

## EVALUATION OF PHYSICAL PROPERTIES OF JIT-TRA-ROM FAST DISINTEGRATING TABLETS PREPARED BY THE DIRECT COMPRESSION METHOD

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Received: 30 Jan 2014, Revised and Accepted: 10 Mar 2014

### ABSTRACT

**Objective:** The aim of this study was to develop a tablet formulation of aromatic powder called "Jit-Tra-Rom", a classical Thai traditional hypnotic drug. In addition, a preformulation study and physical properties of the finish products were investigated to select the best formulation for further study.

**Methods:** Tablets of the six formulations (F1-F6) 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 including weight variation, friability, thickness, hardness, and disintegration time.

**Results:** The F3 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 32°, compressibility index was 23%, and Hausner ratio was 1.29); weight variation was narrowed and friability was less than 1%, hardness was 4.52 kiloponds, and the tablets completely disintegrated within one minute.

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

**Keywords:** Physical properties, Jit-Tra-Rom, Fast disintegrating tablets, Direct compression.

### 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 up to 48% of adults [1]. This problem has many consequences that may impact on health and quality of life, including development of depression, high costs of treatment and health care services, and an increased risk of accidents associated with vehicles or machines [2]. The risk factors of insomnia include older age, female sex, comorbidity disorders (such as medical, psychiatric, sleep, and drug abuse), shift work, and lower socioeconomic status [3].

Insomnia is usually treated by behavioral therapy and/or pharmacological therapy. Hypnotic drugs are also a popular treatment. They have a potent effect to decrease sleep onset and increase sleep duration, but they also have a lot of side effects, such as drug dependence, drug tolerance, anterograde amnesia, central nervous system depression, and drowsiness during the day [4].

"Jit-Tra-Rom" is a herbal remedy found in a classical medical book called Tam Ra Pat Sart Songkraow. This formula contains more than 40 types of herbal which have Jasmine (*Jasminum sambac* Ait.) dried flowers as the main composition. These recipes were used to make hypnotic drugs, and also anxiolytic, cardiotoxic, and migraine treatments. A modified formula was obtained from Suan Moke, Surat Thani province, which changed the pepper (*Piper nigrum* Linn.) ingredient to Chrysanthemum (*Chrysanthemum morifolium* Ramat.). This new ingredient made the treatment appropriate for patients with kidney problems [5]. The original dosage type of "Jit Tra Rom" is powder form, which is inconvenient for the user and has an unpleasant taste. Difficulty in protecting the powder from moisture makes it decompose, and therefore the drug could be administered inaccurately.

The aim of this study was to develop a new dosage form for the drug from powder into tablets using the direct compression method, a cost-effective method, suitable for thermolabile and moisture sensitive drugs. Production also uses fewer equipment and

personnel [6]. In addition, the preformulation studies and physical properties of the finished goods were investigated.

### 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. Then magnesium stearate was added and mixed together for three minutes.

The ingredients ratio is shown in Table 1. Formulations 1-6 are represented by F1-F6. Each formula was also sampled for the preformulation studies (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 (weight variation, friability, tablet thickness, hardness, and disintegration time (DT)) of the finished goods were also tested.

#### Preformulation studies

##### Angle of repose

The angle of repose was investigated by the fixed funnel method. 5 g of powder mixture was poured into a glass funnel. The lower tip of glass funnel was 5 cm from the ground. The height (h) and radius (r) of powder cone was measured, and then calculated using the equation below:

$$\tan \theta = \frac{h}{r}$$

Where  $\theta$  = angle of repose, h and r = height (cm) and radius (cm) of powder cone

**Bulk density**

20 g of powder mixture was accurately weighed and gently poured into a 100 ml glass cylinder without compacting. The volume of

powder mixture was recorded and then calculated using the following equation:

$$\text{Bulk density} = \frac{m}{V_0}$$

Where m = mass (g),  $V_0$  = unsettled apparent volume ( $\text{cm}^3$ )

**Table 1: Ingredients of herbal tablets (mg)**

Ingredients	F1	F2	F3	F4	F5	F6
Herbal mixture	500	500	500	500	500	500
Avicel PH 102	-	143.5	137	117.5	117.5	117.5
Sodium starch glycolate	-	-	-	19.5	-	-
Croscarmellose sodium	-	-	-	-	19.5	-
Crospovidone	-	-	-	-	-	19.5
Colloidal silicon dioxide	-	-	6.5	6.5	6.5	6.5
Magnesium stearate	5	6.5	6.5	6.5	6.5	6.5
Total	505	650	650	650	650	650

**Tapped density**

The glass cylinder with the powder mixture from bulk density testing, and a tapped density tester (Erweka D-63150 Model:SVM 202, Germany) with 1,250 strokes was used for tapped density testing. The volume of tapped powder mixture was recorded, and then calculated using the equation below:

$$\text{Tapped density} = \frac{m}{V_f}$$

Where m = mass (g),  $V_f$  = final tapped volume ( $\text{cm}^3$ )

**Compressibility index**

Data from the bulk density and tapped density testings were used to calculate the compressibility index, using the following equation:

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

Where  $V_0$  = unsettled apparent volume ( $\text{cm}^3$ ),  $V_f$  = final tapped volume ( $\text{cm}^3$ )

**Hausner ratio**

The Hausner ratio for flowability was calculated using this formula:

$$\text{Hausner ratio} = \frac{V_0}{V_f}$$

Where  $V_0$  = unsettled apparent volume ( $\text{cm}^3$ ),  $V_f$  = final tapped volume ( $\text{cm}^3$ )

**Physical property evaluations**

**Weight variation**

Twenty tablets were individually accurately weighed. Each tablet weight was recorded. Results were reported as mean $\pm$ SD 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 5 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 using this equation:

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

Where  $W_{\text{before}}$  and  $W_{\text{after}}$  = Weight of tablets before and after test.

**Thickness**

Ten tablets were individually measured for thickness using the thickness tester (Mitutoyo Corp. Model: ID-C112TB Absolute, Japan). Results are showed as mean  $\pm$  SD in millimeter (mm) units.

**Hardness**

Ten tablets were measured for hardness using a hardness tester (Erweka D-63150 Model: TBH220TD, Germany). Results are showed as mean  $\pm$  SD in kilopond (kP) units.

**Disintegration time**

Six tablets were tested using a disintegration tester (K.S.L. Engineering, Thailand) following the United State Pharmacopoeia method, with water at 37 °C used as the disintegration medium. Individual disintegration time of tablets was recorded in minutes.

**RESULTS AND DISCUSSION**

The angle of repose results revealed flowability of the F2 formulation was "poor-must agitate, vibrate", F1 and F5 were "passable-may hang up", F6 was "fair-aid not needed", and F3 and F4 were "good". Therefore, flowability of the powder formulations was in the following order: F3 > F4 > F6 > F5 > F1 > F2. The compressibility index and Hausner ratio were indirect methods for predicted powder flow characteristics. All formulations showed "passable" flow character, except F4 which showed "fair" flowability [7,8]. Arrangement of flowability was F4 > F5 > F6 > F2 = F3 > F1. The preformulation study data (Table 2) indicated that F1 and F2 were not appropriate for the direct compression technique. Their poor flow characteristics may cause non-uniformity of tablets, which may cause weight variation problems [6]. Thus, F3, F4, F5, and F6 were suitable to continually study. The physical appearances of compressed tablets were brown, smooth and concave in shape, and the odor like the dried jasmine flower: the major ingredient. Table 3 shows that all formulations had a narrow weight variation range. This uniformity indicates that the dosage is acceptable. Friability was less than 1% in all formulations, revealing that the tablets will not erode during transportation [9].

Table 2: Preformulation studies

Parameters	F1	F2	F3	F4	F5	F6
Angle of repose (°)	44	49	32	35	41	39
Bulk density (g/cm <sup>3</sup> )	0.29	0.31	0.33	0.37	0.34	0.33
Tapped density (g/cm <sup>3</sup> )	0.38	0.40	0.42	0.44	0.43	0.43
Compressibility index (%)	25	23	23	16	21	22
Hausner ratio	1.33	1.31	1.29	1.20	1.27	1.29

Table 3: Physical properties of Jit-Tra-Rom tablets

Evaluations	F3	F4	F5	F6
Weight variation (mg)	641.09±3.42	637.03±3.03	645.59±2.19	647.90±2.84
Friability (%)	0.16	0.45	0.61	0.58
Thickness (mm)	6.57±0.05	6.63±0.05	6.76±0.06	6.88±0.07
Hardness (kP)	4.52±0.31	3.58±0.44	3.33±0.25	3.01±0.24
DT (min)	1.01±0.09	0.98±0.13	0.70±0.09	0.71±0.15

The thickness of tablets was not different between formulations (approximately 6.6-6.9 mm). Similar hardness (F3 > F4 > F5 > F6) and disintegration time (F3 > F4 > F5 = F6) results of the remaining four formulations indicate that disintegrants decrease disintegration time. There is some research showed that croscarmellose sodium and crospovidone makes tablets spend less time for disintegration compared with sodium starch glycolate [10, 11]. The result similarly reported with another elsewhere, 5% of each disintegrant revealed the same outcome of disintegration [12]. In addition, this outcome was observed for 3% and 4% disintegrants in other study [13]. However, the disintegration time of F3 is low, meaning that disintegrants are not necessary for this herbal formula. Overall, F3 showed better physical properties compared with the other formulations.

#### CONCLUSION

The F3 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, is the most suitable formula to be studied further. It has 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 goods showed less weight variation, less friability due to appropriate hardness, appropriate thickness, and the tablet completely disintegrated within a minute. The content uniformity, dissolution profile, and stability study for F3 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. We would also like to thank KI Tull for assistance with the English in this paper.

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