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Comparative Binding Effects of Wheat, Rice and Maize Starches in Chloroquine Phosphate Tablet Formulations

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Abstarct: This study was carried out to compare the binding effects of rice and wheat starches with that of the official starch; maize starch BP. Granule properties such as angle of repose, moisture content, bulk and tapped densities, Hausner's ratio, Carr's index and tablet properties which included weight uniformity, friability, disintegration times, and dissolution rates using standard methods. Mucilages of the starches of varying concentrations of 2.5, 5.0 and 7.5%w/v were used to produce chloroquine phosphate granules by wet granulation method and compressed into tablets at 4kgF.An increase in binder concentration led to an increase in crushing strength, decrease in friability and increase in disintegration time of the tablets. Wheat starch produced the hardest tablets and also the least friable tablets, the longest disintegration time and dissolution time when compared to maize starch BP. Wheat starch can be a useful binding agent especially where high bond strength is desired especially in the formulation of chewable tablets and lozenges.

Key words: Binding effect, crushing strength, Wheat, Rice, Maize starch.

INTRODUCTION

Starch is one of the most widely used excipients in the manufacture of solid dosage forms. Starches from different sources have been evaluated and used as excellent binders in either mucilage or the dry powdered form. Although maize starch is the most frequently used excipient in tableting, researchers have tried to develop botanical starches for use tablet excipients. Preliminary evaluation of these starches following official and unofficial protocols showed that they possess some of the desirable features of good excipients (Adebayo and Itiola, 1998).

Nasipuri (1979) evaluated the use of *Dioscorea rotundata* as a binder and disintegrant in tablet formulation and Itiola also investigated the compressional properties of this particular starch (Itiola *et al*, 2006). The effects of pigeon pea and plantain starches on the compressional, mechanical and disintegration properties of Paracetamol tablets have been investigated by Kunle *et al.* (2006). Ibezim *et al.* (2008) have also investigated the role of ginger starch as binder in acetaminophen tablets.

Binders are agents employed to impart cohesiveness to the granules. This ensures the tablet remains intact after compression as well as improving the flow qualities by the formulation of granules of derived hardness and size. The choice of a suitable binder for a tablet formulation requires extensive knowledge of the relative importance of binder properties for enhancing the strength of the tablet and also of the interactions between the various materials constituting a tablet (Mattsson, 2000).

This study investigated the effect of the nature of two starches as binders on physical properties of chloroquine phosphate tablets using the massing and screening method of wet granulation. Chloroquine phosphate was chosen for the work because of its poor tableting properties and hence requires a binder among other excipients to form satisfactory tablets.

MATERIALS AND METHODS

Materials: The following materials were used as obtained from the manufacturers without further purification. Rice grains (Wita-4), Wheat grains (Siete Cerros) (sourced from I.A.R, Zaria). Concentrated Hydrochloric acid (Riedel-dehaen, EC label C.O.O Germany, Lot 42430). Chloroquine powder, Magnesium Stearate powder, Maize starch (BP) powder, Sodium Hydroxide pellets, Talc powder, (BDH chemicals Ltd. Poole England). Gelatin (May and Baker Ltd, Dagenham, England). Xylene (Avondale Lab. Supplies Ltd, Banbury, Oxon, England). The experimental starches (rice and wheat) were prepared in a laboratory in Ahmadu Bello University.

Extraction of Maize, Rice and Wheat starches: The starches were extracted using previously established procedures (Dare *et al*, 2006).

Formulation of chloroquine phosphate granules and tablets: Chloroquine phosphate granules containing 250mg chloroquine phosphate were prepared with wheat, rice starch and maize starch BP as binders respectively in concentrations of 2.5, 5.0 and 7.5%w/v (Table 1). Maize starch at 7.8%w/w acted as disintegrant with 2.0% Talc and 0.2% Magnesium stearate as lubricants. The wet

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Table 1: Formular for chloroquine phosphate granules formulated using the selected starches as binder.

Ingredients	Weight/tablet (mg)	Weight/200 tablets (g)
Chloroquine phosphate	250	50
Intragranular starch (SMS)	15.15	3.03
Binder (batch Ia, Ib, Ic, IIa, IIb, IIc, IIIa, IIIb, IIIc)	7.57	1.514
Extragranular starch (MS, BP)	23.65	4.73
Talc	6.00	1.212
Magnesium stearate	0.60	0.12
Total	303.00	60.60

Key: Ia, Ib, Ic = Official maize starch used at 2.5, 5.0, 7.5%w/v.
IIa, IIb,IIc = Rice starch used at 2.5, 5.0, 7.5%w/v.
IIIa, IIIb, IIIc = Wheat starch used at 2.5, 5.0, 7.5%w/v.
MS, BP = Maize starch BP.

granulation method was employed in the formulation of the tablets. The required quantities of chloroquine phosphate and disintegrant were weighed and mixed with the binder mucilage (wheat, rice and maize starch BP). The resulting wet masses were screened by passing them manually through a 1700 µm mesh size and dried for 20minutes at 40ºC in the oven and then screened through the 1600 µm and then dried to constant weight in the oven. The granules were then mixed with the required quantities of lubricants and then compressed into tablets at 4.0kgF using the Erweka type G. M B. H machine. The tablets produced were stored for 24 hours before the tablet evaluation was carried out to allow for elastic recovery.

Granule analysis

Moisture content analysis: One gram (1g) of the granules was put into a crucible and dried to constant weight in a hot air oven at 105ºC. The moisture content (*MC*) was deduced as difference between the initial (*Wo*) and final weight (*Wf*) of the granules expressed as a percentage and calculated as:

$$MC = \frac{Wo - Wf}{Wo} \times 100 \quad (1)$$

Angle of repose: Fifty grams (50 g) of the granules was placed in a plugged glass funnel which had a distance of 10cm from the flat surface. The granules were then allowed to flow through the funnel orifice by removing the cotton plug from the funnel orifice. The height of the heap (*h*) formed as well as the radius of the heap (*r*) was noted. The angle of repose (*Q*) was calculated as:

$$Q = \tan^{-1}\frac{h}{r} \quad (2)$$

Bulk and Tapped densities: Thirty grams (30 g) of the granules were carefully poured through a short stemmed glass funnel into a 100ml graduated cylinder. The volume occupied by the granules was read and the bulk density calculated in gm/ml (Stanley-Wood and Shubair, 1978). The cylinder containing the granules was tapped fifty times from a height of 2cm and the tapped density calculated in gm/ml.

Percentage compressibility (Carr's index) and Hausner's ratio: The percentage compressibility (*CI*) was calculated from the difference between the tapped (*Dt*) and the bulk densities (*Bt*) divided by the tapped density and the ratio expressed as a percentage (Schwartz, 1975). The Hausner's ratio (*HR*) is the ratio between the tapped and bulk density.

$$CI = \frac{Dt - Bt}{Dt} \times 100 \quad (3)$$

$$HR = \frac{Dt}{Bt} \quad (4)$$

Characterisation of tablets

Tablet thickness: The thickness of ten (5) tablets each selected at random from the formulated batches was determined using a vernier calliper and the mean of these readings was taken as the mean tablet thickness.

Tablet weight uniformity: Twenty (20) tablets were weighed individually on the Mettler electric balance (P163 Mettler instrument AG) from which the mean was calculated and the percentage deviations determined.

Crushing strength: The crushing strengths of the tablets were determined individually with the Monsanto hardness tester, following (Brook and Marsha, 1968). Ten (10) tablets were used and the mean crushing strength was calculated.

Friability: The friability of the tablets was determined using the Erweka friabilator Type A3R. Ten (10) tablets were weighed and put into the Erweka Friabilator and set to rotate at 25 rounds per minute for about four (4) minutes. The tablets were then removed and weighed again.

Disintegration test: Six (6) tablets were placed in each compartment of the Erweka disintegration apparatus, with water thermostated at 37 ± 0.5^{0}C as the medium. The tablets were considered to have passed the test after the six (6) tablets passed through the mesh of the apparatus in 15 minutes.

Calibration curve for chloroquine phosphate: A stock solution of 100mg of Chloroquine phosphate was dissolved in 100ml of 0.1 N HCL. Various dilutions of the stock were made and the absorbances of the various dilutions were taken at 343nm using a UV spectrophotometer. A plot of the absorbance, A against concentration, C was made and the calibration curve was determined from the slope of the graph.

Dissolution test: The dissolution rates of the Chloroquine phosphate were determined using the DGN multipurpose drug test machine (China) Shanghai. The dissolution media was 0.1N HCL at 37 ± 0.5ºC. Samples (10ml) were withdrawn at certain intervals and these were replaced with equivalent volume of the dissolution media. The withdrawn samples were diluted 1 in 10 and analysed at a wavelength of 343nm using the B.Bran Scientific Spectrum Lab 752s spectrophotometer.

Table 2: Granule properties of chloroquine phosphate formulated using the selected starches as binder

BATCH	Ia	Ib	Ic	IIa	IIb	IIc	IIIa	IIIb	IIIc
Binder concentration (%w/v)	2.5	5	7.5	2.5	5	7.5	2.5	5	7.5
Moisture content (%)	4	5	4	4	4	6	6	5	6
Flow rate (g/sec.)	6.08	6.04	5.59	5.79	5.58	5.75	5.92	6.42	4.73
Angle of repose (^{o})	26.6	26.3	25.5	25.3	25.3	23.1	25.5	26.6	25.4
Bulk density (g/ml)	0.51	0.49	0.48	0.51	0.49	0.48	0.49	0.49	0.51
Tapped density (g/ml)	0.64	0.61	0.57	0.61	0.60	0.57	0.65	0.61	0.60
Carr's index (%)	20.3	19.7	15.8	16.4	20	15.8	24.6	19.7	15
Hausner's ratio	1.25	1.24	1.19	1.2	1.22	1.19	1.33	1.24	1.18

Table 3: Tablet properties of chloroquine phosphate tablets formulated using the selected starches as binder

BATCH	Ia	Ib	Ic	IIa	IIb	IIc	IIIa	IIIb	IIIc
Binder concentration (%w/v)	2.5	5.0	7.5	2.5	5.0	7.5	2.5	5.0	7.5
Average tablet thickness (mm)	3.25	3.25	3.32	3.31	3.30	3.25	3.29	3.26	3.29
Crushing strength (kgF)	4.00	5.25	6.25	6.90	7.25	8.25	6.00	10.00	8.90
Tensile strength (MNm)	0.078	0.103	0.120	0.132	0.140	0.135	0.116	0.198	0.143
Friability (%)	4.13	1.08	0.30	1.41	1.06	0.71	1.42	0.71	0.69
Disintegration time (sec.)	141	207	129	141	185	301	261	305	297

RESULTS AND DISCUSSION

The moisture contents of the batches (Table 2) showed that wheat starch formulations has the highest moisture content and this could be attributable to the fact that it has larger average grain size (Olayemi *et al,* 2008) which implies that there are larger pore sizes which may trap water and result in high moisture contents. Investigations have shown that moisture contents of 3-5%w/w were appropriate to produce maximum disintegration and dissolution for chloroquine phosphate/starch tablets (Pilpel *et al*, 1978).

The lower bulk and tapped densities exhibited by wheat and maize starch (Table 2) shows that both materials are not as porous as rice starch although, the three powders prove to be poor flowing powders from the generally low bulk and tapped densities. The low densities have been reported to result when void spaces created by larger powder particles are not filled by smaller particles leading to consolidation of the powder particles (Newmann, 1967). From the Hausner's ratios which are greater than 1.2, all the starch powders can be said to have low interparticulate friction (Staniforth, 1996) and thus, are non- free flowing powders. However, rice and wheat starches possessed better flow properties than maize starch BP as indicated by the Carr's indices. The angle of repose is known to be a measure of flowability and the angles of repose for all the batches were within the same range. The flow rate of granules which is a measure of flowability has been said to be necessary for successful tableting (Newmann, 1967). The flow rates were observed to be comparable although there was a decrease in flow rate with increasing binder concentration, this could be as a result of increased bonding and cohesiveness between particles leading to reduction in the flow of granules (Abdulsamad *et al*, 2008).

Tablet thickness has been established to vary with compressional force and density of granulation. The tablet thickness of all the formulations were similar (Table 3) and this can be attributed to their similar bulk and tapped densities and same compressional force used (4 kgF). The crushing strength and tensile strength of the tablets increased as the concentration of starch increased (Table 3). Binders have been said to promote plastic deformation of particles and thereby increasing the area of contact for interparticulate bonding (Uhumwangho *et al.*, 2006) subsequently leading to the formation of more solid bonds in the tablet. Tablet hardness was observed to be higher with wheat starch at all the concentrations employed compared to those of rice and maize starches. This indicates that lower concentration of wheat starch could be used to achieve the same level of bond strength and probably granules made from wheat starch mucilage were more readily deformed than those produced with either rice or maize starch.

As the more starch is forced into interparticulate spaces thereby increasing the area of contact between the particles leading to formation of additional solid bonds and these confer resistance to tablet fracture and abrasion thereby bringing about a decrease in friability with increase in concentration. This also led to a corresponding reduction in the size of the capillary spaces between the particles (leading to the decrease in the friability). This reduction in capillary spaces led to the reduction in the penetration of water into the tablet to cause bond separation and thus, leading to longer disintegration times. Although all the formulated batches disintegrated within the not more than 15 minutes specified by BP (1988) for uncoated tablets, wheat starch formulation had the longest disintegration time which corresponded to the high crushing strength.

The swelling capacity which reflects increase in volume of the starches showed rice starch having the highest increase in volume followed by maize starch and then wheat starch (Olayemi *et al.*, 2008). This suggests that the low swelling capacity of wheat starch could have resulted in minimal swelling thereby giving rise to particle-particle bonding thus, longer disintegration time.

The dissolution of the tablet formulations was carried out only on 5% w/v formulations (Fig. 1) and it shows that wheat starch formulation attained the specified concentrations at a longer time than the other batches. It was observed that tablets formulated with wheat starch gave the least percent of drug released at the initial time

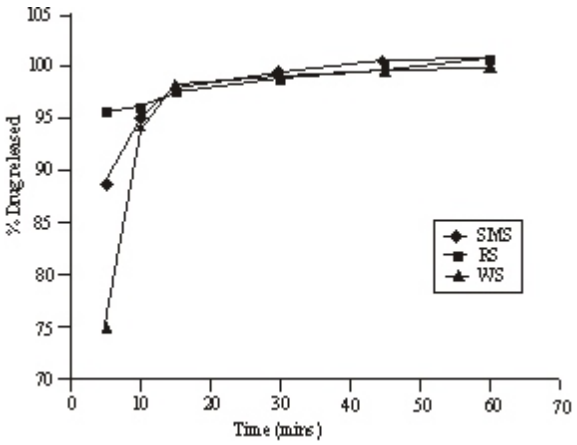

Fig 1: Percent drug released of chloroquine phosphate tablets formulated using the selected starches against time (min).

of dissolution. This could be due to its high bond strength and lower swelling capacity which could be responsible for the increase in dissolution time. Also, the large grain size of the wheat starch could account for the least % of drug released. Underwood and Cadwallder (1972) suggested that tablets containing starch with large particles have a smaller starch particle ratio (less starch separating individual drug particles), so that aggregates of the drug may form and thus, will take a longer time for the drug to be released. The dissolution pattern agrees with the disintegration – dissolution theory which proofs that disintegration usually plays a vital role in the dissolution process since it determines to a large extent the area of contact between the solid and liquid (Odeku and Itiola, 2006). However, all the batches of the tablets formulated passed the BP (2002) dissolution test for tablets which specifies that at least 70% of the drug should be in solution after 30 minutes.

CONCLUSION

The result of this study has established that wheat starch formulations give stronger tablets in comparison to rice and standard maize starches and this is advantageous especially when high bond strength is desired and quick disintegration is not desirable. This makes wheat starch suitable binder for chewable tablets and lozenges.

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