



Formulation of *Dennettia tripetala* Tablets by Direct Compression: Standardization and Quality Control

Onyechi J.O., Chime S.A.^{*}, Onyishi I.V., Eneiga A.

Department of Pharmaceutical Technology and Industrial Pharmacy, University of Nigeria, Nsukka 410001, Nigeria.

*Corresponding author's E-mail: emmyrachi@yahoo.com

Accepted on: 11-12-2012; Finalized on: 30-09-2013.

ABSTRACT

The purpose of the present study was to formulate *Dennettia tripetala* seed tablets by direct compression. The dried powder of *Dennettia tripetala* seed was formulated into tablets using microcrystalline cellulose (MCC) as the filler binder. The tablets were analyzed by determining the tablets thickness and diameter, weight uniformity, disintegration time, friability and hardness test. The *in vitro* release profile of the crude drug was studied in simulated gastric fluid (SGF, pH 1.2). The results showed that the tablets exhibited thickness of 4.25 ± 4.03 mm and diameter of 10.13 ± 0.25 mm. The tablets passed the test for uniformity of weight with percentage deviations not more than 5 %. The tablets had crushing strength of 2.14 ± 7.09 kgf and friability loss of 0.3 %. Disintegration time test showed that the tablets disintegrated at 1.60 ± 16.40 min. The dissolution profile exhibited $T_{62.5\%}$, $T_{71.3\%}$, $T_{72.0\%}$ and $T_{91.3\%}$ release of the crude drug at 2, 5, 20 and 30 min respectively. Therefore, *Dennettia tripetala* seed powder could be produced by direct compression in order to standardize this herbal drug and also improve patient compliance.

Keywords: *Dennettia tripetala*, direct compression, quality control, microcrystalline cellulose.

INTRODUCTION

Dennettia tripetala (G.) (Baker f.) G.E. Schatz (Annonaceae) (Pepper fruit), is a spicy plant, cultivated in Southern states of Nigeria and is also found in Ivory Coast and West Cameroon^{1,2}. The plant is a tropical African plant and its various parts are used in the treatment of fever, cough, it is used as anti-emetics, anti-inflammatory and antinociceptive². The leaves and fruits are used in combination with other herbs for the treatment of cough, infantile convulsion, vomiting, worm infestation and typhoid^{1,3}. *Dennettia tripetala* extracts have also been reported to exhibit insecticidal⁴, and antifungal properties⁵. It is locally called "nmimi" by the Igbo's and "Nkarika" by the Efiks of Nigeria⁶. The fruits of the plants have been reported to be popularly used as stimulants^{1,7,8}. The young leaves and fruits have instinctive spicy taste⁹. The mature fruits constitute the main edible portions. *Dennettia tripetala* is used as masticators, which when chewed produces unique peppery effect¹⁰. The peppery fruits of *Dennettia tripetala* are important in the diets of postpartum women, during which time it is claimed that spices and herbs aid uterine contraction^{9,11}. Okwu *et al* also reported that *D. tripetala* fruits contain important nutritive substances such as vitamins, minerals and fiber¹².

Due to an increase in the use of herbal drugs and the proven efficacy, standardization and quality control are very crucial in order to improve the quality, potency, purity, identity and efficacy of these drugs. It is estimated that today, plant materials are present in, or have provided the models for 50 % Western drugs¹³. Standardization of herbal drugs will encourage its use and also enhance patient compliance due to increase in patient acceptability.

Tablets are the most commonly used dosage form. The ease of manufacturing, convenience in administration, accurate dosing, and stability compared to oral liquids; tamper-proofness compared to capsules; and safety compared to parenteral dosage forms makes them a popular and versatile dosage form¹⁴. Considering the methods of preparation of tablets, direct compression has important advantages compared to traditional granulation methods, such as lower cost, time and energy energy, fewer unit operations, fewer stability issues for actives that are sensitive to heat or moisture, and the possibility to add fewer excipients to the formula¹⁴. Due to these advantages, tablet manufacturing by direct compression has increased steadily over the last years¹⁴. The aim of the work is to formulate *Dennettia tripetala* seed tablets by direct compression and to evaluate the *in vitro* properties of the tablets.

MATERIALS AND METHODS

Collection and authentication of plant

The *Dennettia tripetala* seeds were purchased from Ibagwa market in Nsukka, Enugu state, Nigeria in the month of June, 2012. The plant material had earlier been authenticated by Mr. A.O. Ozioko, a consultant taxonomist with the International Center for Ethnomedicine and Drug Development (InterCEDD) Nsukka. The voucher specimen of the plant studied was deposited in the herbarium of the Department of Pharmacognosy and Environmental Medicines, University of Nigeria, Nsukka.

Chemicals

Microcrystalline cellulose (FMC Corp., American Viscose Division, Pennsylvania, USA), Ac-di-sol (Sheffied Chemicals

Ltd., USA), stearic acid (Merck Darmstadt, Germany), sodium chloride, hydrochloric acid (BDH, Poole, England) and distilled water (UNN Water Resources, Nigeria). All chemicals used were of analytical grade and used as supplied without further purification.

Processing of *Dennettia tripetala* Seed powder

Dennettia tripetala seeds were steeped in water for 24 h to loosen the bark. After dehulling, the seeds were washed three times with clean water and dried under a shed (below 40°C for three days). The dried seeds were milled using a hammer mill (500# grinder/Fuyu Metal, Linyi Fuyu Metal Products Co., Ltd, China) and thereafter, passed through 52 mm sieve (Turgens & Co., Germany).

Preparation of tablets

The tablets were prepared by direct compression; details of tablets composition are given in Table 1. *Dennettia tripetala* powder was mixed with microcrystalline cellulose used as the filler-binder (10 %) and Ac-di-sol (disintegrant) in a tumbler mixer. The powder mix was lubricated with stearic acid and tablets were prepared by compressing the lubricated powder at 46-48 kgf using a 9.0 mm punch and die set fitted into an automated F3 Manesty Single Punch tableting machine^{15, 16}.

Table 1: Composition of *Dennettia tripetala* tablets

Material	Quantity/tablet(mg)
<i>D. tripetala</i> powder	250.0
Microcrystalline cellulose	30.0
Ac-di-sol	17.0
Stearic acid	3.0

Evaluation of tablets

Uniformity of weight

Weight variation was carried out according to the BP 2009 methods¹⁷. The tablets were weighed individually, using an electronic balance (Ohaus Adventurer, China) and the mean weight, standard deviation and percentage deviation were calculated.

Tablet friability test

Friability test was performed using Erweka friabilator (Erweka GmbH, Germany). Twenty tablets were randomly selected from each batch of the tablets, dedusted and weighed. The tablets were placed into the drum of the friabilator and rotated at 25 rpm for 4 min. The tablets were dedusted and reweighed. The friability loss was calculated using equation 1:

$$\text{Friability loss (\%)} = 100 \left[\frac{W_0 - W}{W_0} \right] \quad (1)$$

where W_0 and W are the initial and final weights of the tablets respectively¹⁷.

Hardness/crushing strength test

This test was carried out using Monsanto hardness tester (Manesty, England). Ten tablets from each batch were randomly selected. Each tablet was placed between the jaws of the hardness tester and force was applied by adjusting the knob of tester until the tablet braked diametrically.

Disintegration time test

The Erweka ZT 120 basket and rack assembly was employed in the study, 0.1 N Hydrochloric acid maintained at $37.0 \pm 1.0^\circ\text{C}$ was used as the disintegration medium. Ten tablets from each batch were used for the test and the procedure being as stipulated in the BP¹⁷.

In vitro release studies

Beer's plot was obtained for *Dennettia tripetala* seed crude extract in simulated gastric fluid (SGF) (pH, 1.2) at concentration range of 0.1 to 1.0 mg% at a predetermined wavelength of 284 nm. The *in vitro* dissolution profile for *Dennettia tripetala* tablets was determined using the paddle method (Erweka DT 600, Germany). The dissolution medium consisted of 900 ml of freshly prepared SGF (pH, 1.2) maintained at $37 \pm 1^\circ\text{C}$. The tablet was placed inside a tightly secured basket and the basket was placed in the bottom of the beaker. The paddle was rotated at 100 rpm. About 5 ml sample was withdrawn from the dissolution medium at 2, 5, 10, 15 and 20 min intervals, filtered (Whatman No. 1) and an aliquot of the filtrate was assayed using spectrophotometer (Jenway 6305, UK) at 284 nm. An equal volume of the withdrawn sample was replaced with a fresh medium to maintain sink condition. The amount of drug released at each time interval was determined with reference to Beer's plot for the drug.

Statistical analysis

Data were analyzed using SPSS Version 16.0 (SPSS Inc. Chicago, IL, USA). Data were analysed by one-way ANOVA. Differences between means were assessed using student's t-test. $P < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Dimensional properties of tablets

The results of dimensional properties of tablets shown in Table 2 showed that the tablets exhibited stable thickness and diameter with little variations as depicted by the values of coefficient of variation. The tablets exhibited thickness of 4.25 ± 4.03 mm and diameter of 10.13 ± 0.25 mm. The low coefficient of variation of dimensional properties attests to the reproducibility of the formulation.

Tablets weight uniformity

The results of tablets weight uniformity presented in Table 2 showed that the tablets passed the test for uniformity of weight with percentage deviations not more

than 5 %. According to BP specifications, tablets weight \geq 250 mg should have percentage deviations not greater than 5 %¹⁷. Tablets weight uniformity test is important because variation in tablet weight causes variation in active ingredient content and variability in the bioavailability of the drug.

Table 2: Properties of *Dennettia tripetala* tablets

Tablet weight (mg \pm CV)*	306.00 \pm 4.96
Thickness (mm \pm CV)*	4.25 \pm 4.03
Diameter (mm \pm CV)*	10.13 \pm 0.25
Hardness (kgf \pm CV) [†]	2.14 \pm 7.09
Friability (% \pm CV)*	0.30 \pm 0.08
Disintegration time (min \pm CV) [†]	1.60 \pm 16.40

*Mean for 20 tablets, [†]Mean for 10 tablets, CV: coefficient of variation

Hardness/crushing strength of tablets

The results of tablets hardness are shown in Table 2 and the results indicate that the tablets had crushing strength of 2.14 \pm 7.09 kgf. However, the BP specified a range between 5 to 8 kgf for tablets hardness. The results therefore, showed that the tablets failed the crushing strength test. However, this could be due to the method adopted in the formulation of tablets.

Tablets friability

The results of tablets friability tests also shown in Table 2 revealed that the tablets passed the friability test with percent friability loss of 0.3 %. The results showed that though the tablets had poor hardness, the friability of the tablets was not compromised by this. The BP stipulates that tablets formulated by direct compression should have percent friability loss of \leq 2 %¹⁷. The results therefore, confirmed that the tablets could withstand stress, vibrations and shock during handling, packaging, transportation and use without braking.

Disintegration time

The disintegration time of *Dennettia tripetala* tablets also shown in Table 2 showed that the tablets exhibited fast disintegration within 1.60 \pm 16.40 min. The fast disintegration exhibited by these tablets may be due to the method employed during tablets production, direct compression enhances the disintegration time of tablets. The tablets therefore, complied with BP specifications for a normal release tablet of \leq 15 min¹⁷. Disintegration is central to bioavailability because for the drug to be absorbed, the tablet must first disintegrate in order to make the drug available for absorption.

Dissolution profile

The results of the release profile of *Dennettia tripetala* seed from tablets are shown in Fig. 1. The results showed that the tablets exhibited fast release of the drug characteristic of direct compression tablets. The results showed $T_{62.5\%}$, $T_{71.3\%}$, $T_{72.0\%}$ and $T_{91.3\%}$ release of crud drug at 2, 5, 20 and 30 min respectively. According to US-

FDA guideline, immediate release drug products should release 85 % ($T_{85\%}$) of labeled amount of drug within 30 min of study¹⁸. Therefore, the tablets exhibited good drug release properties as normal release tablets.

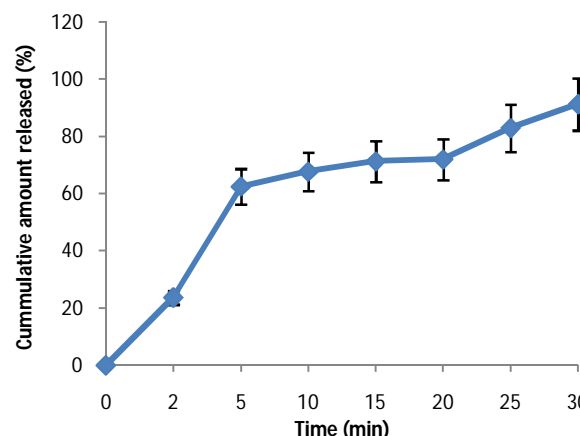


Figure 1: Release profile of *Dennettia tripetala* seed tablets formulated by direct compression

CONCLUSION

Dennettia tripetala tablets were successfully formulated by direct compression using microcrystalline cellulose as the filler binder. The tablets passed the weight uniformity and friability test. The results showed that the disintegration and the dissolution time of tablets were enhanced by direct compression hence, the tablets exhibited fast disintegration and dissolution of the herbal drug. However, further research into the formulation of this plant material is required in order to improve patient acceptability and hence compliance to the use of this herbal drug.

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Source of Support: Nil, Conflict of Interest: None.

