

# Hariyanti-In Vitro Release of Metformin HCl from Polyvinyl Alcohol (PVA) - Gelatin Hydrogels Prepared by Gamma Irradiation

*by Hariyanti Uploded By Wieda*

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# In Vitro Release of Metformin HCl from Polyvinyl Alcohol (PVA) - Gelatin Hydrogels Prepared by Gamma Irradiation

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## ABSTRACT

The aim of this present work is to use polyvinyl alcohol (PVA) – gelatin-based hydrogel prepared by  $\gamma$ -rays irradiation with different gelatin concentrations ranging from 0.5 - 2 %w/v for immobilization of Metformin HCl (MH) at dose range of 0 - 30 mg. The mixture were freeze-thawed for 3 cycles, irradiated using  $\gamma$ -rays with sterilization dose at 25 kGy (dose rates 18 kGy/h). Gel fraction and water absorption were determined gravimetrically. The surface morphology of hydrogels were observed using Scanning Electron Microscope (SEM). In vitro release of MH were taken using UV-Vis spectrophotometer. After evaluated, it was found that with increasing gelatin concentrations, gel fraction increases and water absorption decreases. With increasing gelatin concentration and drug dosage, the cumulative drug released decreases. From SEM observation, the hydrogel had a heterogeneous porous. The hydrogel based on PVA-gelatin can be considered as a matrix for controlled drug release and safe for humans since both PVA and gelatin are non-toxic.

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## INTRODUCTION

Metformin HCl is a type-II antidiabetic drug that works to reduce excessive sugar levels in blood plasma. The advantages of metformin as a water-soluble drug are the low risk of hypoglycemia, and able to reduce the probability of heart damage and death. Metformin is an anti-hyperglycemia drug that is not completely absorbed in the intestine with a bioavailability of about 50 - 60 % in a half-life of 1.5 to 4.5 hours. The disadvantage of metformin is its usage frequency of 2 to 3 times a day with relatively large doses, which can reduce patient compliance. A formula that can maintain the plasma level of metformin and can last for 10 - 16 hours may be adequate in a single dose of metformin. Therefore, sustained products release are needed to entrap metformin which is useful for

extending drug working time and improving patient compliance [1].

Recent progress and attempts were made on the oral sustained or controlled release formulation for metformin. Various methods are available to formulate water-soluble drugs into sustained release dosage forms by retarding the dissolution rate such as matrix tablets, coated tablets, floating tablets, slow release granules, sustained release oily matrix, sustained-release microparticles, and elementary osmotic pump [2-6]. For all these purposes, synthetic or natural polymers are used i.e. ethylcellulose, methylcellulose, PVP, gum, agar, microparticle, HPMC, etc. All the controlled release dosage forms available for metformin claims to release the drug up to 8 hours. These required the drug administration for 2 to 3 times a day, which is unfeasible for a single dose formulation. In some cases, the optimum release of drug was shown but only as an in vitro data. In vivo release was studied

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under animals only. Further clinical studies are needed to assess the benefit of these systems for patients suffering from hypotension. Extensive studies are required to examine the factors that play a role in development of controlled release formulations of metformin. Surprisingly, despite all these research works, there are likely to be no well established metformin controlled release formulations reported to be available in the market. One candidate that has good prospects as a matrix for drug immobilization is a hydrogel. The development of the metformin in the form of immobilization has several advantages, for example reducing the frequency of drug use and minimizing the fluctuations in blood concentrations of drugs that reduce the side effect, among others [7].

Hydrogels are hydrophilic polymers with three-dimensional polymeric network, large molecular weights, and are insoluble in water. They have porous structure, which means that water and small molecules can easily diffuse across the pores. Their unique properties such as biocompatibility, biodegradability, sensitivity to various stimuli and the ability to be conjugated easily with hydrophilic and hydrophobic therapeutic compounds, have made them important candidates in drug immobilization [8-11].

Drug immobilization technique of the hydrogel is one of the drug delivery methods currently being developed intensively in pharmaceutical industries as well as in medicine [12]. Drug immobilization is one of the techniques for an entrapped drug in hydrogels; and released in a medium that can be controlled for a certain period of time. In general, immobilization of drugs in hydrogels can be done in two ways, namely *in situ* loading and *in situ* loading [13,14]. For *in situ* loading, the drug is entrapped after the hydrogels is formed. Whereas for *in situ* loading, the drug is simultaneously entrapped during synthesis process. Basically, drug immobilization technique is physically entrapping the drug in the matrix; the drug does not undergo chemical reactions with the hydrogels and the drug can be separated from the hydrogels in a controlled time interval [15]. One of the potential hydrogels to be used as a drug delivery is gelatin.

Gelatin is a natural, non-toxic, inexpensive polymer compound, biodegradable polymer, denatured protein obtained from the collagen acid and base process [16]. Gelatin has popular properties in the biomedical field including easily degraded, low immunogenicity and toxicity, a very large potential capacity to be modified on the active site of its amino-acids [17]. Gelatin can be easily form hydrogels via temperature changes, but

the result is unstable and has poor mechanical properties [18]. The stability and mechanical properties of gelatin hydrogel can be improved via chemical crosslinking processes using crosslinkers such as genipin, glutaraldehyde, and carbodiimide [19,20]. However, the crosslinker is toxic. One method that is promising, safe, and inexpensive to modify gelatin into hydrogel is to form a physical crosslinking through the freeze-thaw process which is blended with polyvinyl alcohol (PVA) polymers [21] or by combined freezing-thawing and gamma ray irradiation [22,23].

Polyvinyl alcohol (PVA) is a potential hydrophilic polymer raw material for use in the biomedical field, especially in the form of injectable liquid gels [23,24]. PVA is biocompatible, non-toxic, non-carcinogenic, and shows good elasticity and compressive strength. In addition, PVA has the advantage of being able to easily form a physically crosslinked hydrogel with a freeze-thaw process treatment [25]. In the freezing process, water molecules will form ice crystals that are trapped in the PVA matrix. With the thaw treatment, ice crystals trapped in the hydrogel melt out from PVA hydrogel and form pores in hydrogel that are useful for the diffusion of water, drugs, or other molecules. Numerous research has utilized this PVA-based technique which is combined with other polymers/monomers to make hydrogels or other forms [1]. Thus, gelatin should be combined with PVA to obtain new hydrogels as a matrix for drug immobilization such as metformin HCl, which is then sterilized by gamma irradiation.

Drug immobilization method in hydrogel matrix using gamma irradiation technique has advantages such as polymers or monomers as hydrogel matrix can undergo crosslinking reactions, drugs can be trapped in hydrogel matrix simultaneously, there is no need for crosslinkers, and the resulting products are sterile. Based on the previous study, PVA-gelatin hydrogels exhibited the best swelling through gamma rays irradiation at a single dose of 25 kGy [26,27]. In addition, to ensure that the drug does not degrade, the use of PVA as a matrix can be supported with the freeze-thaw process before the irradiation process in the drug-polymer solution mixture.

Based on the description above, PVA-gelatin copolymer hydrogel containing metformin as a model of drug using freezing-thawing and irradiation technique process simultaneously. The hydrogel PVA-gelatin can prolong the release of metformin as well as the effect of irradiation dose or drug compositions.

## METHODOLOGY

The PVA was made by Kuraray, Japan. The gelatin fish scales was prepared by PAIR BATAN. The metformin HCl was made in Mumbai, India. Distilled water was used for drug dissolution.

### Gamma irradiation sources

The samples were irradiated using Co-60 gamma ray facility in IRPASENA, BATAN. The dose rate was 5 kGy/hour and the process was carried out at room temperature. The irradiation doses were calibrated using a Fricke dosimeter.

### Determination of water absorption [9]

Hydrogel samples were dried in an oven at temperature of 60 °C until constant weight, then weighed (27). The dried hydrogels were afterward immersed in 25 ml of distilled water. After 1 hour, the hydrogels were removed from the soaking medium. Then, after removing the water on the hydrogel surfaces with filter paper, subsequently the hydrogel were weighed (Ws). Afterwards, the hydrogels were immersed again in water with the same container to test the water absorption for 1 hour. The same treatment was done for testing water absorption in different time intervals. Finally, the hydrogels were dried in an oven at 60 °C until constant weight. Water absorption can be calculated using the following Eq. (1),

$$\text{Water absorption} = \frac{W_s - W_o}{W_o} \times 100 \% \quad (1)$$

where

Ws = the weight of swollen hydrogel (g)

Wo = the weight of dry hydrogel (g)

### Determination of gel fraction [9]

The dried hydrogels were placed in a tea bag and dried in an oven at temperature of 60 °C until constant weight, then weighed (Wo). In addition, the tea bags were immersed in distilled water and shaken in a shaker incubator at 100 rpm for 24 hours at room temperature to extract unreacted compounds due to radiation treatment. Then, the tea bags were removed from shaker incubator and dried under vacuum at 60 °C, then weighed (W1). The gel fraction can be calculated by Eq. (2).

$$\text{Gel fraction} = \frac{W_1}{W_o} \times 100 \% \quad (2)$$

where,

Wo = the initial weight of dry hydrogel (g)

W1 = the weight of dry hydrogel after extraction (g)

Note: All works were carried in triplicate

### Extraction of gelatin from fish scales

An approximately 200 g of dried fish scales were washed with tap water to remove impurities from the surface. Then it was soaked in a solution of lime soap to remove the fat from its surface. It was then washed again with running water to clean the remaining soap left. Fish scales that have been cleaned were immersed in ± 300 ml of distilled water, and the bottle was closed and put in an autoclave. Afterward, it was heated at a temperature of 121 °C and pressure of 1 atm for 15 minutes. The extracted solution was poured into a plastic tray with a 0.5 cm thickness, and dried in the air for 2 days. Drying products were in the form of gelatin sheets.

### Immobilization of metformin HCl in PVA-gelatin hydrogels

Different amount of gelatin (0.5 g, 1 g, 1.5 g, and 2 g) were dissolved in 100 ml of distilled water. A total of 10 g of PVA was added into 100 ml of distilled water and mixed with the gelatin solutions. Then, the PVA-gelatin solutions were packed in a polypropylene (PP) plastics and heated in an autoclave at 121 °C for 15 minutes. About 5 ml of the PVA-gelatin mixture solution was put into a series of vial containing 10, 20, and 30 mg of metformin, homogenized with a hand shaker. Subsequently the mixture was freeze-thawed for 3 cycles (4 °C, 16 hours and 35 °C, 8 hours) and finally irradiated with gamma rays at a single dose of 25 kGy [26,27]. After irradiation, the vials were broken and the hydrogels were removed from within. Subsequently, the hydrogels were immersed in 100 ml of distilled water, shaken at 100 rpm using an incubator shaker at 37 °C. Every 1 hour interval, 5 ml of the metformin solution released from the hydrogels were measured using a UV-Vis spectrophotometer at a maximum wavelength λ = 232 nm. A total of 5 ml of new solvent was added to the measuring vessel. The amount of drug released was calculated as a cumulative percent. All experiments were carried out in triplicate.

### Scanning electron microscopy (SEM)

The surface characteristics of the PVA-gelatin hydrogel were investigated using Zeiss Scanning

Electron Microscope (SEM), made in Germany. The dried samples were soaked in distilled water up to maximum swelling. Then, the hydrogels were frozen in the freezer at -25 °C for 48 hours. The hydrogels were then lyophilized using freeze drying at -40 °C for 24 hours. Dry hydrogels were then observed for their surface properties using SEM.

### UV-Vis spectrophotometer

UV-Vis mini 1240 Shimadzu, made in Japan, was used to measure the maximum wavelength of the drug as well as measuring the concentration of the drug that were released from the hydrogel.

## RESULTS AND DISCUSSION

### Water absorption

The ability of hydrogels to absorb water is one of the important parameters to predict the capacity of hydrogel in releasing drug. Effect of gelatin concentration on water absorption of PVA-gelatin hydrogels produced from gamma irradiation at 25 kGy is presented in Fig. 1. It can be seen that the irradiated PVA-gelatin hydrogel immersed in water during in the first hour, they absorb water from 100 % to 240 %. By increasing the immersing time up to 12 hours of measurement, the ability of the hydrogel to absorb water was gradually increased to 420 % - 500 % along with decreasing gelatin concentration. In addition, with increasing gelatin concentration up to 2 %, water absorption of the PVA-gelatin hydrogel decreased from 500 % to 420 %. Chemically, the reaction that occurs between PVA and gelatin is the esterification reaction of the OH group from PVA with the COOH group aspartate group and glucose amino acid gelatin to form hydrogel through the crosslinking process [28]. Hence, by increasing gelatin concentration up to 2 % in a mixtures of PVA-gelatin (10:2,wt%) with a relatively large concentrations of PVA, more gelatin will react with PVA. As a result, hydrophilicity of PVA-gelatin hydrogel decreases following with decreasing ability of the hydrogel to absorb water. This might result that, with increasing gelatin concentration, water absorption capacity of the PVA-gelatin hydrogel decreases.

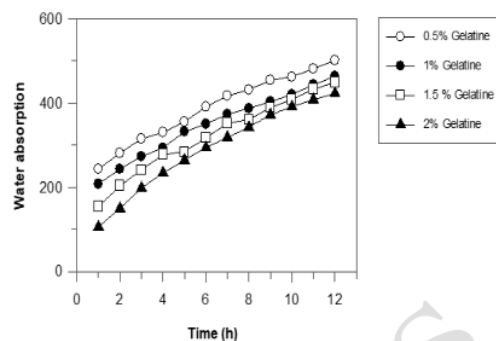


Fig. 1. Effect of immersion time on water absorption of PVA-gelatin hydrogel a result of irradiation at 25 kGy with different gelatin concentrations.

### Gel fraction of hydrogel

Gel fraction is one of the important parameters generally used to determine physical properties of hydrogel. This parameter can also be used to determine crosslinking density of the hydrogels [29]. The results of the gel fraction determination of the PVA-gelatin hydrogel from gamma irradiation for various gelatin concentrations are presented in Fig. 2. It was observed that with increasing gelatin concentration from 0.5 % up to 2 %, gel fraction of the hydrogel increased from 83 % to 94 %. The gel fraction was increased approximately 10 % with the addition of 2 % gelatin at a concentration of 10 % PVA, and raw material wasted due to being dissolved in the water was about 6 %. The wasted material can be either degraded or unreacted PVA or gelatin in the synthesis process. This indicates that the synthesis reaction between PVA with gelatin through the freezing-thawing process combined with gamma irradiation is relatively efficient.

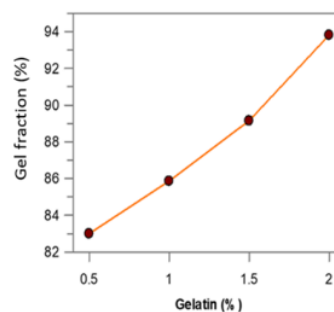


Fig. 2. Effect of gelatin concentration on gel fraction of PVA-gelatin hydrogel prepared using gamma irradiation at 25 kGy.

The mechanism of immobilization of metformin in the PVA-gelatin hydrogel through a combination freezing-thawing and irradiation process is illustrated in Fig. 3. In the freezing-thawing process, the metformin was randomly dispersed in the PVA-gelatin mixture, frozen on the surface and entrapped inside hydrogel, and reacted physically. If the metformin in the frozen form is irradiated, then the relatively small frozen metformin experienced a degradation reaction. This is one of the methods of choice for drug immobilization using irradiation techniques that can simultaneously strengthen the hydrogel matrix from being soluble in water through a radical crosslinking polymerization reaction.

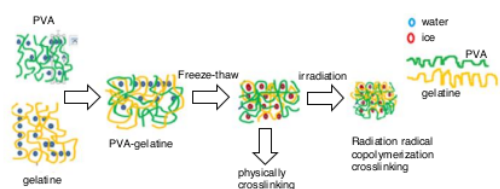


Fig. 3. Mechanism of freezing-thawing and irradiation of PVA-gelatin blended hydrogel preparation.

### Effect of gelatin concentrations on in vitro release of metformin HCl (MH)

The results of the effect of immersion time on the cumulative in vitro release of MH from hydrogel matrix of PVA-gelatin as a function of gelatin concentrations of 1 %, 1.5 % ,and 2 % are presented in Fig. 4.

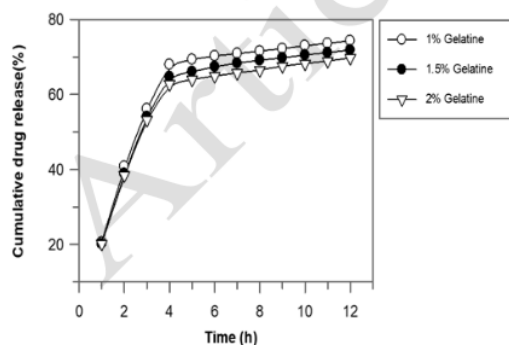


Fig. 4. Effect of immersion time vs cumulative in vitro release of MH from PVA-gelatin hydrogel measured at various gelatin concentrations.

During the first hour of the test, there was a higher cumulative percentage of MH release from hydrogels in the range of 20 - 21 %, known as the burst release. This is due to the release of MH on the

surface of the hydrogel as a result of swelling [30]. Furthermore, with increasing immersion time from 1 hour to 4 hours, cumulative percentage of MH released from hydrogel increased rapidly to a maximum of 65 to 70 % with release rate of 10 - 20 % per hour. As for in vitro release of MH from the 4<sup>th</sup> to the 12<sup>th</sup> hours, the release from each hydrogel was slowly increased with a relatively small range of 0.4 - 1 % and tends to form a slope pattern with increasing immersion time. This release pattern of drug profile follows first-order release kinetics [30]. Hydrogels that are easily degraded (biodegradable) or nano hydrogel particles are generally profiled as an in vitro release kinetics. Drug release was caused by swelling and erosion [23] [30]. This might occur in PVA-gelatin hydrogels. It can also be seen in Fig. 3 that, with an increase in gelatin concentration up to 2 %, in vitro release of MH decreased. This is due to an increase in the concentration of gelatin, so that swelling hydrogel decreased and thereby in vitro release was also decreased.

### Effect of drug dosage on MH in vitro release

The dose of drug-loaded into the hydrogel and released from it is closely related to the capacity of the matrix. The effect of different MH doses from 10 mg to 30 mg immobilized in the PVA-gelatin hydrogel matrix on cumulative MH release is presented in Fig. 5. It appears that at the first hour test of the test, MH was released from the hydrogels as a burst drug release in a range of 9 - 20 %.

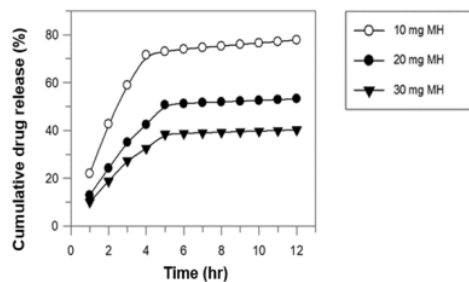


Fig. 5. Effect of immersion time vs cumulative MH release from PVA-gelatin as a function of different doses of MH.

Drug release from the 1<sup>st</sup> hour to the 5<sup>th</sup> hour was relatively rapid, reaching an optimum condition ranging from 33 % to 70 % with a release rate of 3 - 20 % per hour. Then, during measurement from the 5<sup>th</sup> to 12<sup>th</sup> hour, drug release gradually increased with the rate of 0.3 % - 0.6 % per hour, which is

relatively constant. In general, the profile of controlled release of MH drug is that the drug was released faster on the start, and then sloping slowly with smaller drug release rate. The pattern of drug release profile is known as release with first order kinetics [31]. In addition, in Fig. 4, it is clearly seen that as the increase in MH drug dosages to 30 mg, the percentage of drugs released from hydrogel decreased from 75 % to 36 %. This might be due to the increasingly dense hydrogel matrix with increasing MH dose, causing strong interactions between the drug and the hydrogel matrix both physically and chemically. Therefore, the diffusion of the drug within the hydrogel was reduced and its release decreased. It may also be caused by other causes that need further investigation.

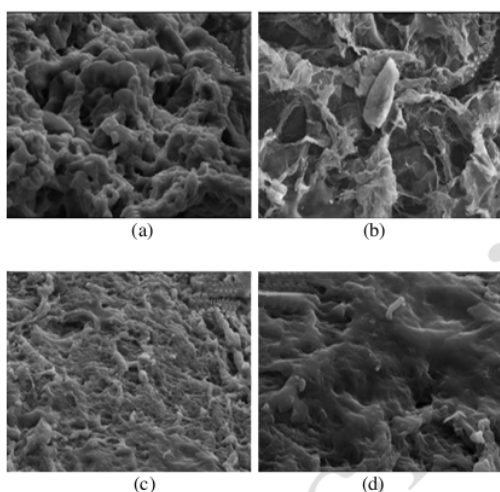


Fig. 6. SEM micrographs of PVA-g-gelatin hydrogels irradiated at 25 kGy with varying concentrations of gelatin; (a). 0.5 %; (b). 1 %; (c) 1.5 %; (d). 2 %.

### SEM hydrogel

The Scanning Electron Microscopy (SEM) test was used to observe porosity or microscopic structures developed in irradiated PVA-gelatin hydrogels. By using SEM analysis, the microstructure of hydrogel surface and the pores can be observed. The results of SEM observations on the PVA-gelatin hydrogel with magnification 1000 times are presented in Figs. 6a-6d. It can be seen that the mixture of PVA and gelatin resulted in a formation of hydrogel with irregular and porous structure. Increasing amount of gelatin produced a hydrogel with irregular structure as expressed in Fig. 6d.

The pores morphology of hydrogel can be related to their water absorption capacity. As shown

in Fig. 3, the increase in gelatin concentration led to decreased in water absorption of PVA-gelatin hydrogels. The hydrogels with denser and tighter structures will have a smaller pore size and hinder the polymer chains, minimizing their water absorption capacity.

### CONCLUSION

It can be concluded that gel fraction of the PVA-gelatin hydrogels increased with increasing gelatin concentration while water absorption decreased. Cumulative metformin releases decreased with increasing gelatin concentrations and doses of metformin. PVA-gelatin hydrogels prepared by combining freeze-thaw and irradiation can be considered as a matrix for drug immobilization.

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### AUTHOR CONTRIBUTION

We declare that all contributors of this paper are equally contributed as main contributors. All authors read and approved the final version of the paper.

### REFERENCES

1. K. J. Wadher, R. B. Kakde and M. J. Umekar, *Int. J. Pharm. Investig.* **1** (2011) 157.
2. J. Sauri, M. Zachariah, R. Macovez *et al.*, *J. Drug Delivery Sci. Technol.* **42** (2017) 215.
3. J. L. J. Blanco, J. M. Benito, C. O. Mellet *et al.*, *J. Drug Delivery Sci. Technol.* **42** (2017) 18.
4. D. W. Kurniawan, D. A. Triyanto and V. V. F. R. Utami, *Kartika: Jurnal Ilmiah Farmasi* **6** (2018) 11. (in Indonesian)
5. K. V. R. N. S. Ramesh, S. Mohanarayam, O. Sarheed *et al.*, *Asian J. Pharm.* **11** (2017) 118.
6. M. T. R. Chikukwa, M. Wesoly, A. B. Korzeniowska *et al.*, *Pharm. Dev. Technol.* **25** (2020) 281.
7. X. Bai, M. Gao, S. Syed *et al.*, *Bioact. Mater.* **3** (2018) 401.

8. Y. C. Qian, P. C. Chen, G. J. He *et al.*, *Molecules* **19** (2014) 9850.
9. Erizal, E. W. Pratiwi, D. P. Perkasa *et al.*, *Jurnal Kimia Kemasan* **40** (2018) 47. (in Indonesian)
10. Z. Velkova, G. Kirova, M. Stoytcheva *et al.*, *Eng. Life Sci.* **18** (2018) 871.
11. D. Singh, A. Singh and R. Singh, *J. Biomater. Sci., Polym. Ed.* **26** (2015) 1269.
12. C. Vasile, D. Pamfil, E. Stoleru *et al.*, *Molecules* **25** (2020) 1539.
13. A. Chyzy, M. Tomczykowa and M. E. Plonska-Brzezinska, *Materials* **13** (2020) 188.
14. S. Amin, S. Rajabnezhad and K. Kohli, *Sci. Res. Essay* **3** (2009) 1175.
15. H. Hariyanti, Erizal, M. Y. Yunus *et al.*, *Jurnal Sains Materi Indonesia* **21** (2020) 143. (in Indonesian)
16. S. Mitura, A. Sionkowska and A. Jaiswal, *J. Mater. Sci. - Mater. Med.* **31** (2020) 50.
17. R. Song, M. W. Murphy, C. Li *et al.*, *Drug Des. Dev. Ther.* **12** (2018) 3117.
18. Q. Xing, K. Yates, C. Vogt *et al.*, *Sci. Rep.* **4** (2014) 4706.
19. G. Thakur, F. C. Rodrigues and K. Singh, *Crosslinking Biopolymers for Advanced Drug Delivery and Tissue Engineering Applications*, in: *Cutting-Edge Enabling Technologies for Regenerative Medicine*, *Advances in Experimental Medicine and Biology* 1078, Springer, Singapore (2018) 213.
20. P. N. Charron, T. A. Braddish and R. A. Oldinski, *J. Mech. Behav. Biomed. Mater.* **92** (2019) 90.
21. K. R. Park and Y. C. Nho, *J. Appl. Polym. Sci.* **91** (2004) 1612.
22. Erizal, D. Pribadi, E. Yulianti *et al.*, *Jurnal Sains Materi Indonesia* **19** (2018) 139. (in Indonesian)
23. M. Kobayashi and H. S. Hyu, *Materials*. **3** (2010) 2753.
24. J. Tavakoli, A. J. Gascooke and Y. Tang, *Top. Curr. Chem.* **379** (2021) 1390.
25. Erizal and Z. Abidin, *Jurnal Ilmiah Aplikasi Isotop dan Radiasi* **7** (2011) 21. (in Indonesian)
26. K. Swaroop, M. J. Gaana, S. S. Shruthi *et al.*, *Studies on Swelling Behaviour of Radiolytically Synthesised PVA/Gelatin Hydrogels*, *AIP Conference Proceedings* 2115, 030050 (2019).
27. K. Swaroop, L. P. Shrikant and H. M. Somashekarappa, *Curr. Perspect. Chem. Sci.* **9** (2021) 125.
28. K. Pal, A. K. Banthia and D. K. Majumdar, *AAPS PharmSciTech* **8** (2007) E1.
29. L. Arens, D. Barther, J. Landsgesell *et al.*, *Soft Matter* **15** (2019) 9949.
30. Z. Xiang, P. Sarazin and B. D. Favis, *Biomacromolecules* **10** (2009) 2053.
31. M. Miotke, J. Strankowska, J. Kwela *et al.*, *Polym. Bull.* **77** (2019) 483.



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H. IRIE, K. TORIMARU, H. TANAKA.  
"Potentiometric titration of IAG gelatins.",  
Journal of The Society of Photographic  
Science and Technology of Japan, 1980

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---

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Jingzhe Sun, Dahye Ahn, Junseo Kim,  
Seongcheol Ahn et al. "Surface-control  
enhanced crater-like electrode in a  
gelatin/polyvinyl alcohol/carbon composite for  
biodegradable multi-modal sensing systems  
with human-affinity", Journal of Materials  
Chemistry A, 2021

Publication

---

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24

Jue Hu, Molamma P. Prabhakaran, Lingling  
Tian, Xin Ding, Seeram Ramakrishna. "Drug-  
loaded emulsion electrospun nanofibers:  
characterization, drug release and in vitro  
biocompatibility", RSC Advances, 2015

Publication

<1 %

---

25 Leandro G. Aguiar, Daniel C. Iwakura, Ana T. S. Semeano, Rosamaria W. C. Li, Esmar F. Souza, Jonas Gruber, Reinaldo Giudici. "Controlled release of an optically active compound by hydrogels of acrylic acid and its online detection", The Canadian Journal of Chemical Engineering, 2018

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