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Establishment of Dissolution Specification for Fa-Tha-Lai Capsules

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Abstract Recently, wide-spread usage of Fa-Tha-Lai capsules or Fa-Tha-Lai Chon capsules dramatically increased as an alternative medicine in Thailand. Apart from the safety and efficacy of the product, its quality control tests were considerably concerned. A dissolution method was one of the crucial tests of quality control because it was considered as a prerequisite to detect a defective product and to maintain content uniformity in batches including reproducibility among the production batches. Consequently, the establishment of dissolution specification for Fa-Tha-Lai capsules or *Andrographis paniculata* capsules in this study was carried out by developing a dissolution method in order to assess the quality of the product. The objective was to evaluate the dissolution behavior of Fa-Tha-Lai extract capsules, which were labeled the content of andrographolide, distributed in Thai markets. Various dissolution media were tested to optimize the dissolution method. The data of the dissolution media were evaluated by a one-way analysis of variance (ANOVA). As a result, the proposed dissolution method used a paddle type dissolution apparatus at the rotation speed 100 rpm, dissolution medium comprising 900 mL of 0.01 M hydrochloric acid containing 0.2% w/v sodium lauryl sulfate maintained at 37.0±0.5 °C, and 45 minutes time-point. Therefore, this proposed method could be suitably used for establishing the dissolution specification of Fa-Tha-Lai extract capsules because it could discriminate the dissolution quality among the products available in Thai markets.

Key words: **dissolution, paddle, Fa-Tha-Lai extract capsules, andrographolide**

Introduction

Andrographis paniculata (Burm.f.) Nees is an herbal medicine in family Acanthaceae, commonly known as Fa-Tha-Lai or Fa-Tha-Lai Chon.[1] It has been widely used in traditional treatments, especially in India, China, Indonesia, Thailand and other countries in Asia for fever, common cold, sore throat and non-infectious diarrhoea. Pharmacological activities of *A. paniculata* (Burm.f.) Nees include hepatoprotective, anti-diarrhoea, anti-inflammatory, antimicrobial, immunostimulant, etc. Clinical studies of *A. paniculata* (Burm.f.) Nees along with its toxicity are performed. Therapeutically active constituent of this plant is andrographolide extracted from leaves and

aerial parts. It is colorless diterpene lactone with bitter taste. Other chemical constituents are neoandrographolide, deoxyandrographolide, dehydroandrographolide, isoandrographolide, bisandrographolide, andrographiside, etc.[2-5] In Thailand, this plant was also officially selected by the Ministry of Public Health as one of the medicinal plants to be included in "The National List of Essential Drugs A.D. 2012" (Guidebook of Herbal Medicine Products).[6] The products of this plant, namely, Fa-Tha-Lai capsules and Fa-Tha-Lai tablets, have been widely marketed as an alternative medicine in Thailand. Nowadays, widespread usage of these products dramatically increases. Their safety and efficacy of the products must be concerned. Therefore, the quality control tests of the products are considerably important.

In this study, the dissolution method for Fa-Tha-Lai extract capsules was developed to assess the quality of the product because it was considered as a prerequisite to detect defective product and to maintain content uniformity in batches including reproducibility among the production batches. It also was performed as an essential evaluation parameter. Additionally, Fa-Tha-Lai extract capsules which specified the content of andrographolide were only selected for this research. Moreover, the data obtained from this study will support establishing the dissolution specification of this product for Thai Herbal Pharmacopoeia (THP) in the future.

Methodology

Chemicals and Apparatus

Andrographolide USPRS, Lot FOI344, % purity 99.5 was from USP, USA. Water was purified by using Milli-Q Advantage A10, Millipore, France. All solvents were HPLC grade and all chemical reagents were analytical reagent grade. Dissolution apparatus Model VK7025 was from Varian Inc., USA and Model 708 DS was from Agilent Inc., USA. HPLC analysis was performed on Waters 2695, Water Corporation, USA and on Dionex Model Summit, Thermo Fisher Scientific Inc., USA. MX5 Microbalance and Mettler Toledo Model AT 200, Mettler-Toledo International Inc., Switzerland were used for weighing the reference standard and sample, respectively. The apparatuses were periodically calibrated as the schedule according to the quality control manual of Bureau of Drug and Narcotic, Department of Medical Sciences.

Sample Selection

Three commercial brands of Fa-Tha-Lai extract capsules were purchased from 3 manufacturers (products A, B, C). Three different lots of each brand of Fa-Tha-Lai extract capsules with labeled claim of andrographolide were provided. The labeled claims of both products A and B were not less than 20 mg of andrographolide per capsule and the labeled claim of product C was 9 mg of andrographolide per 300 mg of Fa-Tha-Lai extract. The product A was sampled as a model of development of the dissolution method which was validated. All the products were at least one year away from their expiration dates at the time of testing. Before subjecting to the dissolution test, each product was tested for uniformity of dosage units (weight variation), loss on drying, andrographolide content, and disintegration test.

Determination of Uniformity of Dosage Units

Ten Fa-Tha-Lai extract capsules in each lot were weighed individually. The content of each capsule was removed by carefully opening the shell without losing any parts of the shell. The shell was cleaned with a

small brush and weighed emptied shell. The weight of the contents in each capsule was calculated by subtracting the weight of the shell from weight of the capsule and was compared with the average weight for the capsules. To meet the requirement of uniformity of dosage units, not more than two of individual weights deviate from the average weight by more than the percentage deviation of 10 percent and none deviates by more than twice that percentage.[7]

Determination of Loss on Drying

Loss on drying was described in THP IV.[8] A weighing bottle was dried in an oven at 105 °C until constant weight. It was replaced with 2 g of the sample and heated as the same condition as above. It was cooled in desiccators and weighed. The procedure was repeated till constant weight. The percentage of loss in weight of the sample was calculated.

Determination of Andrographolide Content

Andrographolide content of Fa-Tha-Lai extract capsules was determined by using HPLC. The andrographolide standard curve was plotted at the concentrations of 5, 10, 15, 20, 25, and 30 mg/mL. For sample preparation, the contents of 20 Fa-Tha-Lai extract capsules were combined, ground and mixed. Accurately weighed about 400 mg of the combined contents were transferred to a 100-mL volumetric flask and a 20-mL portion of methanol was added. The volumetric flask was shaken for a while and adjusted to volume by a mixture of 52 mL of water and 48 mL of methanol as mobile phase. Five milliliters of the sample solution were transferred to a 50-mL volumetric flask. It was diluted with mobile phase to volume, mixed, and filtered through a 0.2 μm PVDF(HL) filter. Twenty microliters of the filtered sample were injected in 3 replicates. Chromatographic peaks were identified by comparison with the retention time of the standard. The chromatographic procedure was carried out using a BDS Hypersil C18 column (150 mm x 4.6 mm, i.d., particle size 5 μm), a BDS Hypersil C18 guard cartridge (10 mm x 4.6 mm, i.d., particle size 5 μm), a mobile phase at a flow rate 1.0 mL per minute, and an ultraviolet photometer at 224 nm.

Determination of Disintegration Test

The procedure of disintegration test for Fa-Tha-Lai extract capsules was described in Supplement to Thai Herbal Pharmacopoeia, 2004[7]. Six Fa-Tha-Lai extract capsules of each lot were used in each test, using water as the immersion fluid. Each lot was performed 3 replicates. To meet the requirement, all capsules disintegrated within 30 minutes.

Dissolution Procedure

Preparation of various dissolution media

The eight dissolution media, namely, water, phosphate buffer pH 6.8, 0.1 M of hydrochloric acid, a series of 0.01 M hydrochloric acid containing sodium lauryl sulfate (SLS) at the concentrations of 0.1%, 0.2%, and 0.3% w/v, and a series of 0.05 M, 0.1 M hydrochloric acid containing SLS at the concentration of 0.2% w/v were employed.

To prepare phosphate buffer pH 6.8, a 250-mL portion of monobasic potassium phosphate solution was transferred to a 1000-mL volumetric flask and a 112-mL portion of 0.2 M sodium hydroxide solution was added. The volumetric flask was adjusted with water to volume. A 900-mL portion was transferred to a 1000-mL dissolution vessel, placed into the dissolution tester's water bath. The medium was equilibrated to 37.0±0.5 °C for about 30 minutes prior to starting the dissolution test.

To prepare 0.01 M, 0.05 M, and 0.1 M of hydrochloric acid, 0.85-mL, 4.25-mL and 8.50-mL portions of hydrochloric acid were transferred to each 1000-mL volumetric flask and adjusted with water to volume to obtain 0.01 M, 0.05 M, and 0.1 M of hydrochloric acid, respectively. A 900-mL portion of each medium was transferred to a 1000-mL dissolution vessel, placed into the dissolution tester's water bath. The medium was equilibrated to 37.0±0.5 °C for about 30 minutes prior to starting the dissolution test.

To prepare 0.01 M hydrochloric acid containing 0.1% w/v SLS (pH 2.04), a 1-g portion of SLS was transferred to a 1000-mL volumetric flask and dissolved with about 400 mL of water. A 0.85-mL aliquot of concentrated hydrochloric acid was added to the solution. It was diluted to volume with water. A 900-mL portion was transferred to a 1000-mL dissolution vessel, placed into the dissolution tester's water bath for equilibration at 37.0±0.5 °C for about 30 minutes.

To prepare 0.01 M hydrochloric acid containing 0.2% and 0.3% w/v SLS (pH 2.10 and 2.14, respectively), proceed as directed in the preparation of 0.01 M hydrochloric acid containing 0.1% w/v SLS but using 2-g and 3-g portions of SLS instead of a 1-g portion of SLS.

To prepare 0.05 M hydrochloric acid containing 0.2% w/v SLS (pH 1.47), a 2-g portion of SLS was transferred to a 1000-mL volumetric flask and dissolved with about 400 mL of water. A 4.25-mL aliquot of concentrated hydrochloric acid was added to the solution. It was diluted to volume with water. A 900-mL portion was transferred to a 1000-mL dissolution vessel, placed into the dissolution tester's water bath for equilibration at 37.0±0.5 °C for about 30 minutes.

To prepare 0.1 M hydrochloric acid containing 0.2% w/v SLS (pH 1.17), a 2-g portion of SLS was transferred to a 1000-mL volumetric flask and dissolved with about 400 mL of water. A 8.50-mL aliquot of concentrated hydrochloric acid was added to the solution. It was diluted to volume with water. A 900-mL portion was transferred to a 1000-mL dissolution vessel, placed into the dissolution tester's water bath for equilibration at 37.0±0.5 °C for about 30 minutes.

Dissolution method

Dissolution profiles in various dissolution media

Dissolution profiles were carried out by using dissolution apparatus with paddles at the rotation speed 100 rpm and 900 mL of various dissolution media maintained at 37.0±0.5 °C. Product A and each dissolution medium were performed in each dissolution test. A 10-mL portion of dissolution medium was withdrawn within the time intervals specified at 15, 30, 45, 60, 90, and 120 minutes. The dissolution medium withdrawn was not replaced. The sample was filtered using a 0.2 μm PVDF(HL) filter. The first few milliliters were discarded. A 5-mL portion of the filtered solutions of the six individual capsules withdrawn was combined as a pooled sample then diluted to 50.0 mL with mobile phase. It was further filtered through a 0.2 μm PVDF(HL) filter before analysis by using HPLC. The amount of andrographolide dissolved for each time interval was calculated from standard curve of andrographolide using linear regression.

Dissolution profiles at different rotation speeds of paddles

Dissolution profiles were performed in different

rotation speeds of the paddles at 50, 75, and 100 rpm, and the same dissolution medium comprising 900 mL of 0.01 M hydrochloric acid containing 0.2% w/v SLS maintained at 37.0±0.5 °C. Product A was performed in each rotation speed. A 10-mL portion of the dissolution medium was withdrawn within the time intervals specified at 15, 30, 45, 60, and 90 minutes. The dissolution medium withdrawn was not replaced. The sample was filtered using a 0.2 μm PVDF(HL) filter. The first few milliliters were discarded. A 5-mL portion of the filtered solutions of the six individual capsules withdrawn was combined as a pooled sample then diluted to 50.0 mL with mobile phase. It was further filtered through a 0.2 μm PVDF(HL) filter before analysis by using HPLC. The amount of andrographolide dissolved for each time interval was calculated from standard curve of andrographolide using linear regression.

Dissolution profiles for different brands

Dissolution tests for products A and B were performed with a paddle type dissolution apparatus at the rotation speed 100 rpm and dissolution medium composed of 900 mL of 0.01 M hydrochloric acid containing 0.2% w/v SLS maintained at 37.0±0.5 °C. A 10-mL portion of this solution medium was withdrawn at 15, 30, 45, 60, and 90 minutes. The dissolution medium withdrawn was not replaced. The sample was filtered using a 0.2 μm PVDF(HL) filter. The first few milliliters were discarded. A 5-mL portion of the filtered solutions of the six individual capsules withdrawn was combined as a pooled sample then diluted to 50.0 mL with mobile phase. It was further filtered through a 0.2 μm PVDF(HL) filter before analysis by using HPLC. The amount of andrographolide dissolved was computed from standard curve of andrographolide.

Validation of dissolution method

The dissolution method of product A was validated for specificity, linearity, precision, accuracy, and robustness according to United States Pharmacopeia (USP)[9] and ICH.[10-11]

Standard curve of andrographolide

The standard andrographolide solution used for establishing the calibration curve in the dissolution test ranged from 5 to 30 mg/mL.

Statistical analysis of data

The analysis of variance (ANOVA) and the test for normal distribution of data (Kolmogorov-Smirnov One-sample Test) were performed. The significance level (α) was set at 0.05.

Results

Weight Variation, Loss on Drying, Andrographolide Content, and Disintegration Test

Three commercial brands of Fa-Tha-Lai extract capsules with labeled claim of andrographolide were tested. The tested products met the weight variation requirement specified in Supplement to THP 2004. The test results for loss on drying found in all products ranged from 1.0% to 6.0% w/w. The content of andrographolide was analyzed by using the method described above and calculated. The andrographolide contents per capsule of products A and B ranged from 20 to 25 mg which complied the labeled claim. On the other hand, the andrographolide content per 300 mg of of Fa-Tha-Lai extract of product C ranged from 5.0 to 7.5 mg. It did not comply with the labeled claim. All products also met the disintegration test requirement specified in Supplement to THP 2004. The mentioned results above were shown in Table 1.

Dissolution Method Result

Dissolution profiles in various media and at different rotation speeds of paddles

The dissolution test was optimized in terms of dissolution media and rotation speeds. The dissolution media and rotation speeds of product A were studied under the experimental condition described above. Dissolution profiles were depicted in Figure 1.

To increase degree of dissolution, the addition of various concentrations of SLS was performed. The suitable amount of surfactant necessary to achieve the maximum percent release of andrographolide within 45 minutes was 0.2% w/v in 0.01 M hydrochloric acid. The mentioned results were shown in Figures 1b and 1c.

Dissolution profiles for different brands

The dissolution profiles of products A and B containing andrographolide in 900 ml of 0.01 M hydrochloric acid containing 0.2% w/v SLS maintained at 37.0±0.5 °C with paddles at the rotation speed 100 rpm were shown in Table 2 and Figure 2.

Validation of dissolution method

Specificity

Specificity of the method was demonstrated in term of spectral as well as peak purity data of the sample and standard. The results showed that the method was specific.

Linearity

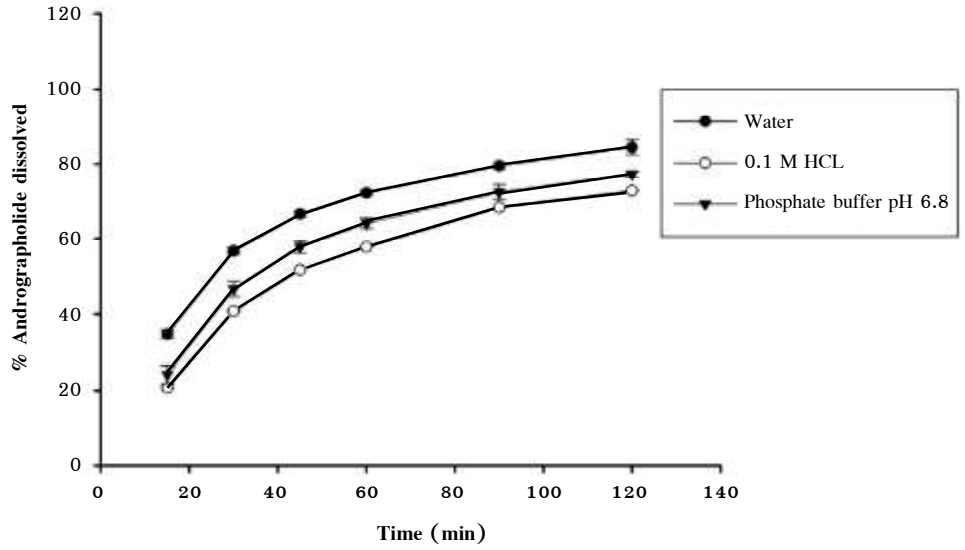
The linearity of andrographolide response was evaluated from the range of 5-30 mg/mL. The line equation was y = 4E+07x with a slope of 10791 and r^2 of 0.998. The percentage of relative standard deviation (%RSD) for each point was less than 1%. These data indicated that the method was linear for andrographolide within the specification limits.

Table1 Summary of the test results for weight variation, loss on drying, andrographolide content, and disintegration test of Fa-Tha-Lai extract capsules

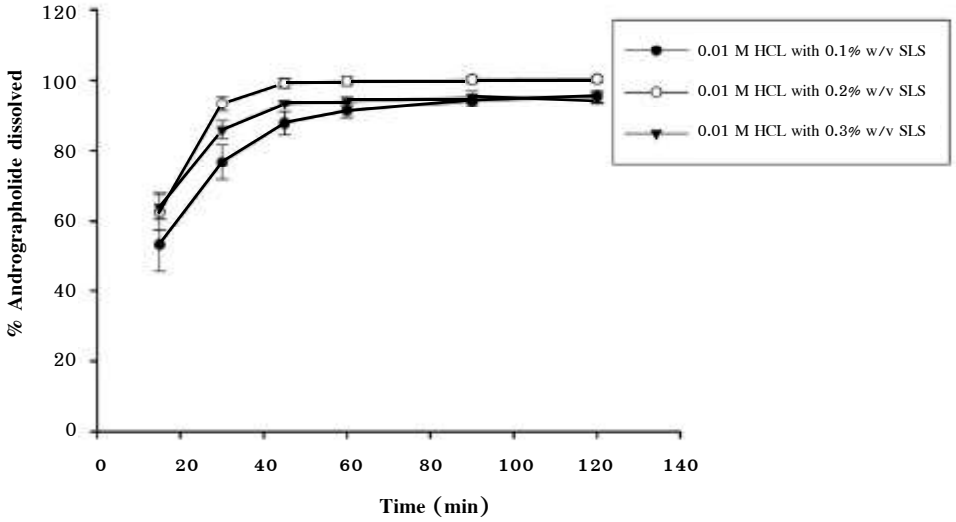
Product	Average weight (mg), SD (n = 10)	Weight variation	Loss on drying (% w/w), SD(n=3)	Andrographolide content (mg), %RSD (n=3)	Disintegration test
Product A					
lot 1	456.1, 0.01	passed	1.3, 0.2	22.5, 0.5	passed
lot 2	461.0, 0.01	passed	1.5, 0.4	22.8, 0.7	passed
lot 3	416.2, 0.02	passed	1.8, 0.1	20.5, 0.3	passed
Product B					
lot 1	387.0, 0.01	passed	4.1, 0.2	23.0, 8.8	passed
lot 2	387.8, 0.01	passed	4.0, 0.3	23.4, 5.2	passed
lot 3	404.6, 0.01	passed	3.3, 0.1	24.6, 3.2	passed
Product C					
lot 1	225.4, 0.01	passed	4.7, 0.1	6.3, 1.3	passed
lot 2	220.5, 0.01	passed	5.8, 0.0	5.4, 0.0	passed
lot 3	299.3, 0.01	passed	5.9, 0.1	7.3, 0.0	passed

Figure 1 Optimization of the dissolution method: (a) effect of dissolution media, (b) and (c) effect of dissolution media and SLS, and (d) effect of paddle rotation speed

(a)



(b)



(c)

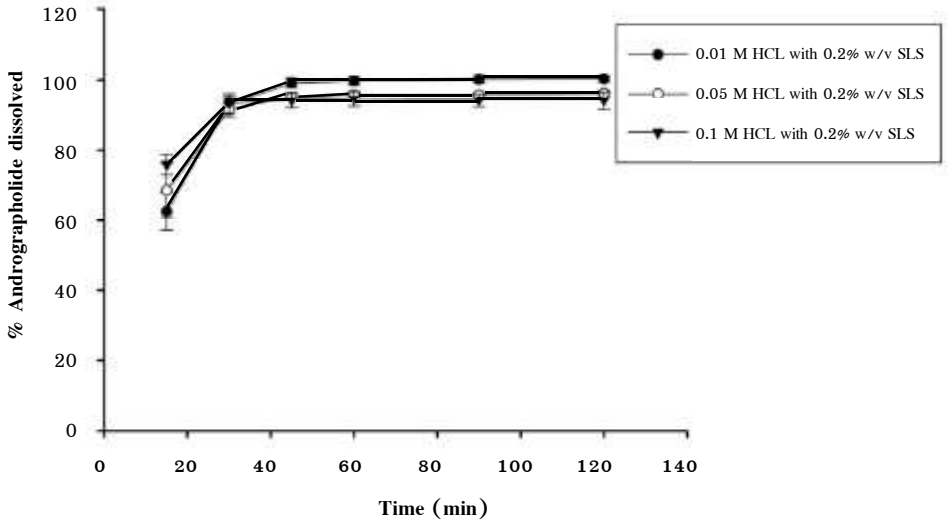
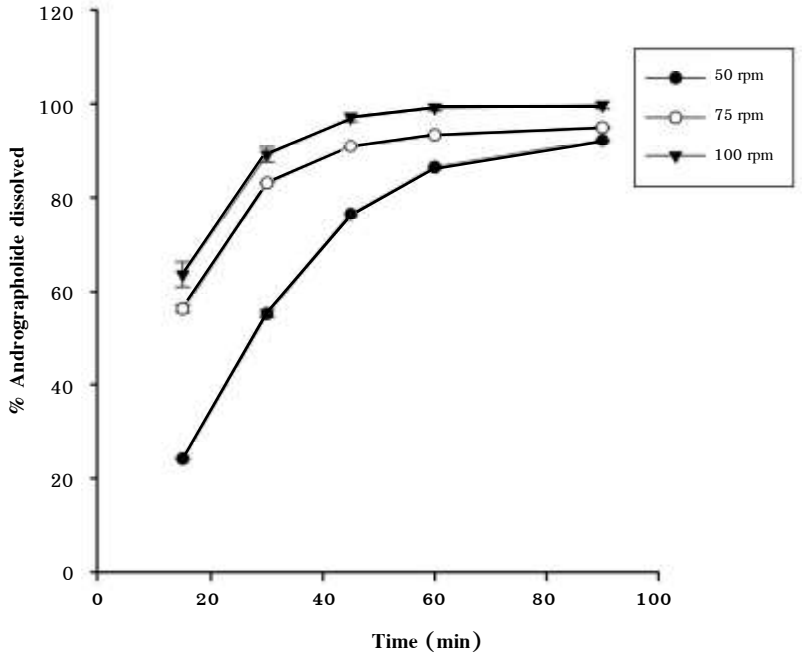


Figure 1 Optimization of the dissolution method: (a) effect of dissolution media, (b) and (c) effect of dissolution media and SLS, and (d) effect of paddle rotation speed (cont.)

(d)



Precision

The precision of dissolution method was determined by measuring the repeatability and the intermediate precision, both expressed as %RSD. All the results were within an acceptance criterion of 2%.

Accuracy

The accuracy expressed the agreement between the accepted value and observed value according to USP. The percent recovery criterion was specified in the range of 95.0-105.0%. The results showed that the percent recovery was in the range of 99.3-100.4%. Therefore, the accuracy of the method was acceptable.

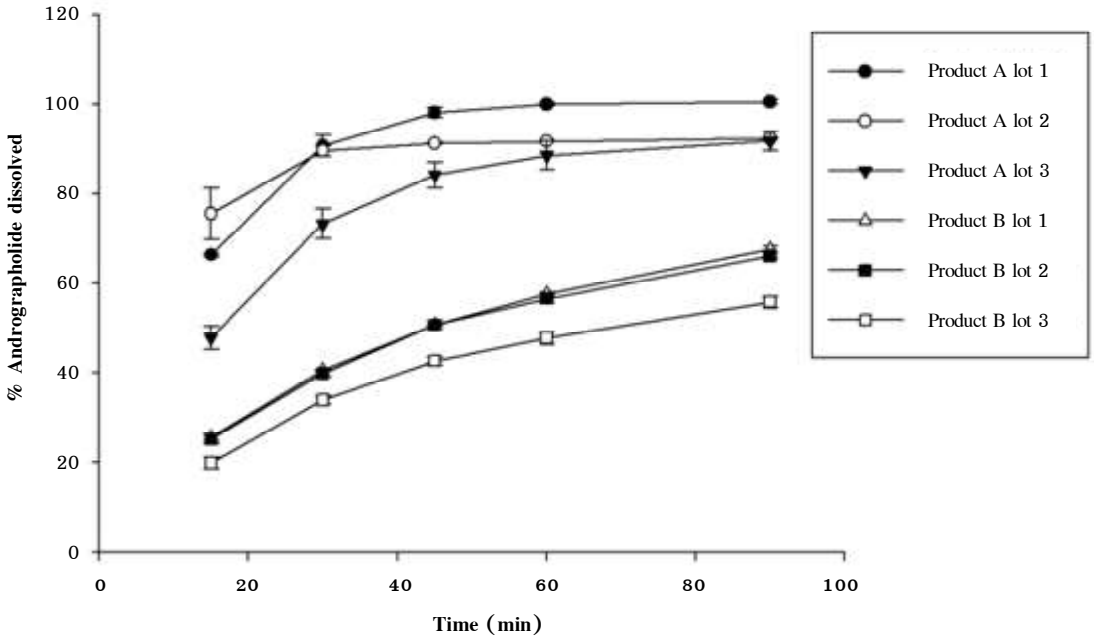
Robustness

The robustness of the method was demonstrated by changing the analysts and instruments. The %RSD

Table 2 Dissolution profiles of 3 lots of products A and B of Fa-Tha-Lai extract capsules (dissolution medium 900 mL: 0.01 M hydrochloric acid containing 0.2% w/v SLS; temperature: 37.0±0.5 °C; paddle: rotation speed 100 rpm)

Product	Lot (each lot, n = 3)	% andrographolide dissolved (mean±SD) at time intervals		
		30 min	45 min	60 min
A	1	90.7±2.5	98.1±1.1	99.9±0.3
	2	89.6±1.2	91.3±0.2	91.7±0.0
	3	72.3±3.3	84.2±2.9	88.6±3.2
B	1	40.5±0.2	50.8±0.9	57.6±0.3
	2	39.8±0.8	50.7±0.1	56.6±0.7
	3	33.9±0.9	42.7±1.0	47.8±1.4

Figure 2 Dissolution profiles of 3 lots of products A and B of Fa-Tha-Lai extract capsules containing andrographolide using the paddle method at the rotation speed 100 rpm and dissolution medium comprising 900 mL of 0.01 M hydrochloric acid containing 0.2% w/v SLS maintained at 37.0±0.5 °C



values were within the specified limit of 2%. These results indicated the robustness of dissolution method.

Discussion

In this study, the development of the dissolution method for Fa-Tha-Lai extract capsules was started with examination of weight variation, loss on drying, andrographolide content, and disintegration test of each brand of Fa-Tha-Lai extract capsules. Weight variation and disintegration test were general requirements for capsule dosage form to control the quality of products according to Supplement to THP[7]. Three commercial brands of Fa-Tha-Lai extract capsules were performed with the tests. All products met the general requirements above. In addition, the determinations of andrographolide contents in all products were also performed. According to the results, the contents of andrographolide in the products A and B met their labeled claims but the andrographolide contents of product C mostly found less than the labeled claim by more than 20%. The product C was excluded for this development of dissolution method. Therefore, the product A was finally selected for the study of the dissolution profile and method validation in order to develop the dissolution method because it had more significant consistency of the contents of andrographolide in each lot than that of the product B.

For selection of suitable dissolution condition, the comparison of dissolved andrographolide profiles was performed with various dissolution media on the steps starting with water, acid, and base conditions. From the study, water was not considered as dissolution medium because the quality of the water could vary depending on the source of the water, and the pH value of the water was not routinely controlled.[9,12] So, the water was not the medium of choice. Addi-

tionally, the base condition should be actually selected for the medium of choice but the acid condition was theoretically selected instead because of absorption information of andrographolide in the stomach.[13,14] Although, over 70% of andrographolide contents were dissolved within 120 minutes in both conditions but they did not reach the dissolution plateau. Thus, the time interval over 120 minutes needed for the complete dissolution was not practical for the dissolution test (Figure 1a). For this reason, an increase in andrographolide solubility with the surfactant was preferably considered. As a result, suitable concentration of SLS at 0.2 w/v was added to 0.01 M hydrochloric acid to enhance andrographolide solubility (Figure 1b). Meanwhile the concentrations of the hydrochloric acid were varied, the amount of SLS at 0.2% w/v was fixed. The results showed that 0.01 M hydrochloric was the best concentration of this testing (Figure 1c). In addition, the influence of rotation speeds was evaluated and the results revealed in Figure 1d. The analysis of ANOVA showed significant difference among the results obtained at 50, 75, and 100 rpm ($p<0.05$). Therefore, 900 mL of 0.01 M hydrochloric acid containing 0.2% w/v SLS maintained at 37.0±0.5 °C for 45 minutes time-point, and a paddle type dissolution apparatus at the speed rotation 100 rpm were proposed to be optimal dissolution method conditions. Subsequently, dissolution tests for different brands (products A and B) of Fa-Tha-Lai extract capsules from Thai markets were performed regarding the dissolution method condition obtained. The percentage of andrographolide dissolved showed significant difference among the products (Table 2 and Figure 2). Assumingly this may be due to the different formulations of the products such as the differences of lubricants, diluents, etc.

Conclusion

The dissolution method developed and validated for Fa-Tha-Lai extract capsules was carried out. The proposed dissolution method used a paddle type dissolution apparatus at the rotation speed 100 rpm for 45 minutes time-point. The dissolution medium comprising 900 mL of 0.01 M hydrochloric acid containing 0.2% w/v SLS maintained at 37.0±0.5 °C. In this condition, the percentage of andrographolide dissolved was higher than 80% in 45 minutes for the product A, on the other hand about 50% for the product B in the same time-point. Therefore, this proposed dissolution method can be suitably used for establishing the dissolution specification of Fa-Tha-Lai extract capsules because it can discriminate the dissolution quality among the products available in Thai markets.

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ที่ผ่านมามีการใช้ยาแคปซูลฟ้าทะลาย หรือยาแคปซูลฟ้าทะลายโจรเพิ่มขึ้นอย่างกว้างขวาง ซึ่งยาดังกล่าวเป็นยาที่ใช้ในการแพทย์ทางเลือกในประเทศไทย นอกจากเรื่องความปลอดภัยและประสิทธิภาพของผลิตภัณฑ์แล้ว การควบคุมคุณภาพเป็นเรื่องที่ต้องคำนึงถึงอย่างยิ่ง วิธีการทดสอบการละลาย เป็นหัวข้อทดสอบที่สำคัญอันหนึ่งในการควบคุมคุณภาพ เนื่องจากวิธีการทดสอบดังกล่าว จะใช้ตรวจสอบความบกพร่องของผลิตภัณฑ์และใช้ควบคุมความสม่ำเสมอในแต่ละรุ่นการผลิต ดังนั้นจึงได้มีการจัดทำข้อกำหนดมาตรฐานการละลายของยาแคปซูลฟ้าทะลาย หรือยาแคปซูลแอนโดรกราฟิส เพนิคุลาตา ในการศึกษานี้ได้พัฒนาวิธีการทดสอบการละลายเพื่อใช้กำหนดคุณภาพของผลิตภัณฑ์ จุดประสงค์ในการศึกษา เพื่อจะประเมินลักษณะการละลายของยาแคปซูล-ฟ้าทะลายสกัด เป็นผลิตภัณฑ์ที่ได้กำหนดปริมาณสารแอนโดรกราโฟไลด์ ซึ่งมีจำหน่ายในท้องตลาด การศึกษาได้มีการทดสอบโดยใช้ตัวกลางการละลายหลายชนิดเพื่อที่จะเลือกตัวกลางการละลายที่เหมาะสมสำหรับวิธีการทดสอบการละลาย ซึ่งข้อมูลที่ได้นำมาวิเคราะห์ความแปรปรวนทางสถิติ ผลการทดสอบของวิธีทดสอบการละลายที่เสนอครั้งนี้ ใช้อุปกรณ์ใบพายที่ความเร็ว 100 รอบต่อนาที ตัวกลางการละลาย 900 มิลลิลิตร ประกอบด้วยกรดไฮโดรคลอริกเข้มข้น 0.01 โมลาร์ โดยมีโซเดียมลอริลซัลเฟตละลายอยู่ในความเข้มข้นร้อยละ 0.2 น้ำหนักต่อปริมาตร ซึ่งตัวกลางดังกล่าวคงอุณหภูมิที่ 37.0±0.5 องศาเซลเซียส และเวลาที่ใช้ทดสอบ 45 นาที ดังนั้น วิธีทดสอบที่เสนอนี้สามารถใช้ในการจัดทำข้อกำหนดมาตรฐานการละลายของยาแคปซูลฟ้าทะลายสกัด เนื่องจากวิธีดังกล่าวสามารถแยกความแตกต่างของคุณภาพการละลายระหว่างผลิตภัณฑ์ที่จำหน่ายในประเทศไทย

คำสำคัญ: **การละลาย, วิธีใบพาย, ยาแคปซูลฟ้าทะลายสกัด, แอนโดรกราโฟไลด์**