Full Length Research Paper

Effect of *Grewia* gum on the mechanical properties of Paracetamol tablet formulations

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Grewia gum has been evaluated as a binder in paracetamol tablet formulations. Compressional properties of the formulations were analyzed using density measurements and the compression equations of Heckel and Kawakita as assessment parameters. Formulations containing *Grewia* gum as a binder show a slower onset and lower amount of plastic deformation than those containing PVP. The Db values for formulations containing *Grewia* gum, increased with increased concentration up to 4% w/w. Formulations containing *Grewia* gum were also found to exhibit higher degree of packing than those containing PVP. Yield values for formulations containing *Grewia* gum was found to be at variance with the binder concentration. The values increased between 1 and 2% w/w and decreased between 2 and 4% w/w. A linear relationship was found to exist between N/C and N for formulations containing *Grewia* gum at all concentrations. *Grewia* gum was found to improve the fluidity of paracetamol granulation better than PVP. This study suggests that *Grewia* gum compares favorably with the standard binder PVP used hence could be a useful substitute binder in paracetamol tablet formulations.

Key words: Grewia gum, PVP, paracetamol, Heckel equation, Kawakita equation, compaction characteristics.

INTRODUCTION

Binders confer structural strength required by tablets during processing, handling, packaging and transporta-tion. A number of plant gums/hydrocolloids have been used as binding agents, suspending or emulsifying agents in both solid and liquid dosage formulations (Chukwu et al., 1994a, b; Nasipuri et al., 1996, 1997, 1999; Odeku, 1998, 2002, 2005). These gums have been used in producing tablets with different mechanical strength, consolidation and drug release properties for different pharmaceutical purposes. These gums are ge-nerally non-toxic and widely available, hence the conti-nued interest (Odeku, 2005).

Grewia mollis juss; F.Tiliaceae is a savanna shrub or a small tree up to 20 ft high. It is known to be a strong fire-resistant. The bark of the tree is black and rough with the young twigs being hairy. The leaves sizes ranges bet-ween 5 – 10 cm long by 2 – 5 cm broad, with shape being ovate to oblong with margin distinctly toothed. The apex is acute and the leaf color is dull bluish green above and silky white below and 3 – nerved at base. The

flowers are brightly yellow and in axillary clusters. Fruit sub globes, about 0.75 cm in diameter and blackish when ripe. *Grewia* gum is obtained from the bark of the tree. The mucilaginous bark is used in cooking soup, or dried and pulverized to mix with bean meal to make cakes called in Hausa "K'osai'. The flowers and young shoots are sometimes used as a soup or sauce vegetable.

The infusion of the bark obtained by cold or hot maceration in water is used in beating mud floors, or mixed with the mud or the walls of huts to give a smooth surface. The mucilaginous property of the bark or leaf is used in application to cuts and sores. The Yoruba in Nigeria use it medicinally at times of child birth (Dalziel, 1937).

In this work, *Grewia* gum has been evaluated for its binding properties in a paracetamol tablet formulation in comparision with a standard binder, polyvinylpyrollidone (PVP), using the density measurements and the com-pression equations of Heckel and Kawakita as assess-ment parameters, while the mechanical properties of the tablets were assessed using the crushing strength and friability.

The Heckel plot is the method most frequently used to evaluate the volume reduction of materials when pres-

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pressure is applied (Luiz et al., 2005). It is assumed that the densification of the powder column follows first order kinetics. Thus, the degree of material densification is correlated to its porosity. Although the literature search reveals some limitations to the Heckel model (Rue et al., 1978; Sonnergaard, 1999), the model has often been applied to study powder mixtures and to evaluate granule manufacture (Isimi et al., 2003; Luiz et al., 2005, Emeje and kunle 2005, Kunle et al., 2005). Of recent, scientists have also made attempts to use the Heckel relation for predicting powder characteristics of active pharmaceutical extracts (Emeje and Kunle, 2005, Kunle et al., 2005). Others have used more than one equation to try to eliminate the shortcomings of the other (Alebiowu and Itiola, 2001; Adebayo and Itiola, 2003; odeku, 2003, 2005). Hence, in this study, both Heckel and Kawakita plots have been used to assess the compression characteristics of *Grewia* mollis in paracetamol tablet formulations.

Heckel (1961) equation is expressed as:

$$\ln [1/1 - D] = KP + A \qquad\qquad i$$

The slope of the linear portion of the curve, K, is the reciprocal of the mean yield pressure, Py, of the material. The intercept of the extrapolated linear region, A, is a function of the original compact volume. It represents two stages of consolidation- one due to the initial relative density of the powder and the other due to densification by particle rearrangement. From the value of A, the relative density Da can be calculated using the following equation;

$$Da = 1 - e^{-A} \qquad\qquad ii$$

The relative density of the powder bed at the point when the applied pressure equals zero, Do, is used to describe the initial rearrangement phase of densification as a result of die filling. The relative density, Db, describes the phase of rearrangement at low pressures and is the difference between Da and Do.

$$Db = Da - Do \qquad\qquad iii$$

The Kawakita (Kawakita and Ludde, 1971) equation is used to study powder compression using the degree of volume reduction, C. The equation describes the relationship between the volume reduction of powder column and the applied pressure;

$$C = [Vo - V/Vo] = [abP/1 + bP] \qquad\qquad iv$$

Where, C, is degree of volume reduction, Vo is Initial volume, V is volume of powder column under the applied pressure P. a, b are constants characteristic to powder being compressed. The equation above can be re arranged in linear form as:

$$P/C = P/a + 1/ab \qquad\qquad v$$

From the graphical presentation of P/C versus P, the constants maybe be evaluated. The constant "a", is given as a reciprocal of the slope from the linear portion of the plot and equivalent to the value of C at infinitely high pressures. 1/ab is the intercept. a, gives an indication of the maximum volume reduction available and is considered to describe the compressibility of a powder, while b is considered to describe an inclination toward volume reduction. However, the actual physical meaning of the constants a and b have been in question (Alderbon and Nystrom, 1996). Consequently, Kawakita et al. (1983) have applied another equation in describing the volume reduction on tapping and vibrating processes, where the pressure P, is replaced by the tapping number, N.;

$$N/C = [(1/a) N \div 1/ab] \qquad\qquad vi$$

Where, N is the tapping number, C is the degree of volume reduction and a and b are constants .C in equation vi is given by;

$$C = [Vo - V_N] \div Vo \qquad\qquad vii$$

Where Vo is the initial apparent volume and VN, the volume at tapping number N. The constants of Kawakita equation can be used to estimate the flow and cohesiveness properties of powders. Constant "a", describes the compressibility and constant "1/b" describes cohesive properties of powders or the fastness of how the final packing stage is achieved (Alderbon and Nystrom, 1996).

MATERIALS AND METHOD

Grewia mollis mucilage (GMM), lactose (sigma-Aldrich, Chemic GmbH, Germany), Paracetamol BP was obtained from NIPCO pharmaceuticals (Nigeria) and Polyvinylpyrrolidone (PVP) obtained from Aldrich chemical company, Inc. USA.

Extraction and Purification of GMM

GMM was extracted and purified as previously described by Nasipuri et al. (1996).

Preparation of granules

Dried powdered GMM equivalent to 0, 1.0, 2.0 3.0, 4.0 and 5.0% w/w or 2.0% w/w PVP was mixed with paracetamol powder respectively and made up with lactose BP. The mixture was blended thoroughly in a tumbler mixer for 10 min and granulated with water in a granulator (Erweka, Germany) fitted with a 1.7 mm sieve and the granules were dried in a hot air oven at 60^OC for 1 h.

Preparation and Evaluation of compacts

Compacts equivalent to 500 mg paracetamol were produced by compressing the granules for 60 s with predetermined loads (at various compression pressures) using a tableting machine (Shangai, China). 50 tablets were compressed at each pressure. All read-
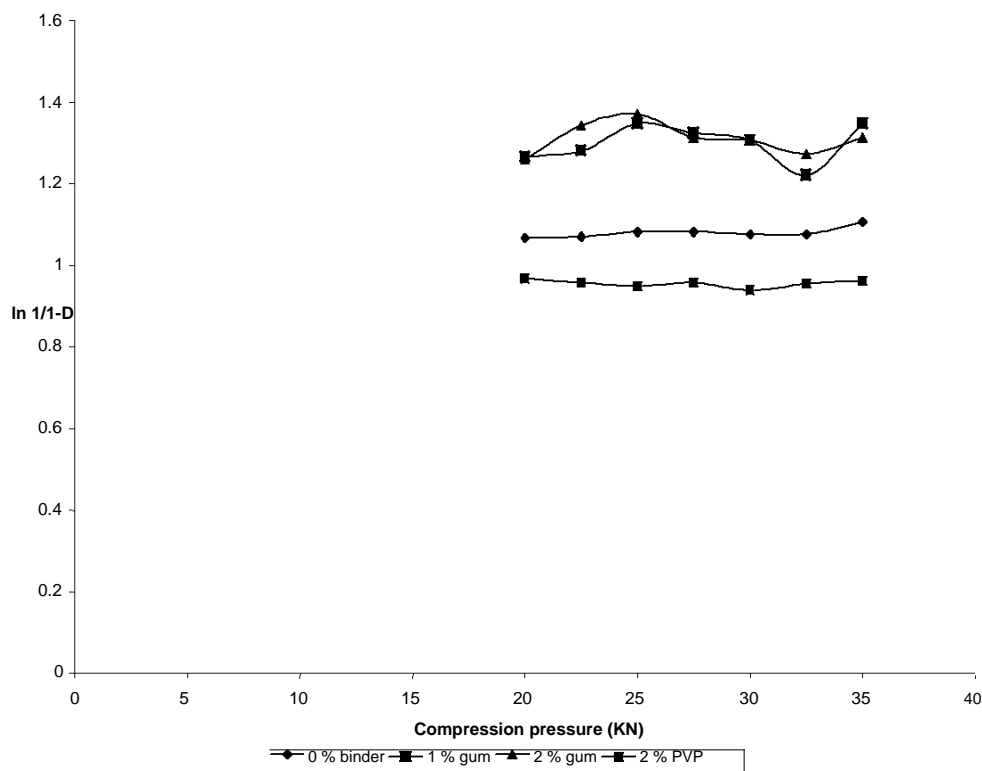
Figure I. plots for paracetamol formulations containing different concentrations of *Grewia* mollis and 2% PVP.

readings are average of 3 measurements. Before each compression, the die (12.5 mm in diameter) and flat faced punches were lubricated with a 1% w/v dispersion of magnesium stereate in chloroform. After ejection, the tablets were stored over silica gel in a dessicator for 24 h to allow for elastic recovery and hardening to prevent falsely low yield values (krycer et al., 1982) and the dimensions of the compact were determined using the mitutoyo model IDC1012EB (Mitutuyo corporation, Japan) thickness gauge to the nearest 0.01 mm. The Heckel and Kwawakita Plots were statistically analysed using the Microsoft Excel computer software. The relative density of the compacts was calculated using the equation;

$$\underline{D =} \qquad w \quad s \text{ -------------} \quad (7)$$
$$Vt$$

Where w is the weight of the compact (g), Vt is the volume of the compact (cm^3), and s is the density of granules ($glcm^3$). The crushing strength of the compacts was determined using an Erweka hardness tester (Erweka, Gmbt, Germany). Ten tablets were tested at each compression pressure. Disintegration time of compacts were determined in 0.I N HCL at 37 ± 0. 5^0C in a BP disintegration test unit (Manesty Machines, Poole, UK).

RESULTS AND DISCUSSION

Figures 1 and 2 show the Heckel plots for paracetamol formulations containing between 0 and 5% w/w GMM and 2% w/w PVP, with those formulations containing PVP showing more compressibility. The addition of GMM as a

binder altered the shape of the Heckel plot from that of linearity at all applied pressures to an initial curve typical of type B plot. Values for the mean yield pressure, Py, of the formulations were calculated from the linear portion of the plots and the intercept, A, was determined from the extrapolation of the region. The values of Py, Do, Da, and Db for all the formulations are presented in table 1.

The phase of rearrangement of particles at low pressure is represented by Db. It can be observed that the Db values for the formulations increased with in-crease in binder concentration up to 4% w/w GMM. These values were higher than that of PVP, suggesting more fragmentation of granules containing GMM at low pressure.

The value of Da representing the total degree of packing achieved at zero and low pressures are higher for the formulations containing GMM than for those containing PVP. The values also increased with binder concentration up to 3% w/w. The values of Do for the formulations did not follow a particular trend. Although the values increased in the presence of both GMM and PVP, concentration of GMM did not have a definable effect on the Do values. The highest Do value was observed to be at 3% w/w and the lowest at 4% w/w. The mean yield pressure is inversely related to the ability of a material to deform plastically under pressure. The value of Py for the formulation containing PVP was much higher than those containing GMM. This implies that onset of plastic
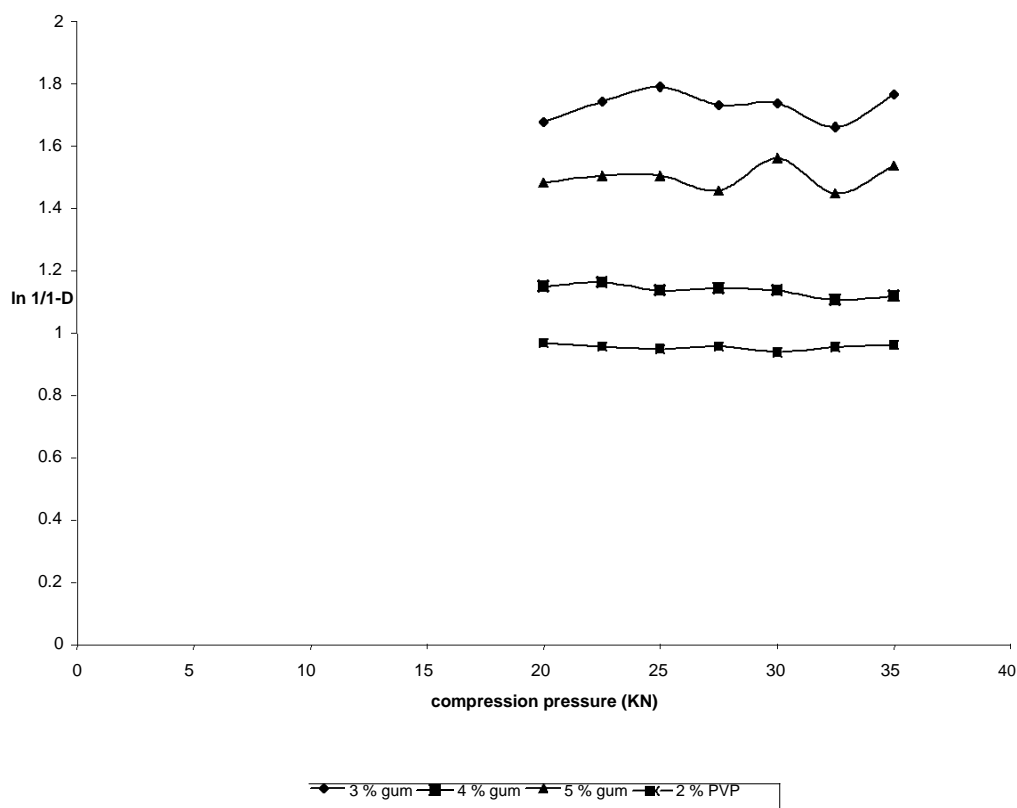
Figure 2. Heckel plots for paracetamol formulations containing different concentrations of *Grewia* mollis gum and 2% PVP.

Table 1. Parameters obtained from Heckel plots for paracetamol tablet formulations.

Binder type	Binder conc. (%w/w)	Do	Py (KN)	Da	Db
Grewia mollis	0.0	0.353	556	0.644	0.291
	1.0	0.466	833	0.718	0.252
	2.0	0.413	1667	0.735	0.322
	3.0	0.491	1429	0.819	.328
	4.0	0.356	345	0.704	0.348
	5.0	0.458	667	0.768	0.310
PVP	2.0	0.431	2000	0.620	0.189

deformation in the formulation containing PVP occurred at much higher pressures. The Py values for formulations containing GMM did not follow any trend, as the values were seen to increase between 1 and 2% w/w and decreased between 2 and 4% w/w. The implication is that, the onset of plastic deformation I the formulation containing 3% w/w GMM occurred at higher pressures than other concentrations. 3% w/w therefore, is the optimum concentration for GMM as a binder in paracetamol tablet formulation.

Figures 3 and 4 show the kawakita plots for paracetamol tablet formulations containing GMM and PVP at different concentrations, where a linear relationship between N/C and N is obtained at all compression pressures used with correlation coefficient 0.99 for all formulations except those containing 2% w/w PVP, and hence, the equation can be used to predict the densification mechanisms of the paracetamol formulations. Values of 1/b and 1/ab were obtained from the slope and intercept of the plots respectively. The tapping experiments were performed on all samples and a and 1/b were evaluated. Table 2 shows the Kawakita constants, it is observed
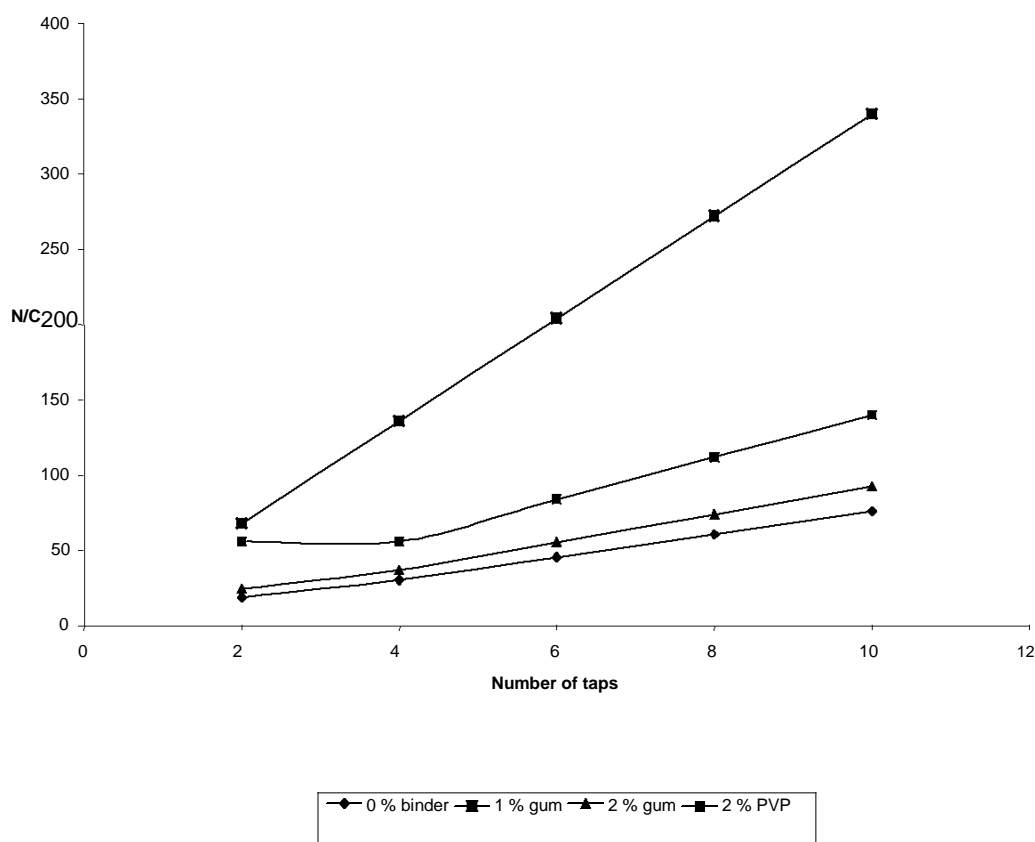
Figure 3. Kawakita plots for paracetamol tablet formulations containing different concentrations of *Grewia* mollis gum and 2% w/w PVP.

Table 2.parameters obtained from kawakita plots for paracetamol tablet formulation

Binder type	Binder conc. (% w/w)	1/ab	1/a	A	1/b	R^2
Grewia mollis	0.5	7.22	3.03	0.330	2.383	0.997
	1.0	34.00	0.00	0.000	0.000	1.000
	2.0	8.63	4.93	0.203	1.751	0.995
	3.0	10.50	9.34	0.107	1.124	0.988
	4.0	8.87	5.06	0.198	1.753	0.995
	5.0	17.50	0.00	0.000	0.000	1.000
PVP	2.0	11.20	22.40	0.045	0.500	0.941

from this table that values of a are larger in formulations without a binder than in the formulation containing GMM and PVP implying that the fluidity of the former is worse. The value of 1/b for formulations without a binder is highest implying that the cohesiveness of the granules would be higher than others. The low value of 1/b in other formulations is indicative of the reduction in cohesion in the presence of a binder. Binders are generally expected to reduce the cohesiveness and increase flow of granulation (Alebiowu and Itiola, 2001). A low value of 1/b is

indicative of materials that are soft and that readily deform plastically under pressure.

Conclusions

The results presented here shows that the mucilage obtained from *Grewia* mollis (GMM) can be used as a binder in paracetamol tablet formulation with good physical properties. From the result obtained, formulations containing G*rewia* gum as a binder show a slower onset
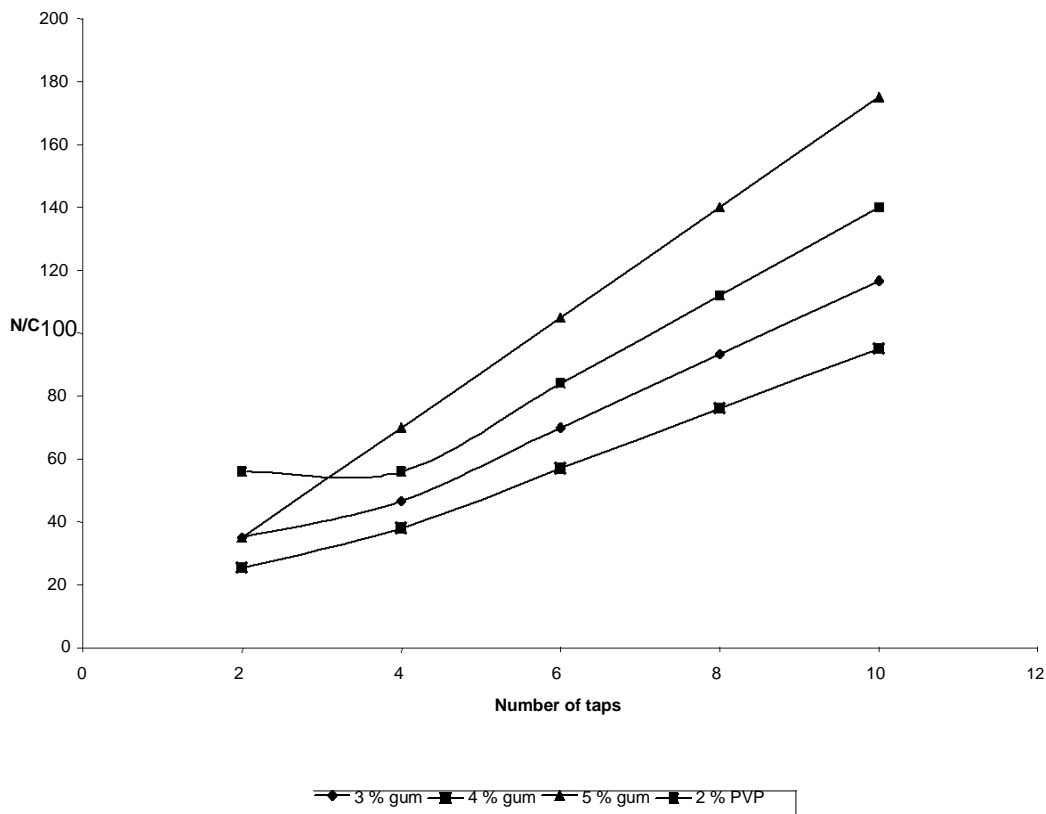
Figure 4. Kawakita plots for paracetamol tablet formulations containing different concentrations of *Grewia* mollis.

and lower amount of plastic deformation than those containing PVP and compared favorably with the standard PVP as a binder.

REFERENCES

Chukwu A (1994). Studies on *Detarium microcarpium* gum II. Investigation as a prolonged release matrix for encapsulated chlorpheniramine maleate. S. T. P. Pharma. Sci. 4: 399-403.

Chukwu A (1994). Studies on *Detarium microcarpium* Gum III. In vitro characteristics of prolonged release chlorpheniramine maleate tablets. S. T. P. Pharma. Sci. 4: 404-408.

Dalziel (1937). The useful plants of West Africa. Crown Agents, 41 Millbank, West minster,London, S.W.1. pp. 98-99.

Emeje MO, Kunle OO (2004). Effect of two surfactants and mode of incorporation on the compaction characteristics of the hot water leaf extract of Ficus Sur. J. Nutraceuticals, Functional and Med. Foods 4: 147-156.

Ismi CY, Nasipuri RN, Ojile JB, Ibrahim YKE, Emeje M (2003). Effects of the diluent type on compressional characteristics of the mixed stem bark extract of Anogeissusleiocarpus and Prosopis africana tablet formulation, Acta Pharmaceutica. 53: 49- 56.

Kawakita K, Ludde KH (1971). Some considerations on powder compression equations, Powder Technol. 4: 61- 68.

Luiz A, George G, Pedro P, Peter C (2005). Dry Granulation and Compression of Spray-Dried Plant Extracts, AAPS Pharm. Sci. Tech. 6 (3): 45.

Nasipuri RN, Igwilo CI, Brown SA, Kunle OO (1996). Mucilage from *Abelmoschus esculentus* fruits – a potential pharmaceutical raw material part 1-physicochemical properties; J. Pharm. Res. Devt. 1: 22-28.

Nasipuri RN, Igwilo CI, Brown SA, Kunle OO (1997). Mucilage from *Abelmoschus esculentus* fruits – a potential pharmaceutical raw material. Part 11-emulsyly properties. J. Pharm. Res. Devt. 2 (1): 27-34.

Nasipuri RN, Igwilo CI, Brown SA, Kunle OO (1999). Mucilage from *Abelmoschus exculentus* fruits – a potential pharmaceutical raw material. Part 111-suspending properties. J. Pharm. Res. Devt. 2: 121 -130.

Odeku OA, Itiola OA (1998). Evaluation of khaya gum as abinder in a paracetamol tablet formulation. Pharm. Pharmacol. 4:183 -188

Odeku OA, Itiola OA (2002). Characterization of Khaya gum as a binder in a paracetamol tablet formulation, Drug Dev. Ind. Pharm. 28: 329-337.

Odeku OA, Itiola OA (2005). Compression and mechanical properties of Tablet formulations containing corn, sweet potato and cocoyam starches as binders. Pharmaceutical Technology (www.pharmtech.com)

Rue PJ, Rees JE (1978). Limitations of Heckel relation for predicting powder compaction mechanisms. J. Pharm. Pharmacol. 30: 642-643.

Sonnergaard JM (1999). A critical evaluation of the Heckel equation. Int. J. Pharm. 193: 63-71.