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FORMULATION OF *CROTON PENDULIFLORUS* SEED INTO TABLET DOSAGE FORM

G. C. ONUNKWO

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ABSTRACT

This paper discussed the formulation of *Croton penduliflorus* seed into a tablet dosage form and an evaluation of some of the granule and tablet properties. The powdered Croton seed was adsorbed onto maize starch and wet granulation method employed to impact flowability and compressibility. Granules properties evaluated were; angle of repose, flow rate, density, Carr's compressibility and Hausner quotient. Tablet properties evaluated were; uniformity of weight, hardness, friability and disintegration time. The angle of repose of the granules was generally lower than that of the powdered drug. Angle of repose decreased with increase in binder concentration. However, flow rate increased with an increase in binder concentration. Gelatin based tablets recorded the highest flow rate and the lowest repose angle. The tablets showed good friability/hardness profiles with exception of the tablet batches formulated with 2 %w/w PVP and acacia. The disintegration time of the tablets also varied with the binder concentration.

KEY WORDS: *Croton penduliflorus* seed, granule properties, friability, hardness and disintegration time.

INTRODUCTION

The plant kingdom constitutes the primary sources of many important drugs used in orthodox medicine. This may explain why the ancient man incorporated many herbs or medicinal plants into his armamentarium to fight against diseases of different kinds (Iwu,1982). Research and development in the field of African medicinal plants would ensure; a scientific exploration of African flora, possible formulation into acceptable dosage forms and a diversification in the sources of our medicines/reduction in our dependence on importation of drugs (Sofowora, 1979). Hence a proper exploitation of our local herbs and eventual formulation into modern pharmaceutical dosage forms could save our nation huge foreign reserves. Since at present more than 90 % of drugs manufactured and sold in Nigeria are imported (Ekwunife, 1978).

Croton penduliflorus contains croton oil, which is obtained from the seed by mechanical expression or by solvent extraction. The gut stimulating principle in *Croton penduliflorus* seed oil was isolated as white crystals (cp crystals) by a bioassay guided chromatographic procedure and identified as arachidonic acid, palmitic acid and stearic acid in approximately equimolar concentrations (Asuzu, 1987). The oil is a very drastic cathartic and is given in cases of obstinate constipation (Asuzu, Shetty, & Anika, 1985).

This paper discussed the formulation of *Croton penduliflorus* seed into a tablet dosage form and an evaluation of some of the granule and tablet properties.

Experimental

Materials

The following materials (of pharmaceutical grades) were employed as obtained from their manufacturers; maize starch, lactose (May and Baker, England); Acacia, Gelatin, Polyvinylpyrolidone (PVP), magnesium stearate (Merck, England).
Croton penduliflorus seed was purchased from the local market.

METHODS

Processing of crude drug

The seed coats of *Croton penduliflorus* were removed and the seeds dried in a hot air oven at 50 °C for 1 h. Size reduction of the seeds was accomplished using a hammer mill (Retch, Germany). The powdered seed was mixed with maize starch (1:3) to mask its oily nature and improve flow.

Preparation of Granules

Wet granulation was adopted for the preparation of croton seed granules. The formula for the production of the tablets is shown in Table I. Three binders (Gelatin, Acacia and PVP) were used at 4 concentrations (2-8 % w/w). The required quantities of croton seed powder, maize starch and lactose were mixed properly for 10 min. The required quantity of binder solution was added and mixed until a damp mass was obtained. The damp mesh was forced through sieve 1.7 mm and dried in a hot air oven at 50 °C for 1 h. The dried granules were rescreened using sieve 1.00 mm. The percent fines were determined by shaking the granules through sieve 0.25 mm mesh size. The fines was first mixed with the lubricant (1 % w/w magnesium stearate) before final blending with the rest of the granulation.

The granules were compressed into tablets using a manesty tableting machine (F_3 single punch size) set at a constant pressure of 50 units.

Evaluation of Granules

Different properties of granules such as flow rate, angle of repose, bulk density, tapped density,

G. C. Onunkwo, Department of Pharmaceutical Technology & Industrial Pharmacy, Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka, Enugu State, Nigeria.

Table 1: Some physical properties of croton seed granules formulated using different binders

Binder . Conc. (w/w %)	Flow time (Secs.)	Angle of Repose (0)	Hausner Quotient (Hq)	Carr's compressibility / (%)
PVP				
2	5.84	41.39	1.39	29.18
4	5.12	41.19	1.35	28.61
6	4.48	40.57	1.32	27.95
8	3.61	40.16	1.27	27.09
Acacia				
2	3.05	40.50	1.29	25.59
4	2.90	39.52	1.27	25.00
6	2.75	38.88	1.24	24.67
8	2.43	38.44	1.22	24.44
Gelatin				
2	2.96	39.45	1.28	25.20
4	2.80	38.88	1.25	24.88
6	2.54	38.14	1.23	24.35
8	2.27	37.62	1.20	23.75

Carr's compressibility and Hausners quotient were evaluated.

Flow Rate

The funnel method of (Carstensen & Chan 1977) was employed. A funnel of specified dimension having orifice and base diameters of 9.8 cm and 9.5 cm respectively was securely clamped to a retort stand. A clean paper was positioned directly at the base of the funnel efflux tube. A 50 g sample was introduced into the funnel while closing the efflux tube by means of a glass sheet. The glass sheet was removed and the powder allowed to fall freely under gravity. The flow rate was calculated from the relationship:

$$\text{Flow rate} = \frac{\text{Amount of powder}}{\text{Time of flow}}$$

Angle of Repose

The technique of fixed funnel, free standing cone (Parrot, 1966) was adopted using funnel of 0.8 cm and 7.5 cm in orifice and base diameters respectively. A cone was formed when a 50 g sample was allowed to flow through the funnel. The height of heap (h) was determined by means of a cathetometer (ebarbatch, Michigan). The base of the line was traced out using a pencil and its radius determined (r). The angle of repose was calculated from the following relationship:

$$\text{Tan } Q = \frac{r}{h}$$

Five measurements were made and the mean value determined.

Bulk and Tapped Densities

A 25 g quantity of sample was introduced into a 100 ml measuring cylinder. The bulk volume (V_B) was recorded. The bulk density (P_B) was calculated from the equation:

$$P_B = \frac{W}{V_B} \text{ g/ml}$$

Five measurements were made and the mean value determined.

Hausners Quotient

This was obtained from the ratio of the tapped to bulk density.

$$Hq = \frac{\ell t}{\ell B}$$

Carr's per cent Compressibility

This was derived by dividing the difference between tapped and bulk density by the tapped density and expressing the result as a percentage.

$$\% \text{ compressibility} = \frac{\ell_t - \ell_b}{\ell_t} \times \frac{100}{1}$$

Evaluation of Tablet Properties

Uniformity of Weight

Twenty (20) tablets selected from each batch were weighed individually and collectively using an electronic balance (Sautorius, Germany). The mean, standard deviation and coefficient of variation were calculated.

Hardness Test

The hardness of ten (10) tablets selected from each batch was determined using an electronic hardness tester (Erweka, England). The mean, standard deviation and coefficient of variation were calculated.

Friability Test

The Roche friabilator was used for the determination. Ten (10) tablets were weighed together in an electronic balance and subjected to shaking in the friabilator (set at 25 revolutions per min.), for 4 min. Friability was then calculated as the percentage loss in weight of the 10 tablets after shaking for 4 min.

Disintegration Time Test

The B. P. disintegration test apparatus was used. Five (5) tablets were placed in the basket of the disintegration apparatus, which makes a steady up and down movement dipping into the disintegration medium in each downward movement. The tablets were regarded as disintegrated when no particle remained above the gauze, which would not pass readily through it. This procedure was repeated five times for each batch and the mean taken.

RESULTS AND DISCUSSION

Granule Properties

The powdered croton seed was adsorbed with maize starch (3:1) and wet granulation employed to impact flowability and compressibility. The angle of repose of the granules was generally lower than that of the powdered crude drug. The angle of repose also decreased with increase in binder concentration (Table I). Gelatin based tablets recorded the lowest angle of repose while tablets formulated with PVP had the highest angle of repose. In general, the angle of repose values of the granules was all below 42 ° indicative of good flow properties (Pathirana, and Gupta, 1976).

As shown in Table 1, flow rate also increased with increase in binder concentration. Granulation perhaps increased the size of the powder particles due to adhesive bonding of the particles by the binder. Larger particles have reduced cohesive forces of attraction (Danish, and Parrot, 1977). Gelatin recorded the highest flow rate.

The Hausner quotient and Carr's compressibility properties (Table 1) also indicate good flow properties. Hausner quotient measures the interparticulate forces in operation while Carr's compressibility determines the case of inducing a powder to flow (Hausner, 1967). A Hausner quotient of about 1.2 shows good flow while Carr's compressibility of more than 24 % indicates poor flow (Ezesobo, and Pilpel, 1976).

Bulk density increased with an increase in binder concentration due to the increase in granular size. Tapped density behaved in the opposite direction. In general, bulk and tapped densities provides an insight into the packing and densification behaviors of powders. An increase from bulk to tapped densities in most powders is usually due to the displacement of air and reduction in the void volume (Chalmers, and Elworthy, 1976).

Tablet properties

Fig. 1 shows the effect of binder on the friability of croton tablets. Tablet friability increased with an increase in binder concentration. This is expected since friability is a measure of interparticulate cohesiveness and could be a measure of tablet hardness. All the batches of tablets had acceptable friability values with

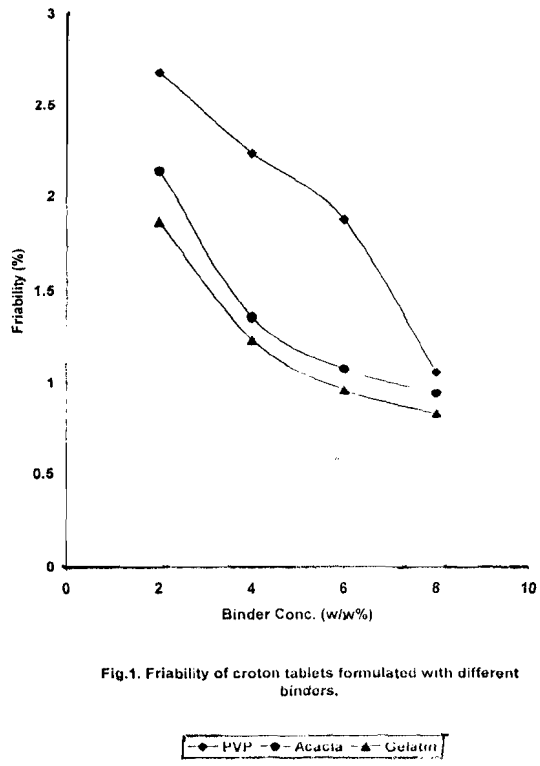

Fig.1. Friability of croton tablets formulated with different binders.

exception of the batches formulated with 2 % w/w PVP and Acacia, which recorded friability values of above 1.0 %. Gelatin based tablets had the least friability. The effect of binder on hardness of the croton tablets is illustrated in Fig. 2. As expected, hardness increased with binder concentration. It has been reported that on drying, binders form bonds between the granules. The adhesion of the binder to the granules and the strength of the bonds contribute in determining the crushing strength of the tablets (Chalmers, and Elworthy, 1976). The binders may be arranged in order of increasing tablet hardness as follows PVP < acacia < Gelatin.

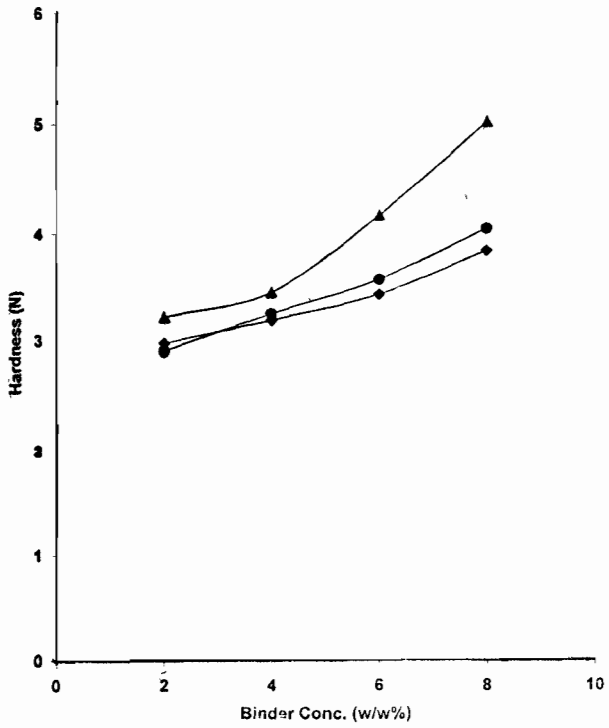

Fig.2. Hardness of croton tablets formulated with different binders.

Fig. 3 presents the effect of the binders in the disintegration time of the croton tablets. There is a direct relationship between binder concentration and disintegration time. Based on the disintegration time data, the increase in the disintegration time could be related to the binding effectiveness, which greatly retards water ingress into the tablets. For instance, tablets formulated with gelatin recorded the highest increase in disintegration time while PVP had the least. Nevertheless, all the tablet batches passed the B. P. 2001 disintegration time limit of 15 min., which show perhaps that the active ingredients will be released promptly from the dosage form. For most tablets, disintegration (breakdown of the tablet into smaller particles or granules) is the first most important step toward dissolution. It is used as a guide to the formulator in the preparation of an optimum tablet

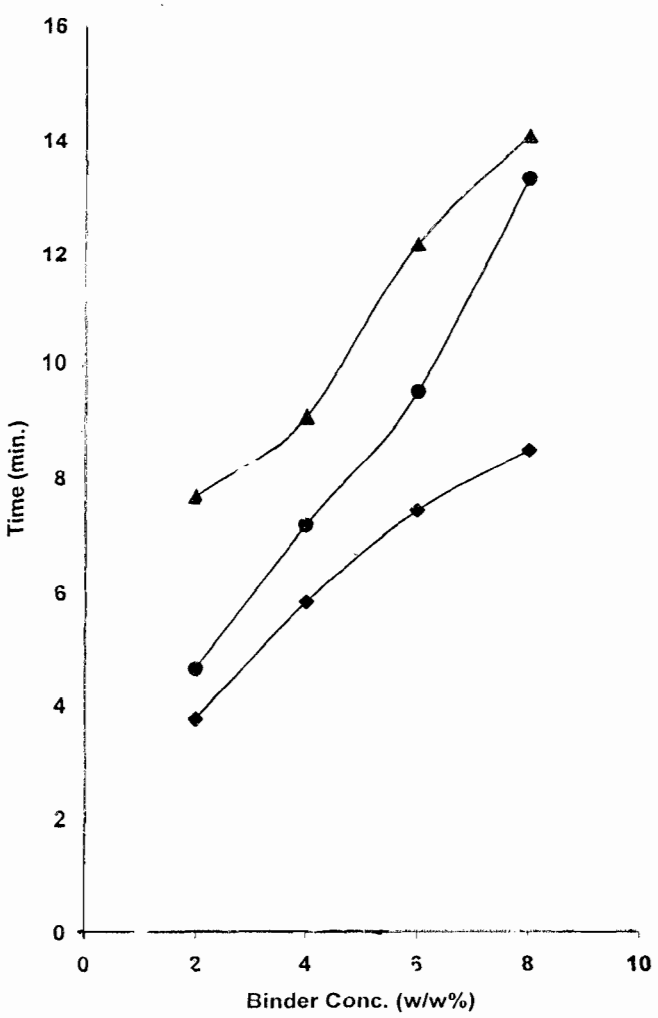

Fig.3. Disintegration time of croton tablets formulated with different binders.

formula and as an in-process control test to ensure batch-to-batch uniformity (Banker, and Anderson, 1992).

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