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Effects of some channelling agents on the compaction properties of the mixed stem bark extracts of *Anogeissus leiocarpus* and *Prosopis africana*

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ABSTRACT

Background & Aim: The hot water extract of a mixture of *Anogeissus leiocarpus* and *Prosopis africana* is widely used in the northern part of Nigeria for the treatment and management of asthma. Since investigations of its pharmacological activities already justify its use, and the need for standardization of herbal medicine and develop appropriate dosage forms has continued to grow, the purpose of this study was to evaluate the effects of some common channelling agents (sodium bicarbonate, calcium carbonate and sodium lauryl sulphate) on the compaction properties of the mixed stem bark extracts of *Anogeissus leiocarpus* and *Prosopis africana*.

Experimental: Granules of the mixed extracts (AA1) were produced using the wet granulation method of massing and screening. The micromeritics and flow properties of the extracts as well as the effects of the three common additives were studied, while the compaction properties of the extract formulated alone and in the presence of these additives were interrogated using the Heckel equation.

Results: Our results showed that, all the formulations containing the channelling agents exhibited poor flow. Granules prepared using sodium bicarbonate (NaHCO3) exhibited plastic deformation during consolidation, those formulated using calcium carbonate (CaCO3) showed initial fragmentation before consolidation by plastic deformation and those formulated using sodium lauryl sulphate consolidated essentially by plastic deformation. Inclusion of additives modified the compressibility profiles of the formulations. Tensile strength of the formulations containing NaHCO3 and sodium lauryl sulphate (SLS) were observed to be concentration dependent while those containing CaCO3 showed no appreciable increase in tensile strength with increased pressure. Generally, formulations containing 5% of the additives gave the highest tensile strength, however, those containing CaCO3 were found to be higher than the other two formulations.

Recommended applications/industries: Considering that, none of the channelling agents altered significantly the compaction properties of AA1, they might be useful in developing standardized and robust tablets of *A. leiocarpus* and *P. africana* admixtures for Asthma therapy.

1. Introduction

The World Health Organisation (WHO) reports that 80 % of the world populace use and are dependent on traditional medicine. Traditional medicine is the treatment of ailments with the use of plant (herbal) extracts. Although, herbal medicines are gaining grounds in developing countries because of poor or lack of adequate health facilities, the major problem with the use of herbal extracts is its formulation into suitable dosage forms and also lack of standardization. Oral solid dosage forms are the most acceptable form of dosage form and its wide acceptability has been attributed to its stability, ease of handling and convenience of dosing (Jivrajet *et al*, 2000).

Anogeissus leiocarpus (Family; *Combretaceae*) known as the "chewing stick" tree, is found widely in Sudan, Ethiopia, The Democratic Republic of Congo, Benin, Senegal, Niger and Nigeria (USDA, 2010). Different parts of this plant have been implicated in treatment of various ailments. It has been reported to possess antimicrobial and anthelmintic properties; in combination with other plants has been used to treat diarrhoea and dysentery (Kubmarawa *et al*, 2007). In Ivory Coast, the plant has been used to treat malaria (Okpeton, 2004); and has also been implicated in the treatment of fungal infections such as dermatitis (Batawila, 2005). In Northern Nigeria, it is widely used in the management of respiratory disease such as asthma (Isimi *et al*, 2003) and also in the treatment of cough and tuberculosis (Victor, 2013).

Proposis africana (Family; Fabaceae) also called "iron wood" is widely distributed in Africa. In Nigeria, it is called "*Ayan*" by the Yoruba, "*Okpeghe*" in Idoma, "*Kiriya*" in Hausa and "*Okpei*" in Igbo (Oguntoyinbo *et al.,* 2007). It has been documented to treat dysentery, malaria, toothache, stomach-ache and gonorrhoea. *Prosopis* also has similar actions with *Anogeissus leiocarpus* in treatment of sore throat and bronchitis. Pharmacological investigations (Isimi *et al,* 2003) revealed that the combination of the hot water extract of the stem bark of *Anogeissusleiocarpus* and *Prosopisafricana* (AA1) is effective in the treatment of asthma.

Formulation of phytomedicines into suitable dosage form enhances their stability and acceptability. It is expedient therefore to establish the suitability of various excipients used in these formulations as they can affect the overall efficiency of the phytomedicines. They could act by delivering or modifying drug release at a required site, eliciting disintegration, useful as a means of identification, for aesthetic purposes and to improve overall product stability (Rutesh, 2008). They are essential components of drug products hence, evaluating the effect and performance of these excipients in any product is necessary.

Heckel equation given below is used by researchers to relate the relative density, D, of powder bed during compression to the applied pressure, P. It determines the compaction characteristics and characterizes consolidation behaviour of materials in a tablet formulation.

$$\ln(1-1)/_D = KP + A \ldots\ldots\ldots\ldots\ldots\ldots \quad \mathbf{(1)}$$

The slope of the straight line portion of the curve, K, is the reciprocal of the mean yield pressure, Py of the material. The relative density, D_A, can be calculated from the intercept A, using the equation;

$$DA=1-e^{-A} \ldots\ldots\ldots\ldots\ldots\ldots \quad \mathbf{(2)}$$

Do is the relative density of a powder at the point when the applied pressure is zero. This connotes the initial phase of powder densification due to particle rearrangement as a consequence of die filling; a high Do value is indicative high densification. DB, is the value indicative of the extent of densification when deformation starts and the phase rearrangement of the particles. It differs from D_A and Do at low pressures.

$$DB = DA - Do \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad \mathbf{(3)}$$

Materials can be classified into A, B and C based on Heckel plot and compaction behaviour of the material. Type A are characterized with plots that remain linear as applied pressure increases; indicative of plastic deformation. Type B show an initial curved plot followed by a straight line; this implies initial fragmentation of particles followed by plastic deformation. Materials that are type C on the other hand exhibits an initial sharp linear curve which becomes superimposed and flattened as the pressure is increased (York, 1992).

In this study, the compaction properties of extracts of the hot water extract *Anogeissus leiocarpus* and *Prosopisafricana* was evaluated; the types of additive and their effect on this formulation was also evaluated.

2. Materials and Methods

2.1 Plant collection

Anogeissus leiocarpus and *Prosopis africana* stem barks were collected from the National Institute for Pharmaceutical Research (NIPRD) garden.

2.2 Extraction

Stem bark of *Anogeissus leiocarpus* and *Prosopis africana* was collected, washed with distilled water, sun-dried and milled to a coarse (1000 µm) powder. The powders were then mixed in a 1:1 ratio and soaked in distilled water in a ratio 1:10 mass to volume, boiled on an electric heater for 10 minutes and left to soak for 24 hours at room temperature. The liquid extract was filtered through a calico cloth and concentrated to a ratio of 5:1 using a rotary evaporator. The concentrated filtrate was then transferred into a tray and dried in an oven at 60 °C until dry. The dry extract was pulverized using a mortar and pestle and then passed through a 150 µm sieve.

2.3 Granulation

Granules of the extract and channelling agents were prepared by the method of wetting and massing. Sodium bicarbonate, calcium carbonate and sodium lauryl sulphate were employed at concentrations of 5, 10 and 15 % in each formulation while water was used as the granulating fluid. The wet mass was passed through the sieve (1.7 mm), dried in the oven and then kept for further analysis.

2.3.1 Granule properties

2.3.1.1 Particle size evaluation

The particle size of the granules was determined by sieving the granules in the Reitsch test shaker with sieves arranged in decreasing order of aperture. The granules (50 g) were placed on the largest screen, the sieves were shaken for 5mins at amplitude of 1.500 mm/g. Granule weight retained on the sieves and the pan was recorded. The percentage cumulative weight undersize was plotted against sieve aperture.

2.3.1.2 Angle of repose

Forty (40) g of the granules was allowed to flow through a funnel. The height and the radius of the heap were determined and the angle of repose (θ) was computed using the equation below:

$$\theta = \tan^{-1} h/r \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad \ldots.\ 3$$

2.3.1.3 Bulk and tapped density

The bulk and tapped density was conducted using the Stampfvolumeter. The granules (30 g) were poured into the 100 mL graduated cylinder using a glass funnel. The volume occupied by the powder was read off and the bulk density was calculated in gm/ml. The cylinder, which contains the granules, was tapped 100 times and the tapped density was calculated.

2.3.1.4 Carr's index

This was mathematically calculated using the equation below:

$$C\,(\%) = {}^{\text{tapped density} - \text{bulk density}}/_{\text{tapped density}}\ X\,100 \ldots\ldots\ldots\ldots\ldots\ldots..4$$

2.3.1.5 Hausner index

It was calculated using the equation below:

$$H = {}^{\text{tapped density}}/_{\text{bulk density}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots.5$$

2.4 Compaction properties

Compacts equivalent to 500 mg AA1 were produced by compressing the granules for 60 sec at various compression pressures using a Manesty tableting machine (Shangai, China). Fifty (50) tablets were compressed at each pressure. All readings are average of 3 measurements.

Before each compression, the die (12.5 mm) and flat faced punches were lubricated with 1 % w/v dispersion of magnesium stearate in chloroform. After ejection, the tablets were stored over silica gel in a desiccator for 24 h to allow for elastic recovery and hardening to prevent falsely low yield values and the dimensions of the compact were determined using the micrometer screw gauge (Mitutoyo model IDC1012EB (Mitutuyo corporation, Japan) thickness gauge to the nearest 0.01 mm. The Heckel plots were statistically analysed using the Microsoft Excel computer software. The plots constructed according to the Heckel equation were used to characterize the consolidation behaviour of the formulations.

The tensile strength (*TS*) the tablets were calculated as:

$$TS = {}^{2CS}/_{Dd} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots..6$$

3. Results and discussion

Figure 1 show more than 50 % of AA1 granules were about 150 µm in size. This implies that the particles of the granules have more cohesive force than gravitational force and are more bounded together.

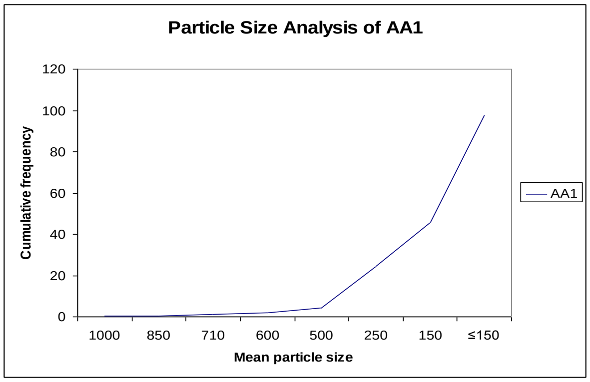

Fig. 1. Particle size analysis of AA1

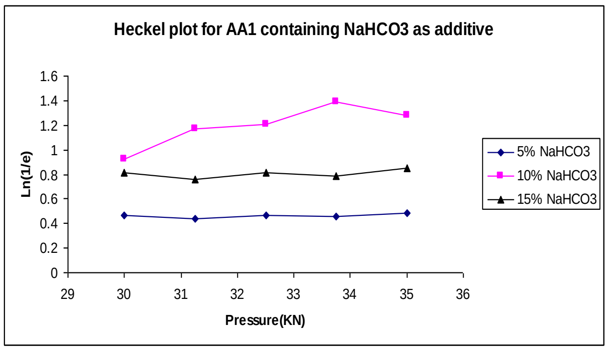

Fig. 2. Heckel plot for AA1 containing $NaHCO_3$ as additive

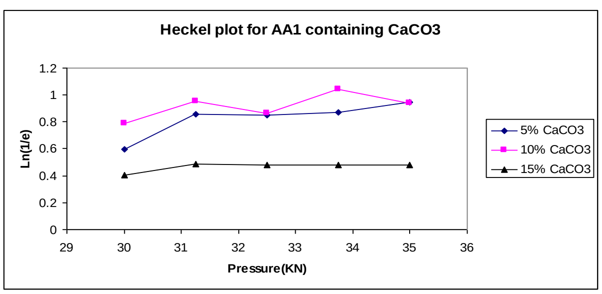

Fig. 3. Heckel plot for AA1 containing $CaCO_3$ as diluent

The flow properties of formulated granules are presented in Table 1. Concentration was observed to have no significant effect on the tapped and bulk density. All the granules were found to have CI > 15 % indicating they are not easily compressible and HI > 1.2 implying the powders are very cohesive. The granules also were found to have poor flow as indicated by angle of repose > 25 %. This is understandable as cohesive materials usually have poor flow.

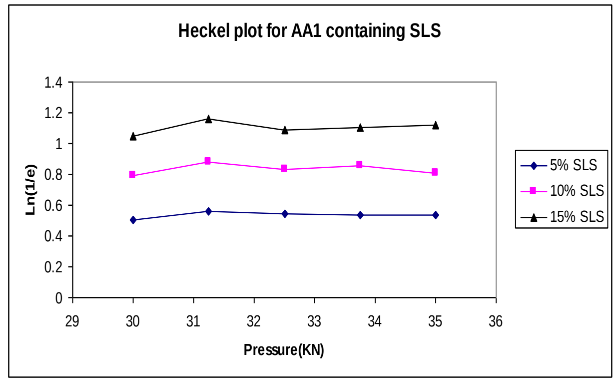

Fig. 4. Heckel plot for AA1 containing SLS as a disintegrant

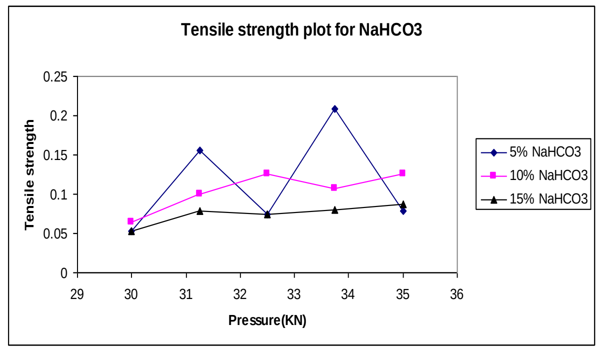

Fig. 5. Compaction plots of AA1 with $NaHCO_3$

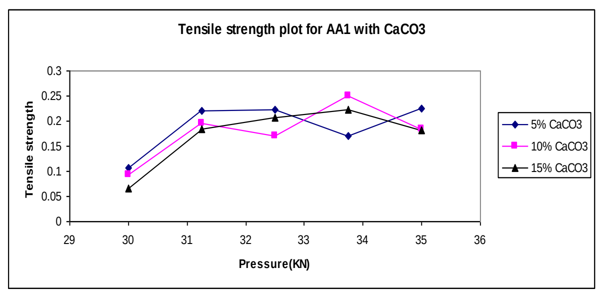

Fig. 6. Compaction plots of AA1 with $CaCO_3$

The Heckel plots presented in Figures 2, 3, 4 show linearity with concentrations employed and at all the pressures, there was no initial curve in the plot thus no initial fragmentation occurred and as such the granules can be said to have deformed plastically.

The Do represents the degree of initial packing in the die as a result of die filling and is said to be related to particle size and of shape of the investigated materials. The type and concentration of additives did not confer any significant effect on the degree of packing as no trend was observed (Table 2). No pattern was observed between particle rearrangement and concentration although DB values for all formulations were generally low; formulations containing SLS had the highest. This suggests that the extent of particle rearrangement in these formulations was low.

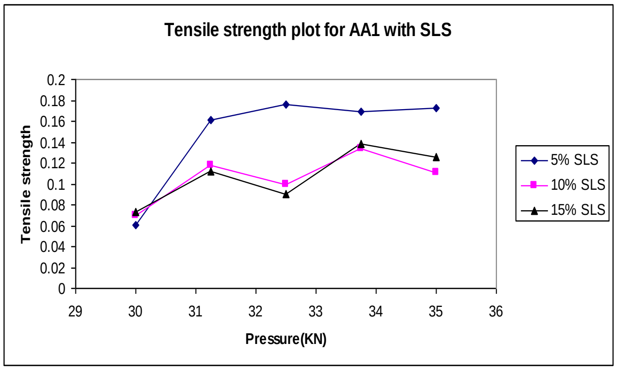

Fig. 7. Compaction plots of AA1 with SLS

Table 1: Powder properties of various batches of AA1

Batch	Bulk density	Tapped density	True density	Angle of repose	Carr's index	Hausner ratio
5 % $NaHCO_3$	0.603 ± 0.003	0.873 ± 0.030	2.637 ±0.240	32.15 ± 2.13	30.47 %	1.438
10 % $NaHCO_3$	0.620 ± 0.010	0.980 ± 0.084	1.440 ±0.050	27.97 ± 0.59	36.73 %	1.581
15 % $NaHCO_3$	0.653 ± 0.007	0.930 ± 0.015	1.762 ± 0.036	30.94 ±1.35	29.78 %	1.424
5 % $CaCO_3$	0.567 ± 0.003	0.920 ± 0.060	1.762 ± 0.083	30.91 ± 2.20	38.37 %	1.623
10 % $CaCO_3$	0.603 ± 0.020	0.987 ± 0.078	1.760 ± 0.090	34.45 ± 2.28	38.91 %	1.637
15 % $CaCO_3$	0.600 ± 0.003	1.010 ± 0.066	2.949 ± 0.071	33.01 ± 1.64	40.30 %	1.675
5 % SLS	0.583 ± 0.008	1.200 ± 0.023	2.615 ± 0.265	28.15 ± 1.60	51.42 %	2.058
10 % SLS	0.567 ± 0.003	0.903 ± 0.013	1.879 ± 0.081	32.40 ± 0.93	37.21 %	1.593
15 % SLS	0.590 ± 0.015	0.950 ± 0.010	1.600 ± 0.060	38.55 ± 0.74	37.89 %	1.610
AA1 only	0.563 ± 0.015	0.800 ± 0.018	1.620 ± 0.040	22.30 ± 0.32	29.63 %	1.421

Da values for all formulations were also found to be low with formulations containing SLS having higher values. There was no significant relationship between the degree of packing and additive concentration although, additive type seemed to influence packing arrangement.

Table 2. Parameters derived from Heckel plots

Batch	Compression parameter	Mean yield pressure	Da	Do	Db
5 % $NaHCO_3$	0.0766	256.41	0.28	0.229	0.051
10 % $NaHCO_3$	0.7751	13.59	-2.31	0.431	-2.741
15 % $NaHCO_3$	0.1141	121.95	0.42	0.371	0.049
5 % $CaCO_3$	0.8826	17.48	-1.82	0.322	-2.142
10 % $CaCO_3$	0.4271	32.15	-0.97	0.342	-1.312
15 % $CaCO_3$	0.2555	847.46	0.08	0.203	-0.123
5 % SLS	0.0942	17.35	0.32	0.223	0.097
10 % SLS	0.0063	-10000	0.57	0.302	0.268
15 % SLS	0.0838	138.87	0.58	0.369	0.211

The mean yield pressure is inversely related to the ability of a material to deform plastically under pressure. The onset of plastic deformation in all formulations at higher additive concentration occurred at higher pressure (Table 2). Values of Py for formulations containing SLS were found to be the lowest, this indicates that additive type influences the pressure at which onset of plastic deformation occurs. Similar findings have been reported in an earlier study where the presence of channelling agents were seen to increase the pressure at which plastic deformation took place (Emeje *et al*., 2006).

The tensile strength of all compacts was observed to be higher at 5 % (Figure 5, 6, 7) and independent on concentration.

4. Conclusion

Presence of sodium bicarbonate, calcium carbonate and sodium lauryl sulphate did not have any significant effect on the compaction properties of AA1 but tensile strength was influenced by concentration. Therefore, any of these additives may be used to formulate standardized tablets of AA1.

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