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Utilizing Alginate to Improve Elasticity and Moisture Balance of Polyvinyl Alcohol/Chitosan Hydrogel Wound Dressing

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Abstract. Uncontrolled hemorrhage is the leading cause of death. The efficient hemostatic dressings are needed to promote coagulation and hold ongoing hemorrhage. Hydrogels are hydrophilic polymers with three-dimensional network structures with high swelling capacity to prevent accumulation of exudates. Hydrogels prepared from polyvinyl alcohol (PVA) grafted with chitosan have attracted considerable attentions due to their biocompatibility, high moisture balance property, and transparency. In this study, alginate was utilized to improve elasticity and thermal stability, also enhance hydrophilicity and increase swelling ability. The hydrogels composed of PVA (7.5 % w/v), chitosan (0.05 % w/v), and alginate (0.2, 0.4, and 0.6 % w/v) were synthesized by gamma irradiation technique at total dose of 15 kGy. The results showed that the increasing of alginate concentration in the total reactant mixture can improve elasticity, swelling capacity and the equilibrium degree of swelling (EDS), and decrease water vapour transmitted rate/moisture vapour transmitted rate (MVTR). The hydrogel wound dressing with 0.6 % of alginate concentration was the best product in this study with 79.49 % gel content, 608.65 % swelling ratio, 628.32 % EDS in 22 hours, elasticity 62.58 KPa, evaporation rate (MVTR) 105g/m2 h, degraded at temperature of 298.89oC, and the weight loss was reached 88.84 % (w/w).

Introduction

A wound is defined as a break or defect in the skin, which formed due to physicochemical or thermal damage [1]. The principle requirements to handle all types of wounds are a clean, adequately perfused wound environment free from infection, necrotic tissue and foreign material [2]. One of the most promising materials in wound care are hydrogel based wound dressings. Hydrogels have attracted considerable attentions due to their high swelling capacity and potential hemostatic ability to prevent accumulation of exudates [3]. Hydrogels are recommended as dressing for wounds because of their usefull properties: keeping the wound moist whilst absorbing extensive exudate, adhesion-free coverage of sensitive underlying tissue, eliminate/minimize pain through cooling, and a potential for active intervention in the wound healing process [4].

Various studies have suggested that chitosan seems to be an excellent material for wound dressings. It has been commonly used to prepare wound dressings in the form of hydrogel [5, 6, 7]. Chitosan has very unique properties as an antimicrobial agent that gets great attention biomedical field for the past few years. Different studies show that chitosan and its derivatives have reasonable antimicrobial activity against bacteria, fungi, yeast, and others [8, 9]. Chitosan also has comprehensive properties such as biocompatibility, biodegradability, excellent hemostatic behaviour and promoting wound healing. Hydrogels prepared from chitosan and its derivatives are promising hemostatic materials with good absorption behaviors and potential hemostatic ability [10].

From several works show that no single material is capable of achieving all the requirements for all the steps of the wound healing process [5]. Chitosan is often combined by grafting method with other materials to get superior properties [11, 12]. Among the many existing materials, polyvinyl

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alcohol (PVA) is one of the longest and most widely used synthetic polymers, and is combined with other synthetic polymers and natural polymers. PVA has good gel properties. It has been proposed as a promising biomaterial suitable for biomedical applications [13]. The combination of chitosan and PVA as a potential hydrogel for wound healing have been studied for mechanical [14] and antibacterial properties [14, 15]. A study reported that the prepared membrane from PVA/chitosan plasticized with glycerol appeared smooth, elastic, and showed significant growth inhibition against pathogens, which recommended for the healing management usage [14].

In addition to chitosan, another biopolymer that has been studied as a potential material for wound dressing is alginate. Alginate is a polysaccharide derived from brown seaweed (Phaeophyceae), which has so many beneficial properties, including biocompatibility and ease of gelation. Alginate based hydrogel has attracted the attention of researchers in wound healing, drug administration, and tissue engineering applications to date, because these gels maintain structural similarity with the extracellular matrix in the network and can be manipulated to play several important roles [16]. Potential wound dressings has been developed from alginate based hydrogels blend with PVA and honey [17], or with chitosan [18, 19]. It has been reported that chitosan/alginate films have a water vapor transmission rate close to the optimum value showed a good antibacterial activity against E. coli and S. aureus [19]. The chitosan/alginate hydrogel produced by a previous research [20] also reported to have high porosity, biodegradable, and suggested to be used to treat the skin injuries in the clinic.

Considering the high performance of chitosan and PVA in the wound dressing development, this study prepare PVA/chitosan blend hydrogels with the addition of alginate then evaluate their swelling ability, mechanical properties, moisture balance, and antimicrobial activity.

Materials and Methods

Materials

Polyvinyl alcohol (Merck, Darmstadt, Germany), Na-Alginate from Kimitsu, Japan, chitosan from PT Biotech Surindo Indonesia, and food grade acetic acid. *Escherichia coli*, *Streptococcus aureus*, and the growth media used for antimicrobial activity test of hydrogel product were purchased from Research Center for Chemistry, Indonesian Institute of Sciences, Serpong, Indonesia. Distilled water used for preparation of the hydrogel and swelling measurement.

Preparation of chitosan solution

Chitosan solution at 1% (w/v) was made by dissolving 1 gr chitosan in 0,25 % (v/v) of glacial acetic acid and stirred constantly using IKA overhead stirrers RW 20 at room temperature conditions.

Preparation of Na-Alginate solution

Na-alginate solution at 2% (w/v) was made by dissolving 3 gr Na-alginate in 150 ml distilled water and stirred constantly using IKA overhead stirrers RW 20 at room temperature conditions.

Preparation of Polyvinyl Alcohol (PVA) solution

Polyvinyl alcohol at 15% (w/v) solution was made by dissolving 75 gr PVA in 500 ml distilled water and heated using autoclave at 121^{o}C for 20 minutes.

Synthesis of hydrogel

An amount of 10 mL chitosan solution, Na-alginate solution in various amount (20, 40, and 60 mL), 100 mL Polyvinyl alcohol solution were added by distilled water until the volume of total solution being 200 mL and mixed well using IKA overhead stirrers RW 20 at room temperature. The homogenized solution was packed in a 20 cm x 10 cm of polypropylene plastic and then ϒ-irradiated at constant total dose 15 kGy.

Gel contents and swelling analysis

The hydrogel products were cut into 3 parts with size 1 x 1 x 0,5 cm^3 and were dried in the oven at 60.5ºC for 24 hours and weighed, then the hydrogels were soaked with distilled water at 60ºC in the 100 rpm spinning shaker for 24 hours. The soaked hydrogels then dried in an oven at 60.5ºC until the weigh being constants, then weighed. The gel content measured twice at room temperature according to a method of [20] and previous study of [21] using the following formula:

$$\text{Gel content (\%)} = \frac{W0}{W1} \text{x } 100\ \% \quad (1)$$

W_1 = weight of dried gel after soaking (g) and W_0 = initial weight of gel (g)

The swelling capacity of hydrogel was determined by immersed the dried hydrogels into distilled water at room temperatures. At 60 minutes time intervals, the samples removed from the distilled water and blotted on a tissue paper to remove the excess surface moisture, then weighed. The swelling ratio calculated according to the following expression:

$$\text{Swelling ratio (\%)} = \frac{Wt}{W0} \text{ x } 100\ \% \quad (2)$$

where W_t = weight of the swollen gel at time t (g) and W_0 is the initial weight of the dried gel (g).

MVTR analysis

The hydrogels cut into 2 x 2 (cm^2), and weighed. Then let the hydrogels in a room temperature for 7 hours and weighed. MVTR calculated according to the following expression:

$$MVTR = \frac{W0-W1}{A} \quad (3)$$

Instrumental Analysis

Fourier Transform Infrared (FTIR) absorption spectra of samples measured by means of Shimadzu IR Prestige-21 spectrometer model 800 series from 4000 to 500 cm^{-1} and recorded with DRS (Diffuse Reflectance Spectroscopy) system. Thermogravimetric analysis is a method of thermal analysis to measure the mass of sample over times as the temperature changes. This analysis was determined using DTG-60. The tensile strength of sample was determined using Instron Tester R-01.

Antibacterial analysis

Antibacterial activity of hydrogel was analyzed in the LIPI Chemical Laboratory. In this study, the measurement method used for antimicrobial analysis is the hole method. The hole method was done by making a hole in the solid agar that has been inoculated with bacteria. The number and location of the hole were adjusted, then the hole was filled with the solution to be tested. After incubation, bacterial growth was observed to see the resistance area around the hole.

Results and Discussion

The effect of alginate concentration to the swelling behaviour and the gel content

From the results obtained can be seen that the increase in absorption time is followed by the increase in swelling ratio (Fig. 1), but this swelling ratio will reach a saturation point, where is the swelling ratio cannot increase dramatically (close to constant) at the boundary certain time. This is because the amount of water absorbed in the hydrogel is already almost exceeding the optimum capacity, so the ability to swell cannot increase dramatically and even close to constant. In this study can be seen that the hydrogel can expand drastically in the first hour and continues to expand drastically for up to 7 hours and reach the saturation within 24 hours. This is suitable with the application as a wound dressing which is indeed used as a first aid to stop bleeding quickly and not to be used continuously in the process of wound healing.

The increase in alginate concentration can also increase the ability of hydrogel to swell. This is due to alginate has an -OH and -COOH functional groups which become the causes of the water absorption process [22]. The highest swelling ratio resulted in this study is 608.65 %, which is reached at 24 hours of absorption with 0.6 % (w/v) of alginate concentration. For 0.2 % and 0.4 % (w/v) of alginate concentration, the value of swelling ratio are 362.09% and 485.66 % after 24 hours of immersing.

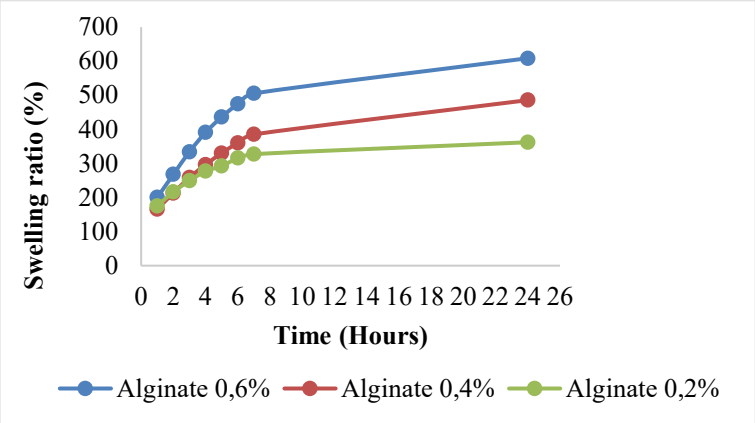


Fig. 1. Swelling properties of the hydrogels.

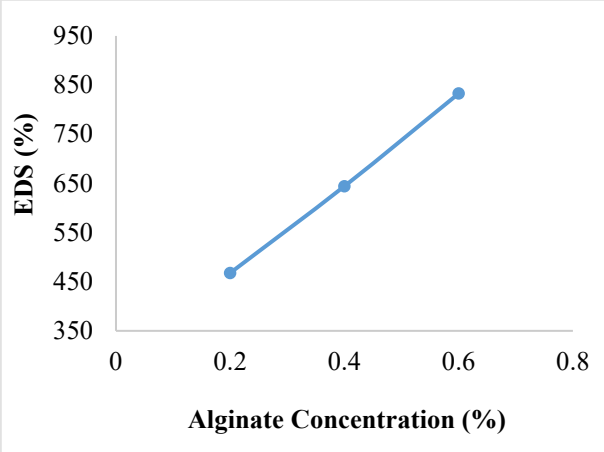


Fig. 2. EDS values of the hydrogels.

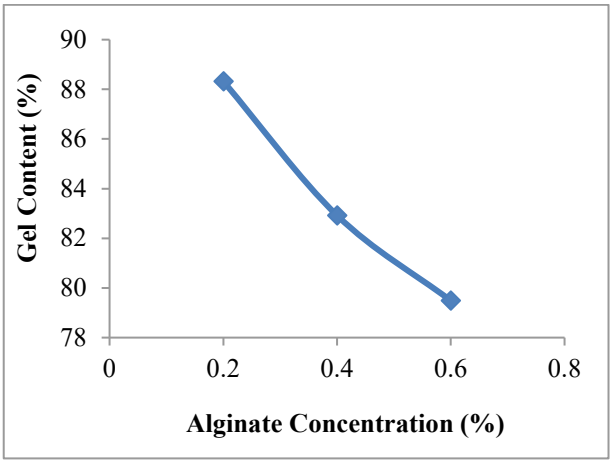


Fig. 3. Gel contents of the hydrogels.

The hydrogel swelling ability for wound dressing has a limit of equilibrium (Equilibrium Degree of Swelling), where the increase of the swelling ratio tends to be constant at certain times. From Fig. 2 can be seen that the increase in alginate concentration affect the Equilibrium Degree of Swelling (EDS) value and the stationary time. At an alginate concentration of 0.6 % (w/v) the hydrogel reaches EDS at 22 hours with the swelling ratio of 628.32 %, while at the concentration of alginate 0.4 % (w/v) achieved EDS at 22 hours with a swelling ratio of 486.4 % and 0.2 % (w/v) of alginate concentration at 17 hours with a swelling ratio of 363.72 %.

Gel content is one of the parameters commonly used in the synthesis of hydrogels. It is reflecting the percentage of the starting material in either the monomer or polymer which is converted into a hydrogel in the synthesis process. In addition, the gel content shows the efficiency of the hydrogel making process which depends on the sensitivity of the material to the emitted gamma irradiation [22]. The gel content analysis in this study can be seen in Fig. 3, with the greatest value of the gel content is 88.32 % at 0.2 % (w/v) of alginate composition. Increasing the concentration of alginate caused a decrease in the gel content formed. This is due to the degradation of natural polymers as raw material for hydrogels when gamma ray irradiation was carried out, so that the number of cross bonds formed in the hydrogel decreased.

The effect of alginate concentration to the mechanical properties

Increasing the concentration of alginate causes the hydrogel produced to be stronger or not easily broken. The elongation ability of the hydrogel is also directly proportional to the addition of alginate. This is because alginate has excellent mechanical properties, so that the easily broken properties possessed by other materials can be well covered by alginate [23]. As a result, the increase in alginate concentration was directly proportional to elasticity, so that the highest elasticity were gained at 0.6 % of alginate concentration, which amounted to 62.58 KPa, while for alginate concentrations of 0.2 % and 0.4 % respectively were 43.6 KPa and 58.61 KPa. From Fig. 4, Fig. 5, and Fig. 6 can be seen the effect of increasing the alginate concentration on the tensile strength, elongation at break, and elasticity of the hydrogels.

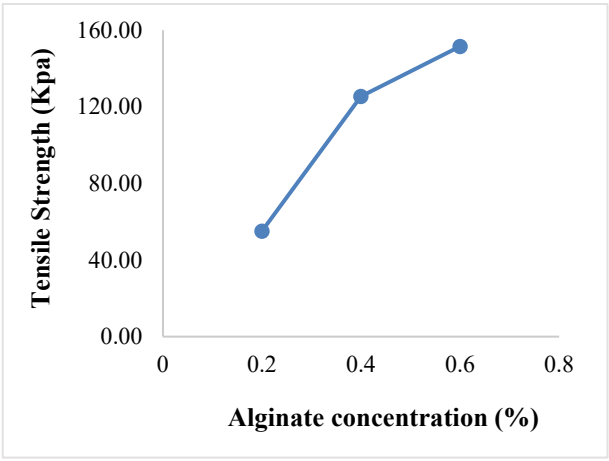


Fig. 4. The effect of alginate concentration to the tensile strength.

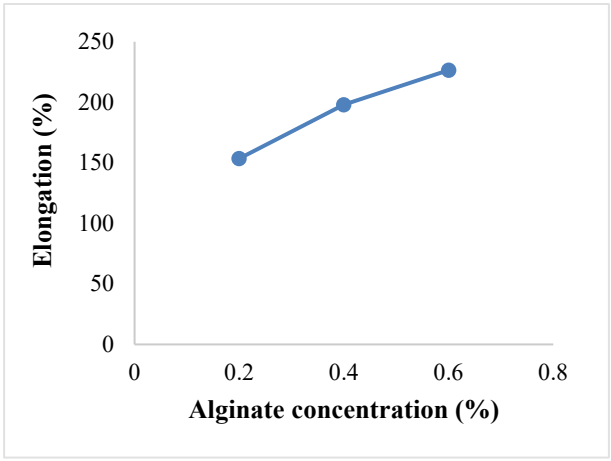


Fig. 5. The effect of alginate concentration to the elongation at break.

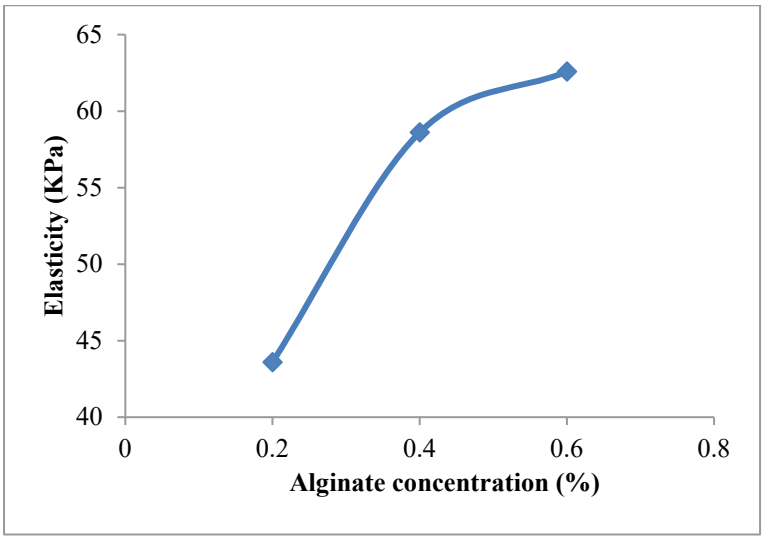


Fig. 6. Elasticity of the hydrogels.

Thermal gravimetry analysis (TGA)

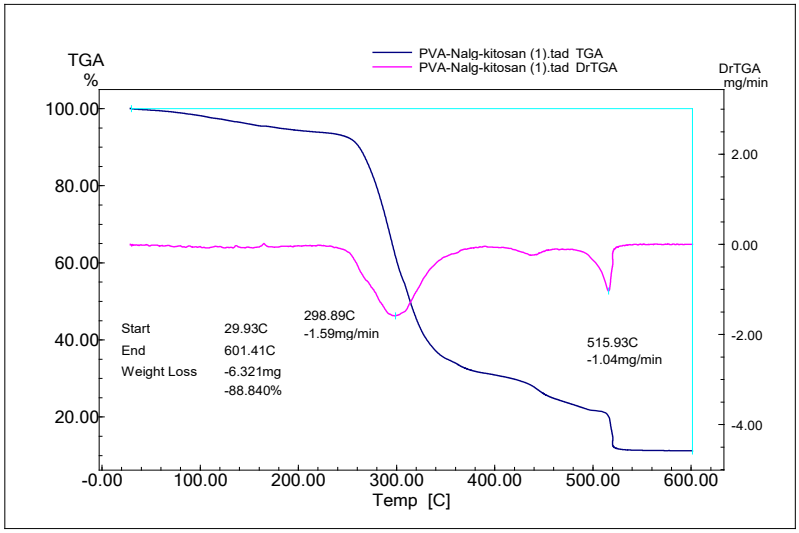


Fig. 7. The thermogram of PVA/chitosan/alginate hydrogel.

Thermogravimetric analysis in this study aims to determine the thermal character when the sample has a decrease in mass, or in other words indicate the condition when the sample undergoes a process of degradation. The decrease in the hydrogel mass is indicated by the thermogram in Fig. 7. The pattern of decreasing sample weight is in accordance with the characteristics possessed by PVA, where PVA has a melting point of 200°C and will melts quickly above that temperature. Based on thermal analysis carried out using TGA, the results showed that the sample decreased by 88.840 %, with the rate of decrease was ± 1.6 mg/minute at a temperature interval of 240-520°C.

FTIR study

The FTIR analysis results for each material before the mixing process and for PVA/chitosan/ alginate hydrogel can be seen in Fig/ 8. It was found that at the wavelength of 3396.64 cm^{-1} there was an amine group (NH) appeared from chitosan and at a wavelength of 2922.16 cm^{-1} there was a hydroxyl (OH) group from PVA. FTIR study is used to measure the success of the cross-linking process. The OH group read on the product spectrum is at a different wavelength with the OH group in the pure PVA spectrum. This difference indicates that PVA has experienced crosslinking with alginate and chitosan. At a wavelength of 140.94 cm^{-1} there is a C-O group derived from alginate.

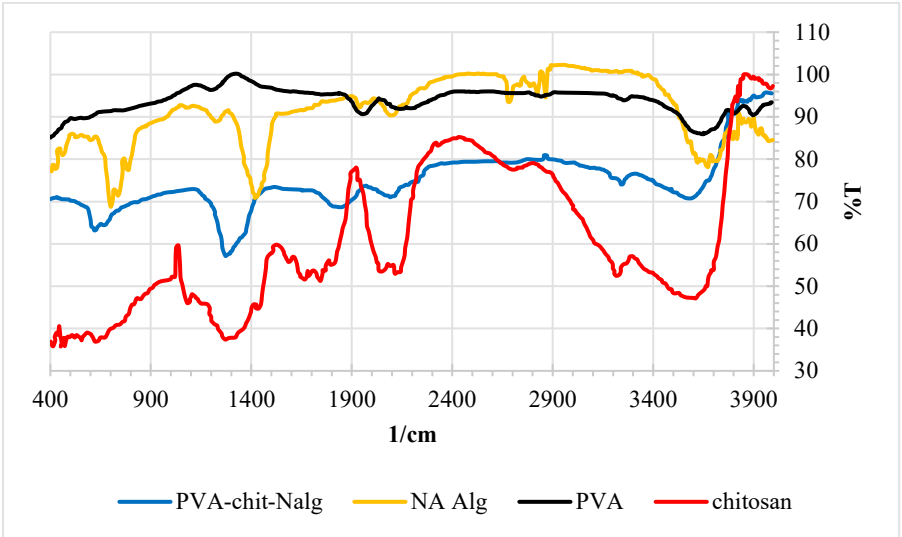


Fig. 8. The FTIR analysis for pure PVA, pure alginate, pure chitosan, and PVA/chitosan/alginate hydrogel.

Moisture vapour transmission rate (MVTR) study

The results of MVTR testing with variations in the concentration of alginate (0.2 %, 0.4 %, and 0.6 %) can be observed in Fig. 9, with the best MVTR in the first hour being at the concentration of alginate 0.6 % which is equal to 105 g/m^{2}h, while for concentrations of 0.2 % and 0.4 % (w/v) the evaporation rate is 117.63 and 110.34 g/m^{2}h respectively. MVTR value after 7 hours of evaporation time with a concentration of 0.2% alginate, 0.4%, and 0.6% w/v respectively are 80.5341 g/m^{2}h, 75.3977 g/m^{2}h, and 64.4318 g/m^{2}h. This is according to the previous research [23], that alginate can maintain moisture in the hydrogel. The duration of evaporation time causes the water content in the hydrogel to be less and the hydrogel is easier to hold water in the hydrogel, so the evaporation rate drops and close to constant when the water content in the hydrogel is almost exhausted.

The rate of evaporation of water or Moisture Vapor Transmission Rate (MVTR) is a test conducted to determine the amount of water content that diffuses into the environment (evaporates). MVTR also shows the ability of a material to maintain moisture (moisture) in the hydrogel wound dressing. The ability of the hydrogel to maintain water content is beneficial in the wound healing process. It prevents the formation of eschar tissue which can inhibit wound healing. The decrease in MVTR causes the hydrogel to be better in the process of wound healing.

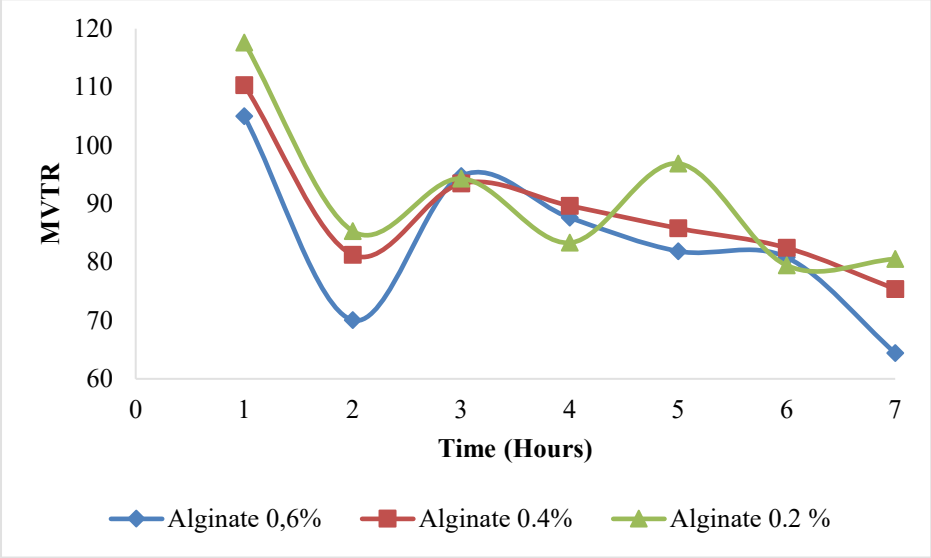
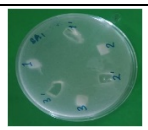
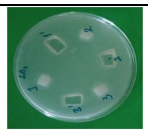
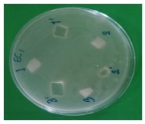
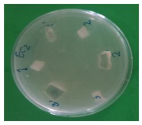


Fig. 9. The effect of time to the MVTR of hydrogels.

Antibacterial study

Based on antibacterial analysis (*E. coli and S. aureus*), the results of this anti-bacterial test can be seen in Table 1. From Table 1, it can be seen that the hydrogel sample cannot inhibit the growth of the test bacteria, this is due to the use of antibacterial substances, namely chitosan in the sample, which has only a small level of 0.05 %.

Table 1. Antimicrobial analysis of the hydrogelю

	trial 1	trial 2	result
S. aureus (InaCC-B4)			No inhibition
E. coli (InaCC-B5)			No inhibition

Chitosan can be used as an inhibitor of bacterial growth [24]. This is due to the positive charge of chitosan can interact with the negative charge on the surface of the bacteria which causes changes in the surface of bacterial cells. Changes in bacterial surface cells causing several constituents of missing cells, namely glucose, protein, and amino acids, so that chitosan inhibits microorganism metabolism and causing the bacterial cells to die. In addition, another mechanism is the positive charge of chitosan will interact with the DNA of *Escherichia coli* and *Streptococcus aureus*, which will inhibit RNA synthesis and protein. However, the use of small levels of chitosan reduces its ability to inhibit bacteria, this is due to the positive charge of chitosan unable to inhibit the bacterial metabolism and the synthesis of RNA, and also protein synthesis in the test bacteria. The use of low chitosan levels in this study are because chitosan cannot mix homogeneously with alginate when the concentration of both are too high. In the preliminary research, product formulations were carried out with alginate levels at the highest concentration and chitosan concentration of 0.1%, but the formulation produced a less homogeneous product, where there were flocs in the hydrogel solution which can be seen in Fig. 10. This is in accordance with the research conducted [25], which states that if the polycation derived from chitosan and polyanion from alginates is mixed, then the mixture clump or form a floc.

Fig. 10. Flocculation during the mixing at high level of chitosan.

Conclusion

Based on the results of this study, it can be concluded that the addition of alginate concentration in the hydrogel reactant mixture reduce the gel content, however increase the swelling ratio and elasticity, and results a better rate of evaporation. The optimum composition is obtained from the hydrogel containing 0.6 % of alginate (w/v) with gel content of 79.49 %, swelling ratio 608.65 %, elasticity 62.58 KPa, and evaporation rate (MVTR) of 105 g/m^2h. Hydrogel produced with the concentration of chitosan 0.05 % (w/v) can not resist the growth of *S. aureus* and *E. coli* bacteria and the hydrogel product is degraded as much as 88.84 % at the temperature of 298.89^oC.

Acknowledgements

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References

[1] E.A. Kamoun, E-R.S. Kenawy and X. Chen, Journal of Advanced Research 8 (3) (2017) 217-233

[2] K. Vowden and P. Vowden, Surgery (Oxford) 35 (9) (2017) 489-494

[3] H.N. Li, J. Yang, X.N. Hu, J. Liang, Y.J. Fan and X.D. Zhang, J. Biomed. Mater. Res. A 98 (2011) 31-39

[4] J. Koehler, F.P. Brandl and A.M. Goepferich, European Polymer Journal 100 (2017) 1-11

[5] T. Wang, X-K. Zhu, X-T. Xue and D.Y. Wu, Carbohydrate Polymers 88 (2012) 75-83

[6] D. Mukherjee, Md. Azamthulla, S. Santhosh, G. Dath, A. Ghosh, R. Natholia, J. Anbu, B.V. Teja and K.M. Muzammil, Journal of Drug Delivery Science and Technology 46 (2018) 498-510

[7] S. Anjum, A. Arora, M.S. Alam and B. Gupta, International Journal of Pharmaceutics 508 (1-2) (2016) 92-101

[8] S. Sharma, R. Kumar, P. Kumari, R.N. Kharwar, A.K. Yadav and S. Saripella, International Journal of Biological Macromolecules 125 (2019) 109-115

[9] E.M. de A. Braz, S.C.C.C. e Silva, D.A. da Silva, F.A. de A. Carvalho, H.M. Barreto, L. de S.S. Júnior and E.C. da S. Filho, International Journal of Biological Macromolecules 117 (2018) 640-647

[10] Y. Chen, Y. Zhang, F. Wang, W. Meng, X. Yang, P. Li, J. Jiang, H. Tan and Y. Zheng, Material Science and Engineering C 63 (2016)18-29

[11] G. Michailidou, E. Christodoulou, S. Nanaki, P. Barmpalexis, E. Karavas, S. Vergkizi-Nikolakaki and D.N. Bikiaris, Carbohydrate Polymers (2019) 208 1-13

[12] Y. Xie, Z-X. Yi, J-X. Wang, T-G. Hou and Q. Jiang International Journal of Biological Macromolecules 112 (2018) 1225-33

[13] S. Jiang, S. Liu and W. Feng, Journal of the Mechanical Behavior of Biomedical Materials 4 (7) (2011)1228-1233

[14] I. Bano, M. Arshad, T. Yasin and M.A. Ghauri, International Journal of Biological Macromolecules 124 (2019)155-62

[15] A. Ali, Md.A. Shahid, Md.D. Hossain and Md.N. Islam, International Journal of Biological Macromolecules In Press Accepted Manuscript DOI 10.1016/j.ijbiomac.2019.07.015 (2019)

[16] K.Y. Lee and D.J. Mooney, Progress in Polymer Science 37 (1) (2012) 106-126

[17] Y. Tang, X. Lan, C. Liang, Z. Zhong, R. Xie, Y. Zhou, X. Miao, H. Wang and W. Wang, Carbohydrate Polymers 219 (2019) 113-120

[18] H. Mndlovu, L.C. du Toit, P. Kumar, T. Marimuthu, P.P.D. Kondiah, Y.E. Choonara and V. Pillay, Carbohydrate Polymers 222 (2019) 114988

[19] H. Kaygusuz, E. Torlak, G. Akın-Evingür, İ. Özen, R. von Klitzing and F.B. Erim, International Journal of Biological Macromolecules 105 (1) (2017) 1161-1165

[20] C.A. Stone, H. Wright, T. Clarke, R. Powell and V.S. Devaraj, Br. J. Plast. Surg. 53 (2000)601-6

[21] M.T. Longaker, E.S. Chiu, N.S. Adzick, M. Stern, M.R. Harrison and R. Stern, Ann. Surg. 213 (1991) 292–6

[22] J.M. Rosiak, I. Janik, S. Kadlubowski, M. Kozicki, P. Kujawa, P. Stasica and P. Ulanski, Nuclear Instruments and Methods in Physics, Research Section B: Beam Interactions with Materials and Atoms 208 (2003) 325-330

[23] E.A. Kamoun, El-R.S. Kenawy, T.M. Tamer, M.A. El-Meligy and M.S.M. Eldin, Arabian Journal of Chemistry 8 (1) (2015) 38-47

[24] D.R. Barleany, I.P. Alim, N. Rizkiyah, U.T. Lusi, H. Heriyanto and Erizal, International Conference on Technology, Innovation, and Society (ICTIS) 2016 Proceeding (Padang July 21-22 Indonesia) 978-602-70570-4-3 DOI 10.21063/ICTIS.2016.1099 (2016)

[25] E.D.T. Atkins, W. Mackie and E.E. Smolko, Nature 225 (1970) 626-628