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FORMULATION OF TABLETS OF *Xylopia parviflora* Benth (ANNONACEAE) LEAVES-A POTENTIAL ANTIMALARIAL DRUG

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Abstract
Xylopia species are widely available in West Africa. *Xylopia parviflora (Benth)* plant is used in folk medicine in the management of a number of ailments, one of these is the use of the leaves in the treatment of malaria fever for which a number of patients have reported its beneficial effects. This study was designed to investigate the possibility of formulating the dried leaves of *Xylopia parviflora (Benth)* into tablets for convenience of administration and consistency of dose. The powdered dried leaves were granulated using three binding agents gelatin, maize starch, and polyvinyl pyrrolidone (PVP). The granules were evaluated for size distribution, moisture content and flow properties while the tablets were tested for hardness, friability, disintegration and dissolution. Results show that the flow properties of all batches of granules are good. The tablets met pharmacopoeial requirement for weight uniformity, disintegration time and dissolution rate. But formulations containing PVP possessed poor disintegration and dissolution properties. *Xylopia parviflora* leaves a potential anti malarial drug can thus be formulated into tablets. Good tablets are obtained when gelatin or maize starch at 0.4% is employed as a binder.

Keywords: *Xyopia parviflora leaves; formulation; tablets*

INTRODUCTION

Xylopia parviflora (Benth) (family Annonaceae) is a shrub or small tree of 0.17 m high in fringing forest and savanna zones from Senegal to Southern Nigeria and into the Sudan, Uganda and Angola. The bark is fibrous from which a cordage is made. In the casamance, an aqueous decoction of equal parts of roots and leaves is taken by mouth as a bechic and expectorant (Burkill, 1985). The leaves of the plant have been used by a herbalist in Babale of Jos North L.G.A Plateau State, Nigeria to successfully manage clinically diagnosed cases of malaria fever (Azija, 1998). Anti-malarial evaluation in confirmed cases showed clearance of parasitaemia after 5-7 days treatment. Results of these are documented in the Department of Pharmacology, University of Jos, Nigeria. The plant has demonstrated some other pharmacological activities (Bukar *et al*., 2005).

Since it is known that it is a medicine and not a drug that a patient receives in the treatment of an illness (Kunle, *et al*., 1998), it is almost always necessary to formulate drugs into suitable dosage forms. The objective of this work, therefore, is to formulate a herbal anti-malarial drug, *Xylopia parviflora* (Benth) powdered leaves, into tablets which are the most common and convenient dosage form.

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Different binders-gelatin, maize starch and PVP were used along with the other excipients to formulate the tablets. Based on the properties of the granules and tablets produced, the most suitable formulation was suggested.

MATERIALS

The following materials were used: Maize starch BP, gelatin powder and polyvinyl pyrrolidone (BDH chemicals England), Magnesium stearate (Boots Co. Ltd England), lactose (Hopkin and William Ltd Switzerland). The *Xylopia parviflora* leaves were obtained from a local forest in Jos

METHODS

Preparation of granules

A 100 mg of fine powder of *Xylopia parviflora* (Benth) leaves was mixed with intra-granular disintegrant (Table 1). Pre-determined quantities of the granulating liquids were then added and mixing was done in a porcelain mortar using a pestle. The granulating solution was 10%w/v solution of gelatin, maize starch or PVP. Screening of the wet mass was on sieve No. 10. The wet mass was dried in a hot air oven at 60°C and the dried granules were then passed through a sieve No. 60. The magnesium stearate (Table 1) was added to the granules and mixed for 5 minutes in a tumbling mixer at low speed.

In the 3 batches of granules made, lactose was used as bulking agent.

Determination of granule properties

i Bulk and tapped density of granules

This was carried out by measuring the volume occupied by a 20g of the granules in a dry 100 ml-glass cylinder. The bulk density was calculated from the formula.

$$\text{Bulk density} = \frac{\text{weight of granules}}{\text{Volume of granules}} \quad (1)$$

The cylinder was tapped until a constant volume result. The tapped density was calculated as

$$\text{Tapped density} = \frac{\text{weight of granules}}{\text{Tapped volume of granules}} \quad (2)$$

ii Percentage compressibility

This was calculated using the formula

$$\%\ Cp = \frac{\text{tapped density-bulk density}}{\text{Tapped density}} \times 100 \quad (3)$$

Cp=Compressbility

iii Angle of Repose

A glass funnel was clamped on a retort stand such that it is over a sheet of paper spread on a flat laboratory bench. The granules were gently poured through the funnel onto the sheet of paper on which they formed a conical heap. The height and diameter of the cone were measured. The angle of repose ɵ was calculated from the relationship.

$$\tan \theta = \frac{\text{height of cone}}{\text{radius of cone}} \quad (4)$$

iv Granule friability

A 5 g quantity of granules that were retained on the sieve No. 16 were used for this test. The granules were later subjected to friability test using a Roche friabilator at 25 rpm for four minutes. The weight of the granules that were retained on the sieve after the test was determined. The granule friability was calculated from the equation

$$\text{Friability} = \frac{\text{weight loss after test}}{\text{weight before test}} \times 100 \quad (5)$$

Compression of tablets

The granule mix was compressed into tablets of target weight of 500±5 mg in a single punch machine (Eagle scientific machine, England). The machine was fitted with 12.5 mm flat-faced punch and dies set. The compression pressure was 5 stretches according to the calibration on the machine. The machine speed was set to 100 tablets per minute. The tablets were stored in airtight bottles for 24 hours before evaluation.

Determination of tablet properties

i. Uniformity of thickness and diameter

The thickness and diameter of the tablets were measured with vernier calipers. The mean value of six determinations was recorded in each case.

ii Uniformity of weight

Twenty tablets were randomly selected from each batch. They were first weighed together and then individually on a mettler balance. The mean weight of the tablets was then calculated and the standard deviation determined.

iii Tablet hardness

Six tablets were randomly selected from each batch. Each of these was in turn placed between the anvil and the spindle of the Monsanto hardness tester and subjected to increasing pressure by turning the Knurled Knob in a clock-wise direction and in as uniform a manner as possible until the tablet was crushed. The unit on the scale where the pointer rested and which corresponded with the pressure required to break the tablet was noted. The mean of six determinations was taken for each batch.

iv Tablet friability

The Roche friabilator was used. Ten tablets were selected from each batch of tablets at random, weighed on mettler balance and placed in the drum of the friabilator. The machine was set for the drum to rotate at a constant rate of 25 rpm and for a period of 4 minutes. Thereafter, the intact tablets were removed from the drum, dusted and weighed. The percentage loss of weight was calculated and recorded as friability value for that batch.

v Disintegration time

The BP (1980) method was used. Six tablets were randomly selected from each batch and placed in the rack of six glass cylinders of the tablet disintegration apparatus such that each cylinder contained only one tablet. The rack of cylinders containing the tablets was raised and lowered at a constant rate in water contained in the glass jar suspended in water bath with temperature thermodynamically maintained at $37\pm0.5^{o}C$. The apparatus was operated for one hour and the time taken for the tablet to completely disintegrate was recorded as the disintegration time for the batch of tablets under investigation. An average of five determinations was taken.

vi Dissolution Rate

The Erweka dissolution rate testing apparatus was used to monitor the dissolution time. The U.S.P type 2 method was applied at a stirring speed of l00 rpm. The medium was 900 ml of distilled water. One tablet from each batch was placed in the medium, where temperature was thermostatically maintained at $37\pm0.5^{o}C$. Samples were withdrawn at specified time intervals. The amount of drug dissolved at each time was determined using a shimadzu spectro photometer (UV-160 A) at λ max 176 nm. Filtered cold water extract of *Xylopia parvioflora (Benth)* leaf powder was used to prepare the standard solutions.

Table 1: Tablet Composition (Quantities per tablet in mg)

	A	*B*	*C*
Xylopia powder	100	100	100
Gelatin	2.3	-	-
Maize starch (paste)	-	2.3	-
PVP	-	-	2.9
Maize starch	11.5	11.5	11.6
Magnesium stearate	1.2	1.2	1.2
Lactose	385	385	384.2

RESULTS AND DISCUSSION

Table 2: Granule Properties

	A	*B*	*C*
Colour	Pale green	Pale Green	Pale green
% moisture content	2.08	2.30	2.36
Bulk density (g/ml)	0.539	0.518	0.561
Tapped density (g/ml)	0.605	0.589	0.675
True density (g/ml)	2.14	2.04	2.24
Angle of Repose	32.17	28.89	32.81
Granule friability (%)	4.6	4.72	18.48
Percent porosity	10.91	12.05	16.89

Table 3: Physical Properties of Tablets

	A	*B*	*C*
Colour	Light Green	Light Green	Light Green
Average weight (mg)	0.49	0.49	0.50
Hardness kg/f	4.5	4.5	4.5
Friability %	0.21	0.14	0.16
% porosity	42.52	44.18	45.98
Disintegration time (min)	11min	3min 20sec	16min 30sec.

Table 1 shows the various ingredients used and their quantities in the different formulations. The disintegrant (maize starch) was added intragranularly (ie in between the other ingredients) to ensure rapid and complete disintegration of the tablets. Based on their angles of repose and percentage compressibility values; all the formulations had good flow properties (Table 2). The angle of repose is a measure of the ease with which particles are able to flow over each other. This affects either the height of the heap, its diameter or both. High values such as between 54-59% (Okhamafe *et al.,* 1991) therefore, indicate poor flow of particles. Materials studied have relatively low values of 32.17, 28.89 and 32.81 for gelatin, maize starch and PVP respectively They are therefore, considered to have good flow properties.

In terms of granule size, the ranking order was PVP greater than gelatin and greater than maize starch (C>A>B). Excessively, large particle flow poorly because they tend to get in each other's way and lack the glidant action imparted by fines.

Formulation C (PVP as binder) produced the most friable granules, followed by formulation B and A (Table 2). The PVP binder solution was the least viscous of the three binders. This might explain the high friability of

the granules produced since viscosity is known to directly affect binding capacity up to a limit (Kunle and Bangudu, 1990). Gelatin on the other hand, was the most viscous of the binders used. The relatively high friability of its granules might be due to poor distribution of the granulating liquid, thereby resulting to some over-wet areas while other parts might have insufficient binder.

All the formulations had good physical strength as indicated by the hardness and friability results (Table 3). Hardness values greater than 3 kg/f are considered suitable for tablets of 1.26 cm diameter. The friability ranking order was gelatin greater than PVP and greater than maize starch (A>C>B). These batches may surely withstand handling ability, such a tablet is considered to have suitable friability properties with ability to withstand handling if it has a percentage loss of less than I percent (Kunle *et al.,* 1998).

The percent porosity is a measure of the number and/or size of the pores in a compact. (Kunle *et al.,* 1998) It is important because it is thought that the disintegration or dissolution medium penetrates the compact through these pores. It would therefore, be expected that percent porosity will be inversely related to the disintegration time. Formulation C had the highest porosity, probably because of its large granule size followed by A and B respectively (Table 3). However, formulation A and B passed the disintegration test (Table 3) since the BP specifies that the tablet must completely disintegrate within 15 minutes. As expected from the porosity results, formulation B, which had a higher percent porosity than formulation A had a shorter disintegration time.

Formulation C that had the highest percent porosity had the longest disintegration time of more that 16 minutes. At the binder concentration used, it may be too high for this particular formulation. Since the range is 1-5%, a concentration lower than 2.5% could be employed.

The dissolution rate profiles of the various formulations are shown in figure 1. None of the formulations was able to release more than 60% of its drug content within the one-hour period. This is thought to be because the amount of drug released was calculated first by determining the amount of extract present in each tablet and then the results used as a basis to calculate the amount of drug release with time for each batch. The relationship between the different formulation with respect to the dissolution rate was the same as obtained for disintegration time of the tablet (Fig 1). Formulation C (with PVP) had the poorest dissolution characteristic while formulation A and B (gelatin and starch) were similar with B better in cold water medium. These results show that the faster the disintegration, the better the dissolution of tablets.

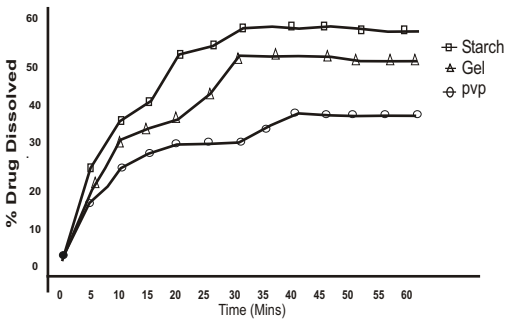

Fig 1. Dissolution rate profile of *Xylopia parviflora* tablets formulation

Conclusion

Based on the work carried out, it can be concluded that tablets can be formulated from *Xylopia parviflora* (Benth) leaves using wet granulation method of massing and screening. The granule properties were found to have suitable properties for tabletting. All the tablets produced had suitable physical characteristics and passed the BP weight variation test. However while the formulations with gelatin and starch passed the disintegration test, that with PVP did not at the concentration used. Although none of the formulations released more than 60% of the drugs, a direct relationship was found between disintegration and dissolution times.

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