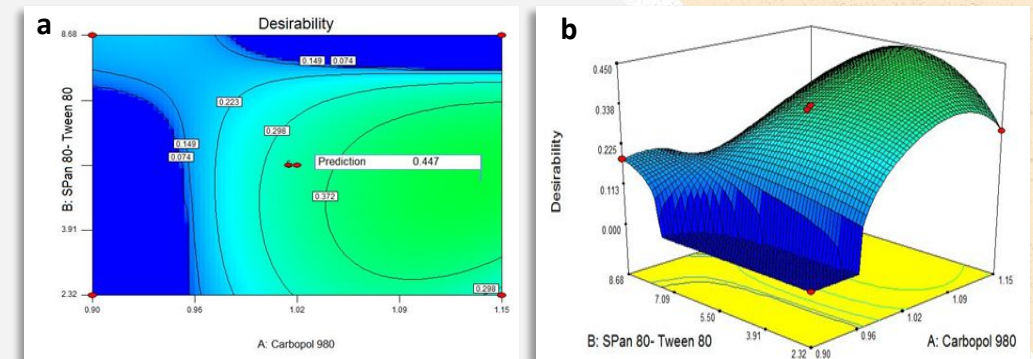


Fig 1. Contour Plot (a) 3D (b) of Desirability

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ABSTRACT BOOK



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FOREWORD

Honorable Dean of Faculty of Pharmacy, Universitas Padjadjaran,
Distinguished speakers, including keynote and invited speaker, and all the participants of the The 5th International Seminar on Pharmaceutical Sciences and Technology (ISPST) and 3rd International Seminar and Expo on Jamu (ISEJ) 2022 embedded 13rd Annual Meeting ISCC.

First of all, please allow me to extend my warmest welcome you at the The 5th International Seminar on Pharmaceutical Sciences and Technology (ISPST) and 3rd International Seminar and Expo on Jamu (ISEJ) 2022 embedded 13rd Annual Meeting ISCC in this morning at online zoom.

The 5th ISPST and 3rd ISEJ are a continuation of the 4th ISPST 2020 and 2nd ISEJ 2017. At the 5th ISPST 2022 and 3rd seminars ISEJ collaborated with the Indonesian Society for Cancer and Chemotherapy (ISCC), an Indonesian-Asian cancer research organization that provides a dynamic network for the exchange of scientific information among academics and practitioners who focus on cancer research.

Distinguished guests, ladies, and gentlemen,

On behalf of the committee of this seminar, we reported that this event involved 27 Speakers including 9 keynotes, and 18 invited speakers from 9 countries, The Netherlands, USA, Japan, South Korea, Australia, Malaysia, India, Thailand, and also Indonesia.

The registered participants were 300 participants with details, 73 participants as oral presenters, 79 participants as poster presenters, and 150 participants as regular participants.

We hope that you will gain a lot of benefits from fruitful discussions during this program. We would like to thank to sponsors that help the funding: rector Universitas Padjadjaran, Director General of Higher Education, Research, and Technology, Ministry of Education, Culture, Research and Technology, and Cendo Pharmaceuticals Industry, also support by Product: Paragon Technology and Innovation and Bintang Tujuh. Of course, I would like to express my expression to the organizing committee of this program. I am indeed delighted and thank you for all your effort and hard working in making this program happened.

For all distinguished guests from abroad and from other cities in Indonesia, enjoy this seminar so that you gain insight into pharmaceutical science and make the best use of your time to discuss with the experts.

Thank you very much.

Wassalamu'alaikum Wr Wb.

Chairman of The 5th ISPST – The 3rd ISEJ – The 13th ISCC

Prof. apt. Muchtaridi, Ph.D

WELCOME SPEECH FROM CHAIRMAN OF INDONESIAN SOCIETY FOR CANCER CHEMOPREVENTION (ISCC)

Dear colleagues,

We are now slowly but surely moving to the new era after the pandemic. The pandemic undoubtedly opens new ways in disseminating science and technology. Instead of an on-site seminar, we are now flexible in having the hybrid system. Thus, following the success of the last two virtual and hybrid events in 2020 and 2021, this year Indonesian Society for Cancer Chemoprevention (ISCC) in partnership with the Faculty of Pharmacy, Universitas Padjadjaran re organizing an international seminar and meeting. On behalf of ISCC, I am honored to welcome all participants to the 5th International Seminar on Pharmaceutical Sciences and Technology (ISPST), the 3rd International Seminar on Expo of Jamu (ISEJ), and 13th Annual Indonesian Society for Cancer Chemoprevention Conference (ISCC 2022). ISCC continuously accelerates the annual scientific forum to disseminate information and update the latest scientific advances in the field of cancer chemoprevention, and facilitate the exchange of ideas and technology and develop networking and communication among participants. Drug discovery and development is the main topic that the Faculty of Pharmacy Universitas Padjadjaran keen on and it is an indispensable area from cancer chemoprevention. Moreover, “jamu” or herbal medicine is also a big topic that is important in pharmaceutical sciences. In collaboration, this year's event with the theme of “Pharmaceutical Technology on Natural Medicines in Post Pandemic Recovery” is being promoted as a communication forum between academicians and researchers in the fields of pharmaceutical sciences, pharmaceutical technology, and integrated research on Jamu or herbal medicine.

As I mentioned earlier, the hybrid system makes this event much more efficient and accessible globally without reducing its quality. We could not thank enough to our distinguishable invited speakers from all over the world, not only Indonesia, but also from Malaysia, Japan, India, Netherland, USA, and Australia – in total 29 speakers –, for accepting our invitation. We also warmly welcome 133 oral and poster presenters and all the participants. We wish that all of the updated knowledge presented in this seminar would be useful as a comprehensive understanding to improve our academic, research, and professional activities. We encourage all participants to take as much as benefit through this scientific meeting.

Lastly, I would like to deliver our gratitude to the committee and Faculty of Pharmacy, Universitas Padjadjaran for working together to make this event possible and facilitating the ISCC annual meeting.

**Indonesian Society for Cancer Chemoprevention
Chairman,**

Prof. Dr. apt. Edy Meiyanto, M.Si

OPENING REMARKS FROM DEAN OF FACULTY OF PHARMACY UNIVERSITAS PADJADJARAN

First of all, I would like to convey my greetings and appreciations to all of the invited speakers especially :

Ir. Budi Gunadi Sadikin, CHFC, CLU. (Ministry of Health)

Prof. Tomoya Uehara, Ph.D. (Chiba University, Japan)

Prof. Edi Meiyanto (President of ISCC/UGM)

Prof. Dr. Sanjay Jachak (NIPER India)

Prof. dr. Maria Yazdanbakhsh (Universiteit Leiden, The Netherlands)

Prof. Taifo Mahmud (Oregon State University, USA)

Prof. Jun-Ya Kato (NAIST-Japan)

Prof. Habibah A. Wahab (President of CADD Asia/Universiti Sains Malaysia)

Prof. Tao Liu (UNSW Australia.)

Thank you for your participation in our event.

Greetings from Universitas Padjadjaran,

Ladies and gentlemen,

It is a great pleasure to welcome you to the joint seminars of the 5th International Seminar on Pharmaceutical Sciences and Technology (ISPST) and the 3rd International Seminar on Expo of Jamu (ISEJ), as a continuation from our previous bi-annual ISPST and ISEJ seminars which are organized by the Faculty of Pharmacy Universitas Padjadjaran and now is also in collaboration with the Indonesian Society for Cancer Chemoprevention (ISCC) which will hold their annual meeting. Similar with our 4th ISPST two years ago, this seminar is also held online. Although now we begin to slowly recover from the COVID-19 pandemic, we realise that we still need to be aware of the spread of the virus.

I would like to start by wishing you and your families for your good health. It's a great opportunity that all of us could gather here on the event which serves as a venue for researcher, professional, and students to build many collaborations for their research project and will also enrich collaborations activity in education, research and community service.

The theme of 5th International Seminar on Pharmaceutical Sciences and Technology (ISPST) this year which is held as join seminar with the 3rd International Seminar on Expo of Jamu (ISEJ) is ***Pharmaceutical Technology on Natural Medicines in post pandemic recovery***. I hope the this theme will explore the opportunities for us to start afresh and positive transformations to improve health and wellbeing.

Moreover, I hope this seminar will accomplish all its aims and earnestly desire that all participants will be able to benefit from the presentations and discussions and this seminar will enrich the development of science, not only in Indonesia but also worldwide. I would like to thank the organizing committee for their tremendous efforts to realize this program.

Once again, I am honored to welcome you at this seminar. I wish all of the speakers and participants will gain many benefits and insightful experience.

With Bismillahirrohmanirrahim. I officially open the 5th International Seminar on Pharmaceutical Sciences and Technology (ISPST) and the 3rd International Seminar on Expo of Jamu (ISEJ) embedded with ISCC annual meeting.

Best Regards

Prof. Dr. Ajeng Diantini, M.Si., Apt.

OPENING REMARKS FROM MINISTER OF HEALTH OF THE REPUBLIC INDONESIA

Excellencies ladies and gentlemen,

In the covid-19 pandemic situation, there was an extreme increase in demand for covid 19 related products. We experience difficulties in obtaining pharmaceutical and medical devices needed for disease control and treatment. Since the pharmaceutical and medical device sectors are still significantly dependent on imports. We realize that Indonesia must build its resilience ensuring that all medicines and medical devices can be produced domestically.

We have developed strategies to build pharmaceutical and medical device resilience. Briefly, the targets are stated in the timeline as shown in the slide. It has indicated the types of raw materials for drugs, vaccines, and medical devices that can be produced domestically. The achievement of these targets is carried out by fixing fundamentals and called processes involving API's stakeholders.

Distinguished guest,

Indonesia is an archipelago country with millions of hectares of tropical forests which consists thousands of species of plants and is home to 80% of the world's medicinal plants.

More than 30 thousand of traditional medicine formulas have been widely used in the community. Indonesia with over 217 million population is a potential market for traditional medicine.

This should be a great opportunity for us to develop an investment in local phytopharmaceuticals manufacturing and contribute to strengthening the resilience of pharmaceuticals.

Excellencies ladies and gentlemen,

I wish you all to have a fruitful discussion during the seminar and it has been a pleasure being with all of you today.

Thank you.

Best Regard

Ir. Budi Gunadi Sadikin, CHFC, CLU

COMMITTEE

Position	Name
Steering Committee	<ol style="list-style-type: none"> 1. Prof. Dr. Ajeng Diantini, Apt. 2. Prof. Dr. Aliya Nur Hasanah, S.Si., Apt., M.Si. 3. Auliya Abdurrohimi Suwantika, S.Si., Apt., MBA.,PhD
Advisory Board	<ol style="list-style-type: none"> 1. Prof. Dr. Apt. Moelyono MW. 2. Prof. Dr. Resmi Mustarichie 3. Prof. Dr. Apt. Marline Abdassah 4. Dr. Apt. Tiana Milanda, M.Si. 5. Dr. apt. Sriwidodo
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Vice Chairman	Prof. Dr. rer. nat. Muhaimin, M.Si
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Tresurer	<ol style="list-style-type: none"> 1. Dr. apt. Nyi Mekar Saptarini, M.Si 2. Dr. apt. Ade Zuhrotun, M.Si
Scientific Committee	<ol style="list-style-type: none"> 1. Dr. apt. Yasmiwar Susilawati, M.Si 2. Prof. Dr. rer. nat. Anis Yohana Choirunisaa, M.Si 3. Dr. apt. Rd. Maya febriyanti 4. Dr. Sri Agung Fitri Kusuma, M.Si 5. Apt. Ferry Ferdiansyah, M.Si 6. Dr. Apt. Iyan Sopyan, M.Si 7. Apt. Gofarana Wilar, M.Si., PhD 8. Apt. Holis A. Holik, Ph.D 9. Dr. apt. Ida Musfiroh, M.Si
Program Activity	<ol style="list-style-type: none"> 1. Dr. apt. Rimadani Pratiwi, M.Si 2. Intan Timur Maisyarah, Ph.D 3. Apt. Miski Aghnia, M.Farm., PhD
Expo	<ol style="list-style-type: none"> 1. Dr. med. Apt. Melisa Intan Barliana 2. Dr. Apt. Sriwidodo, M.Si
Publication and Documentation	<ol style="list-style-type: none"> 1. Apt. Zelika Mega Rhamadania, M.Si 2. Apt. Agus Rusdin, M.Farm.
IT, Multimedia, and Zoom	<ol style="list-style-type: none"> 1. Prof. Apt.,Nasrul Wathoni Ph.D 2. Dr. apt. Sandra Megantara
Consumption Section	Dr. Apt.Ellin Febrina, M.Si
Logistic and Supporting Team	<ol style="list-style-type: none"> 1. Apt. Imam Adi Wicaksono, M.Si 2. Apt. Arif Satria W, M.Si 3. BEM KEMAFAR 4. Himpunan Mahasiswa Pasca Sarjana Fakultas Farmasi Unpad

SCIENTIFIC PROGRAM AND SCHEDULE

Tuesday, 18 October 2022	
Time	Event
07.30 - 08.00	Registration
08.00 - 08.30	Opening Ceremony : Welcome speech of chairman of 5 th ISPST and 3 rd ISEJ Welcome speech of President of ISCC Welcome speech of Dean of Faculty of Pharmacy, Universitas Padjadjaran Welcome speech of Rector of Universitas Padjadjaran, opening of seminar and expo
08.30 - 09.15	Keynote Speaker I: Ir. Budi Gunadi Sadikin, CHFC, CLU. (Ministry of Health)*
09.15 - 09.45	Keynote Speaker II: Prof. Tomoya Uehara, Ph.D. (Chiba University, Japan)
09.45 - 10.00	QnA Speaker II
10.00 – 10.45	Keynote Speaker III: Prof. Edi Meiyanto (President of ISCC/UGM)
10.45 - 11.00	QnA Speakr III
11.00 – 11.45	Keynote Speaker IV: Prof. Dr. Sanjay Jachak (NIPER India)
11.45 - 12.00	QnA Speaker IV
12.00 - 13.00	Lunch Break, Poster Session
13.00 – 15.00	BREAKROOM 1: Plenary session I: Scientific Jamu Assoc. Prof Mohd Razip, Asaruddin (Univesity Malaysia Sarawak) DR (cand.) dr. Ingrid Tania, M.Si. (UI) Assoc. Prof. apt. Dr. Yasmiwar (Unpad) BREAKROOM II: Plenary session II: Drug delivery Assoc. Prof. Rathapon Asasutjarit, Ph.D (Thammasat University, Thailand) Dr. apt. Iyan Sopyan (Unpad) Khaled M. Elamin, Ph.D (Kumamoto University)
15.00 – 15.30	Break
15.30 – 16.00	Keynote Speaker V: Prof. dr. Maria Yazdanbakhsh (Universiteit Leiden, Belanda)
16.00 - 16.15	QnA Speaker V
16.15 – 17.00	Parallel session (Oral Presentation)

Wednesday, 19 October 2022	
Time	Event
08.00 - 08.45	Keynote Speaker VI: Prof. Taifo Mahmud (Oregon State University, Amerika)
08.45 - 09.00	QnA Speaker VI
09.00 - 09.45	Keynote Speaker VII : Prof. Jun-Ya Kato (NAIST-Jepang)*
09.45 - 10.00	QnA Speaker VII
10.00 - 11.00	Paralel Session (Pharmaceutical Technology of Cancer and Microbiology and Biotechnology)
11.00 – 12.00	Parallel Session
12.00 – 13.00	Lunch Break, Poster Session
13.00 - 15.00	<p>BREAKROOM 1: Plenary Session III : Pharmaceutical Technology of Cancer Prof. Nasrul Wathoni (Unpad) Thavasyappan Thambi, Ph.D. (Kyung Hee University, South Korea) Dr. apt. Riris Istighfari Jennie (UGM)</p> <p>BREAKROOM II: Plenary Session IV : Microbiology and Biotechnology Dr. apt. Tiana Milanda (Unpad) Prof. Marlia Singgih (ITB) Dr. Endang Purwantini (Virginia Polytechnic Institute and State University, Amerika)</p>
15.00 – 15.30	Break
15.30 – 16.30	Keynote Speaker VIII: Prof. Habibah A. Wahab (President of CADD Asia/Universiti Sains Malaysia)

Thursday, 20 October 2022	
Time	Event
08.00 - 09.00	Keynote Speaker IX : Dirjen Farmasi dan Alat Kesehatan (Dr. Dra. Lucia Rizka Andalusia, Apt, M.Pharm, MARS)*
09.00 - 09.45	Keynote Speaker X : Prof. Tao Liu (UNSW Australia.)
09.45 – 10.00	QnA Speaker X
10.00 – 12.00	BREAKROOM 1: Plenary Session V : Pharmaceutical Analysis Breakroom 1 : Dr. apt. Ida Musfiroh (Unpad) Dr. Mohamad Rafi, MSi (IPB) Dr. Ezatul Ezleen Kamrulzaman (USM) BREAKROOM 2: Plenary Session VI: CADD Prof. Daryono Hadi Tjahyono (ITB) Dr. Sandra Megantara (UNPAD) Dr Suman Sinha (Tata Institute of Fundamental Research, Hyderabad, India)
12.00-13.00	Lunch Break dan preparation workshop dan annual meeting
13.00 - 17.00	Workshop dan annual meeting secara luring di Lab Workshop 1: Natural Ingredients for Make-up and Skin Care Hybrid Workshop 2: Microwave Syntesis (Maja Bintang) Workshop 3: Encapsulation process technology

ORAL AND POSTER PRESENTATION SCHEDULE

ORAL PRESENTATION

Day 1		
Breakout Room	Number	Presenter
D1-BR1	OP-039	Untung Gunawan
	OP-024	Riska Prasetiawati
	OP-047	Muthi Ikawati
	OP-029	Aiyi Asnawi
D1-BR2	OP-004	Indah Hairunisa
	OP-006	Nasri
	OP-007	Dhiya Ulhaq Salsabila
	OP-013	Vera Estefania Kaban
	OP-015	Ainun Rohmawati Bareta
D1-BR3	OP-017	Dr. apt. Yuliet, S.Si.M.Si.
	OP-018	NOVYANANDA SALMASFATTAH
	OP-021	Endah Puji Septisetyani
	OP-067	apt.Uce Lestari, S.Farm, M.Farm
D1-BR4	OP-002	Marissa Angelina
	OP-008	Ratih Kurnia Wardani
	OP-009	Nisa UI Hasanah
	OP-011	Ahmad Syauby Tafrihani
	OP-045	risna agustina
D1-BR5	OP-016	Nadzifa Nugraheni
	OP-027	Ummi Maryam Zulfin
	OP-042	Hanaan Emilia Adi Hastuti
	OP-043	Dewi Rahmawati
D1-BR6	OP-077	Tri Budi Julianti
	OP-078	Insan Sunan Kurniawansyah
	OP-061	Midori Rahmadhany Putri Adisusilo
	OP-066	Inggita Hasi Rahmah
	OP-068	Dyaningtyas Dewi Pamungkas Putri
D1-BR7	OP-001	Fitriani Jati Rahmania
	OP-003	Ayu Shabrina
	OP-037	Novriyanti Lubis
	OP-082	Tiwuk Susantiningasih
	OP-083	Marko Jeremia Kalalo

Day 2		
Breakout Room	Number	Presenter
D2-BR1	OP-031	Eva Susanty Simaremare
	OP-028	Yeni
	OP-036	Isti Daruwati
	OP-049	Desty Restia Rahmawati
D2-BR2	OP-034	Hesti Riasari
	OP-035	Afifah Kusuma Vardhani
	OP-040	SANTI PERAWATI
	OP-044	Christopher Filando Santoso
D2-BR3	OP-073	Dr. apt. Dewi Astriany, M.Si.
	OP-054	Satriyo Krisna Palguno
	OP-055	Wisnu Cahyo Prabowo
	OP-056	Rina Fajri Nuwarda

	OP-075	Rahma Ziska
D2-BR4	OP-046	Yuni Andriani
	OP-050	Yulia Ratna Dewi
	OP-051	Putri Anggreini
	OP-048	Erlia ANggrainy Sianipar
D2-BR5	OP-058	Emni Purwoningsih
	OP-012	Fathnur Sani K
	OP-041	rizky yulion putra
	OP-085	Husnawati
D2-BR6	OP-052	Siti Hairiah
	OP-053	Tasya
	OP-064	Andi Tenri Kawareng
	OP-079	Vina Maulidya
D2-BR7	OP-084	Andi Khomeini Takdir
	OP-071	Sukmawati. S
	OP-072	Assyifa Cindykia
	OP-074	Purwaniati
	OP-080	Teuku Baihaqi Septiady
	OP-081	Hanggara Arifian

POSTER PRESENTATION

Day 1		
Room	Number	Presenter
1	PP-001	apt. Nining, M.Si.
	PP-002	Anisa Amalia
	PP-003	Garnadi Jafar
	PP-004	I Gusti Ngurah Jemmy Anton Prasetya
	PP-005	Vera Nurviana
	PP-006	Stella Natalia
	PP-007	TUBAGUS AKMAL
	PP-008	Lusi Nurdianti
	PP-009	Novia Permata Hapsari
	PP-010	rahmah elfiyani
	PP-011	Trian Nur'aripin
	PP-012	Ira Rahmiyani
	PP-013	Ade Yeni Aprillia
	PP-014	Deny Puriyani Azhary
	PP-015	Yenni Puspita Tanjung
	PP-016	Nyi Mekar Saptarini
	PP-017	Fith Khaira Nursal
2	PP-018	Fahrauk Faramayuda
	PP-019	Norisca Aliza Putriana
	PP-020	Gofarana Wilar
	PP-021	Norisca Aliza Putriana
	PP-022	Resmi Mustarichie
	PP-024	Sri Agung Fitri Kusuma
	PP-025	Rimadani Pratiwi
	PP-026	Rimadani Pratiwi
	PP-027	Winasih Rachmawati
	PP-028	Apt. Dr. Tina Rostinawati M.Si
	PP-029	Apt. Dr. Tina Rostinawati M.Si

	PP-031	Diah Lia Aulifa
	PP-032	Sri Agung Fitri Kusuma
	PP-033	Sri Agung Fitri Kusuma
	PP-034	Arif Budiman
	PP-035	Arif Budiman
	PP-036	apt. Nur Rahayuningsih, M.Si
	PP-037	Himaniarwati
3	PP-038	Irma Erika Herawati
	PP-040	Raden Bayu Indradi
	PP-041	Lauren Pangestu
	PP-042	Aulia Nur Septiani
	PP-043	Nadiyah Adira Hanun
	PP-044	Ami Tjitraresmi
	PP-045	Ike Susanti
	PP-046	Endah Kartikawati
	PP-047	Marisa Dwi Ariani
	PP-048	Muhammad Ryan Radix Rahardhian
	PP-049	Danni Ramdhani
	PP-051	Intan Timur Maisyarah
	PP-052	Klarissa Nabila
	PP-053	Citra Rosyidah
	PP-054	Faaza Aulia Rahman
	PP-055	Gofarana Wilar
	PP-056	Ratna Asmah Susidarti
4	PP-057	Rohmanika
	PP-058	Ellin Febrina
	PP-059	Silviana Hasanuddin
	PP-060	Silviana Hasanuddin
	PP-061	Raden Maya Febriyanti
	PP-062	Ferry Ferdiansyah Sofian
	PP-063	Andhara Marsha Belinda
	PP-064	Khalisha Qintara Khairunnisa
	PP-065	Hasna Raihan Veninda
	PP-066	Driyanti Rahayu
	PP-067	Resmi Mustarichie
	PP-068	Trisnawati
	PP-070	Yoppi Iskandar
	PP-071	Tita Nofianti
PP-072	Rini Hendriani	
PP-073	Ade Zuhrotun	
PP-074	Yoga Windu Wardhana	
PP-079	Soraya Mita	
PP-080	Muhamad Adam Mustapa	

KEYNOTE AND INVITED SPEAKER

Ir. Budi Gunadi Sadikin, CHFC, CLU. (Ministry of Health, Indonesia)



Ir. Budi Gunadi Sadikin, CHFC, CLU is an Indonesian politician. As of 23 December 2020, he serves as Minister of Health in the Onward Indonesia Cabinet of President Joko Widodo. Ir. Budi Gunadi Sadikin, CHFC, CLU is only the second Health Minister not to graduate from a medical school. He previously served as President Director at Bank Mandiri. He served as President Director of PT Inalum (Persero), then in 2019, he was appointed Deputy Minister of Badan Usaha Milik Negara (BUMN) by President Joko Widodo.

Prof. Tomoya Uehara, Ph.D. (Chiba University, Japan)



Prof. Tomoya Uehara, Ph.D is a professor at the Laboratory of Molecular Imaging and Radiotherapy, Graduate School of Pharmaceutical Sciences, Chiba University. Research field Prof. Tomoya Uehara, Ph.D as follows: (1) Development of radio-metal labeling agents for peptides that reduce non-specific accumulation; (2) Development of radiolabeled agents using alpha-emitting radionuclides; (3) Development of radiometal labeling chelates. Prof. Tomoya Uehara, Ph.D has made more than 60 extraordinary papers during his academic service.

Prof. Dr. apt. Edy Meiyanto, M.Si (President of ISCC/Universitas Gadjah Mada)



Prof. Dr. apt. Edy Meiyanto, M.Si is a professor in the Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Universitas Gadjah Mada. Prof. Edy Meiyanto studied Bachelor of Pharmacy and Pharmacist Profession at Universitas Gadjah Mada. Prof. Edy Meiyanto continued his Master of Science education at Universitas Gadjah Mada and continued his doctoral education in Molecular Oncology at the Nara Institute of Science and Technology, Japan. Currently, Prof. Edy Meiyanto also serves as President of the Indonesian Society for Cancer Chemoprevention.

Prof. Dr. Sanjay Jachak (NIPER India)



Prof. Sanjay Jachak, M. Pharm., Ph.D. is Professor at National Institute of Pharmaceutical Education and Research (NIPER), Mohali, Punjab, India. He has job experiences as Professor, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, Punjab (August 2011- recent); Associate Professor, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, Punjab (August 2006-recent); Assistant Professor, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, Punjab (July 1999 – July 2006); Lecturer, N.D. M.V.P. Samaj's College of Pharmacy, Nashik, Maharashtra Mar (Mar 1998- June 1999); Austrian Research Fellow, Institute of Pharmacognosy, Karl Franzens University, Graz, Austria (1995-Feb. 1998); R & D Officer, Glenmark Pharmaceuticals Ltd., Nashik, Maharashtra Mar (1994-Dec. 1994). He has research interest in phytochemistry (isolation, drug discovery, synthesis and bioassay).

Assoc. Prof Mohd Razip, Asaruddin (Univesiti Malaysia Sarawak)



Assoc. Prof. Dr. Mohd Razip Bin Asaruddin is an associate professor at the Faculty of Resource Science and Technology, Universiti Malaysia Sarawak. He studied Master of Science, Resource Chemistry at Universiti Malaysia Sarawak and Master of Pharmaceutical Science at Kyoto University. He also continued his Doctor of Philosophy, Pharmaceutical Technology, at Universiti Sains Malaysia.

DR (cand.) dr. Ingrid Tania, M.Si. (University of Indonesia)



Dr. (Cand.) dr. Ingrid Tania, M.Si is the Chairperson of the Association of Indonesian Traditional Medicine and Herbal Medicine Development Doctors (PD POTJI) since 2019. She has studied medical professional education at the Faculty of Medicine, University of Indonesia. She continued his Master in Herbal studies at the Department of Pharmacy, Faculty of Mathematics and Natural Sciences, University of Indonesia. She is currently studying for a Doctor of Philosophy in Traditional Indonesian Medicine at the Driyakara School of Philosophy, Jakarta. In addition to being the General Chairperson of PD POTJI, she has also served as Deputy Chairperson of the Department of Herbal Medicine and Nusantara Medicine of the MCB National Management Board since 2020.

Assoc. Prof. apt. Dr. Yasmiwar (Universitas Padjadjaran, Indonesia)



Assoc. prof. apt. Yasmiwar Susilawati, M.Si is the Head of the Center for Herbal Studies at the Faculty of Pharmacy, Universitas Padjadjaran. She studied pharmaceutical science undergraduate at Universitas Padjadjaran. She continued his professional education in pharmacists at the Pharmacist Profession Program at the Bandung Institute of Technology. She continued Masters education at Institut Teknologi Bandung and doctoral education at Universitas Padjadjaran. Assoc. prof. apt. Yasmiwar Susilawati, M.Si has research interests in the fields of herbal medicine for hypertension, diabetes mellitus, immunomodulators, and standardization of herbal medicines.

Assoc. Prof. Rathapon Asasutjarit, Ph.D (Thammasat University, Thailand)



Assoc. Prof. Rathapon Asasutjarit, Ph.D is the associate Dean for Research, Innovation, and Graduate Studies at the Faculty of Pharmacy, Thammasat University. He has research interests on (1) application of polymers and surfactants as drug/cosmeceutical delivery systems; (2) nanotechnology for drug/cosmeceutical delivery; (3) skin and ophthalmic drug delivery. He has served as Head of the Thammasat University Research Unit in Drug, Health Product Development and Application (DHP-DA RU) since April 2020.

Dr. apt. Iyan Sopyan (Universitas Padjadjaran, Indonesia)



Dr. apt. Iyan Sopyan, M.Si serves as Head of the Center for Pharmaceutical Preparation Development Studies, Faculty of Pharmacy, Universitas Padjadjaran. He is a lecturer with expertise in pharmaceutical technology. He studied pharmacy undergraduate at Universitas Padjadjaran and continued his Masters and Doctoral education at Universitas Gadjah mada. He has also joined the Indonesian Pharmacists Association (IAI) organization since 2003.

Khaled M. Elamin, Ph.D (Kumamoto University, Japan)



Assoc. Prof. Khalid Suliman, Ph.D is an assistant professor at the Graduate School of Pharmaceutical Sciences, Kumamoto University, Japan. He has expertise in chemical synthesis, bioconjugation, supramolecular complexations technologies and creating animal cancer models for new drugs or formulation development. He studied pharmacy at the Faculty of Pharmacy, Ribat National University, Sudan. He continued his master of pharmacy studies at the Faculty of Pharmacy, Khartoum University, Sudan. He also continued his PPh.D. in Pharmaceutical and Life Science at Kumamoto University, Japan.

Prof. dr. Maria Yazdanbakhsh (Universiteit Leiden, Netherland)



Prof. dr. Maria Yazdanbakhsh heads the department of Parasitology which engages in basic and clinical research and employs an interdisciplinary group of basic and clinical scientists who focus on understanding host-parasite interactions at the molecular, cellular and population level. The knowledge gained is being applied to contribute to 1) development of effective vaccines against parasitic diseases and 2) identification of parasite-derived immune modulatory molecules to control hyper-inflammatory diseases. Her specific research has been focused on the interaction of helminths along with other coinfections with their human host, immune modulation and vaccine development.

Prof. Taifo Mahmud (Oregon State University, USA)



Prof. Taifo Mahmud is a Professor in the Department of Pharmaceutical Science, Oregon State University, USA. He studied Ph.D in Pharmaceutical Science at Osaka University, Japan and a postdoctoral degree in Bioorganic Chemistry or Genetics at the University of Washington, Seattle. He currently serves as Managing Director, International Indonesian Scholar Association in the U.S. and Canada since 2018 and Co-Director, NIH T32 Training Program at the OSU College of Pharmacy since 2019. Programs and research areas carried out by Prof. Taifo Mahmud, among others, Natural products chemistry, biosynthesis, and drug discovery. Application of a multidisciplinary approach that utilizes cutting-edge technologies in molecular genetics, enzymology, and chemistry to produce novel pharmaceuticals, such as antibiotics, antifungals, anti-malarial, and anti-cancer drugs.

Prof. Jun-Ya Kato (NAIST-Japan)



Prof. Jun-Ya Kato is a professor at the Nara Institute of Science and Technology. Currently, Prof. Jun-Ya Kato serves as Advisor to the President, Nara Institute of Science and Technology since 2017. He studied Ph.D in biophysics at Kyoto University. He is also a member of the Molecular Biology Society of Japan and the Japanese Cancer Association. Research field Prof. Jun-Ya Kato includes cell cycle control and carcinogenesis, hematopoiesis and blood cell differentiation, proliferation, carcinogenesis, cell carcinogenesis, cancer metabolism, and analysis using mouse models.

Prof. apt. Nasrul Wathoni, Ph.D (Universitas Padjadjaran, Indonesia)



Prof. apt. Nasrul Wathoni, Ph.D is a professor in the Department of Pharmacy and Pharmaceutical Technology, Faculty of Pharmacy, Universitas Padjadjaran. He currently serves as Chair of the Bachelor of Pharmacy Study Program at the Faculty of Pharmacy, Universitas Padjadjaran. He studied doctorate at Kumamoto University in the field of physical pharmaceutics. He is also managing editor of the Indonesian Journal of Pharmaceutical Science and Technology, the Indonesian Journal Pharmaceutics, and Pharmacy Magazine. He also founded Farmasetika.com in 2016 which is the latest scientific and practical-based pharmaceutical information site.

Thavasyappan Thambi, Ph.D. (Kyung Hee University, South Korea)



Thavasyappan Thambi, Ph.D memiliki pengalaman di bidang nanomedicine, hydrogels, and tissue engineering. Thavasyappan Thambi, Ph.D current research is mainly focused on the development stimuli-responsive polymeric nanomaterials for the targeted delivery of anticancer therapeutics including chemotherapeutic drugs and oncolytic adenoviruses to cancer cells. Thavasyappan Thambi, Ph.D also develop in situ forming injectable hydrogels for the sustained release of proteins and growth factors for tissue engineering applications. Thavasyappan Thambi, Ph.D research interest includes stimuli-responsive polymers for cancer therapy, therapeutic and diagnostic nanomedicine (theranostics), oncolytic adenovirus for cancer therapy, polymeric biomaterials for cancer immunotherapy, injectable hydrogels for sustained delivery of therapeutic proteins, and hydrogels for tissue engineering.

Dr. apt. Riris Istighfari Jennie (Universitas Gadjah Mada, Indonesia)



Dr. Riris Istighfari Jenie, M.Sc., Apt was the head researcher for the research title Development of Secang (*Caesalpinia sappan L.*) as an Antiaging Cosmetic with a Mechanism of Reducing Senescence Cells in 2021. She studied for undergraduate and mastedegreesgree in pharmacy at Universitas Gadjah Mada and continued his doctoral studies in biological science at NAIST, Japan. She has research interests in Biochemistry, Molecular Pathophysiology, and Molecular Signal Transduction.

Dr. apt. Tiana Milanda (Universitas Padjadjaran, Indonesia)



Dr. apt. Tiana Milanda, M.Si is the Head of the Department of Pharmaceutical Biology, Faculty of Pharmacy, Universitas Padjadjaran. She studied Bachelor of Pharmacy at Universitas Padjadjaran and continued her Masters and Doctor of Pharmacy education at Institute Teknologi Bandung. Dr. apt. Tiana Milanda, M.Si, research field is antimicrobial activities. Her areas of expertise are Pharmaceutical Microbiology, Pharmaceutical Biotechnology, Pharmaceutical Forensic.

Prof. Marlia Singgih (Institut Teknologi Bandung, Indonesia)



Prof. Marlia Singgih, Ph.D is a professor at the School of Pharmacy, Institut Teknologi Bandung. She studied Ph.D in applied microbiology at the University of Strathclyde Glasgow, UK. She served as deputy dean of resources at the School of Pharmacy, Institut Teknologi Bandung in 2015 - 2020. She has expertise in pharmaceutical microbiology.

Prof. Habibah A. Wahab (President of CADD Asia/Universiti Sains Malaysia)



A graduate in BSc in Science and Practice of Pharmacy from Liverpool John Moore University, Habibah A Wahab obtained her PhD in Pharmaceutical Technology from King's College London, University of London in 1999. She is lecturer at the School of Pharmaceutical Sciences where she found a research group "Pharmaceutical Design and Simulation (PhD)" which focuses on research on drug discovery especially those utilizing structural bioinformatics and computer aided drug design approaches. In 2010 Habibah was promoted as a full professor in the School of Pharmaceutical Sciences, Universiti Sains Malaysia.

Dr. Dra. Lucia Rizka Andalusia, Apt, M.Pharm, MARS



Dr. Dra. Lucia Rizka Andalusia, Apt, M.Pharm, MARS is the Director General of Pharmaceuticals and Medical Devices at the Ministry of Health of the Republic of Indonesia since 2021. She has also served as Director of Drug Registration of BPOM (2019 – 2021) and Head of Research and Development (2012 – 2018). She studied undergraduate and professional pharmacist at the Faculty of Pharmacy, Universitas Airlangga. She continued his Masters in Hospital Administration at the Faculty of Public Health, University of Indonesia and master of clinical pharmacy at the University Sains Malaysia. Then, she continued his doctoral studies in Clinical Medicine and Biomedicine at the Faculty of Medicine, University of Indonesia.

Prof. Tao Liu (UNSW, Australia)



Prof. Tao Liu leads the Gene Dysregulation Group at Children’s Cancer Institute and is a conjoint Associate Professor in the UNSW Faculty of Medicine. Originally trained as a medical practitspecializinglising in neurology, Tao joined the Institute in 2003 as a Senior Research Officer after working in cancer research at St Vincent's Centre for Applied Medical Research, Sydney. He was promoted to Project Leader in 2009 and became a Group Leader in 2011.

Dr. apt. Ida Musfiroh (Universitas Padjadjaran, Indonesia)



Dr. apt. Ida Musfiroh serves as Head of Pharmacist Professional Study Program, Faculty of Pharmacy, Universitas Padjadjaran. She received his doctoral education in Pharmacochemistry at Institut Teknologi Bandung. She served as Head of the Basic Analytical Chemistry Laboratory, Faculty of Pharmacy, Padjadjaran University in 2005 – 2012 and currently as an Educational HR Development Staff since 2011.

Dr. Mohamad Rafi, MSi (Institut Pertanian Bogor, Indonesia)



Dr. Mohamad Rafi, MSi is a lecturer at Department of Chemistry, Faculty of Mathematics and Natural Sciences, IPB University, Indonesia and Tropical Biopharmaca Research Center, IPB University, Indonesia. Dr. Mohamad Rafi has researches field include Metabolomics, Analytical Chemistry (chromatography and spectroscopy analysis), Chemometrics, and Natural Product Analysis.

Dr. Ezatul Ezleen Kamarulzaman (USM)



Dr. Ezatul Ezleen Binti Kamarulzaman is a Senior Lecturer at Discipline of Pharmaceutical Chemistry School of Pharmaceutical Sciences, Universiti Sains Malaysia. Dr. Ezatul has research interest in Drug design and discovery of potential natural products, peptides and synthesized organic compounds for anti-viral, anti-cancer and anti-obesity properties. Dr. Ezatul has expertise fields include computational chemistry (molecular modelling), medicinal chemistry (Synthesis of peptide, small molecule and its derivatives), peptide synthesis (Solid phase peptide synthesis) and small molecule synthesis (organic synthesis), natural product chemistry (Isolation and characterization of bioactive chemical compounds using various analytical techniques (HPLC, LCMS, GCMS, NMR, UV, FTIR).

Prof. Daryono Hadi Tjahyono (ITB)



Prof. Dr. apt. Daryono Hadi Tjahjono, M.Sc.Eng is a professor at the School of Pharmacy, Bandung Institute of Technology (ITB). He studied pharmacy at the Bandung Institute of Technology and then continued his master's and doctoral education at Keio University, Tokyo, Japan. Recent projects carried out by Prof Daryono include Virtual In Silico Screening and In Vitro Testing of CDK4/6 Inhibitor Compounds in the Development of Anti-Breast Cancer Drugs (2021), International Conference on Pharmaceutical Sciences and Pharmacy (ICPSP) (2020), and Program Implementation Research and Innovation Consortium Funding for the Acceleration of Handling Corona Virus Disease 2019 (COVID-19) with the title In Silico (2020) Sars-Cov-2 Antivirus Molecular Study.

Dr. apt. Sandra Megantara, M.Farm (Universitas Padjadjaran)



Dr. apt. Sandra Megantara, M.Farm currently serves as Manager of Academic, Student Affairs and Alumni Relations of the Faculty of Pharmacy, Universitas Padjadjaran since 2019. He is pursuing a bachelor's degree in pharmacy, pharmacist profession, and a master's degree in pharmacy at Universitas Padjadjaran. He continued his doctoral education at Institut Teknologi Bandung. He has expertise in pharmaceutical analysis and medicinal chemistry. He has published 7 books in the field of pharmacy and published more than 20 journals. He has also joined the National IAI organization since 2018.

Dr. Suman Sinha (Tata Institute of Fundamental Research, Hyderabad, India)



Dr. Suman Sinha is Assistant Professor-Research, Institute of Pharmaceutical Research, GLA University, Mathura, India. He took his bachelor's degree in pharmacy at Berhampur University and continued his master's studies at Vellore Institute of Technology. He also continued his PhD at Universiti Sains Malaysia. He was an Assistant Professor in the Department of Chemistry at Karunya University (2009 – 2011) and a Post-Doctoral Fellow at the Tata Institute of Fundamental Research Hyderabad (2017 – 2022).

ABSTRACT OF KEYNOTE AND INVITED SPEAKER

ANTICANCER POTENTIAL OF PENTACYCLIC CURCUMIN ANALOGUES TARGETING ON CELL CYCLE PROGRESSION

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ABSTRACT

Numerous developments of synthesized curcumin analogs have been extensively explored to find the potential candidate for antineoplastic with specific targets on tumor cells. A series of 1,5-diphenyl-1,4-pentadiene-3-ones and cyclopentanone were prepared and tested for anticancer activities. Pentagamavunone-0 (PGV-0) and Pentagamuvone-1 (PGV-1) were the first compounds evaluated on breast and colorectal cancer cells. While these PGV analogs exhibited more favorable anticancer properties than curcumin, PGV-1 notably presented more potent cytotoxic effects (IC₅₀ range 0.2-5 μ M) than PGV-0 (10 - 50 μ M) on cancer cell lines. PGV-1 also suppressed tumorigenesis in mice with no detectable side effects. Further evaluation displayed that PGV-1 significantly induced cell cycle arrest on G2/M, similar to curcumin. Interestingly, PGV-1 caused prometaphase arrest, which likely promoted mitotic catastrophe. PGV-1 affected several mitotic regulatory proteins: inhibition of Aurora A, activation of PLK-1, and cyclin B1 that signaled the mitotic checkpoint in cancer cells. Another mediated cellular phenomenon demonstrated by PGV-1 activity includes senescence induction, ROS level modulation, and cell migration inhibition. Recently, we synthesized the modified compound of PGV-1, named CCA-1.1, to improve the solubility in an aqueous solution through the weak reduction in the carbonyl. Indeed, the modification resulted in a slightly different effect on the molecular level, but still, CCA-1.1 similarly presented a similar effect with PGV-1 in cellular physiology activities in cancer cells. Nevertheless, these curcumin analogs deserve chances to continue developing (formulation and clinical studies) as potential antimitotic drugs.

Keywords: curcumin derivative, PGV-1, CCA-1.1, antimitotic drugs

TRANSLATIONAL RESEARCH IN DRUG DISCOVERY FROM MEDICINAL PLANTS

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ABSTRACT

Natural products (NP) have been the most productive source of leads for the discovery and development of drugs over the years. Medicinal plants serves as one of important sources of drugs worldwide since they possess interesting biological properties. About 80% of the world's population uses plant/botanical-derived medicines which are called as herbal medicines. A considerable growth has been seen in the herbal medicine market in recent years as an alternative to medicinal products with chemically derived APIs. In drug discovery and development based on natural products of plant origin, there is requirement of potential plant resources as a source of lead molecules. In this aspect, exploring medicinal plant biodiversity provides rational approach to search for new medicines. At the same time in several traditional medicines throughout the world, medicinal plants constitute an important ingredient of medicines. India with its rich medicinal plant biodiversity in terms of three hotspots viz. Eastern Himalaya, Western Himalaya and Western Ghats, provide an excellent opportunity for drug discovery and bioprospecting. It is estimated that there are around 45,000 higher plant species occur in India out of which around 15,000 species are believed to be of medicinal importance. Thus, there is a great promise to explore Indian medicinal plants for evaluation of various biological activities.

There are several difficulties and challenges associated with the development of herbal drug products. The challenges mainly are related to regulatory guidelines, lack of knowledge of herbal medicines with the drug regulatory authorities, assessment of safety and efficacy, quality control, safety monitoring; for herbal drugs. All these challenges could be addressed effectively by promoting use of herbal drugs through application of modern scientific methodology to herbal drugs/natural products promoting translational research so that the value-added products can be developed. In this presentation translational research approaches in the field of natural products, herbal drugs will be discussed.

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FROM LABORATORY TO COMMERCIALIZATION (SCIENTIFIC JAMU)

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ABSTRACT

In this study, we focus on coconut oil and its derivatives as starting materials to produce various health products. We will provide an overview of the steps required to take an idea from academic discovery and turn it into a commercial entity. This is a guide for academics to be focused on spinning out the technology into a commercial product. Research commercialization is typically a “Technology Push” opportunity. Technology push involves the creation of a technology without a specific end application in mind. The goal of the exercise is to link the technology as closely as possible to a Market Need, a requirement of a customer for such a solution or technology.

CLINICAL TRIAL OF JAMU AS NATURAL IMMUNOMODULATOR IN PANDEMIC SITUATION: LESSON-LEARNED

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ABSTRACT

The COVID-19 pandemic that has swept across the world since the end of 2019 has prompted more research to find safe and effective COVID-19 drugs. In addition to efforts to find antiviral drugs, the search for the right immunomodulator for COVID-19 is pursued through various studies to clinical trials. The immunomodulators that have been used empirically by the society during the pandemic generally come from natural ingredients/ herbs/ jamu. In Indonesia, herbs such as *Andrographis paniculata*, *Zingiber officinale*, *Curcuma xanthorrhiza*, *Curcuma domestica*, *Phyllanthus niruri*, and so on have been used by the people for hundreds to thousands of years as immune boosters (immunomodulators). In 2020 - 2021 PDPOTJI together with LIPI (BRIN), UGM and Kalbe Farma, with the assistance of BPOM, have completed the first clinical trial of herbal immunomodulators for mild COVID-19 in Indonesia^[1], which was followed by the 10 other herbal clinical trials. The implementation of a total of 11 herbal clinical trials during the COVID-19 pandemic has cost a lot of money, involves a lot of human resources, while still implementing rigid Good Clinical Practice (GCP) adapted to the pandemic situation. This paper will describe the results of herbal clinical trials on mild COVID-19 in Indonesia in general and evaluate them, by reflecting on our experiences in conducting herbal clinical trials and reviews of herbal clinical trials in other countries.^[2,3]

Keywords: jamu, herbs, immunomodulator, COVID-19, trial

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HEALTH INDEPENDENCE WITH INDONESIAN HERBAL MEDICINE: A RESEARCH JOURNEY TO FIND NATIVE HERBAL IMMUNOMODULATORS

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ABSTRACT

One of the lessons that we can learn after the COVID-19 pandemic is that Indonesia is still lacking in terms of health independence, especially in raw materials and herbal medicine. This encourages scientist to do more research especially in finding new immunomodulators. As we know immune system is our key mechanism to not only prevent but also to recover from any infectious disease not exclusive to COVID-19^[1]. Three of some plants that has immunomodulatory activity are *Carica papaya* L. leaves^[2], *Phyllanthus urinaria* L., and *Curcuma domestica* Linn^[3]. We study the immunomodulatory activity of each as well as the combinations of the three plants extract using carbon clearance and bacterial induction method with *Shigella dysenteriae*. We found that combination 1:1:1 (*Carica papaya* L. leaves: *Phyllanthus urinaria* L.: *Curcuma domestica* Linn.) has the best activity and formulate a tablet based on the best combination using wet granulation method. But the result shows that consumer need to take 12 tablets per day for it to take effect. So to solve this problem we purify the extract to reduce the mass of the extract by removing the non-active compounds for example chlorophyll, fats, proteins, resins, and waxes. The extracts are purified using Vacuum Liquid Chromatography method. We assess the immunomodulatory activity for the best combination and dose of the purified extract using *Staphylococcus aureus* induction. The result shows that the combination of purified extract 1:1:1 and dose 2 (60 mg/kgBW) gave the best immunomodulatory activity ($p < 0.05$).

Keywords: Indonesian native herbal, immunomodulatory, *carica papaya*, *curcuma domestica*, *phyllanthus urinaria*

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APPLICATIONS OF FLAVONOIDS FOR TREATMENT OF EYE DISORDERS AND DEVELOPMENT OF COLLOIDAL DISPERSIONS AS OPHTHALMIC DRUG DELIVERY SYSTEMS

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ABSTRACT

Flavonoids are a group of natural compounds that are found in various kinds of plants. Their chemical structures are based on a fifteen-carbon skeleton consisting of two benzene rings linked via a heterocyclic pyrene ring. Flavonoids can suppress formation of ROS by inhibition of microsomal monooxygenase, glutathione s-transferase, mitochondrial succinoxidase, NADH oxidase. They also have anti-inflammatory activity via reducing fluid retention and strengthening capillary walls. Recently, many studies showed that flavonoids, for example, quercetin, exhibited promising activities in treatment of ophthalmic disorders, i.e., cataract, diabetic retinopathy, age-related macular degeneration, glaucoma, dry eye syndrome. For the successful ophthalmic delivery of flavonoids, in particular, quercetin, suitable vehicles based on nanotechnology and colloidal dispersions have been applied for this purpose. It was found that quercetin could be effectively delivered to the eye cells and the eye tissues by using the suitable nanoparticles and colloidal dispersion systems. Importantly, they did not cause obvious toxicity to the eyes. The ophthalmic delivery of quercetin by using optimized nanoparticles and colloidal dispersion could be thus accepted for the investigation in further clinical studies.

Keywords: Flavonoids; Quercetin; Ophthalmic Drug Delivery; Nanotechnology; Colloidal Dispersions; Safety.

IMPROVEMENT THE SOLUBILITY AND MECHANICAL PROPERTIES OF CARVEDILOL USING A CRYSTAL MULTICOMPONENT APPROACH

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ABSTRACT

Carvedilol (CVD) belongs to a group of antihypertensive drugs that is poorly soluble in water (0,58 mg/L), and is classified as a BCS Class II drug. In this study, multicomponent crystals of CVD with nicotinamide, fumaric acid, tartaric acid, and succinic acid were made using the solvent evaporation technique, in which the mole ratios were 1:1, 1:2, and 2:1. Cofomer screening was performed *in silico* using the AutoDock software. The performance of multicomponent crystals was evaluated by saturated solubility, phase solubility, and intrinsic dissolution tests. The results showed that CVD-NIC 1:2, CVD-FUM 1:2, CVD-SUC 1:2, and CVD-TAR 2:1 had the best solubility. The multicomponent crystals had a differing pattern of diffractogram from their components. While in the thermogram, a decrease of melting point and heat of melting were discovered, which affected the solubility improvement of the multicomponent crystals. The shift in the FTIR spectrum ($1650 - 1550 \text{ cm}^{-1}$) was assumed to be the result of synthon interaction. CVD-NIC 1:2 and CVD-FUM 1:2 showed Compressibility index, Hausner ratio, and angle of repose of the multicomponent crystals were found to be better than carvedilol, and moreover, CVD-NIC and CVD-FUM experienced plastic deformation based on their tableability profile. In conclusion, the multicomponent crystals approach could be used for CVD using FUM and NIC as the cofomer to improve its physicochemical properties, especially solubility.

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DRUG DISCOVERY FROM AFRICAN NATURAL RESOURCES

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ABSTRACT

Natural products and their structural analogs have previously made significant contributions to pharmacology, particularly in the treatment of cancer and infectious diseases. However, their utilization has declined over the last two decades, owing in part to technological hurdles to screening natural compounds against molecular targets in rising experiments. The use of medicinal plants as a foundational component of African traditional healthcare is one of the oldest and most diversified therapeutic systems. Traditional healers prescribing medicinal plants are frequently the most accessible and cost-effective health alternative available to the local community in many rural African communities, and they are frequently the only remedy available. Therefore, it is crucial to integrate the traditional remedies of African medicinal plants with scientific evidence-based medicine.

We selected two models of infectious diseases, HIV-1/AIDs and the current pandemic COVID-19. Then, we moved to the ground where we will be able to collect information about the traditional remedies in Africa for the intended diseases. Furthermore, using our advanced knowledge of screening systems, we were able to find plant candidates that effectively eliminate HIV-1 virus from the latent host reservoir, as well as some medicinal plants that can be effective in inhibiting the viral breakthrough of SARS-CoV-2 in mutated strains.

To summarize, the incorporation of traditional medicinal plant remedies may become an effective approach for drug discovery as well as improving the quality of life in developing countries by making better use of their resources and combating diseases that originated in their region.

BIOMEDICAL RESEARCH THROUGH COLLABORATION WITH INDONESIA: FINDING PATHWAYS THAT WILL SERVE BETTER HEALTH

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ABSTRACT

There are great differences in burden of infectious diseases and inflammatory disease profiles across the world. Vaccines are needed to combat infections while anti-inflammatory drugs are required to control inflammatory diseases. Both these approaches need a better understanding of the immune system that will be targeted. Using cutting edge methods to phenotype peripheral blood mononuclear cells from different environments, we show that the immune system differ strongly between populations resident in the Netherlands and in rural and urban areas of Indonesia. Using simple methods to measure total IgE levels in infants and young children born in a semi urban area of Indonesia and comparing them to European counterparts, show differences already at one year of age that indicates very distinct immunological footprints early in life determined by environmental exposures. Together these distinct immunological states can affect responses to vaccines and will respond differently to anti-inflammatory drugs. Therefore, it is important to identify immunological pathways that can be targeted in different populations for an optimal health outcome following interventions with vaccines or drugs.

CONTEMPORARY APPROACHES TO THE DISCOVERY AND DEVELOPMENT OF NATURAL MEDICINES

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ABSTRACT

Natural products continue to play an important role in drug discovery and development. About two-thirds of recently approved pharmaceuticals are natural products, botanicals, natural product-derivatives, or natural product-inspired synthetic compounds. Plants, marine animals, algae, and microorganisms are known to be prolific sources of bioactive natural products. Despite their enormous potential, the number of new natural products identified in recent years has significantly declined. This trend has called for alternative approaches to drug discovery and development. Among them is the application of biotechnology to identify and/or generate novel bioactive natural products and their derivatives. Examples of biotechnological tools available for natural product-based discovery and development include genome mining, biosynthetic pathway engineering, biotransformation, and synthetic biology. Combinations of these cutting-edge technologies and state-of-the-art instrumentations may accelerate the discovery and/or development of new drugs.

HYDROGEL MUCOADHESIVE FILM OF α -MANGOSTIN FOR RECURRENT APHTHOUS STOMATITIS

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ABSTRACT

Recurrent Aphthous Stomatitis (RAS) is an ulcerative disease that often causes on buccal, labial and tongue.^{1,2} Many antiseptic drugs, local anaesthetics, and has been widely utilized for RAS therapy; however, it has side effects will harmful on the oral mucosa. α -mangostin (α -M) is a main compound of mangosteen (*Garcinia mangostana* L.) rind has been known as one of anti-inflammation agent.³ In addition, hydrogel mucoadhesive film was designed as a dressings to separate oral ulcer from the oral environment, and improve the effectiveness of RAS therapy.⁴ The purpose of this study was to designed a α -M hydrogel mucoadhesive film based chitosan–alginate (ChAlg/ α -M HF) for RAS therapy. To prepare α -M Alg/Chi-HF, the solvent evaporation and casting methods were used,⁵ then characterized by using SEM, FTIR and XRD.⁶ Based on the characterization studies, the α -M in α -M/EtOH Alg/Chi-HF with ethanol (EtOH) was found to be more homogenous compared to α -M in Alg/Chi-HF with distilled water (H₂O) as casting solvent. *In-vitro* drug release showed that the release of α -M following Higuchi model.⁷ The *in vitro* viability study using NIH3T3 cells showed 100% viability of α -M/EtOH Alg/Chi-HF and Alg/Chi-HF after 24h incubation, indicating well tolerability of this films. Interestingly, the *in vivo* studies using male white rats (*Rattus norvegicus* Berkenhout) proved that α -M/EtOH Alg/Chi-HF with a recovery of 81.47±0.09% in seven days significantly more effective RAS therapy compared to control. These results suggest that α -M/EtOH Alg/Chi-HF has a potential as an alternative for RAS therapy.

Keywords: Recurrent Aphthous Stomatitis, α -mangostin, chitosan, alginate, hydrogel film

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THE DEVELOPMENT OF *Caesalpinia Sappan* BIOACTIVE COMPOUNDS AS CHEMOPREVENTION AND CO-CHEMOTHERAPEUTIC AGENTS

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Sappan heartwood (*Caesalpinia sappan* L.) has been used as traditional medicine, especially in Asia. It has been known that *C. sappan* and its active compounds have various pharmacological activities including anti-inflammation, anti-acne, and anti-oxidant. Our research group explores the potency of *C. sappan* as a chemopreventive agent and the possibility to use it as a co-chemotherapy agent against various cancer cells. We used the extract or the active compounds of *C. sappan* namely brazilin and brazilein and performed the in vitro assay to observe its potency alone or in combination with other chemotherapeutic agents. We also study the molecular mechanism of its activity toward cancer cells.

The common method used to isolate constituents of *C. sappan* was using methanol. Nevertheless, several publications have also done using ethanol, 70% and 50% ethanol solution and followed with further separation. The main compounds that were isolated using the method are flavonoids brazilein and brazilin. Other compounds majorly detected in the extract using HRMS are protosappanin A, protosappanin B, and sappan chalcone. Our in vitro studies using colon cancer and breast cancer cell lines either the subtype of ER⁺, HER2⁺, or triple-negative breast cancer cells revealed that *C. sappan* extract has cytotoxicity activity against these cells with IC₅₀ less than 100 µg/mL. The brazilin and brazilein are also cytotoxic against these cells with IC₅₀ around 50-90 µM. The mechanism involves modulation of the cell cycle which accumulated the cells in the S and G2/M phases by reducing cyclin D expression level. It also induces apoptosis with confirmation from other research groups that the mechanism involves reduced Bcl2 expression. Moreover, we also observed that *C. sappan* inhibited cell migration and invasion in aggressive breast cancer cell lines (HER2⁺ and TNBC cell lines). These findings contribute to the synergism effect of *C. sappan* extract or its active compounds when combined with chemotherapeutic agents such as doxorubicin or cisplatin. The mechanism of migration inhibition involves modulation of PI3K/Akt, MAPK/ERK1/2 that is related to a HER2 signaling pathway, inhibition of NFκB translocation that regulates the MMP2, decreased the expression level and the activity of MMP2 and 9 and modulating Rac-1 expression. Based on our molecular docking study, the docking score of brazilein with PI3Kγ is comparable to that of the native ligand. Taken together, our study indicates the potency of *C. sappan* and its active compounds to be developed as a co-chemotherapy agent to increase the efficacy of chemotherapeutic agents and to halt cancer cell progression.

Keywords: brazilin, brazilein, HER2, breast cancer cells, cell migration, cell invasion

ANTIBACTERIAL COMPOUNDS FROM BACTERIA ISOLATED FROM WADI PAPUYU (*Anabas testudineus* Bloch.) FROM CENTRAL KALIMANTAN

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Wadi is a fermented fish product that is in great demand by the people of Central Kalimantan. Wadi is derived from semi-wet whole fish which is processed with the addition of salt and samu/lamu (rice which is roasted and applied to the fermented fish). Wadi contains bacterial isolates which have secondary metabolite compounds as antimicrobials. The purpose of this study was to identify antibacterial compounds produced from bacterial isolated from papuyu fish wadi (*Anabas testudineus* Bloch.) from Central Kalimantan. The research stages included the collection of papuyu fish, fish determination, preparations of papuyu fish wadi, isolation of bacteria from papuyu fish wadi, identification of bacterial and yeast isolates by 16s and 18s rDNA-sequencing methods and probiotic activity of bacterial isolates test. The result of the determination showed that the fish used was papuyu (*Anabas testudineus* Bloch). From wadi papuyu fish (*Anabas testudineus* Bloch.) from Central Kalimantan, three bacterial isolates were identified, namely *Lactococcus garviae*, *Bacillus altitudinis*, and *Staphylococcus equorum* and one yeast *Candida orthosilopsis*. The bacterial isolates used in the subsequent tests were *Lactococcus garvie* and *Staphylococcus equorum*, because both are bacteriocin-producing bacteria. Both bacterial isolates, especially *Lactococcus garvie*, were viable in MRSA under anaerobic conditions. Both bacterial isolates were tolerant to low pH, because they were able to grow at a pH of 2.0-4.0. Both bacterial isolates were unable to grow at 5°C, but were able to grow at 30°C and 37°C. The drawback is that *Staphylococcus equorum* and *Lactococcus garvie* are not able to grow under the influence of bile salts, nor do they have autoaggregation properties, so these two bacteria cannot be used as probiotics. In the coaggregation test, it was found that the two bacterial isolates were able to provide resistance to *Shigella sp*, *Escherichia coli*, and *Salmonella sp*, with the percentage of coaggregation ranging from 58.5 to 93.2%. This coaggregation ability showed that the two bacterial isolates formed a barrier that prevented the colonization of pathogenic bacteria in the digestive tract. Antibacterial research of the bacteria isolated from the papuyu fish wadi will lead to the search for other types of antibacterials, including bacteriocins.

Keywords : Wadi, *Anabas testudineus* Bloch., Probiotics, Bacteriocin

MICROBIAL QUALITY OF INDONESIAN HERBAL MEDICINE AND DIETARY SUPPLEMENTS

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ABSTRACT

Jamu (traditional herbal medicines) are commonly used in Indonesia, It is predominantly a herbal medicine made from natural materials, such as roots, bark, flowers, seeds, and due to its bioburden, it contain some numbers of natural microbes.

Jamu are regulated in Indonesia by Decree of Indonesian Food and Drug Authority, Republic of Indonesia, no. 32, year 2019, about : Regulation on Safety and Quality of Traditional Medicines. It regulates the quality standard of Indonesian Herbal medicines and Health Supplements, especially for new products such as oral gel preparation, effervescent tablet, etc, to guarantee for its safety, quality and benefits.

Farmakope Indonesia (Indonesian Pharmacopeia) 6th edition , 2020 has specific chapter to regulate herbal medicines for microbial quality, and Farmakope Herbal Indonesia (Indonesian Herbal Pharmacopeia) edition 2, year 2017 and its Supplements, become a standard References for *simplicia* and quality of raw material for Jamu manufacturing.

In Decree no. 32, 2019 for microbiology requirements are mostly on maximum allowable numbers of total microbial counts, .and should be negative for certain microorganisms, such as *Escherichia coli*, *Salmonella sp.* or *Staphylococcus aureus*.

Dietary Supplements including herbal medicines, are regulated in USP chapter 201, 2022 and 2023, which then adopted in BPOM Decree no.16, 2019 about : Supervision of Dietary Supplements. For Dietary Supplements containing herbal ingredients, the number of microbes allowed is higher than the supplements without herbal ingredients, this is due to natural contaminants in herbal sources, but still safe to be consumed within its expired date.

Many microbiological assays have been developed to test the quality of herbal medicines and dietary supplements in Indonesia, and the methods always been updated by PPOMN, Republic of Indonesia, to guarantee the safety and benefit of the products.

Keywords : Herbal Medicines, Dietary Supplements, Microbial quality of products

FROM JAMU TO POTENTIAL INFLUENZA INHIBITORS

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ABSTRACT

Influenza is a major global health threat; and the emergence of drug resistant viral strains have prompted the needs for the discovery of new influenza inhibitors. Here, we report the computational and experimental efforts in the design and synthesis of novel influenza inhibitors from compounds identified in Indonesian (Jamu) and Malay (Ramuan) Traditional Medicine. Virtual screening of compounds from Malaysian and Indonesian Plants used in Traditional Medicine deposited in Natural Product Discovery System (NADI) identified several compounds possessed moderate neuraminidase inhibition activity. Cinnamic acid scaffold unexpectedly discovered through ferulic acid during this virtual screening showed promising anti-influenza activity and was selected for modification and synthesis of new derivatives and anti-neuraminidase activity evaluation. Two proposed ferulic acid analogues, MY7 and MY8 were predicted to inhibit H1N1 NA using molecular docking. From these two analogues, we designed, synthesised and evaluated the biological activities of a series of ferulic acid and vanillin derivatives. The enzymatic H1N1 NA inhibition assay showed MY21 (a vanillin derivative) has the lowest IC₅₀ of 50 µM. In contrast, the virus inhibition assay showed MY15, a ferulic acid derivative has the best activity with the EC₅₀ of ~0.95 µM. In a separate study, inspired from Lawson, compound isolated from henna, a series of dimeric naphthoquinones that containing natural 2-hydroxy-1-4-naphthoquinone moiety was designed, synthesized and evaluated against neuraminidase of H5N1 virus. Compound **GH1** and **GH2** (respectively, percentage inhibition at 250 µg/mL= 86% and 93.5%; IC₅₀: 29 ± 0.9 µM 26.5 ± 0.7 µM) showed better inhibitory profile than DANA (94.8%; 34.82 ± 1.32 µM) while GH 3-7 lawsone and lawsone-dimer showed IC₅₀ between 111-425 µM (Table 3). Although these compounds have similarity in structures with subtle differences in their phenyl group, compounds **GH3** and **GH4** exhibited higher IC₅₀ (Compound **3**: 252 ± 0.1 µM; **4**: 111 ± 0.20 µM) compared to **GH1** and **GH2**. Modelling studies further suggest that these predicted activities might be due to the interactions with conserved and essential residues of NA with ΔG_{bind} values comparable to those of oseltamivir and zanamivir, the two commercial NA inhibitors.

IDENTIFICATION OF BIOACTIVE METABOLITES OF SOME INDONESIAN MEDICINAL PLANTS USING METABOLOMICS ANALYSIS

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Metabolomics has been widely used in natural product research, such as in medicinal plants, for quality control, identifying bioactive metabolites, etc. Metabolomics could identify and quantify small molecules/metabolites resulting from a biological system's metabolism, called metabolome, at a specific time because of a stimulus. As we know, identifying bioactive metabolites from medicinal plants mostly used the bioassay direct fractionation and isolation (BDFI) approach and was very tedious and laborious. So now, many natural product chemists use metabolomics analysis to identify bioactive metabolites. In this approach, we correlated the metabolite profiling of medicinal plant extracts resulting from the different polarities of solvent extraction with the biological activity value like IC_{50} . We can predict the bioactive metabolites using multivariate analysis, mostly PLSR, PLS-DA, or OPLS-DA for that correlation. In this presentation, we will share some research on applying metabolomics to predict bioactive metabolites from Indonesian medicinal plants, such as *Curculigo spp*, *Annona muricata*, etc.

STRATEGY IN NATURAL PRODUCT ANALYSIS USING HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

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ABSTRACT

Natural products have been known to have high structural diversity and unique biological or pharmacological activities as a result of the natural selection and evolutionary processes over hundreds of thousands of years. The structural diversity of natural products far exceeds the capabilities of synthetic organic chemists within the laboratory. Hence, natural products have been utilized in both traditional and modern medicine for treating diseases. The useful of a large numbers of primary and secondary metabolites of natural products are often used as starting points for drug discovery followed by synthetic modifications to help reduce side effects and increase bioavailability. Thus, it is important to have the means available to perform a characterization of the samples in order to provide a selecting species for study. This can be done by combining simple biological assays or Nuclear Magnetic Resonance (NMR) with High-Performance Liquid Chromatography (HPLC) analyses. HPLC is an extremely versatile technique with the reversed-phase method is able to handle compounds of a diverse polarity and molecular mass. Reversed phase chromatography has found both analytical and preparative applications in the area of phytochemical separation and purification. Once a candidate plant has been chosen, a suitable isolation procedure can be employed for the isolation of the active principles. More recently, a recycling preparative HPLC has been used to provide a fast and elegant approach to purify huge (from mg to gram) quantities of starting materials, intermediates and final products.

Keywords: Bioactive compound; Plant extraction; HPLC

DISCOVERING LEAD COMPOUNDS FROM DATA BASE OF NATURAL PRODUCT COMPOUNDS

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ABSTRACT

In a traditional drug discovery and development, it has been known that for launching one molecule for treatment a disease needs 8-15 years and is estimated to be a staggering US\$ 1.8 billion (1). Approximately 75% of the cost is due to failures that happen along the drug discovery and design pipeline. Thus, in the ten years later, global pharma companies have made a serious revitalization of their computation facilities to overcome the great loss in drug discovery. Pharmacophore modelling, molecular docking and molecular dynamic simulation have an important role in supporting virtual screening for drug discovery. On the other hand, natural products have rich structural diversity, and many drugs used today are natural products or natural-product derivatives (2). We have applied those molecular modelling in searching curcumin analogues as DYRK2 inhibitor (3), inhibitor of urokinase-type plasminogen activator (uPA) (4). A repurposing of existing molecules for another target has also been performed, and the results will also be discussed.

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IN SILICO STUDY: COMBINATION OF α -MANGOSTIN AND CHITOSAN CONJUGATED WITH TRASTUZUMAB AGAINST HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2

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ABSTRACT

Breast cancer is a type of cancer with the highest prevalence worldwide. Almost 10–30% of breast cancer cases are diagnosed as positive for HER2 (human epidermal growth factor receptor 2). The currently available treatment methods still exhibit many shortcomings such as a high incidence of side effects and treatment failure due to resistance. This in silico study aims to simulate α -mangostin and chitosan combination conjugated to trastuzumab formulation against HER2 as an effort to improve breast cancer patient therapy. This molecular docking simulation was done through using PatchDock Server. The materials used including the two-dimensional structure of α -mangostin, chitosan, and sodium tripolyphosphate from the PubChem database; trastuzumab FASTA sequence from the DrugBank database; and HER2 structure obtained from a crystal complex with PDB ID: 1N8Z. The results indicated that the particle of α -mangostin and chitosan combinations interacted mostly with the crystallizable fragment (Fc region) of trastuzumab in the conjugation process. The conjugation of trastuzumab to the particle of a combination of α -mangostin and chitosan resulted in the greatest increase in the binding score of the smallest-sized particles (50 Å) with an increase in the score of 3828 and also gave the most similar mode of interaction with trastuzumab. However, the conjugation of trastuzumab eliminated the similarity of the mode of interaction and increased the value of atomic contact energy. Thus, a combination of α -mangostin and chitosan conjugated to a trastuzumab formulation was predicted can increase the effectiveness of breast cancer therapy at a relatively small particle size but with the consequence of decreasing atomic contact energy.

Keywords: breast cancer; α -mangostin; trastuzumab; HER2; in silico; FireDock

APPLICATION OF EQUILIBRIUM AND ENHANCED SAMPLING MOLECULAR SIMULATIONS TOWARDS UNDERSTANDING PROTEIN- PROTEIN AND PROTEIN-SMALL MOLECULE INTERACTION DIASPORA

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ABSTRACT

Modern understanding and interpretation of biology have greatly improved with the gradual development in scientific computing capabilities, such as graphics processing units, multi-core clusters and powerful statistical mechanics-based algorithms. Early state drug discovery has changed over the last few decades as the entire structural biology paradigm has transitioned toward a more quantitative approach with little manual intervention. My presentation will highlight the molecular features of two such relevant protein systems that are accountable for serious clinical conditions like cancer and malaria.

The formation of a moving junction is categorically suggested in a number of literature publications as the final and most important phase in the invasion of human red blood cells by the malarial parasite. Rhoptry Neck Protein-2 and Apical Membrane Antigen-1 (AMA1) are two crucial protein collaborators in this process (RON2). Because of the enormous clinical potential that this complexation offers, understanding the dynamics of the AMA1-RON2 interaction is a significant issue for investigation. I have used biophysical experiments and atomistic molecular dynamics to quantify enumerate the specific functions that certain residues play in this macromolecular recognition process. Subsequently it was tried to comprehend the potential effects on the whole system of the molecular mechanism of binding for various chemically altered RON2-similar peptide ligands. This was motivated by the breathing motion of the Domain II loop and its potential influence on the overall system. The second problem in my talk would relate to one of the most functionally active lectins, Galectin-3, which is being sought after as a key anti-cancer target due to its particular propensity for binding beta-galactosides. Although the end-state bound poses can be seen in the crystal structures that are now available, the precise binding mechanism and the likelihood of the emergence of intermediate states are yet unknown. I have utilized molecular dynamics simulations to clarify how the cognate ligand N-acetyllactosamine and one of its synthetic variants bind to human Galectin-3 dynamically and dissect the molecular determinants responsible for this recognition process.

ORAL PRESENTATION ABSTRACT

[OP-001]

PREPARATION OF CO-METAL OXIDE NANOPARTICLES EMBEDDED CARBON NANOHORN AS THERANOSTICS

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ABSTRACT

Cancer is the second leading cause of death globally. However, conventional cancer therapy still causes some severe side effects. In recent years, combination therapy and diagnostics (theranostics) are explored to overcome unwanted bio-distribution variations and improve therapeutic efficacy. In this work, iron oxide (Fe_3O_4) nanoparticle (NP) as hyperthermia were synthesized using the co-precipitation method, coated with carbon dot (Cdot) which has photothermal/photodynamic activity, and embedded in carbon nanohorn (CNH/ Fe_3O_4 @Cdot).^[1,2] Then, samarium and gadolinium oxide (Sm_2O_3 and Gd_2O_3 , respectively) NP which has radioactivity and radio imaging activity, respectively, were synthesized by the polyol method and combined with CNH/ Fe_3O_4 @Cdot.^[3] The nanocomposite was coated with polyethylene glycol to enhance biocompatibility. Transmission electron microscopy and scanning electron microscopy images showed that the nanocomposites were successfully formed. It was also supported by an energy-dispersive X-ray spectrometer and elemental mapping analysis. Thus, preparing these nanocomposites is a step forward for developing advanced medication as theranostics.

Keywords: Carbon nanohorn, gadolinium oxide, iron oxide, samarium oxide, theranostics.

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CYTOTOXICITY TEST OF *CASSIA ALATA* L. ETHANOLIC EXTRACTS, FRACTIONS, AND COMPOUNDS AGAINST MCF-7 CELLS

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ABSTRACT

Cancer is the primary cause of death worldwide. Conventional cancer treatment is known to be less than optimal because of its chemoresistance and toxicity to normal cells. The invention of cancer drugs from natural product is still being carried out as an effort to overcome these problems. ^[1] *Cassia alata* L. leaf extract is known to have antibacterial and antitumor activities. ^[1,2,3] The main compounds of *Cassia alata* L. leaves (emodin, aloe-emodin, and kaempferol) have been reported to have antiproliferative activity. This study aimed to examine the cytotoxic activity of ethanolic extracts, fractions, and the main compounds of *Cassia alata* L. leaves against breast cancer cells (MCF-7). Cytotoxic activity was carried out by the MTT method. IC₅₀ was determined by linear regression analysis describing the relationship between concentration and % cell viability. The results showed that aloe-emodin, emodin, and kaempferol showed better cytotoxic activity than the extract and fractions of the *Cassia alata* L. leaves with IC₅₀ values respectively 12.7 ppm, 18.1 ppm, and 131.3 ppm.

Keywords: Breast cancer, Cytotoxic assay, *Cassia alata* L., MCF-7.

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STABILITY AND SUN PROTECTION EFFECTIVITY OF SEA BUCKTHORN OIL IN NANOEMULSION SYSTEM USING TWEEN 80-PEG 400 AS SURFACTANT AND COSURFACTANT

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ABSTRACT

Sea Buckthorn Oil (SBO) contains of linoleic acid and β -carotene which can absorb UV-B rays¹. The chemical content of SBO is unstable and difficult to absorb into the skin². Isopropyl myristate (IPM) can be used as stabilizer and enhancer in microemulsion³. The purpose of this study was to determine the stability and effectivity of SBO in microemulsion system with IPM as enhancer. Microemulsion was made using 5% of SBO with Tween 80-PEG 400 (1:2) variations: 60% (F1); 65% (F2) and 70% (F3). SBO microemulsion was stored at $30^{\circ}\text{C} \pm 2^{\circ}\text{C}$, RH $65\% \pm 5\%$ in the climatic chamber 4 weeks (30 days). Physical stability test were organoleptic, pH, viscosity, particle size, transmittance percentage and in vitro SPF value. Effectivity test were carried out by measuring Minimum Erythematous Dose (MED) on rabbit's skin. The stability data were analyzed by multivariate test and MED data were analyzed by one way ANOVA. SBO microemulsion had a clear, transparent, dark yellow color, and there was no phase separation. SBO microemulsion had pH of 7.20-7.50; viscosity in the range of 1.33-2.53 dPa.s; particle size in the range of 52.47-55.43 nm; and transmittance percentage in the range of 97.411-98.281%. All physical characteristic were stable and did not show any significant change after 30 days of storage. SPF value of all formula were in range of $13,61 \pm 0,65$ to $14,52 \pm 1,07$ and categorized as maximum protection. MED of unprotected skin were $13,5 \pm 7,41$ minutes while F1, F2 and F3 were $220,5 \pm 6,34$ (SPF 16); $225,4 \pm 5,41$ (SPF 16) and $240,2 \pm 3,45$ (SPF 17). Microemulsion with tween 80 variation showed physical stability within 30 days of storage. Combination of tween 80 and PEG 400 could increase the effectivity of in vivo sunscreen activity from SBO microemulsion.

Keywords: Sea Buckthorn Oil, microemulsion, stability, sunscreen

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IN-VITRO ANTIOXIDANT ACTIVITY OF WATER AND ETHANOL EXTRACT OF BLACK TURMERIC (*Curcuma caesia*)

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ABSTRACT

Nutraceutical is a concept that emphasizes the benefits of natural products, with the aim of preventing chronic diseases, delaying the aging process, and increasing life expectancy [1]. Black turmeric (*Curcuma caesia*) is a plant that is widely used for traditional medicine [2], and it has potential to be an excellent nutraceutical candidate for maintaining health[3]. This study aimed to determine the phytochemical content and antioxidant activity of *C. caesia* water extract (EWCC) and *C. caesia* ethanol extract (EECC). Samples were extracted using two extraction methods, namely, maceration technique using 96% ethanol and infusion technique using water as a solvent. The phytochemical content, total phenolic content (TPC), and total flavonoid content (TFC) of each extract were determined. Antioxidant activity was measured using the 2,2-diphenyl-1-picrylhydrazyl method, with ascorbic acid as the positive control. Results showed that EWCC and EECC contained flavonoids, alkaloids, and polyphenols. The values of TPC and TFC were 106.08 mg GAE/100 g and 4.32 mg QUE/g for EWCC, respectively, and 73.29 mg GAE/100 g and 3.40 mg QUE/g for EECC, respectively. The inhibitory concentration (IC₅₀) values of EWCC and EECC were 192.34 (moderate antioxidant) and 72.10 (strong antioxidant) g/mL, respectively. Based on the results obtained, EECC showed stronger antioxidant activity when compared to EWCC. This antioxidant activity is thought to be caused by the alkaloid content of EECC.

Keywords: Antioxidant; Black turmeric; *Curcuma caesia*; Nutraceutical

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ANTIBACTERIAL MECHANISM OF SILVER NANOPARTICLES OF ETHANOL EXTRACT OF *VERNONIA AMYGDALINA* DELILE. LEAVES AGAINST METHICILLIN-RESISTANT *Staphylococcus aureus*

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ABSTRACT

Synthesis of silver nanoparticles using plants in the biosynthesis of nanoparticles where secondary metabolites act as reducing agents and stabilizers in the formation of nanoparticles. ^[1] *Vernonia amygdalina* is known to have an antibacterial effect in previous studies. ^[2] This study aimed to synthesize silver nanoparticles of *V. amygdalina* with the addition of AgNO₃ solution and centrifuged. Then analyze its characteristics with a Particle Size Analyzer (PSA) and Scanning Electron Microscopy (SEM). The antibacterial mechanism includes a minimum inhibitory concentration, membrane leakage cell (DNA and protein), and an antibiofilm assay against Methicillin-resistant *Staphylococcus aureus* (MRSA). The results of the analysis with PSA showed nanoparticles measuring 27.21 μm. The results of the SEM analysis showed nanoparticles of various sizes. The test results for the minimum inhibitory concentration of 0.5 mg/mL (7.03 ± 0.15 mm). The results of membrane leakage cell at concentrations of 5 mg/mL and 1 mg/mL showed absorption at wavelengths of 260 nm (DNA) and 280 nm (protein). Formation of antibiofilm obtained values of 74.93 ± 0.61% (5 mg/mL) and 47.19 ± 0.66% (1 mg/mL). The results showed that the silver nanoparticles of *Vernonia amygdalina* had antibacterial potential against MRSA.

Keywords: *Vernonia amygdalina* Delile, silver nanoparticle, SEM, PSA, antibacterial

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ANTI-SENESCENCE EFFECT OF CITRONELLA OIL (*Cymbopogon nardus* (L.) Rendl.) ON VERO CELLS AND PREDICTION OF ITS MOLECULAR MECHANISMS

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ABSTRACT

Doxorubicin can increase intracellular ROS that damage kidney cells through induction of cell senescence.^[1] Citronella oil (CO) and its compounds are known to have antioxidant activity, so they have the potential to be used as kidney protective agents due to cellular senescence.^[2] This study aimed to investigate the nephroprotective effect of CO through bioinformatics and in vitro approaches. CO was obtained using water and steam distillation. The phytochemical profile was analyzed through GC-MS. CO contains citral (15.61%), citronellal (14.92%), methyleugenol (12.55%), hedycaryol (9.08%), citronellol (8.44%), geraniol (8.18%), and geranyl acetate (3.27%). A total of 28 genes play a role in the cellular response to oxidative chemical stress. PTGS2 is a gene that plays a role in the inflammatory process and tissue damage due to doxorubicin induction. Cell viability test was performed using the trypan blue exclusion method on Vero cells as a normal kidney cell model. CO is weakly cytotoxic with an IC₅₀ value of 139 µg/mL. CO was able to significantly reduce the percentage of Vero cells that experienced cellular senescence using SA-β-Gal assay due to doxorubicin induction (p<0.001). Therefore, CO has the potential to be used as a nephroprotective agent in doxorubicin-induced cellular senescence.

Keywords: citronella, nephroprotective, bioinformatics, Vero cell

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NEPHROPROTECTIVE ACTIVITY OF NUTMEG OIL (*Myristica fragrans*) ON VERO CELLS INDUCED BY DOXORUBICIN AND ITS MOLECULAR TARGET IDENTIFICATION WITH BIOINFORMATICS

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ABSTRACT

Doxorubicin can induce cellular senescence by increasing levels of reactive oxygen species (ROS).^[1] Excessive accumulation of free radicals can damage kidney cells causing nephrotoxicity.^[2] Nutmeg (*Myristica fragrans*) oil (NO) has antioxidant activity that can be developed as a nephroprotective agent.^[3] This study aims to explore NO as an anti-aging agent induced by doxorubicin in kidney cells and to study its molecular targets with bioinformatics studies. NO obtained by steam distillation contains sabinene (34.87%), terpinolene (24.63%), safrole (11.67%), α -terpinene (8,60%), β -Pinene (8,46%), dan α -pinene (3,38%) by GC-MS analysis. Bioinformatics studies were carried out to explore the physiological functions of the genes involved in the cellular response to oxidative stress. CASP3 is the most potential target gene for NO compounds that play a role in nephrotoxicity due to doxorubicin administration. NO cytotoxicity was carried out using the Trypan blue exclusion test on Vero cells and had an IC50 value of 100 g/mL. Anti-aging activity test was carried out using the SA- β -Gal assay and found that NO could reduce the number of Vero cells that age due to doxorubicin administration. Therefore, nutmeg seed oil may be as a result of anti-aging agents on renal cells given doxorubicin.

Keywords: Nutmeg (*Myristica fragrans*), senescence, kidney, molecular target

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NEPHROPROTECTIVE EFFECT OF CARDAMOM ESSENTIAL OIL (*Amomum compactum* Soland. Ex Maton) IN CELLULAR SENESCENCE INDUCE BY DOXORUBICIN AND PREDICTING MECHANISM THROUGH BIOINFORMATIC STUDY

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ABSTRACT

Many chemotherapeutic agents cause various side effects, including nephrotoxicity.^[1] Doxorubicin is a chemotherapeutic agent that increases the level of Reactive Oxygen Species (ROS) which leads to cell aging in the kidneys.^[2] Cardamom essential oil (*Amomum compactum* Soland. ex Maton) contains compounds that exhibit antioxidant activity.^[3] This study focused on exploring the potential of cardamom essential oil (CEO) as an anti-senescence induced by doxorubicin using Vero cells and predicting its mechanism through bioinformatics studies. CEO was obtained by steam distillation. The compounds were analyzed by gas chromatography-mass spectrophotometry (GC-MS) which revealed seven compounds with the greatest abundance, namely 1.8-cineole (50.82%), β -pinene (12.43%), α -terpineol (8.50%), fenchone (4.10%), α -pinene (4.00%), sabinene (3.00%), and linalool (1.98%). Bioinformatics were conducted to determine the upregulated genes that play a role in the incidence of cellular senescence. This study confirmed the top 10 genes important in response to chemical and oxidative stress. Cytotoxic assay using trypan blue exclusion showed an IC₅₀ value of 178 μ g/mL. Thus, CEO as weakly cytotoxic. Anti-senescence effect was evaluated using β -galactosidase (SA- β -gal) staining. Concentrations of 50 and 100 μ g/mL were able to reduce the incidence of doxorubicin-induced senescence on Vero cells. Therefore, CEO has the potential as a nephroprotective agent.

Keywords: cardamom, senescence, cytoprotective, bioinformatics, Vero cells

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***Caesalpinia sappan* L. EXTRACT SYNERGICALLY INCREASE PENTAGAMAVUNON-1 CYTOTOXICITY ON TNBC CELL LINE VIA CELL CYCLE REGULATION**

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ABSTRACT

Pentagamavunon-1 (PGV-1) is a curcumin analog that has been known to effectively combat TNBC cell progression and was known to increase its cytotoxicity when combined with many herbal compounds¹. On the other hand, *Caesalpinia sappan* L. has the potency to halt TNBC cancer cells² but it is not yet known particularly how its effects on PGV-1 if combined with PGV-1. This study aims to determine the synergistic properties of *Caesalpinia sappan* L. (CSE) extract with PGV-1 on TNBC cells. 1% yield of CSE is prepared by macerating *Caesalpinia sappan* L. with ethanol. Single cytotoxicity of CSE and PGV-1 was determined using trypan blue exclusion assay and showed IC₅₀ values of 18 µg/mL and 2 µM, respectively. Cytotoxicity synergistic properties between CSE and PGV-1 were determined using a combination index calculation which showed synergism between CSE and PGV-1 (CI<1). Cell cycle regulation by combination treatment was analyzed through bioinformatic exploration via several databases, including CMAUP, Swisstargetprediction, and UALCAN, which reveals putative cell cycle targets of CSE and PGV-1 synergism, including MMP1, PLK1, AURKA, AURKB, NEK2, FEN1, TYMS, KIF11, CDK1, CHEK1, TOP2A, and QPCT. Altogether, CSE was potential to be developed as a companion agent for PGV-1 to combat TNBC progression via cell cycle regulation.

Keywords: sappanwood, pentagamavunon-1, wound healing, senescence, 4T1, triple-negative breast cancer

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HISTOPATHOLOGY OF RENAL MICE POST ADMINISTRATION OF EKOR NAGA (*Rhaphidophora pinnata* (L.f) Schott) LEAVES EXTRACT IN ACUTE TOXICITY

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ABSTRACT

Ekor Naga (*Rhaphidophora pinnata* (L.f) Schott) leaves a traditional plant used by the community. Previous studies have shown this plant has pharmacological effects, including antelmintik^[1], antioxidant, anti-inflammatory^[2], and wound healing^[3]. So it is necessary to do a toxicity test. The study aimed to determine the effect of giving the extract on acute toxicity testing on the histopathological results of renal organs. The research method has used an experimental design. The test animals were divided into 5 groups in each group consisting of 5 test animals: negative control (Na. CMC 0,5%), Treatment 1 (Extract of Ekor Naga Leaves 200 mg/Kg BW), Treatment 2 (Extract of Ekor Naga Leaves 600 mg/Kg BW), Treatment 3 (Extract of Ekor Naga Leaves 1800 mg/Kg BW), Treatment 4 (Extract of Ekor Naga Leaves 5400 mg/Kg BW). The parameters observed were the ratio of the weight of the renal organs and the hispatology of the renals. Data were analyzed using One Way ANOVA test with Duncan's futher test. The results were showed no significant difference in the weight of the renal ($p > 0,05$), and hispatology of the renal after 14 days of acute administration of ekor naga leaves extract from all treatments still looked normal. Administration of ekor naga (*Rhaphidophora pinnata* (L.f) Schott) leaves extract at therapeutic doses, and large doses of single administration do not have a bad effect on the histology of renal organs.

Keywords: Ekor Naga Leaves, Renal, Histopathology, Acute Toxicity

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ANTIOXIDANT ACTIVITY AND DETERMINATION OF ARTOCARPIN LEVEL IN HYDROALCOHOL EXTRACT OF *Artocarpus lacucha* Buch. Ham LEAVES

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ABSTRACT

Antioxidants are molecules that can inhibit the activity of free radicals ^[1]. Antioxidants can be synthesized in the body or obtained from outside, such as from food ^[2]. One of the plants that can counteract free radicals is mobe (*Artocarpus lacucha* Buch. Ham) leaf because of its high flavonoid and phenol content ^[3]. The antioxidant activity of mobe leaves was analyzed by FRAP, CUPRAC, Hydroxyl, and O-Phenantrolin methods. Measurement of artocarpin levels in mobe leaves was measured using a High Performance Liquid Chromatography instrument. The results of the data acquisition of artocarpin levels in the ethanol extract of 80% mobe leaves obtained 37.69 ± 0.97 mg/g extract. The LOD value was $0.35 \mu\text{g/mL}$ and the LOQ value was $1.17 \mu\text{g/mL}$. The IC₅₀ value of extract was 144.36 ± 0.03 (moderate); 82.29 ± 0.07 (stronge); 161.26 ± 0.09 (weak), and 192.56 ± 0.12 (weak) $\mu\text{g/mL}$ respectively. The IC₅₀ value of artocarpine was 127.79 ± 0.06 (moderate); 60.63 ± 0.07 (stronge); 169.43 ± 0.03 (weak), and 301.29 ± 0.29 (weak) $\mu\text{g/mL}$ respectively. From the test results, it can be concluded that hydroalcoholic extract of mobe leaves and artocarpin have antioxidant activity.

Keywords: Hydroalcoholic extract, *Artocarpus lacucha* Buch.Ham, artocarpin, antioxidant, HPLC

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TOXICITY ASSAY OF ETHANOL EXTRACT OF *Enhalus acoroides* AND *Cymodocea rotundata* USING BRINE SHRIMP LETHALITY TEST (BSLT): EARLY STUDY

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ABSTRACT

Marine plants have become a source of phytopharmaceutical raw materials as the potency of anticancer drugs which continue to be researched. For example, seagrass, one of marine angiosperms that is widely distributed in all coastal regions in Indonesia. Bioactive compounds contained in seagrass are known to have potential as anticancer drugs. Several toxicity methods can be used to clarify the anticancer potency of seagrass are cell culture methods (Microculture Tetrazolium Salt/MTT)¹ and Brine Shrimp Lethality Test (BSLT). However, exploration of marine plants, especially seagrass as anticancer from Lampung waters is still minimal. This study aims to determine the bioactive compounds and the anticancer potential based on the LC50 value of ethanol extract of the seagrasses *Enhalus acoroides* and *Cymodocea rotundata* from the waters of Pesawaran and South Lampung, using the Brine Shrimp (*Artemia salina*) Lethality Test (BSLT) method. The results of this study indicate that seagrass *Enhalus acoroides* ethanol extract contained flavonoids, alkaloids, saponins, and steroids has an LC50 value of 126.77 ppm, while the seagrass *Cymodocea rotundata* ethanol extract that contained flavonoids, alkaloids, saponins, tannins, and steroids has an LC50 value of 163.18 ppm. The toxicity value of the two seagrasses in this study is relatively low, which is > 100 ppm.

Keywords: seagrass, anticancer, brine shrimp lethality test (BSLT)

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THE SYNERGISTICALLY CYTOTOXIC EFFECT OF TRIPLE COMBINATION (CURCUMIN, PGV-1, AND PGV-0) AGAINST MCF-7 BREAST CANCER CELLS: IN VITRO AND BIOINFORMATICS STUDY

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ABSTRACT

Background: Combination therapy proved as a promising therapy in inhibiting cancer growth effectively¹. Curcumin and its synthetic analogs (PGV-1 and PGV-0) exhibit growth inhibitory in breast cancer cells^{2,3}. **Objective:** This study aims to examine the singly and triple combination effect of Curcumin, PGV-1, and PGV-0 and explore protein targets that can bind to these compounds in inhibiting the growth of MCF-7 cancer cells. **Methods:** The cytotoxic effect was evaluated using MTT assay singly and in combination on the MCF-7 cell line. The combination index and polygonogram were analyzed using CompuSyn software. The target protein of Curcumin and its analogs that have a role in cell cycle arrest was confirmed using SwissTargetPrediction and then intercepted with the cell cycle regulator protein of MCF-7 retrieved from GeneCards. **Results:** Curcumin, PGV-0, and PGV-1 showed cytotoxic effects against MCF-7 with IC₅₀ values of 80 µM, 21 µM, and 82 µM, respectively. The triple combination of ½ IC₅₀ of Curcumin, PGV-1, and PGV-0 significantly suppressed the cell viability with a combination index of 0.37. Bioinformatics analysis revealed that Curcumin and its analogs target cell cycle regulatory proteins in MCF-7, namely EGFR, BCL2, BRAF, TNF, and CDK2. **Conclusion:** Triple combination of Curcumin and its analogs illustrated synergistically cytotoxic on MCF-7 cells which is likely to target EGFR, BCL2, BRAF, TNF, and CDK2. These findings suggested that the combination of Curcumin and its analogs promising developed as a combination therapy drug for luminal breast cancer.

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ANTIBACTERIAL ACTIVITY AND TLC-BIOAUTOGRAPHY ANALYSIS OF THE TAMOENJU (*hibiscus surattensis* L.) LEAVES EXTRACT AND FRACTION

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ABSTRACT

The tamoenju plant (*Hibiscus surattensis* L.) is one of the plants as traditional medicines to treat infections^[1,2]. Tamoenju leaves contain alkaloids, flavonoids, saponins, tannins, and steroids^[3], a potential antibacterial agent. This study was aimed to determine the antibacterial activity of tamoenju leaves extract and fraction against *Staphylococcus aureus* (ATCC 25923) and *Salmonella typhi* (ATCC 14028). Thin Layer Chromatography (TLC) techniques was carried out to detect the active compounds. The sample was extracted using maceration method with 96% ethanol as the solvent. Fractionation of the ethanol extract using the liquid-liquid fractionation method using n-hexane and ethyl acetate. The agar well diffusion method was used to evaluate the antibacterial activity with various concentrations of 2.5%, 5.0%, 10%, and 20% w/v, followed by TLC bioautography using n-butanol: acetic acid: aquadest (4:1:1) as the mobile phase and silica gel F254 as the stationary phase on the most active fraction. The results showed the extract, hexane, and water fractions were more sensitive to *S. typhi* while the ethyl acetate fraction was more sensitive to these two bacteria. The results of the bioautography TLC showed that the compounds that had the potential as antibacterial in the most active fraction (ethyl acetate fraction) were flavonoids.

Keywords: Antibacterial, *Hibiscus surattensis* L. *Staphylococcus aureus*, *Salmonella typhi*, zone of inhibition

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ERGOTAMINE AS BREAST CANCER DRUG TARGETING ESTROGEN RECEPTOR BETA AND MOUSE DOUBLE MINUTE 2 PROTEIN INTERACTION

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ABSTRACT

Estrogen receptor beta (ER β) is expressed in various cancer cells and becomes a marker of poor progression of breast cancer.^[1] ER β that binds to its ubiquitin ligase, mouse double minute 2 (MDM2), leads to ER β degradation and increases the growth of breast cancer cells.^[2,3] Thus, targeting the interaction between ER β -MDM2 is potential for novel breast cancer drug discovery. This study aimed to screen the FDA-approved drugs, which predicted to stabilize the interaction between ER β -MDM2 virtually. Biovia Discovery Studio 2021, ClusPro 2.0, PyRx 8.0, and PyMOL software were utilized in this study. ER β (PDB ID: 3OLS) and MDM2 (PDB ID: 1T4E) receptors were docked using ClusPro 2.0 to obtain the ER β -MDM2 protein complex. The ligands used in the virtual screening on PyRx 8.0 were from the FDA-approved categories downloaded from the ZINC Database. The results of the virtual screening showed that ergotamine was the drug with the lowest energy score (-12.0 kcal/mol) (native ligand: Estradiol -8.1 kcal/mol) among 1057 drugs docked against the ER β -MDM2 protein complex and able to establish stronger interaction between ER β -MDM2. In conclusion, based on this computational study, ergotamine strengthens the interaction between ER β -MDM2 and thus could be used as new candidate for breast cancer drug. Thorough validation in vitro and in vivo studies are needed to confirm this finding.

Keywords: Estrogen receptor beta, MDM2, Breast cancer, Virtual screening

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CO-CRYSTAL OF CURCUMIN WITH ASCORBIC AND SUCCINIC ACID AS COFORMER: CHARACTERIZATION, SOLUBILITY AND DISSOLUTION PROFILE

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ABSTRACT

Curcumin (*Curcuma Longa L.*) is a naturally occurring polyphenolic molecule with potent pharmacological activity, but poor solubility and bioavailability.^[1,2] Therefore, it is vital to alter curcumin to increase its solubility. Among these is the development of the cocrystal phase.^[3] The purpose of this research is to determine the effects of combining ascorbic acid and succinic acid with curcumin in cocrystal form. Cocrystals are formed by combining solid state grinding and solvent evaporation, with a curcumin to coformer ratio of 6:4. Ascorbic acid as a coformer increased curcumin solubility by a factor of three, but succinic acid had no effect on curcumin solubility in a cocrystal. Curcumin was successfully cocrystallized with both ascorbic and succinic acid, as determined by FTIR, PXRD, DSC, and HSM characterization techniques. At 60 minutes, the solubility of pure curcumin was found to be 27.93%, whereas that of cocrystal curcumin was found to be 48.87% and 45.32% when using ascorbic acid and succinic acid as cofomers, respectively. Thus, it may be concluded that curcumin formed a cocrystal with ascorbic acid and succinic acid. When compared to succinic acid, the characteristics of cocrystal curcumin with ascorbic acid conformer are superior.

Keywords: co-crystal, curcumin, ascorbic acid, succinic acid

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EFFECT OF NARINGIN, A CONSTITUENT OF *Citrus reticulata* PEEL, ON SARS-CoV-2 PSEUDOVIRUS CELL ENTRY

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ABSTRACT

SARS-CoV-2 is a highly pathogenic virus that causes worldwide COVID-19 pandemic [1]. While COVID-19 treatment still focuses on managing the symptoms, Indonesia has struggled to eradicate the illness through widespread immunization and serosurveillance. Due to its extensive biodiversity, Indonesia offers excellent prospect for finding promising herbs for anti-SARS-CoV-2 treatment. This research emphasized the application of reverse genetic technology to synthesize non-replicative SARS-CoV-2 pseudovirus bearing Vesicular Stomatitis Virus (VSV) backbone integrated with a GFP reporter for the purpose of screening cell entry inhibitors. In this study, we amplified VSV-G/G*-GFP using BHK-21 cells injected with a plasmid expressing G glycoprotein. Additionally, we created VSV-G/S*-GFP pseudovirus by pseudotyping VSV-G/G*-GFP in BHK-21 cells overexpressing the SARS-CoV-2 spike glycoprotein. Then, in CHO-K1 cells overexpressing hACE2, we carried out SARS-CoV-2 pseudovirus entry. As a result, we were able to validate the internalization of the SARS-CoV-2 pseudovirus using immunofluorescence analysis, which showed the colocalization of GFP signal from the pseudovirus with spike glycoprotein signal from the antibody reaction. The technique was then utilized to examine the impact of naringin, a constituent of *Citrus reticulata* peel, on the SARS-CoV-2 pseudovirus entry. Our research revealed that naringin might have a concentration-dependent inhibitory effect on the entrance of pseudoviruses.

Keywords: *Citrus reticulata*, naringin, pseudovirus, SARS-CoV-2, viral entry.

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MOLECULAR DOCKING STUDY: ACTIVE COMPOUND OF MENIRAN (*Phyllanthus niruri* L.) AS DENGUE HAEMORRHAGIC FEVER THERAPY

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ABSTRACT

Dengue Haemorrhagic Fever is a disease caused by dengue virus through a mosquito vector *Aedes aegypti*^[1]. NS3 Helicase is known as one of non structural protein consists of some essential enzymes for virus replication. Nowadays ivermectin has been developed as anti-dengue haemorrhagic fever with therapy target NS3 Helicase^[2]. Therapeutics drug of dengue haemorrhagic fever has not been found specifically. Methanol extract of meniran (*Phyllanthus niruri* L.) reported has antiviral activity to dengue virus with concentration 15,63 µg/mL^[3]. The aim of this research was to study the interactions and affinity of the active compound of meniran with the receptor (NS3 Helicase) and to know ADME and toxicity profile. From 56 active compounds of meniran, there was one best candidate as dengue haemorrhagic fever therapy which has energy binding (ΔG) and Inhibition Constanta (IC) lower than natural ligand and ivermectin, it is nirurin with energy binding -4.87 kcal/mol. The candidate of that compound has a good absorption and distribution profile so they can be a therapeutic drug candidate for dengue haemorrhagic fever with NS3 Helicase as the receptor target which better than ivermectin.

Keywords : Ivermectin, meniran, molecular docking, NS3 Helicase.

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ANTI-AGING AND NEPHROPROTECTIVE PROPERTIES OF HYDROCAVITATION EXTRACT OF CITRUS PEELS SUPPORTED BY ITS MAJOR FLAVONOID COMPOUNDS TARGETING MOLECULAR EVENTS

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ABSTRACT

Skin aging is an initial phenomenon of tissue damage involving senescent fibroblast cells, whereas kidney aging and disruption are mainly caused by kidney epithelial cell injury as a result of rising oxidative stress. Natural products are required to protect from these physiological events. Citrus (*Citrus sp.*) is high in antioxidant compounds, particularly flavonoids, which act as radical scavengers. We looked into the molecular markers of fibroblast and kidney aging as the specific anti-aging and nephroprotective targets of hydrocavitation extract of citrus peels (HCE-CP)^[1], including citrus flavonoids like hesperidin (HSD), hesperetin (HST), and diosmin (DSM) as the major compounds. Using cytotoxic and the *senescence-associated beta-galactosidase* assays, HCE-CP and the three compounds were screened on NIH-3T3 and Vero cell lines for their anti-senescence activities. HCE-CP, HSD, HST, and DSM significantly reduced doxorubicin-induced cellular senescence while having no cytotoxic effects. We then conducted three bioinformatics analyses to obtain comprehensive information on anti-aging genes using Genecard, protein targets of HSD, HST, and DSM using SwissTargetPrediction, and molecular docking. We identified specific target genes for each binding pocket, including MMP13 for HSD, MMP2 and MMP9 for HST, and MMP2, MMP9, and PTGS2 for DSM. HST, on the other hand, preferred to interact with catalytic enzymes involved in metabolism, particularly ROS metabolism, whereas HSD and DSM were bound to proteases. These results showed potential anti-aging and nephroprotective activities of HCE-CP and will enhance the evidence of citrus flavonoids as biomarkers for the anti-aging properties.

Keywords: citrus flavonoids, anti-aging, bioinformatics, in vitro

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THE BINDING FREE ENERGY AND TOXICITY PREDICTION OF 1,2,4-TRIAZOLE DERIVATIVES TO ABCG2 AND ABCB1

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ABSTRACT

Cancer is the second most common cause of death after cardiovascular disease. Multi-drug resistance (MDR) in cancer chemotherapy is a major challenge in cancer treatment. MDR can occur due to the efflux of certain anticancer drugs mediated by ABCG2 and ABCB1 transporters. ^[1,2] Several *1,2,4-triazole* compounds have shown anticancer activity and inhibit the efflux activity of ABCG2 and ABCB1. ^[3] The goal of this study was to predict the binding free energy and toxicity of 79 derivatives of *1,2,4-triazole* for ABCG2 and ABCB1 as anti-MDR drug candidates. The molecular docking was conducted using AutoDock 4.2.6 software to predict the binding free energies and toxicity prediction was performed using ProTox-II. The results of molecular docking and toxicity prediction of the tested compounds revealed that there are 16 compounds (code 23, 25, 26, 27, 28, 29, 30, 31, 42, 44, 45, 47, 49, 50, 53 and 78) having low toxicity and more negative value of binding free energies compare to the reference compounds, *Ko143* as ABCG2 inhibitor and *verapamil* as ABCB1 inhibitor. From the 16 compounds, compound 44 is the best-predicted compound with the value of binding free energy -7.58 and -8.92 kcal/mol, against the ABCG2 and ABCB1, respectively.

Keywords: ABCG2, ABCB1, toxicity, 1,2,4-triazole, MDR

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IN SILICO SCREENING OF PHYTOCHEMICALS FROM ASHITABA (ANGELICA KEISKEI K.) AS POTENTIAL MYCOBACTERIUM TUBERCULOSIS KasA INHIBITORS

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ABSTRACT

The infectious disease known as tuberculosis (TB) is brought on by an infection with the bacteria *M. tuberculosis*.¹ The prevalence of *M. tuberculosis* has increased due to the coexistence of antibiotic resistance. Ashitaba (*Angelica keiskei* K.) has been utilized as a traditional medicine and is said to contain a variety of pharmacological properties, including anti-diabetic properties and anti-cancer properties. Several research have also reported that ashitaba extract and chalcone have anti-TB properties.^{2,3} Therefore, the objectives of this paper was to discover of the ashitaba compound has led to the development of a novel lead compound as an anti-TB. At least 40 active compounds from the Ashitaba plant have been reported to be evaluated *in silico* against *M. tuberculosis* KasA using molecular docking and molecular dynamics methods. The results of molecular docking identified the top two compounds as **XAI** and **4HH**, with bond free energies of -12.03 and -11.87 kcal/mol, respectively. Based on the results of molecular dynamics simulations, the XAI was stronger than 4HH in stabilizing complexes with 2WGE with total energy (ΔG_{bind} , MMGBSA) of -54.8512 and -37.8836 kcal/mol, respectively. It can be concluded that **XAI** have the most potential inhibitor of *M. tuberculosis* KasA.

Keywords: Ashitaba, KasA, Molecular docking, Molecular dynamics, Tuberculosis

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GC-MS ANALYSIS OF N-HEXANE EXTRACT FROM ITCHY LEAVES (*LAPORTEA DECUMANA* ROXB. (WEDD))

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ABSTRACT

Itchy leaf (*Laportea decumana* (Roxb.) Wedd) is an endemic medicinal plant from Papua which is widely used by the community as a traditional painkiller/analgesics by applying the leaves to parts of body such as the back, hands, and feet. So far, there is no data that showed active compounds in this plant. The purpose of this study was to determine the compounds contained in itchy leaves by GC-MS. The method were used by collecting leaves from Arso XIII, Keerom Jayapura-Papua Regency. The leaves were cleaned, dried in an oven at $\pm 50^{\circ}\text{C}$ for 7 days, mashed, and sifted so that the size of each simplicia became $100\mu\text{m}$. The powder simplicia was macerated with n-hexane solvent and analyzed by GC-MS to obtain the active components qualitatively. The results showed that there were 31 compounds of n-hexane and dominated by ten compounds, namely: Hexahydrofarnesyl acetone, 4-(1,1,3,3-tetramethylbutyl)-Phenol, Methyl 3-(3,5-di-tert-butyl -4-hydroxyphenyl)propionate, Phytol, Caryophyllene, (E,E,E)-3,7,11,15-tetramethyl-, acetate, 2,6,10,14-Hexadecatetraen-1-ol, 5,5- dimethyl-4-(3-methyl-1,3-butadienyl)-1-Oxaspiro[2.5]octane, 2,4-bis(1,1-dimethylethyl)-Phenol, 4,8,12,16-Tetramethylheptadecan-4 -olide, γ -Cadinene. This study concluded that we found that Hexahydrofarnesyl acetone was obtained as much as 37,94 in Itchy leaves

Keywords: Itchy leaves, (*Laportea decumana* (Roxb.) Wedd), GC-MS, Analgetics

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POTENTIAL OF KABAU LEAF ETHANOL EXTRACT (*Archidendron bubalinum* (Jack.) I.C. Nielsen) TO DECREASE OF BLOOD GLUCOSE LEVELS IN MALE WISTAR RATS INDUCED ALLOXAN

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Abstract

Kabau leaf simplicia was extracted using 96% ethanol solvent by maceration method. The simplicia and extracts were screened for phytochemicals¹, characterized the simplicia, identified using TLC and decreased blood glucose levels. The method used is the GOD-PAP with the induction of alloxan. The data were statistically tested using one way ANOVA. The results of phytochemical screening of the ethanolic extract of kabau leaves showed the presence of alkaloids, flavonoids, phenolics, terpenoid, steroids, and saponins. The results of identification by TLC showed spots with an R_f value of 0.45 which had been evaporated by ammonia which was visible under UV lamp 366 which was suspected to be flavone glycosides, biflavonyls, and unusually substituted flavones. Phenolic compounds were characterized by a color change to blackish green after being sprayed with FeCl₃. Saponin glycoside compounds were characterized by the presence of purple spots after being sprayed with vanillin sulfate³. The increase in glucose levels due to alloxan induction in all groups of test animals was relatively the same statistically except for the 250 mg/kg kabau extract group which experienced the highest hyperglycemia condition compared to other groups of test animals. However, this study was still included in the study because it was included in the criteria for an animal model of diabetes. Measurement of MDA levels in test animals given a dose of 1000mg/kgBW gave a value of 0.024±0.003.

Keyword: Kabau leaves, Induced alloxan, TLC, GOD-PAP and MDA

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DETERMINATION OF GAMMA ORYZANOL FROM ETHANOLIC EXTRACT OF INDONESIAN RICE BRAN (*ORYZA SATIVA*)

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ABSTRACT

Background: Rice bran contains gamma oryzanol, a chemical compound mostly consisted of complex ester trans-ferulate with phytosterols¹. Gamma oryzanol has a strong antioxidant activity, explained by the free radical scavenging activity. This study was aimed to determine gamma oryzanol from ethanolic extract of rice bran. Quantitative analysis was conducted using HPLC analysis with mixture of methanol:acetonitrile:isopropanol (50%:40%:10%) as mobile phase and Inertsil ODS-3 5 µm as stationary phase. The UV detector wavelength was set to 327 nm, and the flow rate was set to 1 mL/min². Gamma oryzanol standard and rice bran ethanolic extract 96% was injected into HPLC system. Ethanolic extract of rice bran (*Oryza sativa*) sample showed four major peaks as those of gamma oryzanol standard and contained 105,981 ppm of gamma oryzanol. As the conclusion, ethanolic extract of rice bran (*Oryza sativa*) contains gamma oryzanol

Keywords: Rice bran, gamma oryzanol, HPLC

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SYNTHESIS OF 17 β -ESTRADIOL-17-HEMISUCCINATE- IODOHISTAMINE AND RADIOLABELING USING IODINE-125 AS RADIOLIGAND BINDING FOR ESTROGEN RECEPTOR

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ABSTRACT

Estradiol is an selective and sensitive ligand agonist of the estrogen receptor (1). For preparation of radioligand binding assay, 17 β -estradiol-17-hemisuccinate was synthesized from 17 β -estradiol then conjugated with iodohistamine (2,3). The 17 β -estradiol compound was synthesized with hemisuccinate to 17 β -estradiol-17-hemisuccinate compound. Furthermore, the ester was synthesized by adding DCC and NHS in ethyl acetate solution to 17 β -estradiol-17-hemisuccinate-NHS. Iodohistamine compounds obtained from the histamine reaction were protected into Boc-histamine then NIS in Dry MeCN was added to form Boc-iodohistamine and deprotected. Then, 17 β -estradiol-17-hemisuccinate-NHS and Iodohistamine was conjugated to 17 β -estradiol-17-hemisuccinate-iodohistamine. These conjugated compounds were confirmed by MS, NMR and HPLC. Radiolabeling of 17 β -estradiol-17-hemisuccinate-iodohistamine was carried out from 17 β -estradiol-17-hemisuccinate-NHS with [¹²⁵I]-histamine and confirmed the percentage of radiochemical and chemical purity by HPLC with UV and radioactive detectors using C-18 column, with mobile phase 0.1%TFA-MiliQ Water and 0.1%TFA-MeCN, gradient phase 0.1% 0.1%TFA-MeCN for 5 min, 5-100% 0.1%TFA-MeCN for 25 min and flow rate 1mL/min. Purification of [¹²⁵I]-17 β -estradiol-17-hemisuccinate-iodohistamine was carried out through HPLC then next purification using Seppak. [¹²⁵I]-17 β -estradiol-17-hemisuccinate-iodohistamine after purification has radiochemical purity above 95% with a yield of 10-20%. In further research, it is necessary to evaluate the stability of the compound in various storage temperatures.

Keywords: Radioligand binding assay, Estrogen Receptor, 17 β -estradiol, Radiolabeling

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STUDY OF EDIBLE FILM CHARACTERISTICS OF PANDAN LAUT FRUIT (*Pandanus odorifer*) PECTIN

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ABSTRACT

Pandan Laut is a tropical plant that mostly grows on the coast. Pandan laut Fruit is a source of pectin^[1]. Pectin is a group of anionic polysaccharides and includes fiber elements that function as adhesives and thickeners in food^[2]. Edible film is a primary wrapper, serves to protect food, is transparent and can be consumed directly with the coated food^[3]. This study aims to determine the characteristics of the edible film of the pectin of the Pandan Laut (*Pandanus odorifer*) fruit. The pectin extraction formula is simplicia Panda Laut, aquades and H₂SO₄ with various conditions of pH 2, 3, and 4. The results show that pectin with a pH of 4 meets the requirements according to the standard consisting of a yield of 2.60%, water content is 8.1%, ash content is 9.2%, methoxyl content is 6.2%, equivalent weight is 631 mg, galacturonic content is 253% and the degree of esterification is 13.9%. The formula for making edible film is Pandan Laut pectin, aquades, with variations of sorbitol added, namely 5%, 10% and 15%. The results showed that at 5% sorbitol concentration produced the best edible film that with the requirements for water content of 6.5%, thickness of 0.13 mm and solubility of 59%. The organoleptic test of edible film with 5% sorbitol concentration was the most preferred by the panelists.

Keywords: Pectin; Edible Films; Pandan Laut

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IN SILICO STUDY OF MOLECULARLY IMPRINTED POLYMER FOR EXTRACTION OF VORICONAZOLE IN HUMAN PLASMA

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ABSTRACT

Aspergillus spp is one of the most prevalent pathogens in coinfections of COVID-19 patients^[1]. Voriconazole is the first-line therapy for aspergillosis, and it's been recommended for therapeutic drug monitoring to increase the probability of a successful outcome and minimize the risk of toxicity^[2]. Bioanalysis of voriconazole requires selective extraction due to the complexity of matrix. Molecularly Imprinted Polymer (MIP) is a solution for increasing extraction selectivity. The interaction between template and functional monomers affects the recognition properties and the resulting MIP^[3]. The purpose of this research was to study the interaction of voriconazole as the template with common functional monomers using *Hartree-Fock (HF) method with basis set 3-21G using* GaussView 5.0.8 dan Gaussian09 software. The result showed that voriconazole forms intermolecular hydrogen bonds and stable complex with functional monomers with negative binding energy. Itaconic acid and acrylic acid were chosen as selected functional monomers based on the change of binding energy (ΔE) and *Gibbs free energy* (ΔG) with ΔE -21,02 kcal/mol, -14,32 kcal/mol, and ΔG -6,92 kcal/mol, -2,06 kcal/mol for itaconic and acrylic acid respectively. Conclusions: in silico study showed that itaconic acid and acrylic acid provided great interaction with voriconazole for MIP design.

Keywords: COVID-19, voriconazole, MIP, in silico

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ANTIPYRETIC EFFECTS OF SEMANGKUK FRUIT EXTRACT (*Scaphium affine*) IN MALE WHITE MICE

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ABSTRACT

Semangkuk fruit (*Scaphium affine*) has been used by Suku Anak Dalam in Semambu Village, Tebo Regency, Jambi Province as a fever medicine (Asridawati et al., 2020). This study aims to prove the antipyretic effect of Semangkuk Fruit extract on male white mice (*Mus musculus*). This study used 35 male white mice with an average body weight of 20-30 grams which were divided into 6 treatment groups, where each group consisted of 5 mice. Group 1 as normal control, group 2 positive control (Paracetamol), group 3 negative control (NaCMC1%) while group 4-6 as the group that was given a variances concentration of semangkuk fruit extract (100, 150 and 200 mg/kgbw). In this study, 5% peptone was used as a fever inducer in mice with an increase in temperature of up to 38°C. The temperature measurement of mice was carried out on the rectal of mice with time intervals of 15,30,60,90, and 120 minutes. The decrease in temperature of mice was analyzed by statistical difference test (Azimatur et al., 2021; Badra & Agustiana, 2017). Based on the results of the research shown all Semangkuk fruit extract doses can reduce the rectal temperature of mice from fever to normal temperature. Statistical results at α 0.05 showed a significant difference between dose and antipyretic activity, so it can be said that the fruit extract semangkuk has antipyretic activity in mice.

Keywords: Antipyretic, Extract, Paracetamol, *Scaphium affine*, Suku Anak Dalam, Semangkuk fruit.

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THE EFFECT DECREASED URIC ACID LEVELS IN BLOOD OF MALE WHITE MICE USED ETHANOL EXTRACT FRACTIONATION CORTEX KAYU MANIS (*Cinnamomum burmannii* (Nees & T.Nees) Blume.)

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ABSTRACT

Preclinical research has been carried out to determine the effect of the effect administration of fraction cinnamom bark fractionation results of cinnamon bark ethanol extract (*Cinnamomum burmannii* (Nees & T. Nees) Blume.) against a decrease in uric acid levels of blood serum of male white mice used experimental methods in vivo. Cinnamon bark contains polyphenol compounds that can be used as a treatment for gout (1–3). The extraction process was carried out used a 96% ethanol solvent and n-hexane, ethyl acetate, and water solvents were used in the fractionation process. Male white mice were used as experimental animals which were then divided into 6 groups to see the influence of ~~the best~~ fraction type category that was most optimal in reduced uric acid levels in the blood at a dose of 100mg/kgBB administration. The Best Fraction was then carried out dose variations used 25mg/kgBB, 50mgkg/BB and 100mg/kgBB. Used inductor chicken liver juice at a dosage of 25 ml / kgBB Orally. Measurement of uric acid levels in the blood is carried out used a uric acid test strip measured device. The result was obtained that the residual fraction of water showed a decrease in the value of uric acid levels with values ($p \leq 0.05$) compared to other types of fractions. The best dose that can lower uric acid levels in the blood from the residual fraction of cinnamon bark water is 100mg/kgBB. It was concluded that research on cinnamon bark fractions has the potential to reduce blood uric acid levels.

Keywords: Fractionation, *Cinnamomum burmannii*, Preclinical, in vivo, gout

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EFFICACY OF CINNAMON OIL AS A NEPHROPROTECTIVE AGENT THROUGH ANTISENESCENT ACTIVITY ON VERO CELLS

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ABSTRACT

Senescence causes nephrotoxicity due to increased ROS that induces cell death through the apoptotic pathway^{2,3}. Cinnamon essential oil (CEO) contains *cinnamaldehyde* compounds that perform antioxidant activity to break the chain reaction to prevent oxidative stress¹. This study aims to explore the potential of CEO as an anti-senescence agent for nephroprotection through an in vitro method on Vero cells. CEO was obtained by hydrodistillation, then identified the compounds by gas chromatography–mass spectrometry. The cytotoxicity of CEO was evaluated using the Cell Counting Kit-8 (CCK-8) assay. The senescence was detected by the senescence-associated beta-galactosidase assay. The CEO contains 31 compounds, of which the highest concentration compound is *cinnamaldehyde*, as much as 66.85%. Cytotoxic test showed that CEO up to 100 µg/mL moderate cytotoxic concentration in Vero cells. Furthermore, administration of CEO at concentrations of 4.5 µg/mL and 9 µg/mL reduced the number of senescence cells that occurred due to the induction of doxorubicin in Vero cells. Based on this study, CEO contains an active compound that has anti-senescence activity on Vero cells, so it has the potential to be used as a nephroprotective.

Keywords: Anti-senescence, essential oil, Vero cells, *Cinnamomum burmanii*

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KNOWLEDGE AND QUALITY OF LIFE IN TYPE 2 DIABETES MELLITUS PATIENTS AND CORRELATION

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ABSTRACT

Diabetes mellitus is one of the chronic diseases suffered by many Indonesian people [1]. Diabetes knowledge, attitudes, and self-management are key factors that can have a direct or indirect impact on quality of life [2]. This study aims to determine patient knowledge and quality of life of patients with DM type 2 outpatient at RSUD Panglima Sebaya Paser Regency. A cross-sectional study design was used in this study. A total of 60 people participated. Data were obtained from medical records, questionnaires DKQ-24 (knowledge), and EQ-5D (QOL). The correlation between knowledge and quality of life of patients with type 2 diabetes and its associated factors was analyzed using univariate statistical tests. The characteristics of DM type 2 patients are the most female sex (61.7%), age 41-60 years (58.3%), high school education level (56.7%), and housewife employment (43.3%). The most widely used drugs are a combination of oral drugs metformin and glimepiride (26.7). The majority of patients with diabetes mellitus have a high level of knowledge (80%) and a moderate level of quality of life (45%). Statistical tests showed there was not significant correlation between knowledge and QOL based on utility value ($p=0.043$).

Keywords: Knowledge, quality of life, diabetes mellitus, patients

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CYTOTOXIC ACTIVITY OF CINNAMON ESSENTIAL OIL AND ITS COMBINATION WITH DOXORUBICIN AS A CO-CHEMOTHERAPEUTIC AGENTS ON MCF-7 CELLS

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ABSTRACT

Doxorubicin, an anthracycline drug, shows resistance to MCF-7 breast cancer cells.¹ Cinnamon (*Cinnamomum burmannii*) indicates anticancer activity in several types of cancer cells.² This study aims to investigate the cytotoxic activity of Cinnamon Essential Oil (CEO) and its combination with doxorubicin as a Co-Chemotherapy agent on MCF-7 cells. CEO was obtained by hydrodistillation, then identified the compounds by gas chromatography–mass spectrometry. The cytotoxicity of CEO and its combination with doxorubicin was evaluated using the WST-1 assay to determine the Combination Index (CI). Cytotoxic test on MCF-7 cells showed that CEO has moderate cytotoxic effect with IC₅₀ values of 125 µg/mL and Doxorubicin has strong cytotoxic effect with IC₅₀ values of 0,78 µM. CEO showed synergistic effect with Doxorubicin on MCF-7 cells. The lowest combination index (CI) with CI values of 0,83 by combination of doxorubicin-CEO 0,2 µM-30 µg/mL. The results of this study indicate the combination of CEO with doxorubicin has synergistic effect and potential to be developed as a co-chemotherapeutic agent for breast cancer treatment especially MCF-7 cells.

Keywords: co-chemotherapy, *Cinnamomum burmannii*, essential oil, MCF-7 cells

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THE EFFECTIVENESS OF PROGRESSIVE MUSCLE RELAXATION THERAPY AND MUSIC THERAPY ON REDUCING STUDENT STRESS DURING ONLINE LEARNING METHODS DURING THE COVID-19 PANDEMIC

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ABSTRACT

During the Covid-19 pandemic, the government imposed restrictions on teaching and learning activities to suppress the spread of the virus so that these activities were carried out from home^[1]. The negative effect is that children become stressed because they feel limited and there are significant changes in social life^[2]. This study aims to see how the effect of progressive muscle relaxation therapy and music therapy on reducing student stress during the Covid-19 pandemic. The research method used is a scoping review where the author uses three databases, namely Google Scholar, PubMed, and Science direct from 2019 to 2022. The results show that progressive muscle relaxation therapy and music therapy given to students can significantly reduce stress during the Covid pandemic. -19. The success of reducing stress levels in students can be optimized by increasing the time interval for giving therapy. Although there are 2 articles which state that there is no relationship between music therapy in reducing student stress. However, there are 22 other articles which state that there is a positive effect of the use of music therapy in reducing student stress. Progressive muscle relaxation therapy and music therapy can significantly reduce student stress during the Covid-19 pandemic.

Keywords: Stress, Music Therapy, Progressive Muscle Relaxation Therapy.

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USE OF ANTIBIOTICS IN FIRST LEVEL HEALTH FACILITIES IN 2019-2021 IN SEVERAL DISTRICTS OF JAMBI PROVINCE

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ABSTRACT

The unwise use of antibiotics is a factor that causes antibiotic resistance. Monitoring of the use of antibiotics is still considered a must to maintain the rational use of antibiotics. This research is one of the initial strategies in designing research in the rational monitoring of the use of antibiotics in first-level health facilities as the front line in health services for the entire community. This study was conducted retrospectively on the use of antibiotics in first-level health facilities. The data used is data for the period 2019-2021. Trends in the use of antibiotics in health facilities I was seen by the ATC DDD/1000/KPRJ method. The results of this study indicate that Amoxicillin is still the largest antibiotic in use, this is indicated by the average value of DDD/1000 KPRJ/year in 3 years of observation of 467.111/DDD/1000KPRJ, PKM S 227,154/DDD/1000/KPRJ, PKM A 170 ,72 DDD/1000/KPRJ, and PKM T of 109.01 DDD/1000/KPRJ. In addition to the value of DDD/1000/KPRJ/year, it was also found that for 3 years at the first health facility, the antibiotics included in the DU90 were Amoxicillin ranked first and followed by quinolones class antibiotics (Ciprofloxacin). This needs to be a concern due to the high use of antibiotics from these two types of groups whether these antibiotics still provide maximum activity. Therefore, the next further study that can be done is to evaluate the rationale for the selection and use of these antibiotics.

Keywords : *ATC/DDD, 90% DU Segment, Amoxicillin, Ciprofloxacin, Health Facilities I*

THE EFFECT OF GALANGIN IN ENHANCING PGV-1 EFFICACY IN COLON CANCER: *IN VITRO* AND BIOINFORMATIC STUDIES

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ABSTRACT

Pentagamavunone-1 (PGV-1) is a curcumin analog with a prominent anticancer potency *in vitro* and *in vivo* including for colon cancer¹. As a new anticancer candidate², to enhance its effectiveness, PGV-1 can be combined with natural compounds such as galangin which possess chemoprevention properties. Galangin has been proved to synergistically enhance the efficacy of PGV-1 in breast cancer cells³. We aim to evaluate the effectiveness of PGV-1 combination with galangin for colon cancer by using *in vitro* and bioinformatic approaches. WiDr cells were used as a model for colon adenocarcinoma (COAD). The cell viability under a single or combination treatment of PGV-1 and galangin was evaluated using direct counting by the trypan blue exclusion test. SwissTargetProtein, UALCAN, and OncoLn were utilized to predict target proteins of the compounds in COAD, the expression level of target proteins, and the survival rate of patients with overexpressed target proteins, respectively. The IC₅₀ values for PGV-1 and galangin were 0.08 nM and 26 μM, respectively. Galangin at low concentration showed the highest synergism effect when combined with PGV-1 at IC₅₀. Six proteins that overexpressed in COAD were identified as targets of the PGV-1 and galangin. Three among them that overlapped targets of PGV-1 and galangin were hepatocyte growth factor receptor (MET), cyclin-dependent kinase 1 (CDK1), and DNA topoisomerase II alpha (TOP2A); the latest two are involved in cell cycle modulation. We concluded that combination PGV-1 with galangin could enhance the effectiveness of its anticancer activity for colon cancer, possibly by targeting overexpressed proteins in COAD.

Keywords: Pentagamavunon-1 (PGV-1), curcumin analog, galangin, colon cancer, combination

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INHIBITORY EFFECT OF *SARGASSUM SP.* ETHYL ACETATE EXTRACT ON CARRAGEENAN-INDUCED INFLAMMATION IN MICE

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ABSTRACT

The prevalences of inflammation-related diseases, such as asthma, hypertension, stroke, osteoarthritis, acute and chronic hyperuricemia, rheumatoid arthritis, and cancer, are still quite high. The bioactive compounds of *Sargassum sp.* have the potential as an antioxidant and anti-inflammatory agent. This study aimed to measure the total phenolic and flavonoid content of *Sargassum sp.* ethyl acetate extract from Ria Beach, Dompu Regency, West Nusa Tenggara, and to evaluate its antioxidant and anti-inflammatory activity. *Sargassum sp.* was macerated in ethyl acetate (1:4 w/v) for 24 hours, then concentrated using a rotary evaporator (40°C). The total phenol and flavonoid contents were measured using the colorimetric method. The antioxidant and anti-inflammatory activities were evaluated using DPPH and carrageenan-induced paw edema models, respectively. The results demonstrated the weak antioxidant of *Sargassum sp.* with an IC₅₀ value of 605,24 ± 26,53 µg/mL. Its total phenolic and flavonoid contents were 103,013 ± 0,479 mg GAE/g and 20,572 ± 0,089 mg QE/g, respectively. The percentages of inflammatory inhibition of *Sargassum sp.* at doses of 200, 400, and 800 mg/kg BW were 53,80 ± 4,68%, 62,35 ± 4,05%, and 60,90 ± 2,88%, respectively. Based on its AUC value, it showed a significant difference (p<0.05) compared to the negative control. This study concluded that *Sargassum sp.* ethyl acetate extract at the dose of 400 mg/kg BW had the highest anti-inflammatory activity.

Keywords: *Sargassum sp.*; Inhibitory effect; Inflammation; Carrageenan; Antioxidant.

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IN VITRO CYTOTOXICITY ASSAY OF PGV-1 IN COMBINATION WITH CURCUMIN ON BREAST CANCER CELL LINES

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ABSTRACT

Pentagamavunon-1 (PGV-1) and its original compound, curcumin, reported to have anticancer activity in a single treatment on breast and colon cancer cell models.^[1,2] This research aims to determine the cytotoxic effect of PGV-1 combined with curcumin on breast cancer cell lines, T47D and 4T1. Cell viability was determined *in vitro* using MTT assay, thus obtaining both IC₅₀ and combination index (CI) values. Firstly, 4T1 and T47D, a TNBC and non-TNBC model cells, were treated with PGV-1 and curcumin in singular, respectively. Next, IC₅₀ values obtained were used as bases of combination dosage. As a result, PGV-1 and curcumin showed a cytotoxic effect against 4T1 cell with IC₅₀ values of 4 µM and 40 µM, respectively, and against T47D cell with 2 µM and 20 µM, respectively. The combination treatment of PGV-1 and curcumin appeared to have a synergistic effect (CI<1) on both 4T1 and T47D cells. In conclusion, the combination of PGV-1 and curcumin seemed to increase the cytotoxic effect of PGV-1 as an anticancer agent. Hence, the combination of these two compounds has the potential to be further investigated as a breast cancer treatment agent.

Keywords: 4T1 and T47D cells, breast cancer, curcumin, cytotoxic, PGV-1

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***Moringa oleifera* AS THE POTENTIAL HERB MEDICINE FOR NEURODEGENERATIVE DISEASES: A NARRATIVE REVIEW**

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ABSTRACT

Neurodegenerative diseases, such as parkinson diseases, alzheimer, dementia, and multiple sclerosis, are commonly occurred in the elderly population and characterized with the progressive decline of neuron function in the central nervous system.¹ *Moringa oleifera* (MO) is commonly used in Indonesia not only as the daily vegetable, but also for the health purposes due to its antioxidant and antiinflammation effects. This effect might be caused by the high nutritional value of this herb medicine such as alkaloids, flavonoids, saponins, sterols, tannins, and phenolics.² Several studies have provided ample evidence that MO has neuroprotective properties in various neurodegenerative disease in animal models.³ This narrative review highlighted the bioactive compounds that can be found in MO and summarized the potential beneficial effect of MO in various rodent models of neurodegenerative diseases.

Keywords: *Moringa oleifera*, neurodegenerative disease, antioxidant, neuroprotective, Bioactive compound

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HEPATOPROTECTIVE EFFECT OF ETHYL ACETAT EXTRACT OF *Lygodium microphyllum* AGAINST PARACETAMOL INDUCED HEPATOTOXICITY IN RATS

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ABSTRACT

Genus *Lygodium* has been used by the Chinese community for traditional hepatitis treatment by drinking boiled water from these plants. *Lygodium microphyllum* is known to have antioxidant and antiinflammation activity. Thus, the present study was design to investigate the effect of *Lygodium microphyllum* extract on paracetamol induced hepatotoxicity. Wistar rat were exposed to ethyl acetate extract of *Lygodium microphyllum* (200, 400, and 600 mg/Kg body weight) for 2 weeks. Paracetamol suspension (3 kg/kg body weight) were given orally at day 8th till 15th. Rats were sacrifice on day 15th, serum and liver were collected and further analyzed.

The result showed that ethyl acetate extract of *Lygodium microphyllum* significantly decreased the level of SGOT ($p < 0.05$) and SGPT ($p < 0.05$) compared to paracetamol only group. Histological analysis also showed that there is no necrosis found in *Lygodium microphyllum* extract group.

Based on result, we concluded that ethyl acetate extract of *Lygodium microphyllum* have a hepatoprotective effect against paracetamol induced hepatotoxicity.

Keywords: *Lygodium microphyllum*, hepatoprotector effect

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MICROEMULSION GEL FORMULATION OF 70% ETHANOL EXTRACT OF KELAKAI ROOT KELAKAI ROOT (*Stenochlaena palustris* (Burm.f.) Bedd)

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ABSTRACT

Kelakai is a plant that lives on peat soil. Kelakai root contains flavonoids that function as antioxidants. The IC_{50} value of kelakai root is 19.06 ppm¹. Gel microemulsions have the advantage of being a good delivery agent for topical preparations². This study aims to formulate microemulsion gel as an antioxidant preparation. Microemulsions were carried out by spontaneous emulsion method using various concentrations of surfactants and co-surfactants, namely Tween 80 and PEG 400. Optimum microemulsion characterization was carried out on particle size, zeta potential, morphology using a Transmission Electron Microscope, and percent transmittance. The gel microemulsion formulation uses Na CMC as a gelling agent with various concentrations. The evaluation was carried out before and after stability. The optimum kelakai root microemulsion had a particle size of 14.6 nm \pm 1.3, potential zeta -42.5 mV, percent transmittance 94.9%. The microemulsion of kelakai root has a spherical shape. The evaluation of the gel microemulsion has met the requirements for before and after stability. Microemulsion gel of kelakai root provides good stability.

Keyword: *antioxidant, kelakai root, microemulsion, gel*

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INCORPORATION OF SOLID LIPID NANOPARTICLES 70% ETHANOL EXTRACT OF KELAKAI ROOT (*Stenochlaena Palustris* (Burm.F.) Bedd) INTO SERUM GEL PREPARATIONS

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ABSTRACT

Kelakai has IC₅₀ value of 19.06 ppm^{1,2}. Antioxidants function to ward off free radicals that cause skin problems. Antioxidant effectiveness can increase by a solid lipid nanoparticle system which is incorporated into a serum gel preparation. The study aims to develop solid lipid nanoparticles into serum gel preparations as an antioxidant. Solid lipid nanoparticles can increase drug penetration into the skin by occlusive properties. Optimization of solid lipid nanoparticle systems has been done by Box-Behnken. Solid lipid nanoparticles were prepared using homogenization and sonication methods. Characterization of optimum solid lipid nanoparticles was particle size, entrapment efficiency, zeta potential, and solid lipid nanoparticle morphology by Transmission Electron Morphology. The optimum formula of solid lipid nanoparticles was incorporated into serum gel preparations, then the physicochemical properties of serum gel were evaluated. The optimum solid lipid nanoparticles have a particle size of 767 nm ± 43, PDI 0.682 ± 0.023, the zeta potential of -53,1 mV ± 0,586 and entrapment efficiency of 86% ± 0,017. Morphology of solid lipid nanoparticles showed a spherical shape. Physicochemical of serum gel showed that pH value with a range of 3-6.5, adhesion of more than 1 second, spreadability with a range of 4.3- 6.2 cm, and a viscosity of 3100-3980 mPa.s. This study concludes that the solid lipid nanoparticles kelakai root gel serum has physicochemical properties that meet the requirements.

Keywords: antioxidant; kelakai root, solid lipid nanoparticles, gel serum

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**ANTIBACTERIAL ACTIVITY TEST OF LIQUID CRYSTAL
NANOPARTICLES GEL METHANOL EXTRACT OF BINJAI LEAVES
(*MANGIFERA CAESIA* JACK. EX. WALL.) AGAINST
*PROPIONIBACTERIUM ACNES***

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ABSTRACT

Binjai leaves (*Mangifera caesia* Jack. Ex. Wall.) contain a distinctive compound mangiferin which is effective as an antibacterial^[1]. This study aims to determine the antibacterial activity of gel liquid crystal nanoparticles of methanolic extract of binjai leaves. Preparation liquid crystal nanoparticles system (LCNPs) of binjai leaf extract were made using the top-down method^[2]. Then the liquid crystal nanoparticle system (LCNPs) was incorporated into the gel preparation. Formulation of gel liquid crystal nanoparticles using Viscolam Mac 10 as a gelling agent. Antibacterial activity test of gel liquid crystal nanoparticles against *Propionibacterium acnes* using cup plate technique. Gel liquid crystal nanoparticles gel of methanol extract of binjai leaves produced a strong antibacterial activity with the inhibition zone is 15.33 mm±1,2413. The antibacterial activity can increased with the LCNPs's application.

Keywords : Gel liquid crystal nanoparticles, Binjai leaves extract, *Propionibacterium acnes*

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PHARMACOGNOSTICAL, PHYTOCHEMICAL, AND ANTIBACTERIAL OF ESSENTIAL OIL FROM *Strobilanthes kalimantanensis* LEAVES: A NEW SPECIES FROM EAST BORNEO INDONESIA

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ABSTRACT

Kalimantan (Borneo) including the Southeast Asian countries, Indonesia, Brunei Darussalam and Malaysia has been recognized by WWF as a center for biodiversity^[1]. East Kalimantan is one of Indonesia's islands rich in tropical rainforest plants. It has abundant natural resources that can be explored to be used for human benefit, especially in medicine^[2]. The aromatherapy plant is known by the Dayak ethnic as the "Lintut" plant with the first species reported as *Strobilanthes kalimantanensis*. Found several morphological characteristics of plants that are identical to hydrophytic plants. The aim was to determine the botanical, chemical characteristics and antibacterial of *S.kalimantanensis*. The results of the steam distillation process of Essential oil (EO) produced a yield of 0.547%, the refractive index at 27°C (1.393-1.401), clear and fresh scent. GC-MS results from EO identified major phytochemicals including anethole and estragole. The antibacterial activity of EO is 100 mg/mL against *Staphylococcus aureus* and 150 mg/mL against *Bacillus subtilis*, *Escherichia coli*, and *Streptococcus epidermidis*.

Keywords: Essential Oil, *Strobilanthes kalimantanensis*, Antibacteria

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VACCINE HESITANCY: THE NEXT CHALLENGE IN THE FIGHT AGAINST INFECTIOUS DISEASES

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ABSTRACT

Despite being one of the most successful public health measures for the prevention and control of infectious disease outbreaks such as smallpox, polio, influenza and COVID-19, an increasing number of people perceive vaccination as unsafe and unnecessary.¹ Anxiety over safety of vaccines and vaccination programs leads to vaccine hesitancy that is caused by a complex mix of social, political, cultural, and religious issues, the availability and ability to interpret health and scientific information, and personal and population experiences with health systems and government policies.² Vaccine hesitancy became one of the WHO's top ten global health issues in 2019.³ Anti-vaccination movements are considered to be as a major contributor to increased vaccine hesitancy worldwide. This talk will discuss vaccine hesitancy and the anti-vaccine movement in their early history and in the modern era, the key drivers of vaccine hesitancy, particularly across different regions of the world, with a focus on countries with low- and middle-, or high-income countries and different socio-economic populations. It will cover vaccine hesitancy's impact on herd immunity and social as well as psychological, and public health measures to counter vaccine hesitancy.

Keywords: vaccines; vaccine hesitancy; anti-vaccine movement; vaccination

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Neuroprotective Effects of Water Extract *Moringa oleifera* leaves on Behavioral Abnormalities of Chronic Stress Mice Models

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ABSTRACT

The brain-derived neurotrophic factor (BDNF) plays a significant role in various stress-related mood disorders¹. Previous literature has demonstrated *Moringa oleifera* positive benefits, including neuroprotective and antioxidant properties². *Moringa oleifera* leaves are enriched in phytochemicals such as tannins, sterols, saponins, terpenoids, phenolics, alkaloids, and flavonoids³. Here we investigate the neuroprotective effect of leaves water extract *Moringa oleifera* (MW) on cognition in chronic stress mice models induced water immersion and restraint stress model. We divided twenty male Balb/c mice into four groups: normal group (control without intervention), stress control group (under chronic stress condition), Fluoxetine group (18 mg/kg), and MW (800 mg/kg) were administered for 23 days to stressed mice. Chronic stress induction was performed by exposing restraint stress and water immersion to mice for 16 days. Furthermore, we measured behaviors, neuroplasticity, and oxidative stress parameters. We found that MW recovered the decline caused by WIRS at levels of anxiety-like was described by the increasing number of returns in the center area and time spent in the center area in open field test. Furthermore, the decrease in depression levels is shown by the increasing number of mobility mice in the force swim test. In addition, the results of this study show that the administration of fluoxetine and moringa leaf aqueous extract can increase by manifesting the level of mRNA BDNF expression in stress mice compared to the stress group ($p=0.024$ and 0.035). In contrast, the values of SOD, MDA, and CAT, in stress mice that obtained fluoxetine and MW were no different from the stress group. Our data reveal that MW as a neuroprotective suppresses the level of anxiety due to chronic stress. This effect is, at least in part, through increased expression of mRNA BDNF.

Key words: *Moringa oleifera*, anxiety, oxidative stress, antioxidant, chronic stress

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REVEALING THE POTENCY OF NUTMEG (MYRISTICA FRAGRANS HOUTT) SEEDS EXTRACT AS A CO-CHEMOTHERAPEUTIC AGENT IN TRIPLE-NEGATIVE BREAST CANCER COMBINED WITH CISPLATIN

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ABSTRACT

Triple-Negative Breast Cancer (TNBC) is one of the breast cancer subtypes with the worst overall survivability^[3]. Treatment for TNBC generally uses chemotherapeutic agent which has dangerous side effects when it used in high doses continuously^[1]. Therefore, exploration of natural products is needed to find synergistic co-agents to optimize chemotherapy and reduce chemotherapy-related toxicity such as nutmeg. This study aimed to reveal the cytotoxic activity of Nutmeg Seed Extract (NSE) as a co-chemotherapeutic agent combined with cisplatin. NSE was obtained by maceration using 96% ethanol for 48 hours. The phytochemical profile of NSE was obtained by thin layer chromatography (TLC) method. The viability of 4T1 cells was determined in vitro using Cell Counting Kit-8 (CCK-8) assay. Meanwhile, WST-1 assay was used to determine combination index (CI) of NSE-cisplatin. Based on result of maceration obtained yield 4,01%. NSE contained myristicin was indicated by appearance of spot at Rf 0,875. At 24 hours of incubation, NSE exhibited moderate cytotoxic effect against 4T1 cells as a model of TNBC with IC₅₀= 61,48 µg/mL, while cisplatin showed strong cytotoxicity with IC₅₀= 2,98 µM. The combination of NSE-Cisplatin exhibited strong synergistic activity with CI<1^[2]. In conclusion, NSE has potency to be developed as a co-chemotherapeutic agent.

Keywords: *Myristica fragrans* Houtt, TNBC, Co-chemotherapy, 4T1, Combination Index

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PREPARATIONS FOR GUMMY CANDY INFUSION OF KEROKOT LEAVES (*LYGODIUM MICROPHYLLUM*) AS NUTRACEUTICALS

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ABSTRACT

Kerokot leaves (*Lygodium microphyllum*) have pharmaceutical potential related to drugs and health protection as well as cosmetics from natural ingredients. The drug category is antioxidant and wound medicine (Rijai, 2012). The antioxidant activity shown by the kerokot infusion has an IC₅₀ value of 65 ppm (Gnanaraj & Charles, 2017), which means it has a relatively high antioxidant activity, namely in the range of 50-100 ppm (Heriad, 2017). Besides Secondary metabolites contain flavonoids, flavonoid glycosides, and naphthoquinones which are included in the phenolic compound group (Kuncoro & Rijai, 2018). This study aims to formulate kerokot leaves into *gummy candy* which has economic value and is favored by various age groups and is beneficial for health. The process of extracting kerokot leaves using the infusion method. The results showed that the infusion of kerokot leaves can be used as a preparation in the form of *gummy candy* with an appropriate base found in the optimization of the F3 base with gelatin: carrageenan ratio of 12: 5, with organoleptic testing the preparation has a slightly sweet, sour taste, tutti frutti aroma, chewy texture, slightly elastic, brownish-yellow color; 1.66% ash content; water content 15.73%; stable at room temperature; pH 5.16%; the uniform weight of the preparation and the dominant hedonic test was preferred, with IC₅₀ preparations of *gummy candy* infusion of kerokot leaves of 146.45 ppm. The conclusion of this study is that the best formulation for the preparation of *gummy candy* infusion of kerokot leaves (*Lygodium microphyllum*) is on the optimization of the F3 basis with a 12:5 ratio of gelatin and carrageenan.

Keywords: Kerokot leaf infusion, Nutrasetical, Gummy preparation Candy

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CYTOTOXIC EFFECT OF LEMONGRASS IN COMBINATION WITH DOXORUBICIN AS A COTREATMENT ON 4T1 CELLS

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ABSTRACT

Lemongrass (*Cymbopogon citratus*) leaves has been known to have anticancer activities by its cytotoxic effect¹, but the cytotoxic effect of the combination of doxorubicin and Lemongrass Essential Oil to 4T1 cells is unknown. Further studies on the combination of Lemongrass and doxorubicin activity are required. This study aimed to provide an exploration of the combination of Lemongrass Essential Oil (LEO) as a doxorubicin cotreatment on 4T1 cells. LEO were extracted by water-steam distillation. LEO was then characterized by Gas Chromatography-Mass Spectrometry (GC-MS). The single cytotoxic activity of the LEO and doxorubicin combination was identified using MTT assay and WST-1 assay to determine the IC₅₀ and Combination Index (CI). The results showed that citral is the major component of the essential oils. LEO and doxorubicin were cytotoxic to 4T1 cells with the IC₅₀ value of 76.60 µg/mL and 4.23 µM, respectively. LEO in combination with doxorubicin showed antagonist effect on 4T1 cells (CI=1,24 - 4,06). The data showed that LEO does not have good synergism with 4T1 cells as a doxorubicin cotreatment.

Keywords: *Cymbopogon citratus*., cotreatment, combination, 4T1

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ANTIOXIDANT ACTIVITIES AND PHYSICAL PROPERTIES OF SCRUB BODY LOTION ETHANOL EXTRACT OF SURIAN LEAVES (*Toona sinensis*) WITH POWDER SCRUB DATE SEEDS (*Phoenix dactylifera*)

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ABSTRACT

Free radicals from exposure to ultraviolet radiation (UVB) cause dull, rough, dry, cracked skin and premature aging so that they can damage skin tissue and result in fatal skin cancer. One way to prevent this is to take antioxidants that come from outside our bodies^[1,2]. Plants that have strong potential as antioxidants are Surian leaves and date seeds which contain lots of flavonoids and phenolics. To make it easier to use, it is processed into a scrub body lotion using a date seed powder scrub (*Phoenix dactylifera*). Date seed powder is able to increase the natural antioxidant function of ethanol extract Surian leaves, besides that, date palm seeds can moisturize and brighten the skin. The aim of this study was to find a scrub body lotion formula that has the best physical properties and is stable during storage and the best formula has the strongest antioxidant activity. In this study, scrub body lotion preparations were made with 5 formulas. Each formula contains ethanol extract of Surian leaves (*Toona sinensis*) with a concentration of 0.1%; 0.3%; 0.5%; 0.7%; 0.9%. After that, an evaluation of the physical properties of scrub body lotion preparation was carried out. From the results of the evaluation of the physical properties of the best scrub body lotion preparations, stable in storage and hedonic tests and safe for irritation tests, formula V contains ethanol extract of surian leaves with a concentration of 0.9% and has antioxidant activity of IC50 22,239 ppm with a very strong category.

Keywords: antioxidant, surian leaf, scrub

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THE POTENTIAL OF PGV-1 AND CCA-1.1 IN DMH-INDUCED LIVER AND COLON CANCER IN RATS MODEL

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ABSTRACT

Background: PGV-is a curcumin analog exhibiting anti-cancer properties against several cancer cells, including K562, WiDr, HCC1954, T47D, MCF-7, 4T1, MCF-7/DOX cell lines⁽¹⁻⁵⁾ and CCA-1.1 its new derivatives exhibits lower IC₅₀ compared to that of PGV-1 in Caco-2 and CT-26 cells⁽⁶⁻⁷⁾. **Objective:** This study aimed to examine steatohepatitis incidence and the proliferation inhibiting of PGV-1 and CCA-1.1 upon DMH 1,2-Dimethylhydrazine induction. **Methods:** Treated DMH-inducing colorectal cancer rat and oral co-administration of PGV-1 and CCA-1.1 for 16 weeks⁽⁸⁾ to analyze the incidence steatohepatitis macroscopic and microscopic. The inhibition of proliferation of PGV-1 in hepar and CCA-1.1 in colon were evaluated by level of Ki67 expression. **Results:** PGV-1 prevented steatohepatitis incidence upon DMH administration and drastically reduced the Ki-67 expression in DMH-induced rat liver indicating its ability to suppress the aberrant liver cell proliferation. In conclusion, PGV-1 and CCA-1.1 promising as chemopreventive effects against DMH liver and colorectal cancer.

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COMBINATION OF MODELING IN SILICO AND IN VITRO ANALYSIS OF ERYTHROCYTE MEMBRANE STABILITY METHODS FROM QUTS AL HINDI (*Saussurea lappa*) AS AN ANTI-INFLAMMATORY

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ABSTRACT

Inflammation is a normal process in the human body as a response to injury from the healing process [1]. Meanwhile, chronic inflammation will cause new health problems to patients. Anti-inflammatory agents generally used for those conditions, have several side effects to patients. [2]. Aims : to determine the anti-inflammatory activity of the ethyl acetate and n-hexan root fractions of *Saussurea lappa* using *in vitro* with erythrocyte membrane stability method and investigate the mechanism of interaction of compounds from the roots of *Saussurea lappa* on COX-2 and iNOS receptors using *in silico*. Methods: Activity tests are performed *in vitro* by measuring anti-inflammatory activity using ultraviolet-visible spectrophotometry Interaction study of compounds of *Saussurea lappa* using Docking simulation with AutoDock Vina package by determining the interaction of sodium diclofenac of sodium diclofenac (as a reference drug) with COX-2 and iNOS as a receptors in terms of hydrogen bonding and free energy bonds. Results: *In vitro* anti-inflammation inhibitory activity assay used 125 ppm of the active fractions of ethyl acetate and n-hexane solvents obtained the inhibition activity of each fraction were 98.927% and 98.761%, respectively. Anti-inflammation inhibition activity *in silico* with molecular docking showed that the interaction between *Saussurea lappa* and COX-2 receptors with its best conformation showed the value of free energy bonding (ΔG) with *Beta Cyclocostunolide* compounds that have a value of -8.6 kcal/ mol and *Costus acid* -8.5 kcal/mol is better than diclofenac as a positive control indicating a value of ΔG -8.4 kcal/mol. While the interaction of iNOS with *Costic acid* compounds have free energy bond of 7.2 kcal/mol, *Dehydrocostus lactone* -7.1 kcal/mol, and *Arbusculin E* -7.1 kcal/mol better than sodium diclofenac -6.5 kcal/mol. Conclusion: This suggests the affinity of the *lappa sauce* is stronger than sodium diclofenac so it can be predicted that *the lappa sauce* has more potential to inhibit the activity of both Cox-2 and iNOS receptors. Thus, *quts al hindi* extract containing the active compounds ***alpha-cyclocostunolide***, ***Beta Cyclocostunolide***, and ***Costus acid*** has the potential to be used as an anti-inflammatory.

Keyword: antiinflammatory, *in vitro*, *in silico*, Quts al hindi, membran stabilization

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MOLECULAR DOCKING REVEALS THE MECHANISM OF LABDANE-TYPE DITERPENE AGAINST CERVICAL CANCER

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ABSTRACT

Labdane-type diterpene from legundi fruit (*Vitex trifolia*) is a compound that can inhibit proliferation and cell cycle in the G0/G1 phase and induces apoptosis.^[1] Many studies have proven its anti-cancer effects, and in this study, labdane-type diterpene had effects on cell cycle regulation by primarily influencing CDK1 to drive cell cycle G2 into mitosis.^[2] But its mechanism in the treatment of cervical cancer is still unclear. Therefore, molecular docking technology is used to explore potential cervical anti-cancer targets and pathways of labdane-type diterpene.^[3] The research stages include the preparation of legundi fruit extract, FTIR Spectroscopy analysis, GC-MS analysis, and molecular docking. The results of the identification of legundi fruit extract using an IR spectrophotometer showed the presence of labdane compounds and confirmed by GC-MS by finding active compound group Labdane-type diterpene in the form of 1,1,4a-Trimethyl-5-6-dimethylenedecahydronaphthalene. Based on the results of molecular docking it was found that the ligand of labdane-type diterpene binds to receptors CDK1 with a result ΔG -5.95 kcal/mol, pKi 47.4 M, 3 hydrogen bonds with type ARG 123 (1,308Angstrom), ARG 151 (1.817Angstrom), TYR 270 (1,735Angstrom). From these results, it is evident that CDK1 has the potential to react with labdane-type diterpene through a cell cycle regulation.

Keywords: Cervical cancer, labdane type-diterpene, mechanism of action, molecular docking, *Vitex trifolia* L.

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CONSTRUCTION OF SINGLE-CHAIN FRAGMENT VARIABLE (SCFV) ANTI NSI DENGUE VIRUS PCR PRIMERS FOR PHAGE DISPLAY LIBRARY PREPARATION

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ABSTRACT

Dengue is an infectious disease that continues to be a public health problem worldwide. The clinical manifestations of dengue infection are difficult to distinguish from other infectious diseases. Rapid and accurate diagnostic tests for dengue virus infection are needed to confirm the disease and treat the patient appropriately. NS1 is the most immunogenic and conserved glycoprotein secreted into the bloodstream¹. Therefore, the dengue virus NS1 antigen assay has been identified as one of the specific markers in laboratory diagnostic tests that can be used to detect primary or secondary dengue infection at an early stage. In this study, we designed PCR primers for amplification of VH and VL domains coding for scFv anti NS1. A primary design of scFv anti NS1 dengue virus has been carried out from available genomic databases using bioinformatics analysis which can be used to create a phage display scFv library^{2,3}. The ScFv gene sequence was amplified by PCR with specific primers incorporating NcoI and XhoI restriction sites for directional cloning into a phagemid vector pComb3d-F expression vector⁴. Cultures of *E. coli* DH5 were transformed with the pComb3d-F derivatives and were then induced with 0.1 mM isopropyl-d-thiogalactopyranoside (IPTG). The phage display technique was used to generate a panel of the single-chain variable fragment (scFv) antibodies specific for the NS1 protein of the dengue virus. This primer pair has been successfully tested and can be used to produce an scFv phage library, characterize antibodies, and/or design recombinant antibodies for the model.

Keywords: Dengue Virus, NS1, scFv; phage display library; Single-chain Fragment variable

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CASTILIFEROL AS A PROSPECTIVE LEAD COMPOUND IN THE DISCOVERY OF NEW ANTIHYPERTENSION DRUGS

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ABSTRACT

Hypertension is a condition where there is an increase in blood pressure to exceed normal limits. The Gotu kola herb (*Centella asiatica* (L.)) has been known to have an antihypertensive effect, but which compound of the herb is responsible for this activity is not yet known. This study aims to analyse the compounds of the Gotu kola herb, which have good affinity and interaction with the renin enzyme. So that new molecular candidates can be found that have the potential as renin inhibitors and allow them to be developed as antihypertensives. The research was conducted in silico with a molecular docking method and molecular dynamics simulation involving 47 test compounds from Gotu kola herb. The research results from molecular docking data showed that there were ten best test compounds with bond-free energy values (ΔG) and inhibition constants (K_i) close to natural ligands. Molecular dynamics simulations showed that castiliferol had the strongest interaction and affinity for the enzyme renin of the ten compounds. So it can be concluded that castiliferol has the potential to be developed as an antihypertensive through the inhibition of the renin enzyme.

Keywords: antihypertensive, Castiliferol, *Centella asiatica*, renin inhibitor

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GENE CLONING, OVEREXPRESSION AND CHARACTERIZATION OF CATALASE-HYDROPEROXIDASE II FROM *Staphylococcus equorum*

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ABSTRACT

Recombinant DNA technology is a potential method to increase enzymes yield in a large scale. The high level of catalase demand as antioxidants in food, textile, cosmetics, and therapeutic industry applications required sustainable availability [1,2]. Biotechnology approaches is one of efforts which promising to overcome the limitations of catalase production. The aims of this study is to obtain recombinant catalase-hydroperoxidase II (HPHII_Seq) from *S. equorum* in *E. coli* BL21(DE3). The complete ORF sequence of *hpII* from *S. equorum* was obtained from *gene bank* NCBI (GenBank accession no. CP013114.1). Synthetic gene of *hpII* was cloned into an expression vector pET-15b. The confirmed pET-15b_HPHIISeq then introduced into *E. coli* BL21(DE3) for protein overproduction. IPTG 0-1 mM was used as inducer and overproduction has been done at variety of temperature (25, 37 and 16°C). Purification of recombinant catalase was performed using prepacked nickel affinity chromatography column (Roche®). Recombinant HPHII_Seq then characterized by the SDS-PAGE method. Overproduction by 0.1 mM IPTG induction gave 77.5 kDa protein, and purification with Ni-NTA resin affinity chromatography showed a thin band of the protein in SDS-PAGE. Enzyme activity identified by catalase zymography.

Keywords: Ni-NTA, recombinant DNA technology, synthetic gene

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CYTOTOXIC EFFECT OF LEMONGRASS IN COMBINATION WITH DOXORUBICIN AS A COTREATMENT ON 4T1 CELLS

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ABSTRACT

Lemongrass (*Cymbopogon citratus*) leaf has been known to have anticancer activities by its cytotoxic effect¹, but the cytotoxic effect of the combination of doxorubicin and Lemongrass Essential Oil to 4T1 cells has not been known certainly. Further studies on the combination of Lemongrass and doxorubicin activity are required. This study aims to provide an exploration of the combination of Lemongrass Essential Oil (LEO) as a doxorubicin cotreatment on 4T1 cells. LEO were extracted by water-steam distillation. LEO was then characterized the phytochemicals by Gas Chromatography-Mass Spectrometry (GC-MS). The single cytotoxic activity of the LEO and doxorubicin combination was identified using MTT assay and WST-1 assay to determine the IC₅₀ and Combination Index (CI). The results showed that citral is the major component of the essential oils. LEO and doxorubicin were cytotoxic to 4T1 cells with the IC₅₀ value of 76.60 µg/mL and 4.23 µM, respectively. LEO in combination with doxorubicin showed antagonist effect on 4T1 cells. **Conclusion:** The data showed that LEO does not have good synergism with 4T1 cells as a doxorubicin cotreatment.

Keywords: *Cymbopogon citratus*., cotreatment, combination, 4T1

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XANTHINE OXIDASE INHIBITORY ACTIVITY OF *Kaempferia parviflora* AND *Kaempferia galanga* ETHANOL EXTRACT

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ABSTRACT

Kaempferia galanga and *Kaempferia parviflora* are members of the Zingiberaceae family, which are widely used in the functional food and nutraceutical industries due to their health advantages^[1]. Both plants contain bioactive substances with powerful anti-inflammatory and alternative therapeutic potential for gout-related inflammation^{[2]–[4]}. Therefore, this study aimed to assess the activity of *K. galanga* and *K. parviflora* rhizome extracts as xanthine oxidase inhibitors in an *in vitro* assay for the treatment of gout. The test tube approach was used to perform a phytochemical screening analysis. The spectrophotometric method 1,1-diphenyl-2-picryl-hydrazyl was then used to measure the antioxidant activity (DPPH method). UV spectrophotometry was used to determine the *in vitro* xanthine oxidase inhibitory activity. Tannins, alkaloids, flavonoids, and polyphenols were discovered through phytochemical investigation. Based on the Folin-Ciocalteu technique, the level of phenolic compounds in *K. parviflora* and *K. galanga* was 52.33 and 50.35 mg Gallic Acid Equivalent (GAE)/100 g, respectively. *K. parviflora* contains 14.42 mg total flavonoid content (TFC) and *K. galanga* have 2.10 mg Quercetin Equivalent (QE)/g. In *K. parviflora*, free radical scavenging activity was measured using the IC₅₀ (DPPH technique), with a value of 547.20 g/mL. It also has the highest inhibitory effect with IC₅₀ of 29.69 µg/mL based on the xanthine oxidase inhibitory activity using *in vitro* assay.

Keywords: *Kaempferia parviflora*, *Kaempferia galanga*, Phytochemicals, Antioxidant, Xanthine oxidase

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THE OPTIMIZATION OF IN SITU OPHTHALMIC GEL CHLORAMPHENICOLE USING 32 FACTORIAL DESIGN: MICROBIOLOGICAL EFFECTIVENESS STUDY

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ABSTRACT

In situ gels are conveniently dropped as a solution into the conjunctival sac, where they undergo gelation after use due to stimulation with its favorable residence time. An antibacterial effectiveness should be performed to determine the ability to resist bacterial contamination during use.^[1,2] This study aims to get the optimize formulation of chloramphenicol ophthalmic gel in situ with a combination poloxamer 407 and HPMC as bases, to determine the mathematical relationship between the inhibition zone diameter and its effectiveness microbiologically against *Staphylococcus aureus*. Optimization of the formulation with a three-level factorial design method response surface. The optimized formula was Formula 1 with a combination of poloxamer 407 5% and 0.45% HPMC, desirability value of 1.00 and classified as very strong in inhibiting *Staphylococcus aureus*. The mathematical relationship was $24.97-0.50A-4.52B+0.29AB$. All preparations still provide effectiveness against bacterial growth during 28 days of storage. The diameter inhibition zone were in the range 17.79-22.66 mm. Conclusion: The best formulation of chloramphenicol in situ gel was the combination bases of poloxamer 407 5% and HPMC 0.45% which viewed from the inhibition zone diameter and had a very strong inhibitory power against *Staphylococcus aureus*.

Keywords: ophthalmic *in situ* gel, three-level factorial design, desirability, poloxamer 407, hydroxypropyl methyl cellulose, *Staphylococcus aureus*.

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STANDARDIZATION OF BLACK BELT LEAF (*Piper acre* Blume.) Ethanol EXTRACT ORIGIN IN EAST KALIMANTAN

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ABSTRACT

Black betel has the species name *Piper acre* (Blume.), family Piperaceae. The purpose of this study was to standardize the ethanol extract of black betel leaf. At five locations, black betel leaf samples were obtained from the East Kalimantan region. The ethanol extract was standardized with two parameters, namely non-specific parameters and specific parameters. The criteria for non-specific parameters were drying shrinkage, total ash content, and acid insoluble ash content. Non-specific parameter data related to drying shrinkage from 5 consecutive samples were 13.75; 12.13; 12.29; 13.36; and 6.12%. Non-specific parameter data related to the total ash content of 5 samples in a row, namely 7.82; 4.36; 6.54; 7.95; and 4.01%. Non-specific parameter data related to acid insoluble ash content from 5 consecutive samples, namely 1.43; 1.73; 4.90; 1.54; and 4.36%. Specific parameter criteria were carried out: identifying extracts, organoleptic, and levels of water-soluble compounds. Identification of the extract in the form of the plant's Latin name, namely *piper acre* (Blume.), and the part of the plant, namely the leaf. Specific parameter data related to organoleptic from 5 samples have similarities. The five extracts are blackish brown, have a distinctive odor, thick consistency, and bitter taste, and are slightly spicy and distinctive. Specific parameter data related to levels of water-soluble compounds from 5 samples in a row are 12.41; 12.38; 12.33; 16.62; and 6.68%. The chemical test results showed that the black betel leaf ethanol extract contains flavonoids, polyphenols, tannins, saponins, and alkaloids. The ethanol extract of black betel leaf based on the standardization test of non-specific parameters did not meet the quality standards of the raw materials. In contrast, the specific parameters had met the standardization of the quality of the raw materials.

Keywords: Black Betel, Standardization, Ethanol Extract

AMINO ACID-CONJUGATED NATURAL COMPOUNDS: AIMS, DESIGNS, AND RESULTS

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ABSTRACT

Protein is one of the essential macronutrients required by all living things. When protein is broken down, it is composed of monomers known as amino acids[1]. The idea of conjugating natural compounds among amino acids for therapeutic goals emerged from the fact that amino acids are important building blocks for life and abundantly provided [2]. This review discussed amino acids that are conjugated to natural compounds, based on urgency, synthetic approach and bioactivity impacts [3]. We proved that amino acids conjugation to specific compounds signifies enhancing the kinetic traits before the absorption and distribution, reducing toxicity and heightened the physiological impacts[4]. Amino acid conjugation provides the feasibility of developing new compounds with useful pharmacological outcomes and a complimentary pharmacokinetic profile[5].

Keywords: Natural compounds, amino acid, conjugation, chemical synthesis.

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NETWORK PHARMACOLOGY AND MOLECULAR DOCKING ANALYSIS OF THE MECHANISM UNDERLYING PYOCYANIN'S EFFECT ON PREMATURE SENESCENCE CARDIOVASULAR

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ABSTRACT

Introduction. Premature senescence cardiovascular maybe induced prematurely by cigarette smoke exposure. Pyocyanin from *Spirulina platensis* phytoconstituent has anti-oxidant activities, however, there is no report about the role of Pyocyanin against premature senescence cardiovascular by cigarette smoke exposure pathways network. The aim of this study was to evaluate Pyocyanin against premature senescence using in silico study. Method. Pyocyanin were obtained *Spirulina platensis* from PubChem database and GeneCards, To reveal the pharmacological mechanism, the component-target and the intersecting protein-protein interaction (PPI) networks were constructed. Molecular docking tools 1.5.6. was carried out to assess the strength of binding between the key active ingredients and protein target. Results. A total of 325 targets from GeneCards. The topology analysis of the constructed PPI network conducted using the Cytoscape software shows that there are 39 hub genes implicated in the effect of Pyocyanin, is VEGFA. The results of molecular docking suggest that the key active ingredients and key protein targets can bind well, with binding energies of less than -5 kJ/mol. Conclusion. The research conducted herein reveals that Pyocyanin can treats premature senescence cardiovascular by cigarette smoke exposure by targeting VEGFA that describe a molecular dynamic signaling pathways.

Keywords: Cigarette smoke exposure, Molecular docking, Network pharmacology, Premature senescence cardiovascular, Pyocyanin *Spirulina platensis*,

IN-SILICO APPRAISAL OF IDENTITY COMPOUNDS FROM THE BOOK FARMAKOPE HERBAL INDONESIA AS CANCER AND DIABETES TREATMENT

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ABSTRACT

Noncommunicable diseases such as Cancer and Diabetes are major health issues in Indonesia of which is a country with high openness to herbal medicines. Although the book Farmakope Herbal Indonesia (FHI) contains rich information regarding Indonesian medicinal plants' identity compounds, the information is poorly used. Therefore, this study aims to explore the potential of medicinal plants listed in FHI for cancer and diabetes treatment. In order to do that, we employ in silico approach where Lipinski's Rule of Five, ADMET prediction, molecular docking, bioactivity prediction, and anti-cancer prediction are addressed. According to the results, we found three promising medicinal plants, sidewayah flower (*Woodfordia fruticosa* (L.) Kurz.) as B-raf inhibitor for melanoma treatment, and for diabetes treatment lime peel (*Citrus aurantiifolia* (Christm.) Swingle) can act as alpha-glucosidase inhibitor and pegagan herb (*Centella asiatica* (L.) Urb.) acts as ChREBP inhibitor.

Keywords: Farmakope Herbal Indonesia, communicable disease, diabetes, cancer, melanoma, BRAF, ChREBP, Alpha-glucosidase

THE ROOT ETHANOL EXTRACTION OF *ACALYPHA INDICAL* AND ITS EFFECT ON NORADRENALINE AS A POTENTIAL TREATMENT TO REDUCE ANXIETY AND DEPRESSION

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ABSTRACT

Background: Anxiety and depression are the major health concern during COVID-19 and post-pandemic. Additionally, a high prevalence metabolic syndrome in Indonesia can contribute to the prevalence of anxiety and depression.¹ Herbal medicines originating from natural ingredients are an alternative treatment with lower side effects compared to modern or western medicine. Indonesia is a biodiversity country with many plants that can be extracted to prevent and treat metabolic syndromes, including *Acalypha Indica* L.² However, a major problem is the standardization of these medicinal plants to determine the dose safety and therapeutic effectiveness for humans is remain challenged. This study aimed to investigate the effectiveness of *Acalypha Indica* L. in treating anxiety and depression in obese rats induced by a high-fructose and cholesterol diet by analyzing the anxiety parameters of serotonin and noradrenalin. **Methods:** Thirty male Sprague-Dawley rats were divided into five groups. An anxiety and depression test were performed. Levels of serotonin and noradrenaline were investigated to analyze the variable changes. **Results:** There was a significant increase of noradrenaline in the group given a high-fructose and cholesterol diet without intervention (27.11 ± 6.74 ng/g). There was a significant decrease in the group treated with Fluoxetine (17.08 ± 4.38 ng/g), *Acalypha Indica* L. (15.97 ± 3.51 ng/g) and a combination of Fluoxetine and *Acalypha Indica* L. (17.67 ± 3.97 ng/g). **Conclusions:** *Acalypha Indica* L is the root ethanol extraction found in Indonesia. This herb can be an alternative therapy for reducing anxiety and depression symptoms due to metabolic syndrome by decreasing noradrenaline levels, particularly in post-pandemic COVID-19. Additionally, we also recommend developing advanced technology to extract *Acalypha Indica* L to obtain an effective dose for human.

Keywords: *Acalypha Indica* L, Metabolic Syndrome, Anxiety, Depression, Noradrenaline

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POSTER PRESENTATION ABSTRACT

[PP-001]

OPTIMIZATION OF GEL-BASED NANOEMULSION OF TURMERIC ESSENTIAL OIL WITH QUALITY BY DESIGN: CHARACTERISTICS AND ANTIOXIDANT EFFECTS

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ABSTRACT

One of the newest research strategies is applying natural products to develop effective formulations with minimal drawbacks and maximum therapeutic effect.^[1-4] Turmeric essential oil (TEO) is one of the essential oils that have the potential as a natural antioxidant^[5-8]. This study aimed to observe the effect of emulsifier concentration and gelling agent in producing nanoemulgel (NEG) and its antioxidant effect from TEO. This study is the first development of a formulation using TEO NE-loaded into a gel base proposed for topical use. Initially, various TEO-loaded NEG formulations were prepared using high-speed homogenization. The formulation design used the Central Composite of the Response Surface Method (CCD-RSM) to obtain the optimal TEO-loaded NEG formula. The optimization variables of the TEO-loaded NEG formula include the concentration of SpanTM 80-Tween 80 (X₁) and Carbopol[®] 980 NF (X₂) with particle size response (PZ) (Y₁), polydispersity index (PDI) (Y₂), zeta potential (ZP) (Y₃), and IC₅₀ (Y₄). The evaluation result of the responses of the actual TEO-loaded NEG was compared with the predicted CCD-RSM. The optimal TEO-loaded NEG developed was made with a 5.13% of emulsifier and 1.14% of gelling agent. The evaluation results showed the optimal nano-metric size of TEO-loaded NEG (178.8 ± 5.3 nm) with PDI (0.430 ± 0.017), zeta potential (-26.29 ± 4.69 mV), and medium potency IC₅₀ (124.84 ± 2.96 m/mL). Statistical analysis results on CCD-RSM showed that the interaction between gelling and emulsifier affected particle size. At the same time, the factors that influence the IC₅₀ are the concentrations of the two types of excipients and the interactions between gelling molecules. The optimal formulation showed unfavourable characteristics in the PDI and zeta potential values, so it was necessary to re-observe other factors to obtain a potential delivery system for topical administration.

Keywords: antioxidant, central composite design, nanoemulgels, response surface methodology, turmeric oil, topical delivery

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FORMULATION OF SALBUTAMOL SULFATE ORALLY DISSOLVING FILMS WITH SODIUM STARCH GLYCOLATE AS A SUPER-DISINTEGRANT

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ABSTRACT

Orally dissolving film (ODF) is a solid dosage form that dissolves immediately in the mouth. A super disintegrant was a substance affecting the film dosage form's dissolving capacity^[1]. One of the super disintegrants in ODF is Sodium Starch Glycolate (SSG), which can expand 7–12 times in less than 30 seconds^[2,3]. This study aimed to investigate the physical characteristics and dissolution of salbutamol sulphate from ODF utilizing pectin as a film-forming agent and SSG as a super-disintegrant at various concentrations. This study utilized SSG concentrations of 0% (F1), 1% (F2), 1.2% (F3), and 2% (F4). The film preparation method used in this study was the Solvent Casting Method, followed by an evaluation of ODF preparations that included organoleptic, pH, thickness, content uniformity, disintegration time, and dissolution test. The film was yellow, odourless, had a faint sour taste, was not sticky, had a pH of 6.03 - 6.7, a folding strength of 225 - 437 folds, content uniformity of 97.77 - 98.81%, and disintegrated in 28 to 75 seconds. Variations in SSG concentration impacted on the film's physical properties and dissolution ($p < 0.05$), where the film rapidly disintegrated and dissolved with higher SSG concentrations.

Keywords: orally dissolving film, super disintegrants, sodium starch glycolate, physical characteristics, dissolution

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FORMULA DEVELOPMENT AND CHARACTERIZATION OF VITAMIN E ACETATE LOADED NANOSTRUCTURED LIPID CARRIER (NLC) USING GLYCERYL PALMITOSTEARATE (PRECIROL® ATO 5) AS SOLID LIPID

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ABSTRACT

Antioxidant effect of vitamin E acetate can neutralize free radicals so it can prevent premature aging of the skin.^[1] It has Log P value of 12.07 ± 0.27 , low topical permeability, and potentially hydrolysed.^[2] Nanostructured Lipid Carrier (NLC) is the second generation of lipid nanotechnology that can improve the delivery and stability of molecules.^[3] This study objective was to obtain NLC that fulfil certain specified parameters. In the formulation, NLC consist of 2% vitamin E acetate, 2-6% Precirol® ATO 5, 1% Myritol®, and 1-3% Tego® Care. Screening of solid lipid, liquid lipid, and surfactant were performed. The compatibility was observed by Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC). NLCs were prepared after screening by homogenization method using magnetic stirrer and then sonicated by probe sonicator. The characterizations were performed by measuring particle size, polydispersity index (Pdl), zeta potential (ZP), and entrapment efficiency (EE). Morphology of NLCs was observed using Transmission Electron Microscopy (TEM). Screening result showed that the solid lipid, liquid lipid and surfactant are compatible. The produced NLCs has 200-400 nm particle size, <0.5 Pdl, <-20 mV ZP, >80% EE and spherical particle morphology. This study concluded that vitamin E acetate loaded NLCs showed excellent results.

Keywords: antiaging; vitamin E acetate; Nanostructured Lipid Carrier

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THE EFFECT OF CATIONIC LIPID COMPOSITION ON PHYSICO-CHEMICAL PROPERTIES OF LIPID NANOPARTICLES AS A VEHICLE FOR TRANSFER GENETIC MATERIAL

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ABSTRACT

Lipid Nanoparticles (LNP) is a lipid-based delivery system. It is widely used to carry out genetical material to the cell^[1]. One of the components of LNP is cationic lipids. The addition of it can affect the size of the resulting particle, up to the effectiveness of the LNP transfection effect^[2]. Therefore, the aim of this study was to observe the effect of adding cationic lipid, 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP), at a concentration of 2.5%; 5.0%, and 7.5% to the characteristics of LNP. These parameters include particle size, polydispersity index, zeta potential, and characteristic observations through the TEM. LNP is formulated using the Emulsification-ultrasonication method. Based on the data obtained, the particle size of LNP increased with the addition of DOTAP concentration^[3]. Particle sizes were 114 ± 2.5 nm, 196.2 ± 4.6 nm, and 261 ± 4.1 nm, respectively. The polydispersity index namely 0.253 ± 0.040 ; 0.290 ± 0.056 ; and 0.273 ± 0.097 significantly. The LNP of each formula shows a spherical and uniform shape. DOTAP is a positively charged lipid. It causes the LNP become more positively charged. In the formulation of LNP with a cationic lipid base, the addition of the concentration used must be considered because it will have an impact on the particle size up to the charge of the LNP.

Keywords: cationic lipid, DOTAP, genetic material, lipid nanoparticle, physicochemical properties.

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CHARACTERIZATION AND ANALYSIS OF ESSENTIAL OIL COMPOUNDS OF REMASON GRASS (*Polygala paniculata*. Linn) FROM CIAWI DISTRICT, TASIKMALAYA, WEST JAVA

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ABSTRACT

Based on empirical data from Ciawi district (Tasikmalaya), remason grass (*Polygala paniculata* Linn.) has been widely used to relieve flu, and treatment for asthma or bronchitis. The *P. paniculata* roots contain volatile compounds (essential oils).^[1] It's pungent, sweet, warming, and tranquilizing.^[2] This study aims to isolate and determine the characteristics of *P. paniculata* roots essential oil. The isolation of essential oil was carried out using the Stahl distillation method with water as a solvent. The quality parameter tests carried out on the *P. paniculata* essential oil included specific gravity, yield, refractive index, and optical rotation as well as analysis of its constituent components using the GC-MS instrument. The evidence of empirical data to relieve flu, asthma, or bronchitis was studied by analyzing the efficacy of each component of the compound using the narrative review method. The results of each parameter characterization of specific gravity, yield, refractive index, and optical rotation, respectively, are 0.919 g/mL, 0.9%, 1.439 (nD 25°), and -14.54. The GC-MS analysis showed the presence of 19 components of the essential oil compound. Based on the results of a narrative review, five compounds have the potential for flu and asthma medicine, namely menthol, 1,8-cineol, mentone, pinene, and limonene.

Keywords: *Polygala paniculata*; Ethnomedicine; Essential Oil; Asthma; Flu

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PALMITOYL PEPTIDE ANTI-AGING COMPOUND: ACUTE TOXICITY TEST ON ZEBRAFISH EMBRYO (*Danio rerio*), INTERACTION STUDY ON RECEPTOR, AND TOXICITY PREDICTION *IN SILICO*

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ABSTRACT

Skin aging is a degenerative process that affects its structure as a result of intrinsic and extrinsic factors, such as an exposure to ultraviolet radiation.^[1] Indonesia, as a tropical country, the citizens are prone to skin aging caused by the sun's ultraviolet radiation. This study aimed to determine the interaction of palmitoyl peptides on human receptors, predict their toxicity *in silico*, and determine their safety level through acute toxicity test on zebrafish embryos. The target proteins used were MMP-1^[2] (PDB ID: 966C), MMP-9^[2] (PDB ID: 5UE4), MMP-3^[2] (PDB ID: 1CIZ), and neutrophil elastase^[3] (PDB ID: 3Q77). Palmitoyl tripeptide-5 (PT5) was predicted to have the best interaction with all target proteins, indicated by $\Delta G = -3.27$ kcal/mol (MMP-1), -6.53 kcal/mol (MMP-3), -3.89 kcal/mol (MMP-9), and -4.93 kcal/mol (NE). The toxicity of all the tested compounds were predicted to have no safety problems. Acute and chronic toxicity predictions using VEGA 1.1.5 for PT5 and palmitoyl tripeptide-8 (PT8) were high and moderate. The LC₅₀ value of PT5 and PT8 were 33.544 mg/L and 2.936 mg/L. Therefore, based on the classification of acute toxicity from Ecotoxicity Categories for Terrestrial and Aquatic Organisms, PT5 and PT8 was classified as slightly toxic and toxic.

Keywords: acute toxicity, anti-aging, molecular docking, palmitoyl peptide, zebrafish

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FORMULATION AND EVALUATION OF PEEL-OFF GEL FACE MASK FROM *PANDANUS AMARYLLIFOLIUS* (Roxb.) LEAVES EXTRACT

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ABSTRACT

UV radiation causes damage to us throughout our lifespan. UV exposure is the most significant environmental risk factor that can be altered for skin cancer and many other skin conditions that are impacted by the environment^[1]. The antioxidant network is examples of endogenous mechanisms for sun radiation defense^[2]. *Pandanus amaryllifolius* (Roxb.), which has fragrant leaves, contains polyphenols that have antioxidant properties^[3]. The objective of this study is to create a pandan wangi leaf extract peel-off gel facial mask and analyze how variations in the extract's concentration affect the preparation's physical and chemical assessment outcomes. In this study, three formulas were made with varying concentrations of the fragrant pandan leaf extract, namely F1 (1%), F2 (3%), and F3 (5%). The preparation was evaluated for 28 days at a controlled room temperature of 15°C and 30°C. Ease of evaluation of physical evaluation (organoleptic, spreadability, homogeneity, viscosity, time) and chemical evaluation (pH). The results of the peel-off gel facial mask preparation of fragrant pandan leaf extract showed that F1, F2, and F3 met the evaluation requirements for physical evaluation (organoleptic, spreadability, homogeneity, viscosity, dry time) and chemical evaluation (pH). Variations in the concentration of pandan leaf extract in the peel-off gel face mask preparation had a significant effect ($p < 0.05$) on the evaluation of the preparation including organoleptic, spreadability, and viscosity. But it did not have a significant effect ($p > 0.05$) on the evaluation of the preparation including homogeneity, dry time, and pH. The findings show that peel-off gel face mask formulations can be created with pandan (*Pandanus amaryllifolius* Roxb.) leaves extract.

Keywords: peel-off gel face mask, pandan wangi, antioxidant, *Pandanus amaryllifolius* (Roxb.)

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FORMULATION AND CHARACTERIZATION OF *BUCCAL FILM* NANOEMULSION APIGENIN AS ANTIDIABETIC

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ABSTRACT

Apigenin (4',5,7-trihydroxyflavone) is one of the flavonoid subclasses of flavones that has antidiabetic therapeutic activity but has limitations including a biopharmaceutical classification system (BCS) Class II low water solubility of 2,16 $\mu\text{g/L}$. To overcome these limitations, the development of nanoemulsion formulation technology, increasing solubility, dissolution, absorption, and bioavailability. It is incorporated into the buccal film for easy application and direct access to the systemic circulation via the jugular vein. This study aims to obtain apigenin nanoemulsion with the best characterization and obtain a buccal film that meets the characterization. The research method was carried out experimentally in the manufacture of nanoemulsions with the spontaneous emulsification method, a buccal film with the solvent casting and characterization including organoleptic, pH, functional group, solubility, %transmittant, globule size, polydispersity index, zeta potential, viscosity, thickness, weight, film surface pH, folding resistance, drug release, and assay. The results obtained were apigenin 10 nanoemulsion formulas that met the characterization with globule size $<20,34$ nm, polydispersity index $<0,131$, zeta potential close to 0 mV, pH 6,23-6,59, %transmittance close to 100%, and best F10 incorporated into buccal film has 29x the solubility compared to apigenin with less $\leq 0,05$. Formulas buccal film met the characteristics with F3 having a 2x faster onset of release time than F1 and F2 with 86,07% diffusion and 97,933 mg/film sheet. Thus, it was concluded that the formulation and characterization of the buccal film met the characterization and that the apigenin F10 nanoemulsion increased the solubility 29x with buccal film F3 having a faster onset of release.

Keywords: Apigenin; BCS; Solubility; Nanoemulsion; Buccal Film

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SYNERGISTIC EFFECT OF *MYRISTICA FRAGRANS*. IN COMBINATION WITH DOXORUBICIN ON MCF-7 BREAST CANCER CELLS

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ABSTRACT

Chemotherapeutics agents plays a good role in causing apoptosis in cancer cells, but it is also toxic in normal tissues and causing side effects.^{[1][2]} Nutmeg (*Myristica fragrans*) seeds has been proven to have cytotoxic activities, but the cytotoxic activity of the combination of doxorubicin and nutmeg extract to MCF-7 breast cancer cells has not been known certainty. This study aims to explore the synergism of Nutmeg Seed Extract (NSE) as a doxorubicin cotreatment on MCF-7 breast cancer. NSE were extracted by maceration using 96% of ethanol for 48. NSE was then subjected to qualitative analysis using TLC. The single and combination of NSE and doxorubicin was tested using a trypan blue exclusion assay on MCF-7 to determine the Combination Index (CI). NSE and doxorubicin were cytotoxic to MCF-7 cells with the IC₅₀ value of 85.42 µg/mL and 0.78 µM, respectively. NSE in combination with doxorubicin showed cytotoxic effect synergistically on MCF-7 cells. The results of this study showed that EBP has good synergism as a doxorubicin cotreatment, especially for MCF-7 breast cancer.

Keywords: cotreatment, *Myristica fragrans*, breast cancer, MCF-7

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CHARACTERISTICS OF DOMPERIDONE PATCH WITH VARIATION OF PENETRATION ENHANCERS (ISOPROPYL MYRISTATE AND EUCALYPTUS OIL)

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ABSTRACT

Domperidone undergoes first-pass metabolism in the liver, indicated a low bioavailability value when administered orally.^[1] To overcome this, domperidone was given transdermally in the form of a patch dosage form. The thing that must be considered in administering drug via transdermal was the diffusion profile of the active substance^[2]. Penetration enhancer was one component that can increase the diffusion of domperidone which was formulated in patch preparations^[3] The aimed of the study was to compare the penetration enhancing ability of isopropyl myristate (IPM) and euacaliptus oil (EO) on the diffusion profile of the domperidone patch (PD). PD was made by solvent casting method using HPMC polymer and penetration enhancer (IPM and EO) with concentrations of 2%, 5%, and 10%, respectively. PD evaluation carried out were organoleptic, weight uniformity, thickness, moisture content, drug content, and diffusion. PD had the appearance of a round shape with a diameter of 0.9 cm, white, dry and not cracked. The results of weight uniformity in PD-IPM ranged from 111.19-140.23 mg while PD-EO ranged from 103.01-128.2 mg, thickness of PD-IPM ranged from 1.64-1.72 mm while PD-EO ranged from 1.65-1.72 mm, moisture content of PD-IPM ranged from 5.71-7.16% while PD-EO ranged from 5.33-6.85%, drug content of PD-IPM ranged from 100.62-101.06% while PD-EO ranged from 99.23-100.35%. The results of the diffusion profile showed that the diffusion kinetics of PD-IPM and PD-EO were zero order, and the rate of diffusion of PD-IPM ranges from 31.448-37.612 ppm/hour while PD-EO ranges from 30.102-35.394 ppm/hour. The conclusion was that penetration enhancers (IPM and EO) do not affect the diffusion kinetics of PD, but the diffusion rate of PD-IPM is higher than PD-EO.

Keywords: isopropyl myristate, eucalyptus oil, domperidone, patch, diffusion

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ANTIHYPERURICEMIA ACTIVITY OF KUPA (*SYZYGIUM POLYCEPHALUM*) SEED EXTRACTS IN MALE WHITE MICE

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ABSTRACT

Hyperuricemia is a clinical condition that increases the concentration of uric acid in the blood beyond normal, high uric acid levels can cause the accumulation of monosodium urate crystals in joint tissue resulting in inflammation and gout.^[1] Kupa seeds contain compounds that have the potential to reduce uric acid levels such as flavonoid compounds, saponins, tannins, and polyphenols.^{[2][3]} This study aims to determine several seed extracts' activity and the best effectiveness in reducing uric acid levels in vivo in male white mice. The uric acid induction method used acetylsalicylic acid 5.04 mg/20gBW in mice and fructose 67.2 mg/20gBW in mice orally for 3 days. On the 3rd day, the mice were given allopurinol test material, 1% CMC and each extract of n-hexane, ethyl acetate, and ethanol as much as 100 mg/kg BW orally for 7 days. The results showed that all extracts of Kupa seeds had activity in reducing uric acid levels with levels of n-hexane 7 ± 0.8 mg/dL, ethyl acetate 4.75 ± 0.95 mg/Dl, and ethanol 3.25 ± 0.5 mg/dL. Ethanol extract has the best effectiveness in reducing uric acid levels compared to n-hexane and ethyl acetate extracts, able to reduce uric acid levels by 68.29% statistically not significantly different from allopurinol as a comparison (73.17%).

Keywords: Antihyperuricemia; gout; Kupa seeds

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ANTI-DIARRHEA ACTIVITIES OF GUAVA SHOOTS LEAVES AND KLUTUK BANANA AND THEIR COMBINATIONS USED BY THE BATTRA OF JAYARATU SINGAPARNA VILLAGE

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ABSTRACT

Knowledge of the use of plants to treat diseases such as diarrhea has been possessed for generations. The healing can be done by self-medication or by asking for help from others such as battra. Commonly used plants are klutuk banana and shoots of guava leaf. This study aims to determine the comparison of the activity of klutuk banana flesh (K) and red shoots of guava leaves with the addition of salt (RS) commonly used by the battra of Jayaratu Singaparna Village with green shoots of guava leaves (G) used by the public and its combination in inhibiting *Escherichia coli*. The samples were red shoots leaves (R); green shoots leaves (G); klutuk banana (K); red shoots leaves and salt (RS); green shoots leaves and salt (GS); red shoots leaves, green shoots leaves, and salt (RGS); red shoots leaves, and green shoots leaves (RG). Each sample was crushed and then extracted. Antibacterial activity tests were carried out using the Kirby Bauer method with cotrimoxazole as a positive control. Data analysis using One Way Analysis of Variance (ANOVA) and continued with the Least Significant Difference (LSD) test. The results showed that samples of R, G, K, GS, RGS, and RG gave inhibition to *Escherichia coli* with inhibitory zone 18.32±0.16 mm; 17.26±0.23 mm; 3.25±0.06 mm; 17.50±0.09 mm, 18.28±0.13 mm, 19.60±0.06 mm, 19.20±0.02 mm respectively. The combination of red and green shoots of guava leaves with salt (RGS) had the highest antidiarrheal activity in the strong category compared to other groups.

Keywords: Shoots leaves, guava, klutuk banana, Battra, *Escherichia coli*

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THE EFFECT OF THE COMBINATION OF ANTHOCYANIN AND WATER HYACINTH CELLULAR COATING ON THE CHARACTERISTICS OF EDIBLE FILM AS PACKAGING ON FRUIT

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ABSTRACT

The edible film is packaged as a thin layer that can decompose spontaneously and is suitable for human ingestion. The water hyacinth's high cellulose content can be used as a component of edible films, and butterfly pea flower anthocyanins can be used as an antibacterial. The goal of this study was to characterize edible films made from a mixture of water hyacinth cellulose and anthocyanins from butterfly pea flowers, as well as to assess how well they work as fruit packing. Edible films made in this study with variations in the concentration of butterfly pea flower anthocyanins include 6%, 8%, and 10%. The tests carried out included the edible film characterization test and the fruit weight loss test during 14 days of storage. The results showed that the addition of butterfly pea flower anthocyanin extracts affected the characteristics of the edible film. The best anthocyanin concentration was obtained with the addition of 10% anthocyanin, which had a thickness of 0.130 mm, tensile strength of 6.306 N/mm², elongation of 45.388%, Young's modulus of 13.7940, water vapor transmission rate of 0.8217 g/m²/day, water solubility of 44, 0557% and 80.9471% water resistance test. The weight of the fruit lost was the least when the edible film was used as a layer for wrapping grapes (0.0564 grams/day). The longer the cellulose chain, the higher the cellulose concentration, and in the end, it will produce a strong and rigid material.

Keywords: Edible film, Water hyacinth, Anthocyanins, Butterfly pea flower, Fruit coating

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FORMULATION OF INSTANT GRANULES CONTAINING THE COMBINATION OF KATUK LEAF (*Sauropus androgynus* L. Merr) AND TURMERIC RHIZOME (*Curcuma longa* Linn.) EXTRACT AS ANTIOXIDANTS

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ABSTRACT

Antioxidants have an important role in preventing disease such as premature ageing. Katuk leaf (*Sauropus androgynus* L. Merr) and turmeric rhizome (*Curcuma longa* Linn.) have antioxidants activity.^[1] This study aimed to formulate instant granules containing the combination of katuk leaf and turmeric rhizome extract as antioxidants. The granule formulation was optimized by the Simplex Lattice Design (SLD) method using Design expert version 13 by varying concentrations of PVP and Sucralose. The instant granules were formulated with variation of PVP to which 1%, 7.75%, 3.25%, 10%, 5.5% and variation of sucralose to which 0.03%, 0.1875%, 0.0825%, 0.24% and 0.135%. Physical stability of instant granules tests was conducted by measuring flow time, angle of repose, compressibility index, moisture content, time of granules to dissolve and also as well as the hedonic test was applied to assess users acceptability. The antioxidant activity was examined using the DPPH method. The results showed that the flow time of granules was 4-5 g/s, the angle of repose was around 36 degrees, the compressibility index was 8-14%, moisture content was around 2%, and the time of granules to dissolve was around 4 minutes. The hedonic test results showed that formula 4 with the concentration of PVP 10% and 0.24% Sucralose is preferred in terms of colour, aroma and taste. IC50 of instant granules was 113.28 ppm, indicating that the instant granules were in the medium category.^[2]

Keywords: Instant Granules, Katuk Leaf (*Sauropus androgynus* L.Merr), Turmeric Rhizome, Antioxidants

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FORMULATION AND EVALUATION OF SECANG (*Caesalpinia sappan* L.) WOOD EXTRACT LIP BALM WITH VARIOUS CONCENTRATION OF BEESWAX AND CANDELILLA WAX

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ABSTRACT

Lip balm plays a very important role in lip skin care, so it needs ingredients such as antioxidants.^[1] Secang wood contains phenolic compounds including brazilin. Brazilin is the main homoisoflavonoid found in secang wood acts as an antioxidant.^[2] One of the important components in determining the physical properties and stability of lip balms is wax which can give shape and maintain the shape of the lip balm. The combination of candelilla wax and beeswax is very good for making lip balms and can produce a smooth and glossy appearance.^[3] This study aims to obtain lip balm preparations of secang (*Caesalpinia sappan* L) wood extract with a combination of beeswax and candelilla wax. In this study, three lip balm formulations were made with three variations in the concentration of beeswax and candelilla wax, namely F1 (8,75%:6,25%), F2 (7,5%:7,5%) and F3 (6,25%:8,75%). Furthermore, evaluation was carried out for 28 days of storage at controlled room temperature (15-30°C) which included evaluation of organoleptic, homogeneity, melting point, pH, oilability, smear test, and spreadability. The results of the evaluation of the lip balm preparation showed that the F2 formula met the all evaluation requirements including organoleptic tests, homogeneity, smear test, melting point, pH, oilability and spreadability, while the F1 and F3 formulas did not meet the spreadability requirements. Variations in the concentration of the combination of beeswax and candelilla wax in lip balm preparations of sappan (*Caesalpinia sappan* L) wood extract significantly ($p < 0.05$) on the evaluation of spreadability but did not significantly ($p > 0.05$) on the evaluation of the melting point, pH, smear test, organoleptic, homogeneity, and oilability.

Keywords: Lip Balm, Secang (*Caesalpinia sappan* L.), Beeswax, Candelilla Wax

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ANALYSIS OF ANTIOXIDANT AND ANTIBACTERIAL ACTIVITY OF LEAVES OF FIG (*Ficus carica* L.) FROM CIWIDEY DISTRICT, WEST JAVA, INDONESIA

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ABSTRACT

Leaves of fig (*Ficus carica* L., Moraceae) contains flavonoids, tannins, phenolic compounds, saponins, alkaloids, steroids, and terpenoids. These compounds create an opportunity to utilize fig leaves as a herbal medicine. This study aimed to analyze antioxidant and antibacterial activity to *Staphylococcus epidermidis* and *Propionibacterium acnes* of fig leaves. Antioxidant activity was conducted by DPPH method, while antibacterial activity was conducted by agar well diffusion method, followed by microdilution method to determine Minimum Inhibitory Concentration (MIC). The results showed the IC₅₀ values of extract, fraction of ethyl acetate, *n*-hexane, and water was 78.79, 22.29, 1052.00, and 133.90 µg/mL, respectively. The diameter of the inhibition zone of the extract was higher in *S. epidermidis* compared to *P. acnes*. The antibacterial activity was proportional to the extract concentration. The extract MICs for *S. epidermidis* and *P. acnes* were in the range of 6.25-12.5% w/v. It concluded that the ethyl acetate fraction had the best antioxidant activity compared to the extract, water and *n*-hexane fraction. The antibacterial activity of the extract was better on *S. epidermidis* than *P. acnes*.

Keywords: DPPH method, *Staphylococcus epidermidis*, *Propionibacterium acnes*, well diffusion, microdilution

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OVERVIEW OF THE PHYSICAL STABILITY OF EXTRACT ETHANOL MANJAKANI SEED (*QUERCUS INFECTORIA GALL*) FEMININE HYGIENE GEL SOAP FORMULA THROUGH VARIATIONS OF USING GELLING AGENT

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ABSTRACT

Formulation of feminine hygiene gel soap has been developed by utilizing natural sources, manjakani seeds (*Quercus infectoria Gall*), in the form of ethanol extract. Manjakani seeds are reported to have an antifungal activity that can inhibit the growth of *Candida albicans* as a cause of leucorrhea^[1]. Stability testing of the formula has been carried out with variations of synthetic (Carbopol 934) and natural (tragacanth) gelling agents^[2,3]. The preparations were made in 6 formulas with the same extract concentration (8%) and variations in the concentration of each gelling agent in the same range. Gel Soap was prepared by developing a gelling agent in aquadest and then homogenizing the preparation through a homogenizer. The formula was obtained with fluctuating viscosity values between carbopol 934 and tragacanth. The physic stability of the preparation at room temperature for six weeks met the pH requirements for feminine soap (3.8-4.5), which was 3.85-4.29. The result of measuring the height of the soap foam shows that the formula using tragacanth meets the standard height of the soap foam, 1.3 – 2.2 cm. At the same time, the formula that uses Carbopol varies between 1.0 - 1.6 cm. Gelling agent affects the physical stability of soap preparations during storage.

Keywords: soap gel, manjakani seed, carbopol 934, tragacanth, physical stability

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THE EFFECT OF EXTRACTION METHOD ON SINENSETIN LEVELS OF *Orthosiphon aristatus* (BLUME) MIQ.

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ABSTRACT

Cat's whiskers (*Orthosiphon aristatus* Blume Miq.) is a plant that has medicinal properties.^[1] Various studies of pharmacological activities have been carried out and it is known that the cat's whiskers plant has a variety of pharmacological activities.^[2] The purpose of this study was to compare the levels of sinensetin from cat whiskers leaf extract obtained by maceration and reflux so that it can be seen which extraction method is better to produce higher levels of sinensetin. The purple variety of cat whiskers samples were obtained from the Unjani Cimahi medicinal plant garden. Prior to extraction, standardization of raw material was conducted, The extraction was conducted by maceration and reflux. Validation of the HPLC method used for assay includes accuracy, precision, linearity, and specificity. The results of the validation of the HPLC method used were % recovery from accuracy of $98.37 \pm 3.44\%$, % RSD of precision 1.12%, correlation coefficient of linearity of 0.999 and no disturbance was found around the retention time of sinensetin so that meet the specificity parameters. The results of the sinensetin test were $0.42 \pm 0.006 \%$ for maceration and $0.30 \pm 0.006 \%$ for reflux. In conclusion, the better extraction method for sinensetin is maceration.

Keywords: *Orthosiphon aristatus* (Blume) Miq., purple variety, sinensetin, HPLC.

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ANALYSIS OF VITAMIN K (VK₁) CONTENT IN SEVERAL TYPES OF VEGETABLES CONSUMED BY WARFARIN-USED PATIENTS

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ABSTRACT

Variations in the response and dose of warfarin between individuals can be influenced by vitamin K-contained foods¹. Vitamin K status in the body that is too high or too low can cause an unstable anticoagulation response, so warfarin-used patients must control their intake of vitamin K to be stable and consistent². The result of a study on the types of vegetables consumed by warfarin-used patients at Hasan Sadikin Central General Hospital Bandung includes spinach, cabbage, napa cabbage, lettuce, cucumber, carrots, tomatoes, red beans, water spinach, potatoes, broccoli, oyong, and beans⁵. This study aims to obtain information on vitamin K₁ content in several types of vegetables consumed by warfarin-used patients at Hasan Sadikin Central General Hospital Bandung and is commercially available in 3 main markets in the Bandung area. The method used in this analysis was HPLC with a UV detector at 245 nm, using isocratic mobile phase containing 100% methanol with a flow rate of 0.6 mL/min, and T3 column set at 25°C. The results showed that vitamin K₁ content in spinach (305,2868 ± 3,3058 µg/100 g - 970,7098 ± 14,1167 µg/100 g), cabbage (27,9531 ± 1,7487 µg/100 g - 217,0457 ± 7,2201 µg/100 g), napa cabbage (56,7445 ± 0,1569 µg/100 g - 273,2828 ± 8,3061 µg/100 g), and lettuce (38,4391 ± 15,2650 µg/100 g - 64,4419 ± 19,0315 µg/100 g). Vitamin K₁ content in all four types of vegetables from 3 main markets in the Bandung area was obtained. In this study, the highest vitamin K₁ content was in spinach and the lowest was in lettuce.

Keywords: Vitamin K, Vegetables, Warfarin, HPLC

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PHARMACOLOGICAL ACTIVITY OF SOY YOGHURT AS ANTI-INFLAMMATORY AGENT RELATED BY ISOFLAVONES COMPOUND

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ABSTRACT

Soybean is a plant that contains isoflavones which have been known have anti-inflammatory activity.^[1] Soy yogurt (soyghurt) is the product of soy milk that go through fermentation process which is known to increase the aglycone component of isoflavones that can improve the biological activity of soybean. Unfortunately, there is no report of anti-inflammatory activity of soyghurt. This research aims to determine the anti-inflammatory activity of soyghurt. The soybean used in this research was collected from Bandung. Soybean was processed into soymilk by using Illinois methods, then added starter bacteria containing *Lactobacillus bulgaricus*, *Streptococcus thermophilus*, *Lactobacillus acidophilus* and *Lactobacillus casei*. The anti-inflammatory activity of the soygurt was determined through acute inflammatory test which is induced by carrageenan. Soyghurt was administered orally at a dose of 2mL, 3ml and 4ml per 200g BodyWeight of rat. Data was then analyzed using ANOVA and Games-Howell test. The anti-inflammatory activity test showed that at doses 2, 3, and 4 mL/200g of rat body weight, soyghurt inhibited inflammatory response by 39.98%; 59.48%; and 48.19%. This research revealed that soyghurt exhibits anti-inflammatory activity.

Keywords: Soybean, Soy Yoghurt, Isoflavones, Anti-inflammatory activity.

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PREDICTION THE EFFECT OF SINGLE NUCLEOTIDE POLYMORPHISMS (SNPs) IN THE CYP2C9 ON WARFARIN METABOLISM BY *IN SILICO* STUDY

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ABSTRACT

Warfarin is an oral anticoagulant that has wide dose variability between individuals. One of the factors that plays a role is Cytochrome P450 Family 2 Subfamily C Member 9 (CYP2C9) or CYP2C9 wild type. It is known that CYP2C9 has many single nucleotide polymorphisms (SNPs) which are thought to cause a decrease in drug metabolic activity.^{[1][2][3]} This study aimed to predict the effect of CYP2C9 polymorphisms on the metabolic activity of S-warfarin in the body. Molecular modeling was performed to obtain CYP2C9 polymorphisms and molecular docking was performed to predict the effect of CYP2C9 polymorphisms on the metabolic activity of S-warfarin. The results showed that wild-type CYP2C9 had the strongest binding affinity (ΔG : -9.76 kcal/mol) indicating that wild-type CYP2C9 had the best metabolic activity compared to CYP2C9 polymorphisms. There was a decrease in hydrogen bond formation and an increase in the distance between C7 S-warfarin and Fe-Heme in CYP2C9 polymorphisms when compared to wild-type CYP2C9. The decrease in binding affinity, decrease in hydrogen bond formation and increase in the distance between C7 S-warfarin and Fe-Heme on CYP2C9 polymorphisms indicated that CYP2C9 polymorphisms had decreased metabolic activity against S-warfarin, which led to an increased risk of bleeding.

Keywords: Warfarin, CYP2C9, CYP2C9 polymorphisms, *in silico*, Molecular Modeling, Molecular Docking

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β-LACTAMASES INHIBITOR-PRODUCING SOIL BACTERIA FOR AMPICILLIN-RESISTANT UROPATHOGENIC *Escherichia coli* ISOLATE

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ABSTRACT

More than 90% of ampicillin-resistant uropathogenic *E. coli* produced TEM β-lactamases.^[1] Before the discovery of uropathogenic *E. coli* resistance to ampicillin and β-lactamases inhibitor, its combination with β-lactamases inhibitor was a solution.^[2] This enables the discoverer of novel β-lactamase inhibitors to repurpose ampicillin. Our earlier research shown the capability of several microorganisms isolated from Indonesian soil to produce inhibitors against clinical isolates of *E. coli*-resistance ampicillin. Therefore, the goals of this investigation were to identify the species of the producers and ascertain the dose-dependent effect of extracellular products of Indonesian bacteria that generate β-lactamases inhibitors. An agar diffusion technique for β-lactamase inhibitor activity assay was carried out. Combining data from phenotypic and genotypic analyses allowed for the identification of the producers. According to our findings, none of the bacteria's extracellular products which contain β-lactamase inhibitors in a range of concentrations showed a discernible impact on the values of the inhibition zone. The producers are *Aeromonas popoffii*, *Alcaligenes faecalis*, *Streptomyces brasiliensis*, *Staphylococcus equorum*, *Pseudomonas putida*, and *Enterobacter hormaechei*. In conclusion, this study clearly showed that our isolated bacteria have the potential to be further investigated in order to maximize the recovery of β-lactamase inhibitor compounds.

Keywords: β-lactamase, marine, soil, inhibitor, *Escherichia coli*, ampicillin

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DETERMINATION OF DEXAMETHASONE IN HERBAL MEDICINE USING UV-VIS SPECTROPHOTOMETRY

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ABSTRACT

Dexamethasone is one of chemical drugs that have been added to some of the traditional herbal medicine to enhance the therapeutic effect in herbal pain relief.^[1] To determine the content of dexamethasone in the herbal medicine, a quantitative analytical method was developed with the reaction of the formation of a dexamethasone-hydroxylamine complex with fluoranil which was measured by UV-Vis spectrophotometry.^[2] In the optimized condition the results of the UV-Vis spectrophotometry showed good results with a linear equation coefficient (R^2) of 0.9965 from a concentration of 1-40 g/mL, LOD and LOQ of 0.21 $\mu\text{g/mL}$ and 0.64 $\mu\text{g/mL}$, %recovery for concentrations of 80%, 100%, and 120%, are 100.14% \pm 0.58; 98.35% \pm 1.19; and 99.00% \pm 1.18, respectively; and %RSD is 0.75%. Sixteen samples were analyzed and six samples were confirmed to contain dexamethasone with varying levels. This method has been compared with HPLC and the results show that the levels obtained are in accordance with the standard method with a deviation range of 0.00 – 0.25. Based on this, this analytical method show good performance and can becomes an alternative method for the analysis of dexamethasone in herbal medicine

Keywords: Dexamethasone, Fluoranil, Herb, UV-Vis Spectrophotometry

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SYNTHESIS OF BIOPLASTIC FROM BANANA TREES (*Musa paradisiaca* L.) WASTE WITH A VARIATION OF STARCH

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ABSTRACT

Cellulose can be used as a bioplastic component because of its natural robustness and ability to be degraded in nature.^[1] Banana stem is one of the cellulose sources with content of cellulose of about 47%.^[2] This research was conducted to find out the process of manufacturing bioplastics made from cellulose waste from banana stem. The stages carried out in this study were collection and determination of banana stem as cellulose source, preparation of banana pseudostem powder, preparation of cellulose powder, bioplastics production, characterization of bioplastics, and biodegradation study of bioplastics. Bioplastic were produced using composite method with phase inversion techniques and variations in the addition of corn starch (0.5 grams; 0.75 grams, and 1 gram). Bioplastics with 0.5 gram starch have better characteristic than others. With the test results of the tensile strength value was $1,7423 \pm 0,083$ MPa, elongation was $43,2484 \pm 1,6328\%$, modulus of elasticity was $5,082 \pm 0,0007$ MPa, density was $1,3180 \pm 0,0089$, water absorption was $368,3887 \pm 5,4714\%$, and completely degraded after planting in the soil on the 5th day.

Keywords: Banana stem, cellulose, bioplastic

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COMPARISON OF PHYSICAL CHARACTERIZATION OF ALPHA MANGOSTIN MIP USING ACRYLAMIDE AS A MONOMER IN BULK AND SUSPENSION POLYMERIZATION

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ABSTRACT

Alpha mangostin is a bioactive compound derived from *Garcinia mangostana* known for its pharmacological activity.^[1] Molecularly imprinted polymers (MIP) is a method that can be used to purify alpha mangostin from other components, allowing identification of the active facet of the compound.^[2,3] Based on a computational study, acrylamide has good binding energy with alpha mangostin and can be used as a functional monomer.^[4] Two types of alpha mangostin MIP have been synthesized in bulk and suspension polymerization. Physical characterization of MIP was determined by FTIR, SEM, and BET instruments. The physical characteristics of the polymer such as shape, porosity, surface area, and average particle size diameter were related to the affinity of the polymer with template. By comparing physical characterization of alpha mangostin MIP, we find that molecularly imprinted polymers made with suspension polymerization method has more uniform shape and the specific surface area are better than bulk.

Keywords: alpha mangostin, acrylamide, molecularly imprinted polymer

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EXPRESSION OPTIMATION OF GENE ENCODING LL37(PJEXPRESS411_LL37) USING CENTRAL COMPOSITE DESIGN AS RECOMBINANT ANTIMICROBIAL PEPTIDE IN *ESCHERICHIA COLI* BL21 (DE3)

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ABSTRACT

LL-37 peptide is an antimicrobial peptide of the cathelicidin group which is naturally produced by epithelial cells and lymphocytes in humans. As an antimicrobial peptide, LL-37 has various activities such as antimicrobial, antifungal, antiviral, and anticancer and can modulate the innate immune system when inflammation occurs. To obtain optimal amounts of this recombinant protein, LL-37 gene expression (Jexpress411_LL37) in *Escherichia coli* BL21 (DE3) was optimized. In this study, optimization of factors affecting the expression of recombinant protein was carried out using a Central Composite Design (CCD) with the optimized factors i.e. the inducer concentration (IPTG) and induction time. The optimization results of LL-37 recombinant protein expression were evaluated using SDS-PAGE protein characterization, then quantified using ImageJ software. The data obtained were re-analyzed statistically. The results of this study obtained the optimal expression of gene encoding LL-37 at an IPTG concentration of 1.3 mM for 4 hours.

Keywords: LL-37, Central Composite Design, IPTG, Induction Time, SDS-PAGE, ImageJ

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SENSITIVITY ASSAY OF RESISTANT *ESCHERICHIA COLI* FROM URINARY TRACT INFECTION PATIENT CLINICAL ISOLATE TO FOSFOMYCIN, KANAMYCIN, RIFAMPICIN, CEFTRIAZONE AND VANCOMYCIN

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ABSTRACT

Antibiotic resistance is a major global health problem and continues to increase, so there is a need for better evaluation and therapeutic advice for urinary tract infection (UTI) patients. This study aims to determine the effect of single and combination antibiotic of fosfomycin, kanamycin, rifampicin, ceftriazone and vancomycin on resistant *Escherichia coli* clinical isolates of UTI. The sensitivity test in this study used the Kirby-Bauer disc diffusion method and data analysis used SPSS version 25. The results revealed the diameter of inhibition zones (mm) of single antibiotic of fosfomycin, kanamycin, rifampicin, ceftriazone and vancomycin respectively i.e. 38 ± 1 ; $31.6 \pm 1,15$; 28 ± 1 ; 36.3 ± 1.15 and 26.3 ± 0.17 . Otherwise the diameter of inhibition zone (mm) of combination antibiotics were $37.3 \pm 0,53$; $33.3 \pm 0,24$; and $41 \pm 0,26$ for kanamycin-fosfomycin, kanamycin-rifampicin and ceftriazone-vancomycin successively. The activity of single antibiotics was significantly difference with combination antibiotic. The combination ceftriazone-vancomycin can increase the activity of each single antibiotic 1.13-1.57 times.

Keywords: UTI, clinical isolate, single antibiotic, combined-antibiotics, diameter of inhibition zone

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MOLECULAR DOCKING OF CHALCONES FROM *ANGELICA KEISKEI* ONTO HMG CO-A REDUCTASE

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ABSTRACT

Angelica keiskei sap contains chalcone compounds, however the molecular mechanism of its anti-hyperlipidemic activities has not been explored. To study the binding affinity of chalcone compounds with HMG-CoA reductase. Molecular docking simulation of each compound using Linux script for AutoDockVina embedded in MGLTools v.1.5.6. Simvastatin (HMG-CoA reductase inhibitor) was used as standards. Prediction of absorption and distribution parameters using PreADMET® software and toxicity properties using SwissADME® software. Simvastatin has binding affinity with Arg590, Ser684, Lys691, Lys735, and Asn755 in HMG-CoA reductase's binding pocket (Ei -6.97 kcal/mol; Ki 10.8 µM). The docking reveals that 24 chalcone compounds had interaction with amino acid in the active sites. One of chalcone has similar interaction, xanthoangelol I (Ei -6.74 kcal/mol; Ki 13.0 µM) interact with Arg590, Ser684, Asp690, Lys692, Lys735, and Asn755. The phytoconstituents in *A. keiskei* might be potential in inhibiting HMG-CoA reductase based on their binding affinity. The binding affinity of xanthoangelol I is almost equal to simvastatin. From the overall results of ADMET predictions, xanthoangelol I meet Lipinski's rules, well absorbed in the intestine, have moderate permeability, well distributed in the body, and not mutagenous.

Keywords: *Angelica keiskei* sap, chalcone, HMG-CoA reductase, molecular docking

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EFFECT OF HEAT TREATMENT ON POTASSIUM CONTENT AND ANTI-SHIGELLOSIS ACTIVITY OF KLUTUK BANANAS (*Musa balbisiana* colla) FRUIT

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ABSTRACT

Our earlier studies demonstrated that fruit of Klutuk banana possessed a strong antibacterial activity against *S. dysenteriae* and might be further developed to be an anti-shigellosis product.^[1] Nevertheless, they have a limited shelf life and must be processed further to have a longer shelf life. It can be preserved as the active ingredients for long-term storage by turning it into banana flour using heat treatment. However, it is well recognized that heat treatment can cause large losses of molecules with biological activity.^[2] In this study, we investigated the effect of heat treatment on potassium content and anti-shigellosis activity of klutuk banana. A validated oven was used to heat-treat the slices of klutuk banana using various conditions: 30-50°C for 15-40h. The selected condition then used to process bananas to meet the stable flour based on its minimum inhibitory concentration (MIC) value and the potassium analysis. As the result, 50° C for 20 h was the optimal heat-treat for the anti-shigellosis activity with the MIC of 3.125 mg/mL. However, the highest potassium content was achieved after heat-treat for 40 h. Thus, heat in flour process was a significant factor that affected the potassium gain and the anti-shigellosis activity of klutuk banana fruit.

Keywords: Klutuk, *Musa balbisiana* colla, heat, potassium, shigellosis.

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SIMPLE CLEANSING METHODS ON MOUTHPIECES DECONTAMINATION OF SHARED WIND INSTRUMENTS

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ABSTRACT

There are few data on bacterial survival in wind instruments. However, the potential for recontamination of players with their own instruments, or cross-contamination of oral and pulmonary microbes between players sharing such instruments, is real.^[1] This study was designed to determine a simple cleaning method that could be used to decontaminate the mouthpieces of shared wind instruments. The study examined four of his wind instruments: the trumpet, mellophone, trombone, and tuba. Total bacteria attached to the device were isolated using a swab method. The decontamination effect was evaluated by a simple cleaning method of immersing the mouthpiece in hot water at 100°C for 5 min and immersing it in soap containing 2% triclosan. Surviving colonies were scored using the plate counting method and counted using a colony counter. The cleaning method of immersing in hot water at 100°C for 5 min significantly reduced the number of bacteria (91.85-99.91%) compared to liquid soap (50.30-91.67%). However, due to the large surface area of the tuba mouthpiece, it was the easiest to disinfect using either method. In conclusion, a 5-min soak in 100°C boiling water can be used as a quick, easy, and easy-to-use method for disinfecting the mouthpieces of shared wind instruments.

Keywords: contamination, mouthpieces, musical instruments, hot water, soap.

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THE PHARMACEUTICAL PROPERTIES OF AMORPHOUS DRUGS LOADED-MESOPOROUS SILICA PREPARED BY SOLVENT EVAPORATION

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Meanwhile, there is an increase in the number of poorly soluble drugs that have been discovered as new chemical entities.^[1] It was also reported that the physical transformation of a drug from a crystalline form into an amorphous state could be used to increase its solubility.^[2] The incorporation of drug into mesoporous silica (MPS) can stabilize amorphous state of drug.^[3] Therefore, in this study, the pharmaceutical properties of amorphous drug loaded-MSP was evaluated. Ritonavir (RTV) was used as a model of a poorly water-soluble drug. RTV was incorporated into MPS (RTV/MPS) using the solvent evaporation method. A halo pattern in the powder X-ray diffraction pattern was discovered in RTV amorphous, indicating its amorphization. While the T_g was not detected in RTV/MPS, indicating that all RTV were completely incorporated into MPS. The interaction between RTV and the surface of MPS were clarified by solid-state NMR and FT-IR spectroscopy. The high supersaturation of RTV in RTV/MPS was not achieved due to its strong interaction between RTV with the surface of MPS. The incorporation of RTV into MPS revealed the improvement of the physical and chemical stability of RTV amorphous. This study demonstrated that the pharmaceutical properties of amorphous drugs could be improved by loaded-MPS.

Keywords: amorphous; pharmaceutical properties; ritonavir; mesoporous silica

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THE INHIBITION OF CRYSTAL NUCLEATION IN A SUPERSATURATED SOLUTION OF ALPHA-MANGOSTIN BY EUDRAGIT

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ABSTRACT

The polymer plays a critical role in an amorphous solid dispersion (ASD) formulation. ^[1] The polymeric additives could inhibit the crystallization of drugs from the supersaturated solutions in order to enhance the delivery of poorly water-soluble drugs.^[2-3] In this study, the impact of eudragit on the supersaturation behavior of alpha mangostin (AM) was investigated to elucidate the role of polymers in enhancing the supersaturation levels of amorphous drugs. Crystal growth rate and nucleation kinetics was evaluated by measuring the induction time for nucleation. The presence and absence of polymers were performed in this experiment. The interaction of AM with eudragit was evaluated and predicted by FT-IR and in silico study, respectively. Moreover, the viscosity of each sample was also evaluated. The eudragit effectively maintained the AM in a supersaturated state for 15 minutes, while in the absence of eudragit, the concentration of AM rapidly decreased even after one minute due to the crystallization of AM. The interaction of PVP-AM was clarified and predicted by FT-IR and in silico study. Moreover, the viscosity of eudragit solution and buffer solution was not significantly different. This indicated that the interaction of eudragit-AM could inhibit the AM crystallization and maintain the concentration of AM in a supersaturated state. This study will be helpful in developing supersaturated formulations of drugs.

Keywords: supersaturation; polymers; eudragit; crystallization; alpha-mangostin

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COST EFFECTIVENESS ANALYSIS OF ANTIBIOTIC USAGE IN DIABETIC FOOT ULCUS PATIENTS IN DOKTER SOEKARDJO TASIKMALAYA HOSPITAL

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ABSTRACT

Diabetic foot ulcers is sores on the skin surface until it penetrates the skin layer caused by infection, which is require high costs for treatment.^{[1][2]} This puts a considerable burden on the patient's family, health agencies and society in general.^[3] This study was conducted to describe the direct medical costs and cost-effective antibiotics for diabetic foot ulcer patients at dokter soekardjo tasikmalaya hospital. The research method is retrospectively with purposive sampling technique. The research subjects included 24 hospitalized diabetic foot ulcer patients who received antibiotic treatment ceftriaxone with metronidazole or meropenem with metronidazole. The effectiveness of therapy is determined by the Length of Stay (LOS). Direct medical costs are obtained from medical costs, treatment costs, laboratory costs, and radiology costs. The average direct medical cost for the combination of ceftriaxone and metronidazole antibiotics is Rp. 4.668.062 and for the combination of meropenem antibiotics with metronidazole is Rp. 9.093.830. The effectiveness of the antibiotic ceftriaxone with metronidazole was 47%. The cost-effective antibiotic is ceftriaxone with metronidazole which has the lowest ACER value Rp. 9,932,046 and the ICER value is Rp. 22,128,840.

Keywords: Antibiotics; Cost Effectiveness Analysis; Diabetic foot ulcers

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THE POTENTIAL OF LANGIR (*Albizia saponaria*) STEM BARK FRACTIONS TO INHIBIT *Malassezia furfur* FUNGUS: *IN VITRO* AND *IN SILICO* STUDIES

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ABSTRACT

The bark of *langir* or whiteflower albizia (*Albizia saponaria*) has been reported as a potential anti-dandruff agent based on empirical use [1], but there is no scientific data showing its activity. Therefore, researchers are interested in testing gynecological fractions with *in vitro* and *in silico* approaches by targeting *Malassezia furfur*, which is a species of fungus that plays a major role in producing dandruff [2]. *In vitro* testing was conducted by agar diffusion method using paper disk to calculate the inhibition zone of *langir* bark fraction, while *in silico* testing was conducted by molecular docking method for the lanosterol 14- α demethylase receptor with a homology model using 48 compounds from the albazia genus as ligands. From *in vitro* testing of 3 fractions, which were n-hexane fraction, ethyl acetate fraction, and water fraction, it was found that the water fraction showed better results, having a moderate inhibition zone of 17.33 mm at 15% concentration and 18.67 mm at 20% concentration. The inhibition was ketoconazole 1% as a positive control with an inhibition zone of 16.67 mm. Furthermore, the *in silico* test revealed 3 metabolites in *langir* plant providing better binding energy than ketoconazole (-10.1 kcal/mol), namely, kaempferol 3-rhamnosyl galactosides (-11.7 kcal/mol), acasioside A (-10.3), and albiziasaponin E (-10.7).

Keywords: Langir (*Albizia saponaria*) bark, *Malassezia furfur*, *in vitro*, *in silico*.

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STANDARDIZATION AND ANTIOXIDANT ACTIVITY OF EXTRACT RUMPUT MUTIARA (*Oldelandia corymbosa* L.) USING DPPH METHOD (2,2-Diphenyl-1-Picrylhydrazyl)

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ABSTRACT

Rumput mutiara (*Oldelandia corymbosa* L.) belonging to the family Rubiaceae, is one of the plants that has been used as herbal medicine because it contains various secondary metabolites.^[1] Flavonoid is the main ingredient in herb rumput mutiara that can be function as antioxidant.^[2] *O. corymbosa* is used for treatment of viral infections, cancer, appendicitis, hepatitis, eye disease, and bleeding.^[2] In order to *O. corymbosa* can be used as raw material for standardized traditional medicines, it was necessary to standardize to determine specific and non-specific parameters, the profile of thin layer chromatography (TLC), and the potential antioxidant activity of *O. corymbosa* extract using DPPH (2,2-diphenyl-1-picrylhydrazyl). The results showed extract has blackish brown in color with a characteristic odor and a bitter taste. The microscopic of crude drug produced fragments such as anther, mesophyll composed of parenchymal cell, lower epidermis with stomata, transport bundles, sclerenchyma, and stem parenchyma. Non-specific parameters showed that the water soluble compounds was 35%; ethanol soluble compounds 72%; moisture extract content of 12%; drying losses of extract was 18%. Specific parameters of *O. corymbosa* extract contained alkaloid, polyphenol, flavonoid, tannin, saponin, steroid, and glycoside as evidenced by phytochemical screening and chromatogram patterns using different mobile phases. The results of the antioxidant activity *O. corymbosa* extract obtained the IC₅₀ was 14.11 ppm. The conclusion showed *O. corymbosa* extract can be standardized to complement the data as a raw material for traditional medicine and also extract has very strong antioxidant activity.

Keywords: *Oldelandia corymbosa* L., specific and non-specific parameters, antioxidant.

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THE CYTOTOXIC EFFECTS OF B-SITOSTEROL AND ITS DERIVATIVES ON MCF-7 HUMAN BREAST CANCER CELLS

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ABSTRACT

β -Sitosterol is one of the most abundant phytosterols in plants. It has been reported that sitosterol have pharmacological activities such as anti-inflammatory, antibacterial, antifungal, antitumor and anticancer. The efficacy of β -Sitosterol and its derivatives are promising as an anticancer drugs.^[1] As one of the most death-causing diseases, cancer, especially breast cancer is the second leading cause of death among women overall.^[2] Therefore, this study aimed to determine the cytotoxic activity of β -Sitosterol and its derivatives, 3 β -galactose sitosterol and 3 β -glucose sitosterol, against MCF-7 human breast cancer cells. Cytotoxic activity was carried out by proliferation assay method using PrestoBlue reagents. MCF-7 cells were treated with 250 ppm, 125 ppm, 62.5 ppm, 31.25 ppm, 15.625 ppm, 7.8125 ppm, 3.90625 ppm, and 1.953125 ppm of each samples. The results showed β -Sitosterol had weak cytotoxic activity against MCF-7 human breast cancer cells with IC₅₀ values 219,193 ppm, meanwhile the derivative compounds had no cytotoxic activity.

Keywords: Breast cancer, β -Sitosterol, Cytotoxicity, MCF-7

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COMBINATION OF CISPLATIN WITH NUTMEG (MYRISTICA FRAGRANS HOUTT) SEED ESSENTIAL OIL EXHIBITS ANTAGONISTIC EFFECTS IN 4T1 BREAST CANCER CELLS

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ABSTRACT

Cisplatin is a drug used for breast cancer chemotherapy, but combining chemotherapy with two or more agents is highly desired as a promising anticancer tool to reduce cisplatin-related toxicity.^[1] The seed of *Myristica fragrans Houtt* (Nutmeg) has anticancer effects on several cancer cell lines.^[2] The study aimed to explore the potential cytotoxic activity of Nutmeg Seed Essential Oil (NSEO) single and in combination with cisplatin on 4T1 cells. Nutmeg seed extraction used the maceration method with 96% ethanol for 48 hours, and the chemical compositions were determined by Gas Chromatography-Mass Spectroscopy (GC-MS). The single cytotoxic activity of the NSEO and cisplatin combination was determined based on the IC₅₀ and the Combination Index (CI) by WST-1 Assay. At 24 hours of incubation, NSEO showed a moderate cytotoxic effect in 4T1 cells with an IC₅₀ of 85.83 µg/mL, while cisplatin showed a strong cytotoxic effect with an IC₅₀ of 4.09 µM. WST-1 assay revealed that the combination of cisplatin with NSEO exhibited an antagonistic effect (CI >3.3) in 4T1 cell line. Our data indicate that combined cisplatin and NSEO produce antagonistic interaction in 4T1 cell line, which is not potential to be developed as a co-chemotherapeutic agent.

Keywords: co-chemotherapy, *Myristica fragrans Houtt*, antagonistic, 4T1 cell lines.

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ANTIBACTERIAL POTENTIAL OF EXTRACT AND FRACTIONS OF SEGARA ANAKAN MANGROVE (*Acanthus ilicifolius*) AGAINST MOUTH BACTERIA AND ITS FORMULATION AS TOOTHPASTE

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ABSTRACT

Controlling mouth microbes is an important thing to do because the uncontrolled microbes will form a hardened dental plaque that can cause dental caries.^[1] This research aimed to provide the antibacterial activities of ethanol extract and n-hexane, ethyl acetate, and water fractions of *A. ilicifolius* leaves and make a toothpaste formulation from the most potential agent. Phytochemicals components tested on extract and fractions obtained from *A. ilicifolius*. Antibacterial activity against *S. mutans* and *B. subtilis* also tested. The toothpaste formulation and some evaluations conducted as the last step. The results showed that ethyl acetate fractions had the strongest antibacterial activity against *S. mutans* with an average diameter of the inhibition in range of 3,5 to 4,5 mm and against *B. subtilis* in range of 19,7 to 22.5 mm. As the ethyl acetate fractions has the strongest antibacterial activity among the rest, it is used as the antibacterial agent in the toothpaste. Evaluations on the toothpaste showed that the color, aroma, scent, flavor, shape, spreadability, and pH of 3, 6, and 9% ethyl acetate fractions met the standard. Based on the results, we know that the ethyl acetate fractions of *A. ilicifolius* leaves could be an antibacterial agent for a toothpaste.

Keywords: *Acanthus ilicifolius*, antibacterial, *Streptococcus mutans*, *Bacillus subtilis*, toothpaste

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ANALYSIS OF MIANA (*Plectranthus scutellarioides* (L.) R. Br.) LEAF EXTRACT WITH LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY METHOD

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ABSTRACT

Miana (*Plectranthus scutellarioides* (L.) R. Br.) belongs to the family Lamiaceae. Miana leaves are a plant material used by Indonesian people in the treatment of various diseases such as malaria by the people in North Sulawesi ^[1], anti-inflammatory by the people in Halmahera ^[2], an also as tuberculosis drugs and immunomodulators by the people in Toraja ^[3]. This study aims to identify secondary metabolites contained in miana extract of miana leaves using Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) instrumentation. The miana leaf was macerated with ethanol 96% as a solvent. The miana extract was analyzed using LCMS/MS-QTOF with UNIFI software which already has a library of the mass spectrum of active substances of natural ingredients from the Waters database. The column used in this study is the C-18 column; the mobile phase was a gradient of 0.1% formic acid in acetonitrile (A) and 0.1% formic acid in aquabidest (B) with a flow rate of 0.6 mL/minute and column temperature of 40°C. The results showed the presence of five compounds from the flavonoid group, namely: kaempferol; baicalein-7-O-β-D methyl glucopyranosiduronic acid; galangin; kaempferol 3-O-β-D-glucuronopyranoside, and kaemferol 3-O-β-D- glucuronopyranosyl methyl ester, and also two compounds from alkaloids group, namely: stachydrine and picrasidine E.

Keywords: Liquid Chromatography-Tandem Mass Spectrometry, *Plectranthus scutellarioides* (L.) R. Br., flavonoids, alkaloids

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SYNTHESIS OF MOLECULAR IMPRINTED POLYMER SALBUTAMOL USING METHACRYLIC ACID MONOMER AND TRIMETHYL PROPANE TRIMETHACRYLATE (TRIM) AS A CROSS-LINKER THROUGH SUSPENSION POLYMERIZATION

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ABSTRACT

Salbutamol is a beta-2 agonist drug used to relieve asthma symptoms through a bronchodilation mechanism. However, this drug is often abused to enhance the performance of athletes and illegally used to promote growth in meat-producing animals. Therefore, a selective and sensitive method is needed to identify and quantify salbutamol. Molecular Imprinted Polymer (MIP) is a synthesis of polymer method to obtain selective and sensitive sorbent that can be used in the analytical preparation process. This study aims to determine the analytical performance and characteristics of MIP salbutamol made with methacrylic acid (MAA) monomer and trimethylpropane trimethacrylate (TRIM) cross-linker through suspension polymerization. Molecular Imprinted Polymer (MIP) showed better analytical performance than Non-Imprinted Polymer (NIP), adsorption ability of MIP reached about 90.43%. The MIP was selective for salbutamol when compared to terbutaline and salmeterol xinafoate with an imprinting factor (IF) of 1.2841. Based on these results, MIP salbutamol has the potential to be developed as a method for the preparation of salbutamol analysis from biological samples.

Keywords: Salbutamol, molecularly imprinted, suspension polymerization, separation

ANTIBACTERIAL EFFECTIVENESS OF MINDI (*Melia azedarach* L.) LEAF EXTRACT AND FRACTION AGAINST THE GROWTH OF *Staphylococcus aureus* ATCC 29213

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ABSTRACT

Diseases caused by microorganisms in the form of bacteria include the bacterium *Staphylococcus aureus*.^[1] In most cases of infection, the use of antibiotics is necessary but if excessive use of antibiotics will cause bacterial resistance, an alternative is needed such as looking for compounds that are antibiotics from plants that have efficacy.^[2] One of the antibacterial plants is the Mindi leaf (*Melia azedarach* L.). This study aimed to determine the antibacterial effectiveness of Mindi (*Melia azedarach* L.) leaf extract and fraction on the growth of *Staphylococcus aureus* bacteria. The methods used are maceration extraction, liquid-liquid fractionation and antibacterial testing using well diffusion. This study used 3 different concentrations of 6.25, 12.5, and 25% with positive control of clindamycin and negative control of DMSO 10% with 3 trials. The medium used for rejuvenation was Nutrient Agar (NA) and the medium used for testing was Mueller Hinton (MHA). The incubation period is 1 day or 24 hours at 37°C. This is done by looking at the inhibition zone marked by the clear zone around the well. The results showed that the greatest inhibition on the growth of *Staphylococcus aureus* bacteria, respectively, was the ethyl acetate fraction of 12.69, the water fraction of 9.78, and the n-hexane fraction of 7.90.

Keywords: *Staphylococcus aureus*, Mindi (*Melia azedarach* L.)

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SYNTHESIS OF MOLECULARLY IMPRINTED POLYMER WITH METHACRYLIC ACID DERIVATIVE MONOMER BY BULK POLYMERIZATION FOR ISOLATION OF ETHYL p-METHOXYCINNAMATE FROM *Kaempferia galanga* L. EXTRACTS

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ABSTRACT

Ethyl p-methoxycinnamate (EPMC) is the main component of the essential oil of *Kaempferia galanga* L., but the isolation yield of EPMC is still meager (0.50%–2.50%) with various isolation methods considering that the EPMC content in *Kaempferia galanga* L. essential oil is dominant^{1,2}. MI-SPE (Molecularly Imprinted Solid Phase Extraction) is currently widely used to isolate active compounds from natural materials because of its good selectivity and high reusability⁵. This study aims to synthesize MIP for isolate EPMC using EPMC as template, methacrylic acid (MAA) as monomer, Trimethylolpropane trimethacrylate (TRIM) or Ethyleneglycol dimethacrylate (EGDMA) as cross-linker, and hexane as porogen with bulk polymerization. In this study, two ratio templates:monomer:cross-linker, were synthesized using 1:4:20 (common ratio) and 1:7:20 (optimized by job plot method) and with 2 variations of cross-linker. The resulted show that the MIP 2 (1:7:20 ratio and TRIM) has better then MIP 1 (1:4:20 ratio and TRIM), MIP 3 (1:4:20 and EGDMA), and MIP 4 (1:7:20 and EGDMA). The adsorption capacity of MIP 2 is about 0.081 mg/g and adsorption capacity of MIP 1, MIP 3, and MIP 4 is about 0.064 mg/g, 0.026 mg/g, and 0.025 mg/g, respectively. Therefore, MIP 2 can be a good choice as an SPE sorbent for EPMC isolation.

Keywords: bulk polymerization, EPMC, molecularly imprinted polymer.

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STUDY OF SUNGKAI (*Peronema canescens*) LEAVES EXTRACT AS AN IMMUNOSTIMULATOR AND ANTIOXIDANT

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ABSTRACT

Immunomodulation is any drug that changes how the immune system works both as an immunosuppressant and as an immunostimulant. ^[1] *Peronema canescens* (PC) is a medicinal plant known as *Sungkai* in Indonesia where the leaves are usually used as an immune booster.^[2,3] However, studies of the immunostimulatory and antioxidant properties of PC are still limited. This study aimed to investigate the immunomodulator and antioxidant properties and determine total phenolic content (TPC) of ethanolic extract from PC using *in vitro* methods. *In vitro* studies to evaluate the immunomodulatory activity of PC on IL-6 with LPS-induced on raw cell 264.7. Antioxidant activity using DPPH, and determination of TFC using AlCl₃ was also carried out. The concentration of 25 µg/mL, with an IL-6 gene expression value of 1.29±0.23 as immunomodulator. antioxidants have IC₅₀ 27.57±2.90 µg/mL, and TPC 175.98±9.33 mg/g GAE. The results not only support the traditional medicine of PC as an immunomodulator and antioxidant but also proved *in vitro* approach.

Keywords: *Peronema canescens*, *In vitro*, immunomodulator, Antioxidant, TPC

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ANTIBIOTIC RESISTANCE PROFILES OF HAEMOPHILUS INFLUENZA ISOLATES FROM ADULT PATIENT: THE CITY HEALTH CENTER STUDY IN INDONESIA

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ABSTRACT

In developing countries, cases of *Haemophilus influenzae* (HI) resistance to levofloxacin, cefixime, and tetracycline have become a serious problem in clinical treatment^{1,2}. This study was conducted to determine the antibiotic resistance profile of HI from adult patient isolates and to provide guidelines for more effective clinical treatment in Indonesia. The patient isolate stock was rejuvenated, cultured on growth media and the *Kirby-Bauer* disc diffusion method was used to test for antibiotic susceptibility. Evaluation was guided by recommendations from the Clinical and Laboratory Standard Institute (CLSI). A total of 643 isolates obtained from the respiratory tract, isolated and identified 73 HI strains. The resistance rates of the HI isolates to tetracycline, cefixime, and levofloxacin were 10.54 %, 4.31%, and 5.67%. Cefixime showed more effective activity than levofloxacin and tetracycline to treat the HI strain.

Keywords : *Haemophilus influenzae*, levofloxacin, cefixime, tetracycline, resistance, clinical isolates.

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PYRIDINE ALKALOID FROM ETHYL ACETATE FRACTION OF *Pouteria campechiana* (Kunth) Baehni STEM BARK WITH CYTOTOXIC ACTIVITY AGAINST MCF-7 CELL LINE

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ABSTRACT

Pouteria campechiana (Kunth) Baehni (campolay or sawo mentega) is well known as a source of consumable fruits as well as traditional medicines.^[1] Ethanolic extract and ethyl acetate fraction of *Pouteria campechiana* stem bark has been reported to exhibit strong cytotoxicity against human breast adenocarcinoma cell line (MCF-7).^[2] This study aimed to investigate the phytoconstituents of cytotoxic fraction of *Pouteria campechiana* stem bark to be developed as a new source of cytotoxic agents. Phytochemical screening of ethyl acetate fraction showed the presence of alkaloid, phenolic, quinone, monoterpenoid and sesquiterpenoid. Further separation and purification by various chromatography techniques yielded alkaloid as a major component. Spectral analysis by ¹H and ¹³C NMR, UV and MS spectroscopy indicated a pyridine alkaloid.

Keywords: *Pouteria campechiana*, stem bark, alkaloid, cytotoxic

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COMBINATION OF CYMBOPOGON CITRATUS ESSENTIAL OIL WITH CISPLATIN ON 4T1 CELLS REPRESENTATIVE TRIPLE NEGATIVE BREAST CANCER: IN VITRO STUDY

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ABSTRACT

Background: Cisplatin widely used to treat multiple types of cancers however it has side effect and might be resistant. *Cymbopogon citratus* essential oil (CCO) known has anti-proliferative and anti-inflammatory activity that potential to be co-treatment with cisplatin and reduce its drawback.^[1] Objective: This study aimed to investigate potency of CCO as a cancer co-treatment with cisplatin toward 4T1 cells. Methods: CCO was obtained by water-steam distillation. Gas Chromatography-Mass Spectrometry (GC-MS) conducted to characterized the phytochemicals in CCO. Cytotoxicity effect of CEO, cisplatin and the combination were done by MTT assay with IC50 and combination index (CI) as parameter. Result: The chromatogram presented 99 compounds and citral was the major compounds as much as 21,12%. The IC50 value show that single treatment of cisplatin and CCO has cytotoxic effect toward 4T1 cells. Combination treatment performed worse cytotoxic effect. CI value was 17,42 at dose 0,5nM cisplatin and 28,125µg/mL CEO that showed combination effect is strongly antagonist. Conclusion: Combination of CEO and cisplatin show antagonist effect and have no potential to be cancer combination treatment.

Keywords: *Cymbopogon citratus* essential oil, cisplatin, combination index

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MECHANISM OF N-ACETYLCYSTEIN (NAC) AND THERAPEUTIC OPPORTUNITIES FOR NEUROPROTECTION: A REVIEW

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ABSTRACT

N-Acetylcysteine (NAC) is a drug approved by the Food and Drug Administration (FDA) and recognized by the World Health Organization (WHO) as an essential drug, widely used as an antidote to acetaminophen overdose¹. NAC can replenish brain glutathione and thus protect against oxidative stress and is likely neuroprotective, with pre-clinical efficacy in reducing oxidative stress markers and the severity of cognitive dysfunction.² NAC regulates pro-inflammatory cytokine production by inhibiting NF- κ B activity (nuclear factor kappa-light-chain-enhancer of activated B cells), which plays a vital role in many elements of the inflammation cascade and immune response.³ Based on these points, this review focuses on recent research on mechanisms of NAC and therapeutic opportunities for neuroprotection, specifically in Alzheimer's disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, traumatic brain injury, and stroke. A literature search was performed in Google scholar, NCBI databases, Elsevier journal, and Nature journal. The conclusion is NAC may be useful in clinical applications for therapeutic treatments in the diseases mentioned above.

Keywords: NAC, neuroprotection, anti-oxidant, anti-inflammation.

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EXPLORING *CYMBOPOGON NARDUS* ESSENTIAL OIL AS A CISPLATIN CO-TREATMENT IN BREAST CANCER VIA THE VERO CELLS MODEL

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ABSTRACT

Cisplatin (platinum derivatives drug) is one of the most common drugs used to treat solid tumors, including breast cancer¹. Cisplatin caused many adverse effects², so combining cisplatin with another compound was desirable. This study aims to explore the potential of *Cymbopogon nardus* essential oil (CNE) as co-treatment in breast cancer via in vitro model. CNE was obtained through steam distillation. Cytotoxic assay of cisplatin and CNE against 4T1 cells performed using MTT. Then, the cytotoxic combination was examined to evaluate CNE co-treatment potential combined with cisplatin. Cytotoxic activity of Cisplatin and CNE against 4T1 cells shown by IC₅₀ = 2.89 μM and 269.43 μg/mL, respectively. CNE has an antagonistic effect on cisplatin. The results of this study shown that CNE has no potential co-treatment activity combined with cisplatin against breast cancer via in vitro model.

Keywords: co-treatment, *Cymbopogon nardus*, combination, breast cancer

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ARTICLE REVIEW: NATURAL PRODUCTS USED FOR SYMPTOMS OF DEPRESSION DURING THE COVID-19 PANDEMIC

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ABSTRACT

COVID-19 is a pandemic disease caused by SARS-CoV-2 which was first discovered in Wuhan, China on the end of 2019. The COVID-19 pandemic has caused many sufferers to experience symptoms of depression¹. Natural products have been used for a long time for various ailments including depression.^[1] This literature review aims to describe various types of plants and their mechanisms that can be used to help deal with symptoms of depression during the COVID-19 pandemic. This article was compiled by conducting a literature search using the keywords “covid-19”, “depression”, and “natural products” on PubMed, Scopus and Cochrane Library engine searching and followed the inclusion criteria, namely, the maximum literature publications from the last 10 years in English and discuss natural products that can be used to help overcome depression during the covid-19 pandemic. We found thirteen medicinal plants are noteworthy to be considered as antidepressant drug candidates. The medicinal compounds need to be developed furthermore in the future since Covid-19 pandemic is not over yet. In addition, these herbal medicines hopefully can be alternatives medicine to treat depression that have mild side-effects compared to synthetic drugs.

Key words: COVID-19, depression, natural products

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CYTOTOXICITY AND CELLULAR UPTAKE EVALUATION OF FPGB-0-SO IN COMBINATION WITH HESPERIDIN FOR BNCT AGAINST BREAST CANCER CELLS

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ABSTRACT

Pentagamaboronon-0 (PGB-0), known as a potential boron-carrier agent but has limited water solubility.^{[1][2]} Thus, we develop a new compound, PGB-0 complexed with sorbitol (FPGB-0-so) which has better solubility than PGB-0. In addition, hesperidin, a citrus flavonoid compound, elicits promising anticancer agents towards several cancer cells. This research aims to evaluate the cytotoxicity of FPGB-0-so and in combination with Hesperidin against MCF-7 and MDAMB-231 breast cancer cells. FPGB-0 was complexed with sorbitol using a simple method. The cytotoxic effect was evaluated using WST assay singly and in combination with Hesperidin on the MCF-7 and MDAMB-231 breast cancer cells. Then, the concentration of boron in the cells was carried out by cellular uptake study using ICP-OES. The FPGB-0-So has a low cytotoxic effect against breast cancer cells. Therefore, the combination cytotoxic effect of FPGB-0-so and hesperidin indicates synergist effect against breast cancer cells. However, the combination of Hesperidin and FPGB-0-so did not affect cellular boron uptake in breast cancer. The cytotoxicity of FPGB-0-so against breast cancer cells was lower than that of PGB-0. The novel compound FPGB-0-ol has low cytotoxicity against breast cancer cells and could be applied in boron neutron capture therapy as a boron carrier.

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IDENTIFICATION OF FLAVONOIDS FROM *ACALYPHA INDICA* L. (EUPHORBIACEAE) AS CASPASE-3 ACTIVATORS USING MOLECULAR DOCKING AND MOLECULAR DYNAMICS

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ABSTRACT

Caspase-3 plays an important role in apoptosis and has become a major target for anticancer therapy. Meanwhile, several reports have shown that *Acalypha indica* extract has cytotoxic activity against several cancer cell lines, and other reports have shown various chemical constituents of this plant. However, until now, there has been no report on the cytotoxic mechanism and what compounds are responsible for this activity. Therefore, in this study, an investigation of structure-based molecular interactions focused on the molecular dynamics between the flavonoids contained in *A. indica* L. and caspase-3 was carried out. In a computer simulation, ten flavonoids from *A. indica* L. (Euphorbiaceae) were evaluated against caspase-3. The X-ray crystal structure of human caspase-3 was retrieved from <https://www.rcsb.org/structure/>. Molecular interactions were studied using AutoDock 4.2 software and followed by molecular dynamics (MD) simulations using Amber18 software. The results of molecular docking identified the top four compounds, namely nicotiflorin, naringenin, hesperetin, and kaempferol, with bond free energies of -6.81, -6.45, -6.33, and -6.10 kcal/mol, respectively. According to the molecular dynamics simulation results, nicotiflorin was most effective in stabilizing the complex with caspase-3, with a total energy (ΔG_{bind} , MMGBSA) of -96.315 kcal/mol. It can be concluded that nicotiflorin is the flavonoid in *A. indica* L. that can most effectively activate caspase-3.

Keywords: *Acalypha indica*, caspase-3, molecular docking, molecular dynamics simulations, MMGBSA

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IN VIVO AND IN SILICO STUDY OF PARSLEY LEAF (*Petroselinum crispum* Mill) FRACTION ON GLUTATHIONE S-TRANSFERASE (GST) RECEPTORS AS AN ANTI-SCABIES

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ABSTRACT

Scabies is an infectious skin disease by *Sarcoptes scabiei* through direct or indirect contact with animals or sufferers of scabies. Parsley leaves (*Petroselinum crispum* Mill.) to contain quinone and coumarin which have antiparasitic and anti-inflammatory activities.^[1,2] The purpose of this study was to determine the anti-scabies activity of the n-hexane and ethyl acetate fractions in vivo and in silico at the Glutathione S-transferase (GST) receptor. The animals treatment in rabbits (*Oryctolagus cuniculus*) which were divided into 5 groups. The first group is control normal the 2nd group was Na CMC 0,5% control, the 3rd group was Pemethrin 5%, the 4th group was 0.15 g/ml n-hexane fraction and 5th group ethyl acetate fraction was 0.15 g/ml. The molecular docking was made in AutoDock Tools and re-docking with AutoDock Vina. 3D structure compound obtained from LC-MS/MS data of n-hexane and ethyl acetate fractions obtained through Knapsack 3D.^[3] Receptor was obtained from the PDB ID :1XW5. The results obtained on the n-hexane and ethyl acetate fractions of parsley leaves (*Petroselinum crispum* Mill.) showed anti-scabies activity at a concentration of 0.15 g/ml on day 7 and The molecular docking evaluation of 1,3-Dihydroxy-2-hydroxymethylantraquinone-3-O-β-D-xylopyranose(1-6)-β-D- glucopyranoside (-8,8 Kcal/mol), aviprin -6.7 kcal/mol and xanthotoxin -6.5 kcal/mol.

Keywords: Scabies, Glutathione S-transferase (GST), *Petroselinum crispum* Mill.

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IN VITRO AND IN SILICO ACTIVITY OF CASSIA ALATA ETHANOL EXTRACT AGAINST MALASSEZIA FURFUR

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ABSTRACT

Malassezia furfur is a fungus considered one of the causes of *Malassezia folliculitis* and associated with dandruff. [2,3] *Cassia alata* which contains saponins, steroids, and flavonoids can inhibit fungal growth. [1]The purpose of this study was to determine the antifungal activity of the ethanolic extract of the leaves of *Cassia alata* against *Malassezia furfur* *in vitro* and *in silico*. This research is make in concentrations of 0.05 g/ml, 0.1 g/ml, 0.15 g/ml, 0.2 g/ml, 0.3 g/ml, 0.4 g/ml. The method used is agar diffusion and molecular docking using AutoDock Tools software and re-docking using AutoDock Vina with the Lanosterol 14-alpha demethylase receptor was obtained from homology modeling. The evaluation results at concentrations of 0.05 g/ml, 0.1 g/ml, 0.15 g/ml, 0.2 g/ml, 0.3 g/ml, 0, 4 g/ml has a very large diameter inhibition zone against *Malassezia furfur* with test results of significant value ($p < 0.05$) and in molecular binding to the Lanosterol 14-alpha demethylase receptor, the compound Nicotiflorin -9.9 kcal/mol, Kaempferol3-O-Gentiobioside -9.5 kcal/mol, Luteolin -8.7 kcal/mol, Kaemferol -8.6 kcal/mol and Chrysoeriol -8.6 kcal/mol. The conclusion of this study shows that the ethanol extract of *Cassia alata* can be recommended as agents of inhibiting the growth of the fungus *Malassezia furfur*.

Keywords: *Malassezia furfur*, *Cassia alata*, Lanosterol 14-alpha demethylase

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DIABETES KNOWLEDGE AND TRANSCULTURAL HEALTH CARE UTILIZATION AMONG PATIENTS WITH DIABETES MELLITUS IN BANDUNG SUB-DISTRICT, WEST JAVA, INDONESIA

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ABSTRACT

Understanding the healthcare utilization among diabetes patients is crucial for encouraging the continuity of care and strengthening it in the communities in general¹. While most studies on health care utilisation are currently limited by the use of one medical system - generally speaking, the modern medical system - the present study has a primary focus on utilisation across medical systems, namely modern, transitional, and modern medical system. This study adopt the Leiden Ethnosystem Approach which is conceptualised in the model of the mutual relation analytical model of transcultural health care utilisation. This study finds that the majority of diabetes patients in the research area have a low to average level of knowledge on diabetes symptoms, risk factors, and treatment. Patients' level of education, income, and occupation have been reported to have a significant association with the level of knowledge on symptoms, risk factors, and treatment of diabetes mellitus. Furthermore, out of 388 utilisation rates, traditional medicine accounted for 27.1% utilisation, transitional 29.5% and modern 43.8% by diabetes patients. Additionally, this study finds that the vast majority of diabetes patients choose transitional medicine as the first choice of treatment (47.2%, n=100).

Keywords: transcultural healthcare, diabetes, traditional medicine

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REPELLENT ACTIVITY OF EXTRACT AND ESSENTIAL OIL FROM ZINGIBERACEAE FAMILY AGAINST *Aedes aegypti*

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ABSTRACT

Aedes aegypti mosquito is the main vector for dengue fever, an endemic infectious disease spreading in tropical areas, especially in Indonesia. The high rate of this spreading encourages to conduct the best prevention in reducing the incidence of this disease by controlling the mosquitoes and avoiding their bites.^{[1][2]} In correlation with this, some Zingiberaceae plants are known to have the potential as a repellent.^[3] So, this study aims to investigate the repellent activity of extracts and essential oil from the rhizome of Zingiberaceae plants against *A. aegypti* mosquitoes. The repellency test was conducted by observing the numbers of mosquitoes that settle on some of the volunteers' hands in a certain time period and then calculating their protection ability.^[4] The results showed that the highest repellency was observed in the essential oils of *Zingiber cassumunar* with a protection ability average of 91.38%. In addition, the GC-MS analysis showed the presence of monoterpene dan sesquiterpene (alpha-terpinolene, γ -terpinene, beta-bisabolene, limonene, and beta-bisabolene, 4-terpineol, sabinene, α -pinene, α -terpinene) components in the essential oils. This study suggested that this essential oil can be developed as a natural repellent product for preventing dengue fever.

Keywords: Zingiberaceae, essential oils, repellent, *Aedes aegypti*,

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ARTICLE REVIEW: CHEMICAL AND PHARMACOLOGICAL PROPERTIES OF SELECTED SPECIES FROM GENUS *Premna* AND THEIR IMMUNOMODULATORY POTENTIALS

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ABSTRACT

Epidemiological data today show an increase in immune diseases, hence increasing awareness to maintain and increase the body's immunity is essential.^[1] Immunomodulators are substances that improve the human immune system by stimulating, inhibiting, or regulating components in the immune system. Immunomodulators can affect the work of cells in the immune system, antibodies, cytokines, apoptosis, and others. Plants are known to produce secondary metabolites which provide beneficial effects on human health including immunomodulatory properties. Some of medicinal plants which have immunomodulatory properties belong to the genus *Premna* from *Lamiaceae*. Given the importance of the immunomodulatory potential of several species from genus *Premna*, the present work reviews the immunomodulatory activity of some species in genus *Premna* by performing web searching through Elsevier, PubMed, Mendeley, and Google scholar. In this review is presented a series of selected plants from genus *Premna* sp. including their chemical and pharmacological properties as well as immunomodulatory potential. Furthermore, this review also discusses biological screening methods for various medicinal plants that focus on revealing the mechanism involved in immunomodulation.

Keywords: *Premna* sp., immune system, immunomodulatory agent, medicinal plants

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PHYTOCHEMISTRY AND PHARMACOLOGICAL POTENTIALS OF *PREMNA SERRATIFOLIA* L.: TRADITIONAL MEDICINAL PLANTS USED BY LOCAL PEOPLE IN KALIMANTAN

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ABSTRACT

Millions of people all over the world are using herbal medicines from thousands of years, due to their great interest in traditional medicines and they believe that herbal medicines are effective for the treatment of certain diseases. The different parts of the plant like leaves, stem, stem barks, root, root barks, and wood have been used for extraction purposes. Based on many research, bebuas (*Premna serratifolia* L.) had many pharmacological activities. Bebuas contains various chemical constituents or secondary metabolites namely flavonoids, saponins, tannins and triterpenoids/steroids that have a role for pharmacological activity¹. The aim of this review article is to review the pharmacological potentials of *Premna serratifolia* L. In this review article, the international research databases including MEDLINE, Google scholar, EBSCO, Academic Search, Web of Science, SciVerse, Scopus (SCOPUS), EBSCO, Academic Search, and Cochrane, were searched using the key words *Premna serratifolia* L., *traditional medicine*, *medicinal plants*, and *pharmacology*. The pharmacological activities which are discussed further in the review including antioxidant, anti-arthritic, anticholesterol, anti-inflammatory, antibacterial, antifungal, antihelmintic, antidiabetic, and anticancer. The study suggest that the plant *Premna serratifolia* L. is a potent source for phytomedicine further development.

Keywords: bebuas, *Premna serratifolia* L., *pharmacological effect*, *traditional medicine*

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REVIEW ARTICLE: MEDICINAL PLANTS WITH MULTIPLE PHARMACOLOGICAL PROPERTIES FOR THE PREVENTION OF INFECTION ON PATIENT WITH CHRONIC METABOLIC DISORDERS

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ABSTRACT

In healthy organism, the immune system maintains homeostasis within the body. The function and efficiency of the immune system are influenced by various exogenous and endogenous factors resulting in either immunosuppression or immunostimulant. Several agents possessing an activity to normalize or modulate pathophysiological processes are called immunomodulators.^[1] The aim of this review article is to introduce the medicinal plants that exert multiple effect not only as immunomodulator but also has pharmacological effect on hypertension, hyperlipidemia, obesity, and diabetes. In this review article, the international research databases including MEDLINE, Google scholar, EBSCO, Academic Search, Web of Science, SciVerse, Scopus (SCOPUS), EBSCO, Academic Search, and Cochrane, were searched using the key words hyperlipidemia, hypertension, diabetes, herbal, obesity, and phytomedicine. The plants that were effective on one, two, three, or all of four diseases were determined. Then for the selected medicinal plants were searched for their immunomodulatory effect. Regarding the findings of this study, we can conclude that some medicinal plants can be used to improve immune system on patient with metabolic disorders.

Keywords: medicinal plants, immunomodulator, chronic disease, metabolic disorders

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SYNTHESIS AND CHARACTERIZATION OF SORGHUM (*Sorghum bicolor* L.) STARCH BASED BIOPLASTICS WITH COMBINATION OF ALPHA-CELLULOSE AND POLYVINYL ALCOHOL

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ABSTRACT

Bioplastics are a type of plastic that can be naturally recycled by biological processes. This type of plastic can be made from renewable resources such as vegetable oils and starches, thus it can be limiting the use of fossil fuels and protect the environmental health^{1,2}. Sorghum (*Sorghum bicolor* L. Moench) is one of the plants that contains a large amount of starch, with a starch content of around 72-85%. Combinations of alpha-cellulose and sorghum starch gave better mechanical properties in bioplastic, but the tensile strength and water resistance still need to be improved³. Adding polyvinyl alcohol (PVA) to bioplastics can increase the value of tensile strength, modulus of elasticity and water resistance^{4,5}. This study aims to produce bioplastic by combining sorghum starch with alpha-cellulose and PVA followed by characterizing the bioplastic product. The research includes several stages which are collecting materials and determination of plants, preparation of sorghum seed flour, extraction and quantitative analysis of sorghum starch, production and characterization of bioplastics, and testing the biodegradability of sorghum starch based bioplastics. The results showed that bioplastics with characteristics closest to those of bioplastics on the market were obtained at a starch:alpha-cellulose:PVA ratio of 7.5:2.5:0.4 (PSV 4) with tensile strength value of 8.625 ± 0.049 N/mm², elongation at break $5.285 \pm 0.601\%$ and modulus of elasticity 1.235 ± 0.092 GPa. PSV 4 has a density value of 1.305 ± 0.01 g/cm³ with water absorption capacity $23.625 \pm 1.571\%$ and was degraded $68.31 \pm 1.243\%$ in 15 days.

Keywords: bioplastic, sorghum, starch, polyvinyl alcohol

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OPTIMIZATION OF ACYCLOVIR SUSPENSION: FORMULATION DEVELOPMENT USING NA-CMC AND QUALITY CONTROL OF FINISHED PRODUCTS

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ABSTRACT

Acyclovir is widely used as a potent antiviral drug to treat viral infections of the herpes and varicella zoster families. Unfortunately, the drug has a very poor oral bioavailability character (15-30 %). The purpose of this study was to develop a formulation of acyclovir suspension with a simple suspension method using Na-CMC (carboxymethylcellulose sodium), and to carry out quality control of the finished product. The formulation was developed by designing variations in Na-CMC concentration, and quality control including pH, viscosity, dispersibility, storage stability, microscopic measurement, sedimentation volume, and evaluation of acyclovir levels. Quality control is to evaluate the suspension in order to obtain good and stable physicochemical properties of the suspension. Design variations of Na-CMC concentrations of 1.4%, 1.5%, and 1.6% resulted in a homogeneous suspension and easily dispersed perfectly. The three formulas did not have a significant difference in the value of viscosity, permeability, and sedimentation volume which were not significant. All formulas have pseudoplastic flow properties, with good particle size uniformity in the range of 0–13 μm . The stability of pH during storage time was shown by the formula with 1.5% Na-CMC. The acyclovir suspension with 1.5% Na-CMC concentration was the best compared to the other formulas in terms of stability and physicochemical properties.

Keywords: acyclovir, suspension, formulation, quality control, Na-CMC, spectrophotometer UV-Vis

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SEAHORSE (*Hippocampus comes* L.) EXTRACT: HOW SAFE IS IT'S USE ON THE HEMATOLOGICAL PROFILE AND BODY WEIGHT?

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ABSTRACT

The seahorse (*Hippocampus comes* L.HcL) is one of the marine fish which is has a medicinal used as a natural product. This value needed to explore the safety use a seahorse extract HcL in hematological profile and body weight on rats induced by depot medroxyprogesterone acetate (DMPA). This experimental study used thirty adult male *Sprague-Dawley* rats (200-250 g; 8 weeks old). All rats were intramuscular administered 1.25 mg/kgbw DMPA. The groups into 5 main groups (6 each), following aquadest (G1), CMC 1% (G2), seahorse extract dose 150 mg/kgbw (G3), 225 mg/kgbw (G4), and 300 mg/kgbw (G5). The hematological profile was analyzed with whole blood from the heart, and the body weight from measurement in everyday until 18 weeks. This present study found there were no significant differences in all groups in hematological profile and body weight. Therefore, we are finding the seahorse extract HcL tends improving hematological profile and body weight, but still in the normal range. Our find out that seahorse extract HcL safety on hematological profile and body weight in rats induced DMPA.

Keywords: Seahorse, safety, hematological profile, body weight, DMPA.

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ANTIHYPERLIPIDEMIC ACTIVITY OF BLACK GARLIC EXTRACTS IN RATS FED A HIGH-FAT DIET

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ABSTRACT

Research has been carried out on the antihyperlipidemic activity of black garlic extract (BGE) on male white rats of the Wistar strain induced during endogenous and exogenous hypercholesterolemia (propylthiouracil 0.01%) and exogenous. Fasting serum lipid levels were determined using the CHOD-PAP, CHOD-PAP and GPO-PAP methods. Ethanol extract suspended in 2% PGA was administered orally every day at doses of 100, 200, and 300 mg/kg BW for twenty-one days. The results showed that BGE at 21 days could reduce total cholesterol, LDL-cholesterol, and triglyceride levels, and significantly increase HDL-cholesterol levels ($\alpha = 0.05$ and $= 0.01$).

Keywords: Black garlic, total cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol

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MORINDA CITRIFOLIA L. AND CINNAMOMUM BURMANNI AND ITS ANTIHIPOGLYCEMIC ACTIVITY

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ABSTRACT

Previous research showed that the combination of 700 mg/kgBW of *Morinda citrifolia* L. (MC) 1.12 g/kgBW of *Cinnamomum burmanni* (CB) and 1.4 g/kgBW of *Trigonella foenum-graecum* L. has hypoglycemic activity.^[1] But the dose of this combination is still too large to be developed into oral preparation such as tablets or capsules and can make the patients uncomfortable. So in this study, will be tested only combination of two plants (MC and CB). MC was collected from Indonesian Medicinal and Aromatic Crops Research Institute (IMACRI/BALITRO) while CB was from Experiment Garden Manoko, West Java, Indonesia. The extraction method using maceration with Ethanol for 3x24 hours. Extract yielded were 14.44% of MCE and 23.01% of CBE. Evaluation of water content showed that 9.81% of MCE and 7.98% of CBE. Phytochemical screening^[2] result reveals that flavonoids, quinone, polyphenols, steroids and mono-sesquiterpens were contains both in MCE and CBE, whereas saponins and tannins only detected in CBE. Hypoglycemic activity test method using Glucose tolerance in male mice.^[3] The results showed that (in mg/kgBW) 4 (MCE 700+CBE 100) gave better hypoglycemic activity compared to 1 (MCE 700), 2 (CBE 100), 3 (MCE 700+CBE 50) and 5 (MCE 700+CBE 200). The reduction in average relative blood glucose levels (%) of 4 were 32.38; 42.51; 48.22; and 45.12 at 30, 60, 90 and 120 minutes, respectively. Statistically, all groups gave a significant difference compared to the negative control at each observation time with 95% confidence. But this value is still smaller than the positive control Glibenclamide.

Keywords: *Morinda citrifolia* L., *Cinnamomum burmanni*, hypoglycemic activity, phytochemical screening

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IN VITRO PERMEATION OF CATECHIN TRANSETHOSOMAL GEL (*Uncaria gambir*, Roxb)

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ABSTRACT

In vitro research on catechin transethosomal gel permeation has been carried out. Gambir (*Uncaria gambir* Roxb.) contains a bioactive component of catechins which have activity against cholesterol reduction through inhibition of HMG Co-A reductase in cholesterol biosynthesis [1]. Orally administered catechins have low bioavailability, so another route of administration is needed, such as transdermal delivery [2]. The formation of catechin transethosomes loaded in the gel preparation aims to increase permeation through the stratum corneum [3]. The aim of this study was to determine the permeation and release kinetics of the catechin transethosomal gel preparation. The permeation test was carried out *in vitro* using Franz Diffusion cells with PTFE membrane. The results showed that the permeation values of the catechin gel preparations and the catechin transethosomal gel were 17.31% and 18.80%, respectively. The release kinetics of the two gel preparations followed the Higuchi kinetic model.

Keywords: catechin, transethosome, permeation, *in vitro*

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ANALYSIS OF ESSENTIAL OIL ACTIVITIES OF INDONESIAN AROMATIC PLANTS COMPOUNDS AS REPELLENT USING HEADSPACE GC-MS

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ABSTRACT

Essential oils are secondary metabolites of the terpene group that can be obtained from cinnamon (*Cinnamomum verum*), clove (*Syzygium aromaticum*), nutmeg (*Myristica fragrans*), patchouli (*Pogostemon cablin*), citronella grass (*Cymbopogon nardus*), lemon grass (*Cymbopogon citratus*), or turmeric (*Curcuma longa* Linn). This research aimed to determine the potential of essential oils from these plants as a repellent against the *Aedes aegypti* mosquitos. The research began by preparing a sample of each plant as much as 5000g, then steam distillation was carried out for each sample to isolate the essential oil. The stages were continued by calculating the rendement of the isolation results where and obtained the rendement of the cinnamon, clove, nutmeg, patchouli, citronella grass, lemon grass, and turmeric of 1.9%, 16%, 16.8%, 2.2%, 1.4%, 0.9%, and 6.8%, respectively. The next stage was making the essential oils at a concentration of 10% and then tested for its repellent activity against the probandus. The test took place from the 0th hour to the 6th hour and was repeated three times so that the average percentage of the repellent activity of the cinnamon, clove, nutmeg, patchouli, citronella grass, lemon grass, and turmeric were 94.7%, 80.4%, 85%, 95.2%, 72.2%, 71.5%, 72.1%, respectively. The results of hypothesis testing using one way ANOVA indicate that the data were normally distributed indicated by the normality significance value of ≥ 0.05 . From the results of the homogeneity test, a significance value of $0.068 \geq 0.05$ was obtained indicating that the repellent data were homogeneous. From the one way ANOVA test, obtained a significance value of $0.00.000 \leq 0.05$. Based on these results, it can be concluded that there are significant differences in the results between the essential oils of the plants as a repellent against the *Aedes aegypti* mosquito.

Keywords: Essential oil, Rendement, Repellent

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