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DRUG DELIVERY HARD SHELL CAPSULES FROM SEAWEED EXTRACTS

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ABSTRACT

Drug delivery concerns the formulation, the technology and and the system of transporting the pharmaceutical compound to the body. It is used for efficacy and safety improvement. Seaweed containing a natural polymer has the potential to be used as a drug delivery material. Hard shell seaweed extract capsules are printed in four compositions (A, B, C and D) containing 0.0 mL,1.0 mL, 1.25 mL and 1.5 mL of sorbitol, which is a plasticizer increasing polymers plasticity by filling the spaces between monomers. The capsules surface morphology is analyzed by SEM. Their swelling degree and dissolutionis determined. It is found that the capsules obtained have moderate-sizenanopores. The average of swelling degree of A, B, C and D refers to 452,4 %, 557,9%, 620,0 % and 754,0 %, respectively. The dissolution of capsules in erythromycin is studied varying pH. The latter values studied are 1.2; 4.5 and 6.8 as the acidity level affects the capsules dissolution profile. It is found that the drug release is the easiest in case of pH of 6.8.The results obtained show also that the increase of sorbitol concentration of D capsules can increase the dissolution rate in absence of medium pH change.

Keywords: seaweed, sorbitol, hard shell capsules, drug delivery.

INTRODUCTION

Drug delivery materials developed in various size or form [1] aim to increase the process efficiency.There are also studies [2] focused at kinetics improvement. Hard capsules are a popular form of drug delivery. There are soft shell and hard shell capsules. The latter need to have great mechanical intensity and elasticity. In general, hard shell capsules are made from natural gelatin of animal bonesand non-animal natural polymers such as starch, chitosan, alginate and carrageenan. Gelatin is a popular material of hard shell capsules preparation which in turn requires the introduction of cuisines are usually used as additives. Gelatin is produced from cow, buffalo and swine bones, so moslem, hindu and vegetarians [3] cannot consume it. Non-gelatin drug delivery materials have been reported. Malviyaet al. [4] for an example use a mixture of chitosan and alginate. Soft and hard shell capsules can be made from starch containing propyl or ethyl groups, namely hydroxyl propyl starch (HPS) [5] or hydroxyl methyl cellulose (HPMC) called hypromellose [6]. Capsugel produces capsules from mixtures of HPMC and carrageenan from seaweed [7]. Cao describes the preparation of hard vegetarian capsules from seaweed extract and galactomannan [8].

We are aimed at developing a non-gelatin drug delivery capsules whose bioavailability and compatibility is similar to those of hard shell gelatin capsules. We use a seaweed extractand sorbitol as a plasticizer agent.

EXPERIMENTAL

Seaweed extract powder (*technical grade*) was purchased from PT. Kappa Carrageenan Nusantara, while sorbitol (*food grade*) – from PT. Brataco Chemica Sura-

baya. The hard shell capsules were prepared in Organic Chemistry Laboratory at the Faculty of Science and Technology of Universitas Airlangga, Surabaya. The dipping pins bar capsule of a zero size were provided by PT. Kapsulindo Nusantara.

Seaweed extract powders were mixed with sorbitol of a content of 0.0 mL,1.0 mL,1.25 mL and 1.5 mL (the hard shell capsules obtained with these mixtures were designated as A, B, C and D). The mixtures were gently poured in water at a ratio of 1:15 (m/v) until colloidal solution were obtained. The latter were stirred at room temperature. Then they were heated in a water bath at 70^0C - 80^0C for 60 min to 90 min. Pins bar device was used for the printing of the hard shell capsules. This was done at room temperature.

The sample was cut to form a cube of 3 mm x 3mm x ^{2} mm. It was then bound to a specimen holder of 1 cm diameter and thickness of 0.5 cm. Finally, the sample was dried and analyzed in a fine coat.

The swelling degree analysis was performed by soaking a sample of hard shell capsules in 100 mL of water for 1 h at 30^0C in absence of stirring. Then the sample was taken out and dried with filter paper for measuring its mass. The analysis was carried out the ground of six replicas.

Dissolution measurements had to be done in a medium close to human body liquids. The pH values chosen referred to 1.2; 4.5 and 6.8 because of the different acidity observed in different parts of a human body. The procedure used followed that of Gohel et al. A 100 mL of Beaker glass was supplied with a siphon. It was filled with 70 mL of the dissolution medium. Each hard shell capsule used was initially filled with 500 mg of erythromycin. The medium was stirred at 75 rpm, while HCl was added drop wise (2 mL/min) in a rate required by the pH value studied. A sample of 1 mL of the medium was withdrawn at the 20th, 40th, 60th and 80th min of the procedure. The accumulated drug concentration was spectrophotometrically determined at 210 nm [9].

RESULTS AND DISCUSSION

The presence of various contents of sorbitol as a plasticizer affects the drug release. Its increase increases the rate of drug release. It may be attributed to the great number of sorbitol –OH groups which facilitate hydrogen bonds formation in the course of mixing with water at the same acidity of the medium. The temperature must be kept constant to keep the solution stabilized. Fig. 1 illustrates the printed hard shell capsules containing a seaweed extracts and sorbitol as a plasticizer. The swelling of a polymer is generally determined to avoid its direct dissolution in the solvent. The swelling degree of the hard shell capsules obtained is shown in Tables 1 - 5. There W_o is the mass of hard shell capsules prior to the contact with the solvent, W_t is their mass after having a contact with the solvent, while Qi stands for the swelling degree.

Fig. 1. Hard shell capsules from seaweed extracts.

The swelling degree is affected by the amount of spaces in the polymer chains [10]. In this case, sorbitol as a plasticizer estranges the intermolecular interactions in the seaweed extract polymer so that it becomes a moderately soft gel. The swelling degree increases with the increase of sorbitol's concentration. It seems probable that seaweed extract capsules can be suitable for the duodenum system.

The analysis of the dissolution kinetics is carried out on the ground of the Noyes-Whitney equation [11]:

$$\frac{dM}{dt} = KS(C_s - C_t)$$

Table 1. The swelling degree of gelatin hard shell capsules.

W_0 (gram)	W_t (gram)	Q (%)
0.0957	0.1897	98.22
0.9090	0.3818	320.0
0.0954	0.1946	104.0
0.0958	0.2088	119.8
0.1342	0.2988	122.6
0.0949	0.1976	108.2
Average swelling degree of gelatin hard shell capsules		**145.5**

Table 2. The swelling degree of A hard shell capsules.

W_0 (gram)	W_t (gram)	Q (%)
0.0850	0.4504	429.9
0.0952	0.2562	169.1
0.0950	0.8174	760.4
0.1101	0.7348	567.4
0.0943	0.4212	346.7
0.0762	0.4121	440.8
Average swelling degree of A hard shell capsules		**452.4**

Table 3. The swelling degree of B hard shell capsules.

W_0 (gram)	W_t (gram)	Q (%)
0.1085	0.6005	453.5
0.1040	0.6134	489.8
0.0960	0.8273	761.8
0.0892	0.5062	467.5
0.1217	0.9692	696.4
0.0860	0.4975	478.5
Average swelling degree of B hard shell capsules		**557.9**

Table 4. The swelling degree of C hard shell capsules.

W_0 (gram)	W_t (gram)	Q (%)
0.1121	0.6346	466.1
0.1097	0.4970	353.0
0.1147	0.8595	649.4
0.1138	0.9181	706.8
0.1032	0.9431	813.9
0.1083	0.9001	731.1
Average swelling degree of C hard shell capsules		**620.0**

Table 5. The swelling degree of D hard shell capsules.

W_0 (gram)	W_t (gram)	Q (%)
0.1018	1.5469	1419.6
0.1215	0.8020	560.1
0.1206	0.8559	609.7
0.1201	0.8649	620.2
0.1438	1.0258	613.4
0.1200	0.8641	620.1
Average swelling degree of D hard shell capsules		**754.0**

where: M is the transferred mass (gram), t is the release time (second), K is a kinetic constant (g^{-1} cm^4 s^{-1}), S is the particle solubility (g/cm^3), C_s is the equilibrium concentration (g/cm^3) of solute, while C_t is the current concentration (g/cm^3) of the solute[11]

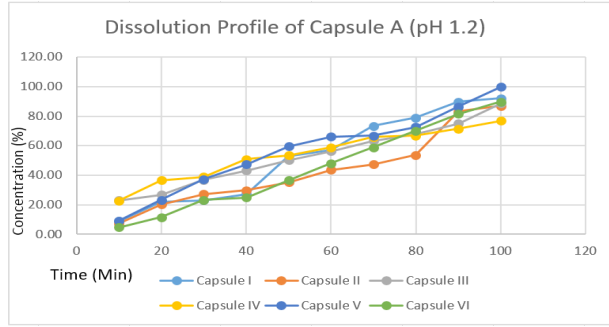

Fig. 2. Dissolution Profiles of capsules of A, at pH 1.2.

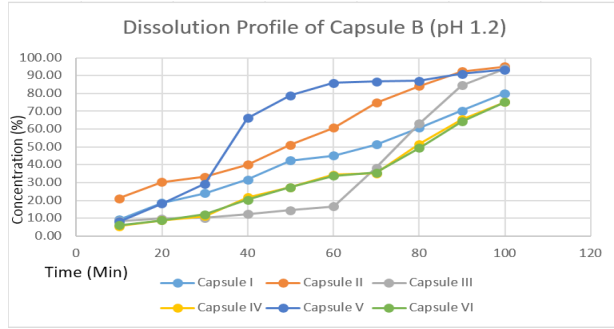

Fig. 3. Dissolution Profiles of capsules of B, at pH 1.2.

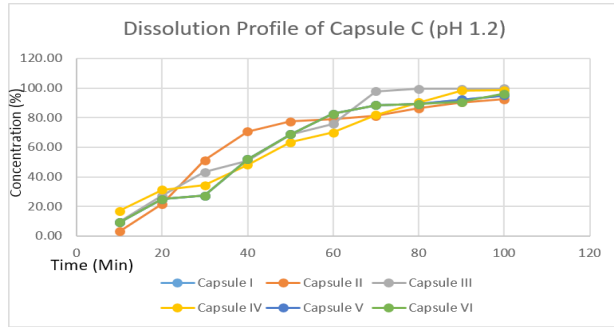

Fig. 4. Dissolution Profiles of capsules of C, at pH 1.2.

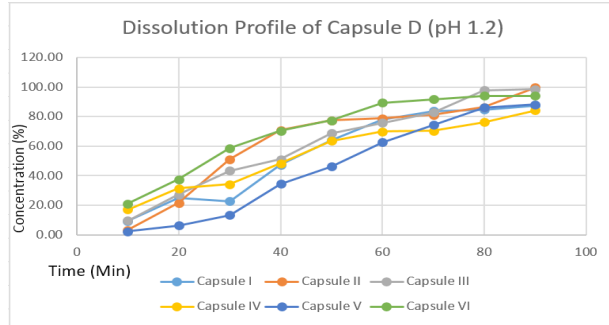

Fig. 5. Dissolution Profiles of capsules of D, at pH 1.2.

Samples of A, B, C and D show different profiles of dissolution kinetics at pH of 1.2. But the accumulated concentration of erythromycin reaches 90 %, which means that they all need 90 min to be released at pH 1.2 (Figs. 2 - 5).

Hard shell capsules of A are released of drug from 40

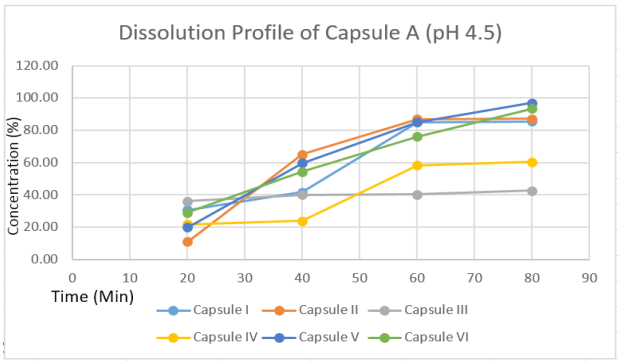

Fig. 6. Dissolution Profiles of capsules of A, at pH 4.5.

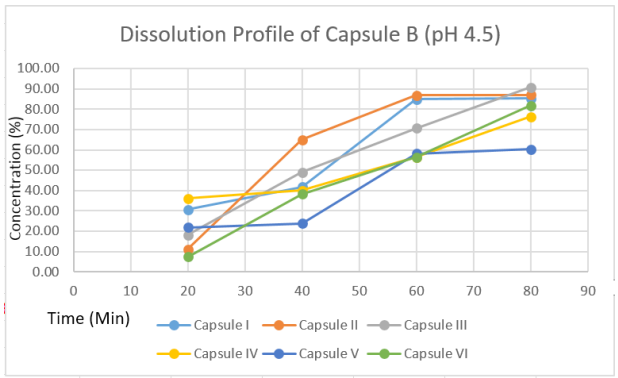

Fig. 7. Dissolution Profiles of capsules of B, at pH 4.5.

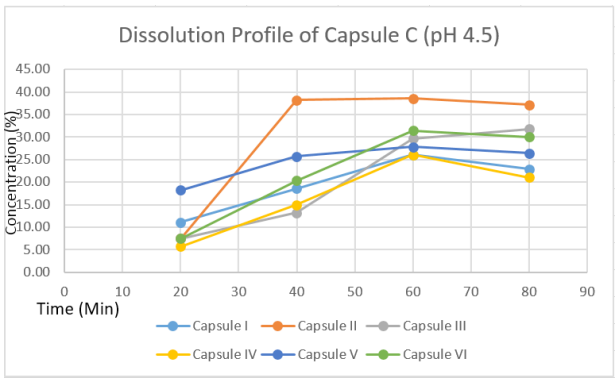

Fig. 8. Dissolution Profiles of capsules of C, at pH 4.5.

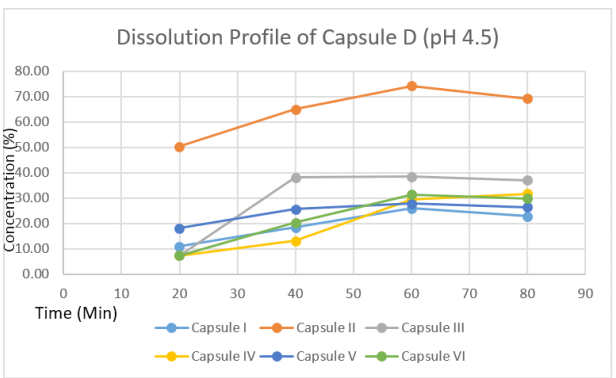

Fig. 9. Dissolution Profiles of capsules of D, at pH 4.5.

min up to 60 min (Figs. 6 - 9). The decreased rate of release is attributed to the smaller pores of the hard shell capsules when compared to those of gelatin hard shell capsules. This data is supported by the higher swelling degree of these capsules compared again to that of gelatin hard shell capsules. Hard shell capsules of B in average have a higher linear rate of diffusion than that of hard shell capsules of A. But hard shell capsules of C and D have a higher swelling degree. A further diffusion rate decrease is indicated. 28.21 % and 36.25 % of the drug in hard shell capsules of C and D are released for 80 min, correspondingly. This leads to the conclusion that capsules A and B are more suitable at pH 4.5 than those of composition C and D.

At pH 6.8 the drug in hard shell capsules of A, B, C and D is released more than 50 % within the first 20 min, while the complete release is achieved for 80 min (Figs. 10 - 13). It is evident that the drug delivery from seaweed extract capsules is easier at pH 6.8.

The characterization of surface morphology of the hard shell capsules shows no nano pores on the surface. This may be due to the magnification used or the bubbles

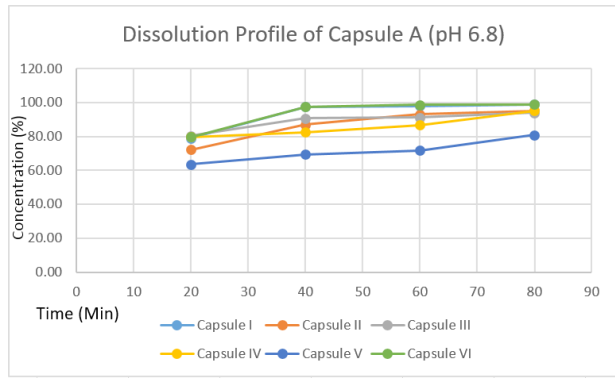

Fig. 10. Dissolution Profiles of capsules of A, at pH 6.8.

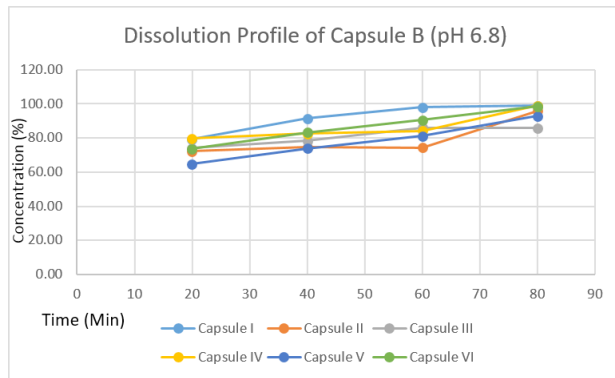

Fig. 11. Dissolution Profiles of capsules of B, at pH 6.8.

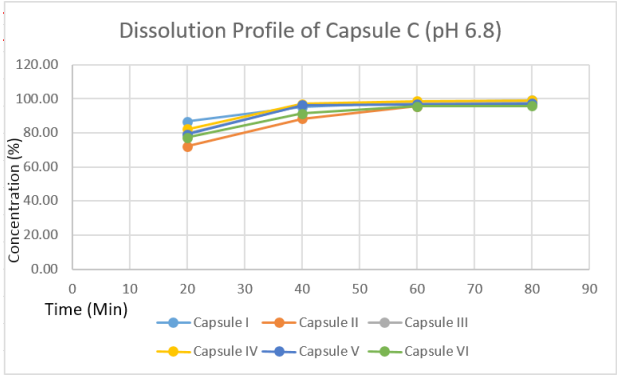

Fig. 12. Dissolution Profiles of capsules of C, at pH 6.8.

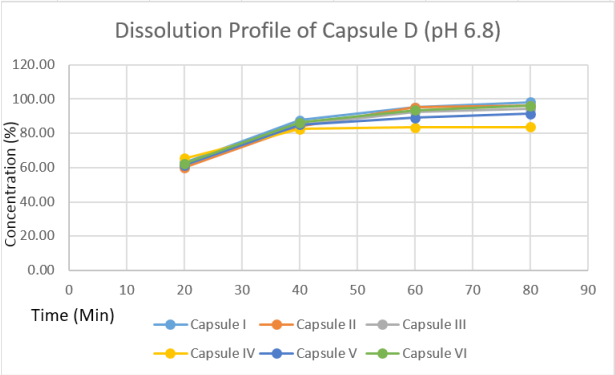

Fig. 13. Dissolution Profiles of capsules of D, at pH 6.8.

formed during the printing procedure. They are seen as white spots on the SEM micrographs.

CONCLUSIONS

Hard shell capsules for drug delivery can be made from seaweed extracts. Indonesia is rich of seaweed, so it has a great potential in this field. Acidity affects the dissolution profiles of the hard shell capsules studied. Unlike gelatin capsules those made of seaweed extract provide drug release at pH of 6.8 which coincides with that of the duodenum.

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