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Research Article

Polymer–Magnesium Aluminum Silicate Composite Dispersions for Improved Physical Stability of Acetaminophen Suspensions

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Abstract. The aims of this study were to characterize the morphology and size of flocculates and the zeta potential and rheological properties of polymer–magnesium aluminum silicate (MAS) composite dispersions and to investigate the physical properties of acetaminophen (ACT) suspensions prepared using the composite dispersions as a flocculating/suspending agent. The polymers used were sodium alginate (SA), sodium carboxymethylcellulose (SCMC), and methylcellulose (MC). The results showed that SA, SCMC, and MC could induce flocculation of MAS by a polymer-bridging mechanism, leading to the changes in the zeta potential of MAS and the flow properties of the polymer dispersions. The microscopic morphology and size of the flocculates was dependent on the molecular structure of the polymer, especially ether groups on the polymer side chain. The residual MAS from the flocculation could create a three-dimensional structure in the SA–MAS and SCMC–MAS dispersions, which brought about not only an enhancement of viscosity and thixotropic properties but also an improvement in the ACT flocculating efficiency of polymers. The use of polymer–MAS dispersions provided a higher degree of flocculation and a lower redispersibility value of ACT suspensions compared with the pure polymer dispersions. This led to a low tendency for caking of the suspensions. The SCMC–MAS dispersions provided the highest ACT flocculating efficiency, whereas the lowest ACT flocculating efficiency was found in the MC–MAS dispersions. Moreover, the added MAS did not affect ACT dissolution from the suspensions in an acidic medium. These findings suggest that the polymer–MAS dispersions show good potential for use as a flocculating/suspending agent for improving the rheological properties and physical stability of the suspensions.

KEY WORDS: magnesium aluminum silicate; physical stability; sodium alginate; sodium carboxymethylcellose; suspensions.

INTRODUCTION

In pharmaceutical product development, polymers have been widely used in coarse dispersion dosage forms, such as suspensions, for minimizing or controlling sedimentation of drug particles (1). They can physically stabilize suspensions by inducing flocculation of drug particles. This can prevent the formation of hard cake sediment which is difficult to redisperse (2). Furthermore, the rheological characteristics of polymer dispersions are very important. A shear thinning or pseudoplastic system is required, that is, the dispersions should have a high viscosity at rest to retard sedimentation of drug particles and have a low viscosity when shaking so as to be easy to pour from a container. Therefore, the concentration of polymers used as flocculating or suspending agents needs to be optimized. High concentrations of polymer lead to a good physical stability of suspensions, but may cause too high a viscosity to pour easily. For this reason, incorporating a material, such as clay, which molecularly interacts with polymers, could enhance viscosity synergism and create a gel-like structure of polymer dispersion (3). This may lead to an increase in the drug flocculating efficiency of polymer.

Magnesium aluminum silicate (MAS) is a mixture of natural smectite clays, in particular montmorillonites and saponites (4). It is composed of a three-lattice layer of octahedral alumina and two tetrahedral silica sheets (4–6); the structure of montmorillonite clays is illustrated in Fig. 1a (5). The surface of the silicate layer contains many silanol groups (SiOH) which have hydrogen bonding potential with other substances (7). The layer structures of MAS can be separated when they are hydrated in water. Once MAS is hydrated, the weakly positive edges are attracted to the negatively charged faces. The face-to-edge attraction of these colloidal layers creates a three-dimensional colloidal structure throughout the dispersion that exhibits a thixotropic property (8). Therefore, MAS has been widely used as a pharmaceutical suspending and stabilizing agent (4). In addition, the positively charged edges on the layers of MAS could interact with anionic polymers such as xanthan gum (9), carbomer (10), and sodium alginate (SA) (11,12), resulting in viscosity

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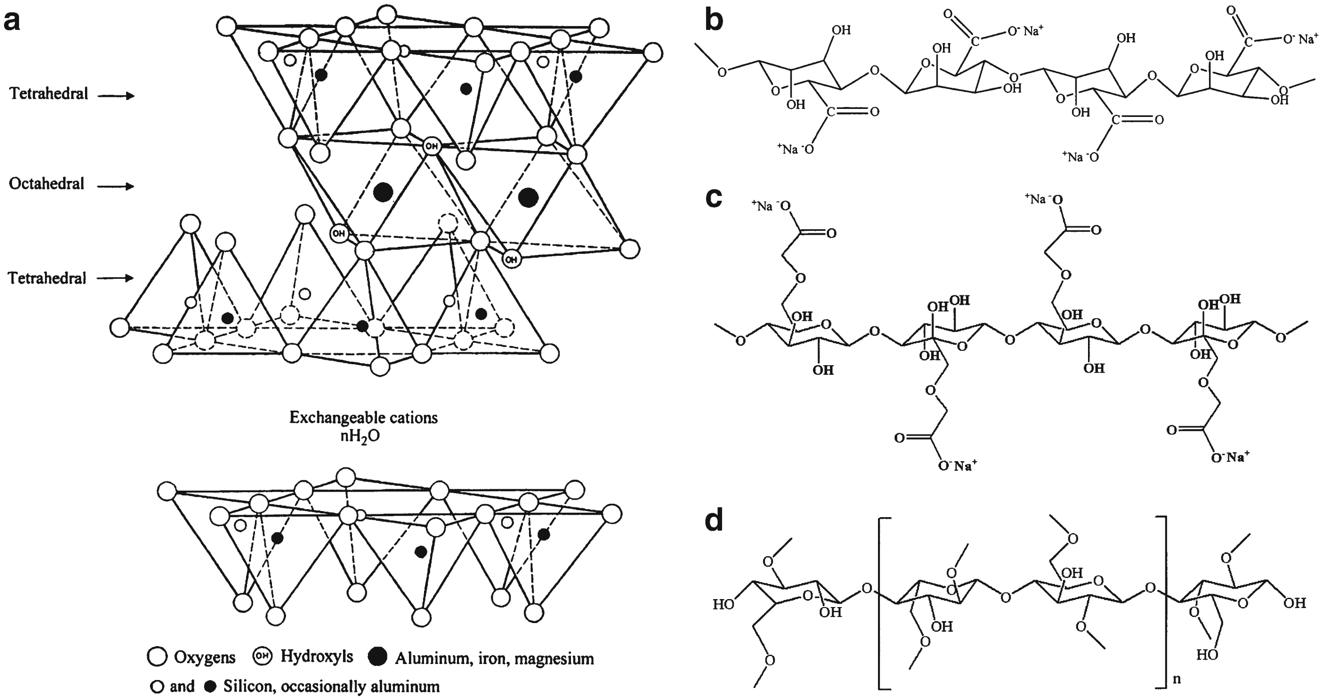

Fig. 1. Molecular structure of **a** montmorillonite clays (5), **b** mannuronic acid of SA, **c** SCMC, and **d** MC

synergism and an increase in the thixotropic properties of polymeric dispersions. To obtain similar results, MAS was also used in combination with sodium carboxymethylcellulose (SCMC) for improving not only physical stability (13) but also the flow behavior of suspensions (3).

Interaction between a polymer and clay could form a flocculate due to an electrostatic force if the polymer had a positive charge, such as chitosan (14), and a bridging mechanism for the polymer chain in the case of non-ionic polymers (15–17). These interactions lead to changes in the particle size and zeta potential of dispersed phase and also the flow behavior of composite dispersions. In a previous study, incorporating MAS into the SA gels provided higher viscosity and changed rheological behavior from Newtonian to pseudoplastic with thixotropic properties. This behavior was due to the formation of an electrostatic force between the negative charge of the carboxyl groups of SA and the positively charged sites at the edges of MAS, as well as intermolecular hydrogen bonding between SA and MAS (12). However, the flocculation and zeta potential of dispersed phase were not investigated in this report.

SA, SCMC, and methylcellulose (MC) have been used as suspending agents in suspensions (4). SA and SCMC are negatively charged polymers that possess carboxyl groups on their polymer chains (Fig. 1b, c, respectively), but SCMC has a carboxylmethyl ether group in which the ether groups may form hydrogen bonds with the silanol groups on the silicate layer surface of MAS. This may lead to the different characteristics of the flocculates formed. MC, a non-ionic polymer, possesses hydroxyl and methoxyl ether groups (Fig. 1d) and also has the potential to form flocculates with MAS. However, there are no data available concerning flocculation between these polymers and MAS. Therefore, the purpose of the present study was to investigate the size and microscopic morphology of the flocculates, zeta potential, and rheological behavior of composite dispersions prepared with different ratios of MAS and these selected polymers. The composite dispersions prepared were used as flocculating/suspending agents for the suspensions of acetaminophen (ACT) which was selected as a model drug because an increase in ACT particle size in suspensions could occur due to the crystallization of ACT saturated solution (18). This led to a hard cake after storage. Thus, the use of the composite dispersion may provide good physical stability to ACT suspensions. Additionally, the dissolution of ACT from the suspensions in an acidic medium was investigated.

MATERIALS AND METHODS

Materials

MAS (Veegum® HV) was obtained from R.T. Vanderbilt Company, Inc. (Norwalk, CT, USA). SCMC (viscosity of 2% dispersion at 25°C: 1,550 cps), MC (Methocel®, 27.5–32% methoxyl content, viscosity of 2% dispersion at 20°C: 3,000–5,500 cps), and SA NF17 (mannuronic acid-rich type) (19) were purchased from Nichirin Chemical Industries, Ltd. (Japan), Fluka (Buchs, Switzerland), and Srichand United Dispensary Co., Ltd. (Bangkok, Thailand), respectively. ACT was obtained from Praporn Darsut Ltd., (Bangkok, Thailand). ACT used in this study was the stable monoclinic form in which the melting peak temperature measured using differential scanning calorimeter was found to be 169°C (20,21). All other reagents used were of analytical grade and used as received.

Preparation of Dispersions

SCMC (0.5 g) or SA (1 g) was dispersed in distilled water (30 ml) by agitation for 2 h, whereas MC (0.5 g) was dispersed in hot water (10 ml) and cold water (20 ml) was then added and stirred for 1 h to get a clear dispersion. MAS (0.1, 0.5, or 1 g) was prehydrated with hot water (20 ml) for 15 min prior to adding into the polymer dispersions. The composite dispersions were obtained after adjusting the final volume to 100 ml with distilled water and were then stirred for 30 min and allowed to fully hydrate at room temperature (25–28°C) overnight prior to use.

Characterization of Composite Dispersions

Microscopic Morphology Studies

The microscopic morphology of MAS particles and the dispersed phase of composite dispersions were investigated using an inverted microscope (Eclipse TS100, Nikon, Japan) and viewed using a digital camera (Coolpix 4500, Nikon, Japan).

Particle Size Determination

The particle size of MAS and the dispersed phase of composite dispersions were measured using a laser diffraction particle size analyzer (Mastersizer2000 Model Hydro2000SM, Malvern Instrument Ltd., UK). The samples were dispersed in 70 ml of distilled water in a small volume sample dispersion unit in which the stirrer revolved at a rate of 50 Hz for 30 s prior to counting. The size–frequency distributions were plotted and particle sizes, measured as volume-weighted mean diameter, were reported. Moreover, $D_{10\%}$, $D_{50\%}$, and $D_{90\%}$, which were the volume number diameters where the given percentage of the particles was smaller than that size, were used to calculate the polydispersity index (PI), indicating the size distribution of the particles. The PI value can be expressed as (22):

$$\mathrm{PI} = \frac{D_{90\%} - D_{10\%}}{D_{50\%}}. \tag{1}$$

pH and Zeta Potential Measurement

The pH of all dispersions was measured using a pH meter (Ion Analyzer 250, Corning, USA). Moreover, the MAS and polymer–MAS dispersions were diluted to obtain appropriate concentrations, and the zeta potentials of all samples were measured using a laser Doppler electrophoresis analyzer (Zetasizer model ZEN 2600, Malvern Instrument Ltd.). The temperature of the samples was controlled at 25°C.

Rheological Studies

The rheological properties of the dispersions were studied using a Brookfield digital rheometer (Model DV-III, Brookfield Engineering Laboratories, Inc., Middleboro, MA, USA). The temperature of all samples was maintained at 32±1°C. A rheogram of the samples was plotted using shear rate and shear stress at various revolution rates of spindle (SC4-34). The rheological parameters of the dispersions, such as the exponential constant and viscosity coefficient, were calculated using exponential formulas as follows (2):

$$F^N = \eta G \tag{2}$$

$$\mathrm{Log} G = N \log F - \log \eta \tag{3}$$

where G, F, N, and η are the shear rate, the shear stress, the exponential constant that defines a type of flow, and the viscosity coefficient, respectively.

Preparation of ACT Suspensions

A 2.5-g portion of ACT was placed into a mortar, wetted using 0.1% (*w*/*v*) polysorbate 80 (2 ml), and levigated until a smooth paste was produced. Next, either polymer or polymer–MAS composite dispersions were added as a vehicle to the ACT smooth paste and mixed well. The resultant mixture was then transferred to a 50-ml graduated cylinder. The mortar was rinsed several times with a small portion of vehicle and the mixture obtained was also poured into the cylinder. Then, the suspension was adjusted to a final volume of 50 ml and mixed well prior to testing. The vehicle of the control suspension in this study was distilled water. In addition, MAS dispersions in concentrations of 0.1%, 0.5%, and 1% (*w*/*v*) were also used as a vehicle for ACT suspensions to investigate the flocculating efficiency of MAS. The suspensions were prepared as described above.

Characterization of Suspensions

Determination of Sedimentation Volume and Degree of Flocculation

The ACT suspension was poured into a 10-ml graduated cylinder and allowed to settle. The volume of the sediment was recorded at predetermined times over a period of 14 days. The sedimentation volume and the degree of flocculation at 14 days were determined. The sedimentation volume is the ratio between the volume of sediment at a given time and the total volume of the suspension, whereas the degree of flocculation is the sedimentation volume of the ACT suspensions using polymer or polymer–MAS composite dispersion divided by the sedimentation volume of the control suspension (2,23,24).

Redispersibility Studies

After the suspension in the 10-ml cylinder settled for 14 days, the cylinder was inverted to redisperse the sediment. The number of inversions required to resuspend the sediment of the suspension is the redispersibility value (24).

In vitro Dissolution Studies

A USP dissolution apparatus II (Hanson Research, Northridge, USA) was used to characterize the dissolution of ACT suspensions. The paddles were rotated at 50 rpm at 37.0±0.5°C. Nine hundred milliliters of 0.1 N HCl was used as a dissolution medium. Five milliliters of the suspension was placed into a 10-ml graduated cylinder and weighed. The suspension was then directly poured into the dissolution medium and the agitation was started (25). The cylinder was reweighed and the difference from the starting weight recorded as the weight of the tested suspension. The corresponding volume was computed using the density of the suspension, which was determined using a 25-ml pycnometer. Samples (5 ml) were collected without replacement of fresh medium at different time intervals. Then, the collected samples were filtered with a 0.45-µm cellulose acetate membrane. The amount of ACT dissolved was analyzed spectrophotometrically at 245 nm (Shimadzu UV1201, Japan).

RESULTS AND DISCUSSION

Microscopic Studies of Polymer–MAS Dispersions

MAS dispersions were opaque in nature. Incorporating MAS into MC, SA, and SCMC dispersions caused a change from clear viscous solutions to dispersions with different turbidities. All composite dispersions showed good homogeneity after fresh preparation. However, different sedimentation behaviors of these polymer–MAS dispersions were observed after settling for 2 days (Fig. 2). The supernatant of the MAS dispersion was not clear, suggesting a deflocculation system (2). Additionally, the MC–MAS and SCMC–MAS dispersions led to a clear supernatant after settling for 2 days (Fig. 2b, d, respectively). In contrast, no sedimentation of the SA–MAS dispersion was observed (Fig. 2c). A photomicrograph of the 0.5% MAS dispersion showed separated particles of hydrated MAS (Fig. 3a), whereas an irregular shape of aggregated particles in the MC–MAS and SCMC–MAS dispersions were readily observed (Fig. 3b, c, respectively). Interestingly, a unique arrangement of the particles was found in the SA–MAS dispersions (Fig. 3d). These results reveal flocculate formation between polymers and MAS. Moreover, the remarkably larger size of the MC–MAS and SCMC–MAS flocculates relative to the SA–MAS flocculates could explain the higher extent in sedimentation of the MC–MAS and SCMC–MAS flocculates. It is likely that the flocculation between these polymers and MAS may affect the characteristics of the composite dispersions, such as zeta potential and flow behavior.

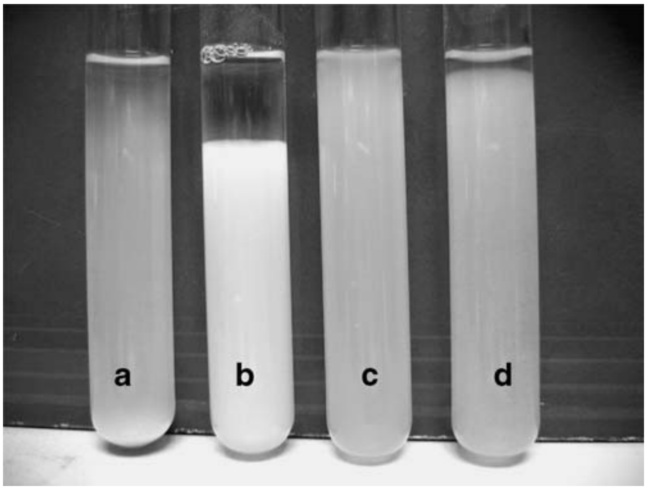

Fig. 2. Photographs of 0.5% MAS dispersions **a** without polymer and **b** with 0.5% MC, **c** 1% SA, and **d** 0.5% SCMC after settling for 2 days

Characterization of Polymer–MAS Dispersions

The addition of polymer into MAS dispersions led to changes in the characteristics of the size–frequency distribution curves, mean particle size, and PI values (Fig. 4 and Table I). As MAS concentration increased, the size–frequency distribution curves of the MC–MAS flocculates were shifted to larger particle size (Fig. 4a). The MC dispersion with 0.1% MAS provided a larger flocculate size than that with 0.5% MAS (Table I). However, the largest flocculate size and the lowest PI value were found when 1% MAS was used. In the case of the SCMC–MAS dispersion, incorporation of MAS provided bimodal size–frequency distribution curves at all concentrations of MAS (Fig. 4b). The peak at the smaller size was in the same range as that of the MAS dispersion. With increasing MAS concentrations, the frequency of the peak at the smaller size was increased, whereas that of the peak at the larger size was reduced. This led to a decrease in particle size with increasing PI values of the SCMC–MAS flocculates. Furthermore, incorporating MAS did not obviously change the size–frequency distribution of the SA–MAS flocculates (Fig. 4c), and the SA–MAS flocculate size tended to decrease with increasing MAS (Table I).

The pH of the polymer dispersions was over the range 6.7–7.2 (Table I), resulting in an ionization of carboxyl groups of SCMC and SA. The zeta potentials of the SCMC and SA dispersions were approximately −49.3 and −81.8 mV, respectively, whereas that of MC dispersion could not be determined due to a very low count rate, indicative of non-ionic polymer of MC. The MAS dispersion possessed a basic pH, and its zeta potential was found to be −44.7 mV (Table I). The addition of MAS into the polymer dispersions caused an obvious increase in the pH because of a mild alkalinity of OH groups associated with Si, Mg, and Al in MAS (11). The basic pH of the composite dispersions suggested that SCMC, SA, and MAS also presented negatively charged molecules. The incorporation of polymer to the MAS dispersion led to changes in zeta potential (Table I). The zeta potential of the MC–MAS dispersions was remarkably lower than that of the MAS dispersion, although MC was a non-ionic polymer. However, the MC–MAS flocculates also presented a negative charge with a small value of zeta potential. The SCMC–MAS dispersions showed an obviously higher zeta potential with a negative charge than both SCMC and MAS dispersions. On the other hand, incorporating MAS did not obviously affect the zeta potential of the SA dispersion. The zeta potential of the SA–MAS dispersions was over the range −78.0 to −84.1 mV, values which were close to the zeta potential of the SA dispersion. Furthermore, it can be seen that the change of the zeta potential of these polymers was independent upon the MAS concentration added. However, the change in zeta potential indicated an interaction between these polymers and MAS, which was related to the flocculation of these dispersion systems.

The flocculation between polymers and MAS is a result of the molecular interaction between both materials, although

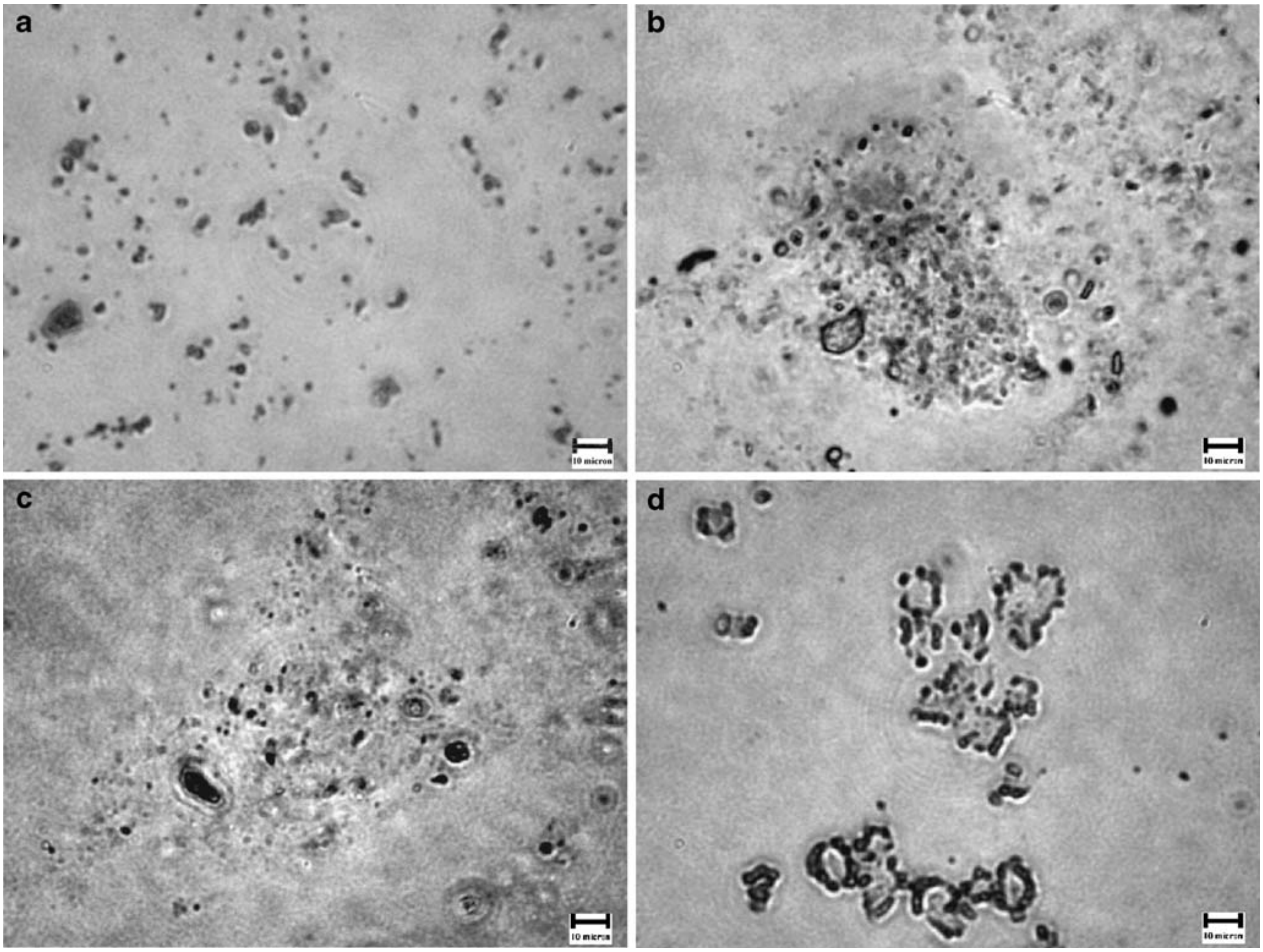

Fig. 3. Photomicrographs of MAS particles in 0.5% MAS dispersion **a** without polymer and **b** with 0.5% MC, **c** 0.5% SCMC, **d** and 1% SA

SA and SCMC have a negative charge that is similar to MAS and MC is a non-ionic polymer. This result suggests that MAS and these polymers could mainly interact via non-ionic electrostatic interaction, such as intermolecular hydrogen bonding, which would lead to flocculation by a polymer bridging mechanism (15). In fact, the surface of the silicate layers of MAS contain many silanol groups (SiOH), which have a high potential to form hydrogen bonds with the oxygen atoms of carboxyl, hydroxyl, and ether groups of these polymers. In the previous study, intermolecular hydrogen bonding between silanol groups at the surface of MAS and hydroxyl or carboxyl groups of SA was demonstrated. Moreover, the negative charges of the carboxyl groups of SA have an electrostatic interaction with the positively charged sites at the edges of MAS (12). This introduces numerous points of contact to create a denser network, resulting in the

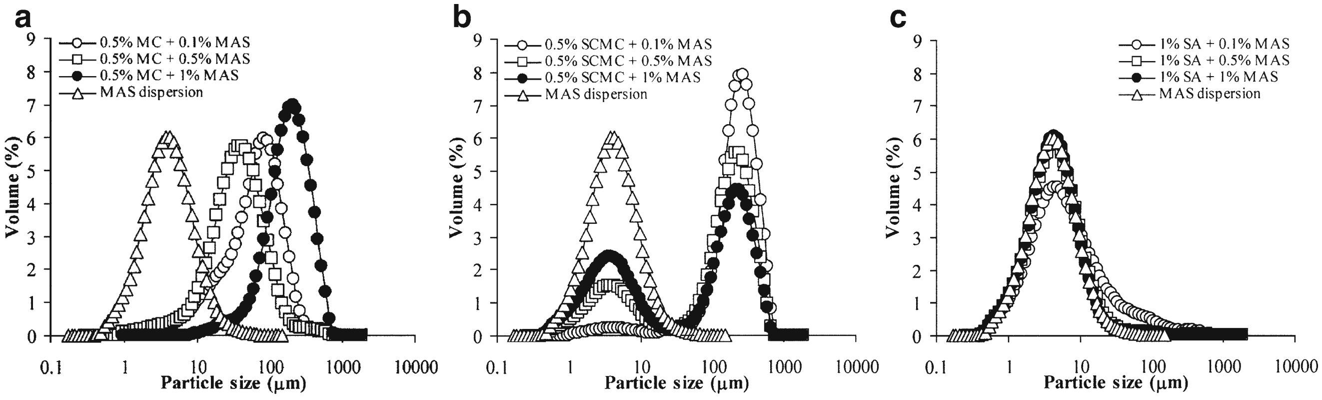

Fig. 4. Size–frequency distributions of flocculates in **a** 0.5% MC, **b** 0.5% SCMC, and **c** 1% SA dispersions containing different concentrations of MAS

Table I. Characteristics of Polymer–MAS Composite Dispersions

Component	Particle size[a] (μm)	Polydispersity index[a]	pH[a]	Zeta potential[b] (mV)	N[a]	Viscosity coefficient[a] [(dyne cm^{-2})^N s]
0.5% (*w*/*v*) MAS	5.5±0.2	2.33±0.09	8.36±0.06	−44.7±2.2	–	–
0.5% (*w*/*v*) MC	–	–	6.85±0.10	––	0.76±0.09	0.08±0.01
+0.1% (*w*/*v*) MAS	82.4±0.8	2.20±0.04	8.58±0.11	−4.34±0.94	0.79±0.12	0.09±0.01
+0.5% (*w*/*v*) MAS	51.9±1.5	2.37±0.20	9.31±0.06	−2.83±0.51	1.22±0.04	0.44±0.03
+1% (*w*/*v*) MAS	217.4±15.6	1.75±0.01	9.23±0.03	−4.36±1.84	1.96±0.01	8.51±1.52
0.5% (*w*/*v*) SCMC	–	–	7.20±0.05	−49.3±14.3	0.96±0.08	0.24±0.05
+0.1% (*w*/*v*) MAS	251.5±17.4	1.55±0.11	7.57±0.03	−84.3±9.4	0.90±0.07	0.24±0.02
+0.5% (*w*/*v*) MAS	169.7±15.0	2.47±0.13	9.23±0.04	−83.1±5.6	1.10±0.05	1.07±0.16
+1% (*w*/*v*) MAS	137.2±14.9	3.53±0.56	9.23±0.02	−79.0±2.8	2.26±0.01	227.6±24.3
1% (*w*/*v*) SA	–	–	6.71±0.02	−81.8±4.5	0.70±0.04	0.18±0.01
+0.1% (*w*/*v*) MAS	16.3±1.3	5.54±0.60	7.37±0.03	−84.1±2.9	0.82±0.07	0.25±0.04
+0.5% (*w*/*v*) MAS	7.1±1.3	2.47±0.04	9.13±0.01	−78.9±2.1	0.95±0.02	0.48±0.01
+1% (*w*/*v*) MAS	5.9±0.1	2.28±0.02	9.12±0.03	−78.1±1.5	1.47±0.11	7.77±2.96

– could not be measured, –– count rate is too low
[a] Data are the mean±SD of three determinations
[b] Data are the mean±SD of six determinations

unique structure of the flocculates observed in the SA–MAS dispersions (Fig. 3d). However, the SA–MAS flocculates were not stable and were dissociated by water dilution and gentle mechanical force during particle size measurement. Thus, the final measured size was in the same range as that of MAS. SCMC has carboxyl groups that are similar to SA, but it could form larger sized flocculates. This can explain why SCMC or SA could interact with MAS via similar interaction mechanisms. However, the aliphatic ether groups on the molecular chain of SCMC could possibly create a hydrogen bond with MAS rather than the ether groups of SA. This resulted to the different characteristics of flocculates. The hydrogen bonding mechanism could also be involved in the formation of the MC–MAS flocculates. However, increasing the concentration of MAS led to a decrease in the amount of the SCMC–MAS flocculates, but it increased the MAS particles that were not involved in flocculation (residual MAS), suggesting that the formation of the SCMC–MAS flocculates was limited in amount and particle size. On the other hand, an almost complete flocculation between MC and MAS occurred, leading to a larger flocculate size with increasing concentrations of MAS. Moreover, the MC–MAS flocculates gave small zeta potentials with negative charges that were obviously less than the zeta potential of MAS, indicating that the flocculates were covered by non-ionic MC molecules. This phenomenon was also found in the SCMC–MAS flocculates, which presented a negative charge, but the zeta potentials of these flocculates were higher than those of SCMC and MAS. This suggests that the coverage of SCMC caused a denser negative charge on the surface of these flocculates.

The effect of MAS addition on the flow curve of the polymer dispersions is shown in Fig. 5. Nonlinear flow curves of the composite dispersions were observed when adding higher concentrations of MAS. In contrast, the flow curves of pure polymer dispersions showed a linear relationship between shear rate and shear stress. The rheological parameters calculated using the shear rate and shear stress of the up-curve are presented in Table I. The exponential constant (N value) that defines the type of flow of the dispersions was approximately unity, indicating Newtonian flow. Incorporation of MAS into the polymer dispersions caused an increase in the N value, suggesting that the flow behavior shifted to pseudoplastic flow. Furthermore, the viscosity coefficient of the polymer dispersion increased with an increasing concentration of MAS (Table I), suggesting viscosity-enhancing properties of MAS. The up- and down-curves of the composite dispersions were coincident when 0.1% and 0.5% MAS were used. A hysteresis loop was found between up- and down-curves of the flow curves when using 1% MAS. The down-curve moved to the left of the up-curve when the MC dispersion contained 1% MAS (Fig. 5a). This phenomenon is called negative thixotropy or antithixotropy (2). On the other hand, the down-curve of the SCMC and SA dispersions with 1%MAS fell to the right of the up-curve (Fig. 5b, c, respectively), indicative of a thixotropic property.

The formation of hydrogen bonds between MAS and SA to create numerous points of contact could produce a loose three-dimensional structure throughout the composite dispersion that is a gel-like structure. The higher the concentration of MAS, the greater the number of contact points in the dispersion. These interactions could result in an enhancement of the viscosity and thixotropic properties of the composite dispersions. The SCMC–MAS dispersions that contained the flocculates and the residual MAS demonstrated that increasing the amount of MAS led to higher viscosities and increased thixotropic properties of the composite dispersions. This suggests that the residual dispersed MAS could possibly act as a cross-linker between SCMC chains to create numerous points of contact. Thus, the SA–MAS and SCMC–MAS dispersions underwent a gel-to-sol transformation and exhibited shear thinning when shear stress was applied. The structure started to reform slowly to the original state after the shear stress was removed. In contrast, the MC–MAS dispersions showed complete flocculation, the largest flocculates were formed when 1% MAS was used, and the flow curve of this dispersion was pseudoplastic with antithixotropy. It is possible that antithixotropy resulted from an increased collision frequency of flocculates in dispersion, leading to an increase in interpar-

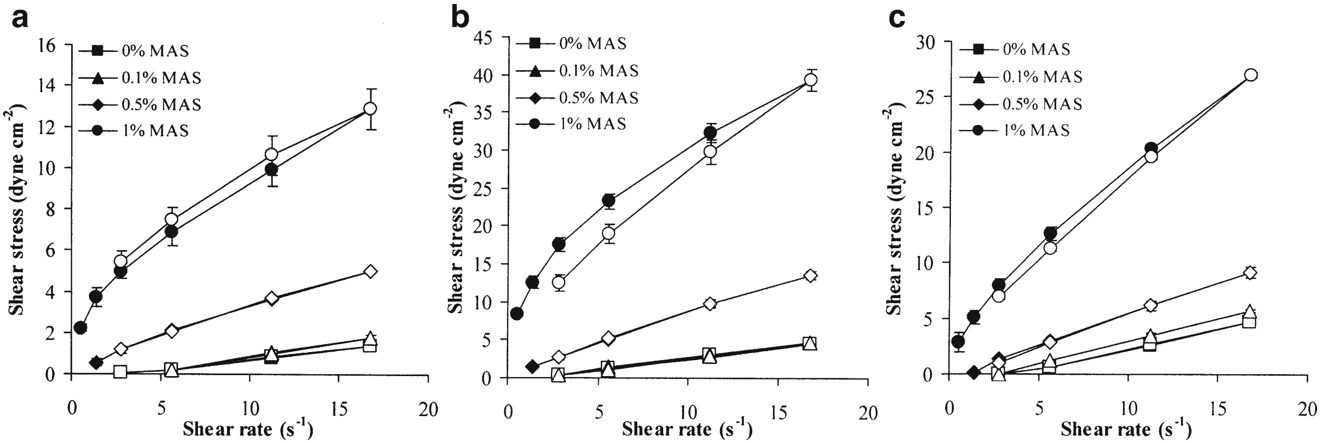

Fig. 5. Flow curves of **a** 0.5% MC, **b** 0.5% SCMC, and **c** 1% SA dispersions containing different concentrations of MAS. *Closed symbols* represent the up-curve; *open symbols* represent the down-curve. Each point is the mean±SD of three determinations

ticle bonding with time. This bonding ultimately led to the formation of larger flocculates, and a gel-like structure was created. At rest, the larger flocculates break up and gradually return to their original state (2).

Physical Properties of ACT Suspensions

The polymer–MAS dispersions were used as flocculating/suspending agents in ACT suspensions. The sedimentation volumes of ACT suspensions prepared using polymer–MAS dispersions at different times are presented in Fig. 6. The sedimentation volume of the suspensions using MC and MC–MAS dispersions decreased rapidly in a similar manner to the control suspension (Fig. 6a). This result was also observed in the suspensions using SCMC dispersions and SCMC dispersions with 0.1% and 0.5% MAS (Fig. 6b). This is likely to be due to the fast sedimentation of ACT particles and polymer–MAS flocculates. However, the sedimentation volume at 14 days increased with increasing concentrations of MAS, and the SCMC-MAS dispersions gave higher sedimentation volumes than the MC-MAS dispersions at all concentrations of MAS. Moreover, it is interesting that the suspensions using the SCMC-1% MAS dispersion had the highest sedimentation volume, which was close to unity, over the 14 days of the test. The suspensions using SA and SA-MAS dispersions showed a slow decrease in sedimentation volume with increasing concentrations of MAS. Moreover, the higher the concentration of MAS added into the SA dispersion, the greater the sedimentation volume obtained at 14 days. The degree of flocculation and the redispersibility value at 14 days of all suspensions are presented in Fig. 7. The degree of flocculation of the suspensions increased with increasing concentrations of MAS in all polymer and polymer–MAS dispersions used (Fig. 7a). The SCMC-MAS dispersions showed the highest degree of flocculation, whereas the lowest degree of flocculation was obtained from the MC-MAS dispersion. When the MAS dispersion was used as a flocculating agent in the ACT suspensions, the degrees of flocculation of the suspensions using 0.1%, 0.5%, and 1% MAS dispersions were found to be 1, 2.8, and 6.1, respectively. The SA–MAS and SCMC–MAS dispersions yielded a remarkably higher degree of flocculation than the MAS dispersions, while the results of the MC–MAS dispersions were similar to those of the MAS dispersion when the same concentration of MAS was compared. The other parameter used to evaluate the suspensions was the redispersibility value. The suspensions with the MC–MAS dispersions demonstrated no differences in redispersibility value when

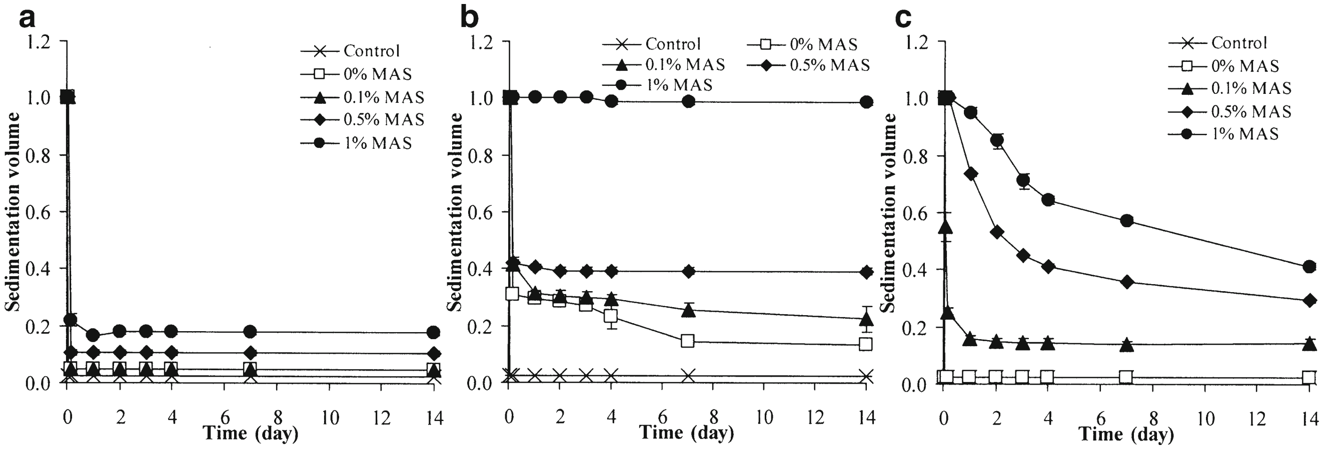

Fig. 6. Sedimentation volume of ACT suspensions prepared using **a** 0.5% MC, **b** 0.5% SCMC, and **c** 1% SA dispersions containing different concentrations of MAS as suspending agents. Each point is the mean±SD, $n=3$

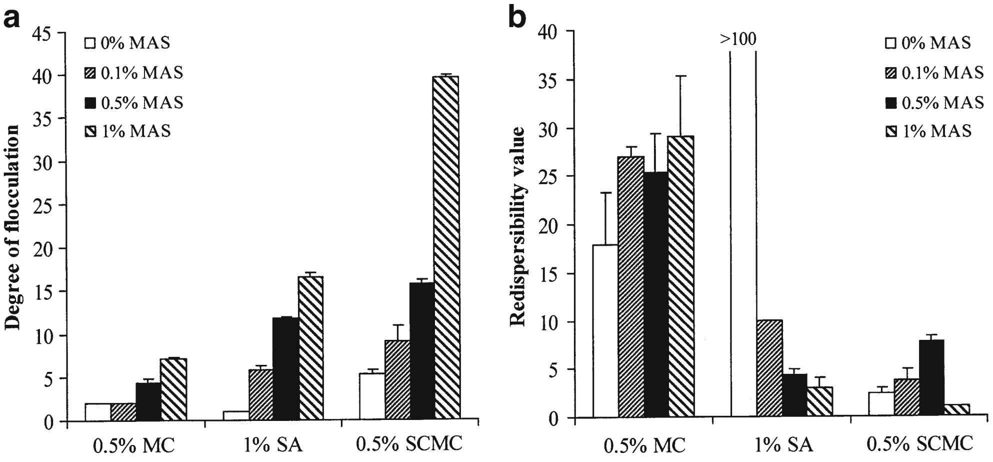

Fig. 7. Degree of **a** flocculation and **b** redispersibility value of ACT suspensions prepared using different polymer–MAS dispersions as suspending agents. Each value is the mean±SD, $n=3$

compared to that using MC dispersion, even though 1% MAS was added (Fig. 7b). On the other hand, the redispersibility value of the suspensions using the SA dispersion decreased appreciably with increasing concentrations of MAS, although this suspension had a tendency to cake, which was also seen in the control suspension (redispersibility value >100). Moreover, the SCMC–1% MAS dispersion gave the lowest redispersibility value, which is likely due to the very low sedimentation volume of this suspension.

The ACT suspension using the SCMC dispersion gave a higher degree of flocculation and a lower redispersibility value than that using the MC dispersion, and the lowest degree of flocculation and the highest caking tendency of the suspensions were obtained when using the SA dispersion (Fig. 7). These results show that the SCMC dispersion provides the highest efficiency in inducing flocculation of ACT particles; the flocculation of ACT particles is formed by a polymer bridging mechanism via hydrogen bonding (26).

Using the MC–MAS dispersion, the degree of flocculation of suspensions increased with increasing concentrations of MAS, but increasing the degree of flocculation of the MC-MAS dispersion had less of an effect than the SA–MAS and SCMC–MAS dispersions. Moreover, the redispersibility value of the suspensions using the MC–MAS dispersions was not noticeably reduced. This result suggests that the large size of the MC–MAS flocculates in the dispersions could induce a fast sedimentation of ACT particles, and a close-packed arrangement of ACT particle sediment and MC–MAS flocculates occurred. However, the close-packed sediment did not cause a hard cake because it was redispersible after shaking. The SA–MAS dispersion led to an improvement not only in the degree of flocculation but also in the redispersibility values of the suspensions. These data indicate that the formation of a three-dimensional structure of SA and MAS and the flocculating efficiency of MAS brought about a loosely packed arrangement of ACT particles, leading to a remarkable reduction in caking tendency and an increased ability to redisperse. The three-dimensional structure formed by the SCMC–MAS flocculates and the residual MAS could improve the degree of flocculation of the suspensions but increase the redispersibility value when using MAS over the range of 0.1–0.5%. This was due to the higher viscosity of the SCMC–MAS dispersions when compared to the other composite dispersions. In addition, the highest degree of flocculation was obtained when using the SCMC–1% MAS dispersion because of the higher viscosity and the denser three-dimensional structure which could retard the sedimentation of ACT particles. This also led to the lowest redispersibility value.

In Vitro ACT Dissolution Studies

The dissolution profiles of the ACT suspensions are presented in Fig. 8. The ACT suspensions using SCMC and MC dispersions led to more than 80% ACT dissolved at 5 min, which was similar to the control suspension. Additionally, the suspensions using SCMC–1% MAS and MC–1% MAS dispersions showed similar results to those using SCMC and MC dispersions. This finding indicated that SCMC, MC, and their composite dispersions can be rapidly dispersed in an acidic medium, which does not affect the dissolution process of ACT particles. On the other hand, SA and SA–1% MAS dispersions could retard the ACT dissolution, for which the

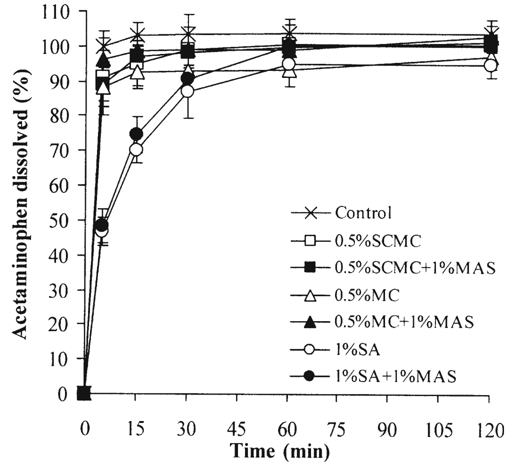

Fig. 8. Dissolution profiles of ACT suspensions prepared using different polymer–MAS dispersions as suspending agents. Each point is the mean±SD, $n=3$

time to 80% ACT dissolved was approximately 30 min. The SA dispersion could possibly form an insoluble gel of alginic acid in an acidic medium (27), resulting in a slower dissolution of ACT particles embedded in the alginic gel. The results indicated that the polymer–MAS dispersions did not affect the dissolution of ACT from the suspensions when compared with the pure polymer dispersions.

CONCLUSION

SA, SCMC, and MC could form flocculates with MAS in dispersions via a polymer bridging mechanism in which the flocculates obtained possessed different characteristics. The residual MAS from the flocculation could create a three-dimensional structure in the SA–MAS and SCMC–MAS dispersions, which led to not only an enhancement of viscosity and thixotropic properties but also an improvement in the ACT flocculating efficiencies of polymers. Moreover, the use of the polymer–MAS dispersions provided a higher degree of flocculation and a lower redispersibility value of ACT suspensions when compared with pure polymer dispersions. The SCMC–MAS dispersions provided the highest ACT flocculating efficiency, whereas the lowest ACT flocculating efficiency was detected in the MC–MAS dispersions. Additionally, the composite dispersions did not affect the dissolution of ACT from the suspensions in an acidic medium. This study suggests that polymer–MAS dispersions demonstrate good feasibility for use as flocculating/suspending agents for improving the flow behaviors and physical stabilities of suspensions.

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