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Full Length Research Paper

Comparative study of some mechanical and release properties of paracetamol tablets formulated with cashew tree gum, povidone and gelatin as binders

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The mechanical and release properties of paracetamol tablets formulated with cashew gum (CAG), povidone (PVP) and gelatin (GEL) as binders were studied and compared. The parameters studied were tensile strength (TS), brittle fracture index (BFI), friability (F), disintegration time (DT) and percentage drug released (PDR). Results showed that the TS and BFI values of tablets formulated with CAG were the lowest at all binder concentrations. The friabilities of all formulations were within accepted limits (<1.0%). Disintegration times were longest for GEL formulated tablets and least for PVP formulated ones. At binder concentrations of 1.0 – 3.0% (w/w) CAG released the highest cumulative amount of drug in 30 min; from 4.0 – 5.0% (w/w) cumulative amount released became highest for PVP formulated tablets. GEL formulated tablets generally released the least amount. CAG gum therefore having imparted better BFI than PVP or GEL, and does not hinder drug release is strongly recommended as an alternative to the more expensive PVP or GEL for immediate release tablet formulations.

Key words: Cashew gum, povidone, gelatin, binder, mechanical, release properties of paracetamol tablets.

INTRODUCTION

Binders are one of the main ingredients required in tablet production. They impart cohesiveness on the powders, thereby improving their flow and compaction properties. Different classes of binders exist in the pharmaceutical industry. Some achieve their effectiveness at high concentrations, while some do so at low concentrations. Povidone and gelatin have been used over the years at low binder concentrations to formulate good tablets. Currently most researchers concentrate on the use of natural gums at high concentrations to formulate matrix tablets intended for controlled release dosage forms. This is because at such relatively high concentrations, their hydrophilic nature ensures the formation of gels in the presence of water thereby modifying the release characteristics of the incorporated drug (Manuel et al, 2000; Sumathi and Ray, 2002). This desire to research mainly on the use of gums to achieve controlled release has led to decline in research on the use of natural gums in the formulation of immediate release tablets, whose formulations are readily undertaken by indigenous manufacturers. Thus, in this study, cashew gum was used at the same concentration range to compare its effectiveness as a binder to those of povidone and gelatin in the formulation of immediate release tablets. Cashew gum is an exudate polysaccharide from *Anacardium occidentale* tree. The physicochemical properties of the gum have been studied (Cunha et al, 2007; Akoto et al., 2007). It has similar rheological properties with gum Arabic and has been proposed as a substitute in the paper industry as liquid glue; agglutinant for capsules and pills, as well as polyelectrolyte complex with chitosan for drug delivery in the pharmaceutical industry; and as stabilizer in the food, and cosmetic industries (Akoto et al., 2007; De Paula et al., 1998).

The compaction characteristics of tablets may be assessed by different techniques: tensile strength, packing

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fraction, brittle fracture index, friability, disintegration time, bonding index, strain index etc (Okor, 2005; Hiestand et al., 1977; Eichie and Amaline, 2007; Itiola and Pilpel, 1986; Uhumwangho and Okor 2004, Uhumwangho et al., 2006; Williams III and McGinity, 1988). Bond strength and lamination tendencies are two important mechanical properties of tablets that are measurable by tensile strength (TS) and the brittle fracture index (BFI) value respectively (Itiola and Pilpel, 1982). Tablet tensile strength is given by the equation (Fell and Newton, 1970):

$$T = 2F/\pi dt \quad (1)$$

Where T is tablet tensile strength (MN/m^2), F is the load (MN) applied to cause diametral fracture of the tablet; d and t are tablet diameter and thickness respectively in metres. Tablet BFI is evaluated by comparing the tensile strengths (T_o) of tablets with a hole at their centers (an in-built stress concentrator defect) with the tensile strengths (T) of tablets without any center hole, both at the same relative density. BFI is computed with the equation (Hiestand et al, 1977):

$$BFI = [(T/T_0) - 1] \times 0.5 \quad (2)$$

BFI is a measure of the ability of the material under test to relieve stress (associated with capping and lamination) by plastic deformation. A low BFI value (close to zero) indicates the ability of the material to relieve localized stress, whereas a value tending to 1 implies a high tendency for capping and lamination to occur. Paracetamol tablets when formulated with a poor binding agent laminate and/or cap easily, thus the selection of paracetamol powder for the study of the binding effectiveness of cashew gum.

MATERIALS AND METHODS

Paracetamol Powder (Mallirickrodt Inc. USA), corn starch BP (Sigma-Aldrich USA)-disintegrant, D(+)-lactose monohydrate (Fluka Netherlands)-filler, cashew gum, extracted from the cleaned tears by the method described by Nasipuri et al. (1996). Povidone (Fluka USA), gelatin-gel strength: 160 Bloom (Fluka Germany), talc (BDH Chem. UK)-lubricant, liquid paraffin (Mopson Pharm. Nigeria), and other reagents are of analytical grade.

Preparation of granules

100 g batches of a basic formulation of paracetamol powder (82%, w/w), lactose (8%, w/w) and corn starch B.P. (10%, w/w) were dry-mixed for 10 min in a planetary mixer (Model A 120, Hobart Manufacturing CO, UK), moistened with the appropriate amount of binder solution equivalent to 1.0, 2.0, 3.0, 4.0 and 5.0% (w/w) in final granules and granulated by wet massing with mortar and pestle. The homogeneous wet mass was then screened through a 1400 µm sieve and the wet granules dried in a hot air oven (Unitemp LTE Scientific Ltd Great Britain) at 50°C for 18 h. After which the dried granules were screened through a 600 µm sieve and stored in air tight containers over silica gel before tableting.

Determination of granule density

Granule density of each formulation was determined using the fluid displacement method (Irwin et al., 2002; Eichie et al, 2005) and applying the equation (Ohwoavworhua et al., 2007):

$$\rho_g = W/ [(a + w) - b] SG \quad (3)$$

Where ρ_g = granule density in grams per cubic centimeter cubed, W = granule weight in grams, SG = liquid paraffin specific gravity = 0.802, a = pycnometer + liquid Paraffin weight in grams, and b = pycnometer + Liquid paraffin + granule weight in grams.

Preparation of tablets

Immediately before tableting, each batch of granules was mixed with 0.5% (w/w) of talc. Tableting was done with a single punch tableting machine (Kilian Frankfurt Germany) having a flat punch surface of diameter 12.55 ± 2.00 mm. Tablets were made by weighing accurately 500 mg of granules and carefully transferring them into the die, and then compressing manually at a pre-determined pressure of 7.50 arbitrary units; with the pressure held on the granules for 30 s before releasing to allow consolidation to take place. The tableting procedure was repeated for tablets with center hole, 1.5 mm in diameter (made with the upper and lower adapters having a hole and a pin at their centres respectively) (Uhumwangho and Okor, 2004). All the tablets were compressed to the same relative density (0.80). Prelubrication of the die and punches in each stage was done by compressing some powder of pure talc before the granules were compressed (Sinka et al., 2004). And the tablets were stored in air tight containers over silica gel for 72 h before the relevant tests were conducted.

Weight and dimension measurements

Tablet weights were determined using electronic balance (Mettler Toledo B154, Switzerland) while the dimensions were measured with Mitutoyo gauge (Model 10C – 1012 EB Japan), to within ±1 mg and ±0.01 mm respectively.

Crushing strength and friability tests

Crushing strengths of tablets were determined at room temperature by diametral compression (Odeku and Itiola, 1998), using a hardness tester (Kal Kolb, Erweka Germany). Results were taken from tablets that split cleanly into two halves without any sign of lamination. All measurements were made in triplicates and their means reported.

Tablets tensile strengths and BFI were then evaluated using equations (1) and (2) respectively. The percentage friabilities of the tablets were determined using Roche Friabilator (Copley/Erweka, Type, TAR 20, GMBH Germany), operated at 25 rpm for 4 min.

Disintegration and dissolution tests

The disintegration times of the tablets were determined in distilled water at 37 ± 0.5°C using the disintegration tester (Manesty, Model: MK 4, UK). Before the dissolution test, 10 µg/ml of paracetamol solution in 0.1 N HCl was scanned between 200 and 800 nm using UV-Visible spectrophotometer (UV-160 A Shimadzu Corporation Japan). Peak of maximum absorption (0.791 A) was shown at a wavelength of 296 nm. Tablet dissolution test was then done using the USP XXIII basket method (Erweka Germany Type: DT 80)

Table 1. Effect of binder concentration on tensile strength (TS), friability, BFI and disintegration times of tablets.

Binder conc. (%, w/w)	TS (MN/m^2)	BFI	Friability (%)	Disintegration time (min)
Cashew gum				
1.0	0.77	0.3015	0.91	0.31
2.0	0.94	0.2713	0.76	0.41
3.0	1.13	0.1700	0.70	2.04
4.0	1.24	0.1448	0.68	3.80
5.0	1.31	0.1391	0.68	9.51
Povidone				
1.0	0.85	0.4362	0.95	0.51
2.0	1.05	0.3614	0.88	0.86
3.0	1.33	0.2622	0.78	0.97
4.0	1.47	0.2408	0.66	1.61
5.0	1.65	0.2057	0.65	3.70
Gelatin				
1.0	0.88	0.3376	0.83	0.51
2.0	1.24	0.3198	0.75	1.24
3.0	1.41	0.2383	0.75	5.00
4.0	1.58	0.2147	0.70	6.61
5.0	1.83	0.2081	0.64	11.28

operated at 50 rpm for 30 min in 900 ml of 0.1N HCl maintained at 37 ± 0.5°C (USP/NF 1995). At 5 min intervals, 5 ml of dissolution fluid was withdrawn and replaced with 5 ml of fresh 0.1N HCl. Each withdrawn sample was filtered and the amount of paracetamol released determined using the UV-Visible spectrophotometer, at 296 nm with 0.1N HCl as blank.

RESULTS AND DISCUSSION

Table 1 shows the effect of binder concentration on tablet tensile strength, brittle fracture index, friability and disintegration time. It is evident that tablet tensile strength increased with increase in binder concentration. Tablet tensile strength is a function of the strength of the bonds between the powder particles that form the tablet lattice structure. Generally, the higher the bond strength, the higher the tensile strength of the compact (Itiola and Pilpel, 1986). Tablets formulated with Cashew gum had the lowest tensile strengths, although the differences between their values and those of tablets formulated with povidone, or gelatin were not appreciable.

Tablets brittle fracture indices displayed inverse relationship to binder concentration. Since BFI is an inverse measure of localized stress relief, it implies that the ability of the binders to reduce the tendency of paracetamol tablets to cap or laminate increased as binder concentration in granules increased. This they achieved by imparting plasticity on otherwise elastic natured paracetamol powder. It therefore implies that the lower the BFI value imparted by the binder, the higher is the binder's ability to prevent capping and lamination in tablets. Thus, cashew gum which produced tablets with the lowest BFI would relief localized stress in tablets better than povidone or gelatin. On friability, the tablets passed the USP 2007 test for friability; with cashew gum yielding tablets of lower friability than povidone up to binder concentration of 3.0% (w/w). All the tablets also passed the BP 2003 tablet disintegration test. Tablets formulated with povidone displayed gradual increase in disintergration time with increase in binder concentration unlike those formulated with gelatin or cashew gum. However tablets formulated with cashew gum had shorter disintergration time than those formulated with gelatin. Table 2 shows the cumulative percent of paracetamol released by all tablet formulations over 30 min intervals. Tablets formulated with povidone generally released the highest amount of drug from 5 to 25 min interval. But the cumulative amount of drug released in 30 min was highest with tablets formulated with cashew gum at binder concentration range of 1.0-3.0% (w/w). Beyond 3.0% (w/w) binder concentration, tablets formulated with povidone had the highest release over those formulated with cashew gum or gelatin. This implies that granules resulting from the disintegration of tablets formulated with povidone disintegrated faster into fine particles thereby enhancing the dissolution of paracetamol particles. The amounts of drug released by tablets formulated with cashew gum were close to those of tablets formulated with gelatin at concentration of 5.0% (w/w) (which is actually not satisfactory for immediate release tablets). Thus it is

Table 2. Dissolution profile of paracetamol tablets formulated with cashew gum (CAG), povidone (PVP), and gelatin (Gel).

Binder conc. (%, w/w)	Cumulative % of drug released/time (min)																	
	5.0 min			10.0 min			15.0 min			20.0 min			25.0 min			30.0 min		
	CAG	PVP	GEL	CAG	PVP	GEL	CAG	PVP	GEL	CAG	PVP	GEL	CAG	PVP	GEL	CAG	PVP	GEL
1.0	26.6	36.9	36.6	62.9	74.1	79.1	77.0	81.8	81.0	79.7	82.5	82.6	81.4	82.9	82.7	85.1	83.1	83.2
2.0	25.8	33.7	28.8	60.7	72.1	46.3	73.8	79.3	64.1	77.0	80.6	67.5	80.3	80.9	70.2	84.2	83.3	75.3
3.0	23.1	28.2	20.1	58.7	60.6	33.5	70.9	79.0	43.7	76.2	79.8	53.5	80.2	80.0	59.8	83.6	80.5	64.1
4.0	18.7	26.4	15.7	30.6	56.8	20.4	40.3	78.3	29.2	50.8	78.4	36.8	62.4	78.6	45.1	70.2	78.9	48.6
5.0	10.0	26.1	11.5	20.7	55.0	16.7	26.8	77.1	22.8	30.9	77.2	29.0	35.4	78.8	34.9	41.2	79.2	39.0

recommendable that the use of cashew gum in the formulation of immediate release tablets should be limited to 1.0-3.0%w/w concentration range in order to achieve good mechanical and release properties.

Conclusion

The mechanical properties of paracetamol tablets formulated with cashew gum as binder at the concentrations used are similar to those of povidone and gelatin. Cashew gum is superior to both binders in its ability to reduce brittle fracture tendency in paracetamol tablets. And because it can achieve very good release profile and mechanical properties at low binder concentration range (1.0-3.0%, w/w) it should be better explored and exploited as an alternative to povidone and gelatin in tablet formulation since its production would generally be cheaper; thus invariably leading to lower cost of tablet production.

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