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### Effect of *Adansonia digitata* Gum on Some Physicochemical Properties of Paracetamol Pediatric Suspension Formulations

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#### ABSTRACT

The purpose of this study was to investigate the effect of *Adansonia digitata* (AD) as a suspending agent in pharmaceutical formulations using paracetamol as the model drug. Paracetamol pediatric 125 mg/5ml suspensions containing AD at 0.1, 0.2, 0.3, and 0.4 % w/v as suspending agent were formulated. Similar formulations of paracetamol pediatric suspension were made using sodium carboxymethylcellulose (Na CMC) as the suspending agent. Some physicochemical properties of the paracetamol pediatric suspensions such as viscosity, easy of redispersion and sedimentation volume were evaluated. The viscosity of the suspension formulations ranged from 71-119 cP, which was a function of the concentration and type of suspending agent as well as the duration of storage of the suspension. Sedimentation volume, ease of redispersion and the flow rate of the formulations were characteristic of the suspending agent used and were influenced by the concentration of the agent. Overall, the profiles of paracetamol pediatric suspension formulations containing AD were better than those of Na CMC irrespective of the concentration of the suspending agent. At the same time the internal phase in all the formulations remained suspended for well enough time to assure withdrawal of accurate and uniform doses during the period of therapy. It was concluded that AD gum could be a potential suspending agent in formulation of pharmaceutical suspensions.

**Keywords:** Pediatric suspension, *Adansonia digitata*, suspending agent, physicochemical characteristics

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## INTRODUCTION

Many people have difficulty in swallowing solid dosage forms and therefore require the drug to be dispersed in a liquid. If the drug is insoluble or poorly soluble in a suitable solvent then formulation of suspension is usually required<sup>1</sup>. In a pharmaceutical suspension settling of the internal phase would settle is a matter of time<sup>2</sup>. The rate and extent of this sedimentation depends on a number of factors such as particle size of the external phase, the difference between density of the continuous external phase and the discontinuous internal phase. It also depends on the viscosity of the continuous phase. According to Stokes' law, changes in the viscosity of the continuous phase affect the terminal velocity of the discontinuous phase<sup>2</sup>. Suspending agents are used in formulations to help the discontinuous phase to remain suspended long enough when shaken and assist in easy redispersion of settled particles on standing<sup>3</sup>. These have the benefit that consistent withdrawal of uniform doses is possible throughout the medication period. Furthermore, a well-formulated suspension should easily be re-suspended when moderately agitated and should allow uniform and accurate doses of the medicament to be withdrawn throughout the period of medication. Natural gums have been reported to provide the needed platform for some of the quality attributes of a suspension due to their ability to swell when in contact with water and their viscous nature<sup>3-8</sup>. Natural gums are generally biodegradable, cheap, easily available, effective, and ecofriendly compared to synthetic and semi-synthetic materials as pharmaceutical excipients<sup>9-11</sup>.

*Adansonia digitata* gum is obtained from the leaves of *Adansonia digitata* (Fam. Malvaceae). *Adansonia digitata* is the most widespread of the *Adansonia* species on the African continent. The plant is found in the hot, dry savannahs of sub-Saharan Africa and grows, having spread secondary to cultivation, in populated areas. English common names include baobab, dead-rat tree (from the appearance of the fruits), monkey-bread tree (the soft, dry fruit is edible), upside-down tree (the sparse branches resemble roots) and cream of tartar tree. The northern limit of its distribution in Africa is associated with rainfall patterns; only on the Atlantic coast and in the Sudan does its occurrence venture naturally into the Sahel. On the Atlantic coast, this may be due to spreading after cultivation. Its occurrence is very limited in Central Africa, and it is found only in the very north of Southern Africa. In Eastern Africa, the trees grow also in shrublands and on the coast. In Angola and Namibia, the baobabs grow in woodlands, and in coastal regions, in addition to savannah. It is also found in Dhofar region of Oman and Yemen in the Arabian Peninsula, Asia. This tree is also found in India, particularly in the dry regions of the country. The plant was investigated for its potential as stickling agent<sup>12,13</sup>. *Adansonia* fruit pulp was investigated for its potential use as additive in

beverages<sup>14</sup>. The gum from the leaves was investigated on the effect of hot and cold water extraction on its potential as a suspending agent in the formulation of sulphadimidine suspension<sup>15</sup>. The workers used hot water and cold water extraction methods to obtain the gum and subsequently used the gum at 1-5 %w/v to prepare sulphadimidine suspension. The gum extracted with cold water had better yield than the hot water extract. Similarly, the cold water extract was shown to have better suspending profile at the same concentration than either the hot water extract of the gum or another natural polymer, tragacanth. Study comparing the effect of *Adansonia digitata* and a semi-synthetic polymer widely used as suspending agent, such as sodium carboxymethylcellulose, in pharmaceutical oral formulations has not been reported.

Paracetamol is an analgesic that could be useful in children when they are febrile as a result of immunization or hurts from experimentations and hyperactivities. The most widely available and used dosage form of this drug is the tablet, which usually comes as a 500 mg paracetamol tablet, requiring two or more tablets as a dose when taken by adults. The most widely used dosage form of paracetamol for children is elixir, usually made possible by dissolving paracetamol in a mixture of ethanol and propylene glycol. Many cases of death from paracetamol elixir poisoning have been reported due to use of ethylene glycol instead of propylene glycol as a solvent in the preparation of paracetamol elixir. Many pediatricians, therefore, prefer the use of tablets from which an extemporaneous suspension of the medicine is prepared for the child. Such preparations may suffer from lack of skills of the care giver or parents to appropriately prepare the medication to meet the pharmacokinetic requirements of the drug. The use of suspension of paracetamol for children may address this challenge and those related to inappropriate use of some solvents in the preparation of elixirs that results in casualties. *Adansonia* gum, like many other gums should provide a suspending function to paracetamol powder, an indiffusible solid in a paracetamol pediatric formulation.

## **MATERIALS AND METHOD**

Paracetamol (Spectrum Chemicals, NJ, USA), Sodiumcarboxymethylcellulose (Na CMC), sodium lauryl sulphate (Spectrum Chemicals, USA) and *Adansonia digitata*(AD).Thematured leaves of *Adansonia digitata* were collected in Jos, Nigeria and were dried and powdered.

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## **EXTRACTION OF GUM FROM THE LEAVES OF *ADANSONIADIGITATA* PLANT**

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Three hundred grams (300 g) of the powdered gum was weighed and was dispersed in 5 liters of hot boiling water. The dispersion was allowed to stand 24 h to extract the gum. The mucilage was filtered through a white muslin cloth to remove any extraneous materials and the mucilage was subsequently precipitated with about 8 liters of ethanol 96 %. The precipitate obtained was redispersed in water and re-extracted with ethanol 96 %. This procedure was repeated until a purified gum was obtained. The gum was dried in the oven at 50 °C for 1 hr. The dried gum granules were pulverized using pestle and mortar to obtain powdered AD gum. The powdered gum was further screened through sieve no. 100 and the resultant powdered gum was stored in air tight polythene bag until required.

### **PREPARATION OF PARACETAMOL PEDIATRIC SUSPENSION FORMULATION**

A pediatric paracetamol suspension to deliver a dose of 25mg/ 5mL was formulated. *Adansonia digitata* powdered gum to give 0.1, 0.2, 0.3, and 0.4%w/v was weighed and dispersed in 500 mL of demineralized water and allowed to stand for 12 h to deaerate. Paracetamol powder was sifted through sieve number 80 and dispersed in about 200 mL of demineralized water, to which 50 mL of sodium lauryl sulfate (1% w/v) had been added to facilitate wetting of paracetamol powder. The dispersed paracetamol suspension was transferred to a 2000 mL beaker and it was mixed on a magnetic stirrer for 30 min. The volume was made up to 1 liter with demineralized water. The paracetamol suspension prepared above was replicated using similar concentrations of Na CMC as the suspending agent.

### **EVALUATION OF PARACETAMOL PEDIATRIC SUSPENSION FORMULATIONS**

#### ***Sedimentation volume***

Triplicate samples of a 100 mL of the suspension was transferred into a 100 mL graduated cylinder and allowed to stand. The volume occupied by the solute in the cylinder below the supernatant (clear surface of the suspension) was recorded daily until there was no visible change in volume in the samples. The average of the triplicate samples was computed.

#### ***Viscosity of suspension***

The viscosity of paracetamol pediatric suspension samples was determined on Brookfield dial rheometer (Brookfield Engineering, USA). A 600 mL sample of paracetamol pediatric suspension was transferred to a 1 liter Pyrex beaker and the viscosity of the sample was determined using RV 2 spindle.

#### ***Flow rate of suspension***

The flow rate of the formulations was compared with distilled water flowing through a 2 mL pipette. The time taken by the distilled water to flow through the 2mL pipette was noted. The flow rates of samples were similarly determined. The results were the average of three determinations.

#### ***Ease of redispersion of paracetamol pediatric suspension formulations***

The ease of redispersion of the suspension formulations was evaluated every other day for two weeks. Triplicate samples of 50 mL paracetamol pediatric suspensions were transferred to 100 mL plain glass bottles for the evaluation of easy of redispersion. The sample was allowed to roll down a 45 cm length by 15 cm width smooth and polished and guarded plank inclined at 45°. The number of cascade required to completely redisperse the suspension was noted. Triplicate samples were evaluated and the results were the average of these samples.

#### ***Determination of pH of paracetamol pediatric formulations***

The suspensions were redispersed by shaking vigorously for homogeneity and the pH was taken when freshly prepared and every other day thereafter on Jenway pH meter.

#### ***Determination of density of paracetamol pediatric suspension formulations***

The density of the samples was determined using a 50 mL glass pycnometer. The weight of the empty pycnometer was first determined.

## **RESULTS AND DISCUSSIONS**

### **General description**

Pale-Whitish deflocculated paracetamol pediatric suspensions were produced. The weight per mL of the paracetamol suspension formulated with 0.4 % w/v suspending agents was  $1.598 \pm 0.006$  g/mL. The pH was  $5.5 \pm 2.39$ . Paracetamol pediatric suspensions containing lower concentrations of the suspending agents had correspondingly lower values of weight per mL.

### **Viscosities and easy of redispersion**

The viscosities of the pediatric formulations are as shown in Table 1. The viscosity of pediatric suspension at 0.1 % w/v suspending agent was 71.49 and  $78.31 \pm 0.28$  cP respectively for paracetamol suspension containing Na CMC and AD gum. The increase in the viscosity of paracetamol pediatric suspension led to decrease in the terminal velocity of the solute particles that would settle.

Consequently, suspensions with higher concentration of the suspending agent produced suspension with correspondingly high sedimentation volume and slow rate of sedimentation.

Table 1: Viscosity of paracetamol pediatric suspensions

Conc. (% w/v)	Suspending agent	
	Sodium carboxymethylcellulose	<i>Adansonia digitata</i> gum
0.1	71.49 ± 1.4	78.31 ± 0.28
0.2	80.23 ± 0.98	90.55 ± 0.28
0.3	92.70 ± 1.1	105.95 ± 0.49
0.4	101.93 ± 0.70	119.10 ± 1.4

Table 2 shows the ease of redispersion of paracetamol pediatric suspensions. It was required that the samples under cascade about 11 and 8 respectively for those containing Na CMC and AD. The number of time required for redispersion of the suspensions decreased with increase in the concentration of the suspending agent. The ease of redispersion of the suspensions was dependent on the type and concentration of the suspending agent incorporated as well as the duration of storage of the paracetamol pediatric suspension. Lower concentrations of the suspending agents (0.1, 0.2, 0.3 %w/v) produced paracetamol suspensions that were relatively more difficult to redisperse than the corresponding higher concentrations. It was easier to redisperse paracetamol suspensions containing AD gum than those with Na CMC as suspending agents. As the concentration of the suspending agent in the continuous phase increased there was a corresponding increase in the viscosity of the suspension. The increase in viscosity retarded the terminal velocity of the particle and at the same time it probably reduced inter particle attraction making the particles to be loosely packed together, thereby making redispersion possible.

Table 2: Ease of redispersion of paracetamol pediatric suspensions after two weeks of storage

Conc (% w/v)	Na CMC	AD
	No. cascade	No. cascade
0.1	11.0 ± 0.86	7.5 ± 0.57
0.2	7.0 ± 1.5	5.0 ± 0.57
0.3	5.0 ± 0.86	3.3 ± 1.00
0.4	3.5 ± 0.86	2.3 ± 0.57

**Sedimentation volume**

Figure 1 shows the typical sedimentation volume of the pediatric suspension at 0.4 % w/v suspending agent. The internal phase settled rapidly within two days and was relatively constant afterwards. High sedimentation volumes were obtained in paracetamol pediatric suspensions containing AD than with Na CMC as suspending agent. High sedimentation volume is an indication that although the internal phase particles have settled, as would be expected with suspensions, the inter particle attraction and bonding were loose and not strong enough to form hard cake during the study period. The result suggested that differences in the sedimentation profiles was probably due more to the suspending agent used than the properties of the internal phase.

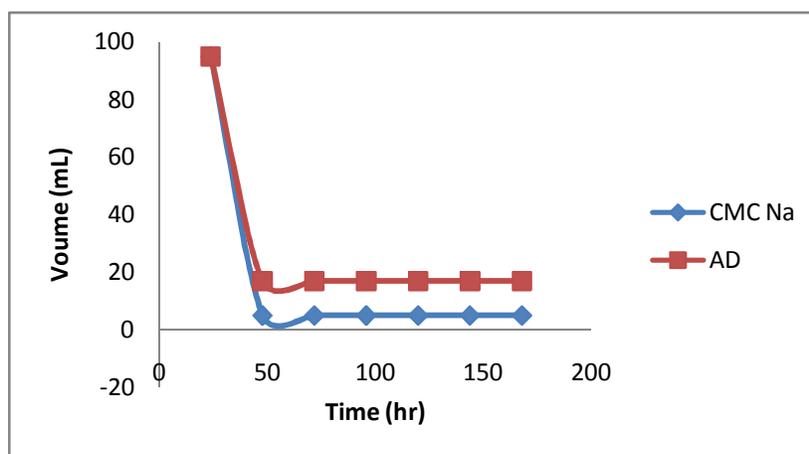


Figure 1: Sedimentation volume of paracetamol 125 mg/ mL containing 0.4 % w/v suspending agent

### **Flow rate of paracetamol pediatric suspension**

The flow rates of paracetamol pediatric suspensions were compared with that of water. The flow rate of water was 0.51 mL / sec and the corresponding values for paracetamol pediatric suspension were 0.466, 0.366, 0.342 and 0.321 mL/sec respectively with Na CMC 0.1, 0.2, 0.3 and 0.4 % w/v as suspending agent. The flow rates of the suspension with similar concentrations of AD as suspending agent were respectively 0.222, 0.21, 0.197 and 0.183 mL/sec. The flow rate decreased with increase in the concentration of the suspending agent. The flow rate of paracetamol pediatric suspension containing Na CMC were higher than those containing AD indicating when equal amounts of Na CMC and AD are used as suspending agent, AD imparted higher viscosity on the formulation than the Na CMC. At concentration of suspending agent the flow rate of paracetamol suspension decreased with storage. This was probably because the attractive forces between the particles of the internal phase became pronounced with storage and the bonding of more particles together with storage retarded the flow of the suspension through the pipette. A good quality pharmaceutical suspension is the one that can easily be withdrawn from the container.

### **CONCLUSION**

Paracetamol pediatric suspensions containing either AD or Na CMC as suspending agent were formulated successfully. Some physicochemical properties of the suspensions were evaluated. The viscosity, sedimentation volume and ease of redispersion as well as the flow rate of the suspensions were characteristic of the suspending agent used. Generally the profiles of paracetamol pediatric suspensions containing AD appeared to be better than those of Na CMC, suggesting its potential as a suspending agent in formulation of pharmaceutical suspensions. The internal phase in all the formulations remained suspended well enough to assure withdrawal of accurate and uniform doses throughout therapy.

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