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Original Article

PHYSICO-MECHANICAL AND FILM-FORMING PROPERTIES OF CARBOXYMETHYL CORN STARCH BUTYRATE

ORNANONG S. KITTIPONGPATANA[1*], NISIT KITTIPONGPATANA[1]

[1]Department of Pharmaceutical Sciences, Faculty of Pharmacy, Chiang Mai University, Chiang Mai, Thailand 50200
Email: ornanong.sk@gmail.com

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ABSTRACT

Objective: This study aims to prepare a new hydrophobic, water-soluble modified corn starch *via* sequential butyrylation and carboxymethylation and to evaluate its physico-mechanical and film-forming properties.

Methods: Butyrylation of corn starch (CS) was carried out in an aqueous suspension using 25%w/w butyric anhydride to yield corn starch butyrate (CSB). CSB was further reacted with chloroacetic acid to carboxymethyl corn starch butyrate (CMCSB). Following the determination of the degrees of carboxymethyl substitution (DS-Cm) and butyrylation (DS-Bu), CMCSB was subjected to analyses by scanning electron microscopic (SEM), X-ray diffraction (XRD), solubility, viscosity, free swelling capacity (FSC), moisture sorption, film formation and water vapor transmission rate (WVTR).

Results: DS-Cm of CMCSB was 0.24, while DS-Bu was 0.09. SEM images revealed significant granules fusion and surface roughness. XRD showed a decrease in the degree of crystallinity. CMCSB was soluble in water, with a three times lower viscosity than that of carboxymethyl corn starch (CMCS). Initial FSC of CMCSB was slightly lower than that of CMCS, but gradually increased to a higher FSC after 30 min. A significant drop of moisture sorption from 20% in CMCS to 11% in CMCSB was observed at 93% relative humidity. CMCSB formed an intact film with slightly better flexibility than that of CMCS. WVTR of CMCSB was decreased by a maximum of 4.9% compared to CS, and 10.2% compared to CMCS.

Conclusion: The introduction of the butyrate group increased the hydrophobicity of the modified starch, altered some of the physico-mechanical properties, and enhanced the barrier property of the modified starch film.

Keywords: Corn starch, Carboxy methylation, Butyrylation, Hydrophobicity, Film-former, Pharmaceutical excipient

INTRODUCTION

The development of starch-based, biodegradable film has been one of the more attractive research topics of starch utilization in pharmaceuticals [1]. Limitations on inherent physicochemical properties of native starch, such as the insolubility in water, poor flow ability, etc., have been overcome by means of chemical and physical modification of starch structure [2]. These alterations allowed the expansion of starch uses from the standard, conventional pharmaceutical excipients such as filler/diluent, binder or disintegrant to the more advanced types of an adjuvant such as emulsifier, a drug carrier, and film former [3-5]. Carboxymethyl starch (CMS), an etherified, anionic modified starch prepared from a reaction that substituted some of the–OH groups in the starch chain with carboxymethyl moieties, has been among the well-studied and commonly employed modified starches in the food and pharmaceutical products. The water-soluble, hydrophilic CMS profiled favorably as a gelling/thickening agent for topical formulation [6]. The development as a film-forming agent, on the other hand, remained problematic despite its decent flexibility and strength compared to that of the native starch film, mainly due to the hygroscopic property that led to the instability of the film upon long storage [5,7]. A number of studies have been reported to increase the hydrophobicity of CMS, including reactions to add hydroxypropyl group [8], esters of fatty acid [9], and conjugation with zein [10].

Esterification of starch to replace some of the–OH group with an ester group was reported as another method to increase the hydrophobicity to starch molecule [11], and the flexibility of starch films [12]. Short chain anhydrides, including propionic anhydride and butyric anhydride, have been successfully used to increase the hydrophobicity of starch. The resulting modified starches, starch propionate, and starch butyrate are reported to have "bioplastic" properties. Preparation of starch butyrate (butyrylated starch) was reported in arenga starch [11]. It was shown that butyrate group imparted the structure with hydrophobicity, which altered the physical and chemical properties. Increases in water-holding capacity, oil-holding capacity, and swelling capacity, together with decreases in crystallinity and solubility were observed from the modified starch. Similar results were also noted in the modification of cassava starch [13].

In this study, we report for the first time the preparation of carboxymethyl corn starch butyrate (CMCSB) and the physico-chemical properties, as well as the film-forming ability of this modified starch compared to carboxymethyl corn starch (CMCS), corn starch butyrate (CSB) and native corn starch (CS).

MATERIALS AND METHODS

Chemicals used in the study

CS (amylose content 19.7%) was obtained from ETC International Trading (Thailand). Chloroacetic acid and butyric anhydride was products of Fluka (Germany). All chemicals used in the preparation and analysis of modified starches were AR grade or equivalent.

Preparation of corn starch butyrate (CSB)

CS powder (100 g) was suspended in 225 ml water, and stirred for 30 min at 25 °C. The pH of the suspension was then adjusted to 10 using 3%w/v sodium hydroxide (NaOH) solution. Butyric anhydride (25%w/w) was added drop wise into the mixture. The reaction was carried out for 60 min, while the pH was maintained at 10. Finally, the pH was adjusted to 4.5 using 0.5N hydrochloric acid (HCl). The modified starch product was washed several times with distilled water, and a final wash with methanol through filtration. The final product was dried in an oven at 60 °C for 24 h.

Preparation of carboxymethyl corn starch (CMCS)

CS powder (138 g) was suspended in 260 ml methanol with 40 g chloroacetic acid. NaOH (50%, 79.5 ml) was then added, and the reaction was heated up to 70°C. After 1 h with continuous stirring, the reaction was neutralized with glacial acetic acid. The liquid supernatant was decanted, and the powder product was washed several times with 90% methanol and dried at 50°C.

Preparation of carboxymethyl starch butyrate (CMSB)

The experiment was carried out as for the preparation of CMCS, except that CSB powder was used in place of CS powder.

Degree of carboxymethyl substitutions (DS-Cm)

Analysis protocol as described previously [14] was followed. The DS value was a combination of the degree of substitution of carboxymethyl acid (A), and the degree of substitution of sodium carboxymethyl (S), which are calculated as follows;

$$A = \frac{1150M}{7120 - 412M - 80C}$$

$$S = \frac{(162 + 58A)C}{7120 - 80C}$$

When, M is the mEq of base required for in the titration to end point. C is the percentage of ash remained after ignition. The reported DS values are means of three determinations.

Degree of butyrate substitutions (DS-Bu)

Butyryl percentage and degree of butyrate substitution were determined based on a titration method described by Tupa *et al.* [12], with a slight modification. Starch sample (500 mg) was placed in a 250 ml flask, and 25 ml of 75% ethanol was added. The flask was agitated at 50 °C for 30 min, and 25 ml of 0.5 M NaOH was added. The excess alkali was back-titrated with 0.1 M HCl using phenolphthalein as an indicator. CS was used as a control. Butyryl (%) was determined as follows;

$$\text{Butyryl}\,\% = \frac{(\text{Blank} - \text{Sample})\text{x Molarity of HCl x }0.071}{\text{sample weight}}\text{x }100$$

DS is defined as the average number of sites per glucose unit that possess a substituent group**.**

$$DS_{bu} = \frac{162 \text{ x Butyryl}\,\%}{7100 - (70 \text{ x Butyryl}\,\%)}$$

Scanning electron microscopic (SEM) analysis

SEM experiments to analyze the granule surface, shape, and size were conducted using a JEOL instrument model JSM-5410LV (JEOL, USA) equipped with a large field detector. The acceleration voltage was 15 kV under low vacuum mode (0.7-0.8 torr). The sample was placed on a copper stub covered with adhesive tape and coated with a layer of gold under vacuum. The images were taken at 1000X magnification.

X-ray diffraction (XRD)

XRD patterns were recorded in the reflection mode on a Siemens D-500 X-ray diffractometer. Diffractograms were registered at a 2θ angle range from 5° to 40°, at a scan rate of 2.5°/min and a step of 0.02°.

Viscosity

The apparent viscosities of 1% w/v solutions of CMCS and CMCSB were measured using a Bob-and-Cup format rotational viscometer (Brookfield Engineering LA, R/S-CC). The measuring system was CC48 DIN. The mode used was CSR (controlled shear rate). The measured parameters consisted of three steps: (1) an increase of the shear rate from 0 to 100 s^{-1} in 1 min, (2) a constant the shear rate at 100 s^{-1} for 1 min and (3) a decrease of the shear rate from 100 to 0 s^{-1} in 1 minute. All measurements were performed in triplicate at a controlled temperature of 25±1 °C. The data were analyzed with Brookfield Rheo 2000 software. Viscosity was expressed in mPa s.

Free-swelling capacity (FSC)

FSC was determined using a method described by Heβ et al [15]. Sample (1.0 g) was accurately weighed into a pre-weighed, dry tea bag. The bag was tied and submerged in a beaker containing an excess amount of water at room temperature. After 1, 5, 15, 30 and 60 min, the bag was taken out, the excess water was wiped out until no visible droplets were observed. The weight of the tea bag and the content was determined. FSC value was calculated as;

$$FSC = \frac{m_t - m_{tb} - m_w}{m_s}$$

when m_t is the weight of the tea bag with water-absorbing gel, m_{tb} is the weight of the empty, dry tea bag, m_w is the weight of the water, absorbed by the empty, wet tea bag., and m_s is the weight of the dry sample.

Moisture sorption

The moisture sorption of starch powder samples was evaluated for 7 d at various relative humidity (RH). Sample (1 g), previously dried to a constant weight at 80ºC, was placed in a calibrated cup with an internal diameter of 2.5 cm. Samples were then placed in desiccators containing different saturated salt solutions which attained 43, 51, 75, 83 and 92% RH at 30ºC. Moisture sorption of samples was determined as a percentage of the weight gained.

Film casting by petri dish method

A 3% w/v aqueous solution of CMCS or CMCSB (30 ml) was placed on a plastic Petri dish and dried at 60 °C for 17 h. Control films were prepared using native starch solution.

SEM analysis of starch film

SEM experiments of starch films were conducted using the instrument and conditions as described for powder samples. The film samples were cut into thin slices, and the cross-section of the film was analyzed. The images were taken at 1000X magnification.

Water vapor transmission rate (WVTR)

The WVTR of the film was determined according to ASTME96-94 (ASTM, 1944). All film samples were cut to be annular 4 cm diameter. The sample was firmly fixed on top of a 4-cm diameter glass bottle containing beads of silica gel. Then, the containers were placed in a desiccator at a 25 °C, with a controlled 50% relative humidity (RH). The containers were weighed daily on an analytical balance for 7 d. The weight of the film was recorded with a precision of 0.0001 g and the WVTR was calculated using an equation:

$$WVTR = \frac{(\frac{G}{t})}{A}$$

Where WVTR is water vapor transmission rate (g/m^2. day), G/t is weight gain over time, and A is the permeation area. The tests were carried out in triplicate.

RESULTS AND DISCUSSION

Determination of degrees of substitution

The degrees of carboxymethyl substitution (DS-Cm) for CMCS and CMCSB were 0.28and 0.24, respectively. Butyryl percentage in starch butyrate was 5.06%, which was equivalent to the degree of butyryl substitution (DS-Bu) of 0.11. For CMCSB, the percentage was 4.14% and the DS-Bu was 0.09. Lower values of DS-Cm and DS-Bu observed in CMCSB, compared to CMCS and CSB, respectively, were likely the results of substitution competition, as both functional groups targeted the–OH groups at positions C-2, C-3 and C-6 in the anhydroglucose units [14, 16].

Scanning electron microscopy

Scanning electron microscopic (SEM) images of native corn starches (fig. 1A) showed granules that were polygonal, with a size range between 6-15 μm. This is in agreement with previous report [17]. Butyrate-modified and carboxymethyl-modified starches showed similar SEM image to that of the native starch. The dual modification, carboxymethyl starch butyrate (CMSB), caused significant changes to the granule appearances. Granule fusion was clearly observed, while surface roughness was visible, with the shape also became irregular. Fusion of granules has been reported for butylated corn starch as a result of partial gelatinization [12].

Table 1: Degrees of carboxymethyl substitution (DS-Cm) and butyrate substitution (DS-Bu) of modified corn starches

Starch type	DS-Cm	Butyryl%	DS-Bu
CS	-	-	-
CSB	-	5.06	0.11
CMCS	0.28	-	-
CMCSB	0.24	4.14	0.09

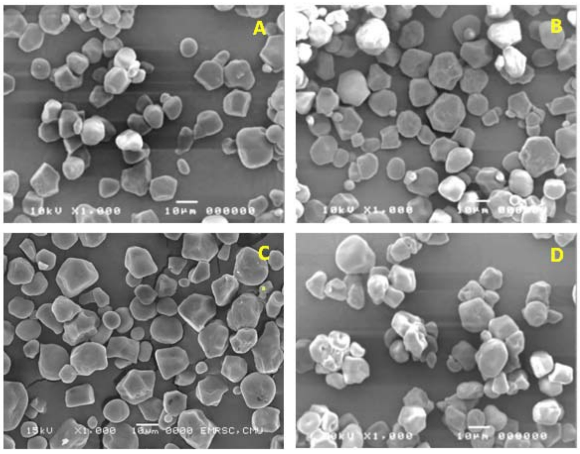

Fig. 1: SEM images of (A) native corn starch (CS); (B) corn starch butyrate (CSB); (C) carboxymethyl corn starch (CMCS); (D) carboxymethyl corn starch butyrate (CMCSB)

X-ray diffraction

X-ray diffraction patterns of native and modified starch powders are shown in fig. 2. XRD of CS showed an A-type diffraction pattern, with major reflections at 15, 17 and 23° of diffraction angle 2*θ*, and small peaks at 20 and 26°. The pattern and values are in agreement with those previously reported [17]. The modification with butyrylation caused a slight increase in the intensity of the reflection signal, indicating an increase in granule crystallinity. Starches modified with carboxymethylation showed decreases in the signal intensity which corresponds with a decrease in the crystallinity of the granules.

Solubility

The addition of butyryl group to the molecule rendered starch hydrophobic, as evidenced by a decrease in solubility of CSB as compared to CS (table 2). This was in agreement with a previous study on butylated corn starch [18]. Upon carboxy methylation, however, the resulting CMCSB became sufficiently hydrophilic that the solubility was 100 % even at room temperature, similar to CMCS.

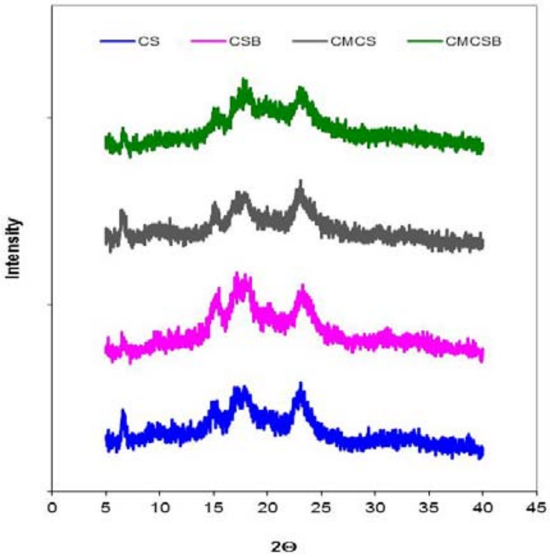

Fig. 2: X-ray diffraction (XRD) patterns of native and modified corn starches

Table 2: Water solubility (g/g of dry starch x 100) of corn and modified corn starches submitted to heat from 50 to 90 °C

Type of starch	Temperature (°C)					
	RT	50	60	70	80	90
CS	0.1±0.0	0.1±0.0	0.1±0.0	1.4±0.1	3.6±0.2	3.9±0.1
CSB	0.0±0.0	0.0±0.0	0.0±0.0	0.3±0.0	1.5±0.1	2.9±0.1
CMCS	100.0±0.0	100±0.0	100.0±0.0	100±0.0	100±0.0	100±0.0
CMCSB	100.0±0.0	100±0.0	100.0±0.0	100±0.0	100±0.0	100±0.0

Values are presented as mean±SD, n=3; CS, corn starch; CSB, corn starch butyrate; CMCS, carboxymethyl corn starch; CMCSB, carboxymethyl corn starch butyrate.

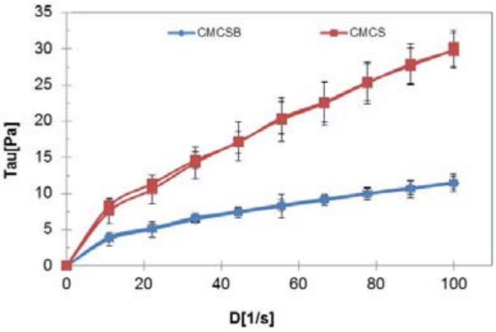

Fig. 3: Rheological profiles of carboxymethyl corn starch (CMCS) and carboxymethyl corn starch butyrate (CMCSB). Values are mean±SD (n=3) Viscosity

The viscosity of 1% w/v aqueous solution of CMCSB was 114.51±9.92 mPa. s, which was almost three times lower than that of CMCS (299.20±19.49 mPa. s). The rheological profile of CMCSB remained pseudoplastic (fig.3). The addition of butyrate groups into the starch polymer chain significantly increased the hydrophobicity and, as a result effectively decreased the viscosity of the solution. Increased hydrophobicity was reported to favour compatibility with synthetic petroleum plastics [19]. The lower viscosity also enhanced the performance of CMCSB as a film former in a film coating system, as the concentration could be further increased while the solution remained dispersible or sprayable.

Free swelling capacity (FSC)

CMCS and CMCSB exhibited superior swelling capacity compared to native corn starch and CSB (Fig.4), mainly due to the addition of hydrophilic carboxymethyl group. For the first 15 min, FSC of CMCSB was slightly lower than CMCS. After 15 min, FSC continued to increase for CMCSB at the rate significantly higher than that of CMCS. This was due to the presence of hydrophobic butyryl group which could retard water mobility during de swelling, resulting in greater water retention ability [20].

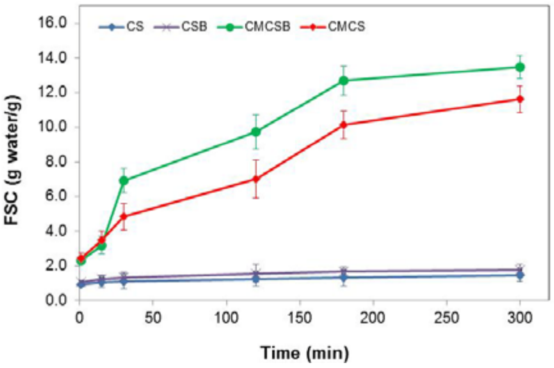

Fig. 4: Free swelling capacity (FSC) of native corn starch (CS), corn starch butyrate (CSB), carboxymethyl corn starch (CMCS), and carboxymethyl corn starch butyrate (CMCSB), n=3

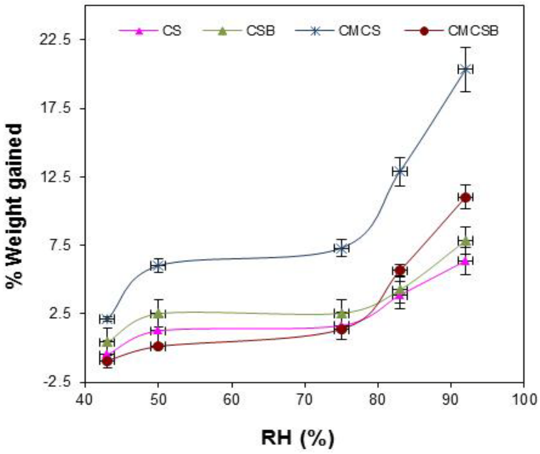

Fig. 5: Moisture sorption profiles of native corn styarch (CS), corn starch butyrate (CSB), carboxymethyl corn starch (CMCS), and carboxymethyl corn starch butyrate (CMCSB), after 7 d at 30 ºC, 43-92% relative humidity, n=3

Moisture sorption

Fig.5 showed the moisture sorption profile of CSB and CMSCB, in comparison with CS and CMCS, at different relative humidity (RH). All profiles showed a similar sigmoid shape, with CMCS and CS being the most and the least hygroscopic, respectively. At RH between 43 to 75%, CS, CSB, and CMCSB exhibited low equilibrium moisture contents (<2.5% weight gained), while CMCS showed a low equilibrium moisture content at 43% RH but then increased to 6.0 and 7.3% weight gained at 51% and 75% RH, respectively. This is likely due to the hydrophilic nature of the carboxymethyl group that enhances the absorption of water molecules [20]. At 83% RH, all samples actively absorbed moisture. The effect became more pronounced at 92% RH, as the weight gained for CMCS reached 20%. The addition of butyryl group into the starch structure before carboxy methylation resulted in a more hydrophobic CMCSB, as indicated by an equilibrium moisture content of 11% at 93% RH.

Film formation and characteristics

CMCS and CMCSB, at 3% w/w concentration, formed plastic-like, intact films that were slightly flexible, while CS film were opaque and brittle. SEM micrographs of CS film showed several air bubbles on the surface and the presence of non gelatinized granules on the cross-sectional image. The unmodified–OH groups formed strong hydrogen bonding, as indicated by the tightly packed appearance of the layer, and caused the brittleness of the film. CMCS film exhibited a more homogenous appearance with slightly loose layer and better flexibility, as a result of water solubility and less hydrogen bonding from carboxy methylation. However, the rough surface suggested that the film could be hygroscopic or that the film formation did not occur evenly due to the high viscosity of the CMCS film-forming solution. CMCSB film showed smooth, homogenous surface, with good flexibility. The cross-sectional image revealed the expansion of the film layer (fig. 6), likely due to the decrease of extended hydrogen bond brought about by the substitution of–OH groups with butyrate groups.

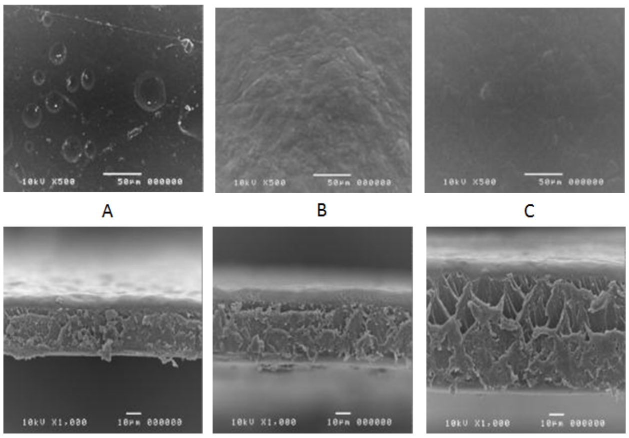

Fig. 6: SEM micrographs of the surface (top) and the cross-section (bottom) of starch films prepared from (A) native corn starch(CS); (B) carboxymethyl corn starch(CMCS); (C) carboxymethyl corn starch butyrate(CMCSB)

Water vapor transmission rate

Under the same test conditions, modification of CS with carboxymethylation caused a significant increase in WVTR, while the butyrylration reaction had the opposite effect. An initial 5.0% increase in WVTR was observed in CMCS on day 1, compared to CS. The value rose to 5.9% by day 7. A dual modification of CS with butyrylation and then carboxymethylation yielded CMCSB with both the initial (day 1) and the final (day 7) WVTRs lower than those of CS (1.4 and 4.9%) and CMCS (6.1 and 10.2%), which suggested that the hydrophobic butyrate group enhanced the barrier property of the starch film (table 3).

Table 3: Water vapor transmission rate (WVTR) of various types of native and modified corn starch films

Type	**WVTR ($g*10^{-2}/m^2/day$)**						
	1	**2**	**3**	**4**	**5**	**6**	**7**
CS	2.82±0.14	1.43±0.11	1.32±0.18	1.20±0.07	1.15±0.08	1.08±0.12	1.02±0.14
CMCS	2.96±0.39	1.58±0.22	1.38±0.13	1.31±0.24	1.24±0.19	1.20±0.22	1.08±0.19
CMCSB	2.78±0.29	1.36±0.22	1.17±0.13	1.10±0.11	1.05±0.07	1.03±0.11	0.97±0.08

CONCLUSION

A new hydrophobic, water-soluble modified starch was successfully prepared from corn starch (CS) *via* sequential butyrylation and carboxy methylation. CS was first subjected to butyrylation in an aqueous suspension with 25%w/w butyric anhydride. The intermediate, corn starch butyrate (CSB), was then reacted with the chloroacetic acid in a methanolic alkaline solvent. The final product, carboxymethyl corn starch butyrate (CMCSB), possessed a degree of carboxymethyl substitution (DS-Cm) of 0.24, and a degree of borylation (DS-Bu) of 0.09. Scanning electron microscopic (SEM) images revealed significant granules fusion and surface roughness, which collaborated with a decrease in the degree of crystallinity observed in x-ray diffractogram (XRD). CMCSB was soluble in water; a 1%w/v solution exhibited a three times lower viscosity than that of CMCS. Dry powder exhibited good free swelling capacity (FSC), with a significant decrease in moisture sorption from 20% in CMCS to 11% in CMCSB, at 93% relative humidity. A 3% w/v solution formed an intact film with slightly better flexibility than that of CMCS. Water vapor transmission rate (WVTR) of CMCSB was decreased significantly compared to CMCS, indicating the effect of the introduced hydrophobic butyrate group on the barrier property of the starch film that could be used in the development/ improvement of a starch-based, aqueous film-coating agent for pharmaceuticals.

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CONFLICT OF INTERESTS

Declared none

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