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Development and Evaluation of *Garcinia parvifolia* (Miq)Miq from Tablet Dosage Forms

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Abstract

Dry and wet methods can be applied for granulation. It is said that final use of prepared granules as tablets dictates the preparation method. At the present study the formulation of the extract of the stem bark of G. parvifolia as tablet dosage form was performewd by use of formulation using dry and wet methods and compared inrespect to characteristics like hardness test, weight uniformity test, friability test, disintegration time and dissolution test and other properties. Results showed that it was concluded that it is better to use wet method for granulation it final aim is produce tablets of the granules. Other wise if the granules will be used as such and there method can be used because of the advantages of this method in respect to low cost of production course, no need to use organic solvents and feasibility in industrial scale production.

Key words

Garcinia parvifolia (Miq)Miq, tablet, dry and wet granulation.

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INTRODUCTION

Garcinia parvifolia (Miq)Miq ′local name is asam kandis, the species of *Garcinia* are found mainly in Kalimantan, Indonesia. It is a rust colored fruit with orange likely rather acid and the young leaf is sometime eaten by residen of Kalimantan as a vegetable [1] The genus Garcinia, which belongs to the family Guttiferae is known to be rich in prenylated xanthones (Chamasathien *et al.*, 2003). *In vitro* antiplasmodial of the xanthone against both drugs sensitive and resistant of *P. falciparum* and *in vivo* antiplasmodial activity against of *P. berghei* [2]. In the extract acute toxicity tests with low toxicity when oral administered, while their active fractions have LD_{50} values more than 8000 mg/kg-weight. According to the classification, these compounds have low toxicity [3].

In spite of their efficacy, herbal medicinal products have been widely criticized due to lack of standarization and poor-quality presentation. Standardization and formulation of traditional herbs into modern phytopharmaceuticals shall provide the solution to most of these problems of traditional medicine (5,6). In traditional medicine, the stem bark of *G. parvifolia* (Miq)Miq., is usually soaked in water and unspecified quantities of the decoction are ingested. However, to improve patient compliance and acceptance, there is need to formulate the stem bark of *G. parvifolia* (Miq)Miq., into dosage form (7). When starting manufacturing of tablets with dry extract from *G. parvifolia* (Miq)Miq., the following assumptions were made: (1) the tablets would be obtained through direct pressing of the tablet mass, (2) to compare, a series would be produced with initial granulation, (3) the tablet should be characterized by quick disintegration and high pharmaceutical availability of biologically active substances, (4) the tablets properties must be in accordance with obligatory standards also after longer time of storage.

Thus, the aim of the present study is to produce conventional tablets of the extracts of the stem bark of *G. parvifolia* (Miq)Miq for oral administration using dry and wet granulation methods to determine the more suitable method for the preparation of the tablets.

EXPERIMENTAL

Plant material and extract

The *G. parvifolia* (Miq) Miq stem barks were sampled in May 2004 from Nang Kalis Village in West Borneo. The stem barks then were identified in the Botanical Research and Development Division Herbarium Bogoriense in West Java, a division under the Center of Biological Research and Development. The stem bark cut into pieces and dried in an oven at 40°C for 48 h. The dried stem bark were ground to a fine powder. The powder of *G. parvifolia* (Miq) Miq stem bark was transferred into a soxhlet apparatus (extractor). The finr powder (2.0 kg) was placed in a soxhlet extractor and extracted with ethanol for 18 h. The extract so obtained was concentrated to a semi-solid mass using a rotary evaporator. A dry mass was obtained by adsorbing the concentrate on Aerocyl® and dryng the mixture at 50°C for 24 h.

Phytochemicals Analysis

The following test were performed on the ethanolic and *n*-hexane extracts of the dried, stem bark.

Assay of Garcinia parvifolia

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The assay procedure was carried out on both the dried, powdered and the crude ethanolic extract. These samples were used for determination of total phenolic content. The procedure used is based on the methods outlined by Folin-Ciocalteu[8]. The method is based on an oxidation-reduction reaction in alkaline conditions, where the phenolate ion is oxidized while Folin's reagent is reduced, turning the solution blue. Many of the active components in the *G. parvifolia* (Miq) Miq stem barks, such as phenolic acids and flavonoids, have a phenolic nucleus and can be evaluated by this method. A calibration curve was built using standard aqueous solutions of phenol.

Preparation of Garcinia tablets

Garcinia tablets each containing 100 mg was prepared by conventional wet granulation and dry granulation methods. All binders were used at 2% concentration of formula. Granules were compressed into tablets of hardness 5 to 6 kg/sq.cm using Cadmach single punch tablet machine.

Evaluation of compressed tablets

- *Hardness test*

Five tablets were selected at random from each batch to perform this test. Monsanto hardness tester (Merk) was used to measure the hardness. Tablet was placed between spndle and anvil of the tester and the calibrated lenght adjusted to zero. The knob was then screwed to apply a diametric compression force on the tablet and the position on the calibrated lenght at which the tablet broke was recorded in kgf units. A mean hardness was calculated for each batch and thus their standard deviations and coefficient of variation and coefficient of variation were calculated.

- *Weight uniformity test*

Twenty tablets from each batch were selected randomly and weighed individually using a highly sensitive electronic balance (merk). Their mean weights were calculated; deviation and coefficients of variation for each batch were calculated.

Friability test

Erweka triabulator was used to carry out this test. Ten tablets were selected at random, dusted and weighed together using the electronic balance (merk) and then placed in the Erweka triabulator (merk). The machine was operator for 4 min at 120 rev/min and then stopped. The tablets were dusted again and reweighed. The percentage losses were calculated for each of the tablets.

- *Disintegration time*

The method specified in the USP/NF (1980) was used. The machine used was (merk). Disintegration medium used was 100 mL of 0.1 N HCl maintained at temperature between 35 and 39°C throughout the experiment. Five tablets selected at random from each batch were placed one in each of the cylindrical tubes of the basket but no disc was used. The time taken for each tablet to break up into small particles and pass out through the mess was recorded. Mean disintegration time was calculated for each batch.

RESULT AND DISCUSSION

The preparation of a dry extract by adsorption of liquid plant extract on inert excipient such as fumed silica has been described by Palma et al. (1999). In this, the performance some common excipients to be used as support for the extractive products, such as lactose starch, PVP and fumed silica have been evaluated. Diluting dry extract wit strach yielded materials with poor flow properties indicating that the selection of suitable inert material for adsorption is fundamental (Palma et al., 1999).

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The crude extracts of the stem bark of *G. parvifolia* have been reported to be highly hygroscopic liquefying at higher relative humidity. Dry extract preparations containing various concentration of Aerosil® were prepared to improve the hygroscopicity and poor flow property of the crude extract of the stem barks of *G. parvifolia* (Miq)Miq. Table 1 and 2 show formulas used in tablet evaluations produced by wet and dry granulation.

Table 1

Formulation of extract of *G. parvifolia* (Miq)Miq by dry granulation methods

Formulation	I (mg)	II (mg)	III (mg)
Dry extract	150	150	150
Lactose	46,75	-	-
$CaHPO_4$	-	46,75	-
Corn starch	-	-	46,75
Potato starch	5	5	5
Talcum	2	2	2
Magnesium stearate	1	1	1
Polivinyl pyrolidon	3	3	3

Table 2

Formulation of extract of *G. parvifolia* (Miq)Miq by wet granulation methods

Formulation	I (mg)	II (mg)	III (mg)
Dry extract	150	150	150
Potato starch	10	10	10
Mucilago amylum	10	10	10
Potato starch	5	5	5
Talcum	5	5	5
Magnesium stearat	2	2	2
Lactose	231,33	-	-
Corn starch	-	231,33	-
$CaHPO_4$	-	-	231,33

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The mechanical properties of pharmaceutical tablets are important test for pharmaceutical tablet that often form part of manufacture's own specification which are quantifiable by the hardness test, weight uniformity test, friability test, disintegration time and dissolution test of the tablets. Based on Table 3, using dry granulation method, formula I and II meet the current tablet requirements, while the tablet from formula III has shorter time of pulverization because the friability and the hardness of the tablets don't meet the current requirements. Using wet granulation, the tablets from formula I and III meet the requirements whereas those from formula II don't meet the requirements in terms of friability and hardness. The phenol content in the tablets produced by wet granulation is higher that those produced by dry granulation. The highest phenol content (2.03%) was found in the tablets of wet granulation formula III.

Table 3

Evaluation tablet dosage forms by dry and wet granulation methods

	Dry granulation methods			Wet granulation method		
	I	II	III	I	II	III
Compressibility (%)	13,3	12,8	14,71	13,79	12,69	11,36
Friability (%)	0,98	0,93	9,39	0,81	5,76	0,65
Weight uniformity (mg)	502	504	507	472	483	507
Mean disintegration time	10′41″	14′41″	5′17″	8′16″	1′14″	4′24″
Mean tablet hardness (Kgf)	4	5,1	1	4,8	2,6	4,5
Assay of phenolic content (%)	1,027	1,029	1,028	2,01	1,39	2,03

Dry plant extracts usualy lack good flow properties to be processed by direct compression. In addition, because the active components of the extracts are diluted by coextracted substances, high dosages are required. This is in conflict with the limited proportion in which the extracts can be incorporated into the final mixture for tablet compression (Vennat et al., 1993). Numerous reports have addresed techniques used to solve these problems, such as wet granulation with non-aqueous solvents (Diaz et al., 1996) and selection of suitable excipients for the formulation of dry extracts in direct compression tablets (Renoux et al., 1996). The analyses shown that the most influent factor on the granulation process for the formulation used in this study was the water addition methods. This is likely to be due to larger droplet sizes from pouring the water resulting in larger granule size, compared with dry and wet granulation. To conclude, the evaluation of granulations properties can be used as important tool to predict the characteristics of final tablets containing high dose granulation.

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