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A COMPARATIVE STUDY OF THE EFFECT OF GRANULATION METHOD ON THE PROPERTIES OF *ANDROGRAPHIS PANICULATA* TABLETS

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Abstract

Comparison between the Wet Granulation and Dry Granulation by Pelletization Methods of Powdered Leaves of *Andrographis paniculata.* Aim: To produce acceptable tablets from powdered leaves of *Andrographis paniculata* (AP) used as an anti hypertensive herbs. AP is a perennial plant called "King of Bitters". It is a member of the plant family Acanthaceae, which has been used for centuries in Asia. The Herbarium member is NIPRB/H/5558. A P is used as an anti hypertensive by the natives in Adamawa State. Scientifically this fact was substantiated by Zhang *et al* 1997 and Mshelbwala *et al* 1998. Comparison was made by formulating the crude powdered leaves into tablet by Wet granulation method as against dry granulation by Pelletization. Wet Granulation Method: Fresh leaves of A P was plucked and dried at 40^{o}C for 24 hours, and it was micronised using a blender and passed through 250μm sieve. The powder was used to formulate 200mg tablets containing 150mg active ingredient of A P. Maize starch was used as a disintegrant. Dry Pelletization Method: Three different disintegrants were used for each set of pellets (Avicel) PGS and ($PGS \leq 75\mu M$). For each disintegrant pellet of 2.5g were compacted at 5, 10, 15 and 20 metric tonne. The pellets were communited and passed through 1.7mm sieve. After the granules analysis. Appropriate amount of lubricant were mixed with the granules. The tablets were compressed at 7 metric tonne pressure using 8.0 mm punch and die set. The results showed that pharmaceutically accepted tablets could be formulated from both wet and dry granulation by pelletization. But the wet granulation method produced tablets of more acceptable physical parameter as compared with the ($PGS \leq 75\mu M$).

INTRODUCTION

Andrographis paniculata (Burn E) is a herbal perennial plant 0.5 – I meter in height. It has a wide variety of therapeutic uses in traditional and ayurvedic practice. It is locally used in India and the Far East for liver disorder, bowel complaints of children, colic pains and cases of general debility, Bently and Trimen 1983. The plant has also been proved to have antidiabetic properties. It has also been proved to have an anti hypertensive effect, Zhang *et a*l 1997 and Mshelbwala *et al* 1998.

Bioassay directed screening of the plant extract have confirmed the presence of andropgrapholide and neo andrographlide (Bentley and Trimen 1983) which posses multiple pharmacological activities such as hepato-protective, antipyretic, anti-inflammatory and immunostimulant (Deng *et al* 1982). In Nigeria the plant is found mainly in Adamawa State, North – Eastern Nigeria, Kaduna State and also in the Federal Capital Territory Abuja. The Herbarium number is NIPRD/H/5558. In Nigeria to be specific in Garkida, Adamawa State where the sample was obtained it is used for an antihypertensive purpose. Since *Andrgraphic paniculata* is used as an anti hypertensive it will be useful

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to formulate it into an oral dosage form. It has been acknowledged that herbal plant is better formulated as a whole rather than isolating the active ingredient for example senna tablets, which are used as laxatives.

Even in developed countries herbal plants are being encouraged rather than orthodox drugs since it is less toxic and more natural. However, in developing countries, the use of herbs is encouraged because it is cheaper than orthodox drugs, which is out of reach of most of the populace. In the case of *Adrographic paniculata* only 10-12 fresh leaves are chewed once or twice daily and this is enough to lower the blood pressure this amount is equivalent to 500mg of powdered leaves. This can conveniently be formulated into tablets. Work has already been done on the direct compression of the powdered leaves but, the tablets could not disintegrate instead they absorbed water and swelled up.

Therefore, in this work various disintegrants are being incorporated into the formation in order to obtain more acceptable tablets which could disintegrate within the specified limits and achieve the therapeutic results.

MATERIALS AND METHODS

The fresh leaves of *Andrographis paniculata* were collected from a garden in Zaria, Northern Nigeria. The leaves were dried in the oven at 40^{o}C for 24 hours. The dried leaves were communicated with a blender and sieved through 250μm sieve size. Granule analysis and all test for granules were carried out on the powered leaves.15 g of the powdered leaves was weighed out for a batch of 100 tablets.

Materials used for the formulations were as written in the table of formulations. Microcrystalline cellulose and pregeletinized starch were used for Method II. The pregeletinized starch was prepared from the Pharmaceutical laboratory of Ahmadu Bello University, Zaria. The slugging machine was a hand press from the Centre of Energy Research, Ahmadu Bello Universtiy, Zaria. Both methods for Dry and Wet granulation i.e., Methods I and II were from "Science of Dosage form Design" 1988 edited by Michael E. Aulton. The sludges compressed weighed 2.5kg and three sludge were compressed at 5, 10, 15 and20 metric tones pressures. The sludge were communicated as mentioned earlier and the granules from both methods were analysed and compressed into 200mg tablets using 8.00mm punch diameter under 7 metric tones pressures. The usual physical parameters were carried out on the tablets according to British Pharmacopoeia (B.P.) specification.

RESULTS AND DISCUSSION:

The results obtained in the various experiments are shown in Table 1 and Figure 1. The yield obtained from gelatinising maize starch formed from 8% W/V mucilage was 83%. Any loss from the product could have ensured by envisaged processing losses. Pre-gelatinization involves the rupture of the organised structure of the starch particles to form a granule. Gelatinisation involves the disorganisation of this crystalline – like, lattice arrangement into a disorganised, amorphous form (Ocheja, 2000). It is also possible that the heat applied for evaporation of the water in the mucilage could partially lead to some level of hydrolysis of the starch into a partially depolymerised form. If at all that was the case, it must have been very negligible as any extensive hydrolised form could have been soluble in the solubility determination which did not reveal any soluble constituents as Table 1 result showed under solubility.

The particle size of the milled dried mucilage flakes showed a mean granule size of 108 μm, much larger than the 21μm size of the maize starch. This larger mean size of the pregelatinised starch showed a high flow rate of 5.7g/sec compared to 1.2g/sec for maize

starch (Table 1). This has also been shown as lower angle of repose (19.6^0) of the heap of PGS while that of MS was 45.7^0. *Larger particles have smaller surface area to volume ratio. Since particulate function is more of a surface phenomenon by generation of resistance to flow. This resistance is directly, related to the surface area of particles.

Most pharmaceutical granules have specific gravity of about 1 or less. Having an admixture with higher bulk and tapped densities, increases the inertia of such mixtures which causes higher densification. Bring in the work or publication of staniforth who showed the range of values of angles of repose, Carr's indices particle sizes that favour flow and ease of packing which favour good glident properties required of granules for filling into the die cavity and therefore higher flow rate.

Nabintu (2001) has shown how close packing had reduced the compaction force needed to density the granules which precedes solidification into compacts. This ease to closer packing is shown with the higher bulk and packed densities of 0.75 and 0.91 g/cm^3 for PGS compared with those of MS were 0.44 and 0.61g/cm^3 respectively (Table 1).The percentage yield of 83% of pregelatinized starch was appreciatively high enough. This shows that the maize starch did not contain a higher amount of other materials other than starch. This contributed to the high yield of pregelatinized starch (Table 1).

Table 2 shows that pregelatinized starch (PGS) has a higher flow rate than that of maize starch. The physical characteristics that make pregelatinised starch, flow or pack more easily to enhance better tableting properties are exhibited the following characteristics there was a lower angle of response, higher powder flow rate due to lower cohesive forces, Martin, et al (1983), Neuman (1976), Carter (1972). Lower difference between bulk and tapped densities and therefore lower value of Carrs packing or consolidating indices. – The lower moisture content, higher packing fraction, lower porosity, and larger mean powder size of PGS result of which are shown on Table 1, all favour more desirable tableting prerequisite. The size distribution of pregelanized starch powder produced from maize starch compared with maize starch powder is shown in Figure 1. The particle size of maize starch powder was not significantly different ($P>0.05$) compared with pregelatinised starch. 15 to 21um and 108 um are by means significantly different pregelatinised starch (PGS) was found to be a good disintegrant in tablets, because, of its excellent pharmaceutical properties when compared with Maize Starch (Musa 2002; Musa, 1999).

Table 1: Comparative physico-chemical characteristics of pregelatinised starch powder produced from maize starch and maize starch.

Parameter	Pregelatinised starch (PGS)	Maize starch (MS)
Yield	83	12.8
Moisture content (%)	7.3	12.8
Mean particle size (μm)	108	21
Efflorescence (%)	1.2	2.1
Solubility	Insoluble	Insoluble
True density (g/cm^3)	1.50	2.13
Flow rate (g/sec)	5.70	1.2
Bulk density (g/cm^3)	0.75	0.44
Tapped density (g/cm^3)	0.91	0.67
Percentage Compressibility (%)	17.6	34.8
Angle of repose (0^0)	19.6	45.7
Powder porosity (%)	50	80
Packing fraction	0.5	0.2

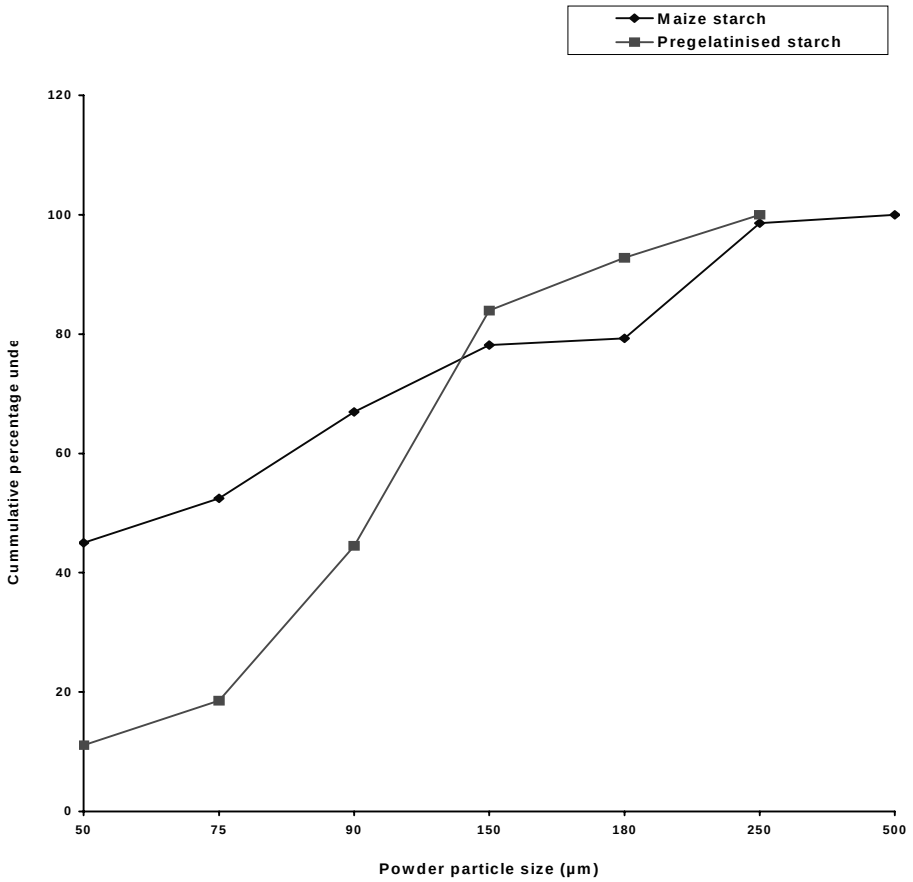

Fig. 1: Size distribution of maize starch powder and pregelatinised starch powder produced from maize starch

CONCLUSION

Nearly all the physical characteristics that favour densification and therefore easier rate of packing in capsule filling and tablet compression such as lower Carr's index, low angle of repose and larger mean particle size were found to be more inherent in pregelatinized maize starch then in maize starch. The move porous PGS and amorphous form favours shorten disintegration time which usually preceeds access to faster dissolution of active ingredients and therefore makes the medication more bioavailable the simple nature of PGS production favours its industrial production even locally.

REFERENCES

Carter, S.J. (1972) Tutorial Pharmacy 6th Edition Pitman Medical Publishing Co. Ltd. Tumbridge Wells Kent England, PP 211 – 233.

Deshpande A.V. and Panya L.B. (1987) Evaluation of sorghum starch as a tablet disintegrant and binder J. Pharm. Pharmacol 39. PP 495 – 496.

Edward G.R, Robert E. O and Joseph BS (1990) Powders in Remintong the Science and practice of pharmacy Editor General Alfonso R.G. etal Lippincott Williams and Wilkins USA 20th Edition Ch . 37 PP 681-699

Martin A. Swarbrick L. and Cammareta A. (1983) "Physical Pharmacy" 3rd Edition Led and Febiger, Philadelphia P 492.

Musa H. (1999) Evaluation of cellulose and sodium carboxymethly cellulose produced from rice husks in Tableting M.Sc. Thesis, Ahmadu Bello University, Zaria, Nigeria.

Musa H. (2002). Tableting properties of low dose formulations containing sodium carboxyl methyl

cellulose (SCMC) derived from rice (*Oryza Sativa*) husks Ph.D, Thesis, Ahmadu Bello University, Zaria, Nigeria.

Nabintu, R.N. (2000) characteristic of wet and dry granulated Folic acid tablets containing alpha and microcrystaline cellulose derived from rice (oryza sativa) husks MSc thesis Ahmadu Bello University, Zaria.

Nasipuri R.N. and Akala E.O. (1986) Effect of concentration and quantity of cassave starch mucilage as a binder on granule and tablet properties Nig. J. Pharm. 17, 13

Neumann B. S (1976), The flow properties of powders Advances in Pharmaceutical Sciences 2, 181 – 221 London Academic Press.

Ocheja, D.A. (2000) Evaluation of pregelatinised starch and maltodextrin from sweet potato (Ipomea batatas) In tablets. MSc, Thesis, Ahmadu Bello University, Zaria, Nigeria.

Staniforth J. N. (1985) Particle Engineering in a direct compression excipient Int. J. Pharm. Tech & Prod Mft, 5,1.

Staniforth J. N. (1993) Particle size reduction in Authon E.M. (ed) Pharmaceutics the Science of dosage form design, Churchill Living Stone, UK, Pp 581 – 590.