

Original Article

PREFORMULATION AND PHYSICAL PROPERTIES STUDY OF FAST DISINTEGRATING TABLETS FROM THAI TRADITIONAL FORMULA

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Received: 27 Feb. 2014 Revised and Accepted: 12 Mar 2014

ABSTRACT

Objective: The aim of this study was to develop a tablet formulation of Wat Pho hypnotic formula, a classical Thai traditional hypnotic drug. In addition, a preformulation study and physical properties of the finished products were investigated to select the best formulation for further study.

Methods: Tablets of the six formulations (D1-D6) were prepared by the direct compression method. The preformulation studies were investigated including angle of repose, bulk density, tapped density, compressibility index, and Hausner ratio. The suitable formulas were compressed into tablets and then were evaluated for physical properties following the United State Pharmacopeial method including weight variation, friability, thickness, hardness, and disintegration time.

Results: The D3 formula contained 500 mg of herbal mixture, 137 mg of avicel PH 102, 6.5 mg of colloidal silicon dioxide, and 6.5 mg of magnesium stearate per tablet. It was the best formulation as it showed good flowability (angle of repose was 35°, compressibility index was 21%, and Hausner ratio was 1.26); weight variation was narrowed and friability was less than 1%, hardness was 5.69 kiloponds, and the tablets completely disintegrated in 1.31 minutes.

Conclusion: The finished products showed less weight variation, less friability due to appropriate hardness and thickness. The tablet completely disintegrated within a few minute. Further studies of this formulation are necessary to evaluate other physical properties and chemical properties of the formulations.

Keywords: Preformulation study, Physical properties, Fast disintegrating tablets, Direct compression, Siamese senna

INTRODUCTION

Recently, many people around the world have reported suffering from a sleeping disorder. Insomnia is the most common sleeping disorder and it has been a major public health problem, affecting 10%-48% of adults [1]. This problem has many consequences; economic, cognitive, social, vocational, and health consequences i.e. mood disorders, depression, and anxiety [2]. Insomnia treatment usually uses behavioral and/or pharmacological treatment. Hypnotic drugs are also a popular treatment, benzodiazepine hypnotics such as diazepam, alprazolam and flunazepam, and non-benzodiazepine hypnotics (Z-drugs) such as zolpidem, zopiclone, and zaleplon. They have a potent effect, but they also have a lot of side effects [3]. Although the Z-drugs are less tolerance and less dependence than the benzodiazepine hypnotics, it should be use the same precautions [4]. Thai traditional medicines are used for treat of many diseases and illnesses for long time ago. Even though, the modern medicines are most popular worldwide, Thai traditional medicines are still used for primary health care in Thailand because they had good therapeutic effects with fewer side effects [5].

Polyherbal hypnotic remedy from "Wat Phra Chetupon Vimolmangkraram Rajworamahaviharn" as known as "Wat Pho", contain six herbs including leaves of *Leonurus sibiricus* Linn., seeds of *Senna tora* Linn., roots of *Glycyrrhiza glabra* Linn., roots of *Albizia myriophylla* Benth., rhizomes of *Ligusticum chuanxiong* Hort., and leaves of *Senna siamea* Lam. *Senna siamea* Lam. is a major active ingredient of polyherbal formula. It contains barakol, an active compound showed good hypnotic effect [6]. Other herbs use as helper and controller ingredient, and flavoring agent to optimize the effect and flavor of *Senna siamea* Lam. follow Thai traditional knowledge.

Original dosage form of this remedy is powder form, make inconvenient for user, unpleasant taste, difficult to protect powder from moisture makes it decompose, and inaccurate amount of drug administer. This study was to develop a new dosage form of Wat Pho hypnotic remedy from powder into tablets by the direct compression method, a cost-effective method because it preferred manufacturing process, improve manufacturing output while lowering processing cost. Compared with the wet granulation method, direct compression shows more product stability, and less unit operation [7, 8].

Fast disintegrating tablet is one of the dosage forms of choice to improve drug solubility rate from the tablet, improve onset of action, and increase bioavailability [9]. Superdisintegrants such as sodium starch glycolate, croscarmellose, and crospovidone are usually added to a tablet formulation to help the disintegration of tablet into smaller particles [10]. The aim of this study was to develop a fast disintegrating tablet formulation of Wat Pho hypnotic formula, a classical Thai traditional hypnotic drug. In addition, a preformulation study and physical properties of the finished products were investigated to select the best formulation for further study.

MATERIALS AND METHODS

All herbal powders were purchased from Chareonsuk Osod, Nakorn Pathom province, Thailand. Avicel PH 102, colloidal silicon dioxide, and magnesium stearate were obtained from Changzhou Kaide Import and Export co.ltd, China. Sodium starch glycolate was obtained from JRS Pharma, Germany. Croscarmellose sodium was purchased from FMC Biopolymer, USA. Crospovidone was purchased from Merck, Germany.

Tablet preparation by the direct compression method

Firstly, herbal powder, avicel PH 102, disintegrant (sodium starch glycolate, croscarmellose, or crospovidone), and colloidal silicon dioxide, were mixed together by the geometric dilution method. Magnesium stearate was then added and mixed together for three minutes. The ingredients ratio is shown in Table1. Formulations 1-6 are represented by D1-D6. Each formula was also sampled for the

preformulation studies including angle of repose, bulk density, tapped density, compressibility index, and Hausner ratio.

The mixture was compressed into tablets using a single punch tableting machine (Charatchai Machinery Model: CMT 12, Thailand) with a die diameter of 10.3 mm. Finally, physical properties including weight variation, friability, tablet thickness, tablet hardness, and disintegration time (DT) of the finished products were also tested.

Table 1: Ingredients of herbal tablets (mg)

Ingredients	D1	D2	D3	D 4	D5	D6	Categories
Herbal powder	500	500	500	500	500	500	Hypnotic
Avicel PH 102	-	143.5	137	117.5	117.5	117.5	Filler
Sodium starch glycolate	-	-	-	19.5	-	-	Disintegrant
Croscarmellose sodium	-	-	-	-	19.5	-	Disintegrant
Crospovidone	-	-	-	-	-	19.5	Disintegrant
Colloidal silicon dioxide	-	-	6.5	6.5	6.5	6.5	Glidant
Magnesium stearate	5	6.5	6.5	6.5	6.5	6.5	Lubricant
Total	505	650	650	650	650	650	

Preformulation studies

Angle of repose

The 5 g of powder mixture was poured into glass funnel; the lower tip of glass funnel was 5 cm height from the ground. The height (h) and radius (r) of pile were measured, and then calculated by equation (1). The study was carried out in triplicate.

$$\text{Tan } \theta = \frac{h}{r} \quad \text{.....(1)}$$

Where θ = angle of repose ($^{\circ}$), h = height (cm), r = radius (cm)

Bulk density

The 20 g of powder mixture was weighted accurately, gently poured into 100 ml glass cylinder without compacting. The volume of powder mixture was recorded, and then calculated by equation (2). The study was carried out in triplicate.

$$\text{Bulk density} = \frac{m}{V_0} \quad \text{.....(2)}$$

Where m = mass (g), V_0 = unsettled apparent volume (cm^3)

Tapped density

The 20 g of powder mixture was weighted accurately, poured into 100 ml glass cylinder. It was tapped using tapped density tester (Erweka D-63150, Germany) for 1,250 strokes. The volume of tapped powder mixture was recorded, and then calculated by equation (3). The study was carried out in triplicate.

$$\text{Tapped density} = \frac{m}{V_f} \quad \text{.....(3)}$$

Where m = mass (g), V_f = final tapped volume (cm^3)

Compressibility index

The volume of powder from bulk density and tapped density testing were used for calculate compressibility index follow equation (4).

$$\text{Compressibility index} = \frac{(V_0 - V_f)}{V_0} \times 100 \quad \text{.....(4)}$$

Where V_0 = unsettled apparent volume (cm^3), V_f = final tapped volume (cm^3)

Hausner ratio

Hausner ratio was calculated by equation (5).

$$\text{Hausner ratio} = \frac{V_0}{V_f} \quad \text{.....(5)}$$

Where V_0 = unsettled apparent volume (cm^3), V_f = final tapped volume (cm^3)

Physical property evaluations

Weight variation

Twenty tablets were individually accurately weighed. Each tablet weight was recorded. Results were reported as mean \pm standard deviation in milligrams (mg) units.

Friability

The tablets had any dust removed before testing. Ten tablets were accurately weighed together, and friability was tested using a friability tester (K.S.L. Engineering, Thailand). After 4 minutes of rotation at 25 rpm, any loose dust from the tablets was removed before accurately weighing again. If friability was not more than 1.0% it was considered acceptable. The friability was calculated by equation (6)

$$\text{Friability} = \frac{(W_{\text{before}} - W_{\text{after}})}{W_{\text{before}}} \times 100 \quad \text{.....(6)}$$

Where W_{before} = weight of tablets before test (g), W_{after} = weight of tablets after test (g)

Thickness

Ten tablets were individually measured using the thickness tester (Mitutoyo Corp. Model: ID-C112TB Absolute, Japan).

Hardness

Ten tablets were measured using a hardness tester (Erweka D-63150 Model: TBH220TD, Germany).

Disintegration time

Six tablets were tested by a disintegration tester (K.S.L. Engineering, Thailand) following the United State Pharmacopeial method, and water was used as the disintegration medium at 37 $^{\circ}$ C. DT of each tablet was recorded in minutes.

Statistical analysis

The average value for each experiment was subsequently calculated and presented as a mean \pm standard deviation.

RESULTS AND DISCUSSION

The angle of repose results revealed flowability of the D3 formula was "good", D4 formula was "fair-aid not needed", and D1, D2, D5 and D6 formulas were "passable-may hang up". Therefore, flowability of the powder formulations was in the following order: D3 > D4 > D5 > D1 = D6 > D2. The compressibility index and Hausner ratio were indirect methods for predicted powder flow characteristics. All formulations showed "passable" flow character, except D1 formula which showed "poor" flowability [11, 12]. Arrangement of flowability were D3 > D6 > D2 = D4 = D5 > D1. The preformulation study data (Table 2) indicated that D1 formula was inappropriate for the direct compression technique. Their poor flow characteristics may cause non-uniformity of tablets, which may cause weight variation problems [13]. The physical appearances of compressed tablets were green, smooth and concave in shape. Table

3 shows that all formulations had a narrow weight variation range. This uniformity indicated that the dosage is acceptable. Friability was less than 1% in all formulations, revealing that the tablets will not erode during transportation [14]. Arrangement of friability were D3 < D4 < D5 < D6 < D1.

The thickness of tablets was not significantly difference in all formulations (approximately 6.32-6.82 mm). The D3 formula showed maximum hardness of 5.69 kP; conversely, the D2 formula showed minimum hardness of 3.22 kP. There are many researches showed that croscarmellose sodium and crospovidone makes tablets spend less time for disintegration compared with sodium starch glycolate [15-17]. The result similarly reported with another elsewhere, 5% of each disintegrant revealed the same outcome of disintegration [18]. In addition, this outcome was observed for 3% and 4% disintegrants in other study [19].

However, the disintegration time of D3 formula is low, meaning that disintegrants are not necessary for this herbal formula. Overall, D3 formula showed better physical properties compared with the other formulations

Table 2: Preformulation studies

Evaluations	D1	D2	D3	D4	D5	D6
Angle of repose ($^{\circ}$)	42	45	35	39	41	42
Bulk density (g/cm ³)	0.39	0.41	0.43	0.43	0.44	0.43
Tapped density (g/cm ³)	0.53	0.54	0.54	0.56	0.58	0.55
Compressibility index (%)	27	24	21	24	24	22
Hausner ratio	1.37	1.31	1.26	1.31	1.31	1.27

Table3: Physical properties of tablets

Evaluations	D2	D3	D4	D5	D6
Weight variation (mg)	647.06 \pm 2.09	650.42 \pm 3.87	648.94 \pm 3.67	647.55 \pm 2.97	649.23 \pm 3.71
Friability (%)	0.85	0.31	0.52	0.61	0.71
Thickness (mm)	6.32 \pm 0.05	6.50 \pm 0.04	6.53 \pm 0.04	6.60 \pm 0.06	6.82 \pm 0.05
Hardness (kP)	3.22 \pm 0.19	5.69 \pm 0.60	4.98 \pm 0.52	4.21 \pm 0.48	3.66 \pm 0.32
DT (min)	2.00 \pm 0.23	1.31 \pm 0.35	1.90 \pm 0.24	1.11 \pm 0.07	1.05 \pm 0.06

CONCLUSION

The D3 formula, which contains 500 mg of herbal mixture, 137 mg of avicel PH 102, 6.5 mg of colloidal silicon dioxide, and 6.5 mg of magnesium stearate per tablet, was the most suitable formula to be studied further. It had good flow property, and a medium compressibility index and Hausner ratio, which refers to probability to be compressed into tablets by the direct compression method. The finished products showed less weight variation, less friability due to appropriate hardness, appropriate thickness, and the tablet completely disintegrated within a few minute. The content uniformity, dissolution profile, and stability study for D3 formula will therefore be further investigated.

ACKNOWLEDGEMENT

The authors are thankful to the Faculty of Pharmacy and Faculty of Oriental Medicine, Rangsit University for research facilities.

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