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Optimization of orodispersible and conventional tablets using simplex lattice design: Relationship among excipients and banana extract

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ABSTRACT

The objective of this study was focused on the optimization of the pharmaceutical excipients and banana extract in the preparation of orally disintegrating banana extract tablets (OD-BET) and conventional banana extract tablets (CO-BET) using a simplex lattice design. Various ratios of banana extract (BE), dibasic calcium phosphate (DCP) and microcrystalline cellulose (MCC) were used to prepare banana extract tablets (BET). The results indicated that the optimal OD-BET and CO-BET consisted of BE: DCP: MCC at 10.0, 88.8, 1.2, 10.0, 83.8: and 6.2, respectively. AFM demonstrated that the surface of BET with BE + MCC was smooth and compacted when compared to BET with BE + DCP + MCC and BE + DCP. FTIR and XRD showed a correlation in the results and indicated that no interaction of each ingredient occurred in the process of BET formulation. Therefore, the experimental design is potentially useful in formulated OD-BET and CO-BET by using only one design simultaneously.

1. Introduction

Oral tablet dosage form is one of the most preferred drug formulations because it is economical, easy to manufacture, easy to handle, accurate dosing, good stability and painless administration when compared to other pharmaceutical dosage forms (Alam, Parvez, & Sharma, 2014). Unfortunately, the conventional tablets are difficult in some geriatric-, pediatric, traveling, unconscious-patients, along with patients who have difficulty swallowing. To mitigate these issues and improve poor patient compliance, the orodispersible or orally disintegrating tablets (ODT) were developed. ODT are the ideal alternative to conventional tablets because of their quick acting effect. ODT are rapidly absorbed and melt in the oral cavity, therefore they do not require water to swallow (Alam et al., 2014). British Pharmacopoeia defines ODT as "*uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed*" and as "*tablets which should disintegrate within* 3 min"(British Pharmacopoeia, 2015). Accordingly, ODT have gained popularity in the market over the last two decades and have adopted the reputation as an alternative to tablets in the pharmaceutical area (Bi et al., 1996; Comoglu & Unal, 2015).

Generally, the active pharmaceutical ingredients (APIs) in tablet dosage forms including ODT were considered inactive ingredients. Pharmacists know that pharmaceutical excipients frequently display considerable effects on the efficacy, stability, safety and quality of the tablets (Bhattacharyya, Schuber, Sheehan, & William, 2006). However, the prediction of excipient interactions and relating them to product specifications is complex, both physically and chemically. Therefore, the known potential interactions of the excipients interaction should be investigated to understand tablet preparation. To develop ODT with a predicable disintegration time (DT) (i.e., within 3 minutes, as stated as the requirement in the pharmacopeia), the response surface method (RSM) is utilized to prescribe and conceptualize the relationships between formulation factors and pharmaceutical responses (Hayashi et al., 2017; Onuki et al., 2018). In this research, we attempted to significantly decrease the amount of sample required in the formulation of ODT by using RSM.

Bananas are one of the greatest economically important fruits that are produced and consumed throughout the world (Zhang, Whistler, BeMiller, & Hamaker, 2005). Bananas have multiple useful elements in their pulp and these elements change significantly during ripening. Starch is the main element of green bananas. As starch is degraded, the amount of sugar, such as sucrose, glucose and fructose is greatly increased (Zhang et al., 2005). Conversely, the considerable high sugar content is found in yellow bananas, which results in a sweeter taste compared to green bananas. In the pharmaceutical field, banana extract (BE) was used as a representative of excipients in the tablet formulation of various drugs (e.g., ondansetron HCl, propranolol, gabapentin) (Alam et al., 2014). Moreover, as a disintegrating agent in tablet

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preparation, banana starch was compared with potato starch. However, to the best of our knowledge, no other group has used ripe banana pulp as a binding agent in ODT formulation. Additionally, taste is very important in the formulation of ODT since patient compliance will be impacted leading to treatment efficacy and bioavailability of drugs. Therefore, the ripe banana pulp used in the ODT formulation had two important functions, binding and flavoring agent.

For the largest pharmaceutical response, this study focused on the application of a primary API utilized in all tableting procedures (i.e., direct compression, wet granulation and dry granulation), such as binding and diluents in placebo ODT. Dibasic calcium phosphate (DCP) and microcrystalline cellulose (MCC) are common pharmaceutical excipients used in tablet formulation. The mixture of DCP and MCC can be helpful in improving hardness and compressibility in tablet preparation. Therefore, the objectives of this study were focused on optimization and elucidation of the relationship between the diluents and BE in preparation of the ODT and conventional tablets. The excipients interaction among BE (X_1), DCP (X_2) and MCC (X_3) was studied using simplex lattice design. The ratio of these three excipients was simultaneous optimization. The physical characteristics of banana extract tablets (BET) (i.e. weight variation (Y_1), thickness (Y_2), hardness (Y_3), friability (Y_4), DT (Y_5) and water content (Y_6)) were evaluated. The accuracy and reliability of the optimal orally disintegrating banana extract tablets (OD-BET) and conventional banana extract tablets (CO-BET) were experimentally evaluated. Moreover, scanning electron microscope (SEM), atomic-force microscopy (AFM), fourier transform infrared spectroscopy (FT-IR) and powder X-ray diffractometry (XRD) were additionally used to investigate the BET.

2. Materials and methods

2.1. Materials

The fruits of *Musa sapientum* (commonly known as banana) were obtained from the local market. DCP (Emcompress®) and MCC (Avicel® PH-102) were purchased from CT Chemical Co., Ltd. and Maxway Co., Ltd., respectively (Bangkok, Thailand). All other chemicals were commercially available and analytical grade.

2.2. Screening of three excipients ratios for banana extract tablets

To determine the proper dose range of the three excipients for BET preparation we used design of experiment for optimization and characterization. Various ratios of three excipients; BE as binder, DCP and MCC as diluent systems were determined. The tablets containing a constant amount of 0.5% colloidal silicon dioxide, 1.0% magnesium stearate, 2.0% sodium starch glycolate and 3.0% talcum, and various ratios of BE, DCP and MCC were formulated. The proper model formulations were selected based on the compressibility for tableting ratios. In a preliminary study, seven pre-model formulations of BET were screened and evaluated (Fig. 1A), then nine formulations consisting of BE (10–20%), DCP (0–90%) and MCC (0–90%) were selected and prepared as model BET (Fig. 1B).

2.3. Simplex lattice design

Response surface methodology using 9 runs, 3 levels and 3 factors for simplex lattice design was utilized to optimize the experimental process, requiring a minimal number of tests to study the effect of causal factors on response variables. The ratio of three excipients of the tablets BE, DCP, and MCC were simultaneously optimized. The components of the model formulations are displayed in Table 1. The three excipients of the tablet, including the BE (X_1), the DCP (X_2) and the MCC (X_3) were defined as causal factors. From the preliminary study, the upper and lower limits of each component were assigned as follows:

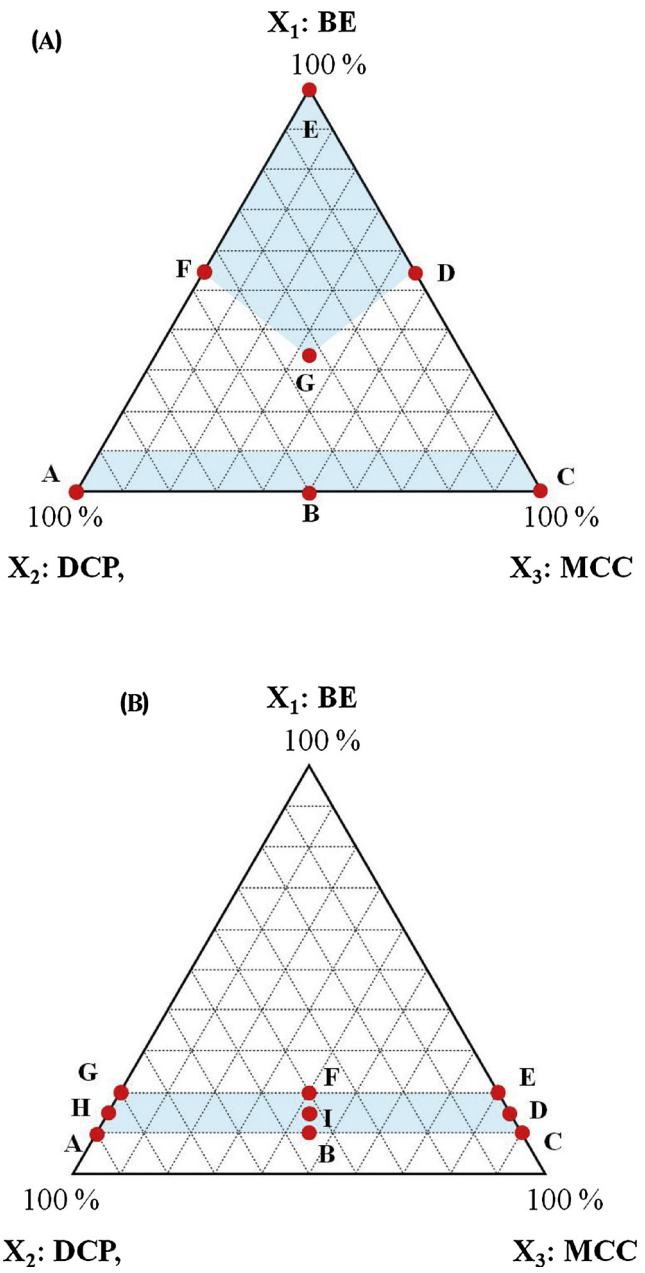

Fig. 1. The model formulation of banana extracts tablets: (A) pre-model formulations and (B) selected formulations (model formulations).

$$10 \le X_1 \le 20\ (\%) \quad (1)$$

$$0 \le X_2 \le 90\ (\%) \quad (2)$$

$$0 \le X_3 \le 90\ (\%) \quad (3)$$

$$X_1 + X_2 + X_3 = 100\ (\%) \quad (4)$$

$$X_1 + X_2 + X_3 = 93.5\ (\%w/w) \quad (5)$$

The three excipients of the model formulations were varied simultaneously and the entire amount was adjusted to 93.5 (%w/w).

2.4. Preparation of BET

The elephant banana (common name) selected from ripe banana pulp aged 7–10 days from green was chosen to prepare BET. The banana was extracted using 50% ethanol, subsequently followed by a freeze-drying process used to evaporate the water and ethanol from the