

Original Article

FORMULATION DEVELOPMENT AND PHYSICAL PROPERTIES STUDY OF THAI TRADITIONAL HERBAL TABLETS: ORIGINAL JIT-TRA-ROM RECIPE

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ABSTRACT

Objective: This work aimed firstly to develop the formulation of original Jit-Tra-Rom herbal tablets by two different methods: direct compression or wet granulation method. The second aim was to evaluate their physical properties, including weight variation, friability, tablets thickness, tablets hardness, and disintegration time.

Methods: Tablets of the four formulations (D1-D4) were prepared by the direct compression method and two formulations (W1-W2) were prepared by the wet granulation 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 direct compression method showed low potential to compress herbal powders into tablets because of their poor flowability and poor tabletability: angle of repose of 44-48°, compressibility index of 17-22%, and Hausner ratio of 1.21-1.28. Thus, the wet granulation method was used for Jit-Tra-Rom herbal tablet preparation that contained avicel PH 102, sodium starch glycolate, colloidal silicon dioxide, magnesium stearate, and different amount of povidone K30. Their granules showed excellent flowability and good tabletability: angle of repose of 26-27°, compressibility index of 13, and Hausner ratio of 1.14-1.15. These formulas had less weight variation of 0.33% and 0.56%, and less friability of 0.07% and 0.02% for W1 and W2 formulas, respectively. This due to had approximately hardness in ranged of 5-6 kP. The Jit-Tra-Rom herbal tablets fully disintegrated within five minutes.

Conclusion: We successfully developed the Jit-Tra-Rom herbal tablet by using the wet granulation method which was the suitable method for tablets preparation than the direct compression method.

Keywords: Physical property, Wet granulation, Herbs, Tablets, Jit-Tra-Rom

INTRODUCTION

Thai traditional medicines are used for treat of patient illness and diseases for long time ago. Even though, the Western 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 [1]. Recently, the Ministry of Public Health has promoted the use of Thai traditional medicines and Thai herbal formulas in the hospital for treatment of health problems [2]. In Thailand, the herbal medicinal products are listed in the 2013 National List of Essential Medicines contains polyherbal formula more than single herbal medicines. The knowledge of the Oriental medicines usually supports the usage multiherbal formula because it takes advantage of synergy and interaction between phytochemicals in herbal recipe to achieve therapeutic efficacy with minimizing side effect [3].

Jit-Tra-Rom (JTR) aromatic powder is a one of the Thai tradition herbal recipe. It is recorded in a classical medicinal book called Tam Ra Pat Sart Songkraow, in the chapter of Kam Pee Cha Wa Darn. It is used as cardiogenic, anxiolytic, and hypnotic drug. The JTR formula that used in this research contains approximate 40 types of different herbs. The jasmine flower (*Jasminum sambac* Ait.) is the main herb that contains of the half part in JTR formula compared to all herbs.

The JTR formula has two formulas which are the original and modified formula. The original JTR formula contains white pepper seed (*Piper nigrum* Linn.). Nevertheless, some Thai traditional doctor believes the white pepper seed is nephrotoxic herb; it may induce to kidney disease in patients. Thus, the modified JTR formula uses chrysanthemum flower (*Chrysanthemum morifolium* Ramat.)

instead of white pepper seed to avoid exacerbation of symptom of kidney disease patients [4]. However, this research used the original formula for JTR formulation development. Because some research reported the discovery of the β -caryophyllene ameliorates, a sesquiterpene in essential oil of black or white pepper, it can prevent drug-induced nephrotoxicity [5]. This result is related to the Indian traditional medicine that uses the pepper seed for nephroprotective application [6]. Original JTR is powder form, which is bulky dose, inconvenient for the user, inaccurate amount of drug administration, and unpleasant taste. These powders are difficult to protect the moisture absorption from environmental which may induce degradation and microbial growth in their powder [7].

However, this problem can be improve by filled the herbal powder into capsule or compressed into tablets, but the capsule preparation may be bulky dose more than tablets preparation. Therefore, both the direct compression and wet granulation methods are considered for preparing a new dosage form of JTR instead of original powder form. Physical properties of these tablets were investigated, including weight variation, friability, tablets thickness, tablets hardness, and disintegration time of finished products.

MATERIALS AND METHODS

All herbs were purchased from Charoensuk Osod, Nakorn Pathom province, Thailand. Avicel PH 102, colloidal silicon dioxide, and magnesium stearate were purchased from Changzhou Kaide Import and Export Co., Ltd., China. Povidone K30 was purchased from Onimax Co., Ltd., Thailand. Sodium starch glycolate was purchased from JRS Pharma, Germany. Croscarmellose sodium was purchased

from FMC BioPolymer, USA. Crospovidone was purchased from Merck, Germany.

Direct compression method for JTR herbal tablet preparation

Initially, mixed herbs, avicel PH 102, sodium starch glycolate (or croscarmellose sodium 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 of D1-D4 formulas are shown in Table 1. The mixture powders were tested and evaluated by preformulation studies: angle of repose, bulk density, tapped density, compressibility index, and Hausner ratio that described in below section before tablets compression

Table1: Ingredient of JTR herbal tablets (mg)

Ingredients	D1	D2	D3	D4	W1	W2	Categories
Herbal	500	500	500	500	500	500	Active ingredient
Avicel PH 102	137	117.5	117.5	117.5	72	85	Filler
Povidone K30	-	-	-	-	19.5	6.5	Binder
Sodium starch glycolate	-	19.5	-	-	19.5	19.5	Disintegrant
Croscarmellose sodium	-	-	19.5	-	-	-	Disintegrant
Crospovidone	-	-	-	19.5	-	-	Disintegrant
Colloidal silicon dioxide	6.5	6.5	6.5	6.5	32.5	32.5	Glidant
Magnesium stearate	6.5	6.5	6.5	6.5	6.5	6.5	Lubricant
Total	650	650	650	650	650	650	

Wet granulation method for JTR herbal tablet preparation

Initially, mixed herbs, avicel PH 102, povidone K30, sodium starch glycolate, and colloidal silicon dioxide were mixed together by the geometric dilution method. Water was then added into the mixture powders until a damp mass occurred, sieved through an 18-mesh sieve to produce granules. The granules were dried in hot air oven at 60 °C for 4 hrs. The dried granules were sieved all over again through a 20-mesh sieve and magnesium stearate was added and mixed together for three minutes. The mixture powders were tested and evaluated by preformulation studies: angle of repose, bulk density, tapped density, compressibility index, and Hausner ratio before tablets compression. Then, the mixture powders were compressed into tablets using a single punch tableting machine (Charatchai Machinery Model: CMT 12, Thailand) with a die diameter of 10.3 mm. The ingredients ratio is shown in Table 1 which designed as W1 and W2 formulas, respectively. After that, the tablets were tested the physical properties: weight variation, friability, tablets thickness, tablets hardness, and disintegration time.

Preformulation studies [8, 9]

Angle of repose

The angle of repose was tested by the fixed funnel method. 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 follow Equation 1. The study was carried out in triplicate.

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

θ = angle of repose (°)

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 follow Equation 2. The study was carried out in triplicate.

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

m = mass (g)

V₀ = unsettled apparent volume (cm³)

Tapped density

The glass cylinder with powder mixture from bulk density testing was used to test tapped density. 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 follow Equation 3. The study was carried out in triplicate.

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

m = mass (g)

V_f = final tapped volume (cm³)

Compressibility index

Data from bulk density and tapped density testing were used for calculate compressibility index follow Equation 4.

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

V₀ = unsettled apparent volume (cm³)

V_f = final tapped volume (cm³)

Hausner ratio

Hausner ratio was calculated follow Equation 5.

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

V₀ = unsettled apparent volume (cm³)

V_f = final tapped volume (cm³)

Physical property evaluations [8, 9]

Weight variation

Twenty tablets were individually accurately weighed. Each tablet weight was recorded. Results were reported as mean ± standard deviation (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 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 follow Equation 6.

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

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). Results were reported as mean±SD in millimeter (mm) units.

Hardness

Ten tablets were measured using a hardness tester (Erweka D-63150 Model: TBH220TD, Germany). Results were reported as mean±SD in kilopond (kP) units.

Disintegration time (DT)

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 °C. DT of each tablet was recorded in minutes.

RESULTS AND DISCUSSION

All formulations that prepared by the direct compression method were tested the preformulation studies for potential evaluation to tablet compression. All preformulation study parameters are shown in Table 2. The angle of repose of all formulation (D1-D4) showed low flowability; D1 and D3 were “passable (may hang up), and D2 and D4 were “poor (must agitate, vibrate), that were classed by the United State Pharmacopeia 33/National Formulary 28 (USP 33/NF 28) [10]. Bulk density of each formulation was 0.39, 0.40, 0.39, and

0.37 g/cm³ for D1, D2, D3, and D4, respectively. Tapped density of all formulation was 0.48 g/cm³. Compressibility index and Hausner ratio revealed that flow character of D1-D3 were “fair”, while D4 was “passable”. Even though, the direct compression method is a cost-effective, faster, simpler, and easier method for tablets preparation [11], all data from preformulation studies indicated that JTR herbal formula could not be prepared by this method, because it had poor flowability and tableability, might cause problems during manufacturing process [12].

After the direct compression method not successfully produced the JTR herbal tablet, the wet granulation method was selected to prepare this tablet. The angle of repose result from preformulation studies of W1 and W2 were found the “excellent” flowability. The compressibility index and Hausner ratio are shown in Table 2 indicated that “good” flow character and tableability, means the wet granulation method was appropriate for JTR herbal formula.

These confirmed by many publications that usually report the excellent flowability when prepared by the wet granulation method [13-16]. And then, W1 and W2 were compressed into tablets and evaluated their physical properties in term of weight variation, friability, tablets thickness, tablets hardness, and DT.

Finished products of JTR herbal tablets had 10.3 mm of diameter and 6.74 mm of thickness are shown in Figure 1. The physical appearance was brown, smooth and concave tablets, and the odor like the dried jasmine flower: the major ingredient. W1 and W2 were less weight variation, 658.80±2.16 mg and 665.17±3.75 mg, respectively, and less friability, 0.07% and 0.02%, respectively due to approximately hardness of 5-6 kP. The W1 fully disintegrated within five minutes but the W2 fully disintegrated within two minutes. This result related to the less amount of povidone K30 as binder in W2 compared to W1 that decreased approximately 2.5 times of DT (Table 3). This results indicated that more concentration of binder make more DT [17-19]. The W1 and W2 were appropriate formula for JTR tablets preparation. Content uniformity, dissolution, and stability will therefore be further investigate

Table2: Preformulation studies of JTR herbal tablets were prepared by the direct compression method (D) and the wet granulation method (W)

Preformulation studies	D1	D2	D3	D4	W1	W2
Angle of repose (°)	44	48	45	46	27	26
Bulk density (g/cm ³)	0.39	0.40	0.39	0.37	0.43	0.42
Tapped density (g/cm ³)	0.48	0.48	0.48	0.48	0.49	0.48
Compressibility index (%)	20	17	19	22	13	13
Hausner ratio	1.25	1.21	1.24	1.28	1.14	1.15

Table3: Evaluations of JTR herbal tablets prepared by the wet granulation method

Formula	Physical properties				
	Weight variation (mg)	Friability (%)	Thickness (mm)	Hardness (kP)	DT (min)
W1	658.80±2.16	0.07	6.74±0.05	4.86±0.44	4.94±0.84
W2	665.17±3.75	0.02	6.74±0.10	5.86±0.55	1.72±0.62



Fig.1: Finished product of JTR herbal tablets (W1 formula)

CONCLUSIONS

The direct compression method is not suitable for JTR herbal tablets preparation, because it is poor flowability and poor

tableability. But, the wet granulation method is preferred. The preformulation study showed the W1 and W2 that prepared by the wet granulation method expressed excellent flowability and tableability.

The physical properties of compressed tablets were studied; both formulas showed less weight variation, less friability due to appropriate hardness, appropriate thickness, and the tablet completely disintegrated less than five minutes.

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