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Preparation of Hard Capsule Shell from Seed Gum of Cassia fistula

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In this study, seed gum from Cassia fistula was used as raw material for preparation of hard capsules. The appropriate condition for hard capsule forming was investigated. The results from viscosity consideration suggest that the formulation for hard capsule forming is a 3 %wt gum solution and 2 %wt plasticiser. The characterisation of hard seed gum capsule was evaluated using standardised tests of Thai Industrial Standard (TIS. 913-2545) and compared to the characterisation of hard gelatin capsule. The water resistance and drug release of hard capsules were observed. The results present that seed gum capsule had more water resistance and drug release for seed gum capsule also took longer than that gelatin.

1. Introduction

Pharmaceutical hard capsule has many advantages such as easy swallowing, tastelessand odour drug protecting. Recently, gelatin is widely used as raw material for hard capsule preparation. However, there are some disadvantages of gelatin capsule, for examples capsule shell become brittle after exposure to a low relative humidity or filling some drugs which are hygroscopic absorb water from the capsule shell (Rabadiya and Rabadiya, 2013) and turn soft when storage condition change or the moisture transfer between the capsule shell and its contents (Chang et al., 1998). Gelatin is one of the proteins derived from animals. The amine groups of gelatin may react with drugs containing aldehyde groups (Ofner et al., 2001). Moreover, cultural, religious, and dietary needs of vegetarian patients are causing a demand of various non-animal origin materials. Hence, various non-animal origin materials have been examined as a substitute for the gelatin such as hydroxylpropylmethyl cellulose (HPMC) (Zhang et al., 2013), mungbean, water chestnut and sweet potato starches (Bae et al., 2008), polyvinyl alcohol copolymer and pullulan (Rabadiya and Rabadiya, 2013).

Cassia fistula is a flowering and ornamental plant in the family fabaceae (Figure 1). The species is native to the Indian subcontinent and adjacent regions of Southeast Asia. It ranges from southern Pakistan eastward throughout India to Myanmar and Thailand and south to Sri Lanka. Various parts of this plant are considered to be a medicines in curing several diseases such as cardiac disorders, diabetes, skin diseases and snake bite (Kirtikar and Basu, 1933).

Its endosperm within seed consists high polysaccharide that called galactomannan. The chemical structure of this seed gum comprises β-(1 → 4) linked d-mannopyranose units with random distribution of α-(1 → 6) linked d-galactopyranose units as side chain having mannose:galactose ratio (M:G) of 3 : 1 (Shrivastava and Kapoor, 2005). This mannose to galactose ratio is intermediate between that for guar gum (2 : 1) and LBG (4 : 1). It has been reported that this gum holds a strong potential to become a good substitute for LBG and tara gum, which is primarily used in the food industry as a thickener and stabiliser (Mathur, 2012). In the present work, seed gum from Cassia fistula might offer a new option of being suitable raw materials for the preparation of plant-derived capsules.

In this study, seed gum from Cassia fistula was used as raw material for coating solution preparation. The appropriate formulation of coating gum solution was explored and then characterisation of hard seed gum

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capsule was observed using standardised tests of Thailand Industrial Standards (TIS, 913-2545). Finally, water resistance and drug release of hard capsule were also investigated.

Figure 1: Flowers and pods of Cassia fistula

2. Material and methods

2.1 Materials

Pods of Cassia fistula were collected in Chonburi province in Thailand. Mature seeds were manually separated and kept in a cool dry place. Propylene glycol was used as plasticiser.

2.2 Seed gum extraction

Seeds of Cassia fistula were crushed and soaked in water for 3 h. The endosperms were manually removed from the germ and the hull. They were then dried in oven at 80 °C, milled and ground through a 355 micron mesh sieve.

2.3 Physicochemical compositions

Moisture and ash contents of crude gums were determined according to the American Society for Testing and Materials methods (ASTM-D2974-87) and AOAC Official Method 923.03. Protein content was obtained from the total nitrogen content (N × 5.7) by Kjeldahl method, as described in the AOAC Official Method of Analysis 981.10. Fat content was determined according to the AOAC Official Method of Analysis 923.06.

The intrinsic viscosity [η] of dilute solution of gum samples was measured at 25 ± 1 °C with a Cannon-Fenske Routine Viscometer (9721-A53) (ASTM-D2515, ISO 3105, and Series 100). Solutions had relative viscosities from 1.2 to 2.0 to assure good accuracy and linearity of extrapolation to zero concentration. The intrinsic viscosity is conventionally obtained by double extrapolation to zero concentration of Huggins', Eq (1), and Kraemer, Eq (2), equations. This extrapolation technique is very popular because it is experimentally simple (Sittikijyothin et al., 2005)

$$\frac{\eta_{sp}}{C} = [\eta] + k'_H [\eta]^2 C \quad (1)$$

$$\frac{(\ln \eta_{rel})}{C} = [\eta] + k''_K [\eta]^2 C \quad (2)$$

Where: C is the concentration of diluted solution. k'_H and k''_K are the Huggins and Kraemer coefficients η_{sp} is the specific viscosity. η_{rel} is the relative viscosity .

2.4 Coating solution preparation

3 %wt gum solution was prepared. Plasticiser was added, which proportion 0 %, 2 %, 5 %, and 10 %. Then the viscosity of coating solutions was determined by a rotary viscometer (Model CV-II+PRO with LV S6-3 spindle) at 30 °C and 30 rpm viscometer speed.

2.5 Capsule formation

Capsules were prepared by dipping stainless steel mold pins (capsule size: 0) into coating solution and dried at 70 °C. The coated steel pins were cold at room temperature and dried again at 70 °C for 30 min and the capsule was taken off from the steel pin.

2.6 Characterisation of hard capsule

The characterisation of capsule was evaluated using standardised tests of Thailand Industrial Standards (TIS. 913-2545), including length, capacity and mass of capsule, also moisture and ash contents of capsule.

2.7 Water resistance and drug release tests

Capsule was drowned by using metal coil in water at 25 ± 1 °C for 15 min for water resistant test and at 37 ± 2 °C until to its breaking or leaking for drug release test.

3. Results and discussion

3.1 Physicochemical properties of seed gum

The endosperm of Cassia fistula seed were obtained about 51.94 % and then they were dried and ground. Hence, this ground form (called seed gum) remain was about 47.35 %. It is mainly composed of a galactomannan, which is a neutral polysaccharide (Mathur, 2012). The main chemical compositions of seed gum was analysed as shown in Table 1. It can be seen that it is rich source of polysaccharide and protein which is quite consistent with previously report (Akiyede and Amoo, 2009). Its intrinsic viscosity was about 10.78 dL/g as determined (Figure 2) by using Huggins' (Eq(1)) and Kraemer (Eq(2)) equations, respectively. When compared with another report such as Pollard et al. (2010) (16.1 dL/g). This variation value can be varied according plant source (Pollard et al., 2010).

Table 1: The chemical composition of gum seed

	Moisture	Ash	Protein	Fat	Polysaccharidea
Cassia fistula	10.08	0.17	10.04	1.03	88.76

Note: all values (%) on a dried weight basis are mean ± standard deviation of three determinations.
[a]Polysaccharide values were calculated by difference.

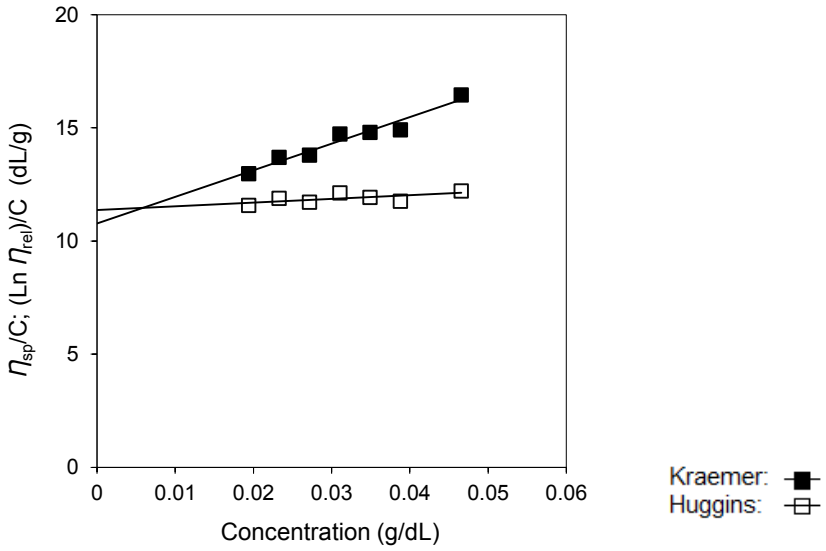

Figure 2: Extrapolation of intrinsic viscosity from Huggins' and Kraemer plots, η_{sp}/C and $(ln\eta_{rel})/C$ against concentration for seed gum aqueous solutions at 25 °C

3.2 Capsule formation

From a preliminary study, varied gum concentrations were prepared and chosen for further used coating formulation by physical appearance from dipping. Figure 3 shows that 3 %wt gum concentration provided suitable viscous solution for dipping. Thus, the coating solution was prepared at fixed 3 %wt gum solution for further coating. Then plasticiser was added with different proportions. Hence the appropriate plasticiser proportion was considered by forming and physical appearance of capsule.

(a) (b) (c)

Figure 3: Photographs of viscous appearance of gum solutions at different concentration: (a) 1 %wt (b) 2 %wt (c) 3 %wt

(a) (b) (c) (d)

Figure 4: Photographs of hard seeds gum capsule shell from 3 %wt gum solution and varied proportion of plasticiser: (a) 0 %, (b) 2 %, (c) 5 %, and (d) 10 %

Table 2: Characterisation of hard capsules as determined under standard of TIS. 913-2545

Hard capsule	Length (mm)	Capacity (cm^3)	Mass (mg)	Moisture (%)	Ash (%)
Gelatin	21.7 ± 0.5	0.68 ± 0.03	98 ± 8	8.48 ± 0.05	0.0013 ± 0.0005
Cassia fistula gum	21.6 ± 0.5	0.64 ± 0.01	95 ± 3	5.33 ± 0.00	0.0019 ± 0.0002

The metal moulds at room temperature were dipped into a hot coating solution, which gels to form a film. The film was dried, cut to length, removed from the moulds and joined together. Figure 4 shows that all capsules present original brown colour from raw material and there are some non-dissolved matter occurring. Increasing plasticiser in coating solution made capsule shell more difficult to take off from the steel pin. By contrast, the coating solution without plasticiser provided the capsule shell fragile. Hence, the coating solution with 2% plasticiser was chosen for capsule formation. The viscosity of chosen coating solution was about 26,667 cP as measured at 30 °C.

3.3 Characterisation of capsule

The hard capsules from 3 % seed gum and 2 % plasticiser was prepared. The characterisation of these hard gum capsules was tested using standardized tests of Thailand Industrial Standards (TIS. 913-2545) and compared to the characterisation of commercial gelatin capsules (Table 2).

The results present that the characterisation of seed gum capsule is close to that gelatin. However, seed gum capsule presents less moisture content than that gelatin capsule. Water resistance of hard capsules was tested at 25 ± 1 °C for 15 min. Seed gum capsule shell was still in shape while shape of gelatin capsule was changed with extended length (Figure 5).

3.4 Drug release

Drug release of hard capsules was tested using the same method of water resistance which measured at normal human body temperature (37 ± 2 °C) until to capsule shell leaking or breaking. The obtained results showed that gelatin capsule shell was completely dissolved within 10 min while seed gum capsule shell still maintained until 27 min before broken (Figure 6). Due to gelatin capsule contained a high percentage of moisture content than that seed gum capsule (Table 2) then moisture can be released from the gelatin capsule to make easily dissolving (Rabadiya and Rabadiya, 2013).

(a) Gelatin (before test) (b) Gelatin (after test)

(c) *Cassia fistula* gum (before test) (d) *Cassia fistula* gum (after test)

Figure 5: Physical appearance of hard gelatin and seeds gum capsules before and after water resistant test at 25 ± 1 °C for 15 min

(a) Gelatin – 10 min (b) *Cassia fistula* gum – 27 min

Figure 6: Visual appearance of hard capsules after drug release test at 37 ± 2°C

4. Conclusions

This work was a preliminary study to form hard capsule shell from seed gum of Cassia fistula plant with convenient forming process. From the observed results, this seed gum has the potentials for utilisation in the pharmaceutical capsule as a substitute for gelatin or animal protein based products. The modified formulation of coating solution can be identified from a mixture design of experiments, in which the fill composition is varied between gum and plasticiser and the responses are the visual appearance. However, the visual appearance of the capsule from gum from Cassia fistula seed for examples clear, colorless, and essentially tasteless needs

further improvement. There is also a need for toxicity studies of gum from Cassia fistula seed before it can be used as a food hydrocolloid additive.

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