THE ROLE OF ACID-HYDROLYSED CASSAVA STARCH AS A BINDER IN PARACETAMOL TABLETS

***Mohammed B.B, Isah A.B, Apeji Y.E**

Department of Pharmaceutics and Pharmaceutical Microbiology Ahmadu Bello University, Zaria, Nigeria.

ABSTRACT

Modified cassava starch has been evaluated as a binder in paracetamol tablet formulations. The starch was extracted from the fresh tubers of manihot esculenta, modified by heat and acid treatments for 24 hours. The binding property of the modified starch was investigated in paracetamol tablets formulated by wet granulation using polyvinlpyrrolidone (PVP) and maize starch BP as basis for comparison at concentrations of 2.5 – 10% w/v. The tablets were evaluated for hardness, friability, weight uniformity, disintegration and dissolution profiles. Results obtained indicated that modified starch performed as good as PVP and maize starch BP as a binder in paracetamol tablet formulations especially at a concentration of 10%w/v.

Key words: Modified starch, Paracetamol, PVP, Maize starch, Binder

INTRODUCTION

Starch is one of the traditional excipients used in the manufacture of tablets. Depending on the application, specific starches are available for use as binders, diluents and/or disintegrants. The use of this natural polymeric material is based on its adhesive, thickening gelling, swelling and film forming as well as its availability.Starch continues to be attractive as a binding material because of its abundant supply, low cost, biodegradability, and ease of chemical modification (4,16).

Binders are agents used to impart cohesive qualities to the powdered material during the production of tablets. They impart cohesiveness to the tablet formulation, which ensures that the tablet remains intact after compression as well as improving the free flowing quality (10). The choice of a particular binder depends on the binding force required to form granules and its compatibility with the other ingredients particularly the active drug (5). Starches from different sources have been evaluated and used as excellent binders in either mucilage or the dry powdered from (9,13 and 17). Maize and potato starches have been in common use and recently cassava starch appeared in British pharmacopoeia as an official starch for use as binder (3).

***Corresponding author:**
Email: disciplebbm@gmail.com

While starch in its unmodified form is satisfactory in many aspects, the increase demand for better binding ability, faster dissolution and disintegration rates and the softening effect that unmodified starch has on tablets at effective concentration levels, has stimulated search for more effective agents, and for forms of starch that exert little effect on tablet mechanical properties. In the present study, the effect of heat and chemical (acid hydrolysis) treatments on the binding property in paracetamol tablet was investigated.

EXPERIMENTAL

Cassava starch (prepared in our laboratory), paracetamol, maize starch, ploy vinlpyrrolidone (PVP), hydrochloric acid and talc powder (May & Baker Ltd, England), magnesium stearate (Merk, Germany).

Extraction and hydrolysis of the experimental starch

The extraction of cassava starch was carried out as described by Linus(12). The method used for the modification was the same as that reported by WIPO (18). A 450 g of an aqueous suspension of (36% wt starch) was poured into a double walled reaction vessel. To this was added 28ml of 6N HCL dropwise with stirring at 55^0 for 24hrs. The reaction was cooled and the product filtered under vacuum.

The product was washed 1:1 with water, it was re-suspended again in 250ml of water and

adjusted to pH of 6 with NaOH solution. The starch was washed with 750ml of water and filtered again under vacuum. A 100g sample of starch was suspended in 800ml of ethanol and stirred for 30 minutes. The product was filtered, air dried, milled and weighed.

Formulation of paracetamol tablets

Twelve batches of the tablet containing 500mg paracetamol were prepared. The batches contained MCS, PVP and maize starch as binders respectively in concentrations of 2.5, 5.0, 7.5 and 10%$^{w}/_{v}$. Maize starch at 10% of the active ingredient acted as the disintegrant with 0.2% magnesium stearate as lubricant, talc 2% as glidant. Wet formulation method was employed in the formulation of the tablet batches.

Granulation and compression

Calculation was made for 250 tablets in each batch. In each case, the weighed quantities of paracetamol powder, maize starch as disintegrant were mixed in a mortar and the binder solution or mucilage added to obtain a damp coherent mass. The damp mass was sieved with 1.7mm sieve and dried at 50 ^{0}C in the oven for 1hr.

The dried granular mass was passed through a 1.6mm seive to obtain uniform sized granules. The different batches of the granules were then mixed with calculated equal quantities of magnesium stearate, talc and maize starch using mixing bottle and then compressed into tablets under constant pressure with a Manesty single punch (Type F3, England) tabletting machine. The punch size and volume of fill were carefully adjusted to give the required tablet size and weight.

The tablets were evaluated for hardness, friability, weight uniformity and disintegration time as reported previously (7). The dissolution tests of the tablets were determined using the dissolution apparatus (Erweka Apparatebau GmbH, DT Germany). One litre of 0.1M HCL thermostatically maintained at 37^{0} C ± 0.5^{0}C was the medium. The apparatus was set to a rotational speed of 100rpm. A tablet was placed in the dry basket and 10ml sample was taken out after 10min, filtered and 1ml of the filtrate diluted to 10ml and the absorbance of the resulting solution taken at the maximum wavelength of 245nm. This was done for formulations containing binder concentrations of 10$^{w}/_{v}$.

Results and Discussion

The prepared granules were considered free flowing based on results of hopper flow rates, angles of repose, compressibility index and Hausner's quotient. These values were omitted for clarity since emphasis is on the role of the modified starch as a binder relative to PVP and maize starch BP as standard binders.

Moreso, acid hydrolysis of starch is known to improve its fluidity and compressibility and possible positive effect on granule flow and compressibility (15).

The tablet properties are shown in Table 1. The hardness values increased with increasing binder concentration. This is in agreement with

Table 1: Tablet properties with Hydrolysed starch, polyvinylpyrrolidone and maize starch as binders

Properties	HS				PVP				MS			
Binder concentration $^{w}/_{V}$(%)	2.5	5.0	7.5	10	2.5	5.0	7.5	10	2.5	5.0	7.5	10
Mean tablet hardess (KgF)	2.0	2.8	4.2	5.2	2.3	4.0	5.1	5.7	3.6	5.0	5.4	6.2
Friability (%)	14	11	3	1.9	12	3.9	2.3	0.3	10	2.3	2.0	0.9
Weight uniformity (mg) SD)	612.5 (19.97)	616.5 (10.14)	618.5 (9.10)	617 (7.14)	623.5 (11.08)	613 (6.40)	598.5 (19.82)	611.5 (6.54)	622.5 (6.98)	633 (15.50)	610.5 (9.21)	635 (5.92)
Mean disintegration time (min)	0.35	0.38	0.52	1.05	0.83	0.92	1.12	1.13	0.42	0.47	0.58	0.9

* Values shown in bracket represent standard deviation

previous studies on starches used as binders in comparison with other binders (17). The hardness of the tablet batches was within accept able range of 4 – 7 kgF for concentrations of 7.5 to 10% for hydrolysed starch, 5 – 10%$^{w}/_{v}$ for PVP and maize starch BP. For those that were not within acceptable range, it could be due to insufficient quantity of binder concentration also for the acid hydrolysed starch, it is logical to state that effect of acid hydrolysed starch in granule compressibility may depend on the extent of hydrolysis achieved (14). The tablet hardness values were in the rank order MS > PVP > HS. This is assumed to result from the heat produced during compression that could cause melting of asperities and of the binding agents. On cooling, these asperities would solidify to form strong solid bonds between the particles (11). The degree of binding depends on the amount of the binding agent present (8) and on the compression force.

Table 2: Dissolution studies for 10%$^{w}/_{v}$ binder concentration

Binder type	Hydrolysed starch	Polyvinyl-pyrrolidone	Maize starch BP
T50% (min)	5	5	5
Percentage released at 45 mins	77%	81%	83%

The same trend was observed with the friability recorded for the three binders. There was a decrease in friability as the concentration increased. The standard binders (MS and PVP) recorded below 1% friability at concentration levels of 10%$^{w}/_{v}$ in the formulation. It should be noted that paracetamol tablets are generally prone to capping when starch binder concentration is less than 7%(^{w}/w) (17). Also, it has been revealed that increase in binder concentration and compression force decreases tablet friability, and that an additive effect exists between the binder concentration and compression force on the friability of paracetamol tablets (1).

As expected, variations in weight uniformity were less with tablets prepared using MS and PVP as binders (standard). Thus the standard binders, produced better flowing granules. The uniformity of weight also indicates probable uniformity of content (6). The die filling of the powder will be uniform. Similarly, the disintegration time increased with increased binder concentration for all three binders. This is due to increase in binder concentration. It has been reported that starch mucilage used as binder forms a thin film around the granules with thickness increasing as the quantity of mucilage increases and this retards disintegration (17). It was also reported that starch added to the dry granules prior to compression improves the disintegration time since the surface surrounding starch acts as a pathway for water penetration in the case of water repellant drugs and for pushing the granule apart due to expansion (2).

The dissolution profiles for tablets formulated with 10%$^{w}/_{v}$ binder concentration of hydrolysed starch, PVP and maize starch BP are shown in Figure 1. There was an increase in the quantity of drug released with corresponding increase in time for all formulations. The $T_{50\%,}$ which is the time taken for 50% of the drug to be released was 5 minutes for all three binders. At 45mins, the percentage of drug released for all three binders was above 70%. This complies with the British Pharmacopoeia (3) requirements for dissolution where it is stated that 70% of the drug should be released at 45 mins. It could be said that hydrolysed starch, PVP and maize starch showed comparative effectiveness as binders to paracetamol tablets.

In conclusion, acid-hydrolysed cassava starch could compete favourably with polyvinylpyrrolidone and maize starch powder as binders in paracetamol tablet formulations.

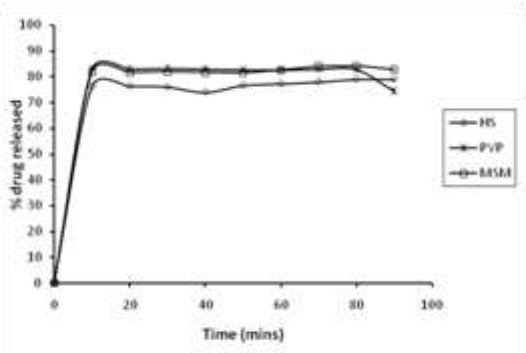

Figure 1: Graph of percentage released versus time for tablets formulated with 10(w/v) binder concentrations of HS, PVP and MSM

REFERENCES

1. Adane, M , Abdel-Mohsen, MG, Gebre-Mariam, T. (2006). Evaluation and Optimization of Godare Starch as a Binder and Disntegrant in Tablet Formulations. Ethiop Pharm. J 24, 106 – 115.
2. Aulton, ME (1988). Pharmaceutics: The Science of Dosage form Design, ELBS, Churchill Livingstone UK pp. 305 – 320.
3. British Pharmacopoeia (2001). Majesty's Stationary Office, London, p. 1576.
4. Gebre-Mariam T, Schmidt PC (1996a). Characterization of enset starch and its use as a binder and disintegrant for tablets. Pharmazie 51:303 – 311.
5. Gordon ER, Rosanke TW, Fonner OE, Anderson NR, Baker GS (1990). In: Pharmaceutical Dosage Forms: "Tablets, Liberman HA. Lachman, L., and Schwartz (Eds), Mercel Dekker, New York. 2:83.
6. Ibezim, EC, Ofoefule, SI, Omeje, EO, Onyishi, VI and Odoh, UE (2008). The role of ginger starch as a binder in acetaminophen tablet. Scientific Research and Essay Vol. 3(2), pp. 046 – 050.
7. Isah, AB, Mohammed, BB, Gwarzo, MS (2009). Evaluation of the Binding properties of Acid hydrolysed starch obtained from manihot esculenta (Euphorbiaceae) in paracetamol tablet formulations.
8. Itiola, AO, Pipel, N. (1986). Tabletting Characteristics of metronidazole formulations. Int. J. Pharm. 31: 99 – 105.
9. Iwuagwu MA (1991) Evaluation of some soluble starches as Lubricants in the formulation of compressed tablets. World Pharm. J. 8(1): 19 – 23.
10. King RE (1975). Tablets in Remington's Pharmaceutical Sciences, 15th Ed. Mack Pub. Coy. Easton, Pennsylvania p. 1587.
11. Kurup, TRR and Pilpel, N (1979). The Effect of binding agents on the tensile strengths of powders and tablets. Asian J. Pharm. Sci. 1: 75 – 90.
12. Linus AJ (1995) Tabletting behaviour of some depolymerized local starches. M.Sc. (Pharmaceutics) Thesis work, Ahmadu Bello University Zaria, Nigeria. P. 42 – 45.
13. Nasipuri RN (1979). Evaluation of Cocoyam Starch as Tablet Binder and Disintegrant. Acta Pharm. Helv. 54(2): 48 – 53.
14. Ofoefule, SI, Osuji, AC and Okorie, O. (2004). Effect of physical and chemical modifications on the disintegrant and dissolution properties of Tacca involucrata starch. Journal of Biological research and Biotechnology, 2(1): 97 – 102.
15. Shangraw, RF, (1986). Formulation of Tablets – Role of Excipients Bulletin E , pp. 22 – 27.
16. Shorgren RL (1998). Starch: Properties and Materials application. In: Kaplan DL ed , Biopolymers from Renewable Resources, Springer, Germany, pp. 30 – 46.
17. Tsige G, Alexander SN (1993). Evaluation starch obtained from Esente Ventricosum As A Binder and Disintegrant for Compressed Tablets. J. Pharm. Pharmacol. 45 (307): 317 – 320.
18. WIPO (1997). World Intellectual Property Organization. Use of microcrystalline starch as tabletting excipient. PCT/NL97/00097.