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PROCEEDING
INTERNATIONAL SEMINAR

CHALLENGES OF THE DEVELOPMENT OF NATURAL COMPOUND AS DRUG FOR INFECTIOUS & DEGENERATIVE DISEASES

Faculty of Pharmacy & Sciences
University Of Muhammadiyah Prof. DR. HAMKA
(UHAMKA)
Jakarta, January 10, 2015

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Assalamu'alaikumWr.Wb.

Distinguished ladies and gentlemen

First of all, on behalf of FFS UHAMKA, I would like to welcome to all of you in FFS UHAMKA Jakarta. Thank you very much for your attention to come and attend the international seminar in FFS UHAMKA. I hope we are all in health condition and in the shadow of God.

The conference is organized by FFS UHAMKA in collaboration with sponsors like PT. Triasindo Jaya , Indolab and UHAMQUA. This event is as part of the routine activities with the purpose are: discuss an update on the challenges of drug development for infectious and degenerative diseases based on natural product and provide a forum for exchange of information on the latest technologies involved in the development of natural compounds as drug.

In this seminar participants from student, lecturer, researchers have been attanded and 4 speakers within field of Pharmaceutical sciences will be presented paper with theme "Natural Compound as Therapy for Infectious and Degenerative Diseases". Besides that, this conference followed by presentation researchers in form of oral and poster presentation. Herewith we would like to express our gratitude to all participants, presenters, and special thanks to plenary speakers for joint us to day to share advance knowledge and expertise in this scientific event in FFS UHAMKA.

The FFS gratefully acknowledges the Rector of UHAMKA University, minister of Health of Indonesia, and sponsors for the nice collaboration in bringing this seminar. Furthermore, personally, I would like to express my deep appreciation to members of the Organizing Committee, for the good teamwork and their great effort to bring success to the seminar.

Finally, I wish all participants could benefit from the seminar and have an enjoyable moment in FFS UHAMKA Jakarta.

I look forward to thank you all for attending this seminar

Wassalamualaikum Warrohamatullahi Wabbarokatuh

Drs. H. Budi Arman, M. Kes, Apt.

COMPARISON OF SODIUM LAURYL SULPHATE, SODIUM BENZOATE, POLYAETHYLENE GLYCOLUM 6000 AS LUBRICANT ON DISSOLVING TIME OF EXTRACT CIPLUKAN (*Physalis angulata* L.) EFFERVESCENT TABLET

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ABSTRACT

Ciplukan is a plant that widely used as a traditional medicine e.g : anti-inflammatory, bronchitis, ulcers, cancer, tumors, leukemia and diabetes mellitus due to chemical compounds like saponin , terpenoids, and alkaloids. This research was conducted by making extract ciplukan effervescent tablet using sodium lauryl sulfat, PEG 6000 and sodium benzoate as lubricant. This tablet was made in 3 formula i.e 2% of sodium lauryl sulfat (F1), 3% of PEG 6000 (F2) and 4% of sodium benzoate. The tablet was evaluated for weight uniformity, size uniformity, hardness, friability, dissolve time, and pH's test. The result shows that the comparison of lubricant can give different in dissolving time. Formula II shows the dissolving time quicker than formula I and formula III. By one way ANOVA analyses with 95% of significance level , among all combinations showed a significant differences.

Keywords: Sodium Lauryl Sulphate, PEG 6000, Sodium Benzoate, Extract Ciplukan Effervescent Tablet

INTRODUCTION

Ciplukan is a plant that widely used as a traditional medicine e.g : anti-inflammatory, bronchitis, ulcers, cancer, tumors, leukemia and diabetes mellitus due to chemical compounds like saponin , terpenoids, and alkaloids. Based research, herbal water extract ciplukan (*Physalis angulata L.*) at a dose of 10 mg / kg body weight can lower blood glucose levels alloxan-induced mice (Sutjiatmo et al. 2011). In this study the yield of the extract obtained 36.26%. The bioavailability of diabetes tablet dosage forms of requires a long time to be absorbed Therefore, the leaf used ciplukan (*Physallis angulata* L.) as antidiabetic drugs in effervescent tablet dosage form.

Effervescent tablets are used to make beverages practical. In the manufacture of effervescent tablets used material soluble lubricant to get the best time of the third comparison of this lubricant. Lubricant materials used in effervescent tablets are sodium lauryl sulfate, sodium benzoate, and PEG 6000. Efficient lubricants are generally insoluble in water and give turbid

solution after disintegration. Magnesium stearate as a lubricant does not cause the release of the drug particles from the unit (Stewart, 1981). Magnesium stearate coating will stick and granule. Magnesium stearate will give a negative effect on disintegration time and dissolution rate of tablets (Bossert, Stamm, 1980). Plus magnesium stearate is hydrophobic so that a layer of magnesium stearate that happens will impede penetration of liquid medium to crush the tablet and the dissolution of the drug (Soebagyo 1994).

Has conducted research that the presence of polyethyleneglycol 6000 as a lubricant material will accelerate the disintegration time of tablets, the higher its level of polyethyleneglycol 6000, faster time destruction. Because polyethyleneglycol 6000 hydrophilic and soluble in water, the contact time with water tablets, polyethyleneglycol 6000 will cause the tablet dissolves easily and quickly destroyed as conducted research that the addition of surfactant sodium lauryl sulfate as a lubricant effective in accelerating disintegration and dissolution of the active substance.

Sodium lauryl sulfate may improve wetting and penetration of the solvent into the tablet as a result of the decline in surface tension between the surface of the tablet particles and solvent (Alatas et al. 2006). Sodium benzoate can be used as a water-soluble lubricant. Has conducted research on sodium benzoate in effervescent tablet tamarind fruit pulp extract with the lowest tablet hardness and friability of tablets were high but longer tablet dissolution (Annisa 2011). Supposedly if you have a tablet hardness and friability of tablets least high then the time should be faster dissolution. For the used lubricants sodium benzoate on this ciplukan extract which is expected to produce a rapid dissolve.So that the resulting effervescent formula can produce a soluble effervescent tablets faster and attract consumers to be used as an alternative dosage form of diabetes mellitus in a more enjoyable. Based on the above background, it is necessary to research on the comparison of the use of sodium lauryl sulfate, sodium benzoate, and PEG 6000 as a lubricant to time ciplukan extract soluble effervescent tablets *(Physalis angulata L.)*

MATERIAL AND METHODS

Ciplukan dry extract powder as made at IPB (Institute Pertanian Bogor) . Ciplukan extract powder was made spray dry methods. Sodium benzoat, PEG 6000 , Sodium Lauril Sulfat , citric acid , tartaric acid, PVP,Sorbitol as a gift sample from Kimia Farma PT. All other chemicals and reagents used were analytical grade and were used as gift.

METHODS

Preparation of ciplukan dry extract powder

Ciplukan extract was made dry powder extract ciplukan in IPB (Institut Pertanian Bogor). Ciplukan extracts diluted with 3 liters of water, then add 35% maltodextrin as filler after it is dried by spray drying at 175^0C inlet and outlet temperature of 75^0C for 2 hours until it becomes dry powder

Evaluation of ciplukan dry extract powder

Organoleptic test include color, smell, taste and the water content test : enter the 1.7 to 2 grams of dry powder into the tool let moisture balance until the temperature rises up to 105^0C for 5 minutes after it will get the percent moisture content of the sample.

Preparation of tablet

All tablet formulations with different drug to lubricant ratio were prepared by wet granulation. (Table. I) All powdered were weighed acctuately in electronic balance then passed separately. A number of citric acid, tartaric acid, cipluka powder, part of sorbiton and part of PVP (diluted at ethanolum) with a specific weight ratio is place, grind in mortar until homogenous and then sieved by 14 mesh sieve and storage in oven at 50^oC for 7 hour . After than sieved granul with 16 mesh sieve .(mass 1). A number of sodium bicarbonat, a part of sorbitol and a part of PVP (diluted at ethanolum) with a specific weight ratio is place, grind in mortar until homogenous and then sieved by 14 mesh sieve and storage in oven at 50^oC for 7 hour (mass 2). After than sieved granul with 16 mesh sieve Mix the acid (mass 1) and alkaline (mass 2) granules then add lubricant. Evaluated the granules. Rotary eight station punch tablet machine was used to press tablets of 4 g weight.

Table I. Formula of Effervescens tablet

Material	F1(mg)	F2 (mg)	F3 (mg)
Ciplukan extract	562,7	562,7	562,7
Citric Acid	630,39	630,39	630,39
Tartaric acid	450,27	450,27	450,27

Sodium bicarbonate	1260,15	1260,15	1260,15
PVP	120	120	120
Sodium Lauril Sulfat	80	-	-
PEG 6000	-	120	-
Sodium Benzoat	-	-	160
Apple Flavour	50	50	50
Sorbitol ad	4000	4000	4000

Evaluation of effervescens granules

Water contents test (Fausett et.al.,2000), fluidity test, angle of rest , compressibility test and granul size distribution.

Evaluation of effervescens tablet

There effervescens tablets of each formulation were examined for their diameter, thickness and height of tablet by using micrometer gauge (MOH, 1979).

Weight variation : to study weight variation, 20 tablets of each formulation were weighed individually using four digital elektronic balance (Sartorius Pioneer).

Determination of tablet hardness. The crushing strength of the tablet was measure by YD-2 Tablet Hardness Tester. Tablet hardness tester which applies compression force diametrically to the tablet. The force required to crush the tablet was recorded as hardness of the tablet in kg/cm^2.

Determination of tablet friability. The friability was determined by weighing 10 tablets and placing them in a Guoming CS-2 type friability apparatus and rotating it at 25 rpm for 4 minutes (i.e 100 drops). After dusting tablets were weighing for the final weight and the % friability was calcilated as follows :

$$\% \text{ friability} : \{ \frac{\text{weight initial-weigth final}}{\text{Weight initial}} \} \times 100$$

Dissolving time. This test was used for guidance to monitor the development of physical changes in tablets morphology when placed in the dissolution medium (Siregar 2010). One of tablet placed in the 200 ml water until the tablet dissolved. Recording the result time.

pH test. Take the effervescent tablet dissolved in 200 ml of water, then measured by using a pH meter pH values obtained are recorded.

RESULTS AND DISCUSSION

Physical properties of Ciplukan powder

Base on phytochemical test result that the ciplukan extract powder contained terpenoids and alkaloid. Organoleptic test is a test that is performed to determine the taste and smell of a material. The resulting dry powder showed that the dry powder form of fine powder, brownish green, bitter taste and distinctive smell. Result of water content are average 3,94%.

Evaluation of granules effervescens

Materials lubricant additives is one important also in the manufacture of effervescent tablets, lubricants used in this research consisted of sodium lauryl sulfate, polyethyleneglycol 6000, and sodium benzoate. The concentration of lubricant F1, F2, and F3 are 2%, 3%, and 4%. The concentration and type of lubricant in this effervescent tablets each different. It is intended as a lubricant want to know which one has the fastest time of the late F1, F2, and F3 and see the impact that would be caused by increasing concentrations of soluble lubricant to time. Evaluation includes water content test, flow velocity, angle of poise, particle size distribution, and tapped bulk density . (Table II)

Table II. Result of granules evaluation

Evaluation	F1	F2	F3
Water content (%)	1,24 ± 0,015	1,20±0,025	1,18±0,030
Flow velocity (g/sec)	9,77 ± 0,332	9,18±0,036	9,38±0,032
Angle of rest (°)	30,16±0,592	29,96±0,648	29,54±0,313
Compresibility (%)	2,671±0,578	3,665±0,578	2,996±0,008
Particle size distribution (µm)	716	729	726

Evaluation of effervescent tablet

Effervescent tablets evaluation included : organoleptic, uniformity size and weight, friability, hardness , pH and solubility time. The results of organoleptic test effervescent tablet has a brown color white and that has been diluted with water has a clear green solution color, slightly sour taste. The comparison of physical properties of the effervecsen tablet (Table III). The weight and thickness of the tablets range from 4.027 to 4.029 and 2.31 respectively.

Tablet hardness is a parameter that affects the solubility time. A tablet must have a certain hardness to resist interference or mechanical shocks. In the persent study , the percentage friability for all the formulation was below 1%, indicating that the friability is within the pharmakopeia limits. The hardness of the tablet was found to be 9,58-9,82 kg/cm2 which show sufficient mechanical strength. All the tablet formulation showed aceptable pharmachotechnicals properties and acceptable acording to pharmacopeia speciffication. Test the pH of the tablet effervescet conducted to determine the acidity of a solution of preparation. Measurements were made by using a pH meter, the results of the study showed that the F1-F3 has pH is 6.83; 6.83; and 6,87. It is proved that the solution is safe to use effervescent tablets orally.At test time effervescent tablets dissolve a process of acid and alkaline reaction which will generate CO2 gas. Time dissolves with the type and concentration of different lubricants, have different solubility time. The results of the formula 1 of 10:15 minutes, the formula 2 at 3:48 minutes, and formula 3 for 4:12 minutes. It shows that the effervescent tablets dissolve meet the timing requirements are less than 5 minutes unless the formula 1. In formula 1 using the lubricant sodium lauryl sulfate. Basically lubricant sodium lauryl sulfate is soluble in water and solubility was fast but because these lubricants include surfactants making the solution generates foam that inhibit this effervescent tablet within a period of dissolution. At the time of effervescent tablets of formula 1 was added to water, the tablet should react more effervescent tablets. CO2 gas produced will produce a layer of foam on top and make effervescent tablets for long pushed to the top, when the effervescent tablet dissolves pushed up process begins to slow down because of the foam covering and inhibiting this tablet to dissolve freely and quickly.Unlike the formula 2 and 3, namely lubricants PEG 6000 and sodium benzoate which produces a rapid dissolve and meet the requirements. Although with different concentrations of PEG 6000 3% and 4% sodium benzoate but these lubricants are both hydrophilic lubricant which makes time ciplukan extract soluble effervescent tablet is fast. Plus sodium benzoate and PEG 6000 which has the form of powder so that the finer the particle size, and it can improve the wetting which makes the tablet will quickly dissolve. The big difference in the results of a late time in each formula due to differences in the type of lubricant used.

Table III. Result of tablet effervescent evaluation

Evaluation	F1	F2	F3
Uniformity of weight (g)	4,029±0,051	4,027±0,034	4,027±0,046

Uniformity of size (mm)	T/D: 0,57/2,31	T/D: 0,57/2,31	T/D: 0,57/2,31
Hardness tes (kg)	9,58±0,385	9,91±0,183	9,82±0,319
Friability test (%)	0,46±0,040	0,59±0,027	0,55±0,058
Dissolving time (min)	10:15	3:48	4:12
pH of solution	6,83	6,83	6,87

The test results were analyzed with the late time statistical calculations. Begins with a normality test to determine the resulting data were normally distributed or not. The results obtained show the data are normally distributed. Furthermore, followed by a one-way ANOVA (One Way ANOVA), to test whether a late third formulas are significantly different or not. Results of one-way ANOVA statistical calculations obtained sig = 0.000 The results showed significantly smaller than 0.05, then the third formula results show significant difference.To see more clearly the existence of significant differences in each formula Tukey HSD test results showed an average difference significant at the formula 1 of the formula 2 and 3, the formula 2 of the formula 1 and formula 3 of the formula 1.

CONCLUSIONS

From the results of this research concluded that the time-soluble lubricant formula PEG 6000 is faster than the lubricant sodium benzoate and sodium lauryl sulfate.
In this research, sodium lauryl sulfate as a lubricant slow time ciplukan extract soluble effervescent tablets, it is necessary to do more research on other additives that may affect the timing soluble tablets of other natural materials.

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