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Evaluation of metronidazole suspensions

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Most of the formulations of metronidazole suspensions available in circulation tend to have the problem of caking or claying probably due to the flocculation behavior of the dispersed phase. The present study attempts to achieve a desirable flocculation pattern by the use of a polysaccharide, *Abelmoschus esculentus* (Okra) mucilage alone and then in combination with a monovalent electrolyte and sodium sesquicarbonate (Trona). Metronidazole formulations with various concentrations (1 to 5%w/v) of *A. esculentus* (Okra), its combination with sodium sesquicarbonate (4:1) and compound tragacanth BP (Reference) were comparatively evaluated using parameters such as sedimentation volume, rheology, pH, redispersibility and particle size. The combined test suspending agents at 5%w/v was found to be superior to the mucilage alone and compound tragacanth BP (P<0.05) at all concentration studied. This result suggests that the combined test suspending agents has the potential of overcoming the problems associated with metronidazole formulations.

Key words: *Abelmoschus esculentus* (Okra), compound tragacanth BP, metronidazole suspensions, sodium sesquicarbonate (Trona).

INTRODUCTION

A pharmaceutical suspension is a coarse dispersion of insoluble solid particles in a liquid medium. The particle diameter in a suspension is usually greater than 0.5 mm. However, it is difficult and also impractical to impose a sharp boundary between the suspensions and the dispersions having finer particles. Therefore, in many instances, suspensions may have smaller particles than 0.5 mm, and may show some characteristics typical to colloidal dispersions, such as Brownian movement (Martin, 2006). A suspending agent is a substance that increases the viscosity of a suspension, so that sedimentation is retarded. The presence of a suspending agent is required to overcome agglomeration of the dispersed particles and to increase the viscosity of the medium, so that the particles may settle slowly. These suspending agents increase sedimentation volume, ease redispersibility, enhance pour ability and prevent compact formation. Suspending agents can be grouped into three classes: Synthetic; semi-synthetic and the natural polysaccharide, which, tragacanth, okra and acacia

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belong.

Gum of the *Abelmoschus esculentus* (okra) family (Malvaceae) is a natural polymer consisting of D-galactose, L-rhamnose and L- galacturonic acid (Agarwal et al., 2001).

Gums of *A. esculentus* (Okra) pods have been reported to have binder potential for tablet formulations (Ofoefule et al., 2001; Chopra et al., 1956). The fresh fruits of *A. esculentus* (L.) are a common component of Indian diet. In addition, the plant has been used medicinally in treatment of several disorders (Chopra et al., 1956; Jha et al.,1997). Anti-cancer, antimicrobial and hypoglycemic activities of the plant are reported (Pal et al., 1968; Tomoda et al., 1987). The anti-ulcer activity of fresh fruits is recently reported (Gurbuz et al., 2003). Studies have also been carried out for its use as a suspending agent (Kumar et al., 2009). Trona is an evaporite mineral also known as sodium sesquicarbonate. A white crystalline hydrated double salt, $Na_2CO_3.NaHCO_3.2H_2O$, soluble in water but less alkaline than sodium carbonate and decomposes on heating. Metronidazole a nitroimidazole antibiotic medication is used particularly for anaerobic bacteria and protozoa. It is antibacterial against anaerobic organisms, an amoebicide, and an antiprotozoal (Cohen et al., 2010). It is the drug of choice for first episodes of mild-to-moderate clostridium difficile infection (Cohen et al.,2010).

This study aims to investigate the suspending properties of the gum, and its combination with sodium sesquicarbonate (Trona) on the stability of metronidazole suspension.

MATERIALS AND METHODS

Metronidazole powder (Medex co. ltd), benzoic acid solution B.P., amaranth solution (E- Merck Darmstardt Germany), raspberry syrup, chloroform water- double strength (BDH Laboratory Supplies Poole, England), compound tragacanth powder (BDH Laboratory Supplies Poole, England) and ethanol 96% (BDH Laboratory Supplies Poole, England) were bused for this study. *A. esculentus* (okra) fruits and trona (Sodium sesquicarbonate) were purchased from the local market in Sagamu, Ogun State, Nigeria and demineralized water was gotten from Faculty of Pharmacy, Olabisi Onabajo University, Ogun State, Nigeria.

Extraction of the gum from the fruit of *A. esculentus* (Family - Malvaceae)

The fruits were sun dried for three weeks and were size reduced using pestle and mortar into powder. The powder was then sifted using a sieve size of 250 µm. Four hundred grams (400 g) of dried powdered okra was dispersed in 8 L of demineralized water and kept in refridgerator for 24 h. The dispersed mucilage was strained through a muslin cloth to remove the fibrous materials. The cloudy mucilage was clarified by centrifugation at 15,500 revolutios per minute using centrifuge (Model LF-400R, Biomaker, China). The clarified mucilage was transferred into a 1 L beaker and the gum was extracted with 8 L of ethanol 96%. The extracted gum was redispersed in water and re-extracted with 4 L of ethanol 96% to get a whitish gum. The gum was dried in an oven at 65°C for 8h. The dried gum obtained was milled into powder.

Purification of trona (sodium sesquicarbonate) $Na_2CO_3.NaHCO_3.2H_2O$

Trona was obtained from a local market in Sagamu, Ogun state, was size reduced in a mortar and pestle. The powder was then sifted using a sieve size of 250 µm. 100 g of the powdered trona was dispersed in 1L of demineralised water. This was passed through a muslin cloth with the residue removed. The cloudy filtrate was allowed to settle for 30 min, after which the supernatant fluid was decanted. The sediment was dried in an oven at 80°C for 3h. The dried flakes obtained were then milled into powder using a blender.

Preparation of metronidazole suspension

5 g of metronidazole powder and 1g of compound tragacanth powder were weighed and triturated in a mortar. Twenty ml of raspberry syrup was added in aliquot proportion and triturated for 3 min until a smooth paste was formed. 2 ml of benzoic acid and 1 ml of amaranth solutions were added gradually with constant stirring and then mixed with 50 ml of chloroform water double strength. The mixture was transferred into a 200 ml amber bottle made up to 100 ml volume with distilled water and then shaken vigorously for 2 min (thus making 1%(w/v) of the gum in the preparation). The procedure was repeated using different concentrations 2, 3 , 4 and 5% (w/v) of compound tragacanth gum. The method above was used for okra gum and combination of okra gum plus trona (4:1) except that in case of okra gum, the appropriate amount was weighed and soaked in 2 ml of dimeneralized water and allowed to soak for 12 h while kept in the refridgerator before triturating with metronidazole powder. Also, the mixture of okra gum and trona (4:1) was first weighed into an evaporating dish and sufficient water was added to form watery mucilage before being heated on a water bath at 100°C for 1 min till viscous mucilage was formed. This was allowed to cool, and then triturated as appropriate with metronidazole powder before other ingredients were incorporated (Table 1).

Determination of sedimentation volume

20 ml of each suspension was stored in 30 ml cylinder in replicate and was left undisturbed. The sedimentation volume of the suspension was then determined at room temperature for 45 days, the result was taken at every 5 days. The sedimentation volume was observed and noted. The sedimentation volume is denoted by (F)

$$F = \frac{V_u}{V_o} \qquad (1)$$

Where V_u is the ultimate volume of the sediment and V_o is the original volume of the suspension.

Rheological assessment

The time to empty 5 ml of the suspension in duplicate from a 5 ml pipette was calculated to give the flow rate and computed thus;

$$\text{Flow rate} = \eta_\alpha = \frac{\text{Volume of pipette (ml)}}{\text{Flow time (s)}} \qquad (2)$$

Likewise, the shear rate was also calculated

$$\text{Shear rate} = \frac{\text{Flow rate (ml/s)}}{\text{Volume of suspension}} \qquad (3)$$

The viscosity behavior of the suspensions prepared with compound tragacanth gum, *A. esculentus* (Okra) gum and a combination of *A. esculentus* (Okra) and sodium sesquicarbonate (Trona) in duplicate were studied using shanghai changji rotational viscometer, spindle number 2 and 3 of low viscosity type with gear speed ranging 30 to 60 rpm. Using these observations, the rate of shear was calculated. The results were recorded as shown in Table 4.

Particle size analysis

The particle size distribution of metronidazole powder was determined micro metrically (Martin et al., 1993). The sieves in descending order of aperture size were arranged from 1000 to 90 μm mesh size and together with collection pan (receiver) was shaken using a sieve shaker. 10 g of metronidazole powder was weighed into the sieve with the largest aperture. After shaking for 5 min, the weight of the particle retained on each sieve was determined and recorded appropriately. The mean particle diameter was determined using the formula:

$$\text{Mean diameter} = \sum(\text{\% weight retained} \times \text{mean aperture}) / 100 \qquad (4)$$

pH determination

The measurement of the pH of all the formulated suspensions was determined in duplicate using the pH meter at 0, 10, 20, 30 and 40 days respectively. The pH meter electrode was allowed to stay in the suspension for 30 s before the reading was recorded.

Redispersibility test

This test was determined quantitatively, in which the effort required to redisperse the sedimented system in a cylinder was evaluated. 5 ml of each suspension was poured into four calibrated tubes, which were stored at room temperature for 5, 10, 15, 20, 25, 30, 35 days at the end of each storage period, each tube was hand shaken at constant moderate rate of 30 shakes to see if the suspension has redispersed.

Statistical analysis

One way analysis of variance (ANOVA) was used to determine if there was significant difference in the sedimentation volume of all the suspending agents investigated. Mean and Standard deviation for values obtained were determined as appropriate.

RESULTS AND DISCUSSIONS

The average yield of dried gum obtained from *A. esculentus* fruit was found to be 16.75 % (w/w). The gum powder obtained was a light brown powder with no taste or odours.

Sedimentation volume

Sedimentation volume is the ratio of the height of the sediment after settling and initial height of suspension. The larger the ratio, the better is the suspendability (Patel et al., 1976). The average sedimentation volume measured for the formulations at different concentration of suspending agents are shown in Table 2 and Figure 1 to 5. The result shows that all the samples settled to form sediments at one time or the other. This is probably due to interaction between the suspended particles which eventually led to generation of energy. This is in conformity with observations of Tabibi and Rhodes (1995) who defined energy of interaction V_T between two particles as

$$V_T = V_R + V_A \qquad (5)$$

Where V_T = Total energy of interaction, V_R = Repulsive forces, V_A= Attractive forces When $V_R > V_A$, there is deflocculation and when $V_A > V_R$, there is flocculation which in either case will eventually lead to sedimentation. Suspension sample produced using okra and the combination of both okra and trona showed a higher sedimentation volume when compared with those prepared using compound tragacanth at all concentrations of prepared samples. Suspension samples containing the combination of okra and trona at concentrations 1, 2, 3, and 4%(w/v), respectively showed only a slight increase in sedimentation volume when compared with those of corresponding concentrations of okra with the exception of those containing 5%(w/v) of the combination of okra and trona, where there is a higher increase in sedimentation volume. Generally, the sedimentation volume of all the formulations were of the order Okra + trona > Okra >Compound Tragacanth

Table 1. Metronidazole suspension formulation.

Ingredients	Quantity prepared														
	Batch 1 (%w/v)					Batch 2 (%w/v)					Batch 3 (%w/v)				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Metronidazole powder (g)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Compound tragacanth (g)	1	2	3	4	5	-	-	-	-	-	-	-	-	-	-
Okra gum powder (g)	-	-	-	-	-	1	2	3	4	5	0.8	1.6	2.4	3.2	4.0
Trona (g)	-	-	-	-	-	-	-	-	-	-	0.2	0.4	0.6	0.8	1
Amaranth solution (ml)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Benzoic acid solution (ml)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Raspberry syrup (ml)	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
Chloroform water double strength (ml)	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
Water for preparation (ml)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total volume (ml)	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

Table 2. Effect of varying concentration of suspending agents on the sedimentation volume of Metronidazole suspension.

Suspending agents	Concentration of suspending agent (%w/v)	Mean sedimentation volume (cm^3)									
		Time (days)									
		0	5	10	15	20	25	30	35	40	45
Compound tragacanth gum	1	1.00	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
	2	1.00	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.10	0.10
	3	1.00	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
	4	1.00	0.14	0.14	0.14	0.13	0.13	0.13	0.13	0.12	0.12
	5	1.00	0.14	0.14	0.14	0.13	0.13	0.13	0.13	0.12	0.12
Okra gum	1	1.00	0.18	0.17	0.17	0.16	0.16	0.16	0.16	0.16	0.16
	2	1.00	0.27	0.27	0.26	0.26	0.25	0.25	0.25	0.25	0.25
	3	1.00	0.36	0.35	0.35	0.35	0.34	0.34	0.33	0.33	0.33
	4	1.00	0.48	0.45	0.45	0.45	0.45	0.43	0.42	0.42	0.41
	5	1.00	0.58	0.53	0.53	0.53	0.53	0.52	0.49	0.48	0.46
Okra and trona in ratio 4:1	1	1.00	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19
	2	1.00	0.29	0.29	0.28	0.28	0.28	0.28	0.28	0.28	0.28
	3	1.00	0.43	0.41	0.39	0.38	0.38	0.38	0.38	0.38	0.38
	4	1.00	0.47	0.43	0.43	0.42	0.42	0.42	0.42	0.42	0.42
	5	1.00	0.77	0.68	0.66	0.65	0.65	0.64	0.64	0.62	0.60

($P<0.05$). This observation could be explained thus, sodium sesquicarbonate (Trona) being acted as flocculating agent by reducing the electrical barrier between the particles, thereby leading to formation of a bridge between adjacent particles linking them together in a loose arranged structure. Okra in the combination formulation however, may be acting in retarding the sedimentation of the floccules so formed by the effect of sodium sesquicarbonate (Trona) behaving as a hydrocolloid suspending agent. As can be observed from Table 2 and Figure 1 to 5 as concentration of the suspending agents increased, the ability to retard sedimentation of floccules increased.

Rheological assessment

The average flow rate of different concentrations of suspension formulation from where shear rate was calculated using equation 3 is presented in Table 3. The

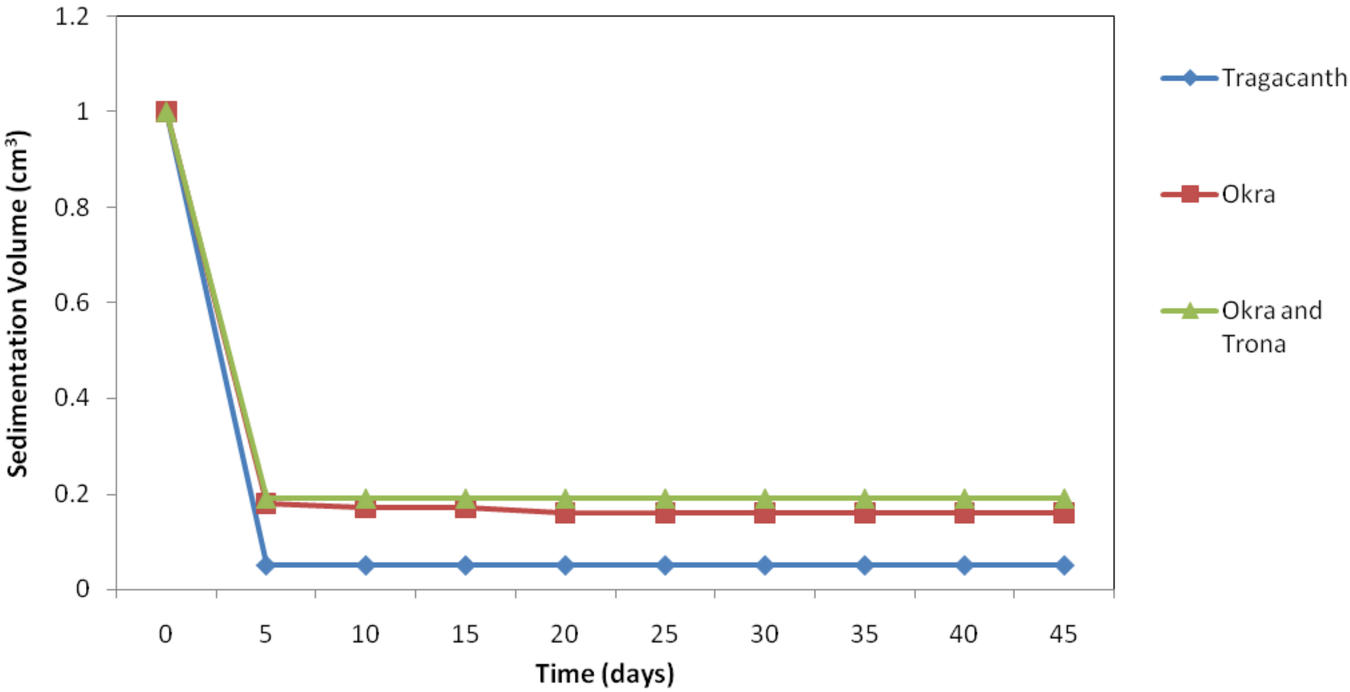

Figure 1. Comparism of sedimentation volume among suspension formulations containing 1% w/v concentration of suspending agents.

Table 3. Effects of varying concentration of suspending agents on the flow rate (ml/sec) and shear rate of Metronidazole suspension.

Suspending agents	Concentration of suspending agent (%w/v)	Mean flow rate (ml/sec)	Shear rate (sec^{-1})
Compound tragacanth gum	1	0.185±0.0001	0.0370
	2	0.035±0.002	0.0070
	3	0.023±0.001	0.0046
	4	0.015±0.001	0.0030
	5	0.013±0.001	0.0026
Okra gum	1	0.100±0.001	0.0200
	2	0.035±0.002	0.0070
	3	0.026±0.001	0.0050
	4	0.019±0.001	0.0040
	5	0	0
Okra and trona in ratio 4:1	1	0.208±0.001	0.0420
	2	0.047±0.001	0.0090
	3	0.027±0.001	0.0050
	4	0	0
	5	0	0

viscosity of these formulations using spindle 2 and 3 are shown in Table 4. Generally, for all formulations, as the flow rate was decreasing along with the increase in concentration of suspending agents, the viscosity was increasing as shown in Tables 3 and 4. For the formulation 5% (w/v) okra gum as suspending agent,

Table 4. Effect of the type and concentration of suspending agent on the viscosity of Metronidazole suspension.

Suspending agents	Concentration of suspending agent (%w/v)	Mean viscosity (Poise)			
		Spindle 2		Spindle 3	
		Spindle speed (revolutions per min)		Spindle speed (revolutions per min)	
		30	60	30	60
Compound tragacanth gum	1	0.38±0.03	0.30±0.01	-	-
	2	2.00±0.15	1.86±0.03	2.05±0.23	1.76±0.01
	3	3.33±0.25	3.06±0.34	3.00±0.29	2.64±0.06
	4	4.15±0.15	3.66±0.27	4.04±0.56	3.70±0.15
	5	4.49±0.23	4.17±0.56	4.17±0.42	3.70±0.12
Okra gum	1	1.39±0.01	1.13±0.001	1.33±0.01	0.92±0.02
	2	4.89±0.62	3.66±0.12	4.68±0.34	3.47±0.06
	3	5.46±0.45	4.07±0.23	5.47±0.23	4.03±0.14
	4	12.06±0.68	8.42±0.34	10.36±0.42	7.27±0.38
	5	20.62±1.12	11.59±0.56	18.38±0.73	12.21±0.98
Combination okra and trona 4:1	1	0.52±0.01	0.43±0.01	0.86±0.01	0.46±0.01
	2	3.39±0.16	2.56±0.17	3.56±0.72	2.63±0.03
	3	7.31±0.97	5.17±0.33	7.51±0.93	5.36±0.09
	4	9.50±0.98	6.75±0.65	9.48±0.94	6.59±0.09
	5	21.64±1.15	11.61±0.71	16.58±0.99	13.41±0.98

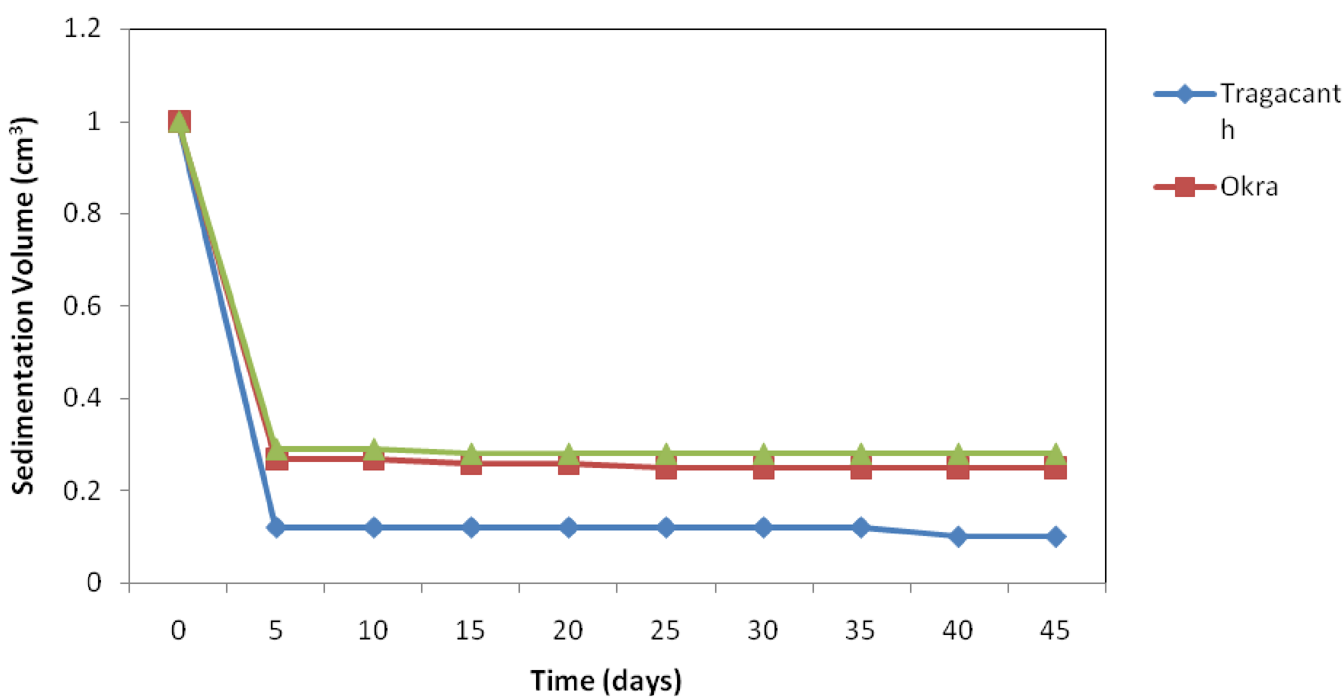

Figure 2. Comparism of sedimentation volume among suspension formulations containing 2% w/v concentration agents.

4%(w/v) and 5%(w/v) respectively for combination of okra gum and Trona (4:1), the viscosities were very high at 30 and 60 revolutions per minutes using spindle 2 and 3 as shown in Table 4. This is so much that the flow rate and shear rate at the stated concentrations above gave zero value as as shown in Table 3. The possible reason

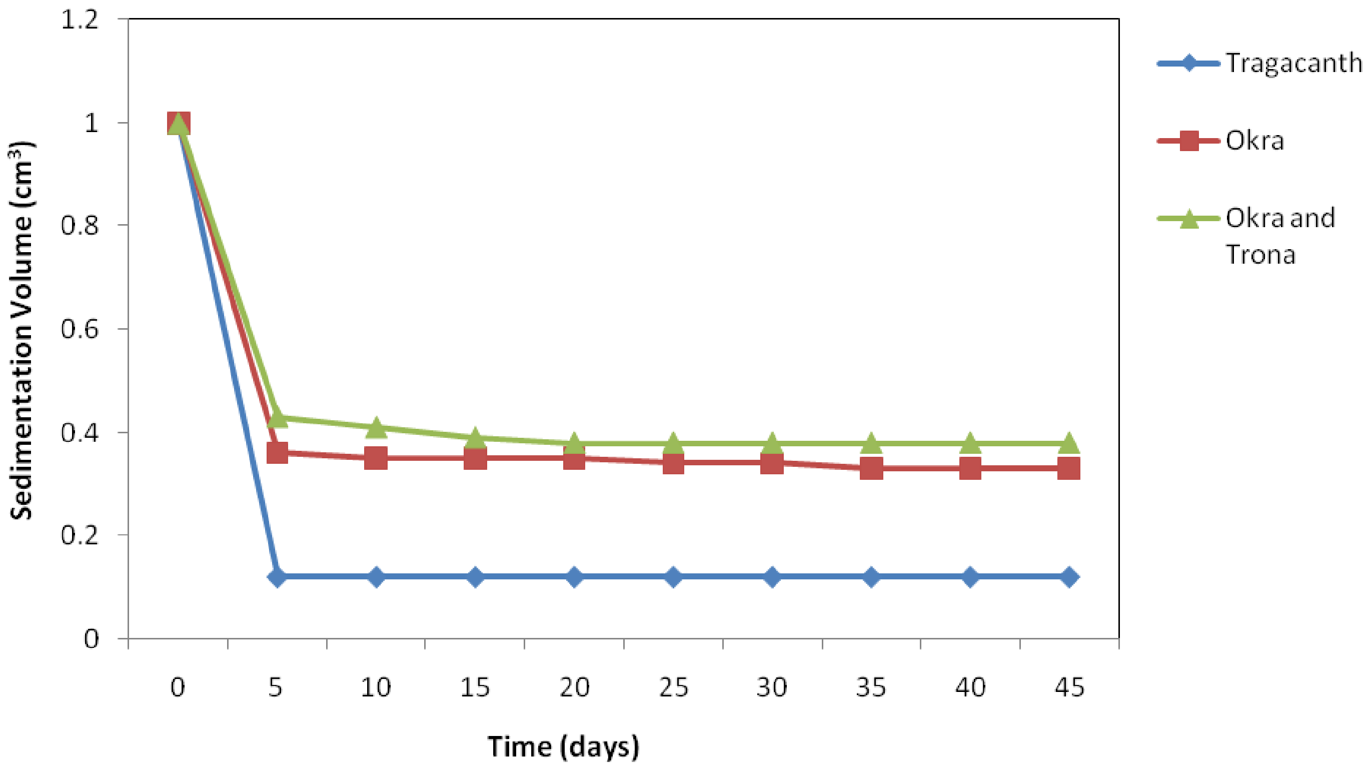

Figure 3. Comparism of sedimentation volume among suspension formulations containing 3% w/v concentrations of suspending agents.

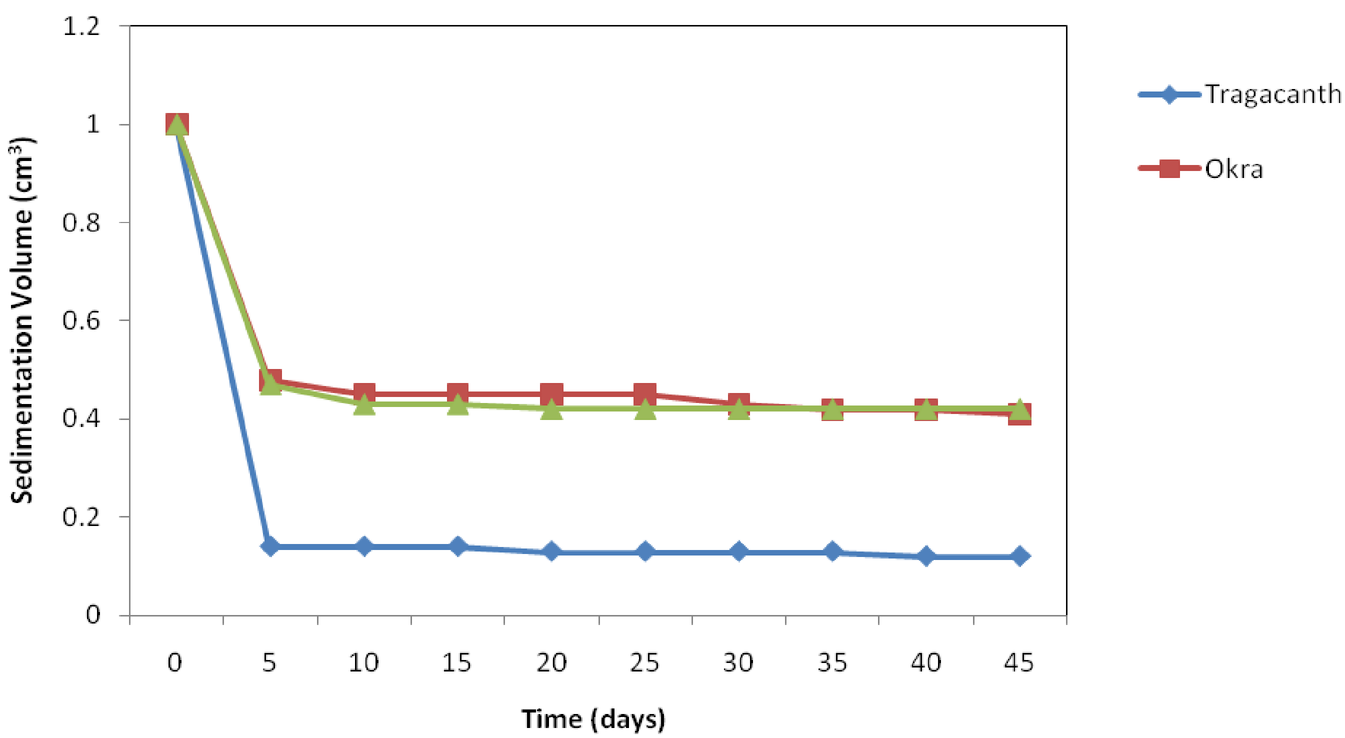

Figure 4. Comparism of sedimentation volume among suspension formulations containing 4% w/v concentrations of suspending agents.

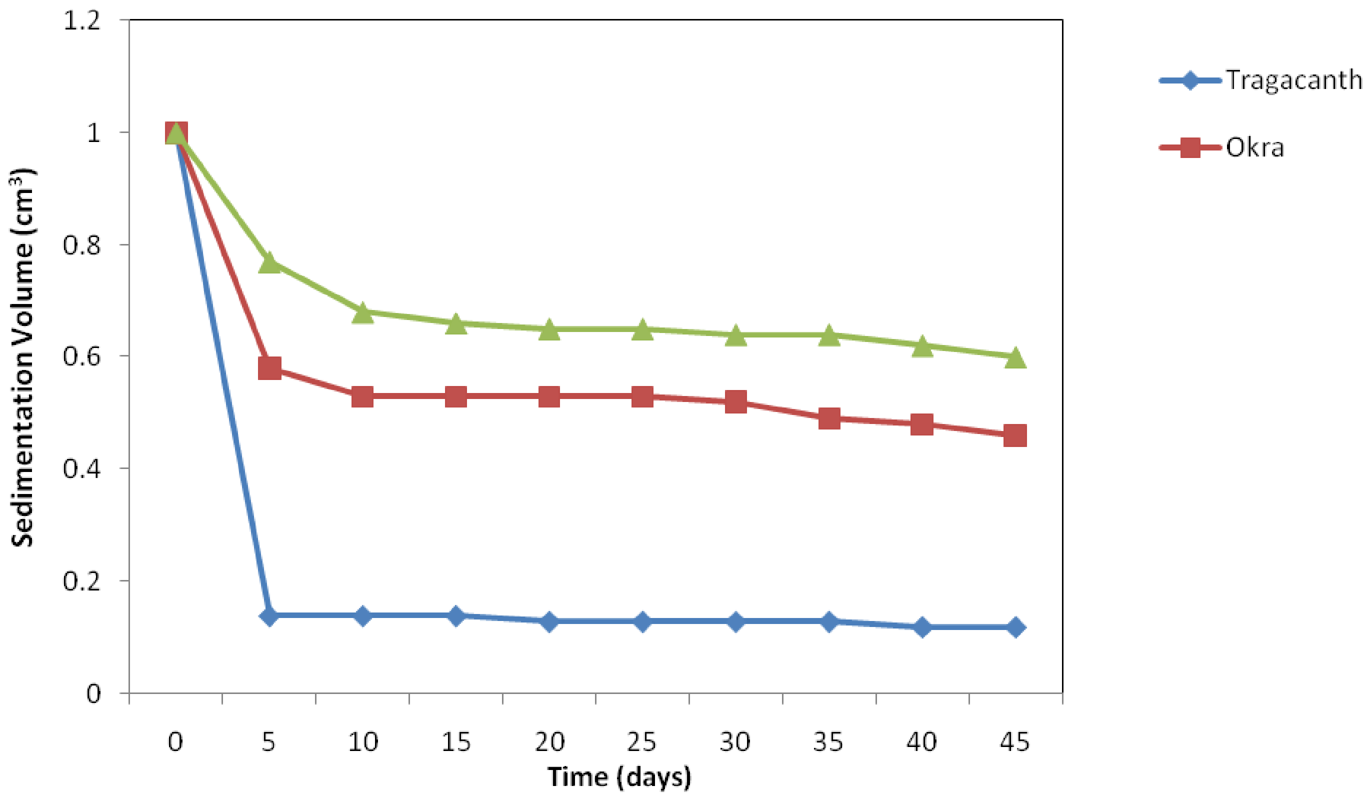

Figure 5. Comparism of sedimentation volume among suspension formulations containing 5% w/v concentrations of suspending agents.

Table 5. Particle size distribution of metronidazole powder.

	Metronidazole powder		
Particle size (μM)	Weight retained (G)	Percentage weight retainded (%)	Cumulative percentage frequency (%)
>1000	1.8	0.9	0.9
>710	2.1	1.05	1.95
>500	4	2	3.95
>355	7	3.5	7.45
>250	96.9	48.45	55.9
>150	39	19.5	75.4
>90	30.3	15.15	90.55
Reciever	18.8	9.45	100

Mean Particle diameter = 379.77μm.

for this observed occurrence is that the degree of flocculation can impede the rheological property of a pharmaceutical formulation. This is because the amount of free continuous phase is reduced as more floccules are formed. The viscosity of the combination of Okra gum and Trona (4:1) at 5% (w/v) was the highest throughout as shown in Table 4. Again the degree of flocculation is possibly responsible for this since it contains an electrolyte flocculating agent as has been explained earlier on. When a disperse system is highly flocculated, the possibility of interactions between floccules increases and structured systems result (Aulton, 1996). If the forces bonding floccules together are capable of withstanding weak stresses, then a yield value will result and below this value, the suspension will behave like a solid that will be difficult to flow, hence the zero flow rate observed for

Table 6. The pH of Metronidazole suspension using varying concentration of suspending agent.

Suspending agents	Concentration of suspending agent (%w/v)	Mean pH				
		Time (days)				
		0	10	20	30	40
Compound tragacanth	1	8.7±0.3	8.1±0.2	6.9±0.1	6.4±0.1	5.9±0.1
	2	9.0±0.5	8.3±0.1	7.5±0.2	7.0±0.3	6.6±0.1
	3	9.3±0.2	8.5±0.2	7.2±0.2	6.9±0.2	6.4±0.1
	4	9.2±0.2	8.2±0.3	7.6±0.1	6.9±0.2	6.7±0.1
	5	9.3±0.3	8.5±0.2	7.9±0.3	6.9±0.1	6.4±0.1
Okra gum	1	8.6±0.2	8.1±0.2	6.7±0.1	6.3±0.1	5.9±0.1
	2	8.7±0.2	8.2±0.2	6.8±0.1	6.2±0.1	6.1±0.1
	3	8.7±0.2	8.0±0.1	6.7±0.1	6.1±0.1	5.8±0.1
	4	8.7±0.2	7.9±0.1	6.5±0.1	6.3±0.1	5.9±0.1
	5	8.9±0.3	8.2±0.2	6.9±0.1	6.1±0.1	5.9±0.1
Okra and trona in ratio 4:1	1	9.3±0.2	8.8±0.2	8.1±0.2	7.6±0.1	7.0±0.1
	2	9.2±0.2	8.6±0.2	8.3±0.2	7.7±0.1	7.0±0.1
	3	10.1±0.3	9.1±0.3	8.2±0.2	7.9±0.1	7.3±0.1
	4	10.3±0.3	9.0±0.3	8.5±0.2	7.9±0.1	7.4±0.1
	5	10.1±0.3	9.3±0.3	8.8±0.2	8.0±0.2	7.4±0.1

this concentration 5%(w/v).

Particle size analysis

The mean particle diameter and the particle size distributions of suspended insoluble drugs are important considerations in formulating physically stable pharmaceutical suspensions. Drug particle size is an important factor influencing product appearance, settling rates, drug solubility, in vivo absorption, resuspendability and overall stability of pharmaceutical suspensions (Nash, 1966). According to stoke's equation,

$$v = \frac{d^2(\rho_1 - \rho_2)g}{18\eta} = \frac{2r^2(\rho_1 - \rho_2)g}{9\eta} \qquad \text{……………… Equation 6}$$

where v is the velocity of sedimentation; d and r are the diameter and radius of the particle respectively; $\rho1$ and $\rho2$ are the densities of the dispersed phase and dispersion medium; g is the acceleration due to gravity; and η is the viscosity of the dispersion medium.

The velocity of sedimentation is directly proportional to the square of the diameter of the suspended particle , this implies that the larger the diameter of the suspended particles the faster such particle sediment thereby, leading to shorter suspending time and ultimately caking, the smaller the particle diameter the slower the sedimentation rate and the longer the suspending time, these results in better suspension as redispersibility is easy and accurate dosage can be withdrawn. The particle size distribution data of metronidazole powder is presented in Table 5, and the size analysis is shown in Figure 6. The figure represents a unimodal frequency distribution. The particle size is in the range of 90 to 1000 µm. The mean diameter for the particle of the powder was calculated and was found to be 379.77 µm. The relatively large size of the suspended particle may be the reason for its initial high rate of sedimentation observed for the first five days of preparation until the terminal settling velocity was reached after which the settling rate remained steady. From Figure 6, it was observed that 7.5% of the metronidazole particles were greater than 250 µm, 68.3 % were less than 250 µm and 24.7 % were less than 90 µm. This shows that the bulk of the

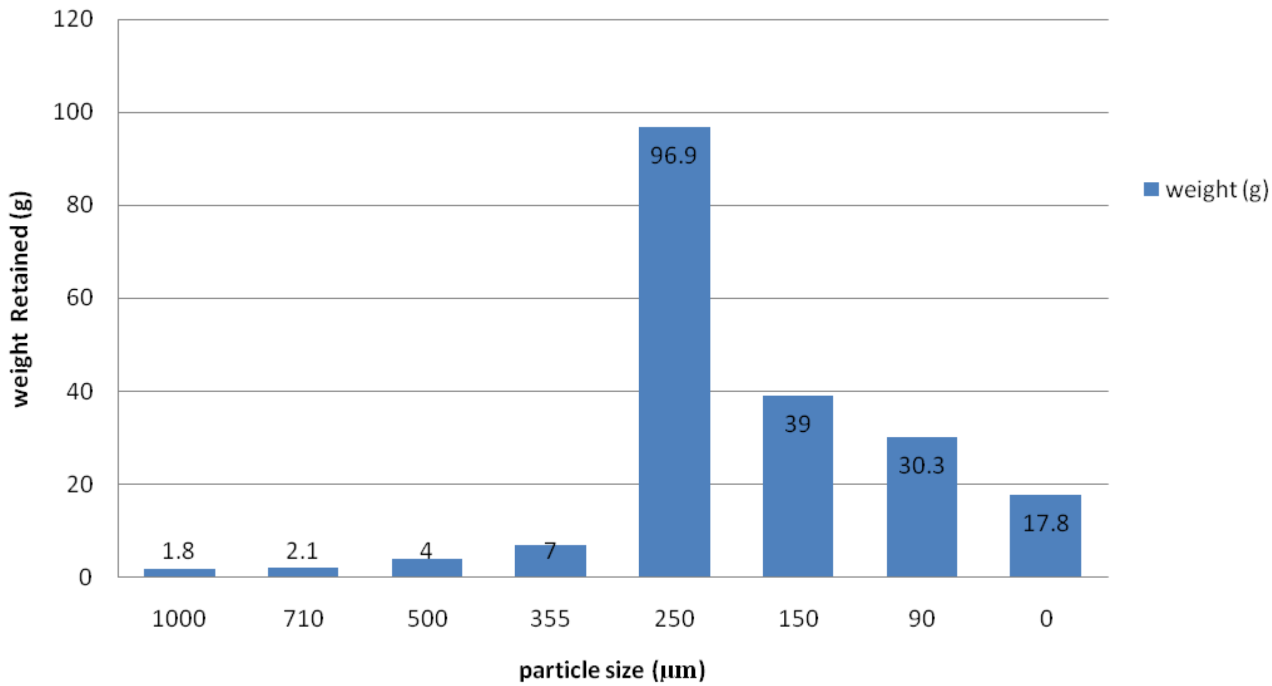

Figure 6. Particle size distribution of metronidazole powder.

size of the particle is less than 250 µm but greater than 90 µm resulting in most of the particles in the formulation being suspended over a longer period of time which reduces greatly the tendency of such formulation to cake, and therefore improves its suspending character.

pH

The pH of all formulations is presented in Table 6. It could be observed that in the first 20 days of the study, pH appears to be in the alkaline to neutral region, as the storage progressed up to 40 days there appear to be a drop in the values of the pH of all formulations tending towards neutral to acidic zone. The change in pH may be a signal to microbial degradation of the polymer suspending agent into constituents like D-galastose, L-rhamnose and L-galactouronic acid. It was also noted that tests formulations containing *A. esculentus* (Okra) and sodium sesquicarbonate (Trona) were found to have the highest pH values throughout the period of study. This is likely to be due to the presence of sodium sesquicarbonate (Trona) that in itself is basic in nature.

Redispersibility

Suspensions tend to settle with time, and therefore, they are designed to be readily redispersed by gentle shaking or stirring, resulting in a homogeneous suspension. Redispersability depends on particle size of the dispersed phase and the nature of suspension formed (floccules, non-floccules or coagule). Since the suspensions produced sediment on storage, it must readily be dispersible so as to ensure the uniformity of the dose. The redispersing ability of the suspendants was shown in Table 7. It was observed that for suspensions prepared using compound tragacanth, the degree of redispersibility reduces as the concentration of the suspending agent increases, inferring that the higher the concentration of the suspending agent the more difficult it would be to redisperse, if the sediments form cake, this was not the case for suspensions produced using okra and those produced using the combination of okra and trona, which showed an increase in the degree of redispersibility as their concentrations increases, inferring that the degree of redispersibility is directly proportional to the concentration of suspending agent used. The observed contrast in the redispersing ability of tragacanth formulated suspension and those formulated using okra and the combination of okra and trona may be attributed to the nature of the suspension formed, since suspensions containing tragacanth formed a deflocculated suspension, they tend to form sediments that eventually cake over time, which are difficult to redisperse, while on the other hand, suspensions

Table 7: Redispersibility of suspensions after shaking 30 times over a period of 30 days.

Suspending agents	Concentration of suspending agent (%w/v)	Redispersibility time (days)					
		5	10	15	20	25	30
Compound tragacanth gum	1	+++	+++	+++	+++	+++	+++
	2	++	++	---	---	---	---
	3	---	---	---	---	---	---
	4	---	---	---	---	---	---
	5	---	---	---	---	---	---
Okra gum	1	+++	++	---	---	---	---
	2	+++	+++	+++	++	---	---
	3	+++	+++	+++	++	++	++
	4	+++	+++	+++	+++	++	++
	5	+++	+++	+++	+++	+++	+++
Combination of okra and trona in ratio 4:1	1	+++	++	+++	+++	++	++
	2	+++	+++	+++	+++	++	+++
	3	+++	+++	+++	++	++	+++
	4	+++	+++	+++	+++	+++	+++
	5	+++	+++	+++	+++	+++	+++

Key + + = re-dispersible with vigorous agitation and stable enough for adequate dose withdrawal, + + + = easily re-dispersed with minimum agitation and stable enough for adequate dose withdrawal, - - - = Not redispersible, formed hard cake.

containing okra and the combination of okra and trona produced a flocculated suspension, which on settling form loose flocs that are easily redispersed on shaking (Lucks et al., 1990). It was also observed that degree of redispersibility decreases as storage time increases for all formulations.

Conclusion

The stability of metronidazole suspension was improved by the addition of the combination of okra and trona in the ratio 4:1, and those formulated with okra alone. The physicochemical properties of the formulations were evaluated. The results showed that the sedimentation volume and viscosity were directly proportional to the concentration of the suspending agents. The reverse case was observed with the flow rate. The present study reveals that metronidazole suspension formulated with the combination of okra and trona and those containing okra alone as suspending agents have better stability indicated by enhancing suspending properties, when compared to the conventional compound tragacanth. On the other hand, metronidazole suspension formulated with the combination of okra and trona showed an observable improvement in its suspending properties when compared with those containing okra alone especially at higher concentrations of okra, inferring that addition of trona improves the suspending property of okra gum. It can therefore, be concluded that addition of trona in concentration ratio of 1:4 to okra gum as suspending agent, influences and impacts a better stability and enhancement of physicochemical properties on the metronidazole suspension especially at higher concentration of okra gum. Therefore, the combination of locally source okra and trona has potential to be used as suspending agent especially in suspensions experiencing caking problem as a result of sedimentation such as metronidazole suspension.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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