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Effect of diluents on the compaction and compressional characteristics of the stem bark extract of *Terminalia avicennoides*

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ABSTRACT

Background & Aim: Herbal medicines have historical use and is currently being used in treatment of various diseases largely due to its relative availability and cheap cost. Standardization and development of suitable dosage forms for herbal medicines is therefore pertinent for both practitioners and patients. This study aims to evaluate effect of diluents (microcrystalline cellulose, lactose and magnesium carbonate) on the compaction and compression properties of the stem bark extract of *Terminalia avicennoides*.

Experimental: The crushed powdered stem bark was macerated in 70 % ethanol for 72 h at room temperature with intermittent stirring. The filtrate was concentrated over a water bath at 100 °C to obtain the dried extract (TAE). Granules of the extract were prepared by wet granulation. Flow properties and moisture content of the granules were determined. Compatibility between the extract and the diluents was investigated by Fourier Transform Infrared (FTIR). Compacts were made and properties evaluated using the Heckel and Kawakita models.

Results: Results of FTIR spectra showed no interaction between the ingredients of the tablet formulations. Granules prepared with microcrystalline cellulose (T-MCC) possessed better flow and showed more propensities to be compacted than the other tablet batches. All the tablet formulations were observed to exhibit plastic deformation but T-MCC showed faster onset of deformation, closer packing, less cohesiveness, greater densification and easier compaction ability than tablets prepared with lactose (T-LAC) and magnesium carbonate (T-MAG). Although T-MAG showed the highest tensile strength, it was the only formulation that disintegrated within the 30 min official specification for herbal tablets.

Recommended applications/industries: However, based on other parameters apart from disintegration time, microcrystalline cellulose is considered as the diluent of choice for preparation of standardized and robust tablets of stem bark extract of Terminalia avicennoides.

1. Introduction

Herbal medicines have been defined by the World Health Organization (WHO) as labelled, finished medicinal products containing either aerial or underground parts or both of a plant or other plant materials (Patil *et al.*, 2012). Herbal medicines have been used to treat various diseases for thousands of years ago. Even with the availability of modern

medicine, traditional herbal medicines still uphold their popularity. The use of herbal medicine has always had historical and cultural reasons and also due to its relatively inexpensive nature and is now being used increasingly worldwide. The WHO has estimated that about 80 % of the world's population use herbal therapies/remedies (WHO, 2015). More recently and frequently herbal remedies are being employed for the treatment of malaria as a large number of people who are infected with malaria parasite cannot afford the cost of the conventional antimalarial drugs.

Malaria is an important world-wide public health problem however, Sub-Saharan Africa alone accounts for about 90 % of malaria cases recorded world-wide. Nigeria along with another African country contributes about 36 % of the world's malaria burden. Malaria is one of the leading causes of mortality on Nigeria especially among children under 5 years and the pregnant women (Nwaorgu and Orajaka, 2011). The risk factors are largely associated with poverty, non-availability of malaria therapies, counterfeiting and the growing resistance to existing antimalarial drugs (Iyiola *et al*., 2020). In line with these challenges, alternate therapies from natural sources like indigenous herbs are now being exploited especially because they are readily available, relatively cheap and resistance to the multicomponent of herbal therapies is less rapid (Afolabi *et al*., 2019). A lot of medicinal plants are used in treatment of malaria either solely or in a recipe for treatment of malaria in ethno medicine one of such is *Terminalia avicenniodes.*

The plant *Terminalia avicenniodes* is a medicinal plant of African descent, it belongs to the Combretaceae family. It is a yellowish-brown shrub-like tree plant with strong hard wood, it is widely distributed in the Savannah region of West Africa, particularly in Senegal, Cameroun and Nigeria (Akanbi *et al*., 2018). All the parts of the plant are used in various forms for treatment and management of different diseases including those of respiratory, skin, gastrointestinal and fungal infections (Akanbi *et al*., 2018). Of particular interest in this study is the use of this plant in the management of malaria, literature reveals studies which show its potential.

The methanol stem bark extract of Terminalia avic*enniodes* (*T. avicenniodes*) has been found to possess significant antiplasmodic activity which confirms the folkloric use in the treatment of malaria. The extract was found to clear malaria parasite up to about 95 % in infected mice after 5 days at minimal doses of 100 and 200 mg/kg (Akanbi *et al*., 2018; Akanbi *et al*., 2017). In another study, the total saponins of *Terminalia avicenniodes* was found to suppress *Plasmodium berghei* in laboratory mice by 80 % after 4 days (Akanbi *et al*., 2018). Similarly, it has been reported that administration of 100 and 200mg/kg of methanol stem extract of *T. avicennioides* to infected laboratory rats reduced parasitaemia by 18 and 11 % respectively (Omonkhua *et al*., 2013). In the same study, the haemoglobin, red blood cell, and lymphocyte counts were restored upon treatment with the extract, in addition, serum and liver superoxide dismutase activities were elevated with concurrent reduction in serum malondialdehyde concentration compared to untreated infected mice. This study suggested that *T. avicennioides* possess potential to offer protection against the severe malaria and its complications.

In a different study, the powdered stem bark of *Terminalia avicennioides* administered as dietary meal to *Plasmodium berghei* infected mice was found to possess similar antiplasmodial activity to the combined artemether lumefantrine drug with no hepatocellular dysfunction observed with the conventional drug (Afolabi *et al*., 2019). Pico Green fluorometric assay used to evaluate *in vitro* antiplasmodial activity of some medicinal plants returned *Anogeissus leiocarpus* and *Terminalia avicennioides* as possessing potent antiplasmodic activity (Shuaibu *et al*., 2008).

In spite of the efficacy of the pharmacological activity of *Terminalia avicennoides*, its use in its unrefined form (decoction, infusion, macerates) is not readily acceptable to most patients. Therefore, developing this extract into suitable dosage forms such as tablets which is one of the most common dosage forms will not only increase their acceptability but will also improve their stability. Tablets are the most common solid dosage forms for systemic administration of active pharmaceutical ingredients manufactured with the aid of various excipients. Tablets are most often preferred due to their simplicity, economy of preparation, stability, convenience in packing, shipping and dispensing, accuracy of dose, compactness and ease of administration. Tablets range from immediate release, extended release, compressed, film coated, sugar coated, enteric coated, chewable, sublingual, etc (Ansel and Loyd, 2011). Excipients are inert substances included in tablet formulation to improve their properties. They are used to achieve

various purposes such as improve dissolution, disintegration, bulkiness, colour, etc. Some categories of excipients for tablet formulations include diluents, binders, lubricants, glidants, etc. Diluents are very crucial in tablet manufacturing because they are used as bulking agents or fillers to make up the required bulk of tablet when the drug dosage itself is inadequate to produce its bulk. Tablet formulations may contain diluents in order to provide better properties such as improved cohesion, direct compression manufacturing and to promote flow properties. Diluents can be classified based on their solubility into hydrophobic diluents like microcrystalline cellulose (MCC), dicalcium phosphate and tricalcium phosphate or into hydrophilic diluents examples include lactose, mannitol, sucrose, dextrose and sorbitol.

This study focuses on the effect of diluent on compaction and compression of ethanol extract of the stem bark extract of *Terminalia avicennoides*as part of formulation studies for standardization since most work conducted on these herbs are limited to their chemical and medicinal properties. This will help determine the technical feasibility and economic viability of producing solid oral dosage forms (tablets) of this extract.

Therefore, the aim of this present study is to evaluate the compaction and compression properties of ethanol extract of the stem bark of *Terminalia avicennoides* prepared *via* the wet granulation method; the effect of diluents of these properties was also evaluated.

2. Materials and Methods

2.1. Materials

Terminalia avicennoides stem bark extract (prepared in the National Institute for Pharmaceutical Research and Technology, NIPRD, Abuja, Nigeria), Polyvinylpyrrolidone (Aldrich Chemicals, Inc. USA), Maize starch (BDH chemicals Ltd), Lactose (BDH chemicals Ltd), Magnesium carbonate (BDH chemicals Ltd), Talc (BDH chemicals Ltd), Magnesium stearate (BDH chemicals Ltd).

2.2. Collection and identification of stem bark of Terminalia avicennoides

Stem bark of *Terminalia avicennoides* was collected from the National Institute for Pharmaceutical Research and Development (NIPRD) botanical garden and identified in the herbarium of the Institute by Mallam Muazam. The plant material was dusted, oven-dried at 40 °C for 24 h and milled using a mechanical grinder to coarse powder. It was then transferred into a plastic container and stored in a desiccator at room temperature until further use.

2.3. Preparation of Terminalia avicennoides extract

About 1 kg of the crushed powdered stem bark was macerated in 70 % ethanol in a ratio of 1:3 for 72 h at room temperature with intermittent stirring. The filtrate was removed from the marc and concentrated over a water bath (Karl Kobb, Dreieich, West Germany) at 70 °C. The resulting dried extract (TAE) was pulverized, packaged in an air-tight container and stored in the desiccator until further analysis (Omonkhua *et al*., 2013).

2.4. Preparation of Terminalia avicennoides extract (TAE) granules

The wet granulation method of massing and screening was used to make granules of TAE. A batch size of 50 tablets was prepared. Appropriate quantities of the extract (TAE), the diluent (microcrystalline cellulose) and disintegrant (maize starch) were mixed in a porcelain mortar and moistened with a solution of the binder (polyvinyl pyrrolidone) according to the composition in Table 1. The damp mass was screened through a sieve (1.4 mm mesh size) and dried in the oven (40 ^{o}C) for 1 h after which the granules were further screened through 1 mm mesh size to break up any agglomerates. The dried granules were stored in air-tight containers and kept in a desiccator until further use. Other batches containing lactose and magnesium carbonate as diluents were prepared similarly according to the composition in Table 1.

Table 1. Composition for preparation of *Terminalia avicennoides* extract (TAE) tablets.

Ingredients (mg)/Batch	T-MCC	T-LAC	T-MAG
TAE	200.0	200.0	200.0
Polyvinyl Pyrrolidone	25.0	25.0	25.0
Maize starch	25.0	25.0	25.0
Microcrystalline cellulose	242.5	-	-
Lactose	-	242.5	-
Magnesium carbonate	-	-	242.5
Talc	5.0	5.0	5.0
Magnesium stearate	2.5	2.5	2.5
Total	500.0	500.0	500.0

Key: TAE = alcohol extract of the stem bark of Terminalia avicennoides, T-MCC = tablet formulation prepared with microcrystalline cellulose as diluent, T-LAC = tablet formulation prepared with lactose as diluent, T-MAG = tablet formulation prepared with magnesium carbonate as diluent.

2.5. Evaluation of Terminalia avicennoides extract (TAE) granules

2.5.1. Particle size analysis

The granules (120 g) were passed through the Reitsch test shaker (Type AS 200 control 'g' GMBH, Germany) with sieves arranged in descending order of aperture. The shaker was allowed to run for 5 min at an amplitude of 1,500 mm/g, the fraction of granules retained on each sieve was weighed and the percentage cumulative weight was determined and plotted against the sieve apertures (Emeje *et al*., 2017).

2.5.2. Moisture content

Moisture content of each batch was determined gravimetrically by drying 2 g sample of the granules in the hot-air oven (BS 6206A ArmouraTech) at 105 °C for 1 h and transferred into a desiccator to cool down before being re-weighed. This cycle of drying and weighing was continued until a constant weight was obtained then moisture content (MC) was expressed in percentage using the equation below (Emeje *et al*., 2017);

$$MC(\%) = {}^{initial\ weight - final\ weight}/_{initial\ weight} \cdots (1)$$

All measurements will be in triplicates and presented as mean.

2.5.3. Determination of flow properties

2.5.3.1. Angle of repose

The funnel method was used in this determination; 50 g of the granules was allowed to flow through the orifice of a clamped funnel. The height and radius of the resulting heap was measured and used to calculate the angle of repose (A) using the equation below (Emeje *et al*., 2005);

$$A = tan^{-1}\, {}^{h}/_{r} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

2.5.3.2. Bulk and tapped densities

The volume occupied by the granules (20 g) in a graduated measuring cylinder was noted as the bulk volume and used to compute the bulk density (g/mL). Similarly, the volume occupied by the granules after tapping the measuring cylinder 100 times in the Stampfvolumeter (STAV 2003JEF, Germany) was noted and used to calculate the tapped density (g/mL) (Emeje *et al*., 2005).

2.5.3.3. Carr's compressibility index (CI) and Hausner ratio (HR):

These were computed with data obtained from the bulk and tapped densities using the equations below (Emeje *et al*., 2005);

$$CI = {}^{tapped\ density - bulk\ density}/_{tapped\ density} X\ 100 \ldots (3)$$

$$HR = {}^{tapped\ density}/_{bulk\ density} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4)$$

2.5.4. True density

The liquid displacement method was adopted and liquid paraffin was used as the displacement fluid. Three determinations were made and true density (Trd) was computed as shown below;

$$Trd = {}^{Wp}/_{[(x + Wp) - y]X\ SG} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (5)$$

Where Wp is weight of starch powder, x is weight of the bottle and fluid, y is weight of the bottle, fluid and starch powder, SG is specific gravity of liquid paraffin (0.865 g/mL) (Emeje *et al*., 2005).

2.5.5. Relative density (RD)

This was calculated as the ratio of the tapped density to the particle density (Emeje *et al*., 2005).

Fourier transform infra-red spectra studies (FTIR)

Granules prepared with the different diluents (T-MCC, T-LAC, T-MAG) were triturated with potassium bromide powder, made into pellets (1 ton/cm^2). The extract alone was similarly triturated to obtain pellets. Infra-red (IR) spectra were obtained between scanning ranges of 4000 and 400 cm-1 from the Magna-IR, 560 spectrometers (Perkin Elmer, USA) (Pongpiachan, 2014).

2.6. Compaction of Terminalia avicennoides extract (TAE) granules

Compacts equivalent to 500 mg were produced by compressing the granules for 60 secs at various compression pressure (22.5, 25, 27.5, 30, 32.5 KN/m^2) in the Manesty tableting machine (Shanghai, China) using the 12.5 mm punch and die set. Fifty (50) tablets were compressed at each of the pressures and they were stored in a desiccator containing silica gel for 24 h to allow for elastic recovery and hardening (Emeje *et al*., 2017).

2.7. Evaluation of Terminalia avicennoides extract (TAE) tablets

2.7.1. Weight variation

The weight of twenty (20) tablets were randomly selected were individually determined using the analytical balance (Mettler Toledo - Type AB54, Switzerland) then the average weight was determined (Adedokun *et al*., 2014).

2.7.2. Tablet diameter and thickness

Diameter and thickness of ten (10) randomly selected tablets was measured using the micrometer screw gauge (Mitutoyo IDC-1012EB, Japan) and the average was calculated (Adedokun *et al*., 2014).

2.7.3. Tablet hardness

The hardness of five (5) randomly selected tablets was determined using the hardness tester (Erweka D-6072 Type HT, GmbH, Germany) and the average was calculated (Adedokun *et al*., 2014).

2.7.4. Friability test

Ten (10) tablets from a batch were collectively weighed (W_1), placed into the Erweka Friabilator and allowed to rotate at 25 rpm for 4 min. Afterwards, the tablets were de-dusted, re-weighed (W_2) and friability (%) was calculated as (Adedokun *et al*., 2014);

$$F\,(\%) = {}^{W1 - W2}/_{W1}\ X\ 100 \quad \ldots (6)$$

2.7.5. Tensile strength

This was determined from data obtained from tablet diameter (d), thickness (t) and hardness (H) using the equation below (Emeje *et al*., 2017);

$$Tensile\ strength = {}^{2H}/_{\pi dt} \quad \ldots (7)$$

2.7.6. Disintegration test

Disintegration time was determined with the aid of a disintegration tester (Type DA, Erweka, Germany). Tablets from each batch was placed in each of the six (6) compartments of the tester containing distilled water maintained at 37 ± 2.0 ºC as medium. The time taken for the tablets particles to pass through the mesh of the compartment was recorded and the average calculated. The same procedure was performed for the other tablets batches (Adedokun *et al*., 2014).

2.8. Analysis of compaction and compressional data

This was done using the Heckel and Kawakita models. The Heckel model utilizes the mechanism of volume of reduction under compression force by linking relative density of powder bed during compression to the applied pressure (Adeleye *et al*., 2015) and is mathematically represented as;

$$\ln({}^{1}/_{1 - D}) = KP + A \quad \ldots (8)$$

by plotting the values of ln [1/1 – D] against applied pressure, P, the values of slope representing K and intercept representing A can be extrapolated from the linear portion of the plot. The value of K also determines the mean yield pressure (1/K = Py) which is a measure of the plasticity of the compressed granules (Adetunji *et al*., 2006).

The value of the intercept A, is used to determine the densification of the granules at different stages; Do, D_A and D_B.

Do is relative density which shows initial granule densification at the die filling stage and is expressed as;

$$D_O = {}^{bulk\ density}/_{true\ density} \quad \ldots (9)$$

The value of D_A is the final compact densification and is calculated as

$$D_A = 1 - e^{-A} \quad \ldots (10)$$

While the D_B value is the densification of the granules when compressed; it indicates the phase rearrangement and is expressed as (Alebiowu and Itiola, 2002);

$$D_B = D_A - D_B \quad \ldots (11)$$

The Kawakita equation was used to assess the flow properties of the granules *viz-a-viz* the compressional behavior of the granules by tapping or from compression. The equation as given below describes the relationship between volume reduction at the limit of tapping (a), cohesiveness of the granules (1/b) and the degree of volume reduction (C) (Chattoraj and Sun, 2018);

$$NC = N/a + 1/ab \quad \ldots (12)$$

The degree of volume reduction (C) is calculated from the initial volume V_0 and tapped volume V as;

$$C = {}^{(Vo - V)}/_{V} \quad \ldots (13)$$

The integrated equation given below was adopted to enable the constants "a" and "b" to be determined by linear regression

$$\frac{P}{C}=\frac{P}{a}+\frac{1}{ab} \quad \ldots\ldots (14)$$

where P is the applied pressure, C is the degree of volume reduction, parameters "a" and "b" are constants relating to the total degree of powder volume reduction and the yield strength of the granules respectively (Chattoraj and Sun, 2018).

3. Results and discussion

3.1. Particle size analysis

Figure 1 shows that granules range from large to small granules with a large percentage of the granules being moderately sized (150 µm). Particle size and its distribution in granules is an important parameter that influences the granules flowability, uniformity of tablet weight, compatibility and rearrangement of particles (Virtanen *et al*., 2010).

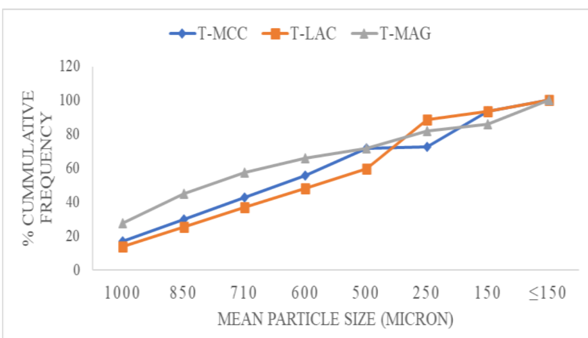

Fig 1. Percent cumulative frequency of *Terminalia avicenniodes* extract (TAE) granules containing lactose (T-LAC), micro crystalline cellulose (T-MCC) and magnesium carbonate (T-MAG) as diluent.

Though, there are exceptions, the flow properties of granules are improved when the particles are large and the particle size distribution is narrow. However, larger particles lead to less strong tablets due to the fact that they have lesser surface areas for bond formation as compared to smaller particles (Sunand Himmelspach, 2006). The different diluents impacted variable effects on the particle sizes of prepared granules. T-MAG prepared with magnesium carbonate as diluent produced larger sized granules than T-MCC and T-LAC prepared with microcrystalline cellulose and lactose respectively. The differences observed in the particle sizes of the granules could be attributed to the difference in the mechanism and rate of fluid uptake of the different diluents during the process of granulation (Chattoraj and Sun, 2018).

3.2. Fourier transform infra-red spectra studies (FTIR)

FTIR was used to identify and compare functional groups in the extract and tablet formulations. The spectra of *Terminalia avicennoides* extract (TAE) and the tablet formulations show that the characteristic functional groups in the parent extract is represented in the formulations. Strong broad O-H stretching (hydrogen-bonded) vibration at 3200-3600 cm^{-1} signifying the presence of alcohols, strong C-H stretching vibration (2850-3000 cm^{-1}) specific of an alkane functional group and strong C-F stretching vibration (1000-1400 cm^{-1}) characteristic of an alkyl halide were observed in Figs. 2a, 2b, 2c and 2d.

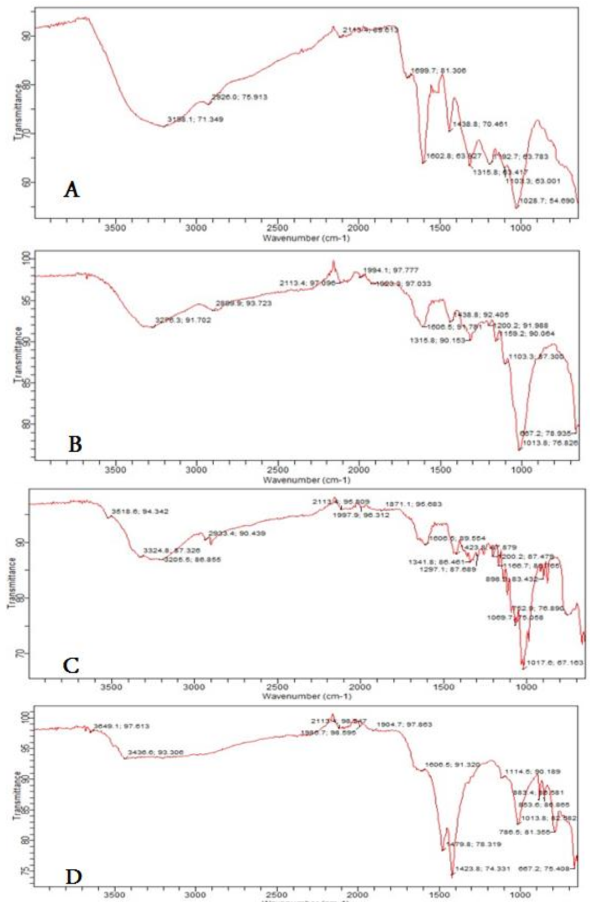

Figure 2. FTIR spectra of *Terminalia avicennoides* extract (A), Tablets containing MCC (B), tablets containing LAC (C), tablets containing MAG (D).

In addition, strong C=C stretching vibration (2100-2260 cm^{-1}) characteristic of an alkyne functional group

was observed in all the FTIR spectra. The presence of C-N stretching vibration (1080-1360 cm^{-1}) and N-H bending vibration (1600 cm^{-1}) typical of amine functional groups and those of aromatic functional groups and the presence of an ester at 1400-1600 cm^{-1} and 1000-1300 cm^{-1} respectively were also observed (Pongpiachan, 2014). As shown in Figure 2, characteristic bands and peaks specific for the extract were not lost in the spectra of the tablet formulations neither were new peaks observed. These parameters have been reported to be indicators of compatibility (Archer *et al*., 2020; *Desai1et al*., 2020).

3.3. Flow and physical properties of Terminalia avicennoides extract (TAE) granules

All the prepared granules had angle of repose values between 25.05 and 29.94 °. Angle of repose reflects the flow ability of materials and values < 30 ° indicate excellent flow, those between 31 and 35 ° show good flow while values between 36 and 40 ° imply that the material possesses fair flow (Kaur *et al*., 2011). Our samples possess good flow with uniform distribution of bridging connecting forces (Geldart *et al*., 2006). The ability of the granules to deform under pressure was assessed using the Carr's index (CI), this is to ensure the suitability of the granules to be tableted while Hausner ratio on the other hand was used to evaluate the cohesive nature of the granules (Panda *et al*., 2018). Both parameters were computed from data obtained from bulk and tapped densities as shown in Table 2.

Table 2. Properties of *Terminalia avicennoides* extract (TAE) granules.

Batch	Moisture content (%)	Angle of repose (°)	Bulk density (g/mL)	Tapped density (g/mL)	True density (g/mL)	Carr's index (%)	Hausner ratio
TMCC	3.50 ± 0.1	29.94 ± 0.2	0.50 ± 0.1	0.40 ± 0.4	0.54 ± 0.2	20.00	0.80
TLAC	3.30 ± 0.2	25.05 ± 0.2	0.76 ± 0.3	0.50 ± 0.2	0.54 ± 0.2	34.21	0.70
TMAG	3.30 ± 0.1	27.37 ± 0.5	0.52 ±0.1	0.41 ± 0.4	0.52 ± 0.1	21.15	0.79

Key: T-MCC = granules prepared with microcrystalline cellulose as diluent, T-LAC = granules prepared with lactose as diluent, T-MAG = granules prepared with magnesium carbonate as diluent. Values are expressed as mean ± SD.

Carr's index value for T-MCC and T-MAG were 20.00 and 21.15 % respectively while that of T-LAC was 34.21 %, and their Hausner values were found to be between 0.70 and 0.80. Granules prepared with microcrystalline cellulose (T-MCC) showed more propensities to be compacted and to be readily deformed under pressure than T-MAG, while that of T-LAC suggests that it possess very low ability to deformation. Values for Hausner ratio showed that all the granules were non-cohesive. True density of all the granules was similar; T-MAG had a value of 0.52 g/cm^3 while T-MCC and T-LAC had 0.54 and 0.54 gm/cm^3 respectively. True density influences the compression properties of granules and can be influenced by the type of excipient incorporated into the formulation. There was no significant difference between the true particle densities of the three batches.

Moisture content plays an important role in tablet formulation especially because it influences tablet stability. The presence of moisture beyond an acceptable limit could lead to loss of material flow, loss of mechanical strength, aids degradation and encourages the growth of microbial contamination in the formulation. In addition, moisture influences the design, packaging and storage of products in which the materials are incorporated (Adane *et al*., 2006). Percent moisture content were shown to be between 3.30 and 3.50, and within the specified limitation for materials intended for pharmaceutical uses (Chattoraj and Sun, 2018).

3.4. Mechanical and release properties of Terminalia avicennoides extract (TAE) tablets

The mechanical properties of the tablets were evaluated and the results are presented in Table 3. Tensile strength of the tablets was observed to increase with increase in compression force across all the tablet formulations in the order T-MAG>T-MCC>T-LAC, although there was no significant difference between that of T-MAG and T-MCC. Tensile strength gives insight into how strong a tablet is, and is associated with tabletability of a material which is expressed by relating the tablet strength to the compression pressure (Lai *et al*., 2013). Higher compression pressure tends to produce denser tablets which eventually gives tablets with higher tensile strength (Lai *et al*., 2013). This is attributed to increase in the number of particle-particle contact which increases interaction between the articles leading to the formation of strong bonds and consequent higher tensile strength (Lai *et al*., 2013).

Table 3. Mechanical properties of *Terminalia avicennoides* extract (TAE) tablets.

Parameters	Batches	Compression pressure (KN/m^2)				
		22.5	25	27.5	30	32.5
Tensile strength (MPa)	TMCC	0.09	0.10	0.11	0.13	0.15
	TLAC	0.04	0.04	0.06	0.08	0.10
	TMAG	0.10	0.10	0.14	0.15	0.15
Friability (%)	TMCC	0.80	0.60	0.11	0.33	0.36
	TLAC	5.74	0.68	0.64	0.73	0.61
	TMAG	0.63	0.62	0.61	0.80	0.66
Disintegration time (min)	TMCC	>30±2.22	>30±0.93	>30±1.15	>30±8.01	>30±2.00
	TLAC	>30±3.80	>30±0.01	>30±0.50	>30±3.36	>30±1.11
	TMAG	1.56±0.40	1.35±1.79	1.10±1.21	1.22±4.13	1.55±1.22

Key: T-MCC = granules prepared with microcrystalline cellulose as diluent, T-LAC = granules prepared with lactose as diluent, T-MAG = granules prepared with magnesium carbonate as diluent. Values are expressed as mean ± SD where applicab.

Friability on the other hand assesses the weakness of tablet; its ability to withstand shock and abrasion which may be encountered during handling, transportation or storage (Adane, *et al.*, 2006). There was general decrease in friability with increased compression pressure. However, all the tablets except T-LAC at the lowest compression pressure, had friability values within the official specified limit of 1 %. Only T-MAG met specification for disintegration. Disintegration is defined loosely as the ability of a tablet to break-up and is often linked to dissolution although, a positive correlation is not always observed. Only tablets prepared with magnesium carbonate at all compression pressures disintegrated within the specified time for herbal tablets (30 min).

3.5. Compaction and compressional properties of Terminalia avicennoides extract (TAE) tablets

Heckle plot basically describes the densification events occurring in a powder bed when pressure is applied. The constants in the Heckel plots are commonly determined by the linear regression analysis; a correct selection of a linear region is a critical factor in the interpretation of the plot, as such, a coefficient value greater than 0.95 is selected to be optimal (Emeje *et al*., 2017).

Figure 3 shows the Heckel plot of the tablet formulations prepared using different diluent types. The applied pressures used for compression of the tablets were from 22.5 to 32.5 KN/M^2. It shows near linearity of the plot with increase in pressure for all the tablet formulations. All bathes showed no sign of initial curves and no initial fragmentation which is an indication of the plastic deformation of the granules (Emeje *et al*., 2017). Materials that have this type of linearity are known as Type A and are usually comparatively soft and readily undergo plastic deformation retaining different degrees of porosity depending on the initial packing of the powder in the die. This is in turn influenced by the size distribution and shape of the original particles.

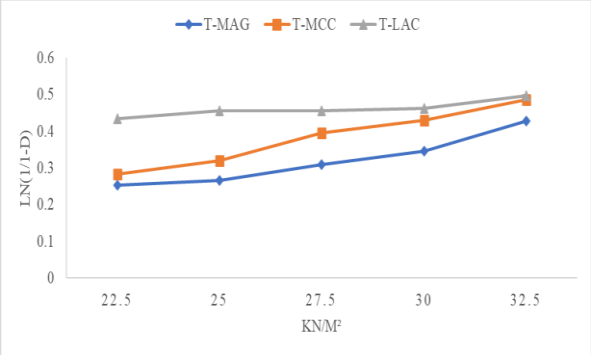

Fig. 3. Heckel plot of *Terminalia avicennoides* tablet containing lactose (T-LAC), micro crystalline cellulose (T-MCC) and magnesium carbonate (T-MAG) as diluent.

The yield pressure value (P_y), which is the inverse of the slope of the linear portion of the Heckel curve, refers to the pressure at which the material begins to deform plastically. The order for P_y is observed to be T-LAC>T-MAG>T-MCC. The order for P_y observed in our work suggests that the onset of deformation of T-MCC was faster, with lower resistance for deformation and easier compression than T-MAG and T-LAC. This indicates that incorporation of microcrystalline cellulose in the formulation promotes rapid densification at low pressure to produce compacts than those prepared with magnesium carbonate and lactose. In addition, it suggests that T-MCC underwent plastic deformation more easily and rapidly than the other batches. The low value observed for T-MCC (19.46) could be attributed to the fact that during compression of microcrystalline cellulose an appreciable amount of interparticulate bonding occurs which influences the

pressure at which onset of plastic deformation occurs (Osamura *et al.*, 2018). High P_y value for T-LAC could be attributed to resistance of the granules to deformation as also reported by (Osamura *et al.*, 2018). The P_y of all the tablets were below 100 MPa which also confirms that the mode of deformation of all the tablets is plastic (Lai *et al.*, 2013). Some reports have also attributed low P_y values to creation of more contacts within the powder bed that culminated in strong interparticulate bonding thus corroborating the observation in this study (Osamura *et al.*, 2018).

The D_A values, which represent the total degree of densification occurring at the initial stages of compressions were 0.20, 0.34 and 0.17 for T-MCC, T-LAC and T-MAG respectively. D_A values shows that the relative density of plastic deformation was similar for T-MCC and T-MAG but highest for T-LAC. Low D_A value for T-MAG and T-MCC is an indication of low contact area between these particles which can be dependent on several variables including particle size, size distribution, shape among others (Osamura *et al.*, 2018). D_B value represents the phase of particle rearrangement in the early compression stages and tends to indicate the extent of granule fragmentation which occurs simultaneously at the same time as plastic and elastic deformation of the granules (Osamura *et al.*, 2018). Negative D_B values for all the tablet formulations implies that the extent of particle rearrangement of the granules was generally low due to high cohesive forces as a result of the amorphous nature of the granules (Osamura *et al.*, 2018) and are related to plastically deforming materials (Panda *et al.*, 2018). However, some other researchers though postulated that zero values indicate that no particle re-arrangement or granule fragmentation took place at low compression pressures, have suggested that negative D_B values cannot be practicably explained using the Heckel plot, which is one of the limitations of the model (Emeje *et al.*, 2017).

Do values represent the degree of initial packing of the granules in the die as a result of filling. Do values for T-MAG (0.79) and T-MCC (0.74) were similar, with T-LAC having a higher figure of 0.93. Our data implies that T-LAC exhibited the highest degree of initial packing, rearrangement and densification during die filling although this did not cumulate into total degree of densification or plastic deformation.

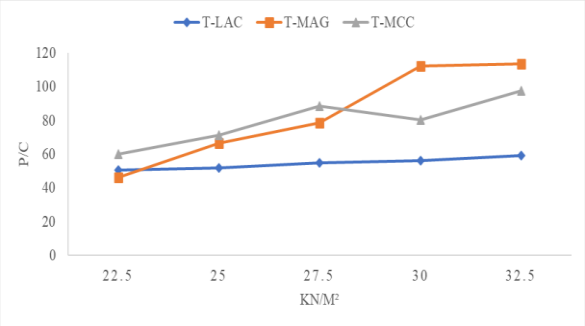

Fig. 4. Kawakita plot of *Terminalia avicennoides* tablets containing lactose (T-LAC), micro crystalline cellulose (T-MCC) and magnesium carbonate (T-MAG) as diluent.

For Kawakita plot, a near linear relationship was also obtained at all compression pressures. Values of constants a and ab were calculated from the intercept and slope, respectively.

The Di value is a measure of the packed initial relative density with the application of small pressures or tapping and is evaluated as (1-a) (Emeje *et al.*, 2005). Lower values of Di are an indication of better flowability of granules (Chattoraj and Sun, 2018). Value of D_i for T-MCC was observed to be higher than its D_O which indicates that granules of T-MCC exhibited closer packing and greater degree of densification than the other batches.

The parameter P_k is the reciprocal of b and is defined as the total amount of plasticity of a material. It represents the pressure required to reduce the volume of the granule bed by 50 % (Osamura *et al.*, 2018). Table 4 also shows that T-MAG had highest P_k value (23.26) followed by T-LAC (5.88) and the T-MCC had the least value (1.61). Low values have been established to be indicative of materials that readily deform plastically under pressure (Lai *et al.*, 2013). On the other hand, high values as observed for T-MAG is indicative of cohesiveness of the granules as was also observed with low Di values. The cohesiveness or fluidity of granules here is indicative of its resistance to flow which is a result of attractive forces between particles of the granules (Osamura *et al.*, 2018). Experimental correlations have shown that less cohesiveness implies high compatibility (Osamura *et al.*, 2018). Overall, this study reveals that tablet formulations containing M-CC exhibits better plastic deformation since M-CC is capable of creating more

contact points for interparticulate bonding under pressure while also forming extremes of deformation spectrum (Osamura *et al*., 2018).

Table 4. Parameters derived from Heckel and Kawakita plots.

BATCH	DA	DO	DB	Py	Di	Pk
T-MCC	0.20	0.74	-0.54	19.46	0.94	1.61
T-LAC	0.34	0.93	-059	74.63	0.89	5.88
T-MAG	0.17	0.79	-0.62	23.36	0.52	23.26

P_y=mean yield pressure, D_A= total degree of densification occurring at the initial stages of compressions, D_B= phase of particle rearrangement in the early compression stages, D_O= degree of initial packing of the granules in the die, Di= measure of the packed initial relative density, P_k= total amount of plasticity of a material, T-MCC = granules prepared with microcrystalline cellulose as diluent, T-LAC = granules prepared with lactose as diluent, T-MAG = granules prepared with magnesium carbonate as diluent.

Marked variations in P_k and P_y values for all tablet formulations observed in this study could be attributed to P_y relating essentially to the onset of plastic deformation during compression while P_k is associated with the amount of plastic deformation occurring during compression (Mahours *et al*., 2017).

4. Conclusion

The results presented in this study, show that ethanol extract of the stem bark of *Terminalia avicennoides* can be formulated into robust tablets using the microcrystalline cellulose, lactose and magnesium carbonate as diluents. However, the compaction behaviors of the formulations were significantly different based on the types of diluents incorporated into the formulation. Granules containing microcrystalline cellulose exhibited the most rapid onset of plastic deformation, exhibited closer packing and easily deformed plastically under pressure and could be the diluent of choice for formulation of *Terminalia avicennoides* tablets. However, incorporation of microcrystalline cellulose into implies that *Terminalia avicennoides* tablet formulation would require a higher concentration of disintegrant than included in this study to facilitate disintegration within the stipulated period.

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