Research Article

Formulation and Evaluation of A New Herbal Tablet from the Stem Bark of *Enatia Chlorantha*

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ABSTRACT

A study was made of the characterization and formulation of stem bark of *Enantia chlorantha* into tablet dosage form. Compacts of powdered stem bark of *Enantia chlorantha* was made with gelatin and polyvinylpyrollidone (PVP) binders; and microcrystalline cellulose and cornstarch disintegrants using direct compression method. The mechanical properties of the tablets were assessed using crushing strength and friability and the crushing strength - friability ratio (CSFR) while drug release properties were evaluated using disintegration and dissolution times. *Enantia chlorantha* powder possesses good flow properties. It had the least densification compared to cornstarch and cellulose; and it is more porous. It also possesses a relatively high bulk density Tablets formulated with PVP had better mechanical strength than those containing gelatin and the mechanical properties of the tablets were affected by the type and concentration of the binder used. Tablets containing gelatin had lower disintegration times than those formulated with cornstarch. Tablets containing 7.5% w/w PVP binder and cornstarch had the best release profile with T_{50} at 60 seconds and T_{90} at 19 minutes. Results suggest that *Enantia chlorantha* bark could be formulated into tablet with good mechanical properties and acceptable release profile.

Keywords: *Enantia chlorantha*, binder, Physicochemical properties, Mechanical properties, Drug release profile.

INTRODUCTION

Enantia chlorantha Oliv [Annonaceae] is an ornamental tree of up to 30 m high, with dense foliage and spreading crown. It is widely distributed along the coasts of West and Central Africa and the Democratic Republic of Congo. This fair-sized forest tree, usually growing in dense shade, may be readily recognized by the bright yellow slash and conspicuous black fruits. The bark fissured geometrically and the outer bark is thin and dark brown; the inner bark is light brown above and pale cream beneath. The stem is fluted and aromatic while the leaves are elliptical in shape[1]. The possible use of the plant in conditions such as rickettsia fever, typhoid fever and infective hepatitis or jaundice has been reported[2]. The active principles have been implicated to be alkaloid berberine (jatrorrhizine and Palmatine), saponins, glycosides and tannin.

Herb is a plant or plant part used for it scent, flavor or therapeutic properties. Herbal medicine products are dietary supplement that people take to improve their health. Many herbs have been used for a long time for claimed health benefits. They are sold as extracts and fresh or dried plants parts[3]. There is a public belief that herbal treatments are safe because they are natural and harmless compared to conventional medicines. Supporters of herbal medicine claim that herbs may both treat and prevent disease[4]. Moreover, herbal products are often free from rigorous regulations and prescriptions are usually not required for these inexpensive products. In spite of their efficacy, herbal medicinal products have been widely criticized due to a lack of standardization and poor quality presentation.

Formulation into tablet dosage form would confer into it many good properties of tablet like ease of administration, greater acceptance due to presentation, prolonged shelf life, greater accuracy in dispensing and reduction in transportation cost arising from formulation into less bulky form. Hence, the objective of the present study is to produce conventional tablets from the stem bark of *Enatia chloranthia* powder for oral administration using direct compression method. The mechanical properties of the tablets were assessed using crushing strength and friability; while the drug release properties were evaluated using disintegration and dissolution times

MATERIALS AND METHODS

The materials used were Corn starch, microcrystalline cellulose, gelatin (BDH chemicals, UK), Polyvinylpyrollidone (PVP) (30,000 Merck, Germany), Lactose (DMV Veghel, Netherlands), magnesium stearate (Hopkin and Williams, UK). The stem bark of *Enantia chlorantha* was purchased from herbal wholesalers at Falawo Market in Sagamu, Ogun state, Nigeria and authenticated at the Department of Botany, University of Ibadan, Nigeria.

Preparation of *Enantia Chlorantia* powder

A 5.0kg weight of fresh *Enantia chlorantha* bark was weighed and spread in the sun for two weeks. The sun drying was done between 9:00hrs and 16:00hrs daily. The average temperature during this period was 33^0C and the relative humidity was 67 %. The sun dried bark was then crushed in a mortar and pestle and then pulverized in an Eurosonic SE-248 blender (UK) to produce powdered *Enantia chlorantha*.

Physicochemical characterization of *Enantia chlorantha*

The following physicochemical parameters were determined on the *Enantia chlorantha* powder.

Moisture content determination

Moisture content of the *Enantia chlorantha* was determined by weighing 10g of the powder in an evaporating dish. This was then dried in the oven at 105^{0}C for 5 hours and the final weight was noted. The percentage weight loss was calculated.

Determination of bulk density and tap density

A 20g of the powder was passed through a 1.00mm mesh screen so as to break up clogs that had been formed during storage. This was then poured carefully into a 100ml cylinder. The apparent volume was determined from the height (h) of the powder bed and the internal radius of the cylinder. The tap density was determined by tapping the measuring cylinder 300 times and recording the new volume occupied by the power.

Particle density determination

The particle density of the *Enantia chlorantha* powder was determined by the pycnometer method using liquid immersion technique with benzene as the displacement liquid. A 50ml pycnometer bottle was weighed when empty (W). It was filled with benzene to the brim till over flows and the excess was wiped off the bottle and the content with the bottle were weighed (W_1). The difference between the two weights was then calculated (W_2). A 2g (W_3) quantity of the *Enantia chlorantha* powder was weighed and transferred into the pycnometer bottle. The excess solvent was wiped off and the bottle weighed again (W_4). The particle density was calculated using the formula:

$$\rho = \frac{W_2 . W_3}{50 (W_1+W_3-W_4)} \quad \text{.....(1)}$$

Angle of Repose determination

The angle of repose was determined using the method adapted by Iwuagwu and Onyekwelli[5]. A short hollow tube was fitted over a flat base whose external dimension was the same as the internal dimension of the tube. A fixed weight of the Okra powder was placed in the tube which was then raised slowly to leave a conical heap behind on the base. The angle of repose was calculated from the geometry of the heap of powder using the equation below:

$$\text{Tan } \theta = 2h/D \quad \text{..... (2)}$$

where h is the height of the heap of powder, D is diameter of the heap of powder and θ is the angle made by the heap with the base

Powder porosity determination

The porosity of the powder was determined using bulk and true densities data using the equation:

$$e = 1 - \text{bulk density/true density} \quad \text{.....(3)}$$

Preparation of Tablets

Three hundred (300) mg of the each of the powders were compressed for thirty seconds into tablet with pre-determined loads using a hydraulic hand press (Model C, Carver Inc., Menomomee Falls, WJ). Before each compression, the die (12.5 mm in diameter) and the flat faced punches were lubricated with a 2 % w/w dispersion of magnesium stearate in 96 % ethanol. After ejection, the tablets were stored over silica gel for 24 hrs to allow for elastic recovery and hardening and to prevent false low yield values.

Determination of uniformity of Weight

Ten tablets were selected randomly from each batch and weighed individually in other to determine the average weight and the weight variation of each tablets from the average weight. The standard deviation and coefficient of variation was also determined statistically.

Crushing strength and Friability Tests

The load required to diametrically break each tablet (crushing strength, CS) was determined using a Monsanto Hardness tester. The friability (F) of the tablets were determined using a friabilator (Veego scientific device, Mumbai, India) operated at 25 revolutions per minute for 4 minutes

Tablet disintegration test

The disintegration times of the tablets were determined in distilled water at 37^{o}C using a BP Manesty disintegration unit (Manesty Machines, Poole, UK. Six tablets from each formulation were placed on the wire mesh just above the surface of the distilled water in the tube and the apparatus was started simultaneously. The time at which each tablet disintegrated completely was observed and recorded. Determinations were made in triplicate and the mean time was recorded.

Tablet dissolution rate test.

The rate of dissolution was studied in a rotating basket BP Apparatus II[6] operated at 100 rpm using a Veego Digital tablet dissolution test Apparatus (Veego, India). The dissolution medium was 900 mL of 0.1 N hydrochloric acid at 37$\pm$ 0.5^{o}C. Five (5 mL) samples were withdrawn at specified time intervals and immediately replaced with 5 mL samples of fresh 0.1N hydrochloric acid maintained at the same temperature. The amount of drug in each sample was analysed spectrophotometrically at 245 nm on a SP6-450 UV/VIS spectrophotometer (Pye Unicam, Middlesex, England). Determinations were made in triplicate.

RESULTS

Table 1 gives values for the various physicochemical parameters of *Enantia chlorantha*, microcrystalline cellulose and cornstarch. *Enantia chlorantha* had higher moisture content and density values compared to

microcrystalline cellulose (MCC) and cornstarch (CS) but the angle of repose is lower.

Table 1: Physicochemical properties of powder samples

Parameters	*Enathia chlorantha*	Microcrystalline cellulose	Corn starch
Moisture content (%)	10.60	4.00	2.00
Particle density(g /cm^3)	1.5418	0.2930	0.2650
Bulk density (g/cm^3)	0.3714	0.2777	0.2439
Tapped density (g/cm^3)	0.5435	0.4347	0.5555
Hausner's ratio	1.50	1.57	2.28
Carr's index (%)	31.50	36.10	56.09
Angle of repose (θ^0)	36.00	45.00	39.80
Powder porosity (%)	76.00	47.90	79.50

Table 2: Statistical data on weight variation

Binder (Disintegrant)	Concentration (%)	Mean tablet Weight (g)	Standard deviation	Coefficient of variance
Gelatin (CS)	0	0.301	0.0053	0.018
	2.5	0.300	0.0062	0.021
	5.0	0.301	0.0051	0.017
	7.5	0.305	0.0058	0.019
	10	0.301	0.0040	0.013
Gelatin (MCC)	0	0.295	0.0089	0.030
	2.5	0.299	0.0051	0.017
	5.0	0.301	0.0050	0.017
	7.5	0.298	0.0056	0.019
	10	0.296	0.016	0.054
PVP (CS)	0	0.306	0.0060	0.020
	2.5	0.302	0.0057	0.019
	5.0	0.300	0.0078	0.026
	7.5	0.302	0.0028	0.009
	10	0.301	0.0037	0.012
PVP (MCC)	0	0.305	0.0061	0.020
	2.5	0.296	0.010	0.033
	5.0	0.300	0.0071	0.024
	7.5	0.303	0.0070	0.023
	10	0.299	0.0058	0.019

PVP- Polyvinylpyrollidone, MCC- Microcrystalline cellulose, CS- cornstarch

Table 3: Effect of binder type and concentration on the crushing strength, friability, crushing strength- friability ratio of *Enatia chlorathia* tablets prepared by direct compression using cornstarch and microcrystalline cellulose disintegrant

Binder (Disintegrant)	Binder conc (% w/w)	Crushing Strength (N)	Friability (%)	CSFR
PVP (CS)	0.0	90.80	0.66	137.58
	2.5	94.40	0.47	200.85
	5.0	111.50	0.41	271.95
	7.5	113.80	0.27	421.48
	10	115.60	0.27	428.15
Gelatin (CS)	0.0	75.60	0.58	130.35
	2.5	76.40	0.38	201.05
	5.0	80.80	0.36	224.44
	7.5	84.90	0.26	326.54
	10.0	89.20	0.21	424.76
PVP (MCC)	0.0	74.1	0.72	102.92
	2.5	101.4	0.67	151.34
	5.0	105.3	0.62	169.84
	7.5	110.2	0.47	234.47
	10	95.5	0.23	234.46
Gelatin (MCC)	0.0	75.8	1.28	59.2
	2.5	76.1	0.86	88.49
	5.0	76.5	0.54	141.67
	7.5	85.5	0.39	219.23

	10.0	88.6	0.23	385.22

Table 2 shows the result of weight uniformity test. None of the tablets varied by more than 1 % of the mean tablet weight. This implies that all the tablets conform to the official standard. The result of the mechanical properties of the tablets formulated with different binders and binder concentrations are presented in Table 3.

The result indicates that the crushing strength increases with increased concentration of the binder. The ranking for the crushing strength values was PVP>Gelatin for all the tablets irrespective of the type of disintegrant that was used. All the tablets formulated had friability values less than 1% except for tablets without binder and tablets containing microcrystalline cellulose disintegrant. The CSFR values also increased generally with increased binder concentration. The ranking for CSFR was PVP>Gelatin

The drug release properties are characterized by disintegration and dissolution times. The amount of drug released was plotted against time and representative plots are presented in Figure 1.

The dissolution times (T_{50} andT_{90}- time taken for 50% and 80% drug release respectively) were obtained from the dissolution profile. The dissolution parameters are presented in Table 4. Disintegration time increased with increased binder concentrations for the two binders employed. The disintegration time for tablets formulated with gelatin binder (when either cornstarch or microcrystalline cellulose was used as disintegrant) was relatively lower than those containing PVP. Tablets containing the binders at concentration of 10 %w/w had the least disintegration time when microcrystalline cellulose was employed as the disintegrant. Tablets containing cornstarch disintegrant had significantly lower disintegration time than microcrystalline cellulose.

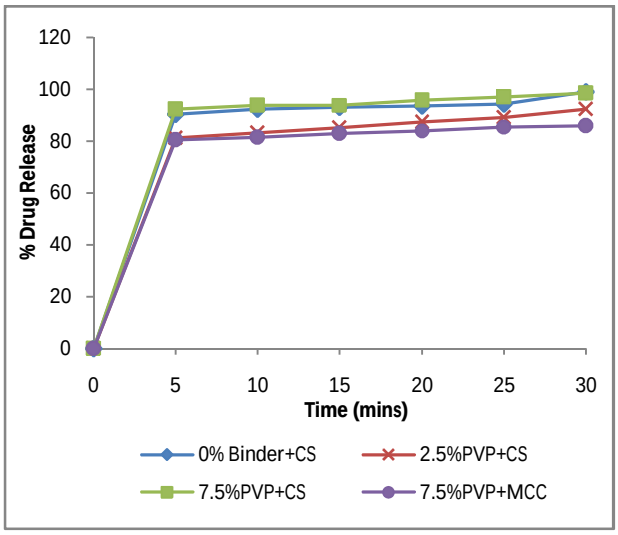

Figure 1: Drug release profile of *Enantia chlorathia*

Table 4: Disintegration (DT) and Dissolution times (t_{50}, t_{80}) of *Enatia chlorathia* tablets prepared by direct compression

Binder (Disintegrant)	Binder conc. (% w/w)	DT (min)	t_{50} (min)	t_{90} (min)
PVP (CS)	0.0	7.50	0.67	18.69
	2.5	13.00	2.64	22.32
	5.0	19.67	25.79	60.90
	7.5	31.67	1.02	19.30
	10	35.0	21.46	55.70
Gelatin (CS)	0.0	6.00	5.40	27.70
	2.5	14.30	31.18	65.51
	5.0	15.20	34.34	74.06
	7.5	22.33	28.49	64.63
	10.0	25.33	4.63	23.86
PVP (MCC)	0.0	28.67	2.11	21.55
	2.5	31.67	5.30	25.03
	5.0	46.67	6.42	27.47
	7.5	22.00	4.11	24.19
	10	8.67	3.65	24.16
Gelatin (MCC)	0.0	9.0	5.19	24.33
	2.5	10.3	32.61	72.65
	5.0	11.3	23.94	53.09
	7.5	34.67	29.43	68.19
	10.0	8.33	38.59	81.37

DISCUSSION

Physicochemical properties of *Enantia chloranthia*

The angle of repose of a powder provides an insight into the magnitude of the cohesiveness of the powder and hence its flowability[7,8]. As a general guide powders with angles of repose greater than 50^0 have unsatisfactory flow properties, whereas minimum angles close to 25^0 correspond to very good flow properties. The results in Table 1 indicate that all the powders possess good flow properties. The Hausners' ratio previews the degree of densification which could occur during tabletting. The higher the ratio, the greater the propensity of the powder to densify. *Enantia chlorantha* powder had the least densification of all the powders and it is more porous. It also possesses a relatively high bulk density which may be of advantage in tabletting because of a reduction in the fill volume of the die [9]

Assessment of tablet mean weight

A fundamental quality attribute for all pharmaceutical preparations is the requirement for a constant dose of drug between individual tablets. In practice, small variations between individual preparations are accepted and the limits for this variation appear as standards in Pharmacopoeia. The British pharmacopoeia (1998) stated that for uniformity of weight determination for tablets, tablets having an average weight of 250mg or more, not more than two tablets should deviate from the mean by greater than 5% and none of the tablets should deviate from the mean by more than 10%. From the results presented in Table 2, it shows that all the tablets conform to this pharmacopoeial standard.

Assessment of Mechanical strength of the tablets

The mechanical strength of a tablet is associated with its resistance to fracturing and attrition. An acceptable tablet must remain intact during handling at all stages, i.e. during production, packaging, warehousing, distribution, dispensing and administration by the patient. Thus, an integral part of the formulation and production of tablets is the determination of their mechanical strength which is often evaluated in terms of certain parameters such as crushing strength (CS) and friability (F) [10]. The crushing strength provides a measure of tablet strength while the friability is a measure of the tablets weakness [6, 11]. Tablets with inadequate mechanical strength may be characterized by excessive friability and variations in crushing strength which may either be too high or too low. Conventionally, tablets that lose less than 1% of their mass during the friability test are generally considered acceptable [11]. From the result in Table 3 all the tablets formulated with either gelatin or PVP binders had friability less than 1%. Increased concentration of the binders resulted in harder tablets. Furthermore, tablets containing gelatin showed the least hardness values compared to tablets containing PVP. The CSFR has been suggested as a better index of tablet quality. The CSFR values of tablets formulated with PVP were significantly higher ($p<0.01$) than those formulated with gelatin. This suggests that tablets formulated with PVP had better mechanical strength than those containing gelatin. In addition, the mechanical properties of the tablets were affected by the type and concentration of the binder used.

Assessment of tablet Release properties

The British pharmacopoeia (1998) stated that the time of disintegration of uncoated tablet should not be more than 15 minutes. At 2.5% binder concentration, all the formulations except those containing PVP binder and microcrystalline cellulose disintegrated within the official specification of 15minutes. Table 4 shows that tablets containing gelatin disintegrated faster than those formulated with PVP. Furthermore, tablets containing gelatin had lower disintegration times than those with cornstarch. Formulations containing a combination of gelatin binder and microcrystalline cellulose disintegrant had the fastest disintegration. The effect of binder concentration on the dissolution times did not follow a particular trend. However, all formulations containing microcrystalline cellulose and PVP at all concentration used had T_{50} less than 7minutes and the time taken for 90% drug dissolution (T_{90}) was less than 30minutes. However, tablets containing 7.5% w/w PVP binder and cornstarch had the best release profile with T_{50} at 60 seconds and T_{90} at 19minutes.

CONCLUSION

This study has shown that the stem bark of *Enantia chlorantha* could be formulated into tablets and the tablet properties could be controlled to obtain optimal drug release. This is the first step in the standardization of traditional remedies for use in orthodox medical practice

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