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EVALUATION OF *STERCULIA FOETIDA* L. GUM AS NATURAL BASED DISINTEGRATING EXCIPIENT

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Abstract. Natural adjuvants have received increasing attention in recent years. *Sterculia foetida* L. gum (SFG) has been considered as multifunctional polymer for various applications in both food industry and pharmaceutical dosage forms. *Sterculia foetida* L. is widely grown in Binh Thuan Province, Viet Nam. The aim of this study was to elucidate the role of *Sterculia foetida* L. gum in hydrophilic tablets. Therefore, the physicochemical properties of *Sterculia foetida* L. gum, including solubility, grain shape, melting point, swelling index, pH, viscosity and loss on drying were determined. Furthermore, compressed tablets were successfully prepared for *in vitro* studies at many different particle sizes, concentrations of gum, rotational speeds and media in order to evaluate the effects of these parameters on the rate of drug release. Besides, SFG tablets were compared with the tablets prepared with Hydroxymethylcellulose E15. The findings indicated that SFG exhibited an excellent potential in managed release dosage forms. Tablets based on SFG prolonged the drug release as opposed to HPMC E15 forms. The scanning electron micrographs showed that most gum particles were of multi-morphology. The viscosity, pH, loss on drying, melting point and swelling index were 176 cP, 5.21, 10.9 %, 225 ^{o}C and 44.4 %, respectively. The formulation containing 40 % of gum was suitable for prolonging drug release. There was no significant impact of fillers on drug release profile while rotational speed had a huge effect. The outcomes demonstrated that *Sterculia foetida* L. gum could be used as a potential candidate for novel drug delivery system.

Keywords: Sterculia foetida L. gum, controlled release excipient, HPMC E15, *in vitro* release testing.

Classification numbers: 1.4.2, 1.2.4.

1. INTRODUCTION

Recently, exploiting natural polymers has been put into research because they possess a highly complex, branched structure which exhibit high cohesive and adhesive abilities. Such specific properties are essential for preparing pharmaceutical dosage form. Hence, they have a variety of applications not only as pharmaceutical adjuvants in pharmaceutical formulations but also as stabilizer in food and beverages industry and as preservative, thickener in cosmetics,

paints, textiles and paper manufacture [1]. In fact, both gums and mucilages can be collected from diverse natural resources, such as plants, marine algae, bacteria or animals. For plant-derived gums and mucilages, the basic difference between them is that gums are pathological products while mucilages are physiological products. Furthermore, gums dissolve in water while mucilages form slimy masses. Besides, various commercial excipients, natural-derived polysaccharides are preferred due to its chemically inert, biodegradation and abundant source. The sustained release of drug is a major concern of researchers and producers. In addition to particle size, compression force, excipients play a key role in drug release. These excipients were added into pharmaceutical dosage forms as binders, diluents, lubricants, glidants, disintegrants, polishing, coating agents, plasticizers, colorings or preservatives to provide necessary accurate weight, enhance stability and bioavailability [2]. The drug delivery undergoes three main processes: solvent transport, swelling, solute diffusion. In details, the release rate of active pharmaceutical ingredient (API) from tablets depends on swelling step as well as erosion mechanism. However, there is a profound difference between hydrophilic polymer and hydrophobic polymer matrix, rapid hydration and polymer chain disentanglement along with both swelling and erosion occur in hydrophilic system whereas only erosion happens in hydrophobic one.

Among plant-derived gums such as Arabica gum (*Acacia Arabica*, Combretaceae), Ghatti gum (*Anogeissus latifolia*, Combretaceae), Karaya gum (*Sterculiaurens*, Sterculiaceae), Guar gum (*Cyamopsis tetragonolobus*, Leguminoseae), Tamarind gum (*Tamarindus indica*, Leguminoseae) and Trom gum (*Sterculia foetida* L., Sterculiaceae) have not been well documented in pharmaceutical manufacturing industry. *Sterculia foetida* L. is a tropical plant belonging to the family Sterculiaceae. This plant is well known as Java olive, naturally distributed from Europe, through Africa to Asia [1]. Many parts of this tree have been well known for several applications. Leaves has been used in Ayurvedic medicine for various treatments such as aperients, diuretic, anti-epileptic [2]. Moreover, leaves were also used for repelling insect [2]. Oil extracted from seeds was applied for itches treatment and skin diseases. Furthermore, seeds oil was capable of antifungal, antiviral and antitumor [2]. Gum, exudates from stem bark of trunk and branches of this plant, is taken consideration as a very promising hydrophilic polymer which can replace commercial excipients. *Sterculia foetida* L. gum (SFG) possesses high acetyl content D-galactouronic acid and little of L-rhamnose, D-galactose and ketohexose [2]. In addition, SFG also contains around 37 % uronic acid and minerals such as calcium and magnesium. After hydration, the compressed tablets became a highly viscous gelatinous surface barrier layer. Therefore, SFG is a potential candidate for the preparation of hydrophilic matrix tablets.

In 2008, Chivate and colleagues evaluated SFG in regulating the drug delivery and revealed that there was no interaction between SFG and diltiazem hydrochloride (DIZ) [3]. Besides, swelling and erosion behavior of SFG compressed tablets in comparison with diltiazem hydrochloride and microcrystalline cellulose in drug release profile was reported by Namdeo and colleagues in 2010 [4]. Two years later, this research group published a paper in regarding the effective prolongation of drug release from hydrophobic rice bran wax coated with hydrophilic SFG in a three-layer matrix tablets containing a highly soluble drug, DIZ [4]. Their results explained swelling and erosion of exposed hydrophilic layer and increased in surface area per unit time. The bioavailability testing on ocular mini tablets based on SFG was demonstrated as a promising novel trend for ocular drugs without causing irritation. In recent study, the buccal film of ranitidine HCl was optimized using different concentration of SFG and the drug release profile was obeyed diffusion mechanism. The outcome proved that the optimized formulation with 53 % (w/w) of SFG could sustain drug release (98.79 %) for 12 hours [5]. In Viet Nam, Vo

Thi Lieu, a pharmacist from the Vinh Tam cosmetics company, has developed skincare products from SFG [6].

Thus this study was focused on determining characterization of *Sterculia foetida* L. gum, namely solubility, morphology, melting point, swelling index, pH, viscosity and loss on drying. Another objective was that evaluation of swelling behavior of the SFG along with different types of excipients. Compressed tablets preparation for *in vitro* release testing at various conditions was conducted. The influences of particle sizes (60, 80, 100 and 120 µm), concentrations of SFG (10 - 40 %), rotational speeds (50, 75 and 100 rpm), media (7.4, HCl 0.1 N and DW), and other fillers (none filler, MCC, lactose and DCP) on API release rate. Moreover, a comparison between SFG matrix tablets and HPMC E15 tablets was carried out. The concentration of methylene blue released was measured.

2. MATERIALS AND METHODS

2.1. Materials

Sterculia foetida L. gum was purchased from Binh Thuan Province, Viet Nam. The gum was washed thoroughly to remove dust and impurities. After that, it was dried in Memmert oven at 100 ^{o}C for 24 hours and then cooled down to room temperature before being ground into small particles. Thereafter, it was sieved through a wide range of mesh (60, 80, 100 and 120 mesh) prior to clarifying the influences of SFG's particle size on tablets properties.

Methylene blue (Megha International, India), Dicalcium phosphate (Quingzhou company, China), Microcystalline Cellulse - MCC, Avicel PH 102 (Dupont, Italia), lactose (Lacteos Caprinos, Spain) and Magnesium stearate (F.D&C company, France) were prepared for experiment.

2.2. Properties of *Sterculia foetida* L. gum

2.2.1. Determination of solubility

The solubility of SFG (0.5 g of SFG: 50 ml of solvent) determined at room temperature for an hour, in various solvent, namely ethanol, distilled water (DW), hydrochloric acid (5 %), sodium hydroxide (5 %) and phosphate buffer (pH 7.4) by magnetic stirrer (Benchmark Scientific, USA).

2.2.2. Determination of morphology

The surface morphology of SFG was observed by a scanning electron microscope (Model S-4800, Hitachi, Japan). The photomicrographs were taken at 100X, 200X, and 500X magnifications.

2.2.3. Determination of melting point

Fill a capillary tube with SFG about 3 mm high. Place the capillary tube in melting point apparatus. Set the MEL-TEMP (Stuart, SMP3) at a high enough level to make a rapid determination of melting point. The melting process was observed through the magnifying lens and recorded the temperature at which it melts.

2.2.4. Determination of swelling index

SFG (1 g) was dispersed in 99 ml of distilled water (DW). The weight of mixture was measured and then calculated the swelling index (SI) as weight of mixture after 24 hours (W_t) divided by the original weight of dried SFG (W_o) [3].

$$\text{Swelling index (SI)} = \frac{(W_t - W_o) \times 100\%}{W_o} \quad (1)$$

2.2.5. Determination of pH

The pH value was recorded after mixing vigorously 1 g of SFG with 100 ml of DW at room temperature [3].

2.2.6. Determination of viscosity

The sample was prepared by adding exact amount of water (1 %, w/w) into a beaker in order to immerse completely the spindle. Brookfield viscometer (Brookfield, DV2T-LV, USA) was used for determining the viscosity at rotational speeds 100 rpm with suitable type of spindle 61 at room temperature [3].

2.2.7. Determination of loss on drying

1 g of SFG was put into the porcelain crucible and weighed. After that, it was put in an oven maintained at 105 °C for 4 hours. Next, it was removed and placed in desiccator and allowed to cool for 15 minutes prior to weighing as quickly as possible. The loss on drying was calculated by moisture loss divided by fresh weight of sample.

$$\text{Loss on drying (\%)} = \frac{(W_3 - W_2) \text{x} 100\%}{W_2 - W_1} \quad (2)$$

where W_1 is the weight of container (g), W_2 is the weight of container and SFG (g), W_3 is the weight of container and SFG after drying (g).

2.3. Preparation of compressed tablets

Table 1. Formulations of compressed tablets.

Compositions (%)	Formulations (g)						
	1	2	3	4	5	6	7
Methylene blue (MB)	89	79	69	59	21	21	21
SFG	10	20	30	40	40	40	40
Magnesium stearate	1	1	1	1	1	1	1
Lactose	-	-	-	-	40	-	-
Avicel	-	-	-	-	-	40	-
Dicalcium phosphate	-	-	-	-	-	-	40

In order to demonstrate the effects of several fillers (lactose/Avicel/DCP) and the role of SFG (10 to 40 %) on releasing of active pharmaceutical ingredient (API) in tablets, numerous formulas of tablets were investigated as in Table 1. All compositions of tablets were mixed thoroughly in mortar and pestle before being undergone direct compression (8-10 kg/cm^2). The diameter and thickness of tablets were 15 mm, 3 mm, respectively [7].

2.4. Determination of hardness

According to U.S. Pharmacopeia, compressed tablets require a certain amount of hardness and resistance to friability and more significantly, it can affect disintegration, dissolution and bioavailability. Therefore, the hardness and friability of tablets were evaluated. The tablets were placed between anvils and the breaking forces of 10 tablets were recorded using Tablet hardness tester (ERWEKA, TBH-220TD, Germany). The limit of tablet hardness is 15 kP to ensure all tablets can withstand during the process and transportation.

2.5. Determination of friability

The friability of 20 tablets was randomly examined by tablet friability tester (Vanguard, LIC-1, USA). Twenty tablets were weighed accurately (W_1). These tablets were subjected to a rotating drum at the speed of 25 rpm for 4 min. The tablets were de-dusted and re-weighed (W_2). Compressed tablet that lose less than 0.5 to 1.0 % of the tablet weight are accepted. The friability was calculated by using the following formula:

$$\text{Friability (\%)} = \frac{(W_1 - W_2) \times 100\%}{W_1} \quad (3)$$

2.6. *In vitro* drug release studies

According to USP 26 Apparatus 2 (Paddle), the release profile of tablet using methylene blue as a model drug was evaluated at different speeds of 50, 75, 100 rpm in DW at room temperature using 900 ml of HCl 0.1N (Pharmatest, Germany). 10 ml of solution was taken out every 30 minutes and then was passed through a filter (0,45 µm) before being determined the concentration of methylene blue at the wavelength of 237 nm (PharmaSpec UV-1700, Shimadzu, Japan) [8].

2.7. Size of SFG particles

In this section, 40 % of SFG with different particle sizes (60, 80, 100 and 120 µm) were prepared with 59 % g of MB and 1 % of Magnesium stearate.

2.8. Concentration of SFG

To evaluate the effect of SFG concentration on release rate of tablets, compressed tablets with various concentrations, 10 %, 20 %, 30 % and 40 % of SFG were prepared. Each tablet contained 1 % of Magnesium stearate and the remaining belonged to MB.

2.9. Rational speeds

Dissolution of tablets (40 % of SFG, 1 % of Magnesium stearate) at different rational speeds 50 rpm, 75 rpm and 100 rpm were investigated.

2.10. Type of media

Prepared tablets were dissolved in different media such as HCl 0.1N, distilled water and phosphate buffer pH = 7.4 separately.

2.11. Type of fillers

Tablets containing DCP/Lactose/MCC were used as a filler in formulation as compared to non-filler tablets.

3. RESULTS AND DISCUSSION

3.1. Characterization of *Sterculia foetida* L. gum

3.1.1. Solubility

The results showed that SFG was not dissolved in absolute ethanol and DW while it can be dissolved easily in hydrochloric acid (5 %), sodium hydroxide (5 %) and phosphate buffer (pH 7.4). These results are similar to the report of Chivate and co-workers [3]. However, SFG adsorbed DW and swelled extensively as compared to the original volume, becoming a viscous colloidal solution. SFG was suitable for sustained release tablets because of its high viscosity and suspension properties. The swelling behavior of SFG is assumed to be resulted from the presence of acetyl groups in its structure [3].

3.1.2. Morphology

The morphology of SFG was observed by scanning electron microscope as seen in Figure 1. It showed the surface smoothness of SFG at three different magnification levels, which support to develop better cohesion force during tablet compression. Overall, particles of SFG were mostly multi-morphology in shape and ranged from 20 to 200 μm in size as compared to 125 μm in the previous study of Chivate [3].

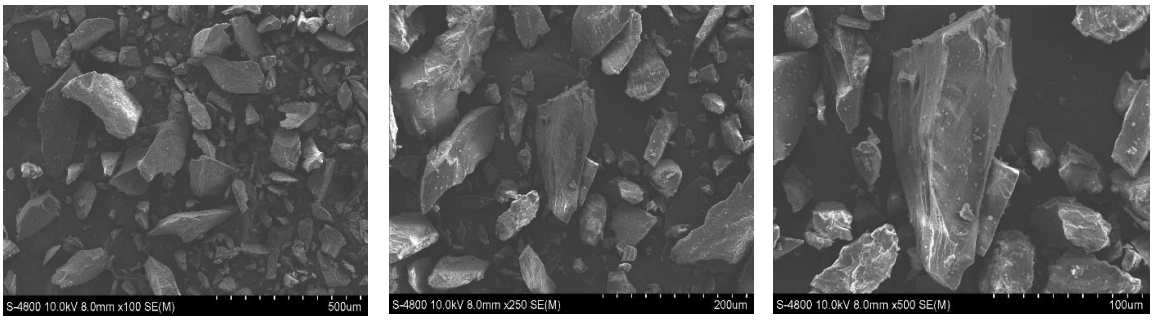

Figure 1. The scanning electron microscopy of *Sterculia foetida* L. gum powder at three different magnifications (500X, 200X and 100X).

3.1.3. Physicochemical properties

The physicochemical properties of SFG were shown in Table 2.

Table 2. The characteristics of *Sterculia foetida* L. gum.

Parameter	Result
Melting point	225°C
Swelling index	44.4 %
pH	5,21
Viscosity	167cp
Moisture	10.9 % (w/w)

3.2. Hardness and friability

The hardness and friability of tested tablets were found to be 22.84 kP and 0.79 % respectively; while these quantities reported in Namdeo's study ranged from 6.5 to 7.0 kg/cm^2 and 0.94 to 0.99 %, respectively [4].

3.3. The influence of particle sizes, concentrations, rotational speeds, media and fillers on release rate

3.3.1. The influence of particle size

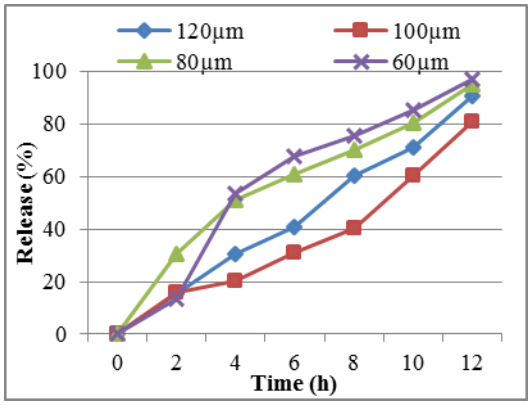

Figure 2. The effect of SFG particle size on *in vitro* MB release.

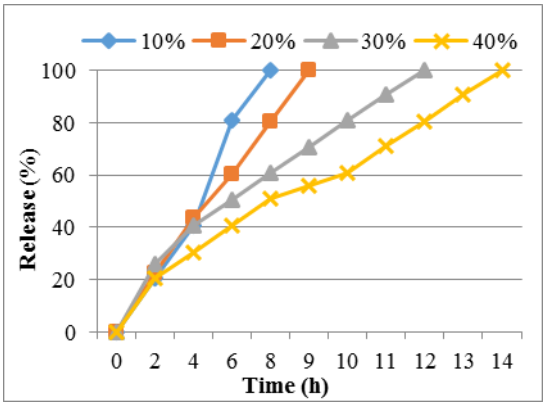

Figure 3. The effect of SFG concentration on *in vitro* MB release.

The experiment was conducted in DW at 100 rpm. According to Figure 2, it indicated that after 12 hours the release of MB completed for smaller particles ranged of 60 and 80 µm whereas in case of 100 µm and 120 µm just released around 80-90 % at the same time. Based on the conclusion of Chivate's research [3] related to hydration, it can be explained that the bigger particles could not hydrate fast enough to form a protective gel layer as compared to the smaller

particles. In that case, small particles swelled easily and released the MB faster. Therefore, a significant sustained release was observed in tablets with coarse particles.

3.3.2. The influence of concentration

The dissolution of SFG matrix tablets containing 10 to 40 % of SFG were prepared in DW at 100 rpm. The MB release profiles were depicted in Figure 3. It would be noticed that the release rate is significantly affected by concentration of hydrophilic polymer (SFG). The formulation with 40 % SFG witnessed a very slow release in MB concentration while others obtained MB completely within 12 hours. The outcomes indicated that when the concentration of SFG in tablets went up, the ability to release MB from compressed tablets went down. Indeed, increasing polymer concentration in a matrix tablet generally increased polymer chain in gels, which caused widespread the barrier and lowered the diffusion. Therefore, the release of MB from tablets was slower. In contrast, at lower level of SFG, thanks to swelling behavior and rubbery state, the mobility of the polymer chains was improved, consequently, the drug release accelerated. Moreover, electrostatics caused by interaction between negative-charge carboxylated polymer chain and positive-charged of MB molecules could explain this phenomenon.

3.3.3. The influence of rotational speed

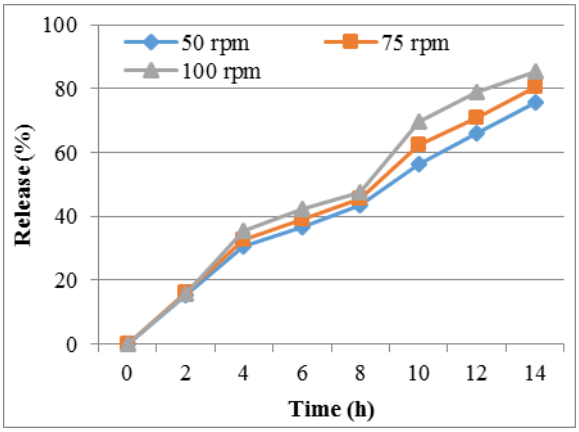

Figure 4. MB release as a function of time at different rotational speeds.

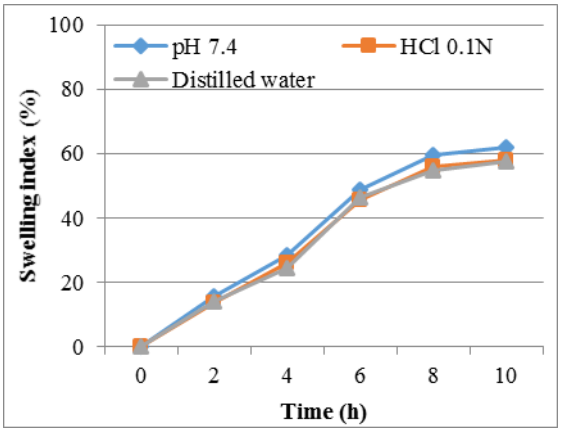

Figure 5. Swelling index of SFG tablets performed in various media versus time (h).

The influence of rotational speed on MB profile release (Figure 4) were evaluated in DW based on USP, apparatus 2 at 50, 75 and 100 rpm. The amount of MB in 1 tablet was 354 mg. The formulation containing the 40 % SFG was applied for testing. It was observed that the release rate of MB at 3 speed levels increased steadily from 0 % to over 40 % within 8 hours before a profound difference in MB release happened in the rest of experiment. In fact, rotational speed had no significant effect during first 8 hours and then the amount of MB release rose when the rotational speed was enhanced. As Chivate mentioned in the previous study [3], the drug release was improved by diffusion process which occurred within tablets. On the other hand, since the rotational speed grew, the surface erosion and the disruption of gel could occur rapidly; hence, there was an upward trend in drug release. Obviously, both the diffusion and the erosion play a significant role on release rate of MB.

3.3.4. The influence of dissolution media

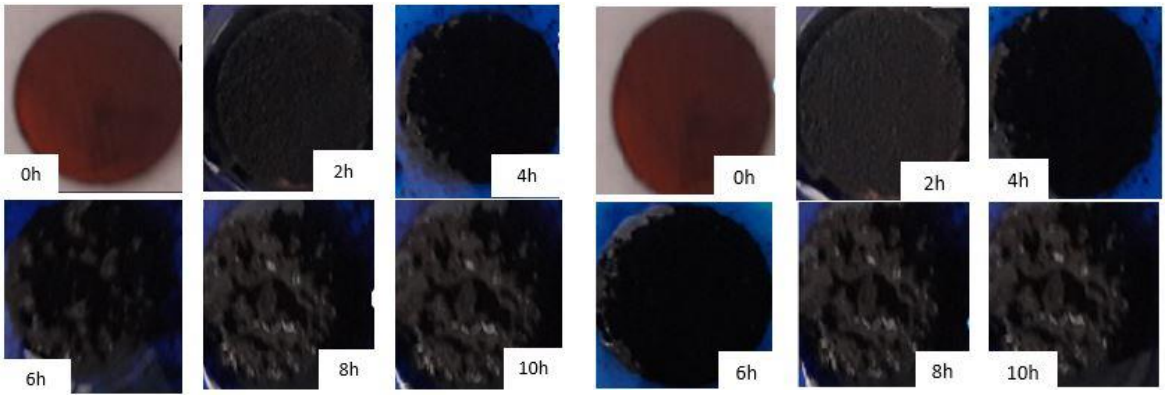

Figure 6. Photos of SFG tablets in distilled water (left) and HCl 0.1N (right) versus time (h).

Figure 5 indicates the testing results of swelling behavior of SFG tablets in 3 media, namely HCl 0.1N, phosphate 7.4 and DW at 100 rpm. The Figure showed that there is no significant difference between the tablets dissolved in three media. It means that pH did not impact on the swelling behavior of SFG matrix tablets. The same finding was found in the research of Chivate [3]. Figure 6 illustrated that the gel structures formed were different from between DW and HCl 0.1 N. It is clear that the gel structure was transparent in HCl 0.1 N whereas it was vague in distilled water. After 8 hours, the surface erosion of tablet showed an anomalous diffusion in comparison with others.

3.3.5. The influences of fillers

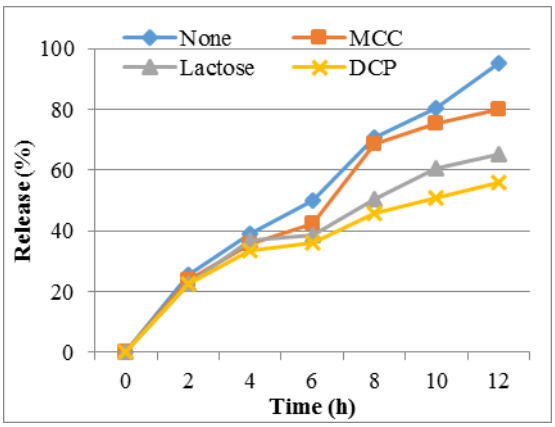

Figure 7. The effect of fillers on *in vitro* MB release.

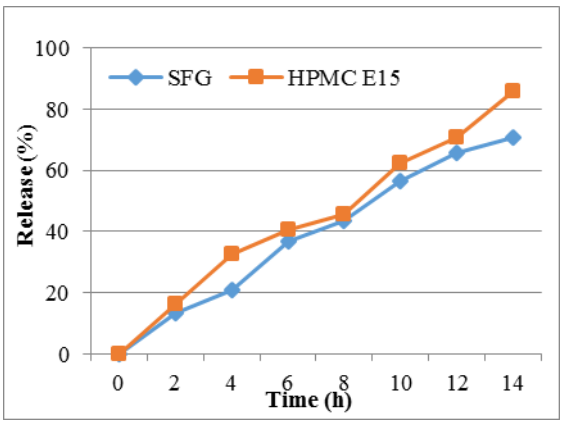

Figure 8. Comparison of *in vitro* release of MB from SFG and HPMC E15 tablets.

The influence of fillers on tablets containing 40 % SFG was shown in Figure 7. The thickness of gel can controll the release of MB. The release study was performed in DW at 100 rpm. The release of MB witnessed a significant different among the fillers, including none filler, MCC, lactose and DCP. It depends on the nature of fillers. In detail, MCC is a swelling,

insoluble, dispersible filler and therefore, it enhanced the rate of swelling on the tablet's surface. At the same time, MB released better into the medium. In contrast, in the case of using DCP, its nature is both insoluble and non-swelling. As a result, DCP could create the cracks on the surface during gelling, preventing MB diffusion into the medium. Moreover, insoluble parts were trapped until the polymer chains were destroyed whilst soluble ones dissolved easily during swelling of polymers [8]. The tablet without filler possessed the highest release rate due to lack of trap as filler, followed by tablet used MCC, lactose and DCP. Generally, the addition of soluble filler such as lactose improved to the dissolution of drugs.

3.4. Comparison with HPMC E15 tablets

HPMC E15, a commercial hydrophilic polymer, was used for preparation of controlled release tablets in contrast to that of SFG. The experiment was conducted in DW, at 100 rpm, every tablet containing 40 % of specific polymer (SFG or HPMC E15). From Figure 8, the amount of SFG from HPMC E15 tablets was released much more than that from SFG tablets. The significant feature was noted that although the viscosity of 1 % solution of HPMC E15 was around 15,000 cP that was 90 times higher than the viscosity of 1 % solution of SFG, SFG could prolong the drug release time than HPMC E15 during 14 hours.

4. CONCLUSIONS

In general, the physicochemical properties of SFG indicated that it met the meet the quality requirements of pharmaceutical excipients. The drug release was improved as concentration of SFG and rotational speed during dissolution was enhanced. Moreover, tablets containing SFG was also demonstrated that it controlled the drug release better than tablets using HPMC E15. Thus this study concluded that SFG is promising sustained release adjuvant in pharmaceutical industry.

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