Drug Development and Industrial Pharmacy, 32:809–820, 2006

ISSN: 0363-9045 print / 1520-5762 online
DOI: 10.1080/03639040500529978

informa
healthcare

Development of Suspending Agent from Sodium Carboxymethyl Mungbean Starches

O. S. Kittipongpatana and J. Sirithunyalug
Department of Pharmaceutical Sciences, Faculty of Pharmacy, Chiang Mai University, Chiang Mai, Thailand

ABSTRACT Three sodium carboxymethyl mungbean starches (SCMMSs) were selected, based on the physicochemical profiles and evaluated as potential pharmaceutical suspending agent in comparison with a sodium carboxymethyl tapioca starch and other five commercial suspending agents. Ibuprofen suspension was employed as a model formulation with 0.5, 1.0, and 2.0% w/v of suspending agents. Evaluation parameters included the determination of sedimentation volume ratio, redispersibility, viscosity and rheological properties and content uniformity studies. The results revealed that a high-viscosity modified mungbean starch, MMS-M-04, possessed suitable properties as a suspending agent and, at 1% concentration, was as effective as sodium carboxymethylcellulose and xanthan gum, two most-commonly used suspending agents. This modified starch could be further developed and employed as a new commercial suspending agent in the pharmaceutical industry.

KEYWORDS Suspending agent, Sodium carboxymethyl mungbean starch, Suspension, Modified starch

INTRODUCTION

Sodium carboxymethyl starch (SCMS) is a modified starch (MS) prepared essentially by a chemical reaction between native starch and chloroacetic acid in an alkaline condition. The major characteristics of this starch ester derivative are the solubility in unheated water and the ability to form viscous paste with smoother texture, and higher flexibility and strength than those of pregelatinized starches (Mishra et al., 1990). SCMS is also recognized as "generally safe" and is officially listed in the United States Pharmacopeia (USP) and the British Pharmacopoeia (BP). It has been widely used in the food industry as ingredients in many types of sauces and instant foods (Chen and Jane, 1994) and has also been evaluated and employed in the preparation of pharmaceutical dosage forms as important excipients. Such applications included the use of SCMS as directly-compressible excipient for tablet (Timaroon and Kulvanich, 1992), tablet binder (Pitaksuteepong, 1995), disintegrant (Teruya, 1995), and suspending agent (Suwannapakul, 1997). These studies showed that

Address correspondence to O. S. Kittipongpatana, Department of Pharmaceutical Sciences, Faculty of Pharmacy, Chiang Mai University, Chiang Mai, 50200 Thailand; E-mail: ornanong@pharmacy.cmu.ac.th

SCMSs prepared from different types of native starch (i.e., potato, tapioca, corn, and rice) possessed different characteristics and therefore had different applications, which suggested that the starch from other sources could also be studied for broader applications.

The seeds of mungbean (*Vigna radiata* L. Wilczek, Papilionaceae), the legume crop most cultivated in Thailand, contain a high amount of starch which is mainly amylose (30–45%) (Jung et al., 1991; Kasemsuwan et al., 1998). The physicochemical and rheological properties, as well as structural characterizations of mungbean starch, have been reported (Hoover et al., 1997; Ohwada et al., 2003). Initially used predominantly in the food industry, the unique characteristic of mungbean starch to form transparent gel with resiliency and strong gel-strength has attracted the interest for pharmaceutical research. Sinchaipanid (1989) reported that pregelatinized and crosslinked mungbean starch had a potential as tablet disintegrant. Recently, our group has prepared 15 sodium carboxymethyl mungbean starches (SCMMSs) using various solvents and reaction conditions and reported the physicochemical properties of these modified starches (Kittipongpatana et al., 2006). It was found that these SCMMSs possessed different properties that could be employed as many types of pharmaceutical ingredients such as film-coating agent and suspending agent.

The amount of pharmaceutical suspension marketed and prescribed in Thailand each year means that a large quantity of suspending agents is required. Most of the suspending agents currently used in the preparation of such dosage form, for examples – acacia (AC), sodium alginate (SA), sodium carboxymethylcellulose (SCMC), tragacanth (TG) and xanthan gum (XG) – are imported and are generally expensive. The development of new suspending agents based on domestically and abundantly available materials, such as starch, proposes a way to decrease the amount of imported materials, the price of the dosage form, as well as benefits the growers of starch-containing plants will receive through the value-added procedure and application of otherwise cheap materials.

In this subsequent study, we focus our interest on the evaluation of SCMMSs as suspending agent. Three SCMMSs were selected and employed, in comparison with some commercial suspending agents and a sodium carboxymethyl tapioca starch (MTS), in the formulation of pharmaceutical suspension containing ibuprofen as active ingredient. The prepared formulations were then evaluated to determine the effectiveness of the suspending agents which included the determination of sedimentation volume, redispersibility, viscosity and rheological characteristics and content uniformity.

MATERIALS AND METHODS

Materials and Reagents

Mungbean starch was from Sitthinan Co. Ltd. (Pine brand, Thai Industrial Standard, TIS 948–2533). Chemicals and solvents used in the preparation and analysis of modified starches were of analytical grade or equivalent. Methanol used to wash the final products was of commercial grade but was double-distilled before use. Acacia, sodium alginate, sodium carboxymethylcellulose (average MW 250,000; D.S. 0.70), tragacanth and xanthan gum were from Fisher, USA. A water-soluble sodium carboxymethyl tapioca starch (MTS) (D.S. 0.3447; pH $_{(1\%\ w/v)}$ 8.4; viscosity $_{(1\%\ w/v,\ at\ shear\ rate\ 1,000\ s-1)}$ 57.33 mPa.s) was prepared using the same procedure as for SCMMS, with 2-propanol as a solvent and the reaction temperature of 50°C for 60 min. Ibuprofen was a gift from Siam Pharmaceutical Co. Ltd. Chemicals used in the preparation of tested suspensions were of pharmaceutical grade or equivalent.

Selection of Sodium Carboxymethyl Mungbean Starches

Three SCMMSs, namely MMS-E-01, MMS-I-01, and MMS-M-04, were among 15 SCMMSs prepared in the previous study (Kittipongpatana et al., 2006) and were selected, based on their physicochemical properties, as potential suspending agents. The criteria for selection were the water solubility, pH of solution, paste clarity, viscosity, and rheological profile.

Preparation of Ibuprofen Suspensions

Three SCMMSs, a sodium carboxymethyl tapioca starch (MTS) and five commercial suspending agents – acacia (AC), sodium alginate (SA), sodium carboxymethylcellulose (SCMC), tragacanth (TG) and xanthan gum (XG) – were used in the preparation of ibuprofen suspensions (100 mg/5 mL). Three concentrations

(0.5, 1, and 2% w/v) were prepared for each suspending agent, i.e., 27 suspension formulations were prepared and comparatively evaluated. The ibuprofen suspension formulation is as follow;

Ibuprofen	2 g
Suspending agent	0.5, 1.0, 2.0%
Syrup USP	15 mL
Sorbitol 70%	15 mL
Tween® 80	0.52 g
Sodium saccharin	0.02 g
Methyl paraben	0.18 g
Propyl paraben	0.02 g
Flavor (orange oil)	10 drops
Color (2% sunset yellow)	5 drops
Water qs. to	100 mL

The pourability of the prepared suspension was tested by placing 60 mL of the suspension into a bottle and clamped it on a stand. The clamp was rotated 45° down and the ability of the suspension to flow out completely from the bottle was observed.

Evaluation of Suspension and Effectiveness of Suspending Agents

The following parameters of each suspension formulation were evaluated: sedimentation volume, redispersibility, viscosity and rheology, and content uniformity. All evaluations were done in triplicate and, unless noted otherwise, at room temperature. In addition, redispersibility and viscosity study were also conducted on samples treated through eight freeze-thaw (FT) cycles. Each cycle consisted of a cold storage at 8°C for 2 days and a warm storage at 45°C for 2 days (British Pharmaceutical Codex, 1996).

Sedimentation Volume

The sedimentation volume of the suspension was determined over a period of two months, using the cylindrical graduate method (Nasipuri and Ogunlana, 1978). The procedure was as follow: 50 mL of triplicated samples were stored in 100 mL glass graduate cylinders. Each sample was shaken to ensure uniformity prior to the study. Sedimentation height was measured and recorded every day for the first five days, then every five days until day 40 and every 10 days afterward, without disturbing the suspension. The sedimentation volume (F) was calculated from the ratio of the ultimate height (Hu) of the sediment to the initial height (Ho) of the total suspension.

Redispersibility

The ease of redispersion was deduced from the number of vertical inversion required for each test tube containing the studied suspension which had to be inverted before the sediment was completely resuspended. The triplicated test tubes that were allowed to settle for 1, 2, 3, and 4 weeks, as well as test tubes subjected to freeze-thaw cycles, were tested. The vertical inversion was conducted by clamping the test tube vertically on a stand. The tube was then manually rotated, at a constant rate, up 180° and back down. In case the tube had been inverted 30 times and the sample was still not fully resuspended, the tube was vigorously shaken until homogeneity was achieved and the result recorded "vg," If the sediment remained solidly flocculated at the bottom of the test tube even after "vg," the test result would be recorded as "cake."

Viscosity and Rheology

The rheological profile of each formulation was characterized using a Brookfield R/S-CPS rheometer (Bob-and-Cup format). 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 1,000 s^{-1} in 1 min, (2) held at 1,000 s^{-1} for 1 min and (3) a decrease of the shear rate from 1,000 to 0 s^{-1} in 1 min. All measurements were performed at a controlled temperature of 25 ± 1°C. The data were analyzed with a Brookfield Rheo 2000 software. The apparent viscosity for all samples in this study was measured at a shear rate of 1,000 s^{-1}. Viscosity was expressed in mPa.s. The flow curve was plotted between shear rate and shear stress. Thixotropic quantity of each formulation was also determined as a value of thixotropic breakdown which was calculated from the area of a hysteresis loop formed between the upcurve and the downcurve of the flow curve of each suspension.

Content Uniformity

Fifty milliliters of aliquot of suspension sample were individually withdrawn at three different depth levels from a cylinder containing the suspension

which was allowed to stand undisturbed for 1, 2, and 4 months and transferred into a 50 mL volumetric flask. The sample was dissolved, diluted, and adjusted to volume with phosphate buffer pH 7.2, which is composed of 0.68% KH_2PO_4 and 0.14% NaOH. The absorbance of ibuprofen was measured at 223 nm by a UV spectrophotometer, using matrix solution as a blank, and the concentrations of ibuprofen at each depth level were calculated. The deviation of ibuprofen concentration among the three depth levels of each suspension was used to determine the content uniformity of the formulation. Total deviation can be calculated from the triplicate of each formulation as follows

$$\text{Total deviation} = \sqrt{SD_1^2 + SD_2^2 + SD_3^2}$$

when SD_n is the deviation among three depth levels of triplicate # n

Statistical Analysis

The statistical tests, for significant differences in the sedimentation volume, redispersibility, viscosity, and content uniformity among samples containing different types and amounts of suspending agents, were performed using Duncan's multiple range test at 95% confidence level ($p < 0.05$).

RESULTS AND DISCUSSION

Selection of SCMMSs with Potentials as Suspending Agent

Three previously prepared SCMMSs – MMS-E-01, MMS-I-01, and MMS-M-04 – were selected based on their physicochemical properties that showed potentials as suspending agent (Kittipongpatana et al., 2006) (Table 1). All three SCMMSs were soluble in cold water and formed clear, viscous gel with high degree of thixotropy, a preferable property of a suspending agent.

Preparation of Ibuprofen Suspensions

Based on general appearances of the prepared suspensions, most suspending agents showed optimum effectiveness, i.e., exhibited the ability to suspend drug particles, with pourable viscosity, at 0.5 and 1.0% concentration, with the exception of AC and SA which required at least 2.0% concentration to obtain a good suspension. At 2.0% concentration, the viscosity of the formulations that contained MMS-M-04, SCMC, and XG as suspending agent were too high and the evaluation of some tested parameters was not possible.

Evaluation of Suspension and Effectiveness of Suspending Agent

Sedimentation Volume (SV)

At 0.5% w/v, the formulations that contained SCMMSs as suspending agent showed lower SV ratio compared to those of SCMC-, TG-, XG-, and MTS-containing formulations (Fig. 1). However, at 1.0% w/v of suspending agent, formulations that contained SCMMSs showed improved SV ratio during a 60-day evaluation. MMS-M-04-containing formulation was completely suspended (SV = 1.00) while those contained MMS-E-01 and MMS-I-01 yielded good SV ratio (Fig. 2). At 2.0% w/v suspending agent, the formulations that employed SCMMSs were all completely suspended and only those which contained AC, SA, and MTS showed significant degree of sedimentation (Fig. 3).

TABLE 1 **Physicochemical Properties of Selected SCMMSs**

Sample	Solvent	D.S.	pH (1% w/v)	A*$_{650\ nm}$	Viscosity at SR 1,000s^{-1} (1% w/v; mPa.s)		Thixotropic quantity (mPa.s)
					normal	FT	
MMS-E-01	ethanol	0.2011	9.0	0.01–0.02	31.33 ± 0.58	27.67 ± 1.53	1,557.57 ± 16.75
MMS-I-01	2-propanol	0.3443	9.2	0.02–0.03	37.33 ± 0.58	29.67 ± 1.53	1,599.16 ± 38.61
MMS-M-04	methanol	0.3597	9.0	0.13–0.16	149.67 ± 1.53	59.33 ± 0.58	8,795.51 ± 458.80

*Absorption of a 1% w/v solution measured spectrophotometrically at 650 nm.

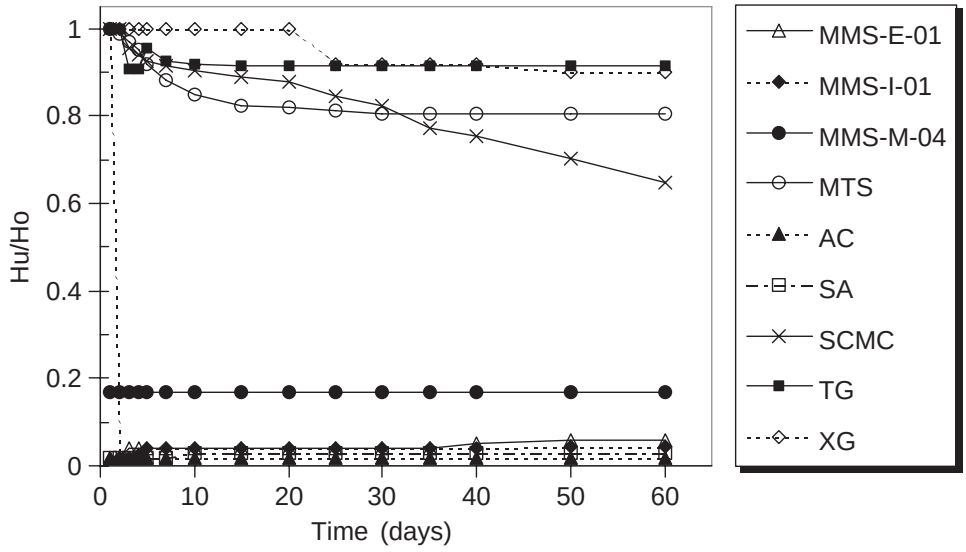

FIGURE 1 **Comparison of Sedimentation Volume Ratio Among Ibuprofen Suspension Formulations Containing Different Suspending Agents at 0.5% w/v.**

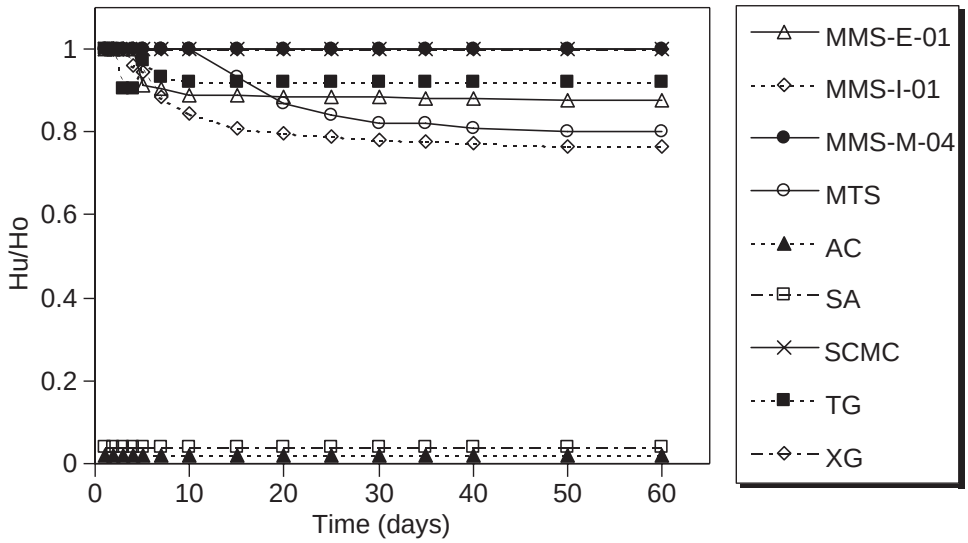

FIGURE 2 **Comparison of Sedimentation Volume Ratio Among Ibuprofen Suspension Formulations Containing Different Suspending Agents at 1.0% w/v.**

Redispersibility (RD)

Suspensions that contained MMS-M-04, TG, SCMC, and XG possessed excellent redispersibility. At 0.5% concentration (Fig. 4), these suspensions required, at any tested period, less than five inversions to completely resuspend the sediment at room temperature, while the subjection of samples through FT cycles did not affect the redispersibility. The formulations that used MMS-E-01, MMS-I-01, MTS and SA as suspending agent required more number of inversion before a homogenous suspension could be obtained. The redispersibility of these suspensions, however, was affected by FT cycles so that these formulations required less number of inversion to resuspend the sediment. This is partly due to the loss of viscosity caused by FT treatment. AC-containing suspension showed lower redispersibility as the storage time increased and FT treatment resulted in the aggregation

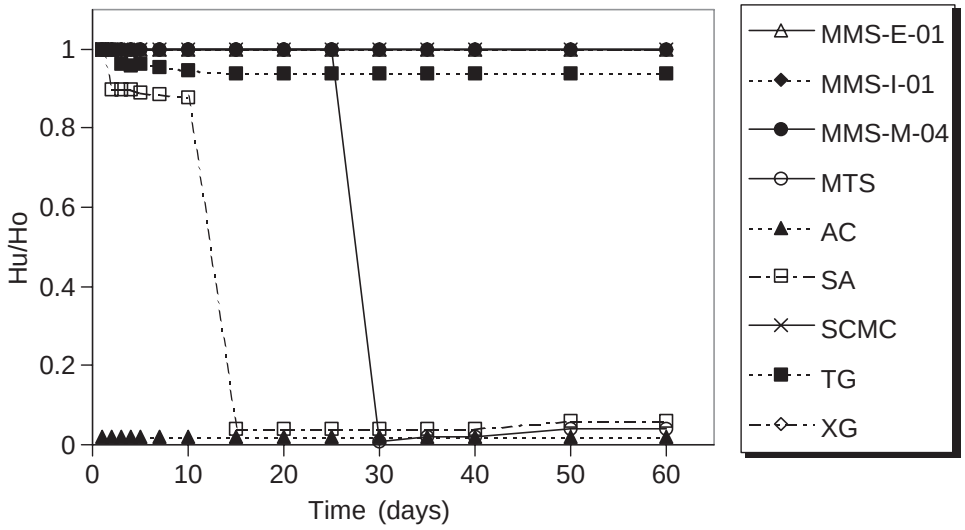

FIGURE 3 **Comparison of Sedimentation Volume Ratio Among Ibuprofen Suspension Formulations Containing Different Suspending Agents at 2.0% w/v.**

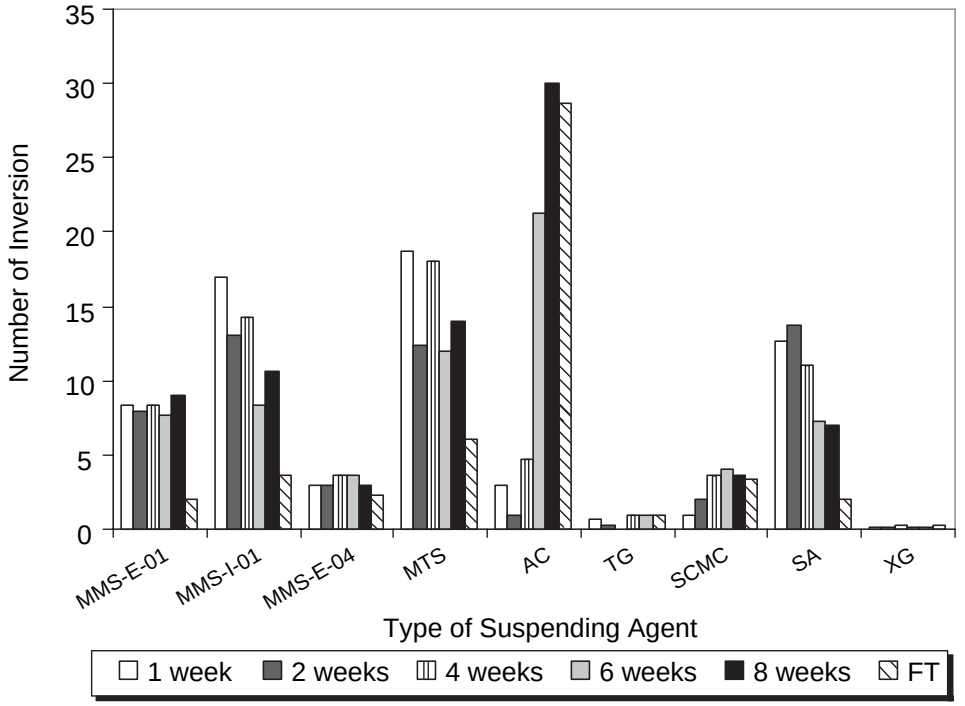

FIGURE 4 **Number of Inversion Required to Completely Resuspend to Homogeneity of the Ibuprofen Suspension Formulations Containing Different Suspending Agents at 0.5%w/v.**

of sediment that required vigorous shaking (vg) to redisperse the suspension. At 1% w/v of suspending agent (Fig. 5), suspensions containing MMS-M-04, SCMC, and XG required no inversion as the formulations were completely suspended, while TG- and MMS-E-01-containing formulations required only a few inversions. In contrast, suspensions that used MMS-I-01, MTS, and SA as suspending agent required vigorous shaking to resuspend the formulation due to a high increase in viscosity. FT treatment yielded results similar to those observed in 0.5% formulations. Similar trend was also observed for 2.0% formulations (data not shown).

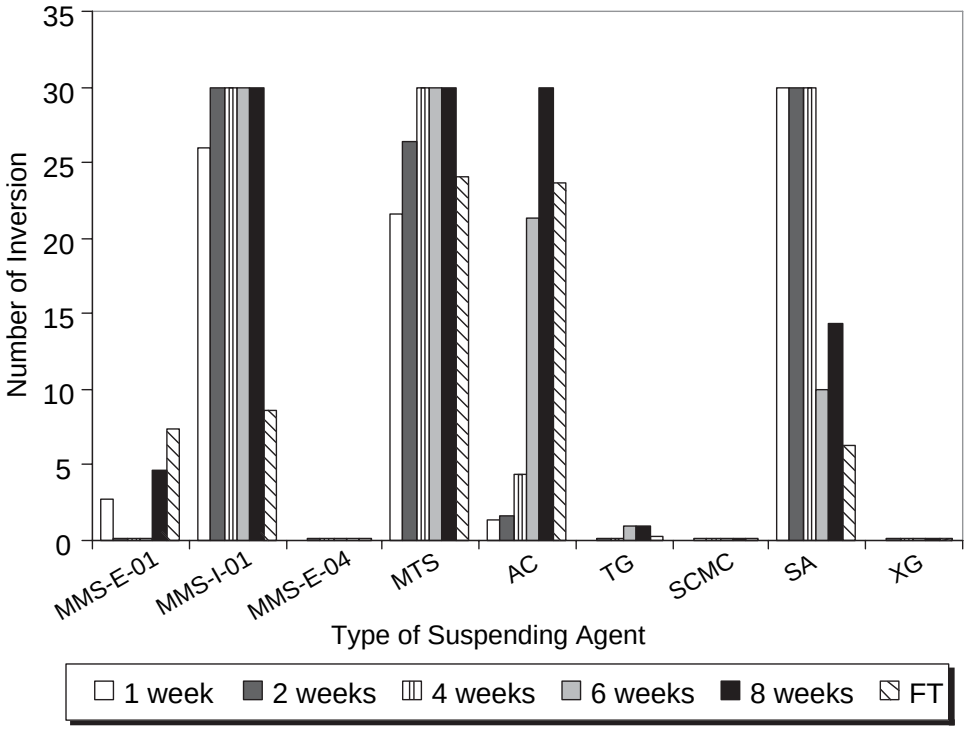

FIGURE 5 **Number of Inversion Required to Completely Resuspend to Homogeneity of the Ibuprofen Suspension Formulations Containing Different Suspending Agents at 1.0%w/v.**

Viscosity and Rheological Studies

At 0.5% w/v concentration (Fig. 6), the apparent viscosity of MMS-M-04-containing suspension was slightly less than that of the SCMC-containing suspension but was significantly higher than that of the XG-containing suspension. Formulations that employed MMS-E-01 and MMS-I-01 as suspending agent exhibited lower apparent viscosity but the values were comparable to those which contained MTS and

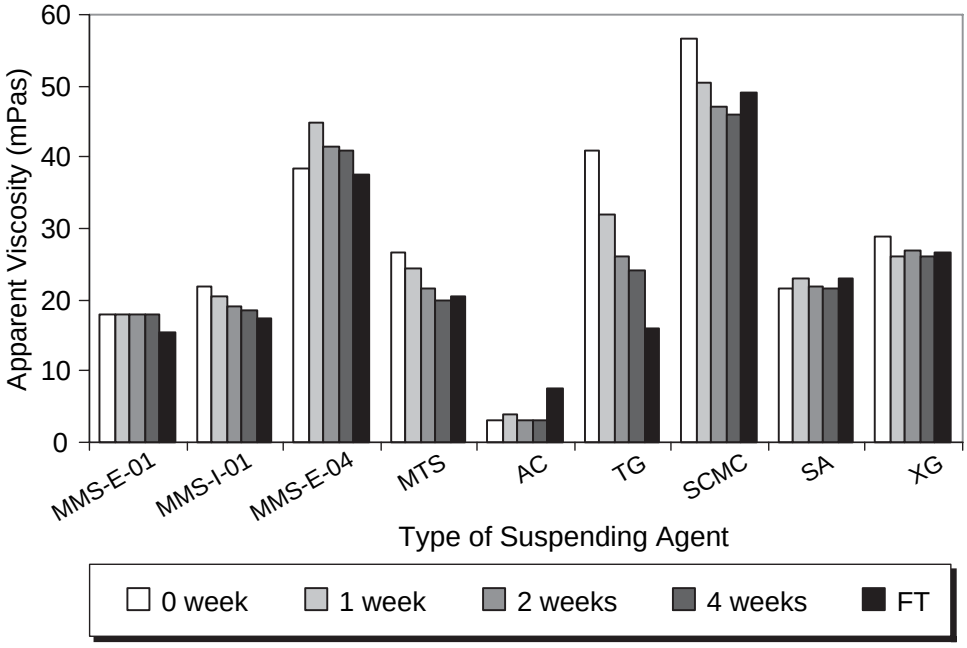

FIGURE 6 **Apparent Viscosity of Ibuprofen Suspension Formulations Containing 0.5% w/v Suspending Agent.**

TG. All formulations showed good viscosity stability upon storage at room temperature for 1, 2, and 4 weeks, as well as after passing through FT cycles, with the exception of SA-containing suspension of which the viscosity decreased significantly after treatment through FT cycles compared to week 0. Similar results were observed for the formulations containing 1.0% suspending agents (Fig. 7) with the concentration-dependent increase of viscosity. At 2.0% w/v, the increase of the viscosity of most formulations followed the same trend (data not shown). However, the formulations that utilized MMS-M-04, SA, SCMC and XG as suspending agent became thick pastes and the determination of viscosity using the same sensor and conditions as for other formulations was not possible.

A plot between shear stress and shear rate for each formulation revealed that at both 0.5 and 1.0% concentrations of suspending agent, most suspensions exhibited pseudoplastic flow characteristic with the non-superimpose upcurve-downcurve, forming a hysteresis loop or thixotropy (Figs. 8 and 9). This parameter represents an ability to undergo gel-sol-gel

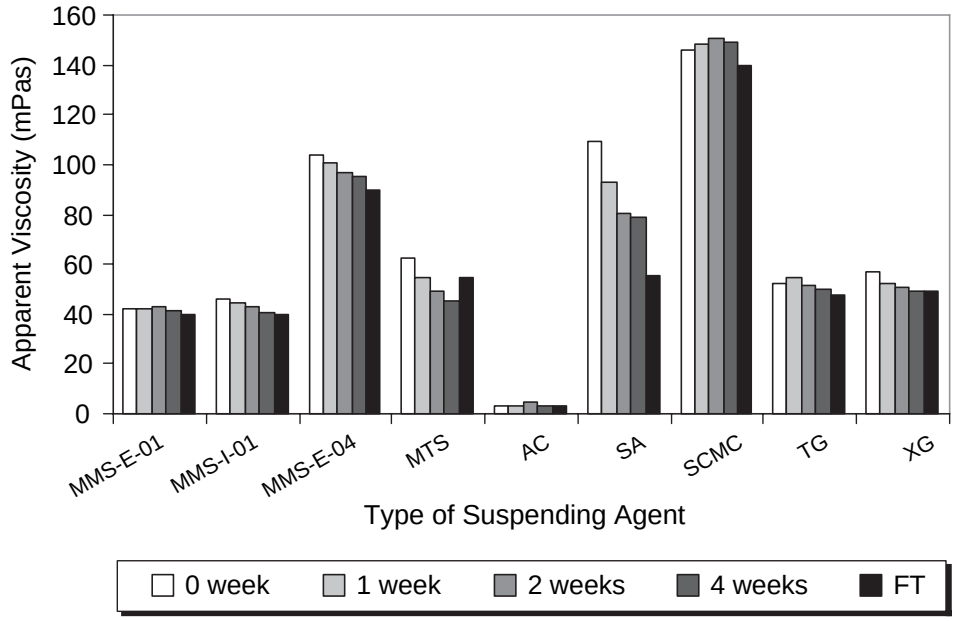

FIGURE 7 **Apparent Viscosity of Ibuprofen Suspension Formulations Containing 1.0% w/v Suspending Agent.**

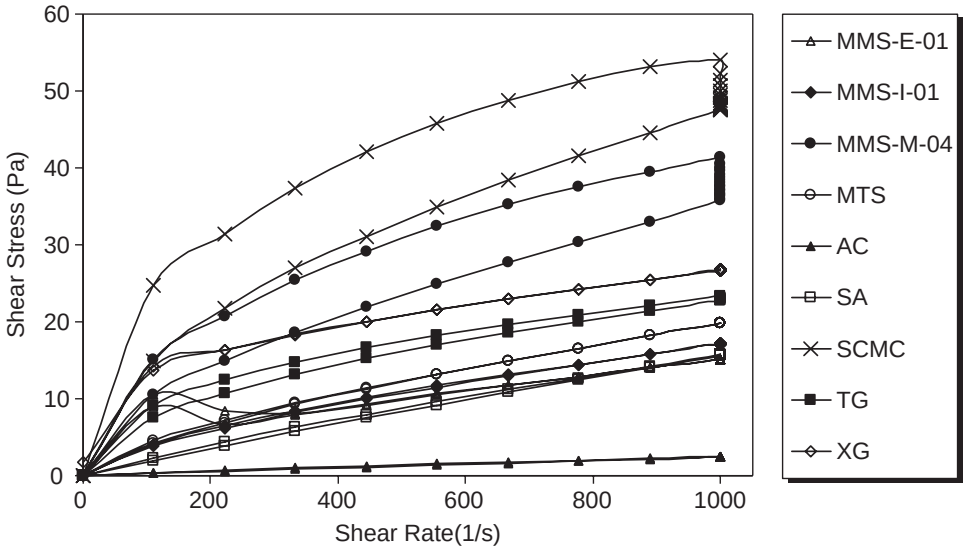

FIGURE 8 **Rheological Profiles of Ibuprofen Suspension Formulations Containing 0.5% w/v Suspending Agent.**

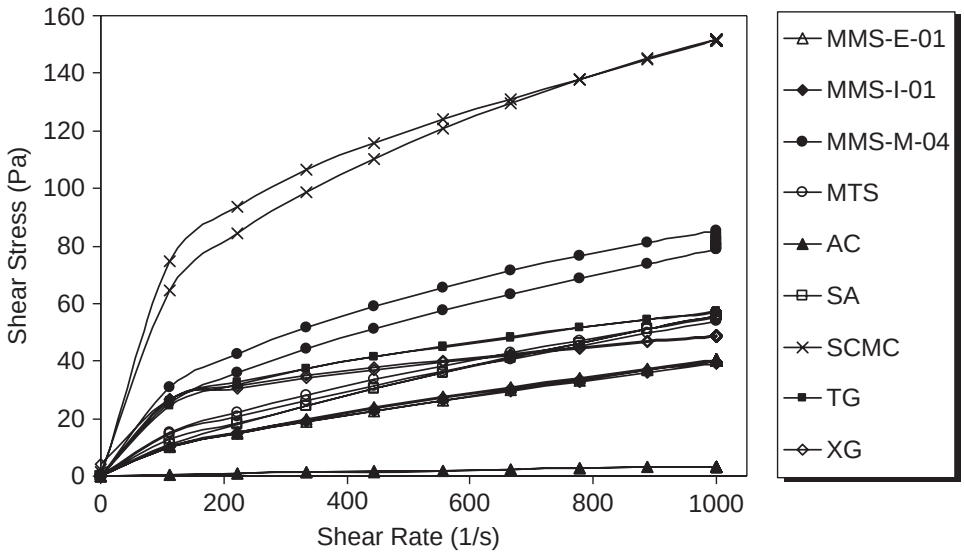

FIGURE 9 **Rheological Profiles of Ibuprofen Suspension Formulations Containing 1.0% w/v Suspending Agent.**

conversion of a suspension. A high thixotropic quantity is a preferable property for a good suspension formulation as it becomes "thinning" and allows a uniform distribution of the sediment upon shaking, then "stiffening," and reforms a gel upon standing to maintain the suspendibility (Wood, 1986).

Thixotropic quantity, calculated as an area of the hysteresis loop, varied from one formulation to another (Table 2). At 0.5% concentration, suspensions that contained MMS-M-04 and SCMC showed comparable thixotropic quantity, both were much higher than that of other formulations. Unlike the viscosity, thixotropic quantities are not necessarily concentration-dependent.

TABLE 2 **Thixotropic Quantity of Ibuprofen Suspension Formulations Containing Different Suspending Agents at 0.5 and 1.0% w/v**

Suspending agent	Thixotropic quantity (mPa.s) of the formulation	
	0.5% w/v	1.0% w/v
MMS-E-01	426.02 ± 22.47	827.61 ± 21.05
MMS-I-01	137.56 ± 41.87	612.71 ± 47.87
MMS-M-04	6,034.20 ± 284.60	6,287.81 ± 875.37
MTS	212.40 ± 158.25	1,670.74 ± 123.41
AC	185.00 ± 423.55	137.89 ± 45.57
SA	308.81 ± 70.67	257.28 ± 54.52
SCMC	8,360.86 ± 1,322.46	3,601.28 ± 568.44
TG	1,081.59 ± 90.39	227.19 ± 2.22
XG	62.16 ± 14.59	772.40 ± 124.12

The differences in the viscosity observed among the three MMSs and the MTS could be attributed to two major factors – the nature of the materials and the modification conditions. Amylose molecules are less soluble in water but, when dissolve, can form gel better than those of amylopectin. In addition, amylose molecules are likely more susceptible to the modification reaction due to their short, straight chain properties that allowed easier access of the reactants to the –OH groups, compared to the branched amylopectin molecules. Upon modification with carboxymethylation, amylose molecules become more soluble in water and form gel. Therefore mungbean starch, which contains higher amylose content (30–45%), is likely to form more viscous gel than the less-amylose (17–22%) tapioca starch. The significance of the modification conditions was also observed in case of the three MMSs. The reaction parameters, such as temperature, time, amount of reactants, type of solvent, as well as the amount of water in the reaction all play important roles in the physicochemical properties, particularly the degree of substitution (D.S.) and the granule properties, of the obtained modified starches. An increase in the D.S. generally results in an increase in the water solubility and, to a certain point, an increase in the viscosity of the solution (Sangseethong et al., 2005). This relationship was observed for the three SCMMSs in this study. In addition, the significant (5X) difference between the viscosities of MMS-E-01 and MMS-I-01 and that of MMS-M-04 can be

explained by the properties of MMS granules. X-ray diffraction (XRD) and scanning electron microscopic (SEM) studies on these MMSs revealed that while the granules of MMS-M-04 were mainly modified by carboxymethylation, those of the other two MMSs also showed characteristics of "pregelatinized" starch. Such characteristics, including the loss of crystallinity observed in the XRD and the roughness or indentation of granule surfaces seen in the SEM, are brought about by the rupture of starch granules in the presence of water and heat treatment (Kittipongpatana et al., 2005). Pregelatinized starch was reported to possess low viscosity (Liu, Ruan, Wang, & Wu, 2003) which explained the lower viscosities observed for MMS-E-01 and MMS-I-01 compared to the "true" carboxymethylated modified starch. In the case of MMS-M-04, the use of methanol as solvent hindered the pregelatinization by increasing the gelation temperature of the starch granules (Gerlsma, 1970; Hizukuri & Takeda, 1978), thus allowed carboxymethylation to take place predominantly. SEM of MMS-M-04 showed granules with similar appearance to those of the native starch, and with more size uniformity, while XRD exhibited presence of crystallinity (Kittipongpatana et al., 2006). These two characteristics possibly contributed to the high viscosity of MMS-M-04 when dissolved in solution.

Content Uniformity

The comparison of content uniformity among different suspensions at 0.5 and 1.0% w/v of suspending agents (Figs. 10 and 11) indicated that MMS-M-04 was as good a suspending agent as SCMC and XG as far as distribution of active ingredient was concerned (total deviation less than 0.3 and 0.1 at 0.5 and 1.0% w/v, respectively). The effectiveness of MMS-E-01 and MMS-I-01 in this aspect was comparable to that of MTS, TG, and SA.

CONCLUSION

Sodium carboxymethyl mungbean starches (SCMMSs), especially the one with high viscosity such as MMS-M-04, can be used as a suspending agent in a pharmaceutical suspension. Results from the comparison of parameters relevant to key properties of suspending agent suggested that the effectiveness of this SCMMS was comparable to that of xanthan gum and sodium carboxymethylcellulose and was significantly better than that of acacia, tragacanth, sodium alginate as well as the modified tapioca starch (MTS)-counterpart. The highlight physicochemical properties, which include the solubility in cold water, the formation of

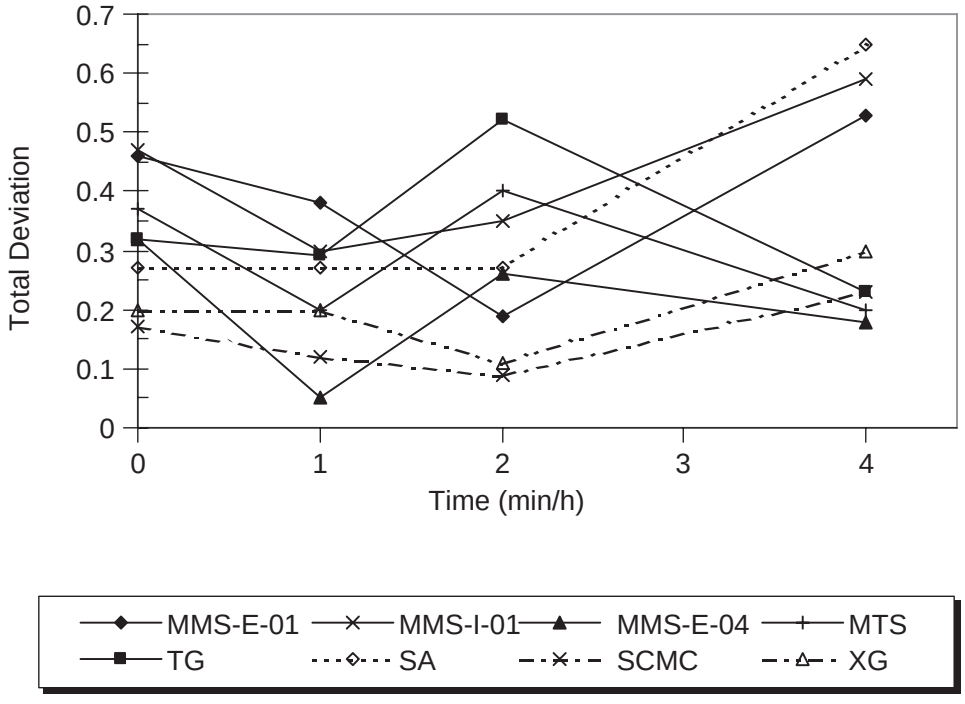

FIGURE 10 **Total Deviation of Ibuprofen Content Among Three Depth Levels of the Formulations Containing Different Suspending Agent at 0.5% w/v.**

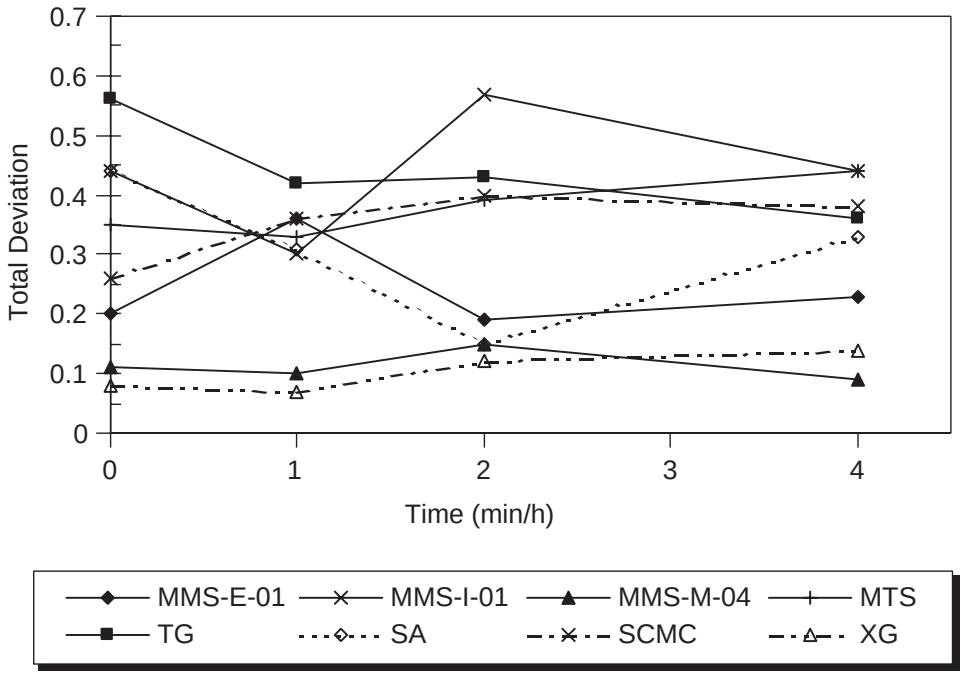

FIGURE 11 **Total Deviation of Ibuprofen Content Among Three Depth Levels of the Formulations Containing Different Suspending Agent at 1.0% w/v.**

transparent, viscous and stable paste at relatively low concentration (0.5–1%), the good sedimentation volume ratio, redispersibility, and rheological profile, as well as the ability to maintain a uniform distribution of drug content in the formulation, provide a legitimate possibility for this type of modified starch as a candidate for a new pharmaceutical suspending agent. In addition, the reported safety as food ingredient, together with the relatively low cost of production (~1,500 Thai Baht or ~37 US$/kg in lab scale) and an abundant availability of mungbean in Thailand could facilitate its production and uses in the industrial scale in the near future.

ACKNOWLEDGEMENTS

This work was supported by a research grant from the National Metal and Materials Technology Center (MTEC) – the National Science and Technology Development Agency (NSTDA), Thailand and the New Generation Researcher Fund, Chiang Mai University. The authors thank Siam Pharmaceutical Company Limited, Bangkok, for providing ibuprofen powder for the preparation of model formulations, and Associate Professor Dr. Poj Kulvanich for his valuable advice on the modification of starch.

REFERENCES

Chen, J., & Jane, J. (1994). Preparation of granular cold-water-soluble starches by alcoholic alkaline treatment. *Cereal Chemistry*. 71, 618–622.

Gerlsma, S. Y. (1970). Gelatination temperatures of starch, as influenced by polyhydric and monohydric alcohols, phenols, carboxylic acids and some other additives. *Staerke*, 22(1), 3–9.

Hizukuri, S., & Takeda, C. (1978). Studies on the gelatinization of starches. Part 2. Effect of lower alcohols on the gelatinization of cereal starches. *Staerke*, 30(7), 228–33.

Hoover, R., Hynes, Y. X. L., & Senanayake, N. (1997). Physicochemical characterization of mung bean starch. *Food Hydrocolloids*, 11(4), 401–408.

Jung, S. H., Shin, G. J., & Choi, C. U. (1991). Comparison of physicochemical properties of corn, sweet potato, potato, wheat and mung bean starches. *Han'guk Sikp'um Kwahakhoechi*, 23, 272–275.

Kasemsuwan, T., Bailey T., & Jane, J. (1998). Preparation of clear noodles with mixtures of tapioca and high-amylose starches. *Carbohydrate Polymers*, 32, 301–312.

Kittipongpatana, O. S., Sirithunyalug, J., & Laenger, R. (2006). Preparation and physicochemical properties of sodium carboxymethyl mungbean starches. *Carbohydrate Polymers*, 63(1), 105–112.

Mishra, P., Jain, A., & Agrawal, R. K. (1990). Studies on starch derivatives – Part I: Sodium O-carboxymethyl starch as a suspending agent. *Indian Journal of Natural Product*, 6(1), 22–25.

Nasipuri, R. N., & Ogunlana, E. O. (1978). Formulation and evaluation of a sulphadimidine suspension for infants. *The Pharmaceutical Journals*, 221, 258–259.

Ohwada, N., Ishibashi K., Hironaka K., & Yamamoto, K. (2003). Physicochemical properties of mungbean starch. *Journal of Applied Glycoscience*, 50, 481–485.

Pitaksuteepong, T. (1995). Tablet Binder Property of Carboxymethyl Starch, Master's Thesis (Manufacturing Pharmacy), Graduate school, Chulalongkorn University, Thailand.

Sangseethong, K., Ketsilp, S, & Sriroth, K. (2005). The role of reaction parameters on the preparation and properties of carboxymethyl cassasva starch. *Starch/Starke*, 57, 84–93.

Sinchaipanid, N. (1989). Tablet disintegration property of mung bean starch. M.S. Thesis, Mahidol University, pp. 1–122.
Suwannapakul, O. (1997). Preparation and evaluation of sodium carboxymethylstarch as suspending agent, Master's Thesis (Manufacturing Pharmacy), Graduate School, Chulalongkorn University, Thailand, 185 pp. ISBN 974-635-207-5.
Teruya, T. (1995). Development of Superdisintegrant from Tapioca Starch, Doctoral Thesis (Manufacturing Pharmacy), Graduate School, Chulalongkorn University, Thailand.
Timaroon, S., & Kulvanich, P. (1992). Pharmaceutical technology of starch: Invention of directly compressible starch, Thai Journal of Pharmaceutical Science, 16(4): 309–315.
United States Pharmacopeia (USP) XXIII and the National Formulary (NF) XVI, The United States Phamacopeial Convention, (1995) Taunton: Rand McNally.
Wood, J. H. (1986). Pharmaceutical Rheology. In *The Theory and Practice of Industrial Pharmacy*, 3rd Ed. Lachman, L.; Lieberman, H. A.; and Kanig, J. L.; Eds., Philadelphia: Lea & Febiger: P.