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Carrageenan-based hard capsule properties at different drying time

M A Hamdan[1], S S Lakashmi[1], K N Mohd Amin[1], F Adam[1,2]*

[1]Faculty of Chemical & Natural Resources Engineering, Universiti Malaysia Pahang, Lebuhraya Tun Razak, 26300 Kuantan, Pahang, Malaysia
[2]Centre of Excellence for Advanced Research in Fluid Flow (CARIFF), Universiti Malaysia Pahang, Lebuhraya Tun Razak, 26300 Kuantan, Pahang, Malaysia

Abstract. Shelf life of biocomposite can be monitored by many preservation methods such as drying of biocomposite. Upon drying, water molecule will be removed due to evaporation to surrounding and effect the biocomposite quality, chemical and mechanical properties. Over drying process will lead to the reduction of chemical and mechanical properties of biocomposite. In this work, determination of the best drying time for carrageenan biocomposite hard capsule was performed and compared with commercial hard capsules which are gelatine (GHC) and hydroxypropyl methylcellulose (HPMC). Carrageenan was mixed with crosslinker, cellulose nanocrystal (CNC) and toughening agent at various drying time. The colloid solution was dipped using size "1" dipping bar and dried at 60 ^{o}C for various drying time from 40 to 60 minutes in an oven. The carrageenan hard capsule (CHC) was analysed for weight variation, functional group and capsule hardness test. The result showed that increasing the drying time decreased the properties of the CHC. The CHC had higher hydroxyl group absorbance area in comparison to GHC and HPMC. Meanwhile, the GHC had the highest hardness load followed by HPMC and CHC. Material hardening occurred in CHC biocomposite upon increasing drying time thus lead to material shrinkage and water loss from the sample.

1. Introduction

Interest in the development of biocomposite from natural carbohydrate polymers is rapidly growing especially in food packaging and pharmaceutical application. This is to replace the current petroleum-based synthetic polymers that lead to rubbish dumping and water pollution, globally. Carrageenan is one of the potential carbohydrate polymers to replace the plastic in pharmaceutical application due to its processability and abundance. Carrageenan is a natural and water soluble sulphated polysaccharides [1]. There are three common type of carrageenan which are kappa, iota, and lambda carrageenan [2]. Among those types, kappa carrageenan is commonly used in food and pharmaceutical application as it can form a hard, strong, and brittle mixture or gels. However, biocomposite film from carrageenan itself cannot form a high mechanical strength and easily torn biocomposite [3]. It requires additives such as crosslinker, filler, and toughening agents especially in the making of pharmaceutical products such as hydrogel and hard capsule. In hard capsule formation, if carrageenan is used, the hard capsule cannot disintegrate in water because carrageenan will swell. As a result, the drugs in the hard capsule will not be released in the body. In order to overcome the problem, crosslinker shall be used to crosslink the carrageenan structure and the hard capsule will disintegrate when in contact with water.

Meanwhile, filler such as nanocellulose (NC) is proven to increase the mechanical strength of biocomposites [4,5]. NC is a naturally available polymer which consist of repeating units of *β-D-glucopyranose* group [6]. NC also consists of both crystalline and amorphous region with high aspect

ratio [7]. The properties provide an extensive network of molecules that result in superior properties. Incorporation of NC in carrageenan hard capsule application is expected to increase the mechanical strength of the product.

Other than raw materials, process parameter such as drying is an important parameter in the development of stable and high mechanical properties of carrageenan biocomposite. Drying is a preservation method that will affect the sensory quality and consumer acceptability of the products [8]. Determination of biocomposite quality depends on the physical and chemical properties such as hardness, tensile strength, thermal stability, functional groups determination, and others [8]. In carrageenan pallets, increasing the duration of drying cause a decrease in dissolution time, tensile strength, and disintegration time [9]. Higher drying time more than 70 ^{o}C leads to the decrease in molecular weight of carrageenan pallet due to degradation in the carbohydrate backbone [9]. Extensive drying in bamboo shoot slices leads to the decrease in protein content, water activity, and development of locked in pores due to cellular collapse and severe tissue shrinkage [10]. Additionally, reducing the drying time at higher drying temperature in maize (*Zea mays*) kernels lead to a poor final quality which adversely affected seed viability [11]. At low drying time and high drying temperature, stress-cracking index (major quality concerns in maize processing) was high which caused maximum grain damage [11]. Moreover, increasing the drying time of powdered *Asam sunti* up to 8 hours lead to the decrease in moisture content, but increase in ash content and oxalic acid levels [12]. The increment of drying time cause the hardening of the outside skin of dried fruit hence increase the mineral content in the product [12].

In this study, hard capsule from carrageenan was prepared using dipping method as same as the gelatin hard capsule. The hard capsule was dried a various drying time to analyze the effect on the stability and properties of the hard capsule. The properties of carrageenan hard capsule were compared with the commercial hard capsule materials which were gelatin (GHC) and hydroxypropyl methylcellulose (HPMC). This work is important to ensure that the developed carrageenan hard capsule can withstand the fluctuation of temperature during storage or transportation.

2. Methodology

2.1. Materials

Semi refined carrageenan was supplied by TACARA, Sabah, Malaysia. Food grade crosslinker, toughening agents, and microcrystalline cellulose (MCC) were obtained from Sigma-Aldrich, USA, meanwhile plasticizer, polyethylene glycol (PEG) was obtained from Merck, Germany. Nanocellulose (NC) was obtained via ultrasonication of MCC for 50 minutes at an amplitude of 20% in deionized water.

2.2. Preparation of carrageenan hard capsule

Semi refined carrageenan, crosslinker, nanocellulose (NC), PEG, and alginic acid were mixed with deionized water in a double jacketed glass reactor. The formulation solution was mechanically stirred at 60 °C for 3 ½ hours. The hard capsule solution was dipped using self-fabricated capsule dipping machine using size "1" capsule shell. The pin bar was dried at 60 °C for 40, 50, and 60 minutes in drying oven (BINDER, Germany). The samples were labelled as DT40, DT50, and DT60. The hard capsule physicochemical and mechanical properties were compared with commercial gelatine and HPMC hard capsule material.

2.3. Hard capsule characterization

The hard capsule samples were characterized for functional group and thermal analysis, weight variation and mechanical strength.

2.3.1. Functional group analysis

A Perkin Elmer ATR-FTIR spectrometer (Frontier, USA) was used to analyses the functional group presence in the hard capsule sample. FTIR was operated at spectra range of 400 to 4000 cm^{-1}. A total of

32 scans were acquired at 0.15 s/scan and with a spectral resolution of 8 cm^{-1}. The spectra were analyzed using OMNIC software.

2.3.2. Thermal analysis
Thermogravimetric analysis (TGA) was conducted to analyse the thermal effect on hard capsule sample through changes in weight using Universal TA Instrument (V.47A, New Castle). The thermographic profiles of approximately 5 mg samples heated between 20 °C to 600 °C at heating rate of 10 °C/min, were analysed.

2.3.3. Weight variation
20 hard capsules were selected randomly and weighed using weighing balance. The average net weight was calculated from the sum of the individual net weights. The percentage deviation from the average net weight of each sample was determined using Equation 1;

$$Deviation = \frac{|Average\ weight - Weight\ of\ hard\ capsule|}{Average\ weight} \times 100\% \quad (1)$$

2.3.4. Hard capsule hardness test
Mechanical strength analysis was conducted via breaking force test using CT3 Texture Analyzer (Brookfield, USA). The texture analyser was loaded with a 50 kg load cell. An average of at least three measurements was taken for each formulation. A flat-end probe (TA-10) with diameter of 12.7 mm was used for the analysis. Hard capsule was placed on the texture analyser platform and positioned at the centre of the probe. Testing mode of 'compression' and target option of 'distance' approximately 4.0 mm was programmed. Upon analysis at speed of 1.0 mm/s, the probe was compressed onto the capsule and the breaking force was recorded [13].

3. Result and Discussion

3.1. Functional group analysis
Fourier transforms infrared analysis was conducted to study the presence of specific functional groups in hard capsule biocomposite. Figure 1 shows that infrared spectroscopy of carrageenan hard capsule at different drying time, gelatine and HPMC hard capsules. The wavelength between 3500 to 3200 cm^{-1}, 1335 cm^{-1}, and 1160 cm^{-1} at DT40, DT50 and DT60 are associated to the vibration range of intra- and intermolecular hydrogen bonded OH groups from the NC [14]. Meanwhile the band absorption at 3430 cm^{-1} represents the amorphous properties of cellulose. It is attributed to the OH stretching related to the intra-molecular hydrogen bonds at the C3 position. It may also possible for intra-molecular hydrogen bonds between the functional groups at the C2 and C6 positions of the cellulose [14].

Presence of C-O of 3,6-anhydrogalactose and C-O-SO_4 on galactose-4-sulphate from carrageenan are observed at wavelength of 922 cm^{-1} and 841 cm^{-1} respectively [15]. Meanwhile the functional group for D-galactose-4-sulphate, 3,6 anhydro-D-galactose, glycosidic linkage and ester sulphate are attributed at wavelength of 1033 cm^{-1} and 1220 cm^{-1}, respectively [16]. As the formulation of carrageenan and NC were kept constant throughout the study, no switch of wavelength observed from the spectrum.

The manipulation of drying time affected the absorbance of hydroxyl group in the hard capsule biocomposite. Increment of drying time from 40 to 60 minutes reduced the absorbance of hydroxyl group from 471.13 to 460.55. This was due to the loss of water from the surface of hard capsule to the surrounding as the occurrence of evaporation phenomena in the system during the drying process.

Absorbance areas of hydroxyl group in GHC and HPMC hard capsules were lower which represented that the product had low water content. This result proved that the commercial products had a longer shelf life thus could prevent the growth of microorganisms that could cause contamination of the hard capsule. The spectroscopy showed that carrageenan hard capsule contains chemical groups that were also presence in both GHC and HPMC hard capsule samples, at wavelength of 840-850 cm^{-1} (C-O-SO_4) and 925-935 cm^{-1} (C-O).

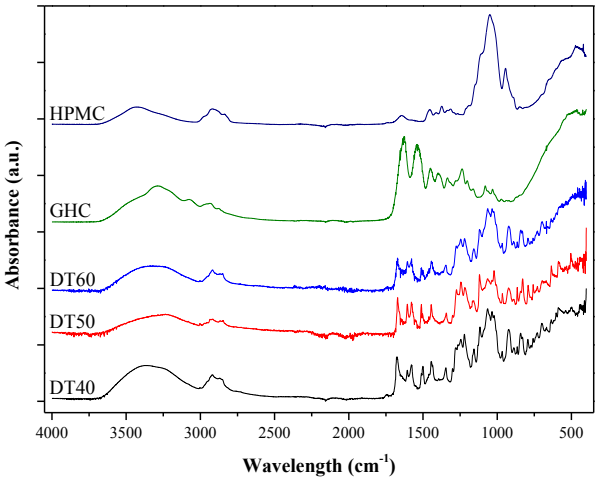

Figure 1. FTIR spectrum of carrageenan hard capsule biocomposites, gelatine, and HPMC hard capsules.

3.2. Thermal stability analysis

Figure 2 shows the derivative weight loss (TG) curves for 5 hard capsule samples which are CHC at DT40, DT50, and DT60, GHC, and HPMC. At the first stage up to 150 ^{o}C, it was related to the loss of adsorbed and bound water in the sample. Meanwhile, at the second stage, the weight loss was attributed to the formation of carbonaceous residue and decrosslinking of polymer networks [17]. The second thermal event of HPMC hard capsule happened at higher temperature as compared to GHC and CHC. The result showed that the HPMC hard capsule presented a higher thermal stability when compared with other samples. This was probably caused by the presence of charged group in HPMC molecule such as OH stretching vibration, CH stretching vibration (water in the amorphous region), and C-O-C stretching [18].

Among the developed CHC, it was found that the onset temperature of weight loss for the DT60 is higher than DT50 and DT40. This indicated that increasing drying time had improved the thermal stability of the carrageenan biocomposite. DT60 hard capsule sample is expected to be more stable than DT40 and DT50 hard capsules to withstand the fluctuation of storage and transportation temperature.

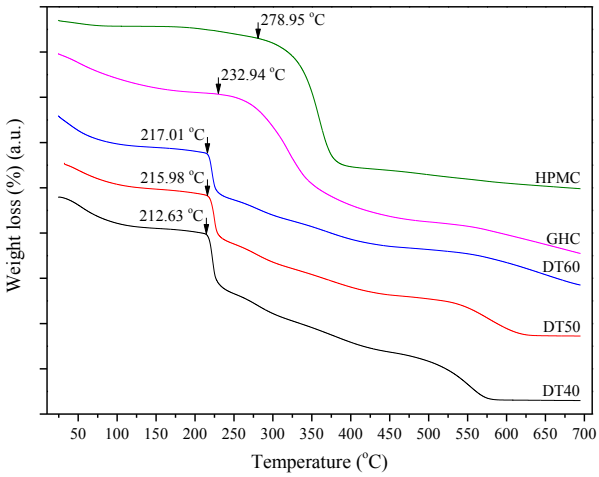

Figure 2. Thermogravimetric curves for CHC at various drying temperature, GHC and HPMC hard capsules.

3.3. Weight variation

The weight variation analysis represents the uniformity of the hard capsule during the production process. Deviation of less than 10% shows that the product is having a uniform weight, while deviation of more than 10% shows that the product is not having a uniform weight or having a problem in the production line.

Based on the result presented in table 1, all the hard capsules from 40 to 60 minutes were having a deviation of less than 10% which means that the hard capsules had a uniform and accepted weights. Besides, as the drying time increased, the weight variation decreased from 9.28 to 4.93%. The results showed that the increment of drying time may cause an improvement in the product uniformity for the hard capsule. At a longer drying time, more water molecules were evaporated to surrounding thus caused the hard capsules to have a consistent weight.

The weight variations of GHC and HPMC hard capsules were 3.30% and 2.18% respectively. Both products have the lowest weight variations as they are commercially marketed products. Thus, the products already have standard and also an optimum drying parameter in production line.

Table 1. Weight variation of carrageenan based hard capsule biocomposites, gelatin and HPMC hard capsules

Formulation	Weight Variation (%)
DT40	9.28 ± 5.28
DT50	7.93 ± 4.91
DT60	7.99 ± 4.86
GHC	3.30 ± 2.15
HPMC	2.18 ± 1.37

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3.4. Hard capsule hardness test

Hardness is defined as resistance to an indentation in sample specimens [19]. The graph in figure 3 shows the trend of hard capsule hardness test and hard capsule photographs upon application of mechanical testing. The line graph shows that the hardness of hard capsule decrease as the drying time increase. At 40 minutes, the capsule hardness was only 3.44 N. When the drying time increased to 60 minutes, the capsule hardness decreased up to 19% to 2.78 N. Moreover, at DT60, the pictograph of hard capsules showed that the CHC were dented in comparison to DT40 and DT50. As the drying time increase, it creates a formation of more tight structure and restricts the movement of molecules in the carrageenan network that causing the drop in CHC mechanical properties [14].

In addition, crosslinking of carrageenan with crosslinker in the matrix also affect this situation. Crosslinking prevents the swelling of carbohydrate and restricts the movement of water molecules in the matrix [14]. Thus, it led to a decrease in the amount of absorbed water, as proven in functional group analysis. It is in agreement with the mechanical properties of the carrageenan biocomposites. Besides, the physical properties of hard capsules were dented due to extreme loss of water in the biocomposite matrix. The results showed that the modification of drying time did not only affect the chemical properties of carrageenan hard capsules, but also the physical properties.

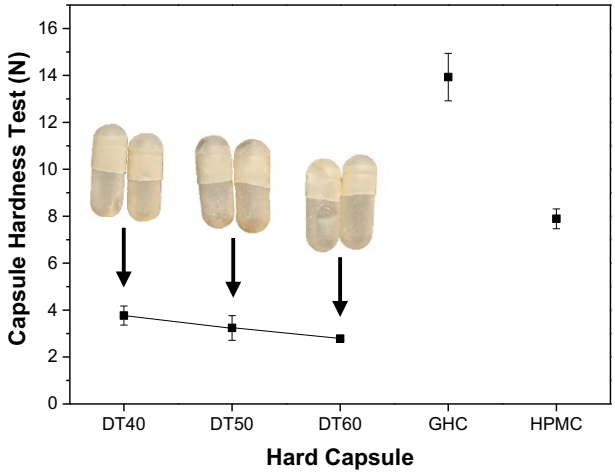

Figure 3. Hard capsule hardness test and pictographs for CHC at different drying time, GHC and HPMC hard capsule.

4. Conclusion

Drying is an important parameter to evaluate the stability, uniformity, and mechanical strength of carrageenan hard capsule. Increasing drying time has increased the thermal stability of the carrageenan biocomposite. Prolong drying also reduced the sample weight variation which represents the improvement in the product uniformity. This is due to a maximum water loss is achieved upon longer drying time. However, the hardness of hard capsule is reduced as the drying time increase from 40 to 60 minutes. It is expected that cased hardening has occurred. There is a formation of more tight structure in the carrageenan network and restricts the movement of molecules in the matrix. In comparison to GHC and HPMC hard capsules, CHC has similar functional group properties as both GHC and HPMC. GHC and HPMC hard capsules have better weight variation, thermal stability, and mechanical strength as compared to CHC. The drying time modification of carrageenan biocomposite hard capsule effects the chemical and physical properties of the biocomposite.

Acknowledgments

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