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Evaluation of suspending properties of *Afzelia africana* gum in paracetamol liquid formulation

Olorunsola EO* and Ebigbo BO

Department of Pharmaceutics and Pharmaceutical Technology, University of Uyo, Uyo, Nigeria

ABSTRACT

Advances in drug delivery have stimulated the discovery of excipients which are safe, useful and economical. In this research, *Afzelia africana* gum was evaluated for its suspending properties in paracetamol liquid formulations. The pH of 1% w/v gum dispersion and viscosity of 1, 2, 3 and 4% w/v gum dispersions were determined. Paracetamol suspensions were prepared using the test gum and acacia gum (as reference suspending agent) at the concentrations used for viscosity determination. The preparations were assessed for sedimentation volume, flow property and redispersibility. *Afzelia* gum had a higher pH, and the viscosity of its dispersions was over twenty five times that of acacia gum. Suspensions containing afzelia gum had higher sedimentation volume, lower flow rate and poorer redispersibility compared to those containing similar concentrations of acacia gum. The gum was found to be 2 to 3 times better than acacia gum in terms of suspendability but slightly lower in terms of redispersibility. Concentration of 2% w/v afzelia gum is the optimal for acceptable paracetamol suspension. The gum is a good alternative to standard acacia gum.

KEYWORDS: *Afzelia gum, suspending properties, sedimentation volume, flow, viscosity, redispersibility*

INTRODUCTION

Drugs are rarely administered alone; rather they are given as part of formulations in combination with one or more non-medicinal agents that serve specialized pharmaceutical functions [1]. Proper and selective use of these non-medicinal agents, also known as pharmaceutical excipients, produces dosage forms of different types. The age of the intended patient plays an important role in selecting the form a medication is to be presented. For infants and children younger than 5 years of age, pharmaceutical liquids rather than solid forms are preferred for oral administration [2].

A well formulated suspension, according to Eraga *et al*. [3], is superior to tablets and capsules in terms of bioavailability. Though bioavailability might be dissolution-limited, a suspension of a finely divided powder will maximize the potential for rapid dissolution. Advantages of suspension as a dosage form include: ease of dose adjustment, possibility of modifying duration of action, masking of disagreeable tastes, suitability for children, suitability for patients who have difficulty in swallowing tablets or capsules *et cetera* [4].

According to Sudan *et al*. [5], a pharmaceutical suspension is thermodynamically unstable. This makes it necessary to include in the dosage form, a stabilizer or suspending agent which reduces the rate of settling and permits easy re-dispersion of any settled particulate matter [6]. Suspending agents act by protective colloidal actions and by increasing the consistency of the suspending medium. They may also act by reducing interfacial tension thereby

**Corresponding author:* olorunsolaeo@yahoo.com; +2348035067306

allowing liquid penetration. The presence of suspending agent increases viscosity and density of the dispersion medium thus reducing the rate of settling of dispersed particles [4].

Afzelia africana is widely distributed in Africa being found from the extreme of West Africa to the extreme East of the continent. The seed gum is a non-starch polysaccharide [7]. The seed contains about 7% gum which is a xyloglucan hemicellulose [8]. The swelling characteristics of the gum showed that the gum is a hydrogel and the moisture sorption characteristics showed that it is moderately hygroscopic [7]. Differential scanning thermogram of the polymer showed an endotherm which peaked at 77°C and an exotherm which peaked at 325 °C. The endotherm was ascribed to enthalpy relaxation while the exotherm was ascribed to crystallization [9]. Since the polymer exists in two forms [7], it was suggested that the endotherm of melting of one form might have been superimposed by the exotherm of crystallization of the other form [9].

Paracetamol is used in the management of mild to moderate pain and in pyrexia [10]. It is available in a wide range of proprietary over-the-counter preparations. Paracetamol is only sparingly soluble, and appears difficult to be produced in solution form. Therefore, there is a need for formulation of suspension for pediatric use [2]. Natural gums have been shown to be effective suspending agents [1]. The aim of this research is thus, to evaluate the suspending properties of *Afzelia africana* gum in paracetamol liquid formulation.

MATERIALS AND METHODS

Materials

Materials used include: paracetamol powder (May and Baker, Nigeria), acacia gum (BDH Chemicals, England), benzoic acid BP (BDH Chemicals, England), amaranth solution (Merck, Germany), chloroform water double strength (BDH chemicals, England) and raspberry syrup BP (Best Ltd., England). Afzelia gum was extracted from *Afzelia africana* seeds (obtained from Abuja, Nigeria) using the method described by Olorunsola *et al*. [8].

Determination of pH of gum dispersions

The pH of 1 % ^{w}/v dispersion of *Afzelia africana* and *Acacia* gums were determined 24 h after preparation using pH meter.

Determination of viscosity of gum dispersions

The viscosity of different gum dispersions (1, 2, 3 and 4% ^{w}/v) was determined at 25 ^{0}C using a Brookfield viscometer, model LVF (Brookfield Laboratories, Massachusetts) operated at 60 revolution per minute (spindle #$_2$).

Formulation of paracetamol suspensions

Different batches of the suspension were prepared based on Table 1. *Afzelia* gum at concentrations of 1, 2, 3 and 4% ^{w}/v were used as suspending agent. Similar concentrations of standard acacia gum were also used as suspending agents. The required quantities of *Afzelia africana* gum and paracetamol powder were weighed and triturated together. Raspberry syrup (20 ml) was measured, added to the powder mix and triturated together to form a smooth paste. The required volumes of benzoic acid solution and amaranth solution were measured and added gradually with constant stirring. A 50 ml volume of chloroform water double strength was measured and added with continuous stirring. The mixture was transferred into a 100 ml calibrated bottle, made up to volume with distilled water and then shaken vigorously for 20 min.

Table 1: Suspension formula

	Batches			
Ingredient	**1**	**2**	**3**	**4**
Paracetamol powder (g)	2.5	2.5	2.5	2.5
Acacia or afzelia gum (g)	1.0	2.0	3.0	4.0
Raspberry syrup (ml)	20.0	20.0	20.0	20.0
Benzoic acid (ml)	2.0	2.0	2.0	2.0
Amaranth solution (ml)	1.0	1.0	1.0	1.0
Chloroform water double strength (ml)	50.0	50.0	50.0	50.0
Water to (ml)	100.0	100.0	100.0	100.0

Determination of suspension characteristics
Sedimentation volume

The sedimentation volume F was determined using the modified form of the method described by Femi-Oyewo *et al*. [11]. A 50 ml sample of each suspension was placed in a 50 ml capacity measuring cylinder for 24 h at room temperature. The volume of sediment was taken every 3 h over the period of 24 h. The sedimentation volume was calculated as the ratio of the ultimate volume of the sediment V_u and the original volume of the suspension V_o.

Flow

The time required for each suspension sample to flow through a 10 ml pipette was determined and the flow rate (ml/s) was calculated as the ratio of volume of pipette (ml) to flow time(s).

Redispersibility

A 50 ml sample of each preparation was placed in different plain bottles. The bottles were covered and kept on a vibration-free platform. After 7 days, each suspension was shaken 3 times manually to find out the level of redispersibility. Thereafter, they were shaken vigorously to also find the level of redispersibility.

RESULTS

Afzelia gum at concentration of 1 % ^{w}/v had a pH of 5.58 while acacia gum at the same concentration had a pH of 4.73. The viscosity of different gum dispersions measured at a speed of 60 rpm using spindle number 2 is shown in Table 2. The viscosity of 1% ^{w}/v of afzelia gum is over 25 times that of same concentration of acacia gum and the number of folds increased with increase in concentration.

The sedimentation volumes of suspensions taken at different times for different concentrations of suspending agent are shown in Table 3. The sedimentation volume increased with increase in concentration of suspending agent and decreased with increase in time. The values for suspensions containing afzelia gum were higher than those containing acacia gum at all concentrations used. The plots of flow rate of suspension versus concentration of suspending agent (gum) are shown in Figure 1.

Table 2 Viscosity of different concentrations of gum dispersion

Gum concentration (% ^{w}/v)	Viscosity (mPa-s)	
	Afzelia gum	Acacia gum
1	113.7	4.2
2	210.6	5.2
3	334.5	5.6
4	558.7	7.1

The redispersibilities of suspensions containing different concentrations of gums are shown in Table 4. All the concentrations of acacia gum used produced suspensions that were redispersible with minimum agitation, stable enough to allow dose withdrawal. Concentrations of afzelia gum above 2 % w/v did not produce suspensions that were redispersible enough to allow dose withdrawal.

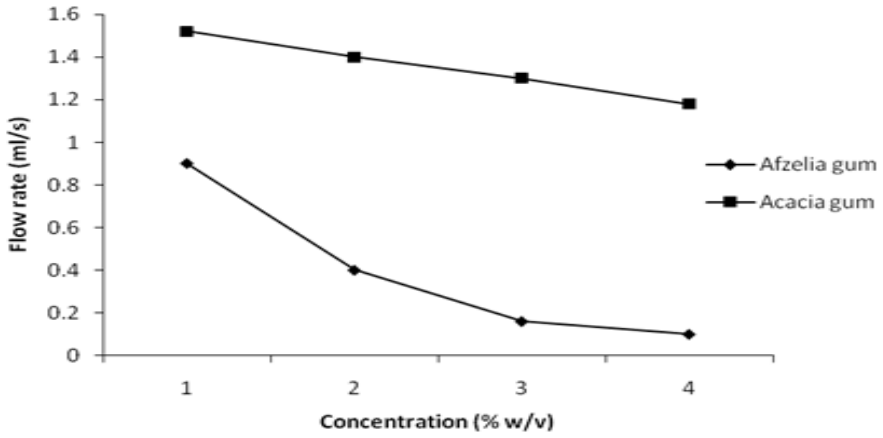

Figure 1: Plot of flow rate of suspension against concentration of suspending agent

Table 3 Sedimentation volumes of suspensions at different times

Suspending Agent	Conc. (% w/v)	Sedimentation volume at different time								
		0 h	3 h	6 h	9 h	12 h	15 h	18 h	21 h	24 h
AFG	1	1.00	0.60	0.56	0.53	0.50	0.47	0.45	0.43	0.42
	2	1.00	0.72	0.64	0.60	0.53	0.52	0.51	0.50	0.50
	3	1.00	0.89	0.80	0.75	0.72	0.68	0.68	0.68	0.68
	4	1.00	0.92	0.88	0.80	0.74	0.74	0.74	0.74	0.74
ACG	1	1.00	0.49	0.43	0.41	0.39	0.37	034	0.32	0.30
	2	1.00	0.58	0.51	0.48	0.46	0.44	0.41	0.40	0.39
	3	1.00	0.62	0.55	0.50	0.48	0.45	0.42	0.41	0.40
	4	1.00	0.68	0.64	0.58	0.52	0.49	0.45	0.45	0.45

Table 4: Redispersibility of suspensions containing different gum concentrations

Gum concentration (% w/v)	Redispersibility	
	Afzelia gum	Acacia gum
1	+++	+++
2	++	+++
3	+	+++
4	- - -	+++

Key

+++ = Easily redispersible with minimum agitation and stable enough for dose withdrawal

++ = Redispersible with vigorous agitation and stable enough for dose withdrawal

+ = Partially redispersible with vigorous agitation, not adequate for dose withdrawal

- - - = Not redispersible, formed hard cake

DISCUSSION

The knowledge of pH of an excipient is an important parameter in determining its suitability in formulation since the stability and pharmacological activity of most preparations depends on this parameter [12]. The pH of afzelia gum falls within the range of pH of gastrointestinal tract. It is also close to the neutral pH. Hence, it is not likely to adversely affect the stability and pharmacological activity of most drugs.

The high viscosity of dispersion of afzelia gum could be responsible for the traditional use of the gum as a soup thickener which was reported by Builders *et al*., [7]. The viscosity of the dispersion is several folds that of acacia gum (Table 2). It is advantageous in that little quantity of *Afzelia africana* gum can produce same effect as far larger quantity of acacia gum. Therefore, it is more economical to use afzelia gum for pharmaceutical suspensions. Ability of a polymer to increase viscosity in aqueous preparations even at small concentrations is desired of a good suspending agent [13].

Stoke's law shows an inverse relationship between sedimentation rate of a disperse system and the viscosity of the dispersing medium. Afzelia gum, with higher viscosity will give a lower sedimentation rate since other parameters such as particle size of the dispersed phase and acceleration due to gravity were constant. Therefore, afzelia gum will produce a more stable suspension compared to acacia gum.

Sedimentation volume and flow rate are important parameters for assessment of suspensions [14]. The trends of sedimentation volume against time for the two gums are similar to that of *Khaya senegalensis* gum reported by Mahmud *et al.* [2]. Sedimentation volume gives a qualitative account of flocculation; and the value ranges from 0 to 1. When the value equals to 1, it means that no clear supernatant and no sedimentation occurs. Suspensions containing afzelia gum had higher sedimentation volumes at all concentrations used. The sedimentation volumes of suspensions containing 1% ^{w}/v afzelia gum are comparable to those containing 3% ^{w}/v acacia gum; and the values for those containing 2% ^{w}/v of the gum are comparable to those containing 4% ^{w}/v acacia gum. Hence, afzelia gum is 2-3 times better than acacia gum in terms of suspendability.

The viscosity and sedimentation values have shown afzelia gum to be an effective suspending agent even at low concentration. It is however, limited by its low

flow rate; the flow rate of suspension containing 1% w/v afzelia gum being lower than that containing 4% w/v acacia gum (Figure 1). To ensure good suspension and good flow, it is required to use low concentration of afzelia gum. The effectiveness of the gum at low concentration is an indication that it is highly economical to employ the gum as a suspending agent; the gum being 2-3 times as effective as acacia gum.

Redispersibility is a qualitative assessment which is carried out by simple agitation of a product inside a container. It is one of the methods for assessing pharmaceutical suspensions [5]. All the concentrations of acacia gum used produced suitable suspensions in terms of redispersibility. Suspension containing 2% w/v afzelia gum is appropriate for use as it was redispersible with vigorous agitation and stable enough for dose withdrawal. The gum at concentration of 3% w/v is not suitable for formulation of suspension because the suspension was not sufficiently redispersible to allow accurate dose withdrawal not to talk of 4% w/v with which there was caking.

CONCLUSION

Afzelia africana gum is not likely to adversely affect the stability and pharmacological activity of most drugs. It is 2-3 times better than acacia gum and can be used at half or one-third of the concentration of acacia gum to achieve similar suspending properties. The gum is associated with poor redispersibility and must be used at low concentration. Concentration of 2% w/v is the optimal for acceptable suspendability, pourability and redispersibility.

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