Evaluation of admixture of starches and acacia gum a binders for sulphaguanidine granules and tablets

By
FRANCIS A. OLADIMEJI* AND ISAAC O. DAGUNDURO
Department of Pharmaceutics,
Faculty of Pharmacy,
Obafemi Awolowo University, Ile-Ife.

* *Address for correspondence*

ABSTRACT:

The effects of combining starches (Cassava, maize and potato) with acacia gum on the physical properties of sulphaguanidine granules and tablets were investigated. The starches were found to have higher binding capacity than acacia gum but stepwise substitution of the starch with the gum produced more friable, smaller, and less porous granules with improved flow ability. Combination of starch and acacia gum also produced tablets with improved weight uniformity and decrease in hardness and disintegration values. However on storage for six months, tablets formulated with increased proportion of acacia to starch in the binder solution showed increase in hardness and disintegration values because of the increase in hardness and disintegration values of the tablets on aging, it is suggested that starch should be minimally substituted with acacia gum.

INTRODUCTION

The choice of a binder in tablet formulation is dictated among other things by the degree of binding required (Shubair and Dingwall, 1976) Starch has been found to be a better binder than acacia gum since starch gave harder, glossier and less friable tablets (Alam and Parrott, 1971 and Nasipuri, 1979). Acacia gum has also been found to increase the hardness and disintegration values of tablets on aging (Alam and Parrott,1971 and Nasipuri,1979). However, synergistic effects between starch and gum like guargum have been reported by Nath and Gaitonde (1976). Improvement in granules flow ability and tablet weight uniformity was exhibited when guargum and starch (Maize, potato tapioca and arrowroot) combinations were used in preparing lactose (Nath and Gaitonde 1976). No conclusive ratio between the guargum and starch at which the combination was optimally effective was however arrived at. Nath and others (1985) using guargum and locust bean gum in combination with different starches, reported that binder formulations containing guargum were most effective. The results indicated that all natural gum containing galactomannan may not compare favourably with one another when combined with starch.

This present study involved the use of acacia gum in combination with three starches namely cassava, maize and potato to produce sulphaguanidine granules and tablets. The physical properties of the granules and tablets were evaluated with the aim of determining the optimal effective ratio between acacia gum and the starches at which satisfactory granules and tablets were produced.

EXPERIMENTAL

Materials: Acacia powder (BDH, England), Maize starch (BDH, England), Magnesium stearate (Hopkins and Williams, England), Talc (BDH, England), Sulphaguanidine (BDH, England). Cassava starch was prepared in our laboratory using the method adopted by Nasipuri (1979) in preparing cocoyam starch.

Preparation of Sulphaguanidine granules: The starches (cassava, maize and potato) and acacia gum were combined and coded as indicated in Table I. The starch and acacia gum were heated together using distilled water until a homogenous mucilage was formed. The final weight of the binder solution was adjusted to 100g with hot distilled water.

Predetermined quantity of the binder solution was added in three to four portions to 700g of sulphaguanidine power and massed at regular time intervals for 8 min. using a Hobart bowl mixer. The wet mass was passed through a 12 mesh screen (i.e. 1400 um) and the wet granules dried in a fluidized bed dryer at 45-60^{o} for 25min. The dried granules were screened through sieve No 10 (i.e. 1700 um).

Granule size analysis: Endecott test sieves ranging from 2000 um (8 mesh sieve) to 150 um (100 mesh sieve) and a receiver were used with a shaking time of 10 min. 50% comulative over size was taken as average granule size.

Friability: 10g sample from fraction retained by a 22 mesh sieve but passing through a 16 mesh sieve i.e. (710 - 1000 um) was used in the determination, using a Roche friabilator with the drum set to rotate at 25 rpm for 4 min. The percentage loss of weight due to abrasion was calculated from the weight of granules retained by the 22 mesh sieve after the test. The results given are the means of three determinations

Bulk density (P_b): Bulk densities were determined the method of Neumann (1967). 50g (W) of granules fraction from -16 + 22 mesh sieve i.e. (710 - 1000um) was poured into a 100cm^3 graduated measuring cylinder and dropped gently 100 times on a pile of cloth until no decrease in bed height occurred. The volume of the granules bed was measured at three places around the measuring clylinder. The mean volume (V) was used to calculate the bulk density from the expression:

$(W/V)\ Cm^{-3}$ ..... (1)

The results given are the means of the three determinations.

True density (P_t)

True density was determined using the displacement of benzene method in $50cm^3$ pycnometer bottle. The empty bottle was weighed (W), filled with benzene and reweighed (W_1). The difference gave the solvent weight (W_2) 5g sample (W_3) of granules fraction -16 + 22 mesh sieve i.e. (710- 1000 um) was introduced into the empty pycnometer bottle, filled with the benzene and weighed (W_4). The true density was calculated from the expression

$$P_t = \frac{W_2\ W_3}{50\ (W_1 + W_3 - W_4)} \quad \text{..... (2)}$$

The results given are the means of three determinations.

The total porosity (E_T) of the granules was estimated from the expression (Martin **et al**, 1983).

$$E_T = 1 - \frac{P_b}{P_t} \quad \text{..... (3)}$$

And the percentage porosity is expressed as

$$E_T\% = (1 - \frac{Pt)}{(\ Pt)} \times 100 \quad \text{..... (4)}$$

Angle of repose

Granules retained by 44 mesh sieve (355 um) but passing through a 16 mesh sieve (1000 um) were used for the determination. A fixed - funnel and free standing cone method was used (Train, 1958) the funnel was secured with the tip at a known height (h) above a calibrated graph paper placed on a flat horizontal surface. Granules were carefully poured through the funnel until the apex of the conical pile touched the top of the funnel. The diameter (d) of the cone was measured and the angle of repose calculated from the expression.

$$0 = \arctan(2h/d) \quad \text{..... (5)}$$

The results given are the means of four determinations.

Flow Index

A flow tube with an orifice of 10 mm was vertically secured to a retort clamp. The orifice was covered with a cardboard flap and a weighted receiver placed below it. 100g of -16 + 44 mesh granules (355 - 1000 um) was introduced into the tube and the cardboard flap covering the orifice gently removed to allow the flow of the granules for 60 sec. The quantity of granules discharged was weighted and the flow index calculated from expression below:

$$\text{Flow Index} = \frac{W\ \ (g\ min^{-1})}{W_a\ (g\ min^{-1})} \quad \text{..... (6)}$$

w = Weight of granules discharged

w = Weight of granules discharged using acacia as binder.

The results given are the means of four determinations.

Preparation of the tablets

Granules retained on 44- mesh screen (355 um) were used with 10% $^{w}/_{w}$ of granules that passed through 60-mesh screen (250 um) added to them as fines. 5% $^{w}/_{w}$ potato starch was added as disintegrant while 1% $^{w}/_{w}$ of a mixture of magnesium stearate and talc (1:1) sifted through 60-mesh screen were added as lubricant. The mixtures were then mixed by gently rolling them in a container for 5 min. 400 mg granules sample was used in calibrating the die fill. The granules were then compressed on a single punch tabletting machine (Diaf A/S, Type TM20, Denmark) using a 10 mm diameter flat faced punch/die at 5 units compressional pressure. The tablets were stored for seven days to allow elastic recovery before they were evaluated.

Evaluation of the tablets

Tablet hardness was determined by the Pfizer hardness tester using ten tablets. Twenty tablets from each batch were weighed individually and the mean tablet weight, standard deviation, and coefficient of variation calculated. Friability value was determined by rotating ten tablets in a Roche friabilator (Erweka) with the drum set at 25 rpm for 4 min. The percentage loss in weight due to abrasion was then calculated. The disintegration times of the tablets were determined by the method prescribed in British Pharmacopoeia (1973) for uncoated tablets using a manesty tablet test unit except for elimination of guide discs. The results given are the means of three determinations.

Results and Discussion

The physical properties of sulphaguanidine granules are given in Table II. The effect of combining starch with acacia gum on the physical properties of the granules were almost the same for the three starches used, hence the results will be discussed in general. The mean granule size decreased as the concentration of starch in the starch-acacia gum combination decreased. This also correlated with a decrease in the quantity of starch-gum combination used in formulating the granules. The trend of the result could be due to increase in the fluidity of the starch-gum solution as the concentration of starch in the combination decreased resulting in decrease in the solution tackiness/adhesiveness thereby promoting solid/liquid adhesion rather than solid/solid adhesion. It has been reported that solid/liquid adhesion yields granules with smaller sizes (Chalmers and Elworthy, 1976). Also a stepwise decrease in the concentration of starch in the starch-gum mixture yielded more friable granule. Replacing part of the starch by the gum is analogous to dilution of the binder mixture (decreased viscosity), which has been reported to increase friability (Davies and Gloor,1973).

There was no significant difference in bulk densities and true densities of the granules as the starch-gum component of the binder solution is varied. However, granules produced using starch mucilages alone were more porous than those of acacia gum, while combinations of the two binders showed intermediate values. To some extent, the porosity of the granules could be correlated with the granule size, as smaller and dense granules yielded less porous granules (Batches M_4, P_4 and A). The flow index is a measure of flowability of the

TABLE I: COMPOSITION OF THE GRANULATING FLUID (% W/W)

Cassava	Maize	Potato	Acacia gum	Code	Quantity used (Gram)
6	-	-	-	C_1	157.5
4	-	-	2	C_2	149.4
3	-	-	3	C_3	132.0
2	-	-	4	C_4	129.6
-	6	-	-	M_1	149.7
-	4	-	2	M_2	137.8
-	3	-	3	M_3	133.2
-	2	-	4	M_4	135.0
-	-	6	-	P_1	143.4
-	-	4	2	P_2	128.4
-	-	3	3	P_3	121.8
-	-	2	4	P_4	123.3
-	-	-	6	A	121.5

TABLE II: PHYSICAL PROPERTIES OF SULPHAGUANIDINE GRANULES PREPARED WITH ADMIX TURE OF STARCH AND ACACIA GUM AS BINDER

	C_1	C_2	C_3	C_4	M_1	M_2	M_3	M_4	P_1	P_2	P_3	P_4	A
Mean granule size (um)	1590	1400	1360	1320	1460	1400	1330	1090	1730	1600	1400	1220	1140
Friability, %	4.9	5.5	9.2	9.9	5.7	6.0	6.3	7.4	2.1	5.3	6.8	7.2	5.8
Bulk density,gcm^{-3}	0.44	0.46	0.50	0.50	0.45	0.46	0.48	0.51	0.42	0.44	0.48	0.54	0.52
True density, gcm^{-3}	1.29	1.28	1.36	1.38	1.31	1.31	1.34	1.38	1.28	1.31	1.35	1.36	1.37
Porosity, %	65.9	64.1	63.2	63.8	65.6	64.9	64.2	63.0	67.2	66.4	64.4	60.3	62.0
Angle of repose	38.1	37.2	36.1	30.6	38.6	38.1	36.5	35.4	40.4	39.5	37.4	36.4	38.4
Flow index	0.73	0.75	0.90	1.04	0.70	0.74	0.75	0.88	0.68	0.80	0.77	1.13	1.00

TABLE III: PHYSICAL PROPERTIES OF SULPHAGUANIDINE TABLETS PREPARED WITH ADMIXTURE OF STARCH AND ACACIA GUM AS BINDER

	Weight Variation			Friability (%)	Hardness (kg)		D.T (min)	
	Mean wt (g)	S.D (g)	C.V. (%)		X	Y	X	Y
C_1	0.385	0.023	5.97	1.53	8.8	9.3	27.03	26.92
C_2	0.382	0.017	4.45	1.40	9.2	10.1	30.07	31.19
C_3	0.395	0.014	3.54	1.70	8.2	10.4	16.22	20.89
C_4	0.410	0.008	1.95	2.16	7.3	8.1	10.43	14.22
M_1	0.385	0.034	8.83	1.69	10.5	11.3	33.67	34.81
M_2	0.380	0.026	6.84	1.73	9.1	9.4	26.42	32.00
M_3	0.381	0.021	5.51	2.08	8.5	9.5	16.72	25.03
M_4	0.415	0.011	2.65	2.74	6.4	7.6	10.28	16.25
P_1	0.365	0.038	10.41	1.20	10.8	11.1	*	*
P_2	0.379	0.029	7.65	3.22	4.9	5.5	27.55	28.36
P_3	0.392	0.009	2.30	4.15	5.2	5.7	18.40	21.42
P_4	0.390	0.013	2.33	4.70	4.8	5.9	6.48	10.78
A	0.408	0.021	5.15	2.12	6.2	7.9	14.20	18.36

S.D. - *Standard Deviation*
C.V. - *Coefficient of variation of weight*
X - *Immediate value*
Y - *Value after 6 months;*
D.T. - *Disintegration time;*
* - *Disintegration time greater than 120 min.*

granules with reference to the flowability of those granules produced using acacia gum alone as binder. A decrease in angle of repose with improved flowability was therefore observed (Table II) as the concentration of starch in the binder combinations was decreased stepwise.

The physical properties of tablets compressed from the granules are reported in Table III. A stepwise decrease in the concentration of starch in the binder mixture improved the mean weight of the tablets. Increase in flow rate associated with smaller and less porous granulations manufactured using less viscous binder solution might have contributed to the increase in the mean tablet weight and diminished variation in the weight of the tablets. As indicated in table III, when part of the starch is substituted with acacia gum, the tablet hardness decreased, while the friability increased. This may be an indication that the effectiveness (binding capacity) of the binder mixture depends on the concentration of starch mucilage in the admixture of starch-acacia gum.

The disintegration times for the sulphaguanidine tablets are given in Table III. Starch mucilage alone prolonged the disintegration time when compared with acacia mucilage. This finding was contrary to earlier reports of Mital (1968), who observed that starch mucilage gave a lower disintegration time when compared with acacia mucilage in this case, a heavier coating of the granules by the high viscous starch mucilage may be responsible for the prolonged disintegration time there was a significant decrease in the disintegration time with stepwise decrease in the starch concentration of the binder mixture. This could probably be due to decrease in binding capacities of the solutions.

Storage at room temperature for six months affected the disintegration and hardness of the tablets as indicated in Table III. This has earlier been noted by Alam and Parrott, (1971), and Nasipuri (1979). The increase in disintegration time with aging became more pronounced as the concentration of acacia gum in the binder solution increased. On physical inspection of the tablets after six months, batches C_3, C_4, M_3, M_4, P_4 and A showed brown colouration. The intensity of the colour was found to depend on the concentration of gum in the binder mixture.

From the physical properties of the granules and tablets, it could be concluded that starch has a higher binding capacity than acacia gum. This higher binding capacity may not necessarily mean improved granule and tablet properties as evidenced from the results in Tables II and III. Blends of starch and acacia gum produced granules and tablets which exhibited better physical properties than when starch or acacia was used alone. Starch mucilages are highly viscous and their efficiency in producing uniform wet mass may be reduced while acacia gum mucilage due to its low viscosity may produce over wetted granule. The synergistic effect noted earlier on by Nath and Gaitonde (1976) when starch was combined with guargum may therefore not necessarily be as a result of chemical reaction between the amylopectin fraction of the starch and the galactomannan molecule of the gum. It could be as a result of reduction in the viscosity of the starch gum mixture which improved the wetting and penetration ability of the binder solution.

Though stepwise substitution of the starch with the gum continuously improved the tablets properties (at the concentrations studied) as also noted by Nath and Gaitonde (1976), this was found to increase the hardness and disintegration time of the tablets on storage for six months. Therefore, high substitution of the starch with gum may not be desirable.

REFERENCES

1. Alam, A.S. and Parrott, E.L. (1971) Effect of Aging on some physical properties of Hydrochlorothiazide tablets. J. Pharm. Sci. 60 263-266.
2. British Pharmacopoeia (1973) Disintegration Test for Tablets. Appendix XIXA A131.
3. Chalmer, A.A. and Elworthy, P.H. (1976) Oxytetracyline Tablet Formulation: Effect of Variations in Binder Concentration and Volume on Granule and Tablet Properties. J. Pharm. Pharmacol. 28. 228 - 233.
4. Davies W.L. and Gloor Jr. W.T. (1973) Batch Production of Pharmaceutical, granulations in a fluidized bed III: Binder dilution effects on granulation. J. Pharm Sci. 62 170 -171.
5. Martins, A.N; Swarbrick J. and Camarata, A. (1983) "Densities of Particles" in Physical Pharmacy 3rd Edition. Lea and Febiger hiladelphia. p. 513 - 517.
6. Mital, M.C (1968) Methyl Cellulose in Non-aqueous Solvent as a Granulating Agent for Aspirin. Pharm. Acta Helv. 43, 91 - 94.
7. Nasipuri, R.N. (1979) Evaluation of Cocoyam starch as Tablet Binder and Disintegrant. Pharm. Acta Helv. 54, 48 - 53.
8. Nath, B.S. and Gaitonde, R.V. (1976) Effect of Admixture of Guargum and Starch Mucilage on Micrometrics of Granules and Tablets of Lactose. Indian J. Pharm 38, 99 - 101.
9. Nath, B.S; Kamamai, E. and Borcar, D.V. (1985) Effect of Admixture of Natural Gums and Starch Mucilage as Binder for Lactose Granules and Tablets. Indian J. Pharm. 47 181 184.
10. Neumann, B.S. (1962) "The Flow Properties of Powder" in Advance in Pharmaceutical Science No. 2. Edited by Beans, H.; Beckett, A.H and Carless, J.E. Academic Press New York. p. 200 - 205.
11. Tran, D. (1958) Some Aspects of the Property of Angle of Repose of Powders. J. Pharm. Pharmacol. 10 127T - 137T.
12. Shubair, M.S. and Dingwall, D. (1976) Starch Binder Dilution and Tablet Properties. Mfg. Chem. Aerosol News 47(11) p. 43 - 47.