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EVALUATION OF THE SUSPENDING PROPERTY OF GREWIA GUM IN METRONIDAZOLE SUSPENSION

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Abstract

The suspending property of grewia gum in metronidazole suspension was evaluated. The gum was extracted by maceration, filtration, precipitation and drying techniques. It was used at 0.3 to 1% w/v as a suspending agent for metronidazole. Sodiumcarboxymethylcellulose (SCMC) and tragacanth were used as basis for comparison. The suspending properties evaluated included the sedimentation rate, sedimentation volume, ease of redispersibility, apparent viscosity and degree of flocculation. The effect of electrolyte, pH, temperature and ageing on the viscosity of the suspension was also investigated. Results obtained after 8 weeks of storage showed that the optimum suspending concentration for grewia gum in the drug was 1% w/v. The sedimentation rate, sedimentation volume and the viscosity of the suspension containing grewia gum were superior to those made with SCMC. No significant (P >0.05) difference in these properties was observed when compared with suspension containing tragacanth. The suspension containing grewia gum was moderately redispersed. The degree of flocculation increased in the order SCMC<grewia<tragacanth. Moderate concentrations of electrolyte, pH, temperature and storage did not adversely affect the viscosity of metronidazole suspension containing grewia gum. On the basis of these, grewia gum may find application as a suspending agent in metronidazole suspension.

Keywords: Grewia gum; metronidazole; suspension, evaluation.

INTRODUCTION

Because of the overdependence on imported pharmaceutical raw materials for most of our pharmaceutical products in Nigeria, there has been marked increase in the search for pharmaceutical excipients from our abundant potential raw materials yet untapped. This will help reduce the depletion of our foreign reserves and also the cost of production leading to affordability of raw materials for foods and pharmaceutical products. Shrubs or tree exudates may serve as a potential source of commercially useful gums and hydrocolloids that are employed in foods, pharmaceutical and cosmetics preparations. Gums such as tragacanth and acacia are plant exudates that are commonly used (Carter, 1987) these are now scarce and expensive.

Plant gums are naturally occurring water soluble polymers widely found in nature. They are derived from seed extracts, plant exudates, seaweed extracts and fermentation processes of certain microorganism (Zatz *et al.*, 1988). They find application in pharmacy as viscosity – building agents, deflocculants and, sometimes, as emulsifying agents.

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Grewia gum is a polysaccharide derived from the inner stem bark of the edible plant *Grewia mollis,* Juss (family Tiliaceae). The plant is a savannah shrub, which grows widely but is usually cultivated. Its local source is in the guinea savannah region of the middle belt of Nigeria where it is called *dargaza* in Hausa language. Indigenous people use the powdered inner stem back as thickening agent in local dishes (Okafor, 2001; Audu-Peter, 2007).

Works have been done on the rheological, binding, sustained release and film forming properties of grewia gum (Okafor, 2001; Okafor and Chukwu, 2003; Audu-Peter, 2007). The aim of this work is to evaluate the suspending property of the gum in metronidazole suspension formulation. Similar suspensions made with tragacanth and sodiumcarboxymethyl cellulose (SCMC) were used as basis for comparison.

MATERIALS AND METHODS

Materials

. The following materials were used as procured from their manufacturers: Sodium metabisulphite, hydrochloric acid (Sigma-Aldrich, Germany), sodium benzoate, sodium chloride and Magnesium Chloride, (BDH Chemical, England), Sodium hydroxide (Avondale lab, England), 95% w/v Ethanol (Philip Harria, England), Sodium carboxymethyl cellulose (SCMC) (Merk, Germany), tragacanth, aluminium chloride and metronidazole (M&B Chemicals, England

Methods

Extraction of grewia gum

Grewia gum was extracted and processed from our laboratory according to the method of Okafor (2001). All other materials where used as obtained.

Preparation of metronidazole suspension

A 1.0 g quantity of grewia gum was dispersed in enough distilled water contained in a beaker to make some dispersion. The dispersion was allowed to stand for 24 h with occasional stirring to facilitate the dispersion of the lumps. Similar procedure was carried out to obtain 1.0% w/v aqueous dispersions of tragacanth and SCMC.

Table 1 shows the formula for preparing metronidazole suspension. A 4 g quantity of metronidazole was weighed out in an Ohaus balance (Model 310, USA) and transferred to a clean porcelain mortar. The aqueous dispersion of grewia gum was added in successive portion to make a smooth paste. A 0.1 g of sodium benzoate was weighed and then dissolved in 10 ml of distilled water and added to the content of the mortar. The content was transferred to a 100 ml measuring cylinder. The suspension was made up to volume with rinsing from the mortar. The procedure was repeated for dispersions of SCMC and tragacanth gums.

Evaluation of the suspensions

Sedimentation rate analysis

The original height Ho of the suspension was read off on the cylinder immediately after preparation. The measuring cylinder containing the suspension was allowed to stand on a vibration free stand. The height of the sediment Hu was read off daily for 7 days. It was subsequently read off on weekly basis for 7 weeks. The sedimentation rate analysis of the suspension was calculated and presented graphically either as ultimate height against time.

Sedimentation volume.

The sedimentation volume was determined according to the expression. Hu/Ho (or Vu/Vo) where Ho (orVo) is the original height or volume of the suspension and Hu (or Vu) is the ultimate height or volume of the sediment at any given time.

Degree of flocculation

A 100 ml quantity of 4% w/v metronidazole suspension containing 1%w/v each of grewia, SCMC or tragacanth was prepared. A similar suspension containing no suspending agent was also prepared. The suspensions were kept for 6 months on a vibration-free stand. The volume of sediment (vu) after the time interval was recorded. The volume of the suspension containing no suspending agent after 6 months (v∞) was also recorded. The degree of flocculation (β) was calculated using the equation:

$$\beta = Vu/V\infty.$$

Re-dispersibility test

The suspensions were prepared as described previously. At the end of the six months period, they were gently shaken for 1 min in order to determine the ease with which the particles disperse. The result was recorded as not easily-, moderately-, easily- and very easily redispersed.

Viscosity determination

A 50 ml quantity each of the suspension was transferred into the cup of a rotational viscometer (contraves rotational viscometer, model 1698, Switzerland) and the spindle dipped into it and rotated at 50 rpm. The viscosity was read off from the viscometer after one minute. This was repeated after 2 months of storage.

Effect of viscosity.

The viscosity of batches of metronidazole suspension was immediately determined after preparation with the aid of a pH meter (Jenway Ltd model 3310, UK). A 1 ml quantity of 1.0N hydrochloric acid or sodium hydroxide was added and the suspension was made up to 100 ml. The viscosity of the suspensions was determined using contraves rotational viscometer as described earlier. The average of three determinations was recorded.

Effect of electrolytes on viscosity

A 100 ml volume of metronidazole suspension containing 1%w/v grewia gum and 0.5% w/v each of sodium chloride, magnesium and aluminium chloride was prepared and allowed to stand for 24 hours. The viscosity of the suspension was determined in a contraves rotational viscometer as described before. The average of three determinations was recorded.

Effect of temperature on viscosity

A 100 ml quantity of metronidazole suspension containing 1%w/v grewia gum was kept in thermo regulator (Controller OV/75/F/DIG, Genlab, Ltd, UK) and refrigerator (HR 170T) at 4, 25 and 45^{o}c for 24 h. The viscosity of the suspension was determined in the rotational viscometer. The average of three determinations was recorded.

RESULTS AND DISCUSSIONS

Sedimentation Rate

Fig1 shows the effect of grewia gum concentration on the sedimentation rate of metronidazole suspension. It can be seen that the rate at which the metronidazole particles settled in the suspension was high for suspension containing 0.3 or 0.5% w/v grewia gum. This is evident from the slope of the graph which was steep especially in the first 2 days. On the other hand, metronidazole particles contained in the suspension containing 1%w/v grewia gum settled slowly. It could be seen that the rate of sedimentation was gum concentration dependent. It has been reported that the viscosity of gum dispersions increases with increase in the concentration of the gum (Carter 1986; Patel et al, 1986). One of the factors that affect the sedimentation rate of particles in a suspension according to Stoke's law is viscosity. The higher the viscosity, the slower is the rate of sedimentation. The viscosity of the suspension containing 1%w/v grewia gum is 75 cps. The corresponding value for suspension containing 0.3 or 0.5% w/v grewia gum are 20 cP and 50 cP respectively. The slow rate of setting of particles in the metronidazole suspension containing 1%w/v grewia gum is therefore attributed to the high viscosity achieved in the suspension.

Sedimentation volume

Table 2 shows the sedimentation volume of metronidazole suspension containing grewia gum, tragacanth or SCMC. The sedimentation volume of both grewia and tragacanth was higher than SCMC, and when sedimentation volume of grewia gum was compared to that of tragacanth, they did not differ significantly (P>0.05) but there was significant difference (P<0.05) between that of grewia gum and SCMC.

Fig 2 shows the effect of gum type on the sedimentation volume of metronidazole suspension. The sedimentation volume of the suspension containing grewia gum is about 0.7 after 60 days of storage. This is the same with that of similar suspension containing tragacanth. The suspension containing SCMC exhibited only 0.2 sedimentation volume after 60 days.

Sedimentation volume is an important parameter for assessing the physical properties of a good suspension. The higher the sedimentation volume, the better is the suspension (Martin 1993, Patel et al., 1986). High sedimentation volume of suspension enhances ease of redispersibility and eliminates cake formation (Martin, 1993; Patel *et al*., 1986). High sedimentation volume is therefore desirable in a suspension. The high value of sedimentation volume obtained for the suspension containing grewia gum and tragacanth is good. The result shows that SCMC is not a good suspending agent for metronidazole.

Degree of flocculation

Table 2 shows the degree of flocculation of metronidazole suspension after 6 months using tragacanth, grewia and SCMC gums. The degree of flocculation is in the order SCMC<grewia<tragacanth. The degree of flocculation of grewia gum is about four times higher than SCMC while that of tragacanth is only about 1.5 times that of grewia gum. It therefore means that grewia gum has better suspendability of metronidazole particle than SCMC.

Redispersibility

Table 2 also shows the ease of redispersibility of the suspension containing 1% w/v suspending agents after 6 months of storage. Although the metronidazole suspension containing SCMC are easily redispersed, it settles quickly while that of tragacanth and grewia gums redisperse easily and moderately respectively at similar concentrations.

Viscosity

Table 3 shows the effect of storage on viscosity metronidazole suspension containing 1%w/v

Table 1: Formula for preparing the suspensions

Ingredients	Batches (g or ml				
	I	II	III	IV	V
Metronidazole	4	4	4	4	4
Grewia Gum	1	-	-	0.5	0.3
Tragacanth	-	1	-		
SCMC	-	-	1		
Sodium benzoate	0.1	0.1	0.1	0.1	0.1
Water	100	100	100	100	100

Table 2: Physical properties of metronidazole suspension containing 1% w/v suspending after 8 months

Gum Type	Sedimentation Volume		Ease re-dispersibility	Degree of Flocculation
	2 Months	6 months		
SCMC	0.24	0.17	Easily redispersed	1.411
Tragacanth	0.64	0.09	Easily redispersed	7.111
Grewia	0.65	0.13	Moderately reds	5.000

Table 3: Effect of storage on the viscosity of metronidazole suspension containing 1%w/v suspension agents.

Suspension	Viscosity reading in cP	
Metronidazole Tragacanth	125	50
Metronidazole SCMC	270	115
Metronidazole	75	53

Table 4: Effect of some factors on the viscosity of metronidazole suspension containing 1% w/v grewia gum.

Sample	Electrolyte (0.5%)	Viscosity(centipoise)
	Electrolyte	
	Nil	75
Metronidazole	Sodium chloride	70
suspension	Magnesium chloride	65
	Aluminium Chloride	Coagulation
	pH	
Metronidazole	6.17	75
Suspension	8.40	65
	5.50	62
	Temperature(^oC)	
Metronidazole	25	75
Suspension	4	70

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45	74

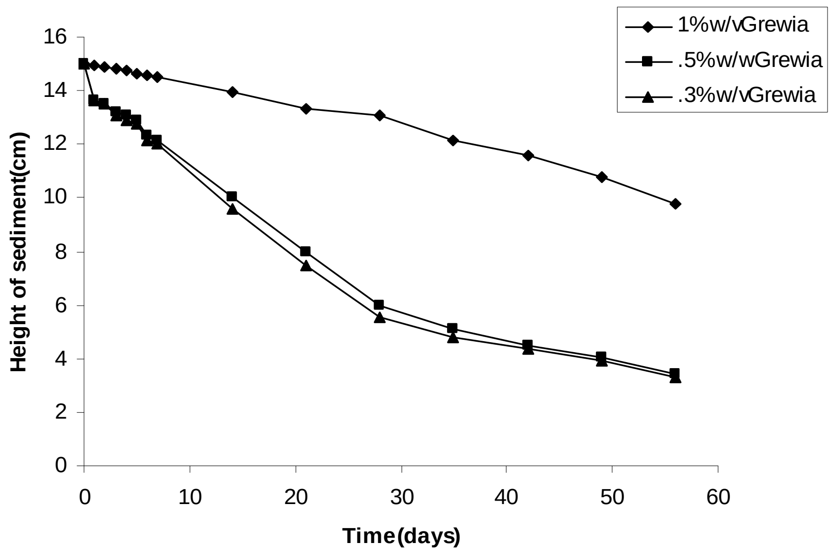

Fig. 1: Effect of grewia gum concentration on the sedimentation rate of metronidazole suspension.

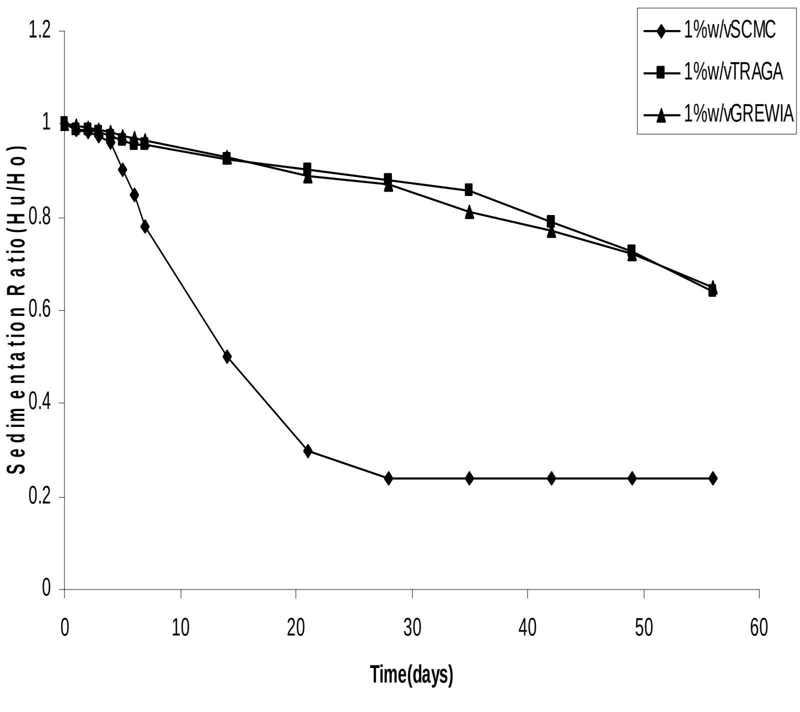

Fig 2: Effect of Gum type on the sedimentation volume of Metronidazole suspension

suspending agent. Freshly prepared metronidazole suspensions containing tragacanth, grewia and SCMC gums had viscosity value of 125, 75 and 270 cps respectively but the viscosity dropped to 50, 53 and 115 respectively after 2 months. Although the viscosity of the suspensions containing tragacanth and SCMC was initially higher than grewia gum, those containing grewia gum did not drop drastically on storage when compared with those made with the two standard gums.

Effect of pH

From Table 4 it could also be seen that alkaline or acidic pH affects the viscosity of the suspension, but the suspension is more affected by acidic pH than alkaline. Although grewia gum contain uronic acid, it is a weak acid and stronger acids such as HCl have more impact on the viscosity of the gum.

Effect of electrolyte

Table 4 shows that addition of 0.5% w/v sodium cholride, magnesium chloride or aluminium chloride led to reduction from 75 to 70 cP, 75 to 65 cP and coagulation respectively. This agrees with Schulze-Hardy rule which states that the valence of ions having a charge opposite to that of the hydrophobic particle appears to determine the effectiveness of the electrolyte in aggregating the particles. Divalent ions are ten times as effective as monovalent ions while trivalent ions are one thousand times as effective as monovalent (Patel *et al.*, 1986, Carter, 1986, Martin, 1993).

Effect of temperature

Table 4 also shows the effect of temperature on the viscosity of metronidazole suspension containing 1% w/v grewia gum. The viscosity of the gun is not affected adversely, at 4, 25 and 45^oC but viscosity is affected more at 4^oC than 45^oC. Temperature changes may affect the rheology of the suspension especially towards the extremes or when kept for a long time at slightly elevated temperatures or reduced temperature.

CONCLUSION

From the study carried out so far, grewia gum is a good suspending agent for metronidazole suspension formulation. The viscosity of the suspension containing the gum is not adversely affected by storage. It also has moderate degree of flocculation.

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