



## COMPRESSION, MECHANICAL AND RELEASE PROPERTIES OF PARACETAMOL TABLETS CONTAINING ACID TREATED GREWIA GUM.

\*J Muazu<sup>1</sup>, H Musa<sup>2</sup> and KY Musa<sup>3</sup>.

<sup>1</sup>Department of Pharmaceutical Services, University of Maiduguri Teaching Hospital, Nigeria.

<sup>2</sup>Department of Pharmaceutics and Pharmaceutical Microbiology, Ahmadu Bello University Zaria, Nigeria.

<sup>3</sup>Department of Pharmacognosy and Drug Development, Ahmadu Bello University Zaria, Nigeria

### Abstract

Grewia gum a natural gum from the bark of plant *Grewia mollis* was treated with hydrochloric acid at three different concentrations and three different times. The gum have been evaluated as a binding agent in comparison with both untreated gum and gelatin in paracetamol tablet formulations. Compressional properties of the formulations were analyzed using density measurements and assessed by compression equation of Heckel. The mechanical properties of the formulations were assessed using crushing strength and friability as well as crushing strength friability ratio. The drug release properties of the tablets formed were assessed using disintegration and dissolution times. Tablet formulations containing treated grewia gum exhibited low onset of plastic deformation, while that untreated gum and gelatin were relatively high onset of deformation. The friability of paracetamol tablet formulation increases with increase in acid concentration and treatment time. The crushing strength, disintegration and dissolution times decreased with increase in acid concentration and treatment time. Tablets produced with untreated gum showed higher crushing strength, disintegration and dissolution times and low friability than the gelatin and the treated gum. Depending on the desired onset of action of medicament acid treated rewia gum can be used in formulation of conventional tablets especially if the formulation does not require sustained release.

**Keywords:** Grewia gum, acid treated, binder, compression, Heckel equation, mechanical and release properties.

### Introduction

Binding agents are used to impart the structural strength required during the processing, handling, packaging and transporting of tablets (Odeku, 2005).

A number of plant gums have been used as binding agents in tablet formulations (Rama Prasad et al, 1998, Odeku and Itiola, 1998, Kalu et al 2007 and Odeku, 2005). These gums have been used in producing tablets with different mechanical strength, consolidation and drug release properties (Emege, 2008). The grewia gum was sourced from the inner bark stem of *Grewia mollis* shrub or tree of family *Tiliacaea*, locally distributed within the Northern and middle belt of Nigeria. In Northern Nigeria, the mucilage from the bark is used as a thickener in cooking soup, bean cake called kosai in Hausa. Phytochemical and histopathological studies were carried out on the leaves and stem bark extracts of *Grewia mollis*, the result revealed the presence of tannins, saponins, flavonoids, glycosides, balsam, phenols, terpenes, steroids and the absence of alkaloids in *Grewia mollis* bark while toxicological result showed that the

plant is safe for human consumption (Onwuliri et al, 2006)

Many researchers have carried out studies on compaction characteristics of pharmaceutical powders with many equations and expressions reported (Train 1956, Heckel 1961, Cooper and Eaton 1962, Kawakita and Ludde 1970, Pilpel 1973). However the Heckel equation is one of the most widely used equation for describing the compaction properties of powders (Oladapo et al 2006, Odeku 2005, Ravindra et al 2006, Ohwoavworhwa 2007 and Emeje 2008). The Heckel equation analyses the ability of granules to undergo volume reduction, i.e compressibility. It describes the relationship of the compact, density to the applied pressure (Ravindra et al 2006).

The Heckel equation relates the relative density,  $D$ , of a powder bed during compression to the applied pressure,  $P$ , which provides information on the mechanism of powder consolidation during compact formation by the equation

$$\ln(1/1-D) = kP + A \dots \dots \dots (1)$$

Where  $k$  and  $A$  are constants.

The slope of the straight line portion,  $K$ , is the reciprocal of the mean yield pressure,  $P_y$ , of the material. The intercept of the extrapolated linear portion,  $A$ , is a function of the original compact volume. From the value of  $A$ , the relative Density ( $D_A$ ) can be calculated using the following equation.

$$D_A = 1 - e^{-A} \dots\dots\dots (2)$$

The relative density of the powder bed at the point when the applied pressure equals zero,  $D_0$ , is used to describe the initial rearrangement phase of densification as a result of die filling and this is obtained from the ratio of the loose density to the particle density. The relative Density,  $D_B$ , describes the phase of rearrangement of particles during the initial stages of compression. The extent of rearrangement phase depends on the theoretical point of densification at which deformation of particles begins.

$$\text{Thus, } D_B = D_A - D_0 \dots\dots\dots (3)$$

In the present study, Grewia gum has been treated with acid and evaluated as a binding agent in paracetamol tablet formulations in comparison with a standard binder, gelatin BP using the compression equations of Heckel. Mechanical strength of the tablets was assessed using crushing strength and friability while the release properties of the tablets were assessed by disintegration and dissolution times. Paracetamol was used as the model drug for the present work because of its poor compression properties; hence it needs a binding agent among other excipients to form satisfactory tablets (Odeku 2005).

### Materials and Methods

The following materials were used as procured from their manufacturers; Hydrochloric acid, sodium hydroxide, magnesium stearate, maize starch, (B.D.H. Ltd, England), water bath with temperature regulator, mettler electronic weighing balance (Gallenkamp), drying cabinet (mono model N53 Gallenkamp), absolute ethanol, Erweka tablet machine (GMBH)

Germany.

### Methods

#### Extraction of Grewia gum

The method of Nasipuri et al was adopted for the extraction of grewia gum (Nasipuri et al 1996). The gum was size reduced using a laboratory blender and the size fraction < 180  $\mu\text{m}$  was used.

#### Modification of Grewia gum.

The method of Audu-Peter et al (Audu-Peter et al, 2007) was adopted. Twenty grams of gum powder was weighed and carefully transferred into a round bottom flask and 80ml of hydrochloric acid was poured into the flask to make slurry. The mixture in the flask was then placed into a water bath of temperature 50°C and then clamped using retort stand and then allowed for time interval of 1, 2 and 3 hours respectively while constantly stirring using glass rod. This was repeated for each concentration (0.1N, 0.2N and 0.3N HCl. It was then removed from the water bath and allowed to cool. Equal volume of equimolar concentration of sodium hydroxide was used to neutralize the acid. About 80ml of ethanol was used to precipitate the gum after which it was placed in 80ml of distilled water and then a drop or two of silver nitrate solution was introduced – To test the presence of salt which is indicated by observed precipitate of silver chloride. Finally, ethanol was used to precipitate the gum and then dried.

#### Preparation of granules

The wet granulation method of massing and screening was employed and the batch size was 250 tablets.

Quantities of paracetamol powder, lactose and maize starch were dry-mixed for 5 minutes in a planetary mixer (Model A120, Hobart Manufacturing Co., UK.) and then moistened with distilled water or appropriate amounts of binder solutions to produce granules containing different concentrations of grewia gum or gelatin as binders.

**TABLE 1:** Shows the working formula for studying the binding properties of Grewia gum comparing with Gelatin B.P in Paracetamol 500mg tablets.

Ingredients	Quantity per Tablet	Quantity per Batch (250)
Paracetamol 77% <sup>w/w</sup>	500mg	125.00g
Lactose 10% <sup>w/w</sup>	64.9mg	16.23g
Disintegrant Maize starch BP 7.8% <sup>w/w</sup>	50.6mg	12.65g
Binder: Grewia or Gelatin B.P 2% <sup>w/w</sup>	2% <sup>w/w</sup>	2% <sup>w/w</sup>
Mg. Stearate	1.30mg	325mg
Talc	13.0mg	3.25g
Theoretical weight	649mg	

**Table 2:** Showing Heckel's parameters in paracetamol tablet formulation with treated and untreated gum and gelatin.

Binder	Acid conc.	Acid treatment time (hours)	D <sub>0</sub>	P <sub>v</sub> (MNm <sup>-2</sup> )	D <sub>A</sub>	D <sub>B</sub>
Grewia	0	0	0.409	148.62	0.731	0.322
	0.1N	1	0.388	98.89	0.631	0.243
	0.1N	2	0.391	112.46	0.664	0.273
	0.1N	3	0.358	118.74	0.671	0.313
	0.2N	1	0.336	121.74	0.697	0.361
	0.2N	2	0.317	136.11	0.708	0.391
	0.2N	3	0.293	142.03	0.719	0.426
Gelatin	0	0	0.304	162.41	0.629	0.325

**Table 3.** Crushing strength, friability and crushing strength friability ratio (CSFR) of tablets from treated, untreated gum and gelatin.

Binder	Acid conc.	Acid treatment time (hrs)	Crushing strength (N)	Friability (%)	CSFR
Grewia	0	0	67.53±1.13	0.71±0.04	99.11
	0.1N	1	64.14±2.01	0.86±0.02	74.58
	0.1N	2	61.02±1.18	0.88±0.03	69.34
	0.1N	3	58.71±2.14	0.91±0.04	64.52
	0.2N	1	57.13±1.62	0.87±0.03	65.67
	0.2N	2	54.28±1.63	0.92±0.01	59.00
	0.2N	3	52.40±1.78	0.98±0.02	53.47
Gelatin	0	0	56.92±1.24	0.79±0.05	72.05

Massing was continued for 5 minutes and the wet masses were granulated by passing them manually through a wire mesh (1600  $\mu\text{m}$ ), dried in a hot air oven (Gallenkamp, UK) for 18 hours at 50 °C. Dried granules were sieved through a mesh (1400  $\mu\text{m}$ ) and then stored in airtight containers.

#### *Formulation of tablets*

The granules were lubricated with appropriate weight of lubricant/glidant (table 1) Paracetamol tablets (500 mg) were prepared from the 250 to less than 100 mm size fraction of granules by compressing them for 60 s with predetermined loads at various compression pressure, on an Erweka single punch tableting machine (Erweka, AR400 Germany) coupled with 12.5 mm die and flat-faced punches. After ejection, the tablets were Stored in a desiccator containing silica gel for 24 h. There relative densities (R) were calculated using the equation:

$$R = m / V_t \rho_s \dots \dots \dots (4)$$

Where  $V_t$  is the volume of tablet ( $\text{cm}^3$ ) and  $\rho_s$  is the particle density of solid material.

#### *Crushing strength and friability tests*

Crushing strengths of the tablets were determined at room temperature using Erweka Hardness tester (Erweka TBH 100, Germany).

The percent friability of the tablets was determined using an Erweka friabilator (Erweka, Germany) operated at 25 rpm for 4 minutes.

#### *Disintegration and dissolution tests*

Disintegration times of the tablets were determined in distilled water at  $37 \pm 0.5^\circ\text{C}$  using a disintegration tester (Erweka ZT 71, Germany).

The dissolution test was carried out on the tablets using the USP XXIII basket method (Erweka dissolution tester, Type DT 700, Germany) rotated at 50 rpm in 900 mL of 0.1N HCl, maintained at  $37 \pm 0.5^\circ\text{C}$ . Samples (15 mL) were withdrawn at

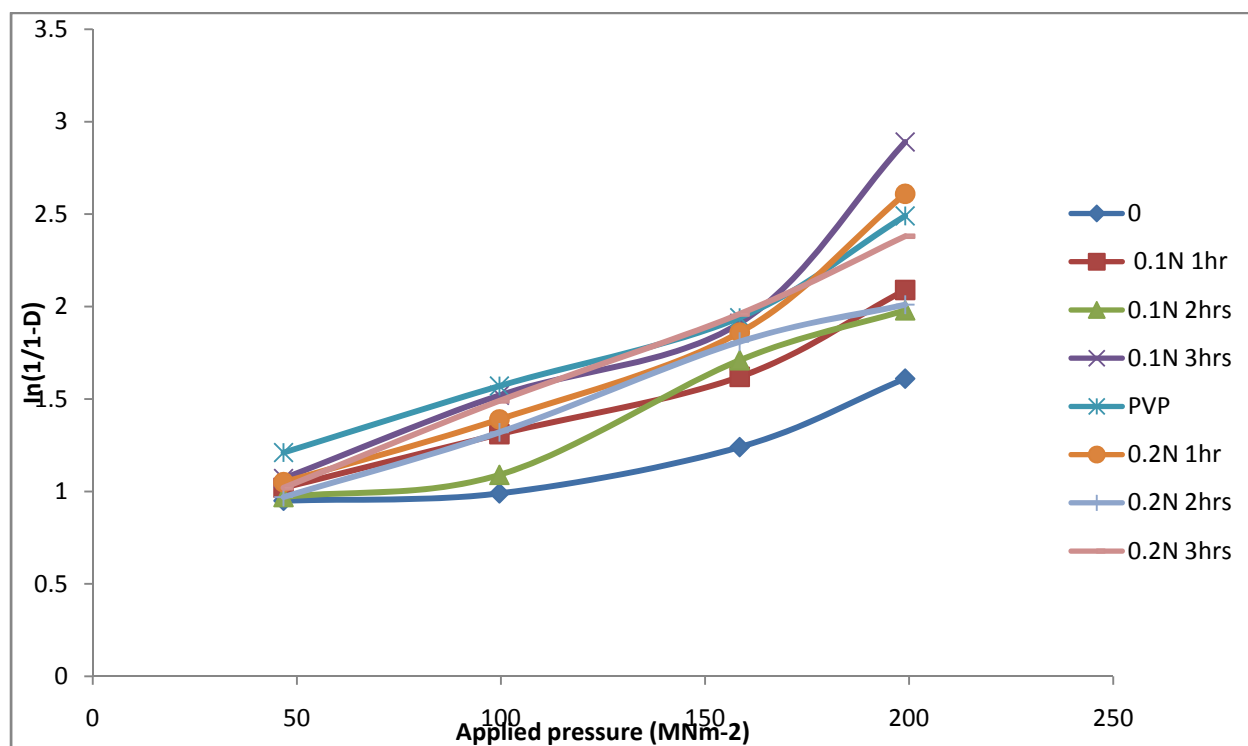
different time intervals and replaced with equal amounts of fresh medium (0.1N HCl). The sample was diluted and the amount of paracetamol released was determined using a UV spectrophotometer (Beckman and Coulter DU 520 series, UK) at 243 nm.

#### **Result and discussion**

Fig. 1 shows representative Heckel plots for paracetamol formulations containing 2.0%w/w binder. The mean yield pressure,  $p_y$ , was calculated from regions of the plots showing linearity. The intercept, A, the point at which an intact tablet was just formed during compression, was determined from the extrapolation of the region used for the determination of  $p_y$ . The  $D_A$  and  $D_B$  values were calculated from equations 1 and 2 respectively. The values of  $D_0$ ,  $P_y$ ,  $D_A$  and  $D_B$  for the formulations are presented on Table 2.

The  $D_0$  value, which represents the degree of initial packing in the die as a result of die filling for all formulation increased as the binder concentration is increased, implying that initial packing of the granules as a result of die filling increased with increase in binder concentration which confirmed the earlier work (Oladapo *et al*, 2006). In general formulation containing grewia gum treated with 0.2N for 3 hours has the lowest  $D_0$  value. As the time of treatment is increased the  $D_0$  value decreases, also as the concentration of acid used in treatment is increased the  $D_0$  value decreases.

The  $D_B$  value represents the particles rearrangement phase in the early compression stages and tends to indicate the extents of particles or granules fragmentation, although fragmentation can occur concurrently with plastic or elastic deformation of constituent particle,  $D_B$  value generally decrease with increase in the concentration of acid and time of treatment. This indicates that granule fragmentation decreased with an increase treatment time and acid concentration.



**Figure 1.** Heckel plots for Paracetamol tablet formulations containing gelatin, untreated grewia gum and grewia gum treated with different acid concentration and time.

The  $P_y$  value (mean yield pressure) is inversely related to ability of material to deform plastically when compressed (Itiola, 1991), the value of  $P_y$  was observed to increase with increase in treatment time and acid concentration, implying that the onset of plastic deformation in the formulation occurred at lower pressure.

Treatment of grewia gum with 0.1N for 1hour was observed to have lower  $P_y$  value, indicating less force might be possibly needed to deform them. The relative higher  $P_y$  value observed in gelatin and untreated gum indicated that the granules were softer more plastic and hence could deform readily.

The crushing strength values increased and those of friability decreased with an increase in acid concentration and treatment time. It is a well known fact that a high concentration of a plasto-elastic binding

agent leads to an increase in plastic deformation of the formulation and consequently to the formation of more solid bonds with increase in tablet strength and resistance to fracture and abrasion (Odeku, 2005). Untreated grewia gum has higher crushing strength than gelatin, while gelatin has crushing strength higher than all treated gums. The crushing strength-friability ratio (CSFR) can also be used to measure the mechanical strength of tablets. The values of CSFR for the tablets were also shown on table 3; there was decrease in CSFR values as a result of increased concentration of acid and treatment time. Treatment with acid therefore disorganizes the structure of the gum and hence the low crushing strength and high friability.

The release of medicaments from tablets can be assessed by disintegration and dissolution times, the disintegration and dissolution

times of the formulation were shown on table 4. The disintegration and dissolution times both decreased with increase in acid concentration and treatment time. However, tablets containing untreated grewia gum have highest disintegration and dissolution times. This might be as a result of the gum been intact (not disorganized)

All the tablets conformed to the British pharmacopoeia requirement (BP, 2002) for uncoated tablets on disintegration, i.e. tablet to disintegrate within 15mins. The time required for 50% and 70% (t<sub>50</sub> and t<sub>70</sub> respectively) of paracetamol to be released were shown on Table 4. It also followed the pattern of disintegration, disintegration is the first step of dissolution and the explanations are similar.

### Conclusion

The present study showed that formulation containing treated grewia gum as a binder show similar onset of plastic deformation under applied compression pressure, similar mechanical and release properties with the standard (gelatin) however the untreated gum exhibit higher plastic deformation, mechanical and release properties. This suggests that treated gum can be used as a binder in uncoated tablets and where sustained release is desired, untreated grewia can be used.

### References

- [1] Audu-Peter JD, Isah S and Limasaya I (2007) Evaluation of modified grewia gum as binder in paracetamol tablet. *Nig. J. Pharm. Res* 6 (1); 25-30
- [2] British Pharmacopoeia. Her Majesty's stationery office, University Press Cambridge. 2002 Vol. I and II.
- [3] Emeje M, Isimi C and Kunle O. (2008) Effect of *Grewia* gum on the mechanical properties of Paracetamol tablet formulations. *Afr. J. Pharm. Pharmacol.* 2: 1-6.
- [4] Heckel RW. (1961) An analysis of powder compaction phenomenon. *Trans. Metall. Soc. AIME.* 221: 671-675.
- [5] Itiola OA. (1991) Compression Characteristic of Three Starches and the Mechanical Properties of their Tablets. *Pharm. World J.* 8(3): 91-97
- [6] Kalu VD, Odeniyi MA, and Jaiyeoba KT. (2007) Matrix Properties of a New Plant Gum in Controlled Drug Delivery. *Arch Pharm Res* 30 (7): 884-889
- [7] Kawakita K, Ludde, KH. (1970) Some Considerations in Powder Compaction Equation. *Powder Tech.* 4:61-68.
- [8] Odeku OA (2005) Assessment of *Albizia zygia* gum as a binding agent in tablet formulations. *Acta Pharm.* 55; 263-276
- [9] Odeku OA and Itiola OA. (1998) Evaluation of khaya gum as a binder in a paracetamol tablet formulation, *Pharm. Pharmacol. Commun.* 4; 183-188.
- [10] Ohwoavworhwa FO, Adelakun TA and Kunle OO. (2007) A comparative Evaluation of the Flow and Compaction Characteristics of  $\alpha$ -Cellulose obtained from Waste Paper. *Trop. J. Pharm. Res,* 6 (1): 645-651
- [11] Oladapo AA, Michael AO and Oludele AI. (2006) Compression, mechanical and release properties of chloroquine phosphate tablets containing corn and trifoliate yam starches as binder. *Trop. J. Pharm. Res.* 5 (2): 589-596.
- [12] Onwuliri FC, Wonang DL, Onwuliri EA and Mawak JD (2006) phytochemical, Toxicological and Histopathological studies of some medicinal plants in Nigeria. *Intern Journal of Natural and Applied Sciences* 2 (3): 225-230, 2006
- [13] Rama Prasad YV, Krishnaiah YSR and Satyanarayana S. (1998) In vitro evaluation of guar gum as a carrier for colon-specific drug delivery, *J. Control. Rel.* 51; 281-287.
- [14] Ravindra SD, Shamkant LS, Bhaskar C, Kakasahib RM and Anant P. (2006) Evaluation of a drug with wax-like properties as a melt binder. *Acta Pharm.* 56: 451-461.
- [15] Train D. (1956) An investigation into the compaction of powders. *J. Pharm. Pharmacol.* 8: 745-761
- [16] United States Pharmacopoeia 23/National Formulary 18, United States Convention, Rockville. 1995, pp. 1942-1943.