Synthesis of Sodium Carboxymethyl Cellulose (Na-CMC) from Water Hyacinth with Mixed Solvent using Succinic Acid and Epichlorohydrin as Crosslinker

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Abstract
Water hyacinth (Eichhornia crassipes (Mart.) Solms.) is an aquatic weed which has high cellulose content which it could serve potentially as raw material for Na-CMC synthesis. This study aimed to synthesize and determine Na-CMC quality using variations of solvent of isopropyl alcohol, isobutyl alcohol and isobutyl alcohol-isopropyl alcohol (1:4) and crosslinked by succinic acid and epichlorohydrin. This study involved isolating α-cellulose, synthesis of Na-CMC through alkalization and carboxymethylation, crosslinking Na-CMC by succinic acid and epichlorohydrin and their characterization as pharmaceutical excipient.

The results of characterization showed that values of degree of subtitusion (DS), Water Holding Capacity (WHC), Oil Holding Capacity (OHC) using isopropyl alcohol, isobutyl alcohol and isobutyl alcohol-isopropyl alcohol (1:4) as solvent without crosslinker were 0.66, 4.79 g/g, 3.37 g/g; 0.77, 4.53 g/g, 3.26 g/g; and 0.80, 4.62 g/g, 3.31 g/g respectively.

Meanwhile, Na-CMC synthesized using crosslinker of epichlorohydrin and succinic has decreased the values but Na-CMC syntesized using isopropyl alcohol as solvent worked better than other solvents with the value of DS, WHC and OHC parameters as 0.16, 3.22 g/g, 2.99 g/g; and 0.5, 4.33 g/g, 3.19 g/g respectively. The results showed that Na-CMC synthesized from Water hyacinth with the best characteristics is shown using isobutyl alcohol-isopropyl alcohol (1:4) as solvent.

Keywords: Na-CMC, water hyacinth, solvent, succinic acid, epichlorohydrin.

Introduction

Carboxymethyl cellulose sodium (Na-CMC) is one of the most popular and widely used carboxymethyl cellulose (CMC) derivatives. In pharmaceutical, Na-CMC is used as coating material, binder and desintegrant on tablet, suspending agent and also stabilizer. In addition, Na-CMC is the preferred choice for topical dosage formulations and oral preparations because of their viscosity-enhancing properties[7]. Based on its usefulness, Na-CMC became a compound of interest and much studied.

Na-CMC synthesis has been studied many years ago. The synthesis of Na-CMC by utilizing the wastes continues to be developed. Initially, Na-CMC was widely synthesized from wood cellulose. This is because the content of cellulose in wood is usually quite high which is about 42-47%. However, not only from wood, nowadays it has been widely developed to non-wood based Na-CMC synthesis, but agriculture wastes such as water hyacinth.[8]

Water hyacinth is a weed of water and the most troublesome plant because it grows very easily[6]. However, water hyacinth turned out to have high cellulose content of 66.87%[5]. In addition, the utilization of this plant has not been optimized, so this plant has great potential to be used as raw material in Na-CMC synthesis.

Na-CMC was synthesized from water hyacinth cellulose, but had deficiency in the value of Water Holding Capacity (WHC), Oil Holding Capacity (OHC) and Degree of Substitution (DS) compared to standard Na-CMC[4]. One of the things that can be done to improve WHC and OHC values is by adding crosslinkers. Based on this, add epichlorohydrin crosslinker in Na-CMC synthesis and generate 5.68 g/g of WHC, 2.87 g/g of OHC and 0.035 of DS value.[3]

The other studies reported that using mixture solvent of isobutyl alcohol-isopropyl alcohol improved the resulting DS value of Na-CMC. As well as, WHC and OHC value can be improved by using crosslinkers. Succinic acid, malic acid and citric acid were used as crosslinkers in Na-CMC synthesis and it is reported that succinic acid gave the most optimum results among those three.[2] Physical and chemical properties of Na-CMC are affected by DS value. DS influences on Na-CMC ability to absorb water, rheological behavior and viscosity of Na-CMC solution.[13] This research used epichlorohydrin and succinic acid as crosslinkers and different solvent of isobutyl alcohol, isopropyl alcohol and their combination (4.1) to synthesize Na-CMC from water hyacinth cellulose.

Material and Methods

Materials: Water hyacinth was obtained from Lembang, West Java, Indonesia. Aquadest, sodium hydroxide, sodium hypochlorite, isopropyl alcohol, isobutyl alcohol, isopropyl alcohol, isobutyl alcohol, isobutyl alcohol, sodium monokloroacetate (Sigma Aldrich), methanol, ethanol, acetic acid glacial, ammonium hydroxide, epichlorohydrin, succinic acid and olive oil (Dougo) were the chemicals used.

Synthesis of Na-CMC using different solvent: The synthesis of Na-CMC was started by performing α-Cellulose isolation, α-Cellulose isolation from water hyacinth performed the same procedure as the previous study[7], as well as the procedure made into Na-CMC. However, this study was performed with three types of solvents : isopropyl alcohol, isobutyl alcohol and mixture of isobutyl: isopropyl alcohol (4:1) using succinic acid and epicholohydrin as crosslinker.

Crosslinking Na-CMC from Hyacinth Cellulose using Epichlorohydrin (1:10): Na-CMC synthesis of water hyacinth cellulose weighed 5 grams of dry weight, then mixed with 50 grams of 17.5% NaOH and stirred at 50°C for 20 minutes. Epichlorohydrin with a ratio of 1:10 was mixed with 25% NH_4OH (1: 1) and added to the sample. The sample was refluxed for 4 hours at 40°C. The insoluble crosslink product is collected, washed with ethanol and aquades, then dried. Obtain by product of crosslinking Na-CMC.[3]

Crosslinking Na-CMC using Succinic Acid: A total of 3 g of Na-CMC was added to 1.5 g of succinic acid and dissolved in 20 mL of distilled water while continuously stirred to produce a homogeneous mixture. The formed mixture is then poured onto the teflon, dried in the oven at 55°C to dry and then blended until smooth.[5]

Determination of quality of Na-CMC Synthesized from Cellulose Hyacinth: Quality test of Na-CMC synthesis of water hyacinth cellulose includes pH determination of 1% solution, Water Holding Capacity (WHC) and Oil Holding Capacity (OHC) and sodium content using Atomic Absorption Spectroscopy (AAS).

The determination of total sodium content is obtained by first making the sodium raw curve with concentration variation so that the sodium concentration can be determined. Then the degree of substitution is made. Functional groups of Na-CMC of synthesis and Na-CMC of crosslinking of water hyacinth cellulose used fourier transform infrared (FTIR). Transmission is measured at wave numbers 4000-400 cm^{-1}.[9]

The other characterization of these Na CMC used Scanning Electron Microscope (SEM) - Energy Dispersive X-Ray (EDX). Dry samples of Na-CMC are applied on aluminum surfaces. After drying, the sample is allowed to stand for 30 seconds with gold using a Polaron machine. Furthermore, SEM is run under a Stereoscan microscope.

Results and Discussion

Isolation of α-cellulose from water hyacinth was obtained as in the previous study with 19.87% yield of 40 g of simplicia which is consistent with previously studies from 50 g water hyacinth fine grains used and boiled in 2000 mL NaOH 25% (1:40) to give α-cellulose white grain with 15.278% rendement[5]. The higher NaOH concentration will get higher rendement also. 30% NaOH can dissolve other cellulose forms such as β-cellulose, γ-cellulose, hemicellulose and holocellulose so that what remains is α-cellulose.

Na-CMC was synthesized with three types of solvents isopropyl alcohol, isobutyl alcohol and mixed isopropyl alcohol and isobutyl alcohol (4: 1) with a mechanical stirrer at room temperature. The mixed solvent was used to obtain a solvent having a relatively small polynomial rate of 4.22. Isobutyl alcohol has a polarity index of 3.9 and isopropyl alcohol of 4.3 but isopropyl alcohol has a deficiency, it is not good for sodium hydroxide, so in this study a higher concentration of sodium hydroxide[10] is used. The reaction medium or solvent affects the yield of Na-CMC formed because relatively small polarity will increase the rate of Na-CMC formation reaction. The reaction medium causes cellulose decrystallization to play an important role in alkalization. The reaction medium as a dispersion medium will disperse the cellulose, increase the degree of substitution, increase the reaction kinetic rate and as a heat exchange medium[5]. The yield of synthesis using isopropyl alcohol solvent, isobutyl alcohol and mixture were 111.97%; 83.35 and 100.64%.

Characterization of Na-CMC result of synthesis and crosslinking: The first test was pH testing. The pH test was done on 1% Na-CMC solution, the pH was in accordance with the standard that ranged from 6.00 to 7.00. The results can be seen below.

WHC showed the amount of water that can be tied to 1 g of dry matter or often called water holding capacity while OHC (Oil Holding Capacity) shows the amount of oil that can be fastened to 1 g of dry matter and is often referred to as the oil binding power. WHC and OHC are important characters given the function of Na-CMC in the pharmaceutical field as emulsifying agent, gelling agent and suspending agent. The results of WHC and OHC Na-CMC testing can be seen in fig. 2. and fig. 3.

WHC is influenced by pore size, conformational structure of molecules and hydrophilic interactions through hydrogen bonding. The high WHC shows an increase in hydrophilic character of the molecule. The highest WHC of the product synthesized which used isopropyl alcohol was 4.79. This can make isopropyl alcohol as the most polar solvent. The OHC values are influenced by the chemical and conformational structures of the Na-CMC molecules such as the ratio of hydrophobic groups and hydrophilic groups to Na-CMC structures. High OHC values are associated with an increase in hydrophobic character[11]. However, the source of raw water hyacinth ingredients has a significant effect on the value of WHC.[8]

The requirement of sodium content in Na-CMC as excipient is 6,5 - 9,5%. In addition, this sodium content also determines the value of degrees of substitution (DS) Na-CMC produced. The determination of sodium content was performed using AAS instrument with calibration curve method. DS has an influence on the ability of Na-CMC to absorb water, rheological behavior and viscosity of Na-CMC solution to be produced[13]. The results of sodium and DS Na-CMC content are given in fig. 3. and fig. 4.

Sodium content of Na CMC synthesized with mixed solvents due to the effects of mixed solvents which have low polarity but stereochemically not too steric, causes the soluble etherification agent to increase access into the cellulose structure.[4] This also occurs in the isobutyl alcohol solvent but due to the steric isobutyl alcohol structure generated by the three methyl groups around the primary carbon.

Content levels of sodium that have been obtained are used in determining the value of degrees substitution (DS). The degree of substitution is the number of substituted groups in each hydroglucose unit. The value of the degree of substitution required is divided into two i.e. the quality of I is not less than 0.7 and not more than 1.2 while quality II is not less than 0.4 and not more than 1.0. Solvents used in carboxymethylation may affect the DS. When the solvent polarity decreases, the reaction efficiency will increase, thus increasing the DS[1]. It is also proven in this study that Na-CMC with the highest DS value is Na-CMC synthesis with mixed solvent and isobutyl alcohol solvent. Although the isobutyl alcoholic polarity is lower than that of the isopropyl alcohol-isobutyl alcohol (1: 4) isopropyl mixture, the resulting DS is higher in Na-CMC with mixed solvent. This may be due to a steric factor in the isobutyl alcohol solvent.

The results of FTIR analysis showed spectra with the absorption at similar wave numbers between standard Na-CMC and crosslinked Na-CMC broad band at wave number 3392.82 cm^{-1} to 3433.35 cm^{-1} caused by strain of hydroxyl group (-OH) and band at wave number 2900.02 cm^{-1} up to 2934.74 cm^{-1} show cluster strain -CH. There are strong bands on standard Na-CMC, Na-CMC synthesized and Na-CMC crosslinked by epichlorohydrin at wave numbers 1588.41 cm^{-1} to 1647.24 cm^{-1} indicate the presence of carbonyl group (-C = O) which is an indication of Na-CMC[12]. However, these bands shifted to the 1700s wave number on crosslinked Na-CMC with succinic acid. This indicates the occurrence of crosslinking between Na-CMC and succinic acid forming the ester compound.[2]

Bands of about 1414.81 cm^{-1} to 1431.21 cm^{-1} are given by the scissoring vibration $-CH_2$. These bands in the 1600 cm^{-1} and 1400 cm^{-1} are an indication of the formation of carboxymethyl groups in Na-CMC. Bands at 1016.5 cm^{-1} to 1048.33 cm^{-1} wave numbers show the $CH\text{-}O\text{-}CH_2$ group.[1]

Based on SEM-EDX analysis, Na-CMC shape is irregular and porous. Judging from its size, synthesized Na-CMC size is ranging from 76.8 - 128 µm whereas standard Na-CMC has a slightly larger size which is 113-190 µm. The size of crosslinked Na-CMC ranged between 204 - 545 µm. The Na-CMC constituents of both standard Na-CMC, synthesized Na-CMC and crosslinked Na-CMC are carbon (C), oxygen (O) and sodium (Na). However, there are other atoms detected in Na-CMC synthesized with mixed solvents and crosslinked Na-CMC by epichlorohydrin i.e. Cl atoms, it might be caused by residues of epichlorohydrin itself from crosslinking process.

Table 1
Result of pH measurement test

Na- CMC	**pH**	
	Non *crosslink*	***Crosslink***
Standard	6.73	-
Crosslinker : Epichlorohydrin		
Isopropyl alcohol solvent	6.61	6.41
Isobutyl alcohol solvent	6.71	6.53
Mixture solvent	6.66	6.33
Crosslinker : Succinic acid		
Isopropyl alcohol solvent	6.61	6.28
Isobutyl alcohol solvent	6.71	6.6
Mixture solvent	6.66	6.44

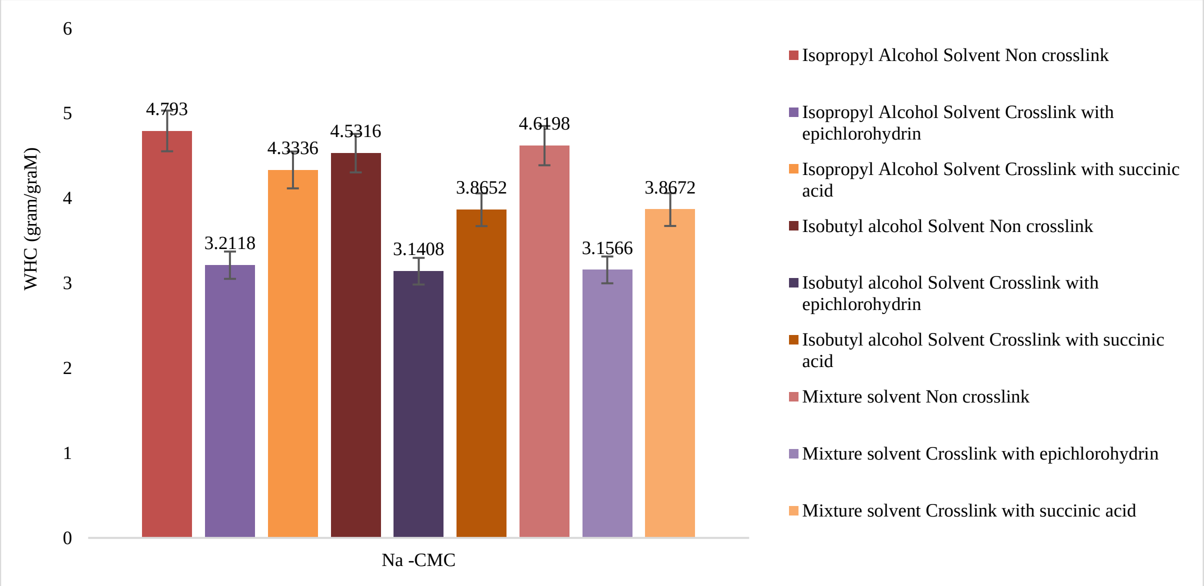

Fig. 1: Water holding capacity (WHC) of Na-CMC

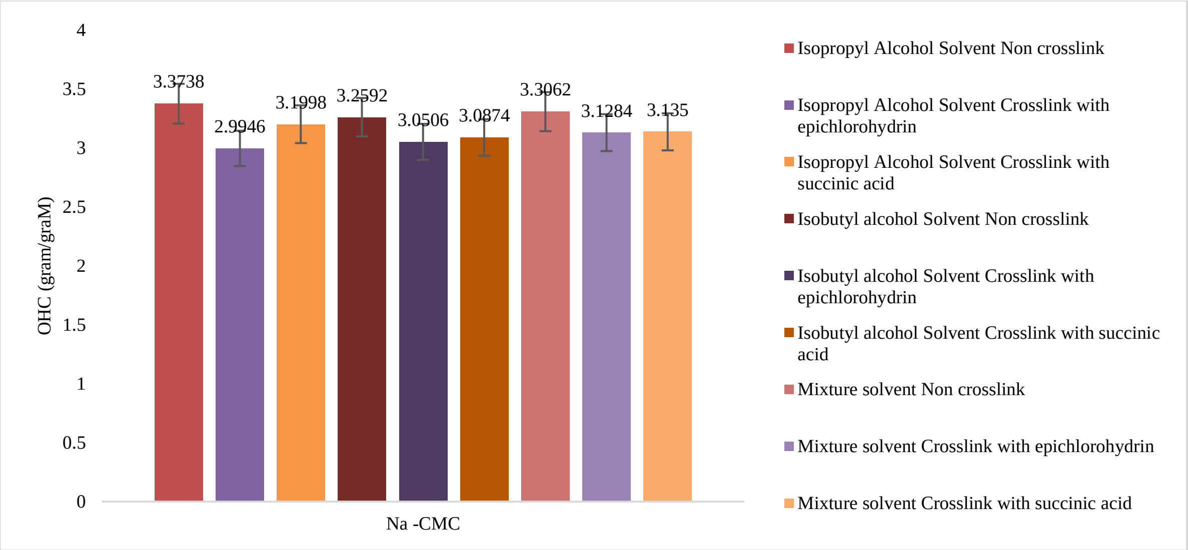

Fig. 2: Oil holding capacity (OHC) of Na-CMC

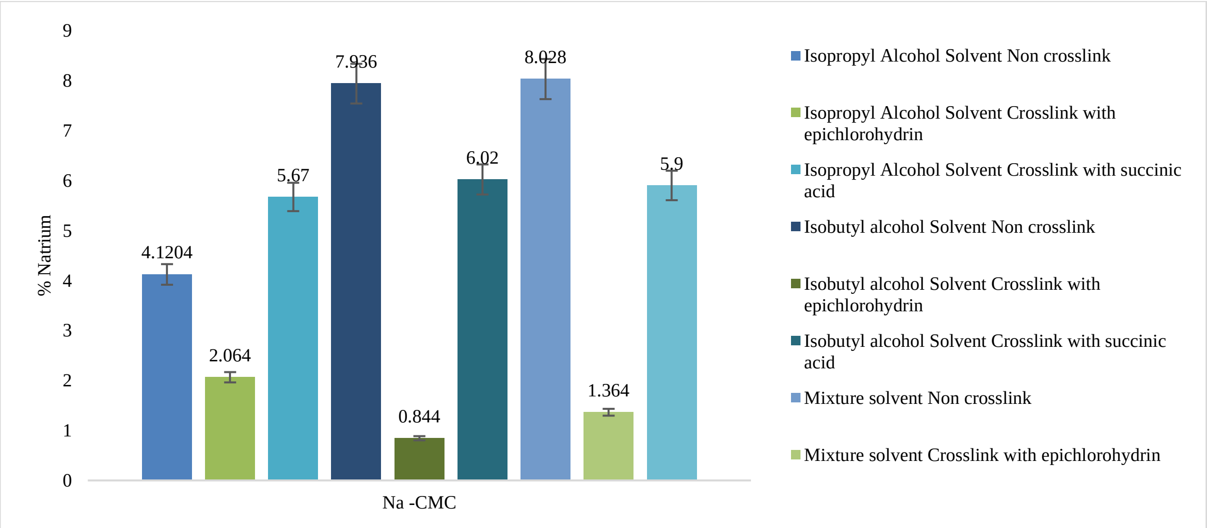

Fig. 3: Sodium content (% Na) of Na-CMC

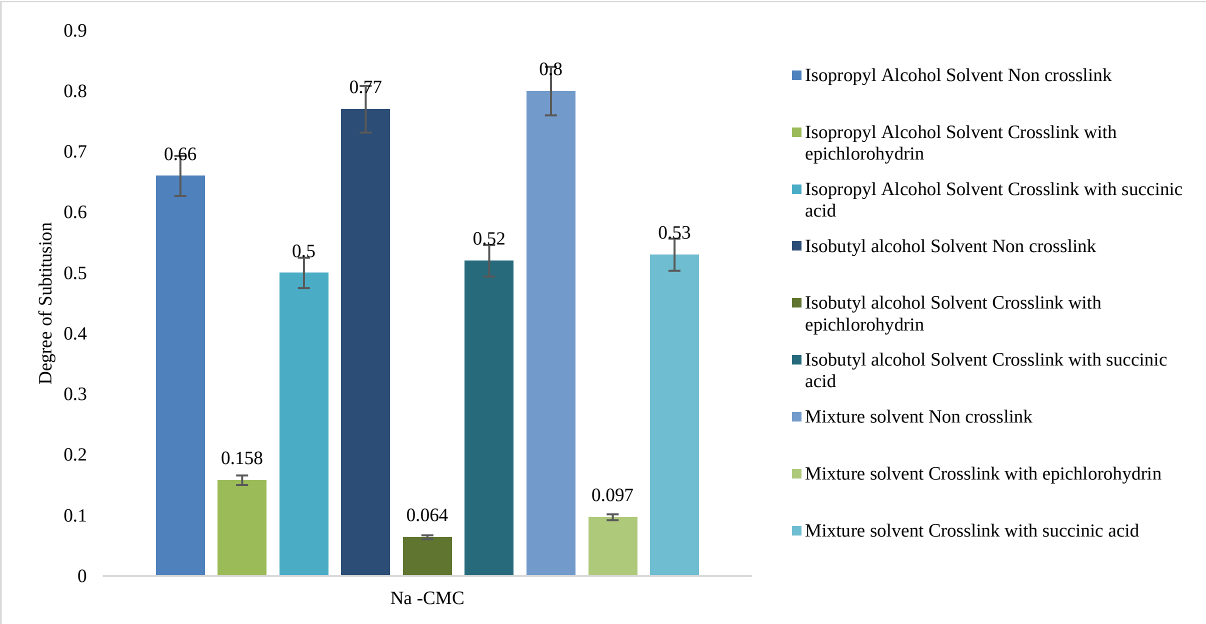

Fig. 4: Degree of substitution (DS) of Na-CMC

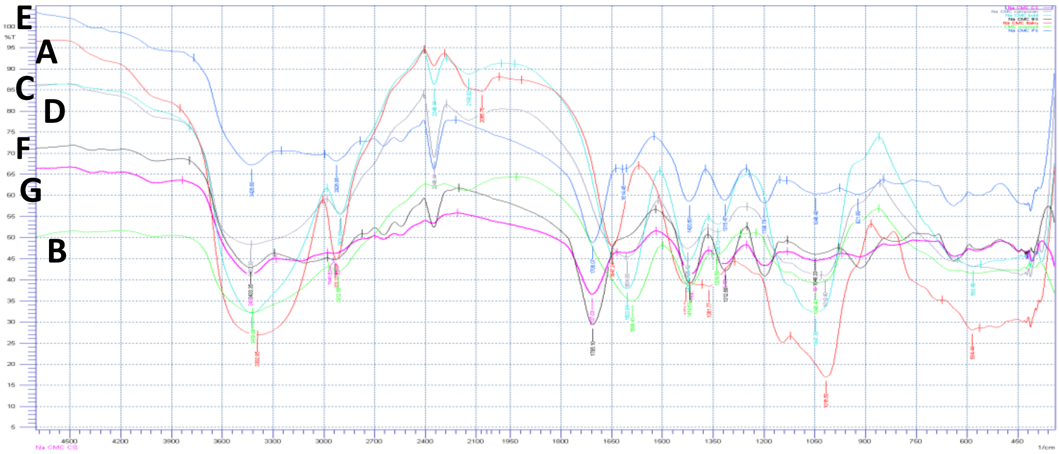

Fig. 5: FTIR spectrum of (A) standard Na-CMC, (B) Na-CMC synthesized by isopropyl alcohol, (C) isobutyl alcohol, (D) mixture solvent, (E) Na-CMC crosslinked by succinic acid synthesized by isopropyl alcohol, (F) isobutyl alcohol and (G) mixture solvent

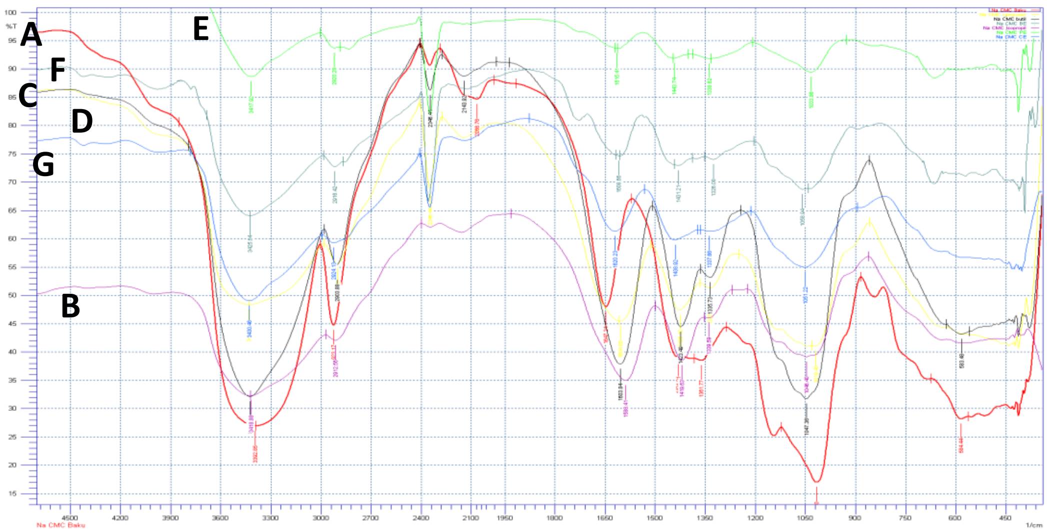

Fig. 6: FTIR spectrum of (A) standard Na-CMC, (B) Na-CMC synthesized by isopropyl alcohol, (C) isobutyl alcohol, (D) mixture solvent, (E) Na-CMC crosslinked by epicholorohydrin synthesized by isopropyl alcohol, (F) isobutyl alcohol and (G) mixture solvent

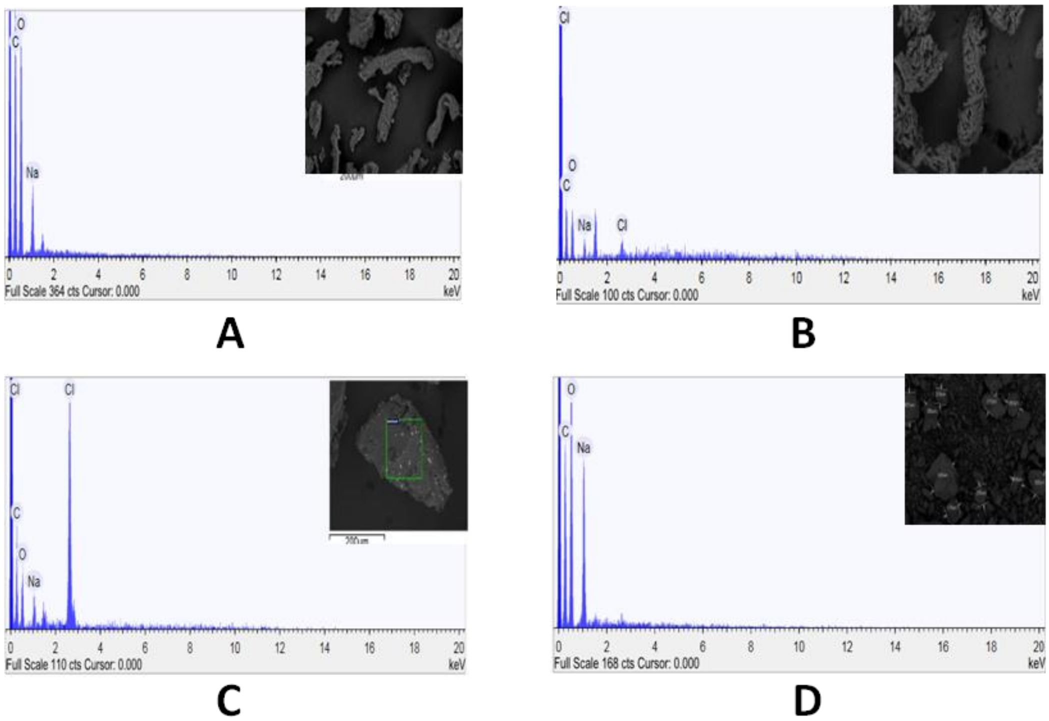

Fig. 7: SEM-EDX result analysis of (A) standard Na-CMC, (B) Na-CMC synthesized by mixture solvent, (C) Na-CMC synthesized by isopropyl alcohol crosslinked by epichlorohydrin and (D) Na-CMC synthesized by isopropyl alcohol crosslinked by succinic acid

Conclusion

Characteristics of Na-CMC synthesized from water hyacinth cellulose with isopropyl alcohol, isobutyl alcohol and mixed solvent of isopropyl alcohol-isobutyl alcohol (4:1) meet the requirements of Na-CMC as pharmaceutical excipients. Na-CMC with the best characteristics is shown by Na-CMC synthesized with mixed solvent. However, characteristics of Na-CMC crosslinked with succinic acid and epichlorohydrin showed differences in various characters such as decrease of DS, WHC, OHC, viscosity and sodium content.

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