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Research Article

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Physical and mechanical effects of starch-gelatin binary binder mixtures on sodium salicylate tablets

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ABSTRACT

Starch- gelatin binary binder mixtures were applied in the formulation of sodium salicylate tablets. Locally developed cassava starch (tapioca starch) was used as a co-binder with gelatin. Wet granulation method was used to formulate different batches of sodium salicylate tablets with varying binder concentrations (1-5%w/w) and starch – gelatin binder ratios (25:75, 50:50, 75:25 and 0:100). The sodium salicylate granules were evaluated for flow properties, friability, moisture uptake while the tablets were assessed for crushing strength, friability and crushing strength-friability ratio (CSFR). Formulations prepared with gelatin, had lower granule friability than those produced with cassava starch – gelatin binder mix. Flow properties did not follow any definite pattern ,whereas moisture uptake studies showed that gelatin batches absorbed more moisture than cassava starch-gelatin batches. As the gelatin content decreased, the tablet crushing strength and CSFR decreased while the friability increased. The mechanical strength and moisture uptake of the gelatin based granules or tablets reduced with the incorporation of cassava starch

Keywords: Wet granulation, starch, gelatin, binary, binder.

INTRODUCTION

In various solid dosage forms, starches are widely employed as multipurpose excipients especially as fillers, disintegrants, and binders due to their versatility, ready availability, cheapness and inertness [1]. Starch and gelatin are two of the most widely used pharmaceutical excipients. As binders they function by holding powder particles together in cohesive agglomerates thereby converting them into granules that are free-flowing and compressible. They act as adhesives to bind powders together in the wet granulation process. Starch and gelatin are usually employed as binders in the form of starch mucilage (2-5%w/w) and gelatin solution (1-3%w/w) respectively. Tapioca Starch (cassava starch) is obtained from the rhizomes of *Manihot utilissima pohl.* Sodium salicylate was used as the model drug due to its poor compressibility and flow. The aim of this research is to investigate the application of starch-gelatin binary binder mixture in the formulation of sodium salicylate tablets.

EXPERIMENTAL SECTION

Materials

The following materials were utilized as supplied by their manufacturers; sodium salicylate, magnesium stearate (Merck, Germany); Lactose , maize , sodium metabisulphite, potassium hydroxide (BDH , England); Gelatin (Sigma ,USA) ;Hydrochloric acid , sulphuric acid (M&B England).Cassava tubers were obtained from Nsukka farm, Nigeria.

Extraction of Starch from Cassava Tubers

Cassava starch was extracted from the tubers of *manihot utilissima* through the process of communition and stepwise treatment with, sodium metabisulphite, 0.1N potasium hydroxide and 0.1N sulphuric acid.

Formulation of sodium salicylate granules

Wet granulation method was used to produce sodium salicylate tablets containing different concentrations of binders. The general formula given below in table 1, was used in the formulation of sodium salicylate granules.

Table 1: Formula for the production of sodium salicylate granules/tablets

Ingredients	Weight per tablet
Sodium salicylate	100mg
Binder	1-5% w/w
Dry maize starch	30mg
Magnesium stearate	3mg
Lactose qs	300mg

The various binder levels (1-5% ^{w}/w) were comprised of binary binder mixtures of cassava starch: Gelatin or Gelatin alone. The binary binder mixtures were formulated in 3 different ratios of 25:75, 50:50, and 75: 25 for each of the 1%, 2%, 3%, 4% and 5% binder levels.

Evaluation of granules

Granule friability was evaluated using the Roche friabilator and calculated as 100 times the ratio of loss of weight to initial weight of the granules. The Bulk density (ρ_b) of the sodium salicylate granules was determined as the quotient of weight to the volume of the granules while the tapped density (ρ_t) was determined as the quotient of weights to the volume of granules after tapping the measuring cylinder containing the bulk sample 500 times from a height of 1 cm from the bottom of the cylinder. Hausner's quotient of the granules was derived as the ratio of the tapped density to the bulk density [2].The percent compressibility was calculated as one hundred times the ratio of the difference between the tapped density and bulk density to the tapped density [3]. The flow rate of the various batches of sodium salicylate granules were determined simultaneously with the angle of repose using the fixed height funnel method [4]. The mean height of the heap and diameter of the base of the powder heap were determined and the angle of repose was then calculated from the geometry of the powder heap:

Flow rate = weight/time ----------2

Θ=height of powder heap (h)/radius (r)----------3

Θ is the angle of repose and the radius is half of the diameter of the heap base.

Moisture uptake by the various batches of sodium salicylate granules was studied based on static method using saturated salt solution in closed chambers [5].

Evaluation of Tablet

Monsanto hardness tester was used to determine the force required to diametrically break ten randomly selected tablets from each batch of sodium salicylate tablet. The tensile strength of the sodium salicylate tablets were calculated using equation 4

$T_s = 2P/\pi dt$ ----------4

$T_s$is tensile strength, P is crushing strength, d is diameter and t is thickness of the tablets

Friability of tablets was evaluated using the Roche friabilator and calculated as 100 times the ratio of weight loss to initial weight while crushing strength-friability ratio was calculated by dividing the crushing strength by the friability. Statistical evaluation was performed by Analysis of variance (ANOVA) at 95% confidence limit.

RESULTS AND DISCUSSION

Flow Properties of Granules

The bulk density, tapped density, hausner's quotient, carr's compressibility index, flow rate and angle of repose of the sodium salicylate granules are shown in table 2.

Table 2: bulk density (ρ_b), tapped density (ρ_t) ,hausner's quotient (H.Q), carrs compressibility index (C.I), angle of repose, flow rate, granule friability (F) and moisture uptake (%) of sodium salicylate granules

Formulation	ρ_b(g/ml)	ρ_t(g/ml)	H.Q	C.I	angle of repose (°)	flow rate (g/sec)	F (%)	Moisture Uptake %
Ac_1	0.44	0.54	1.22	17.78	33.59	5.13	2.20	20.60
Ac_2	0.45	0.69	1.52	34.10	33.28	5.13	2.15	20.25
Ac_3	0.45	0.74	1.63	38.64	33.94	5.00	2.24	20.00
Bc_1	0.48	0.59	1.24	19.04	33.24	5.26	1.93	21.70
Bc_2	0.45	0.58	1.28	21.60	32.72	5.13	2.00	21.10
Bc_3	0.45	0.58	1.28	21.60	32.78	5.00	2.15	20.55
Cc_1	0.45	0.57	1.26	20.46	33.04	5.56	1.95	21.90
Cc_2	0.46	0.58	1.26	20.68	33.16	5.41	2.06	21.20
Cc_3	0.47	0.59	1.26	20.93	32.02	5.41	2.10	20.90
Dc_1	0.45	0.59	1.29	22.73	32.45	6.67	1.90	23.20
Dc_2	0.44	0.56	1.25	20.01	32.72	6.67	2.00	22.10
Dc_3	0.44	0.59	1.32	24.45	32.55	6.45	2.00	21.50
Ec_1	0.44	0.56	1.25	20.01	32.41	8.00	1.90	24.40
Ec_2	0.43	0.53	1.25	20.21	32.85	7.70	1.98	23.00
Ec_3	0.44	0.61	1.36	26.68	32.76	6.67	2.05	22.65
A-gel	0.46	0.61	1.32	24.14	32.91	5.00	2.10	21.10
B-gel	0.44	0.59	1.32	24.45	32.47	5.56	1.96	22.15
C-gel	0.43	0.58	1.33	25.00	30.88	5.88	1.90	22.35
D-gel	0.43	0.58	1.33	25.00	31.92	6.90	1.90	23.95
E-gel	0.43	0.57	1.34	25.53	30.65	8.00	1.18	24.80

Key : A-E represents 1-5% binder concentrations
: c and gel represents cassava starch-gelatin and gelatin respectively
: 1,2 and 3 represents 25:75, 50:50 and 75:25 starch: gelatin binder ratio respectively

The crushing strength, tensile strength, friability and CSFR of the formulated sodium salicylate tablets are presented in table 3 and ranges from 5.0-12.5Kgf, 0.10-0.21MNm^{-2} , 0.35-1.47%, 3.40-35.31 respectively.

Table 3: crushing strength, tensile strength, friability, CSFR of the sodium salicylate tablets

batch	Crushing strength (Kgf)	Tensile strength (MNm^{-2})	Friability (%)	CSFR
Ac_1	6.40	0.11	1.21	5.31
Ac_2	5.80	0.10	1.43	4.05
Ac_3	5.00	0.10	1.47	3.40
Bc_1	7.00	0.12	0.77	9.13
Bc_2	6.55	0.13	0.87	7.57
Bc_3	6.25	0.11	0.95	6.55
Cc_1	9.30	0.16	0.63	14.83
Cc_2	9.05	0.15	0.87	10.37
Cc_3	8.80	0.17	0.75	11.69
Dc_1	10.60	0.18	0.42	25.30
Dc_2	9.75	0.16	0.58	16.70
Dc_3	9.25	0.16	0.65	14.25
Ec_1	12.20	0.20	0.39	31.69
Ec_2	11.45	0.19	0.42	27.46
Ec_3	10.25	0.17	0.61	16.89
A-gel	7.00	0.12	0.95	7.33
B-gel	8.20	0.14	0.63	12.98
C-gel	9.35	0.16	0.65	14.39
D-gel	11.00	0.16	0.39	28.42
E-gel	12.50	0.21	0.35	35.31

Physical properties of sodium salicylate granules

The granule friability of the batches is a measure of their strength. The granule friability decreased with increasing binder concentration and gelatin content . The general hardness and resistance to abrasion exhibited by these granules may have been caused by intragranular migration which may have deposited the soluble binder (gelatin) at the periphery of the granules during drying. Earlier studies have shown that this migration can aid the bonding process and is therefore sometimes beneficial [6]. The result from tests of flow rate, angle of repose, Hausner's quotient and Carr's compressibility index (table 2) were compared in order to fully understand the flow properties of the sodium salicylate granules. In free-flowing granules, the bulk and tapped densities would be more similar than in poor flowing granules which yield greater differences between the two values. At 84% relative humidity, the moisture absorbed by the granules increased as the binder concentration and/or gelatin increased. This result may be due to the higher hygroscopicity and swelling capacity of gelatin. Gelatin absorbs 5-10 times its own weight of water [7]. The batches containing cassava starch absorbed less environmental moisture.

Evaluation of sodium salicylate tablets

The Crushing strength and tensile strength of the sodium salicylate tablets are presented in table 3. The result showed that the crushing strength or hardness of the tablets generally increased as the binder concentration and gelatin increased.

There was a decrease in friability as the binder concentration and gelatin increased. Most of the batches exhibited friability values of less than 1% which is acceptable, with exceptions observed at 1% binary binder concentrations. Tablets prepared with 25:75 starch-gelatin binary binder ratio exhibited lower friability than those prepared with 50:50 and 75:25 binder ratios. Furthermore tablets formulated with 50:50 binder ratio showed a relatively lower friability compared with the corresponding batches prepared with 75:25 binary binder ratio.

Generally the higher the CSFR value, the stronger the tablet. Formulations prepared with gelatin alone as binder exhibited higher CSFR than the corresponding batches produced with cassava starch-gelatin mix. In terms of binder ratio, the CSFR values followed an approximate order : 0:100 > 25:75 > 50:50 > 75:25 binder ratio.

CONCLUSION

The mechanical strength and moisture uptake of the gelatin based granules or tablets, reduced with the incorporation of cassava co-binders. The choice of component, concentration and ratio of composite binder mixtures would depend on intended use and prevailing environmental conditions. The flow properties of the formulations did not show any definite rank order and changes in the binary binder components of the formulations may be permissible with respect to flow behaviour. This research work would contribute positively to the mobilization of local raw materials like cassava and stimulate the mass production of cost effective pharmaceutical products.

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