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COMPARATIVE EVALUATION OF THE SUSPENDING PROPERTIES OF FOUR NATURAL GUMS IN ALBENDAZOLE SUSPENSION FORMULATIONS

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ABSTRACT

Background: Natural gums and mucilages are utilized as excipients in pharmaceutical formulations. This study was done to comparatively evaluate the suspending property of tragacanth (TG), *Sida acuta* (SAG), *Detarium microcarpum* (DMG), *Brachystegia eurycoma* (BEG) gums in albendazole suspension formulations. **Method:** The gums were isolated from their natural sources and utilized as suspending agent in the preparation of nine different albendazole suspensions (AS1-AS9). Distilled water was added respectively to the gums to form colloidal dispersions. Albendazole and benzoic acid were added to the respective mixtures and triturated properly to form a suspension. They were transferred into the respective measuring cylinders and made up to 50 ml using distilled water. The measuring cylinders were sealed properly using adhesive tapes and were kept on undisturbed surface for 35 days. The suspensions were then evaluated based on physical appearance, pH, viscosity, sedimentation volume and redispersibility index. **Results:** Albendazole formulations AS2 (containing 2% SAG) and AS8 (containing 2% TG) were the most stable of the suspensions. The pH of the suspensions ranged from 4.3 ± 0.1 to 5.9 ± 0.1 on day 0 to 5.0 ± 0.0 to 6.7 ± 0.1 on day 35. The viscosity of the albendazole suspensions ranged from 1428.2 to 5436.6 mPas on day 0 and 771.3 to 2470.0 mPas on day 35. The redispersibility index ranged from 3-80. **Conclusion:** The albendazole suspensions prepared with TG and SAG were the most stable based on sedimentation volume but the suspensions prepared with tragacanth gum have lower redispersibility index.

KEYWORDS: Suspension, *Sida acuta* gum, Tragacanth gum, *Detarium microcarpum* gum, *Brachystegia eurycoma* gum.

INTRODUCTION

Natural gums and mucilages are utilized as excipients in pharmaceutical formulations. They are utilized as binders, diluents and disintegrants during production of tablets and also as suspending agents and emulsifying agents for suspensions and emulsions production respectively. They are usually isolated from plants, animals and microbes. Gums are obtained from plants parts such as seeds, leaves and barks. Natural gums and mucilages have the advantages of being easily available, biocompatible, cheap and non-toxic.[1, 2] Gums are pathological substances which arise due to injury to the plant or disapproving conditions, such as breaking the cell wall. They easily dissolve in water and examples include tragacanth and mangifera gums.[3] Mucilages are natural products of metabolism and are formed in the cell and do not dissolve easily in water. Mucilages exist in various plant parts. Mucilage, a thick, sticky material is manufactured by majority of plants and some microorganisms. Gums and mucilages are plant hydrocolloids. They are mixtures of clear amorphous polymers and monosaccharide polymers and are combined with uronic acid. Gums and mucilages are composed of hydrophilic molecules which when combined with water produce viscous or gel-like solutions.[3, 4] The properties of each of the various gums are influenced by nature of the compounds involved. Linear polysaccharides take up more space and they have higher viscosity when compared to compounds of the same molecular weight that are highly branched. More stable gels are produced more easily by the branched compounds, because extensive interaction along the chains is not possible.[4]

Pharmaceutical suspensions are liquid dosage forms that are thermodynamically unstable, and are composed of

liquid continuous phase containing dispersed insoluble solid particles.[5] Suspensions are utilized as dosage forms to administer medicaments to patients that experience difficulty in swallowing tablets and capsules such as children and the elderly. They are utilized to formulate and deliver poorly water-soluble drugs.[6] The dispersed particles in a suspension usually sediment at the bottom due to their sizes (usually greater than 1 μm). Different medicaments have formulated in suspension form such as antacids,[7] ciprofloxacin,[8] paracetamol,[9] metronidazole[10] and albendazole.[11] Suspensions Formulation of stable suspensions demands that particles of the active ingredient are suspended in a uniformly distributed manner for a prolonged period of time and this is achieved by the inclusion of a suspending agent.[5, 12] Suspending agents are materials that are utilized in keeping the suspension stable by increasing the viscosity of the suspending medium, reducing the sedimentation rate, increasing the sedimentation volume, improving ease of redispersibility, and reducing cake formation.[5, 13] Suspending agents could be prepared from synthetic, semisynthetic, and natural origin.[12] Natural gums from plants have been utilized as structured vehicles to prepare deflocculated suspensions to enhance their viscosity in order to reduce the rate of sedimentation of suspended particles.[14] Examples of natural gums include tragacanth gum, acacia gum, *Detarium microcarpum* gum, *Brachystegia eurycoma* gum and *Sida acuta* gum.

Detarium microcarpum gum (DMG) is extracted from the seeds of *Detarium microcarpum*, Guill. and Perr. (Fam. Fabaceae).[11] *Detarium microcarpum* plants exist in the wild in some parts of the semi-arid sub-Saharan and tropical zones of Africa. The seeds are powdered and used as soup thickeners in some towns in Nigeria. It exhibits various degrees of viscoelastic properties in hot water.[15] *Sida acuta* gum is extracted from the dried leaves of *Sida acuta*, which is a shrub that belongs to Malvaceae family. The plant exists widely in the wilds in subtropical regions of the world.[16, 17] *Brachystegia eurycoma* Harms (synonym *B. spiceaform-is*) is a plant that is widely spread in the forest zone in southern Nigeria and Cameroun. It belongs to the *leguminosae* family.[10, 18]

Tragacanth gum is a natural polysaccharide that is derived from the dried sap of various species of Middle Eastern legumes that belong to the genus *Astragalus*. The polysaccharide is made up of an insoluble but a water-swellable fraction known as bassorin and a water-soluble fraction known as tragacanthin.[19] It is a viscous, odorless, tasteless, water-soluble mixture of polysaccharides. Tragacanth gum makes a solution thixotropic (forms pseudoplastic solutions). Different suspensions have been formulated utilizing natural gums as suspending agents. The natural gums include *Sida acuta* gum,[9] *Brachystegia eurycoma* gum,[10] *Abelmoschus esculentus* leaves gum,[20] *Detarium microcarpum* gum,[21] and *Hygrophila spinosa* seed mucilage.[22]

Albendazole, a benzimidazole derivative, belongs to the biopharmaceutical classification system (BCS) class II (high permeability and low solubility) category of products. It is poorly and erratically absorbed when taken orally, because of its low aqueous solubility. It is formulated in suspension form for paediatric use. It has bioavailability of less than 5% in humans.[11]

This study comparatively evaluates the suspending property of *Detarium microcarpum* gum, tragacanth gum, *Brachystegia eurycoma* gum and *Sida acuta* gum in albendazole suspension formulations.

MATERIALS AND METHODS

Materials

Albendazole, benzoic acid and tragacanth. *Detarium microcarpum* gum, *Brachystegia eurycoma* gum and *Sida acuta* gum were isolated in the Pharmaceutical Technology laboratory of the Faculty of Pharmacy, Delta State University, Abraka, Nigeria.

Isolation of *Sida acuta* gum

The gum was isolated using the method of Okafo & Chukwu.[9] A 200 g quantity of the powdered dried leaves of *Sida acuta* was macerated in 1500 ml of distilled water for 6 h. The mixture was heated at 100 °C for 1 h. It was kept for 2 h and then filtered with the aid of a muslin cloth. The filtrate (900 ml) was precipitated with equal volumes of isopropyl alcohol and kept in a refrigerator for 6 h at 8–10°C. The crude gum was filtered out with the aid of a muslin cloth and washed two times using isopropyl alcohol and once with acetone. The purified gum was dried in the oven at 40 °C for 8 h and stored separately in a clean, dry, and closed container.

Isolation of *Detarium microcarpum* gum

DMG was isolated using the method of Okafo et al.[21] The seeds of *Detarium microcarpum* were pulverized and 100 g of it was transferred into a small bucket. It was mixed properly and macerated with 1.5 liters of distilled water for 24 h. The mixture was filtered with muslin cloth and the filtrate (1.2 liters) was precipitated with equal volumes of acetone. The crude gum was washed with 100ml of acetone twice. It was dried for 6 h at 50°C in an oven. The dried gum was kept in an airtight container until when needed.

Isolation of *Brachystegia eurycoma* gum

The method of Okafo et al[23] was in the isolation of BEG. *Brachystegia eurycoma* seeds were boiled, dehusked, dried, and pulverized. A 200 g quantity of powder from the pulverized *Brachystegia eurycoma* seeds was macerated for 24 h in 1000 ml of distilled water. Muslin bag was used to filter the mixture and an equal volume of acetone was added to the filtrate to precipitate the gum. The gum was washed with 100 ml of

acetone twice and dried in an oven for 6 h at 40 ^{o}C. The gum was stored in a dry, airtight container until used.

Preparation of albendazole suspensions

Albendazole suspensions were prepared following the formula in Table 1. Distilled water was added respectively to the gums (TG, SAG, BEG and DMG) to form colloidal dispersions. Albendazole and benzoic acid were put in the respective mixtures and triturated properly to form a suspension. They were transferred into the respective measuring cylinders and made up to 50 ml using distilled water. The measuring cylinders were sealed properly using adhesive tapes. They were kept on undisturbed surface for 35 days.

Table 1: Composition of albendazole suspension formulations AS1 to AS9.

Ingredient	AS1	AS2	AS3	AS4	AS5	AS6	AS7	AS8	AS9
Albendazole (mg)	1.34	1.34	1.34	1.34	1.34	1.34	1.34	1.34	1.34
Benzoic acid (mg)	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Tragacanth gum (mg)	-	-	-	-	-	-	0.5	1.0	-
Sida acuta gum (mg)	0.5	1.0	-	-	-	--		-	-
Detarium microcarpum gum (mg)	-	-	0.5	1.0	-	-	-	-	-
Brachystegia eurycoma gum (mg)	-	-	-	-	0.5	1.0	-	-	-
Distilled water to (ml)	50	50	50	50	50	50	50	50	50

Evaluation of albendazole suspensions

Sedimentation volume: The measuring cylinders containing the various suspensions were kept on an undisturbed surface for 35 days. The volume of sediment on day 0 (50 ml) was recorded and the volume sediment was recorded daily for the 35 days. Sedimentation volume was Type equation here.calculated using equation 1:

$$Sedimentation\ volume = \frac{ultimate\ volume\ of\ sediment\ (Vu)}{initial\ volume\ of\ sediment\ (Vo)} \quad \ldots 1$$

pH: This was measured using a digital pH meter (Hanna Instruments, India) on day 0 and day 35.[24-26]

Viscosity: The suspensions' viscosity was determined using spindle 2 of a Brookfield viscometer (NDJ viscometer, India) at 6 and 12 rpm respectively on day 0 and day 35.[13, 27]

Redispersibility: After 35 days storage on an undisturbed surface, the sealed measuring cylinders were turned clockwise and anticlockwise to form one cycle. The number of cycles it took for sediments to redisperse completely from the bottom of a measuring cylinder was recorded as ease of redispersibility.

RESULTS AND DISCUSSION

Physcical appearance: Albendazole suspension formulations AS1 and AS2 were brown in colour, AS3 – AS6 were cream coloured while AS7 – AS9 were white in colour. The colours of the different suspensions were influenced by the colour of the gum used as the suspending agent.

Sedimentation volume: The results in Table 1 showed that after 10 days of storage, only formulations AS1, AS2 and AS8 had sedimentation volume of up to 60%. After 20 days, only formulations AS2 and AS8 had sedimentation volume of up to 50% while only AS7 and AS8 had sedimentation volume of up to 30% on day 35. It shows that albendazole formulations AS2 (containing 2% *Sida acuta* gum) and AS8 (containing 2% tragacanth gum) are the most stable of the suspensions. As reported by previous researchers,[6, 14, 28] the concentration of the suspending agent is directly proportional to the sedimentation volume. One of the good qualities of an ideal suspension is that the suspended particles should not settle very fast to allow for uniformity of dose administration.[29, 30]

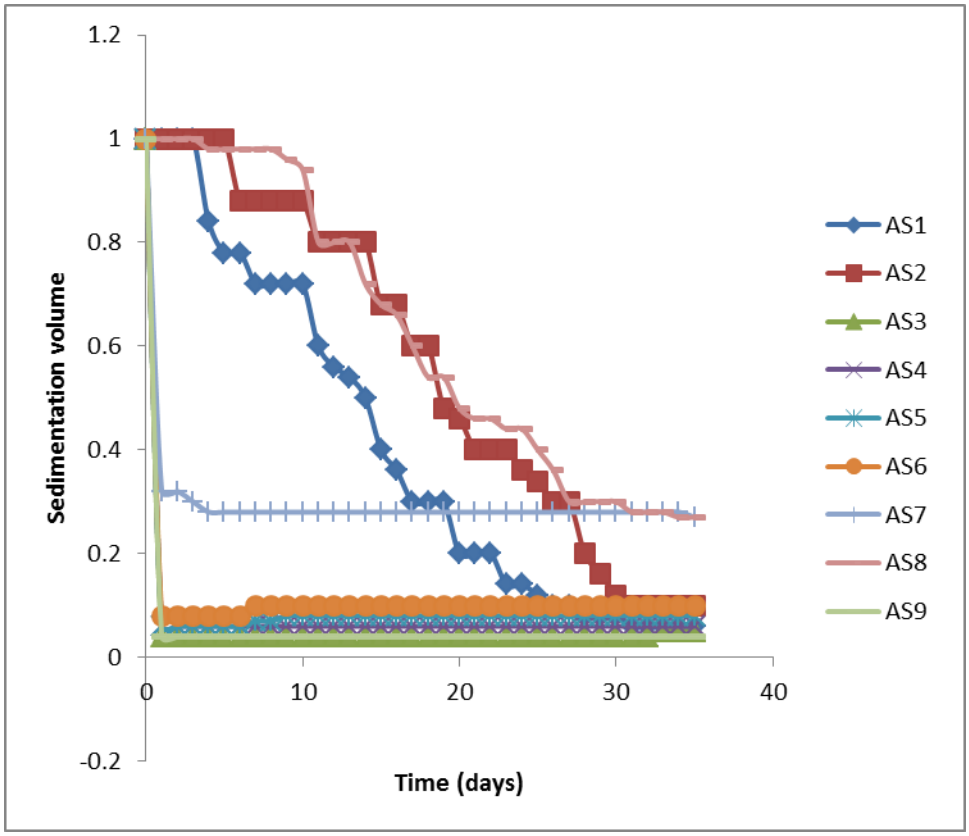

Figure 1: Sedimentation volume for albendazole suspension formulations AS1 to AS9.

pH: The pH of the suspensions ranged from 4.3 ± 0.1 to 5.9 ± 0.1 on day 0 to 5.0 ± 0.0 to 6.7 ± 0.1 on day 35. The pH values for the various suspensions were within the range that is acceptable (2-6) for oral administration. There was increment in pH for formulations AS1, AS3 - AS7 and AS9 after 35 days of storage whereas there was reduction in pH for formulations AS2 and AS8. The stability criteria for pH must indicate that changes in pH should not deviate as much as possible from the original pH if the preparation is deemed stable.[31]

Table 2: Physicochemical property of albendazole suspension formulations AS1 to AS9.

Formulation	pH on day 0	pH on day 35	Viscosity (mPas) on day 0	Viscosity (mPas) on day 35	Redispersibility Index
AS1	4.8 ± 0.1	5.4 ± 0.0	2658.8	771.3	10
AS2	5.9 ± 0.1	5.1 ± 0.0	3398.9	1197.5	20
AS3	4.3 ± 0.1	5.2 ± 0.0	1672.0	942.9	3
AS4	4.4 ± 0.1	5.5 ± 0.0	5436.6	2470.0	5
AS5	4.7 ± 0.1	5.5 ± 0.0	4455.7	918.9	55
AS6	4.6 ± 0.1	5.0 ± 0.0	3790.9	1314.7	80
AS7	5.3 ± 0.0	6.2 ± 0.0	3680.8	1278.4	5
AS8	5.9 ± 0.0	5.0 ± 0.0	1428.2	1146.7	3
AS9	4.7 ± 0.1	6.7 ± 0.1	3661.8	908.4	4

Viscosity: The viscosity of the various ibuprofen suspension formulations ranged from 1428.2 to 5436.6 mPas on day 0 and 771.3 to 2470.0 mPas on day 35. The marked reduction in viscosity for all the formulations may be due to loss of viscosity on storage by the suspending agents which is one of the disadvantages of natural gums.[1]

Redispersibility: This shows the ease with which the sedimented particles will be re-suspended through moderate agitation. The higher the redispersibility index the more difficult it is for the settled particles to be re-suspended in the dispersion medium. One of the desirable qualities of an ideal suspension is that settled particles in a suspension should not form a hard cake and that they should easily be re-suspended homogeneously upon moderate agitation of the container to allow for uniform dose administration.[8, 29] From Table 2 it can be seen that albendazole suspension formulations AS3, AS4, AS7, AS8 and AS9 have low redispersibility index and therefore, could be easily redispersed by mild agitation. Formulations AS1 and AS2 have moderate redispersibility index and could be redispersed by moderate agitation while Formulations AS5 and AS6

have very high redispersibility index and would not be easily redispersed with moderate agitation.

CONCLUSION

The albendazole suspensions prepared with tragacanth gum and *Sida acuta* gum were the most stable, based on sedimentation volume. However, the suspensions prepared with tragacanth gum have lower redispersibility index when compared to those prepared with *Sida acuta* gum and therefore are the optimized formulation. The suspensions prepared using *Brachystegia eurycoma* gum (AS5 and AS6) gave the worst values for both sedimentation volume and redispersibility index.

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