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Relationship between Lactose and Microcrystalline Cellulose as Diluents on Physical Characteristics of Banana Extract Tablet using Computer Program

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Abstract

Introduction: The utilization of banana in pharmaceutics has gained attention as an alternative excipient for tablet formulation. Banana starch obtained from *Musa sapientum* has been used as disintegrant in comparison study with other disintegrating agents. However, a few research works have been done to investigate the feasibility of banana extract as binding agent in tablet formulation. To overcome this problem, the development of banana extract tablets was performed using Design-Expert® Software. **Methods:** The model formulations of banana extract tablets were processed according to the formulation obtained from the experimental design. In this study, lactose (X_1) and microcrystalline cellulose (X_2) (as formulation variables) were varied and used as diluents of banana extract tablets. The physical characteristics i.e., weight variation (Y_1), hardness (Y_2), thickness (Y_3), friability (Y_4) and disintegration time (Y_5) of banana extract tablet (as response variables) were evaluated. **Results:** The response surface predicted by Design-Expert® Software reveals an obvious relationship between the diluents and physical characteristics. The banana extract tablets having the appropriate physical characteristics followed the United States Pharmacopeia (USP35) criteria. **Conclusion:** The results indicated that the experimental design was beneficial for the development of pharmaceutical tablets formulation. The finding provided an understanding of the relationship between formulation variables and response variables as exhibited in the response surface.

Keywords: Banana extract tablets, Tablet formulation, Design Expert®, Lactose, Microcrystaline cellulose

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1. Introduction

Oral tablet administration is the most widely utilization because it's safe and most convenient route (Alam, 2014). Wet granulation is the method of choice that can be applied for various drug tablets including a high dose and a very low dose, thus most of tablets formulation in pharmaceutics are processed by this method. The required practicality of a compression is good compactability, good content uniformity, good flowability which wet granulation method, is a master key process in tablet manufacturing (Cai, 2013, Westerhuis, 1997). Generally, wet granulated tablets composed of one or more diluents for bulk, a binder to facilitate granule growth, a lubricant for aid processing and a disintegrant for supporting the disintegration of tablets. Nowadays, the mobilization of natural polymers as tablet pharmaceutical excipients is extensive studied. Because natural polymers are biodegradable, biocompatible, low price and local accessibility as compared to synthetic polymers. Moreover, the natural polymers are mainly preferred by the patients as they are safer than the synthetic polymers. Therefore, the utilization of polymer obtained from natural sources is more patient compliance and acceptance.

Bananas are economically one of the most important fruit produced and consumed in the world. Because of their sweet and soft, bananas become a tropical fruit in South-East Asia enjoyed by the people from around the world. Bananas contain vitamin A, which can be used in the treatment of diarrhea and gastric ulcer; vitamin B6, which can be utilized for stress and potassium, which can be responsible for predominant brain functioning. Furthermore, banana is a good source of energy because of its high carbohydrate content (Alam, 2014). Recently, banana starch obtained from *Musa sapientum* has been used for binding agent in comparative study with official corn starch (Odeku, 2009). Moreover, banana starch also availed for disintegrating agent in aceclofenac tablet formulation compared with potato starch (Raj., 2013). Banana starch is found to compare favorably with corn starch as binding agent in tablet formulations (Babalola and Odeku, 2014).

However, no work has been done to evaluate the physical characteristics and feasibility of banana extract as binding agent in tablet formulation. Moreover, the effect of diluents (e.g. lactose and microcrystalline cellulose) was also compared in this study, because both lactose and microcrystalline cellulose are the most used excipients in the pharmaceutical industry and are generally considered the diluents that having a good binding properties (Bolhuis and Armstrong, 2006, Knöös, 2014). The object of this study was to investigate the effect of diluents (types and amount) on the physical characteristics (i.e. weight variation, hardness, thickness, friability and disintegration time) of banana extract tablet. Moreover, the Design expert® computer program was used to estimate the relationship between the formulation variables (i.e., types and amount of diluents) and response variables (i.e., weight variation, hardness, thickness, friability and disintegration time).

2. Materials and methods

Materials

The fruits of *Musa sapientum* (com monly known as banana) were purchased from local market. Lactose and microcrystalline cellu lose were purchased from CT Chemical Co., Ltd. and Maxway Co., Ltd., respectively (Bangkok, Thailand). All other chemicals were commercially available and of analytical grade.

Preparation of banana extract tablets

The extraction of banana from banana pulp with 50% ethanol was utilized as binder. The ripe banana of elephant banana (common name) age between 7 to 10 days from green was used in this study. Different contents of lactose and microcrystalline cellulose as diluents were used to prepare banana extract tablets by wet granulation method (Table 1). The desired amounts of lactose and microcrystalline cellulose were dry mixed for 5 min using mortar and pestle. Then, the proper amount of banana extract was added and mixed thoroughly until the wet mass was homogeneous. The wet mass was granulated by screening through sieve number 16. Sodium starch glycolate, magnesium stearate, talcum and colloidal silicon dioxide were added into the granules and manually mixed together in polybag. Granules were dried in a hot air oven at 50 C for 3 h, and then the dried granules were collected and passed through sieve number 18. Lastly, the blend was directly compressed using a manual hydraulic press (Model 15011, Specac, USA) with 12.7 mm diameter flat-faced tooling. The tablet was compressed at 1 ton for a dwell time of 10 s.

Characterization of banana extract tablet

The physical characteristics of banana extract tablet e.g., weight variation (Y_1), hardness (Y_2), thickness (Y_3), friability (Y_4) and disintegration time (Y_5) were determined at room temperature. Briefly, the weight variation was obtained from twenty individually weighed tablets using Sartorius balance (model AC 210 S, Sartorius, Germany). The thickness of ten tablets was determined individually using Erweka thickness tester (model TBH 225 TD, Erweka, Germany). The hardness of ten tablets was measured by hardness tester (model TBH 225 TD, Erweka, Germany). The friability was determined using Erweka tablet friabilator (model TAR 220, Erweka, Germany) performed at 25 rpm for 4 min. Disintegration testing was operated at 37±2 C in distilled water using a disintegration tester (model DT 3, Sotax, Switzerland). The disintegration times were reported as mean values of six determinations.

Table 1 Formulation variables of banana extract tablets

Ingredients	%	Function
Banana extract	18.5%	Binder
Lactose (X_1)	15-35%	Diluents
Microcrystalline cellulose (X_2)	40-60%	Diluents
Sodium starch glycolate	2.0	Disintegrant
Magnesium stearate	1.0	Lubricant
Talcum	3.0	Antiadherent
Colloidal silicon dioxide	0.5	Glidant
Total weight	100	

Experiment Designs

The experimental design was utilized for optimization of pharmaceutical formulations in accordance with previous study (Duangjit, 2012). The content of diluents in banana tablets including lactose (X_1) and microcrystalline cellulose (X_2) were selected as formulation variables. Base on our pre-formulation study as summarized in Table 1, the upper and lower limits of the levels of each composition were set as follows:

$$15 \; X_1 \; 35 \; (\%) \qquad (1)$$

$$40 \; X_2 \; 60 \; (\%) \qquad (2)$$

Thus, the diluents in banana extract tablets were studied by varying their content simultaneously, and the total content of the diluents was adjusted to 75% as defined in equation (1)-(2). The response surfaces of all model formulations were estimated and sketched by Design-Expert® Software, Version 8, Approved No. 009503 (Stat-Ease, Inc., MN, USA).

3. Results and discussion

Physical characteristics of banana extract tablets

Figure 1A represents the visual inspection of the banana extract granule and Figure 1B represents the banana extract tablet. The physical appearance of the banana extract granule and the banana extract tablet was evaluated by visual observation. The granule and the tablet were yellowish, and the banana extract tablet had a smooth surface. The upper and lower value of weight variation, hardness, thickness, friability and the disintegration time of all banana extract tablets was illustrated in Table 2. According to the United States Pharmacopeia (USP35) criteria (2011), a maximum loss of mass of banana extract tablets was not greater than 1%, and all of the tablets disintegrate completely at the end of 30 min. These results indicated that our banana extract tablets were considered acceptable for the official USP35 criteria.

Table 2 Physical characteristics of all banana extract tablets

Characteristics	Lower value	Upper value
Weight variation (mg)	543.9	547.80
Hardness range (N)	172.4	301.2
Thickness (mm)	2.97	3.06
Friability (%)	0.003	0.069
disintegration time (min)	10.55	12.35

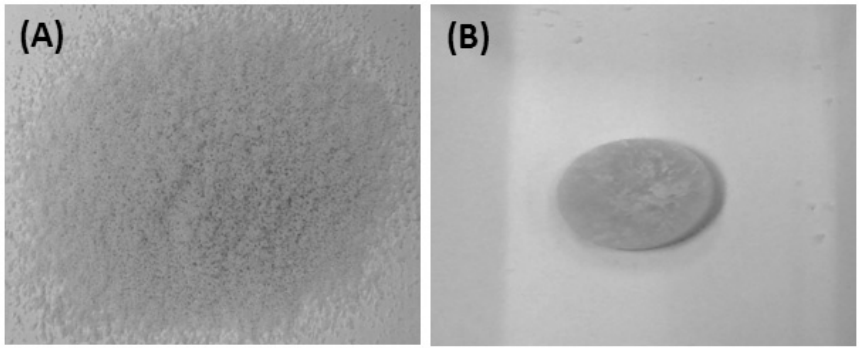

Figure 1 the visual inspection of the banana extract: (A) granules and (B) the banana extract tablets.

Prediction of response surface

The response surface of each physical characteristic was estimated by Design-Expert® Software. The content of lactose and microcrystalline cellulose were selected as formulation variables. The physical characteristics e.g., weight variation, hardness, thickness, friability and disintegration time of banana extract tablets were selected as response variables. Generally, a tablet formulation in pharmaceutics composes of several formulation variables. The relationships between the formulation variables and response variables were often complicated. Our results indicated the response surface predicted by Design-Expert® Software reveals an obvious relationship between the diluents and physical characteristics. The predicted values and experimental values were evaluated to validate the reliability of response surface (Adjusted R^2 = 0.71 to 0.89).

The relationship between lactose and microcrystalline cellulose as diluents on physical characteristics of banana extract tablets is displayed in Figure 2. The response surface showed that an increase in lactose content resulted in a slightly increase in weight variation, while an increase in microcrystalline cellulose did not affect the weight variation of banana extract tablets (Figure 2A). In the other hand, an increase in lactose content resulted in a slightly decrease in hardness and thickness, while an increase in

microcrystalline cellulose did not affect the hardness and thickness of banana extract tablets (Figure 2B and 2C). Moreover, the friability and disintegration time of banana extract tablets increased when the content of lactose increased, as shown in Figure 2D and Figure 2E, respectively. Although, the results revealed that the content of microcrystalline cellulose seem to slightly affect the physical characteristics of banana extract tablets. However, the previous study reported that microcrystalline cellulose may improve the flowability and decrease tablets weight variation of acetaminophen tablets (Hasegawa, 2002). Thus, microcrystalline cellulose is still selected as diluents in our study for improving the appropriate characteristics of banana extract tablets. Furthermore, microcrystalline cellulose is a stable through hygroscopic condition, as the present of abundant hydroxyl group in cellulose chains (Thoorens, 2014). However, the response surface indicated that the physical characteristics of banana extract tablets were directly affected by the content of lactose (Kubbinga, 2014). In this study, it could be concluded that lactose and microcrystalline cellulose can be used for improving the physical characteristics of banana extract tablets by varying its content in the tablet formulation.

4. Conclusion

Based on our experimental design using Design Expert® Software, the response surface revealed a clear relationship between formulation variables (i.e., lactose and microcrystalline cellulose) and response variables (i.e., weight variation, hardness, thickness, friability and disintegration time). Using the response surfaces, we could predict the physical characteristics of banana extract tablet without actual prepared by the experiment. Considering the USP35 criteria, the results suggested the feasibility for using banana extract as binder in tablets formulation. However, the tablet formulation contained banana extract as binder should be continually developed for the optimal banana extract tablet formulation in further study. The Design Expert® Software was beneficial as a powerful statistical program for the development of pharmaceutical tablet formulation.

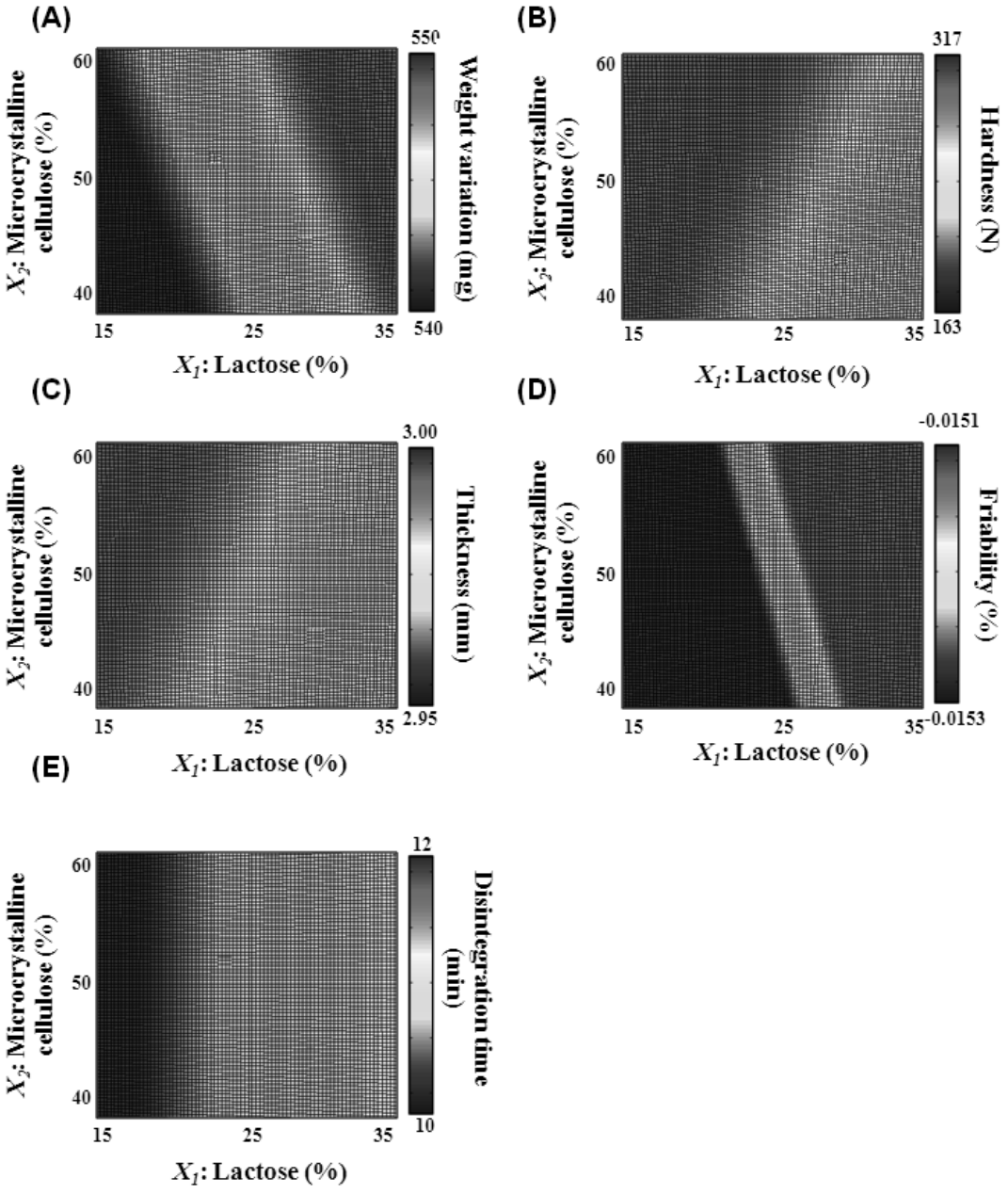

Figure 2 : the response surface of the physical characteristics of banana extract tablets estimated by Design Expert® Software, as a function of the percentage of lactose (X_1) and microcrystalline cellulose (X_2) included: (A) weight variation, (B) hardness, (C) thickness, (D) friability and (E) disintegration time.

5. Acknowledgements

The authors gratefully acknowledge the financial support from the National Research Council of Thailand (NRCT) and Thammasat University, Thailand. We acknowledge the Faculty of Pharmacy, Silpakorn University, Nakhon Pathom, Thailand for supporting the facilities.

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