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INTRODUCTION

Traditional Thai medicine (TTM) to relieve health disorders has been used for many years. It has been widely accepted that TTM has a good potential for new pharmacotherapy from medicinal plants. Jatu-Phalathika, a TTM formula, has been used as mild laxative, expectorant and to relieve cough. This formula composed of equal proportions of four medicinal plants which are *Terminalia bellirica* (Beleric Myrobalan), *Terminalia chebula* (Chebulic Myrobolans), *Phyllanthus emblica* (Emblic Myrobolans) and *Terminalia sp.* (Arjun). Jatu-Phalathika is prepared by boiling the plant materials with water before use. The composition of herbs within a boiled solution can be changed depending on the condition of the patient. This preparation has some disadvantages such as the time needed to prepare, appearance or taste that might be considered unpleasant for some patients. Therefore, this study is interested in developing Jatu-Phalathika into a modern formulation, the effervescent tablet. This will provide a viable solution for delivering active ingredients using a cost-effective technology.

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MATERIALS AND METHODS

Materials Gallic acid was purchased from Sigma Chemical Co. (USA). All four medicinal plants: *Terminalia bellirica* (Beleric Myrobalan), *Terminalia chebula* (Chebulic Myrobolans), *Phyllanthus emblica* (Emblic Myrobolans) and *Terminalia sp.* (Arjun) were purchased from drug store in Nonthaburi Province, Thailand. Pharmaceutical excipients including lactose, sodium bicarbonate, citric acid, tartaric acid, polyethylene glycol 6000 and sodium saccharin were purchased from TTK Science, Bangkok, Thailand. The solvents for HPLC including acetic acid, water and acetronitrile (Labscan, Thailand) were also purchased from TTK Science, Bangkok, Thailand.

Methods

Preparation of crude extracts The Jatu-Phalathika preparation was formulated by using equal amount (500 g) of *Terminalia bellerica, Terminalia chebula, Phyllanthus emblica* and *Terminalia sp.* (Arjun). The mixture was then boiled in water (3 L) and left to freely evaporate in order to obtain 1 liter of the aqueous extract. Next, the water was removed from the extract by using freeze dry method (EYELA FD-1, Tokyo Rikakikai, Japan).

Preformulation study In order to estimate the suitability of mixture for formulation, preformulation studies to check the physical properties of Jatu-Phalathika extract with other excipients were required. The results of the preformulation studies provided data necessary for the formulation and manufacturing of the effervescent tablet. Preformulation studies were performed concerning the angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio, using appropriate techniques.

Formulation development of Jatu-Phalathika effervescent tablets All ingredients shown in Table 1 were mixed and compressed by direct compression using a single punch tablet machine to make an effervescent tablet following the formula. First, Jatu-Phalathika extract was absorbed by lactose, sheared by the pestle and put through a 60-mesh sieve. The powder of Jatu-Phalathika was tray-dried at 60 °C using a hot air oven for 1 hour. Then, the powder was mixed with sodium bicarbonate, citric acid, tartaric acid, PEG 6000 and sodium saccharin. Humidity in the room was controlled to lower than 30%RH. Amount of gallic acid from effervescent tablets was analyzed by validated HPLC method.

Table 1 Formula of effervescent tablets

Ingredients	Weight per tablet (mg)				Function
	F1	F2	F3	F4	
Jatu-Phalathika extract	250.00	250.00	250.00	250.00	Active ingredient
Lactose	750.00	750.00	750.00	750.00	Absorbent/Filler
Sodium bicarbonate	500.00	489.90	479.90	469.90	Alkalizing agent
Citric acid	166.67	163.30	159.97	156.63	Acidifying agent
Tartaric acid	333.33	326.60	319.93	313.27	Acidifying agent
PEG 6000	-	20.00	40.00	60.00	Lubricant
Sodium saccharin	-	0.20	0.20	0.20	Sweetening agent
Total weight (mg)	2000.00	2000.00	2000.00	2000.00	-

Physical properties of Jatu-Phalathika effervescent tablets The evaluation data composed of weight variation, thickness, hardness, friability, and disintegretion.

Quantitative analysis of gallic acid by high performance liquid chromatography (HPLC) Quantitative analysis of gallic acid was performed using high performance liquid chromatography (HPLC) method with UV detector at 292 nm. The HPLC system consisted of a quaternary pump system (Agilent, 1260 VL), autosampler (Agilent, 1260 TCC) and UV/VIS with diode array detector (Agilent, 1260 DAD VL). A reversed-phase Inertsil ODS3 C-18 column (4.6 x 250 mm) was eluted by using a gradient system of acetronitrile (A) and 1.0% acetic acid (B) as the mobile phase with a flow rate of 0.8 ml/min. The condition of mobile phase gradient elution was 10–40% (A) in 0–15 min, 40–60% (A) in 15–30 min, 60–80% (A) in 30–40 min, and 80–100% (A) in 40–60 min. The injection volume was 5 µl. Validation parameters of linearity, accuracy, and precision were confirmed for this method.

RESULTS AND DISCUSSION

Preformulation study The preformulation studies to check the physical properties of the Jatu-Phalathika extract with other excipients were shown in Table 2.

Table 2 Data of preformulaton studies

Preformulaton studies	F1	F2	F3	F4
Angle of repose (°)	47.52	44.11	40.29	38.25
Bulk density (g/ml)	0.38	0.41	0.39	0.43
Tapped density (g/ml)	0.43	0.48	0.48	0.50
Carr's Index (%)	11.63	14.58	18.75	14.00
Hausner's Ratio	1.13	1.17	1.23	1.16

Formulation development of Jatu-Phalathika effervescent tablets The formula of F1, F2, F3 and F4 contained lactose at the amount of 37.50% by weight. Lactose could effectively absorb Jatu-Phalathika extract in the formulation. F1, which composed of Jatu-Phalathika extract and acid-base agent, poorly flowed and stuck to the punch and die set. Then, we added PEG 600 in F2, F3 and F4 at the amount of 1%, 2% and 3% by weight, respectively. The effervescent tablets of F2 and F3 showed a better flow than F1 but still stuck to the punch and die set. F4 formulation, which contained 3% of PEG 6000, exhibited good flow, good compressibility and did not stick to punch and die set. When dissolved F4 effervescent tablet in water, it disintegrated and produced clear solution. The physical appearance of effervescent tablet of F4 was brown, round shape with smooth surface. The evaluation data of weight variation, thickness, hardness, friability, and disintegretion time were shown in Table 3.

Table 3 Data of physical properties

Physical properties	F1	F2	F3	F4
Weight variation (mg)	2003.12±8.76	2007.15±2.25	2011.47±5.13	2006.62±5.81
Thickness (mm)	7.28±0.15	7.44±0.09	7.49±0.17	7.50±0.11
Hardness (kP)	45.23±0.02	43.56±0.11	48.25±0.13	49.68±0.05
Friability (%)	0.27	0.20	0.23	0.29
Disintegretion time (min)	3.05±0.05	3.11±0.09	3.11±0.13	3.20±0.06

Quantitative analysis of gallic acid by high performance liquid chromatography (HPLC)

Validation method of HPLC analysis Linearity was studied by preparing standard stock solution of gallic acid at different concentration levels. When the concentrations of gallic acid and their respective peak areas were subjected to regression analysis by least squares method, a good linear relationship (r^2 = 0.9990) was observed between the concentrations of gallic acid and the respective peak areas in the range 20-200 µg/ml. The regression equation was found to be y = *13.8469x- 24.0172*, where Y is the peak area and x is the concentration of gallic acid.

To ensure the accuracy and reliability of the method, recovery studies were carried out in triplicate at three concentration levels. The recovery of gallic acid was found to be in the range of 98.47-99.10 %

The intra-day precision of the assay method was evaluated by carrying out six independent assays of gallic acid test samples against qualified reference standard on the same day and these studies were also repeated on six consecutive days to determine inter-day precision. The percentage of RSD of six assay values was calculated. On day 1, 2 and 3, % RSD of gallic acid was found to be 0.533, 0.701 and 0.354, respectively.

To determine the specificity of the analytical method, standard stock solution of gallic acid, placebo solution and Jatu-Phalathika solution dissolve in the same solution. All solutions were filtered through 0.2 µm Nylon filter. Equal volume (5 µl) of each sample was injected into the HPLC by autosampler and diode array scanning was measured from 220-400 nm. The retention time and UV absorption spectrum of Jatu-Phalathika solution were compared with the standard and placebo. As a result, the chromatogram of placebo was not shown the peak area at 7.129 minutes.

CONCLUSION

Jatu-Phalathika effervescent tablets were prepared successfully by direct compression method. Lactose can effectively absorb Jatu-Phalathika extract and other excipients. The formulation overcomes the problems associated with hygroscopic excipients like sodium bicarbonate, citric acid and tartaric acid. The analytical HPLC method is validated for quantitative determination of gallic acid in effervescent tablet. This research demonstrates the new dosage form for TTM preparations to be a new way to promote traditional medicine usage for modern lifestyle.

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