https://doi.org/10.31351/vol33iss4pp115-125

Extraction and Characterization of Carrageenan from Seaweed (*Kappaphycus alvarezii*) Produced by South Lampung Indonesia Farmers and Utilization as a Tablet Binder using Metformin as a Drug Model

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Received 2/8/2023, Accepted 16/10/2023, Published 20/12/2024

Abstract

Indonesia is known as one of the countries with the biggest biodiversity worldwide. The aim of this study is to determine the characteristics and the strength of carrageenan as a tablet binder from *Kappaphycus alvarezii* seaweed that is produced by farmers in South Lampung District, Province of Lampung. Carrageenan that was produced was characterized by its physical, chemical, and functional characteristics. Carrageenan then was formulated in a tablet dosage form as a binder and compared to tablets that used carbopol as a binder. The data obtained from the physical, chemical, and functional characteristics was described qualitatively and the test results of some parameters from the physical characteristic tablets were analyzed theoretically as compared to the standard literature. The statistical tests used an independent T-test at a 95% confidence interval. The results showed that carrageenan has the following characteristics: pH 10.7; moisture content of 5.001%; particle size distribution of 76.8% (120 mesh); compressibility index of 21.9%; inflate index of 240% (pH 1.2); repose angle of granule is 30,48º; flow rate of 5 g/s; viscosity at 45.922,85 cps (75ºC) and 53.690 cps (50ºC); SEM results indicate that carrageenan particle shape was irregular; FTIR showed that there were ester sulfate, 3,6- anhydrogalactose, and galactose-4-sulfate. Based on the result, it was concluded that the metformin tablet that was made using carrageenan and carbopol as binders qualified the physical characteristics of tablets, but there were significant differences in the granule flow rate, tablet disintegration time, and dissolution profiles of tablets. It was stated that carrageenan can be used as a good tablet binder in this research.

Keywords: Binders, Carrageenan, Characterization, *Kappaphycus alvarezii*, Tablet.

Introduction

Indonesia is a country that has huge biodiversity, both of land and marine. Various types of nutritious plants thrive in this country, most of them had been not explored well, especially the potency of biodiversity in the sea [(1)]. Good exploration and utilization of the potency of biodiversity will provide many impacts for the country such as health, welfare, and prosperity [(2)]. One of the resources marine plants have many utilities is seaweed, well known produce a lot of materials as alginate, agar, and carrageenan which are applied in foods and pharmaceutical fields [(3)]. Alginate had been applied in many fields of pharmaceuticals and food, even, this material had been investigated in micro/nanoparticulate drug delivery systems [(4)]. Carrageenan is one of the seaweed products that were studied by a few researchers as compared to alginate and agar. Moreover, in Indonesia, we have to import from abroad for applying carrageenan in the pharmaceuticals field. Carrageenan obtained from the extraction of red algae (rhodophyceae) using hot water or alkaline solution at high temperature [(5)].

Carrageenan-producing seaweed species such as *Eucheuma cottonii* and *Eucheuma spinosum* can be obtained from the Indonesian ocean. Since the carrageenan is produced from *Eucheuma cottonii* generally kappa-carrageenan type hence this red algae is also called *Kappaphycus alvarezii* [(6)].

Carrageenan is a biopolymer that has many implications not only in food and pharmaceutic fields but also in biomedical applications, which is widely used due to its low toxicity, biodegradability, stability, renewable nature, and its functions [7,8]. Carrageenan can be used as a thickening agent, gelling agent, stabilizer, binder (former film), and deterrent of water release (syneresis inhibitors) [9]. Salamat-Miller et al. [10] categorized carrageenan as a mucoadhesive polymer for a buccal drug delivery system. Buccal drug delivery with a mucoadhesive system will increase the contact time in buccal hence the drug efficacy will raise maximally.

Furthermore, carrageenan had been explored in various drug delivery systems, such as in oral extended-release tablets, as an extrusion aid for the preparation of pellets, and in micro/nanoparticles delivery systems [11]. In the general tablet formulations, carrageenan plays a role as a binder. The binder must provide an affinity for the powder mass during the granulation process. The binder can hold the particles together powder in granules [12]. Normally, the amount of carrageenan used as a binder is 0.25 – 2 % [13].

A tablet binder is a vital component of tablet formulation, it provides the adhesion and cohesiveness quality of the tablet [14]. Through its characteristics, the binder contributes to form tablet granules and tablet compression as well as the standard required [15]. Another reference used granulating agents as a synonym of tablet binder, especially in terms of wet granulation and dry granulation as the methods of tablet preparation. The materials commonly used as tablet binder such as starch, pregelatinized starch, acacia, polyvinyl pyrrolidone (PVP), hydroxy propyl methyl cellulose (HPMC), and methyl cellulose (MC) [16]. Some researchers tried to explore carrageenan used for binder in sustained release tablet [17] and modified release tablet [18]. We also applied agar as another marine product which is well-known has similar characteristics with carrageenan for tablet binder [19] and explored it into mucoadhesive excipient [20].

Accordingly, in this study, we used carrageenan from *Kappaphycus alvarezii* was produced by farmers in South Lampung District, Province of Lampung Indonesia as a binder in tablet formulation. We then characterized the properties of the carrageenan as an excipient included physical, chemical, and functional characterization in which the binding capacity was measured in the metformin tablet formulation as compared to Carbopol which is known as a commercial tablet binder. Carbopol had been examined as a tablet binder since a few years ago [21].

Materials and Methods

Materials

The materials used seaweed was purchased from farmers in the South Lampung District, Province of Lampung. Metformin HCl was received as a gift sample from PT Pyridam Farma, Indonesia. Carbopol was purchased from Shadhong Biotechnology, Shanghai, China. All other chemicals were of analytical grade purchased from local suppliers in Indonesia.

Plants determination

Determination of seaweed used in this study was performed at the Laboratory of Plant Taxonomy, Faculty of Biology, Universitas Jenderal Soedirman, Purwokerto, Indonesia.

Preparation of carrageenan

Extraction of carrageenan from Seaweed *Kappaphycus alvarezii* is performed according to the method by Naseri et al. [22]. Seaweed soaked for 24 hours with water, washed, cut, and crushed using a blender. Then extracted the seaweed with 1 % NaOH at 90^{o}C while stirring for 3 hours and filtering the extract with nylon 150 and 300 mesh. The precipitation process was carried out by adding isopropyl alcohol (IPA) with a volume ratio of seaweed extract and IPA 1:1.5 (v/v). Afterward, the carrageenan obtained was dried in the oven at 60^{o}C until a constant weight.

Physical characterization of carrageenan

a) Physical appearance

Physical appearance is carried out by organoleptic observations on carrageenan, including taste, colour, and smell [23].

b) Particle shape

The observation of the particle shape and the morphology of carrageenan were carried out using scanning electron microscope (SEM). The sample put on the holder and insert to coating unit then observed with SEM [24].

c) Particle size distribution

Determination of the particle size distribution was done by the micromeritic method (sieve). The sieves are arranged starting from the top, from the smallest sieves (40 mesh) to the biggest (120 mesh). About of 50 grams of carrageenan powder was put into the smallest sieve then sieved for 20 minutes [25].

d) Hygroscopicity

Each 1 gram of carrageenan powder placed in the plastic pots with four treatments, i.e.: 1. The plastic pot without lid, 2. The plastic pot with lid, 3. The plastic pot without lid with silica gel, and 4. The plastic pot with lid with silica gel. All of plastic pots was placed in a desiccator at room temperature and relative humidity (RH) 70%. Samples were observed every week to see changes in physical characteristics encompass the changes in colour and weight for 1 month [26].

e) Determination of powder moisture content

A total of 5.003 grams of carrageenan powder was weighed and added carefully in a container. Powder dried at 105°C for 5 hours and weighed then the drying was continued for 4 hours [27]. The moisture content of carrageenan powder was calculated according to the equation: $\frac{W0-W1}{W1} x\ 100\%$, whereas W0 is the initial powder weight and W1 is the powder weight after drying.

Chemical characterization of carrageenan

a) Identification of functional groups

Identification of functional group of carrageenan is carried out by an infrared spectrophotometer. About of ± 2 mg of the sample to be tested was weighed together with 98 mg of potassium bromide (KBr) and then analysed using spectrophotometer infrared (Fourier Transformation Infra-Red/FTIR) [28].

b) pH Measurement

The pH measurement was determined by preparing a 2% of carrageenan solution, then the pH was measured using a pH meter [29]. The 2% carrageenan solution is used to determine its pH because it is a common concentration applied in scientific research to study the properties of carrageenan [30].

Functional characterization of carrageenan

a) Carrageenan viscosity measurement

Viscosity of the sample was determined by making a 5% w/v solution of carrageenan in distilled water, then measured using a Brookfield viscosimeter, from 0.5 rpm, 1 rpm, 2 rpm, 2.5 rpm, 5 rpm, 10 rpm, and 20 rpm, then back to 10 rpm, 5 rpm, 2.5 rpm, 2 rpm, 1 rpm , and 0.5 rpm [31]. As we know that carrageenan is a natural polysaccharide, a 5% solution is commonly used to measure its viscosity [32].

b) Determination of powder flow properties

The flow properties of carrageenan powder were determined by measuring the flow rate and angle of repose of the samples. Amount of 100 gram of carrageenan powder was weighed and put in flowmeter, to calculate the flow rate, note the time of powder flowing until it runs out, and to determine the angle of repose measured the height and the diameter of the pile is formed [33].

c) Compressibility index

Determination of the compressibility is started by measuring the bulk density, the measurements were carried out by weighing about of 20 grams carrageenan samples were put into a 100 mL of volumetric flask, then the volume was measured (V_1). Compressed density was measured by continuing the carrageenan sample in bulk density determination, then the volumetric flask containing the sample was tapped about 300 times. The experiment was repeated by 300 times tapped and the volume was measured (V_2) [34].

d) Swelling behaviour test

Carrageenan was put into a 10 mL volumetric flask up to a limit of 1 mL (V_0). Added a solution of HCl pH 1.2 and phosphate buffer pH 7.4 each as much as 10 mL in different containers. Carrageenan was allowed to swell at room temperature. Observations were performed at certain time intervals until constant (V_t) [35].

e) Tablet formulation

Carrageenan was added into a metformin HCl tablet formulation as a binder tablet. This formula then compared to another formula that used carbopol as a binder tablet. We used carbopol which is known as a good binder tablet [21], commonly. Both of formula as seen in **Table 1**. The preparation of metformin tablets with carrageenan and carbopol as the binders using the wet granulation method. We used metformin HCl as a model drug, as a filler that is lactose, and Ac Di Sol as disintegrant were mixed, then added with carrageenan (F1) and Carbopol (F2). After that, the mixture was sieved with a 14-mesh sieve into granules and was dried in an oven at a temperature of 60-70°C for about 60 minutes. Afterward, talc and Magnesium stearate as lubricant were added [36].

Table 1. Tablet formulation

Component	**F_1**	**F_2**
Metformin HCl	500	500
Carrageenan (%)	2.0	-
Carbopol (%)	-	2.0
Lactose (%)	qs	qs
Ac Di Sol (%)	3	3
Talc (%)	1	1
Magnesium Stearate (%)	2	2

f) Evaluation of granules

1. Determination of granules flow properties. The granules flow properties that are flow rate and angle of repose are determined using a flowmeter. 100 g of granules is weighed and put into flowmeter, to calculate the flow rate, note the time of granules flowing until it runs out, to determine the angle of repose measure the height and diameter of the pile formed [33].

2. Determination of granules moisture content. Amount of 5 g granules (W_0) dried in an oven at a temperature of 40ºC, then weighed until a constant weight (W_1) is obtained [37].

g) Tablet compression

The granules are put into the hoppers and compressed with both movements upper and lower punch to form tablets [38].

h) Determination of the physical properties of metformin tablets

1. Tablet organoleptic
The organoleptic test of tablets was performed by observing the colour, shape, smell, taste, surface form, tablet physical disability [39].

2. Tablet hardness
The tablet hardness test is done by put one tablet in the middle hardness tester in an upright position, the condition of the device was initially in the zero position, then the tool was rotated slowly until the tablet crush. Read the scale (kg) when the tablet is ruptured [40].

3. Tablet fragility (friability)
The tablet friability is determined by friabilator, that is total of 20 tablets weighed (W_0), then entered in the friabilator operated 100 times for 4 minutes. The tablets were then taken and weighed again (W_t), the percentage difference or weight loss was calculated [41].

4. Tablet disintegration time
A total of six tablet samples were put in a basket-shaped tube, then the tube was up and down regularly 30 times per minute in a water medium at a temperature of 37°C. The tablet is declared disintegrated if there is no part of the tablet left on the gauze [40].

5. Tablet weight uniformity
For the weight uniformity test, 20 tablets had been cleaned of dust were weighed one by one and the average weight was calculated [40].

6. Tablet size uniformity
Determination of tablet size uniformity was carried out by taking a sample of 20 tablets. The diameter and the thickness of each tablet were measured using calipers. The diameter of the tablet is not more than three times and not less than one-third of tablet thickness [40].

7. Tablet dissolution test
The rate of drug release from the tablet is tested using the type II dissolution test (paddles). The tablets were tested in 900 mL of phosphate buffer pH 6.8 as a dissolution medium, at 37 ± 0.5ºC and 100 rpm. A total of 5 mL samples were taken after 5, 10, 15, 20, 30, 45, and 60 minutes and with the same volume medium added again every after taking the collected sample. Samples were then analyzed using spectrophotometry at a wavelength of 233 nm to measure the concentration of the drug contained in [40]. The absorbances were read on the UV-Vis spectrophotometer and plotted into the regression equation of the metformin HCl standard curve, namely $y = 0.3106x + 0.0082$; $R^2 = 0.9708$.

Data analysis

Data obtained from the physical, chemical, and functional characterizations of carrageenan powder were described qualitatively, then the results of testing several parameters of the characteristics of tablets were analysed literally as compared to Indonesian Pharmacopoeia Edition VI, and other literatures. Statistical tests were performed by an independent T test with a 95 % confidence level to determine whether there was a significant difference in the characteristics of tablets formulations using carrageenan and carbopol as binders.

Results and Discussion

Plants determination

The determination of seaweed demonstrated that the red algae was used in this research is truly *Kappaphycus alvarezii* from Solieriaceae family.

Physical characterization of carrageenan

According to the carrageenan extraction, which is from 1.5 kg seaweed to 142.3 gram of carrageenan, the yield was 9.48%. In this study, the carrageenan was obtained in the form of a fine powder that was light yellow in colour, tasteless, had a typical carrageenan odor, and was slightly fishy. The results of observations using SEM (Figure 1) show the shape of carrageenan particles that is solid pebbles, with various sizes but there are still large chunks, the shape of the particles is irregular and has a rough surface texture.

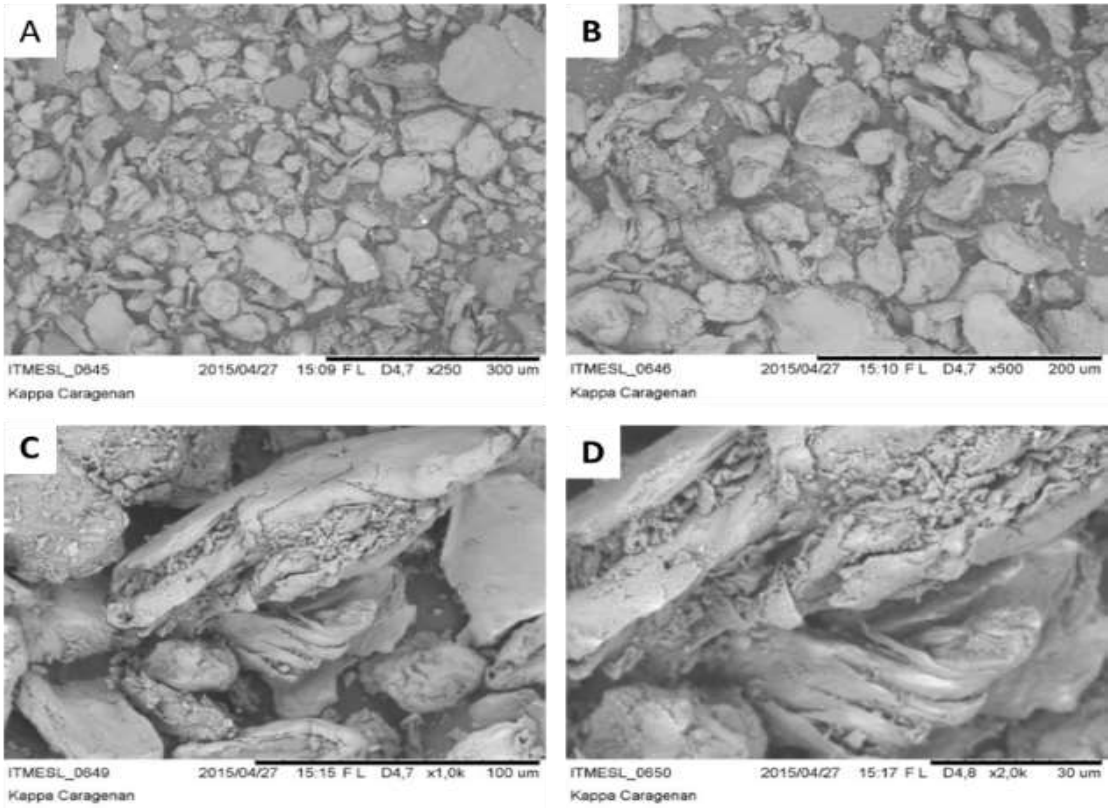

Figure 1. SEM images of carrageenan powder with 250x magnification (A), 500x magnification (B), 1000x magnification (C), and 2000x magnification (D)

Determination of particle size distribution using sieves showed that carrageenan powder is distributed as much as 76.8 % at 120 mesh, 13.4 % at 45 mesh, 8 % at 100 mesh, 0.8 % at 40 mesh, and 1 % which did not pass the sieve. The particle size distribution of carrageenan powder visualized as bar chart can be seen in the **Figure 2**.

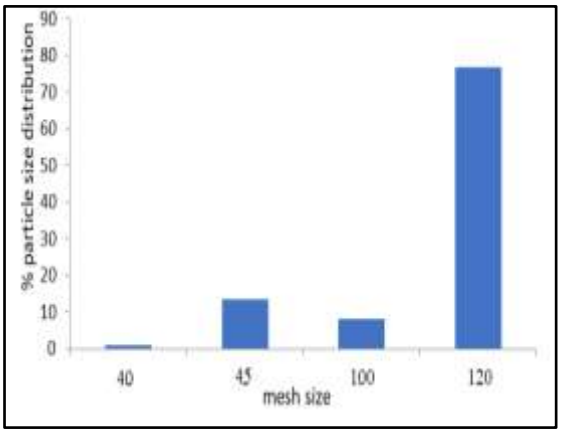

Figure 2. The bar chart of particle size distribution

The hygroscopicity characterization displayed during 4 weeks of treatment there was no change in the colour of carrageenan powder. The highest increase in average of carrageenan weight is 5.075% in the pots I without lids and without silica gel. While the samples stored in closed pots IV with silica gel, has the lowest percentage for the weight increasing, that is 2.825%. This data indicates to store carrageenan powder should be in the container tightly closed with silica gel inside. The bar chart as visualization for results characterization of carrageenan powder hygroscopicity can be seen in **Figure 3**.

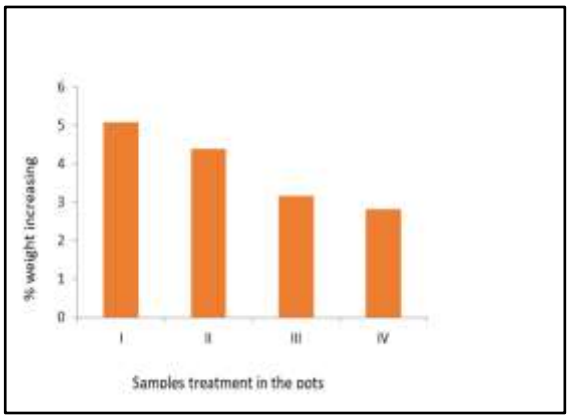

Figure 3. The bar chart of % carrageenan weight increasing

From the experiment, the result for moisture content of carrageenan powder is 5%. This data meets the Food Agricultural Organization (FAO) standard (2014) that stated the moisture content of carrageenan powder should be no more than 12% [(42)].Lower moisture content will be more

advantageous because the material will be more resistant in the water storage [43].

Chemical characterization of carrageenan

The results of functional groups identification with FTIR, the carrageenan from this research has a peak curve of 3390.86 cm^{-1} which shows presence of OH, the infrared spectrum also on a peak curve of 2933.73 cm^{-1} which indicates the presence of CH alkane. The carrageenan has absorption from sulfate esters at 1220-1260 cm^{-1}, carrageenan also has a strong and broad absorption, related to a typical absorption of all polysaccharides at 1000-1100 cm^{-1}, absorption of 3.6-anhydrogalactose at 928-933 cm^{-1}, absorption of galactose-4-sulfate at 840850 cm^{-1} [44]. All the functional groups indicate that carrageenan as produced *Kappaphycus alvarezii* from South Lampung District, Province of Lampung, Indonesia is like kappa-carrageenan. The complete infrared spectrum of carrageenan was made in this research could be seen in Figure 4.

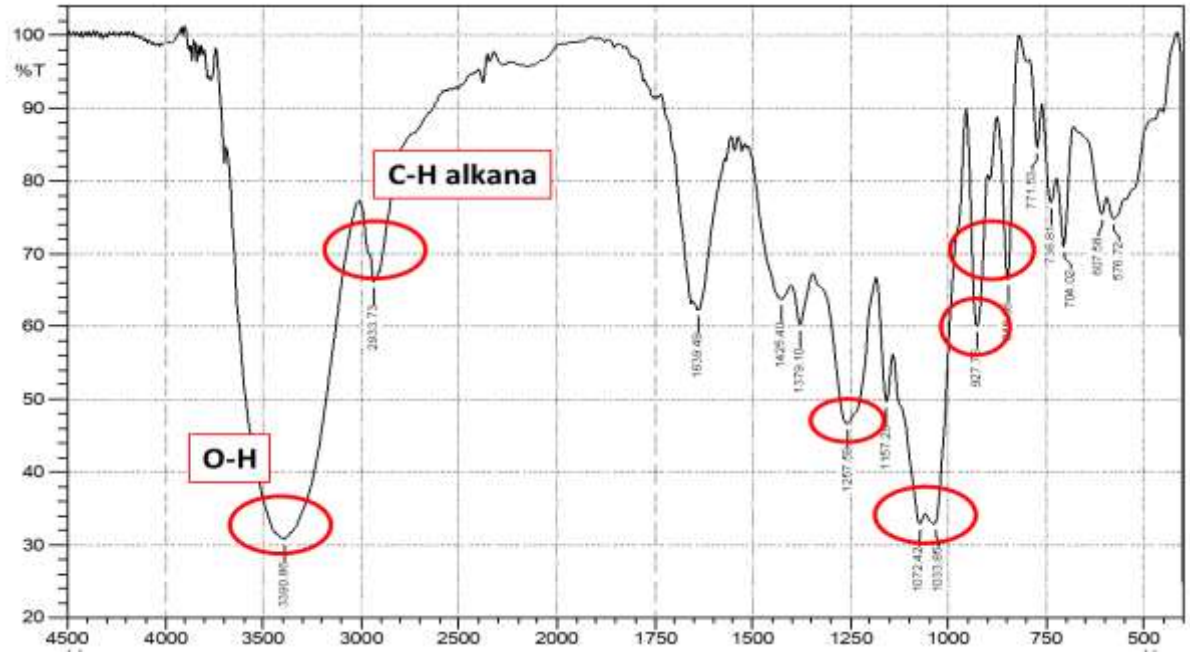

Figure 4. Infrared spectrum from FTIR characterization for carrageenan

After measure the carrageenan pH using pH meter, the result showed the pH was 10.7. This data meets the FAO (2014) requirement that carrageenan has a pH between 8-11.

Functional characterization of carrageenan

Carrageenan viscosity was measured at a concentration of 5% w/v using spindle 64 at a temperature of 75°C the average viscosity is 45922.85 cps, at a temperature of 50°C had an average viscosity of 53690 cps, and at a temperature of 25°C, its viscosity could not be measured. Carrageenan viscosity belongs to the pseudoplastic flow type, pseudoplastic flow is usually indicated by the polymer in solution [31].

The results of the measurement of the angle of repose of carrageenan have an average of 30.48° which is categorized as a good and shows a good flow property. Carrageenan also has a good flow rate, which is 5 g/second. The compressibility index test results showed that the value of kappa-carrageenan was 21.9%, which means classified in the medium category [45].

After performed the swelling behaviour test, the results demonstrated that the highest swelling of carrageenan was found in HCl medium pH 1.2. In this pH, the swelling volume can reach 240% of the initial volume. The swelling behaviour of carrageenan at phosphate buffer pH 7.4 and aquadest pH 6 only had 200% and 190%, respectively. This is due to the nature of carrageenan which is hydrophilic so that it is more easily hydrated by the medium used [46]. The summary of carrageenan functional characterization results could be seen in Table 2.

Table 2. Summary of functional characteristics result test in average

Characteristics	Average Results
Viscosity	45922.85 cps (75°C) 53690 cps (50°C)
Angle of repose	30.48°
Flow rate	5 g/sec
Compressibility index	21.9%
Swelling behaviour index	240% (pH 1.2)

Based on the results of measurement of the granules angle of repose showed that each tablet formula has a different value. Metformin HCl tablet with carbopol as a binder has granules angle of repose of 28.79° and granules with carrageenan as a binder has 31.15°. It can be stated that the granules with carbopol as a binder meet the requirements, namely having an angle of repose no more than 30° [45]. However, the result of the T-test on the average

angle of repose of granules with carbopol as a binder and granules with carrageenan as a binder is p> 0.05 and it can be concluded that there is no significant difference between the two formulas.

The result of the granules flow rate measurement exhibited that granules with carbopol as a binder has 6.66 second and granules with carrageenan as a binder was 26.33 second. It means that granules with carrageenan as a binder is categorized bad flow rate due to the requirement for a good granules flow rate from 100 grams granules should less than 10 second [47]. Referring to the flow rate result, the T-test showed p<0.05, it could be decided that there is a significant difference in the average flow rate between carbopol formula and carrageenan formula.

From the moisture content measurement, the results show that both carrageenan granules and carbopol granules meet the requirements, which is in the range of 2%. Following this data, the T-test of carbopol formula and carrageenan formula is p>0.05 and it can be concluded that there is no significant difference in the average moisture content between the two formulas [48]. All the measurements result of the granules characterization for each formula on average could be seen in **Table 3**.

Table 3. The measurements result of granules characterization on the average

Granule Characteristics	Formula	
	Carbopol	**Carrageenan**
Angle of repose	28,79 °	31,15 °
Flow rate	6.66 s	26.33 s
Moisture content	2.55 %	2.14 %

The tablet appearance test was performed by physical organoleptic showed that the resulting tablet is relatively good [49]. All formulas have a brownish-white colour and a uniform surface shape. But there is a striking difference from the smell of tablets, tablets with carrageenan as a binder has a little fishy belong to the typical smell of carrageenan [29].

Regarding the tablet hardness test results, showed that both carbopol as a binder and carrageenan as a binder meets the requirement, which has a hardness scale of 4-8 kg [39]. The friability test of both tablets' formula also meets the requirements, namely weight loss of not more than 1% [50]. All formulas qualified the tablet disintegration time test requirements, namely for uncoated tablets should not be more than 15 minutes [40]. The disintegration time of tablets using carrageenan as a binder is only 37 seconds, this shows that the carrageenan binds or adsorbs water quickly thus accelerates the tablets to disintegrate.

Both tablet formulas did not differ significantly in weight and met the requirements for weight uniformity because none of the tablets deviate from 5% or 10% of the average weight of the tablets [40]. From the size uniformity test, the results showed that all tablets meet the requirements since they are still within the allowable range that is the diameter is not more than three times the tablet thickness and not less than one-third of the tablet thickness [51]. The T-test results of tablet hardness, friability, weight uniformity, and size uniformity between tablets with carbopol as a binder and tablets with carrageenan as a binder were p>0.05, which means there was no significant difference between the two formulas [52]. However, there was a significant difference between the two formulas for the tablet disintegration time due to the T-test results showed p>0.05. The summary of the tablet's physical characterization results on average can be seen in Table 4.

Table 4. Summary of tablet's physical charactarization results on average

Characteristics	Formula	
	Carbopol	**Carrageenan**
Tablet hardness	4,740 kg	4.250 kg
Friability	0.07 %	0.33 %
Disintegration time	494 s	37.33 s
Weight uniformity	592.75 g	597.3 g
Tablet Diameter	1.35 mm	1.34925 mm
Tablet Thickness	0.4415 mm	0.43925 mm

Based on the tablet dissolution test, the result displayed that the release percentage of metformin HCl tablets with carbopol as a binder was increased gradually over time. But metformin HCl tablet with carrageenan as a binder showed weird drug release as showed in **Figure 5**.

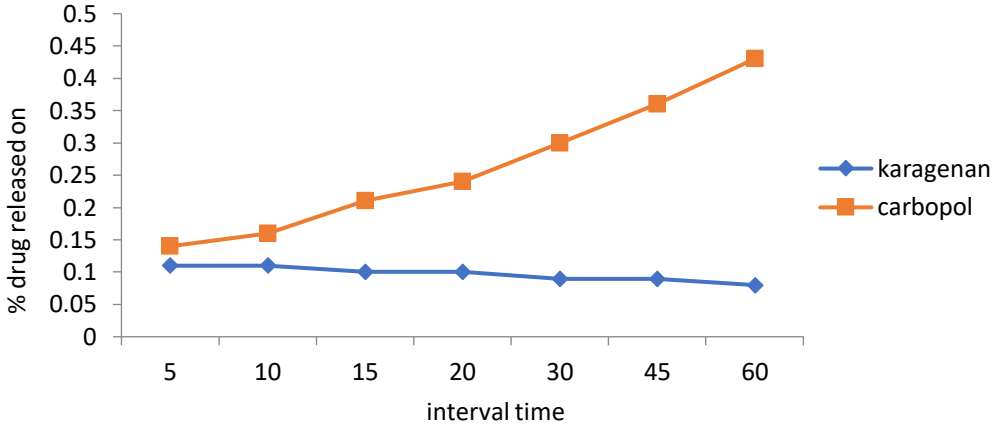

Figure 5. The dissolution profile of metformin HCl tablet with different binders

The carrageenan used in this study was produced by standard method thus the particle size and the particle shape were less uniform. This case can be solved when the production of carrageenan using some size reduction technologies such as micronizing, microfluidic particle size reduction, spray drying, and sonocrystallization. These technologies provide a better quality of carrageenan since particle size and particle shape influence many other things in the pharmaceutical field [53].

Regarding the functional groups' identification, carrageenan in this research is like kappa-carrageenan. This property is also supported by the other characterization which are viscosity, pH, and swelling behaviour. Therefore, it can be claimed that the carrageenan used in this research is categorized as kappa-carrageenan [54].

Based on the results of the carrageenan characterization when used as a binder in metformin tablets, the performance met the requirements of the literature. All the parameters such as tablet hardness, friability, uniformity of weight, and uniformity of tablet size are good. Interestingly, metformin tablets with binder carrageenan disintegrated very quickly, i.e., 37 seconds. This indicates that the bond between the particles in the metformin tablet is very strong but is easily wetted by the presence of water [55].

The results of this study indicate that carrageenan can be a good excipient to be used as a tablet binder. This enriches the list of natural excipients that can be used as tablet binders [56]. Meanwhile carrageenan has not been widely studied when it is used as a tablet binder. Both origins the marine natural products, the utility of carrageenan as a tablet binder is less familiar when compared to alginate [57]. Metformin tablets using binder carrageenan have a slightly distorted dissolution profile can be caused by several things, including there is potential for carrageenan to be used as a slow-release matrix thus metformin is restrained from its release, the raw material for carrageenan has not been standardized, and the metformin HCl tablet formulation is not optimal. The T-test result on the dissolution of the tablets with carbopol and carrageenan as binders showed $p<0.05$, which means there is a significant difference between the two formulas [58].

Referring to the results of the hardness test, friability test, disintegration time test, and dissolution test of metformin tablets using a carrageenan binder, the carrageenan used in this study is promising to be used as a binder in the formulation of sustained-release tablets [59]. This is also confirmed by [60] in their research about combination kappa-carrageenan with HPMC and guar gum as excipients in the formula of metformin HCl modified release tablet. In this study it was stated that this combination could be used well as a drug carrier with matrix system.

Following the profile of releasing the metformin from the tablet, it can be hypothesized that the mechanism is the dissolution medium enters into the tablet, then the polymer (carrageenan) is gelatinized, dissolution of the drug and diffusion through the resultant layer. Simultaneously, the outer layer is fully hydrated and dissolved. This process is known as erosion [61] and this mechanism is followed by a lot of natural polymer in the releasing of the drug from its dosage forms [62]. Metformin tablets that use carrageenan as the binder have slightly aberrant dissolution profiles, which can have several causes things, including carrageenan proven can be used as a sustained-release matrix, carrageenan raw materials have not been standardized, and the tablet formulation has not been optimal [23].

Conclusion

Carrageenan produced of seaweed *Kappaphycus alvarezii* from South Lampung District, Province of Lampung, Indonesia has following characteristics such as pH 10.7; moisture content 5%; particle size distribution of 76.8% at 120 mesh; compressibility index 21.9%; the highest swelling index 240% at pH 1.2 for 30 minutes; angle of repose 30.48º; flow rate 5 g/s; viscosity at 5% w/v of 45.922.85 cps (75ºC) and 53.690 cps (50ºC); SEM images show a less uniform particle shape; FTIR showed that there were OH groups, CH alkanes, sulfate esters, 3,6anhydrogalactose, and galactose-4-sulfate that similar to kappa-carrageenan. The metformin tablet formula was made using carrageenan and carbopol as binders met the requirements for tablet physical properties (physical appearance, size uniformity, weight uniformity, hardness, friability, and disintegration time) but there were significant differences in the granule flow rate of the two formulas, tablet disintegration time, and the profile dissolution. Altogether, this carrageenan is promising to utilize as a tablet binder.

Acknowledgment

Thanks to Hilman Husna Pratama and Nadial Uzmah for helping some of the experiments.

Conflicts of Interest

The authors have no conflicts of interest regarding this study**.**

Funding

This study was funded by The Institute for Research and Community Service (Lembaga Penelitian dan Pengabdian Masyarakat/LPPM) Universitas Jenderal Soedirman, Purwokerto, Indonesia.

Author Contribution

Study conception and design: DWK and KAR; data collection: KAR; analysis and interpretation of results: DWK, KAR, RAS, and SS; draft manuscript preparation: KAR and RAS. All authors reviewed the results and approved the final version of the manuscript.

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