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PHYSICO-TECHNICAL PROPERTIES OF THE GRANULES AND TABLETS OF MICRONISED MORINGA OLEIFERA LEAF: THE EFFECT OF BINDERS

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ABSTRACT

Background: An important challenge militating against the general acceptance of herbal medicines is the formulation of appropriate dosage form that meets conventional quality standards. Thus, the objectives of this study are to formulate the micronized leaf of *Moringa oleifera* into robust tablets and evaluate the effect of some traditional binders on the quality of the tablets. **Methods:** The leaves of *M. oleifera* were micronized to a particle size < 150 µm. Granules of the powder were respectively produced using water, aqueous dispersions of acacia, and maize starch paste as binders. Various physicochemical properties of the granules such as the flow, equilibrium moisture uptake (EMU) were evaluated. The granules were respectively compressed into tablets and the quality of the tablets was evaluated by standard methods by testing the friability, disintegration time, tensile strength, and EMU of the formulated tablets. **Results:** The results showed that granules produced with aqueous dispersion of acacia as binder had higher EMU than the granules produced with water and maize starch. Tablets formulated with water as binder had higher tensile strength; similarly the disintegration time of the tablets produced with water, acacia and maize starch were all within the British Pharmacopoeia limits of acceptance. **Conclusions:** the granules of microniized leaf of *M. oleifera* prepared with water, aqueous dispersion of acacia and starch paste showed variable physicochemical

properties. On compression of the granules robust tablets that met official criteria for quality acceptance were successfully formulated with the binders.

KEYWORDS: *Moringa oleifera* leaf, herbal formulation, physico-technical properties, tablets properties, granule properties

INTRODUCTION

Herbal medicine is increasingly becoming popular because they have found success in treating certain diseases for which conventional medicines have failed. Other attributes of herbal medicines includes better tolerance and fewer side-effects, efficacy, widespread availability and low costs.[1] *Moringa oleifera* Lam. (family Moringaceae); a herb, native to South Asia, America and now found abundantly in the tropics including Nigeria has been used in the treatment of various diseases including hepatitis, hypertension, diabetes, cancer, HIV-AIDS, diarrhea, ulcer, rheumatism, anemia, alopecia and urinary tract infections. It has also been reported to be beneficial in enhancing lactation and management of several nutritional deficiencies such as obesity, scurvy, marasmus, kwashiorkor etc.[2-6]

In Nigeria, *M. oleifera* Lam is popular. The leaf is widely consumed as tea, vegetable, seasoning and a condiment in many traditional herbal recipes. This makes the formulation of herbal medicines into an acceptable dosage form important especially with the increased use of herbal medicine. However, certain factors are known to militate against the general acceptance of herbal medicines and their inclusion into primary healthcare. One of such factors relates to the difficulty in presentation of the herbal materials into convenient, effective and stable conventional dosage forms. The reason for this has been tracked to some of their intrinsic physico-technical properties such as poor flow, large volume per dose, poor compactibility, disintegration and dissolution.

The formulation of *M. oliefera* leaf into conventional tablet is to make available a simple, convenient and conventional dosage form that is elegant, easy to handle, dispense and use by the patient. It also affords other primary advantages of tablets such as maintenance of physical and chemical stability, easy identification and low cost of production.

Tablets often contain other excipients apart from the active component; one of such excipients is the binder. Binders are ingredients that impart cohesiveness to the drug materials and hold the tablets together. Some of the classical binders used in pharmaceutical

manufacture include starch and acacia. The choice of a suitable binder in tablet formulation requires extensive knowledge that is gained often by empirical evaluations.[7] As such, investigating the suitability of different binders in the formulation of herbal tablets is important. The aim of this work is to evaluate water, acacia and maize starch respectively as suitable binders in the formulation of the dried micronized leaf of *M. oleifera* into tablets.

MATERIALS AND METHOD

Materials

Maize starch and acacia gum (Sigma Aldrich, Germany), Water was supplied by the water plant of National Institute for Pharmaceutical Research and Development (NIPRD), Abuja, Nigeria and further purification and distillation was carried out in the Department of Pharmaceutical Technology and Raw Materials' Development, NIPRD. *Moringa oleifera* leaves were collected from the botanical garden of NIPRD.

Methods

M. oleifera leaves were collected and identified by Mallam Mauza at the National Institute for Pharmaceutical and Drug Research and Development (NIPRD), Abuja, Nigeria. The leaves were dried in a hot air oven (Salvis ISG 160, Germany) set at 40 ^{o}C for 48 h. The dry leaves were then pulverized for 10 min using a Braun homogenizer (Type-4142, Germany) set to maximum speed. The powder was then screened through a 150 µm mesh size sieve. The fine powder (Mo-P) was then packed into an opaque, large mouthed screw capped plastic container and kept in a desiccator for further study.

Preparation of moringa granules

Appropriate quantities of Mo-P corresponding to 500 mg/tablet and maize starch as disintegrant (200 mg/tablet) required to produce 60 g of granule per batch of binder sample were geometrically mixed together in a mortar. Adequate quantity of water and the binder dispersions (7.5 %w/w: maize starch and acacia gum) were respectively added to the powder mix in a mortar to form a damp coherent mass. The mass were respectively screened through a 1.6 mm mesh sieve and dried in the hot air oven set at 60 ^{o}C for 5 min the granules were again screened through the sieve and finally dried in the oven at the same temperature for 20 min then appropriately packaged for further use.[8]

Characterization of granules

Bulk and tapped densities: The volume occupied by 50 g of each of the granules was determined using a 200 mL graduated measuring cylinder. The tapped volume which corresponds to the final volume of consolidation after tapping with an automated tapping machine (Stampfvolumeter, STAV 2003JEF, Germany) was determined. The bulk and tapped densities were evaluated.

Compressibility index: The Compressibility index (CI %) was extrapolated from the bulk and tapped densities using equation Eq1:

$$CI = [\text{Tapped density} - \text{Bulk density}] \div [\text{Tapped density}] \times 100\% \quad \text{Eq 1.}$$

Hausner ratio: The Hausner ratio (HR) was also extrapolated from the bulk and tapped densities using equation Eq2:

$$HR = [\text{Tapped density} \div \text{Bulk desnsity}] \quad \text{Eq 2.}$$

Angle of repose: A 50 g quantity of the granules samples were respectively poured into a plugged funnel whose tip had been placed at a distance of 10 cm from the flat surface of a table. The height (h) and the radius (r) of the resulting horizontal heap were noted and used to compute the angle of repose (A) as presented in equation Eq 3.

$$A = \tan^{-1} h/r \quad \text{Eq 3.}$$

Equilibrium moisture uptake profile: A 5 g quantity of each of the granule samples were respectively placed in a Petri dishes which was put into a desiccator containing activated silica gel, after 24 h the granules were weighed again and the readings taken as initial dry weight. The granules contained in the Petri dishes were then placed in a desiccator containing saturated solution of sodium chloride maintained at 27 ^{o}C for one week. At the end of the one week the Petri dishes were reweighed. The increases in weight (%) were determined as the equilibrium moisture uptake (EMU) at tropical climate condition. The EMU was evaluated using equation Eq 4:

$$EMU = \frac{M_e \times 100}{M_d} \quad \text{Eq 4.}$$

Preparation of Moringa tablets

The target tablet weight was 700 mg and all the granules were compressed un-lubricated with a single punch tableting press (Shanghai Tianxiang and Chentai Pharmaceutical Machinery

Co Ltd, China) at 9 kgN. The tablets were then left for 24 h before the properties were evaluated.

Evaluation of Moringa tablets

Tensile strength: The mean thickness and diameter of 10 randomly selected tablets from each batch were determined using a digital Vernier calliper (Mitutoyo, Japan). The crushing strength of the selected tablets was also respectively determined with a hardness tester (Schleuniger -2E/205, Switzerland). The tensile strengths of various sample batches were then evaluated using the equation Eq5:

$$T = \frac{2F}{\pi d H} \quad \ldots . 5.$$

Where: F (Nm^{-2}) is the crushing strength, d and H are the diameter and thickness Respectively.[8]

Friability: Ten tablets of each batch sample were weighed collectively and allowed to rotate at 25 rpm for 4 min in a friabilator (Erweka Gmbh, Germany). The tablets were dusted, re-weighed and the percentage loss in weight was determined as the friability.[9]

Disintegration time: The British Pharmacopeia method was adopted to assess the disintegration time of six tablets selected from each batch of the Moringa tablets.[10] The disintegration apparatus (Erweka ZT4, Germany) and distilled water maintained at 37^{o} C ± 2 ^{o}C were used for the test .[10] The time taken for each tablet to break up and pass through the mesh screen was considered as the disintegration time.

Equilibrium moisture uptake: Tablets produced from each batch were placed in a desiccator containing an activated silica gel for 24 h before the weight corresponding to the initial tablet weight was determined. The tablets were again placed in a crucible containing sodium chloride solution and reweighed after 1 week.[8,11] The percentage increase in weight corresponding to equilibrium moisture uptake (EMU) was then evaluated according to equation 6.

$$EMU = \frac{M_e \, x}{M_d} 100 \quad \ldots . . . .6.$$

Where M_e is the amount of moisture absorbed at equilibrium and M_d is the dry weight of the material.

RESULTS

Preparation of moringa granules

Dark green elegant multiparticulate granules were produced by the wet granulation processing of the micronized *M. oleifera* leaf using water, acacia gum dispersion and maize starch paste respectively as binders. During the wet massing the *M. oleifera* leaf powder formed coherent masses when blended respectively with water, acacia gum dispersion and maize starch paste.

Equilibrium moisture uptake (EMU) of Moringa granules

The EMU of the powder of the micronized *M. oleifera* leaf (Mo-P) and the granules prepared with the water (Gra-Wat), starch paste (Gra-StP) and acacia dispersion (Gra-Ac) are presented in Fig. 1a. The three granule batches and the ungranulated micronized leaf powder showed variable but low EMU at the tropical weather condition simulated with hermetically sealed desiccator containing saturated sodium chloride solution maintained at 27 ^{0}C, corresponding to the room temperature. In accordance with the EMU profile shown in Fig. 1a, the EMU of the different granule in comparison with the ungranulated micronized powder can be represented thus: M-Pow< Gra-Wat< Gra-StP < Gra-Ac.

Flow characteristics

The CI, HR and AR of the moringa leaf powder (Mo-P) and the granules are present in Table 2. The CI, HR and AR for Mo-P were 36.5 ± 1.6 %, 1.5± 0.1, 47±3^{o} respectively generally corresponds to poor flow. The values obtained from similar parameters for the different granulated motifs as shown in Table 1 all corresponds to good flow. The granules produced with maize starch paste and water showed CI and HR that corresponds to lower particle cohesiveness as compared to Mo-P (the ungranulated fine powder) and to a lesser extent the granules produced with acacia gum (Table 1).

Properties of Moringa tablets

Mo-P formed compacts that were unstable to handling at the compression pressure at which all the granules formed coherent stable tablets. Table 2 shows some of the physico-technical properties of the moringa tablets: tensile strength, friability and disintegration time.

The disintegration time for the various batches of the moringa tablets are presented in Table.2. The tablets of the different batches of the micronized moringa leaf all disintigrated within 8 minutes using the BP method of disintigration evaluation. This is within the

acceptable time limit of 15 minutes prescribed by the BP for rapid release uncoated tablets on which this test was based.

The % EMS of all the tablets is presented in Fig. 1b. The tablets prepared with the granules showed comparatively lower EMS than their respective granule types. Also the EMS of the tablets followed similar profile as shown by the granules: Gra-Wat< Gra-StP < Gra-Ac. (Table 1). The % EMU of the tablets prepared with water and starch paste as binder were relatively lower than those of the tablets, apart from that of the acacia gum which showed remarkable higher % EMU than that of the granules.

DISCUSSION

The mass of Mo-P produced by wetting and blending with water showed as much good cohesion similar to that produced when acacia dispersion and maize starch mucilage were used, thus, indicating the presence of an intrinsic adhesive substance in Mo-P probably present as one of the biochemical constituents of the leaf such that by wetting and massing with water the adhesive was activated.[12,13]

The moisture content at which a solid material produces a vapor pressure equal to that of the surrounding environment is known as the equilibrium moisture content. Saturated solution of sodium chloride in a hermetically sealed system furnishes a relative humidity (RH) of 75 %. The RH of 75% and a temperature of 27 ^{o}C corresponds to a typical tropical humidity and temperature as simulated by the by the saturated sodium chloride solution maintained at 27 ^{o}C [7]. The evaluation of the moisture uptake characteristic of Mo-P and the granules is important because Mo-P which is the active ingredient in the formulation of moringa tablets are known to contain substance(s) with the potential to undergo hydrolysis in the presence of moisture.[14-16] The relative low moisture content of the granules could be linked to the intrinsic properties of the bulk material (Mo-P). The bulk material consists largely of pulverized leaf which consists largely of lignin and cellulose. Cellulose is basically more crystalline than being amorphous. Lignin and cellulose are basically hydrophobic hence, insoluble in water. These are probably responsible for the low relative moisture absorption observed for Mo-P and granules produces water as the binder agent. The comparatively highest moisture absorption observed for granules prepared with acacia may be related to the relative moisture absorption potential of acacia. Thus the variability of the EMU could be related to the properties of the binders used for the granulation. Generally, low moisture content is essential for maintenance of physical, chemical and microbiological stability.[16]

Optimum granule moisture content is necessary to achieve good granule flow and strength of the tablets by increasing the density of the particles within the tablet.[17] Nevertheless, excessive moisture content can decrease the tablet hardness by causing an increase in compression pressure required to form a stable robust tablet; it can also result in the increase in cohesion between particles thus, resulting in caking of the powders.[18] Thus, the empirical evaluation of the EMU will as well give insight into the proper selection of excipients required for the formulation of Moringa leaf tablets and possibly the tablets of other herbal materials.

CI, HR and AR are simple indirect techniques used for predicting the flow of powders.[19] The flow properties of the Moringa granules were evaluated using CI, HR and AR. The AR as a parameter for flow is based on the inter-particulate cohesion of the granules: values less than 25° is indicative of *very-good flow* whereas values equal and greater than 25° but less than 50° indicate *good flow* while values greater than 50° indicate *poor flow*.[20] Basically CI and HR predict granule flow by measuring the interparticulate interaction and are determined by the densification of the granules as determined by the evaluation of bulk and tapped densities. CI greater than 10 % is termed to correspond with excellent flow, values between 11 and 15 % correspond with good flow while higher values (> 26 %) indicate poor flow; similarly HR values less than 1.00 - 1.18 portrays the material as less cohesive and free-flowing while values greater than 1.2 indicate cohesiveness.[20] The more cohesive a material, the less its ability to flow into the die cavity during tablet compression therefore, the higher the chances of having tablets with irregular weight and drug content. Thus, the relative values of the CI and HR correspond to good flow for granules prepared with water and maize starch and fair for granules prepared with acacia and poor for the ungranulated powder (Mo-P).The poor flow shown by the Mo-P basically will be due to cohesive properties of the fine particles of the powder. While the results presented using the AR show the granules of the three sample batches as having excellent flow. The differences in the results as given by CI and HR versus AR show the apparent drawback in using these indirect methods for predicting the flow of powders.[21]

The formation of stable compacts by the granulated motifs of Mo-P as compared to the ungranulated powder reiterates the advantage of granulation in the production of tablets. The mechanical strength of tablets is an important quality parameter and measures the cohesiveness and structural strength. The tensile strength measures the mechanical strength of

tablet in relation to thickness and diameter of the compacts.[22] The mechanical strengths of the various tablets produced using the different binders did not show any remarkable differences in terms of their tensile strength and friability as shown in Table 2. However, tablets produced with water as binder showed a relatively higher tensile strength than those of acacia gum and maize starch paste. Visual observation showed that granules produced with water as binder were quite small as compared to those of acacia gum dispersion and maize starch paste. Thus, the smaller sized granules of this batch had greater surface area for contact binding and cohesion during compaction.[23] While the tablets of granules produced with maize starch paste, which had the largest particle size had a comparative least tensile strength, attributed to the large void spaces and weaker inter-particulate bonds between the granule particles.

Tablet friability is another important parameter used for evaluating the mechanical strength of tablets. This official test is used to assess the resistance of tablets to abrasion, shock or deformation. By interpretation, lower friability (%) of tablets proposes higher mechanical strength, thus, better resistance to shock and abrasion during the processes of manufacture, handling, transportation or storage.[24] Tablets produced using the ungranuleted powder was totally friable as they were not able to form coherent compacts due essentially to the massive elastic recovery of the particles. Tablets produced with water as binder were observed to be relatively more friable, this could be attributed to insufficient binder quantities in the smaller granules thus produced. Some researchers have also documented the production of friable tablets even though the tablets had high crushing strength.[25-27] However, all the tablets produced irrespective of the binder type, had values less than 1 % (Table 2) an indication of good mechanical strength. The official limit for acceptance of a rapid release tablet is a friability of less than 1%.[27]

Disintegration test is an official test that provided information as regards the ability of the tablets to break apart within the time limit prescribed officially for acceptance when the tablet is placed in the prescribed liquid medium.[9,28]

Though the granules because of the higher sourface area is expected to have a higher % EMU than the tablets. The observed phenomena may be linked to the probable high porosity of the tablets that allowed ingress of moisture into the core of the tablets. However the general low % EMU showed by all the formulations will favour physicochemical and microbial stability of the Moringa tablets.

CONCLUSION

This study has shown that the dried micronized leaves of *M. oleifera* can be formulated into robust conventional tablets intended for immediate release. Water as well as dispersions of acacia gum and maize starch paste was shown to be efficient binders in the production of Moringa leaf granules. The various granules showed acceptable flow properties and moisture uptake that did not adversely affect the compaction and stability of the granules. All the tablets produced by the conventional wet granulation method showed acceptable mechanical strength, disintegration time, moisture content and stability. However because of the relative higher moisture uptake potential, special attention may be required when acacia mucilage is intended for the formulation of dried micronized Moringa leaf powder.

Table 1: Effect of binder type on the flow properties of Moringa leaf granules.

Batch (Binder)	Angle of repose (Θ^o)	Compressibility index [CI] (%)	Hausner ratio (HR)
No binder (Mo-P)	47.00 ±3.0	33.5 ±1.6	1.50 ±0.1
Water	23.50 ±1.5	14.5 ±0.8	1.16 ±0.3
Acacia	28.90 ±3.5	19.43 ±0.7	1.27 ±0.2
Starch paste	21.50 ±1.0	11.11 ±0.8	1.12 ±0.2

Table 2: Effect of binder type on some tablet parameters of Moringa leaf tablets.

Batch (Binder)	Tensile strength (Kg/cm^3)	Friability (%)	Disintegration time (min)
Water	0.06	0.79	8
Acacia	0.05	0.70	8
Starch paste	0.04	0.75	8

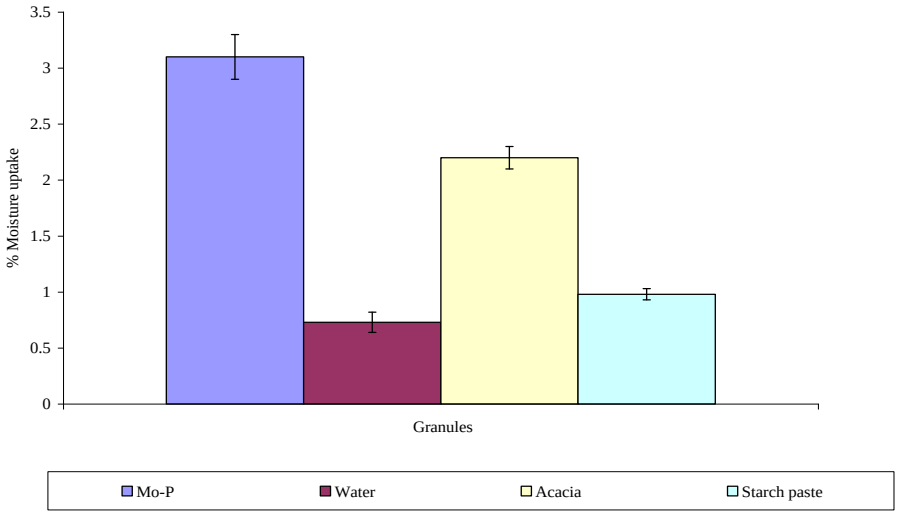

Fig. 1a: Moisture uptake of Moringa leaf powder and Moringa granules.

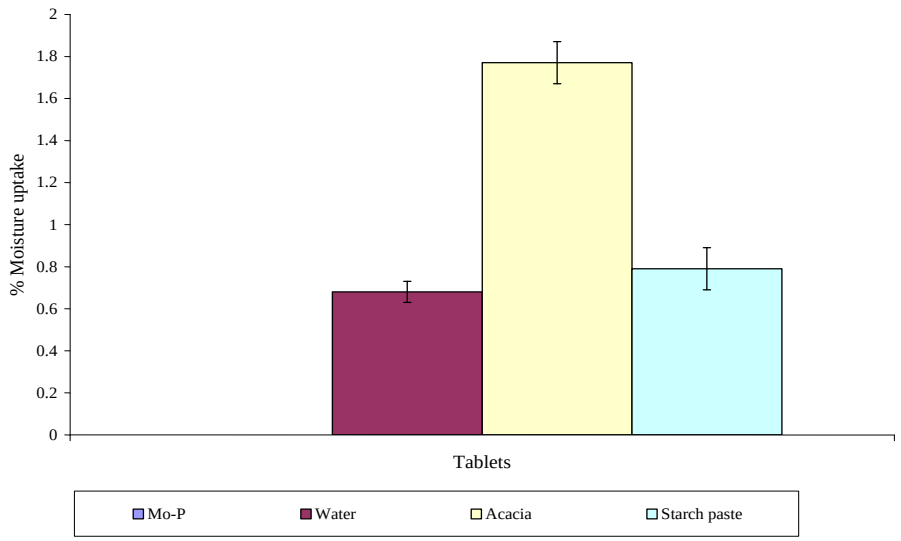

Fig. 1b: Moisture uptake of Moringa leaf tablets.

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