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Full Length Research Paper

Evaluation of okro gum as a binder in the formulation of thiamine hydrochloride granules and tablets

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The aim of this study is to examine the suitability of okro gum as a binder for pharmaceutical tablet formulations. A comparative evaluation of *Abelmoschus esculentus* (okro) gum as a binder in the formulation of thiamine hydrochloride granules and tablets was performed. Gelatin, acacia and polyvinylpyrrolidone (PVP), were employed as standard binders for comparison. The properties of granules and tablets evaluated were; flow rate, angle of repose, density, weight uniformity, hardness, friability, disintegration time and dissolution rate. The granules had good flow properties. However, binder concentration influenced flow characteristics. Okro gum gave the highest hardness/friability ratios. It also prolonged disintegration time and dissolution time and dissolution rate. Hence, okro gum may not be useful as a binder in conventional tablet formulation. Nevertheless it could be a good candidate for evaluation as a binder or hydrophilic polymer in sustained release tablet formulation.

Key words: *Abelmoschus esculentus* gum, binder, granules, tablets.

INTRODUCTION

Research on many flowering plants growing in Nigeria as sources of pharmaceutical recipients have yielded interesting results. Recently, a polysaccharide gum from *Abelmoschus esculentus* popularly known as okro was shown to have favourable suspending and emulsifying properties (Brown, 1991). The plant belongs to the plant family Malvaceae. Okro fruits are edible. The generic name Abelmoschus is suggestive of the musky odour of the seed. The fruits are larger than those of the two other related species; *A. cannabis* and *A. sabdarifta*. It is both a tropical and temperate crop but grows more extensively in the tropics. It is an annual crop native to Africa, probably Ethiopia, but is now cultivated widely in other parts of the world like India and United States of America (Martin and Robert, 1965). The fruits are normally sliced into small bits or ground. Water is usually added to facilitate the production of mucilage. Okro gum produces high viscosity mucilage even at low concentrations. Nasipuri et al. (1996) have determined the molecular weight of okro gum mucilage by gel filtration chromatography and light scattering methods and obtained a value of about 150,000. The charge on the gum mucilage was also determined by paper electrophoretic method. The particles were found to be negatively charged. The results obtained from the surface and interfacial tension studies show that okro mucilage has little surface activity (Nasipuri et al., 1996).

The present investigation was aimed at comparing the effectiveness of this edible gum as a binder in tablet formulations. Thiamine hydrochloride was used as a soluble drug that can be easily assayed.

MATERIALS AND METHODS

Materials

The following materials were used as supplied by their manufacturers: maize starch, stearic acid, lactose (May and Bakers, England); acacia, gelatin, microcrystalline cellulose, polyvinylpyrrolidone (Merck, W. Germany); ethanol (95%), thiamine hydrochloride and acetone (BDH, England).

Methods

Processing of okro-gum: A one kg quantity of unripe and tender fruits of okro gum was used. The fruits were washed, sliced and ground by means of a blender. The crushed mass was soaked in distilled water to hydrate with occasional stirring six hours. A white muslin cloth was used to express the viscous solution to produce the gum extract. Acetone was used to precipitate the extract at a ratio of 3 parts of acetone to 1 part of extract. Filtration of the precipitated gum was performed using a vacuum pump, attached to a Buckner funnel with filter paper (Whatman, 12.5 mm). Finally, the gum was dried in a desiccator containing anhydrous calcium

chloride. Size reduction and screening of the dried gum was carried out using an end runner mill (Manesty, England), and a 250 µm stainless steel sieve. Airtight powder bottles were used to store the undersized fraction (less than 250 µm).

Production of thiamine hydrochloride granules

The granules were produced using the moist granulation method. Four binders, gelatin, acacia, polyvinylpyrrolidone (PVP) and okro gum were used at five concentrations (1 - 5% w/w). Microcrystalline cellulose (5% w/w) was employed as the disintegrant. Lactose, microcrystalline cellulose and the drug were mixed intimately in a mortar for 10 min and binder solution added to obtain a damp mass. The moist mass was forced through a 1.7 mm sieve and the granules dried at 40°C in a hot air oven (Gallenkamp) for one hour. The dried granules were further forced through a 1.0 mm stainless steel sieve stored in clean air-tight powder bottles and evaluated for flow properties.

Compression of granules

The fines of the granules were first mixed with 3% w/w stearic acid and then the coarse fraction for 5 min. The tablets were compressed in a tabletting machine (Model F_3, Manesty) fitted with 9.5 mm concave faced punches at a tablet target weight of 300 mg.

Evaluation of granule properties

Flow rate determination: The funnel method of Carstensen and Chan, (1977) was employed. A funnel of specified dimensions having orifice and base diameters of 0.8 cm and 9.0 cm respectively was used and securely clamped to a retort stand. A 50 g sample was introduced into the funnel and the powder allowed to fall freely under gravity. The flow rate was calculated from the following expression.

$$\text{Flow Rate} = \frac{\text{Amount of powder}}{\text{Time of flow}} \quad (1)$$

Each experiment was conducted five times. The mean value and coefficient of variation was determined.

Angle of repose

A funnel of 0.8 and 8 cm in orifice and surface diameters respectively, was used, adopting the method of fixed funnel and free standing cone (Parrot, 1966). A 50 g sample was allowed to flow through the funnel to form a cone. A cathetometer (Eberbatch, England) was used to determine the height of the heap (h). The base of the cone was traced out using a pencil and its radius (r) determined. The angle of repose was determined from the following relationship:

$$\text{Tan } e = \frac{h}{r} \quad (2)$$

Each experiment was conducted five times. The mean value and coefficient of variation were determined.

Bulk and tapped densities

The bulk volume (V_B) was determined by recording the volume occupied by a 50 g sample introduced in a 100 ml measuring cylinder. The bulk density (P_B) was calculated from the equation:

$$P_B = \frac{w \text{ g/ml}}{V_B} \quad (3)$$

The tapped volume was determined by tapping the cylinder from a fixed height on a soft base, until there was no further reduction in volume (V_t). The tapped density (P_t) was calculated from the equation:

$$P_t = \frac{W}{V_t} \quad (4)$$

Tablet evaluation

Uniformity of weight determination

Twenty tablets were randomly selected from each batch and then weighed individually and collectively using an electronic weighing balance (Mettlers). The mean weight and standard deviation were determined.

Hardness test

The hardness of 10 tablets selected randomly from each of the batches after equilibrating at room temperature for 24 h was determined in an automatic hardness tester (Erweka, Model TBH - 28). The mean hardness was calculated.

Friability

The weight of 20 tablets selected from each batch at random was determined collectively as initial weight, W_A. The tablets were placed in a friabilator (Erweka Apparatabeau); set to rotate at 25 rpm for 4 min. At the end of the run, the tablets were de-dusted and weighed (W_B). Friability was calculated from the equation.

$$F = \frac{(W_A - W_B) \times 100}{W_A} \quad (5)$$

The test was repeated five times and the mean value determined.

Disintegration time determination

Erweka disintegration test apparatus (Model DT4) was used based on the British Pharmacopoeia, 2003 method. The disintegration medium was 0.1 N HCl, maintained at 37 ± 0.5°C. Five tablets from each batch were used for the test. The disintegration time was taken as the mean time needed for the tablets to break into particles small enough to pass through the screen into the disintegration medium.

Table 1. Physical properties of thiamine hydrochloride granulations.

Binder conc. (% w/w) Acacia	Bulk density	Tapped density	Angle of repose	Flow rate
1	0.4015	0.4625	37.75	3.32
2	0.3951	0.4580	37.60	3.36
3	0.3902	0.4515	37.42	3.40
4	0.3866	0.4478	37.45	3.43
5	0.3802	0.4395	36.65	3.41
Gelatin				
1	0.3825	0.4550	37.45	3.34
2	0.3770	0.4460	37.16	3.37
3	0.3722	0.4385	36.79	3.44
4	0.3689	0.4310	36.21	3.46
5	0.3656	0.4270	35.90	3.44
PVP				
1	0.4225	0.4821	38.75	3.26
2	0.4186	0.4775	38.40	3.30
3	0.4107	0.4710	37.90	3.38
4	0.4075	0.4660	37.55	3.55
5	0.4020	0.4605	37.06	3.52
Okro gum				
1	0.3750	0.4325	36.50	3.40
2	0.3702	0.4250	36.15	3.45
3	0.3675	0.4202	35.76	3.50
4	0.3608	0.4155	35.32	3.55
5	0.3555	0.4095	34.82	3.52

Dissolution rate determination

Erweka dissolution apparatus was used, employing the British Pharmacopoeia 2003 method. One tablet was placed in the apparatus and rotated at 100 rpm. The dissolution medium was 1000 ml 0.1 N HCL, maintained at 37 ± 0.5℃. Five milliliter portions of the dissolution medium were withdrawn using a pipette fitted with a non-adsorbent cotton wool at predetermined time intervals. Each 5 ml sample withdrawn was replaced by an equivalent fresh dissolution medium, maintained at 37 ± 0.5℃. The solution was analyzed after colour development using a Sp6-450 UV/VIS spectrophotometer at 430 nm.

RESULTS AND DISCUSSION

Granule properties

The flowability of thiamine hydrochloride granules was expressed as flow rate, angle of repose and density as shown in Table 1.

Flow rate

Flow rate increased with increase in binder concentration and then decreased after an optimum value. Granules formulated with okro gum had the highest flow rate at 1 - 2%w/w binder concentrations. The large average granule size formed at high binder concentration of the binder may have affected the flow rate. Large granule size has been shown to obstruct flow through funnel orifice especially when the granule size approaches the size of the orifice diameter. The relationship between flow rate and orifice diameter has been reported by Danish and Parrot, 1977.

Angle of repose

Angle of repose decreased as binder content of the granules increased. This may be attributed to the reduced cohesive forces of the larger granules formed at higher binder concentration (Shotton and Ganderton, 1961). Granulations produced with okro gum demonstrated the highest reduction in angle of repose and the angle of repose values for all the granulations were below 42°. This suggests good flow properties (Shah and Mlodezeniex, 1977). Angle of repose is a measure of powder resistance to flow under gravity due to frictional forces resulting from the surface properties of the granules.

Tablet properties

Weight Uniformity: There was no significant variation in

Table 2. Content and weight uniformity of thiamine hydrochloride tablets formulated with different binders.

Binder conc. (% w/w) Acacia	Content uniformity drug content (mg)	Weight uniformity (mg)
1	25.50	306.0 (1.69)*
2	24.75	305.9 (1.55)
3	24.50	307.9 (2.80)
4	25.00	302.7 (1.98)
5	25.00	300.10 (1.70)
Gelatin		
1	25.25	304.80 (1.25)
2	24.75	295.70 91.57)
3	25.00	300.60 (12.70)
4	24.25	303.60 (1.87)
5	25.00	308.20 (1.32)
PVP		
1	26.00	301.25 (1.62)
2	25.00	303.05 (2.11)
3	24.50	298.05 (2.04)
4	24.75	300.45 (1.82)
5	24.75	306.75 92.15)
Okro gum		
1	25.25	301.75 (2.43)
2	25.00	300.35 (1.63)
3	25.25	303.33 (2.01)
4	24.25	303.10 (2.01)
5	24.75	301.60 91.67)

*Values in bracket represent standard deviations.

the mean weights of thiamine hydrochloride tablets since all showed low coefficient of variations of below 2% (Table 2). A good tablet weight uniformity is an indication of a good uniformity of tablet contents.

Hardness and friability

The effect of binder concentration on tablet hardness and friability are shown in Table 3. An increase in binder concentration increased the hardness of the tablets. On the other hand, friability decreased as binder concentration increased. An increase in binder concentration will enhance the formation of stronger interparticulate bonds between the granules during compression in a tabletting machine (Esezobo and Pilpel, 1976). This means that the tablets would offer greater resistance to shock and abrasion since there is a stronger adhesive bonding of the granules at high binder concentrations. In general, the tablets showed good friability profiles, since most had friability values of less than 1.0% (Harwood and Pilpel, 1968). Moreover, the tablets made from okro gum had high hardness/friability ratios, since the tablets recorded the highest hardness and least friability values.

Disintegration time

The effect of binder concentration on tablet disintegration time is shown in Table 4. The tablets formulated with okro gum failed the British Pharmacopoeia 2003 disintegration time test. However, tablets containing polyvinylprrolidone (PVP), acacia, and gelatin as binders disintegrated in less than 15 min. The binders follow this order of increasing tablet disintegration time: PVP < acacia < gelatin < Okro gum.

Dissolution profile

The dissolution data of the tablets are presented in Table 5. Tablets made with PVP gave the highest drug release while okro gum had the lowest. As the binder concentration increased, there was a general decrease in the release rate of thiamine hydrochloride from the tablets. Okro gum displayed a very remarkable delay in the

Table 3. Hardness and friability values of thiamine hydrochloride tablets formulated with different binders.

Binder Conc. (% w/w) Acacia	Hardness (N)	Friability (%)	Hardness / Friability Ratio
1	2.73 (2.27)*	0.95	2.87
2	2.54 91.69)	0.91	3.89
3	4.83 (1.26)	0.87	5.55
4	6.15 (0.85)	0.81	7.59
5	7.17 (0.45)	0.76	9.43
Gelatin			
1	3.33 (1.59)	0.92	3.62
2	3.90 (1.23)	0.89	4.38
3	5.04 (1.39)	0.85	5.93
4	6.65 (1.07)	0.80	8.31
5	7.55 (0.78)	0.74	10.20
PVP			
1	2.51 (1.59	1.02	2.46
2	3.12 (0.99)	0.98	3.18
3	3.95 (1.04)	0.90	4.39
4	4.81 (0.91)	0.85	5.66
5	5.51 (0.47)	0.82	6.72
Okro gum			
1	4.20 (0.93)	0.86	4.88
2	6.28 (1.00)	0.81	7.75
3	8.46 (0.79)	0.78	10.85
4	10.23 (1.86)	0.73	14.01
5	11.55 (0.95)	0.65	17.77

Table 4. Disintegration time of the thiamine hydrochloride tablets formulated with different binders.

Binder conc. (% w/w) Acacia	Disintegration time (min)
1	5.96 (0.36)*
2	7.12 (0.26)
3	10.36 (0.54)
4	12.46 (0.34)
5	14.24 (0.25)
Gelatin	
1	6.44 (0.29)
2	7.76 (0.30)
3	11.10 (0.26)
4	13.14 (0.59)
5	15.24 (0.63
PVP	
1	4.70 (0.29)
2	6.40 (0.60)
3	8.16 (0.38)
4	10.10 (0.31)
5	11.94 (0.33)

Table 4. Contd.

Okro gum	
1	21.60 (1.14)
2	31.20 (1.30)
3	51.20 (1.64)
4	76.60 (1.82)
5	111.80 (2.05)

* Values in brackets represent standard deviations.

Table 5. Dissolution rate data (per cent of drug released) of thiamine hydrochloride tablets formulated with different binders.

Binder Conc. (% w/w)	Dissolution Time (min)					
Acacia	**5**	**10**	**15**	**20**	**25**	**30**
1	47.06	58.82	75.49	85.29	98.04	101.96
2	40.40	50.51	65.66	11.78	84.85	94.95
3	38.78	44.90	57.14	69.39	78.57	88.76
4	32.00	38.00	50.00	60.00	70.00	78.00
5	28.00	34.00	44.60	56.00	66.00	72.00
Gelatin						
1	39.60	47.52	55.45	69.31	93.07	100.99
2	36.37	44.45	70.71	65.65	78.79	92.93
3	32.00	40.00	46.00	50.00	62.00	74.00
4	24.74	37.11	41.24	47.42	57.73	72.16
5	18.00	28.00	36.00	42.0	48.00	60.00
PVP						
1	42.31	57.69	76.92	98.08	101.92	105.77
2	40.00	54.00	70.00	92.00	100.00	100.00
3	36.73	51.02	65.31	83.67	95.92	97.96
4	30.30	46.46	56.57	74.75	84.85	90.91
5	26.26	40.40	52.53	68.69	76.77	84.85
Okro gum						
1	27.72	33.60	41.58	45.54	51.49	55.45
2	24.00	30.00	38.00	42.00	46.00	56.00
3	19.80	25.74	33.66	39.60	43.46	45.54
4	16.49	22.68	28.87	39.18	41.24	43.40
5	10.10	16.16	24.24	32.32	34.34	36.37

release rate at higher binder concentrations since none of the tablet batches formulated with okro gum released up to 75% of drug in 30 min (Esezobo and Pilpel, 1976).

Conclusion

A. esculentus gum could not be suitably employed in conventional tablet formulation as a binder since it prolongs tablet disintegration time and also remarkably delays drug dissolution rate. Perhaps it may be a good candidate for evaluation as a binder or hydrophilic polymer in sustained release tablet formulation.

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