Effects Of Physical And Chemical Modifications On The Disintegrant And Dissolution Properties Of *Tacca involucrata* Starch

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Abstract

The effects of physical (pregelatinization) and chemical (acid hydrolysis) modifications on the distintegrant and dissolution properties of *Tacca involucrata* Starch (Tacca starch) were investigated in lactose based tablets containing 0.001% w/w of riboflavin as tracer substance, 10% w/w Tacca starch as disintegrant, 3% w/w acacia as binder, 1% w/w stearic acid as lubricant and enough quantity of lactoşe as diluent. The starch was incorporated intragranularly, extragranularly and intra/extragranularly. Regardless of the mode of incorporation, Tacca starch was most efficient in effecting the disintegration of the tablets and releasing their riboflavin contents in its unmodified form. In this regard, pregelatinized Tacca starch was more effective as a disintegrant than the acid hydrolysed form of the starch. Generally, fastest disintegration and dissolution were obtained with extragranular incorporation of the three forms of the starch. On the basis of dissolution efficiency values ($D>E^{15}$), the modifications did not result in any retardation in riboflavin release from the tablets.

Keywords: Tacca starch, pregelatinization, acid hydrolysis, extragruanular, intragranular intra/extragranular, dissolution efficiency.

Introduction

Starches from different plant sources are employed as disintegrants, binders and diluents in tablet formulations. They are usually employed in their unmodified form in this regard. The role and mechanisms of disintegrant action were extensively reviewed (Lowenthal, 1972). *Tacca involucrata* starch (Tacca starch) has been evaluated in its unmodified form as a binder and as a disintegrant in tablet formulations (Ofoefule *et al*, 1998; Ofoefule, 1998). The effects of the mode of incorporation on its disintegrant properties in chloroquine phosphate tablets were also reported (Ofoefule, 1998). It is recognized that among many factors which play a role in the rate at which a tablet disintegrates or the active ingredient dissolves, the role of the disintegrating agent is paramount. While starch in its unmodified form is satisfactory in many aspects, the increase demand for faster disintegration and dissolution 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 effects of physical treatment (pregelatinization) and chemical treatment (acid hydrolysis) on the disintegrant properties of this new

starch isolate in lactose based tablets containing riboflavin as a tracer substance were investigated. The effects of mode of incorporation of the modified starch on disintegration and dissolution profiles of the compressed tablets were also investigated.

Material and Methods

The following materials were used as procured from their manufacturers: Riboflavin powder (Hosanna Int. Co. Nigeria), concentrated hydrochloric acid, lactose (May and Baker, England), stearic acid, acacia gum powder (Merck, Germany), sodium metabisulphite, acetone (B.D.H. England). *Tacca involucrata* starch was extracted according to previously reported method (Ofoefule *et al*, 1998).

Modifications of tacca starch

Pregelatinization of tacca starch: Tacca Starch forms a thick gel in the temperature range of 65 – 70 ^{0}C (Ofoefule *et al*, 1998). Five portions of 10 % w/w slurry of the starch in deionised water were heated in a thermostated water bath for 10 min with constant stirring at 63.5 ^{0}C. The starch slurries were filtered and dried in an oven set at 40 ^{0}C for 24 h. Dried starch was stored in well-closed amber coloured bottle until used.

Acid hydrolysis of tacca starch: Five 10% w/w portions of tacca starch in 7.5 % hydrochloric acid were stored in well closed 250 ml volumetric flasks at 28 ± 1 ^{0}C for seven days (Rohwer *et al*, 1984). The starch slurries were drained of fluid, washed several times with distilled water until it was about pH 6. The starch was dried in an oven at 40 ^{0}C for 24 h, and stored in well-closed amber coloured bottle until used.

Preparation of granules and tablets: Granules containing 10 % w/w Tacca starch (disintegrant) 3 % w/w acacia (binder), 0.001 % w/w of riboflavin and sufficient quantity of lactose were prepared using the conventional wet granulation method – involving wet and dry screening of granules through 1.7 mm and 1.0 mm stainless steel sieves respectively. Granules containing 10 % w/w of pregelatinized or acid hydrolysed starch and equivalent quantities of the other ingredients were similarly prepared. These batches of granules were lubricated with 1% w/w stearic acid previously screened through a 0.20 mm stainless steel sieve prior to compression in an F –3, Manesty Single Punch tabletting machine fitted with 0.95 cm flat faced punches, after assessing their flow properties with standard methods (Carstensen, 1973). Target weight of tablets was 300 ± 5 mg and compression load was kept at 45 units of the machine pressure gauge.

Batches of tablet containing Tacca starch (unmodified, pregelatinized and acid hydrolysed) were prepared such that the starch was incorporated intragranularly, extragranularly and intragranular/extragranularly (ratio, 1:1). The tablets were evaluated for hardness, and friability as reported previously (Ofoefule *et al*, 1998). The disintegration times of the tablets were determined using Manesty single unit disintegration assembly. Disintegration medium was distilled water maintained at 37 ± 1 ^{0}C. Results presented are mean of six determinations in each case. The static basket – rotating basket assembly, was adopted in the dissolution studies. The dissolution medium was 500 ml distilled water maintained at 37 ± 1 ^{0}C by means of a thermostated hot plate. Samples were

withdrawn at predetermined time intervals and analysed for riboflavin content at 444 nm in a spectronic 20 colorimeter.

Results and Discussions

Prepared granules were considered free flowing based on results of densification behaviour, hopper flow rates, angle of repose, compressibility index, and Hausner's quotient. These values were omitted for clarity since emphasis is on disintegrant and dissolution properties of the modified Tacca starch relative to that of unmodified form of the starch. More so, pregelatinization and acid hydrolysis of starch is known to improve its fluidity and compressibility and possible positive effect on granule flow and compressibility (Shangraw). It is evident from Table 1 that pregelatinized Tacca starch increased the hardness of the tablets regardless of the mode of incorporation as against a decrease observed with the unmodified form. The acid hydrolysed form of the starch increased the hardness of the tablets only when it was incorporated intragruanularly. From the hardness values of tablets containing the acid hydrolysed Tacca starch, it is logical to state that effect of acid hydrolysed starch on granule compressibility may depend on the extent of hydrolysis achieved. In a previous study, the distintegrant properties of varying concentrations of unmodified Tacca starch in chloroquine phosphate based tablets were reported (Ofoefule, 1998). In the present study the unmodified starch was most effective in the disintegration of the lactose based tablets at extragranular incorporation (Table 2). This result is in agreement with the earlier finding (Ofoefule, 1998). Similar behaviour was exhibited by Pregelatinized and acid hydrolysed

Table 1: Mean Hardness of Lactose Based Tablets (kgf)

Starch Form	Mode of Incorporation		
	Intra.	Intra ./Extra	Extra
Unmodified	6.16 ±0.91	5.94 ±0.59	5.09 ± 0.38
Pregelatinized	9.79 ± 1.02	10.24 ± 1.62	50.40 ± 0.81
Acid hydrolysed	10.30 ± 0.49	3.97 ± 0.89	4.82 ± 0.78

Table 2: Mean Disintegration Times (Min.) and Dissolution efficiency (%) of Tablets

Starch Form	Mode of Incorporation		
	Intra.	Intra. /Extra	Extra
Unmodified	1.74 ± 0.17	1.13 ± 0.15	0.70 ± 0.10
Pregelatinized	5.32 ± 0.44	3.33 ± 0.08 (79.50)	0.97 ± 0.17 (80.0)
Acid hydrolysed	17.80 ±0.41 (49.5)	4.0 ± 0.21 (71.5)	3.03 ± 0.60 (81.0)

Values in bracket represent Dissolution efficiency, D.E.[15]%

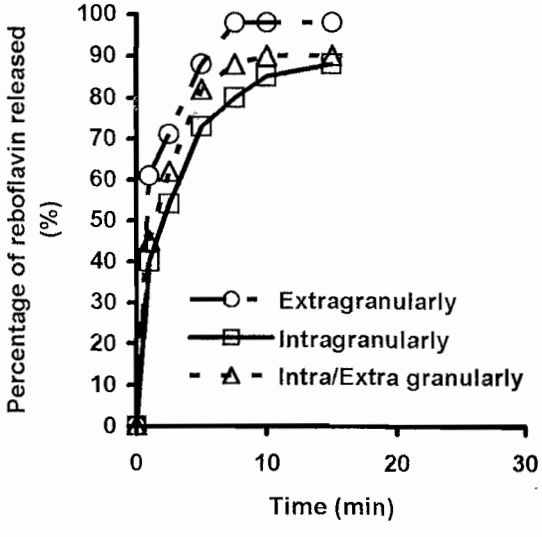

Fig. 1: Dissolution profiles of riboflavin tablets containing unmodified Tacca starch

forms of the starch. This behaviour could be explained on the basis of two hypotheses. First, the effectiveness of disintegrant is a function of its accessibility to water or disintegration medium. Consequently the more the

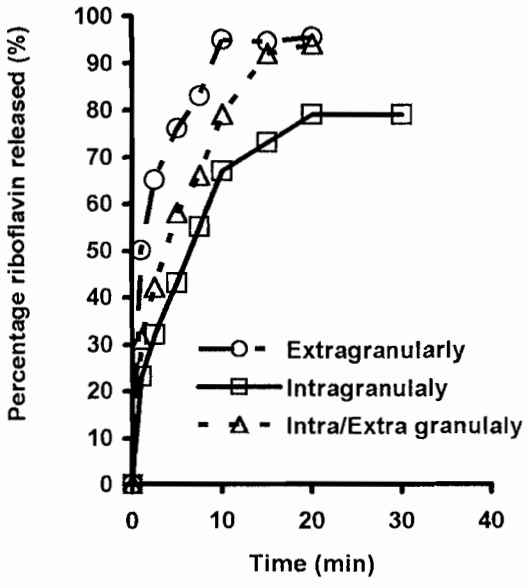

Fig. 2: Dissolution profiles of riboflavin tablets containing 10% w/w pregelatinized Tacca starch

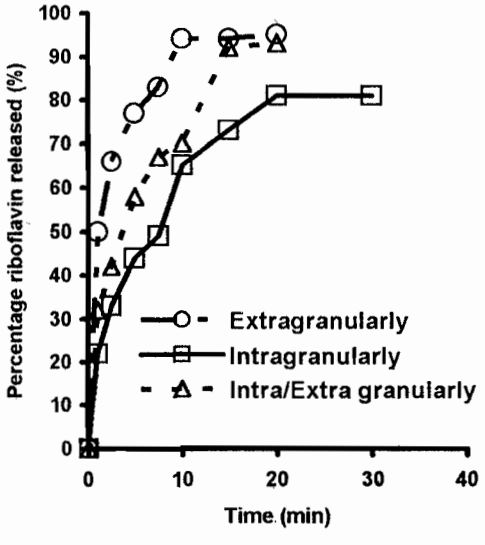

Fig. 3: Dissolution profiles of riboflavin containing 7.5% acid hydrolysed Tacca starch

disintegrant is on the surface of the granules, the more its accessibility to the disintegrating medium. This may result in faster disintegration of the tablets. Secondly, the fluid repelling property of the incorporated lubricant, stearic acid might have been reduced by the increased wetting brought about by the presence of Tacca starch on the surface of the granules. The later hypothesis agrees with earlier findings (Lieberman *et al*, 1990; Shotton *et al*, 1976). In addition it was reported that starch added to the dry granules prior to compression improve 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 granules apart due to expansion (Aulton,1988). Wagner (1968) have similarly shown that when starch is used as extragranular disintegrant, it appears in the channels between the granules causing increase in the tablet porosity. Kolariski and Krowezynski (1970) using potato starch and various cellulose derivatives claimed that the wetting time for disintegrants varied with the method of addition to the other ingredients. The results of the present study when taken together with the results of an earlier study (Ofoefule, 1998) establish that Tacca starch either in its unmodified or modified form, is most effective as a tablet disintegrant when incorporated extragranuarly in tablet formulations. Table II, also shows that modification of the starch led to an increase in the disintegration time of the tablets. One of the properties of Pregelatinized starch is that it is difficult to disperse in water since the grains tend to hydrate rapidly, thus giving lumps and clots that contain unwetted starch in the centre (Snyder, 1984). During pregelatinization, a great proportion of the starch grains gelatinize. Gelatinization is dominated by the amylose content of the starch, a component which is now known to account for the disintegrant property of starch (Manudhane *et al*, 1969). The gel portion is capable of forming a gelled plug thereby hindering further movement of the disintegration medium into the interior of the tablet. It is perhaps on the basis of this that it was concluded that substantial mounts

of Pregelatinized starch (> 5%) in tablet formulations hinder rather than aid disintegration (Ingram *et al*, 1968). These could account for the increased disintegration time of the tablets containing Pregelatinized Tacca starch. Acid hydrolysis on the other hand, may or may not affect the disintegrant property of starch. In situations where acid treatment brings about hydrolysis of mainly the amorphous phase, leaving the crystallites disconnected from each other, a gel network is formed which makes swelling impossible (French, 1984). When starch in water is treated with acid below the gelatinisation temperature, the product can be expected to have the same granular appearance and essentially the same insolubility in cold water as the parent starch (Walton, 1928). Since the concentration of acid and reaction time affect the degree of hydrolysis of starch, and hence its properties, it is logical to conclude here that acid hydrolysis of Tacca starch achieved in this study may have been such that gel network may have been formed by the crystallites which resulted in limited swelling of the starch grains. This is thought to be responsible for the relatively longer disintegration time of tablet containing the hydrolysed Tacca starch. Manudhane *et al* (1969) had earlier reported the superiority of compressible starch (acid hydrolysed) over starch USP in terms of fluidity and compressibility. Their result indicated that effect of compressible starch on disintegration and dissolution of tablets was comparable to that of starch USP. The result of the present study, however, suggests that the effect of acid hydrolysed starch on tablet disintegration and dissolution may depend on the extent and degree of hydrolysis achieved. The effectiveness of the forms of Tacca starch in disintegrating the tablets was in the order unmodified > pregelatinized > hydrolysed starch.

The dissolution profiles of the tablets are shown in Figures 1 – 3. All the tablet batches released above 70 % of riboflavin within 15 min. The relative effect of modification of the starch on dissolution profile of riboflavin was evaluated using the concept of dissolution efficiency (D.E.) at 15 min. using trapezoid rule (Khan *et al*, 1972). The concept of D.E. was adopted because results obtained with it is reported to correlate with *in vivo* performance of a dosage form (Khan *et al*, 1972). The D.E.[15] values presented in Table II indicate that tablets formulated with expected since hydrophilic fillers, such as unmodified starch have been shown to enhance the dissolution of drugs, particularly when starch was granulated with the drug (Marlowe *et al*, 1967). There appears to be a positive correlation between the mode of incorporation of the Tacca starch forms, disintegration time and dissolution efficiency of the tablets. For instance, under extragranular incorporation, fastest disintegration times and highest D.E were obtained for all the tablet batches. Overall, modification of Tacca starch did not retard the dissolution of riboflavin from the tablets.

Conclusion

Tacca starch could be employed in its unmodified or modified forms as disintegrant in tablet formulations. Detailed study on its physico-chemical properties have been done and results from study on binary mixtures of this starch and gelatin (coded Takagel), in the formulation of paracetamol tablet showed very good performance application. It is believed that after extensive characterization of the physico-chemical properties of this

novel starch, it could receive wide acceptance by tablet manufacturing pharmaceutical companies.

Acknowledgement

One of the authors, S. I. Ofoefule is grateful to Bassir – Thomas Biomedical Foundation for her Financial assistance of this research.

References

Aulton M.E. (1988) Pharmaceutics: The Science of Dosage Form Design, ELBS, Churchill Livingstone U.K. PP. 305 –320

Carstensen J.T. Disintegration of Tablets, Theory of Pharmaceutical systems, Academic Press, New York, 1973 pp 258 – 262.

French D. (1984): In, Starch Chemistry and Technology Op. Cit. P. 235.

Ingram, J.T. and Lowenthal, W. J. (1968). Mechanism of action of starch as tablets disintegrant III. *Pharm Sci.,* 57: 393.

Khan, K.A. and Rhodes, T.C. (1972). Effects of compaction pressure on the dissolution efficiency of some direct compress system. *Pharm Acta, Helv.*47: 597 –607.

Kolarski, K. and Krowezynski, L. (1970). Effect of mode of incorporation on disintegrant action of some disintegrants. *Acta Pol. Pharm.* 27: 477

Lieberman W.A., Lachmn L. and Schwartz J.B. (1990). Pharmaceutical Dosage form: "Tablets Vol. 1 2nd Ed. Marcel Dekker inc. New York. P. 108.

Lowenthal, W.J. (1972). Disintegration of Tablets *Pharm* Sci. 61: 1695 –708

Manudhane, D.S. Contractor A.M. Kim, HY and Shangraw R.F. (1969). Tabletting properties of a directly compressible starch. *J. Pharm. Sci.*, 58: 616 620

Marlowe, E. and Shangraw, R.F. J. (1967). Dissolution of sodium salicylate from tablets matrices prepared by wet granulation and direct compression. *J. Pharm. Sci.* 56: 498 (1967)

Ofoefule S.I. and Esimone, O., (1998). Studies on the tabletting properties of *Tacca involucrata* starch: evaluation as a binder. *Bol. Chim. Farmaceutico* 137 (1); 7 – 12

Ofoefule, S.I. (1998). Studies on the tabletting properties of *Tacca involucrata* starch: evaluation as a disintegrant. *Boll. Chim. Farmaceutico,* 137 (6): 218 – 222

Rohwer, R.G. and Klem, R.E. (1984): In, Starch Chemistry and Technology, Whistler, R.L. Bemiller, J.N. and Paschal E.F. (eds) Academic press London, P. 535.

Shangraw, R.F. (1986) Formulation of Tablets – Role of Excipients Bulletin E, pp. 22 – 27.

Shotton, E. and Leonard, G. S. J. (1976). Effects of intragranular and extragranular disintegrating agents on particle size of disintegrated tablets. *Pharm. Sci* 65: 1170 – 1176 (1976).

Snydner, E.M. (1984): In, Starch Chemistry and Technology Op. Cit, P. 671.

Wagner J. (1968). *In-vitro* testing of conventional tablets and capsules. *J. Pharm. Sci.*, 58: 1254.

Walton, R.P, "Comprehensive Survey of Starch Chemistry, Chemical Catalog Co., New York Vol. 1., 1928 p. 170.