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EFFECT OF PARTICLE SIZE OF OKRA GUM AS A SUSPENDING AGENT ON SOME PHYSICOCHEMICAL PROPERTIES OF RECONSTITUTED DRY PARACETAMOL SUSPENSION

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ABSTRACT

Objective: The purpose of this study was to investigate the effect of particle size of okra gum as a suspending agent on the physicochemical properties of oral dry paracetamol suspension. **Materials and Methods:** Batches of pediatric paracetamol (125 mg/ 5 mL) dry suspension powder containing okra gum particles undersize 180, 250 and 355 µm were formulated for reconstitution. Similar batches of paracetamol dry suspension were made using tragacanth gum as a suspending agent to provide a basis for comparison. Some physicochemical properties of the paracetamol suspensions such as sedimentation volume, viscosity, redispersibility, degree of flocculation and dissolution rate profile were evaluated. **Results:** The results showed that the physicochemical properties differed among the batches of the paracetamol dry suspension and were influenced by particle size of the suspending agent. **Discussion:** Although all the samples met the dissolution profile requirements by releasing more than 80 % of the content within 30 minutes, there were obvious differences in the viscosities of the samples that may influence the acceptability and compliance by the patients to therapy. The study showed that particle sizes of okra gum used in the formulations were responsible for the observed characteristics. **Conclusion:** Among the three okra gum samples, particles undersize 180 µm yielded paracetamol suspension with desirable physicochemical properties thus implying that there is an optimum particle size of suspending agents that should be used in a suspension. Therefore, when ascertaining the quality of a dry suspension, particle size of the suspending agent is critical as it affects the physicochemical properties of a suspension.

KEYWORDS: Particle size, Suspending gent, Physicochemical properties, Oral dry suspension, Paracetamol.

INTRODUCTION

Pharmaceutical suspensions are dosage forms where insoluble or sparingly soluble drug is dispersed uniformly in aqueous or non-aqueous continuous phase.[1] Oral pharmaceutical suspensions are convenient to use and are suitable for patients such as geriatrics and pediatrics who have difficulty in swallowing solid medications. Oral suspensions are also used to achieve controlled drug release.[2] In addition, oral dry suspensions are employed to improve stability and increase shelf-life of moisture sensitive drugs.[2]

Pharmaceutical suspensions are thermodynamically unstable due to particle-particle interactions.[1] Therefore, it is important to include suspending agents such as povidone, microcrystalline cellulose, sodium carboxymethylcellulose, acacia, tragacanth, okra gum to increase the viscosity of the disperse medium and reduce sedimentation of the suspended drug particles. Suspending agents allow easy redispersion of the settled drug particles and thus maintain uniform suspension of the drug particles for accurate dosing.[3]

A study has shown that the properties of suspending agent such as concentration, particle size, molecular weight, and hydration rate affect the physicochemical properties of a pharmaceutical suspension.[4] Physicochemical properties of a reconstituted dry suspension are critical to performance of the suspension in terms of withdrawal of correct dose of drug and release of drug in the body. Although dry suspensions may confer better stability on the formulation than a factory reconstituted formulation that might have stayed on the shelves for long before use, it has been demonstrated in some formulations that properties of a suspending agent influence some of the physical properties of the suspension formulation. It is not known how different particle sizes of a suspending agent incorporated in a dry suspension to be reconstituted would affect the profile of the physicochemical properties of the suspension.

The purpose of this work was to study the effect of different particle sizes of okra gum as a suspending agent on the physicochemical properties of pharmaceutical suspensions using paracetamol as a model drug. Oral reconstitutable paracetamol suspension was formulated and the effect of particle size of a suspending agent on viscosity, dissolution and sedimentation volume of the reconstituted suspension was evaluated.

MATERIALS AND METHODS

Materials

Okra gum (extracted), Tragacanth gum (Lab Tech Chemicals), Paracetamol powder (A.H.A International Co. Ltd, Batch No. Y142870). All chemical and reagents used were of analytical grade.

Methods

Collection and Identification of Okra Plant Pods

Okra pods were obtained from Faringada market at Jos, Plateau State in September, 2018. Whole okra plant with pods was taken to a botanist at the College of Forestry, Jos for identification and the herbarium voucher number was FHJ 241.

Extraction of Okra Gum

Fresh Okra pods were washed with purified water, sliced, air-dried in the laboratory and weighed. The dried sliced okra was macerated in cold water for 24 hours to extract the mucilage and the dispersion was separated from the chaff using a muslin cloth. The mucilage was centrifuged (Centrifuge, Mistral 1000, UK) at 4500 rpm for ten minutes and then treated severally with 96% ethanol to precipitate the gum. The gum was air dried, pulverized, weighed and packaged in a well-closed container for subsequent use.[5] The percentage yield of the gum from dried okra was calculated using equation.

$$\text{Percentage yield} = \frac{\text{Mass of dry okra gum x 100 \%}}{\text{Mass of dry sliced okra pods}} \quad \text{(Equation 1)}$$

The powdered okra gum was passed through a nest of three sieves (sieve size 355 µm, 250 µm and 180 µm) to separate it into fractions of different particle size distribution. The sieves were shaken for ten minutes and particle size distribution of undersize 180, 250 and 355 µm. Tragacanth gum was treated in similar way and used for comparison.

Preparation of Oral Reconstitutable Paracetamol Suspension

A paracetamol suspension to deliver a dose of 125 mg/5 mL was formulated using 0.6% w/v of suspending agent particles undersize 180, 250, and 355 µm. Desired quantities of paracetamol powder and excipient powders (Table 1) were finely ground, screened through a sieve of undersize 180 µm and weighed. Sodium lauryl sulphate and sodium citrate were uniformly mixed. To the mix, sodium benzoate was added and mixed to form a uniform mix. Gum powder was added to mix and mixed gently using a spatula. Paracetamol powder was

added to the mix and mixed to form a blend of dry powder suspension.[6] Mixing of the powders was done gently using a spatula in a mortar to avoid modification of the okra powder particle size. Six batches of the suspension (S1-S6) were prepared using the three samples of okra gum and tragacanth gum. Batch S1 contains okra gum undersize 180 µm, S2 contains okra gum undersize 250 µm, S3 contains okra gum undersize 355 µm, S4 contains tragacanth gum undersize 180 µm, S5 contains tragacanth gum undersize 250 µm, and S6 contains tragacanth gum undersize 355 µm. The components of the oral reconstitutable suspensions are shown in the Table 1.

Table 1: Formulation components of oral reconstitutable paracetamol suspension containing different particle sizes of suspending agents.

Ingredient	Batches					
	S1	**S2**	**S3**	**S4**	**S5**	**S6**
Paracetamol (% w/v)	2.5	2.5	2.5	2.5	2.5	2.5
Okra gum powder (% w/v)	0.6	0.6	0.6	-	-	-
Tragacanth gum (% w/v)	-	-	-	0.6	0.6	0.6
Sodium benzoate (% w/v)	0.5	0.5	0.5	0.5	0.5	0.5
Sodium citrate (% w/v)	0.5	0.5	0.5	0.5	0.5	0.5
Sodium lauryl sulphate (% w/v)	0.02	0.02	0.02	0.02	0.02	0.02

Reconstitution of the Dry Suspension

A 46 mL of distilled water was added to the powder in the bottle and the cap was replaced. The constituents of the bottle were shaken until there was uniform dispersion. The displacement volume was 4 mL.

Evaluation of the Reconstituted Paracetamol Suspensions

Sedimentation volume

Each batch of the reconstituted paracetamol suspension was shaken vigorously to form a uniform dispersion and 50 mL transferred to a measuring cylinder and the volume (H_u) occupied by the suspensions was recorded. The measuring cylinders were left to stand on a vibration free stand and the volume (H_o) occupied by the solid in the measuring cylinder below the supernatant at 5 min, 10 min, 15 min, 20 min, 30 min, and 1 hour was recorded. The sedimentation volume (F) was determined using equation;[7]

$$F = \frac{H_u}{H_o} \qquad \text{(Equation 2)}$$

Where F is the sedimentation volume, H_u is final volume of sediment and H_o is the original volume of the suspension. The sedimentation rate was calculated from a plot of sediment height against time.

Redispersibility

Each batch of the reconstituted paracetamol suspension was shaken vigorously to form a uniform dispersion and 50 mL transferred to a measuring cylinder. The suspensions were left to stand for fourteen days to form a sediment. Redispersibility was determined by gently inverting the suspensions and the number of inversions required to disperse the particles to form a uniform suspension were recorded.[3]

Degree of flocculation

Each batch of the reconstituted paracetamol suspension was shaken vigorously to form a uniform dispersion and 50 ml transferred to a measuring cylinder. The suspensions were left to stand for fourteen days to form a sediment. The volumes of the sediments (Vu) were recorded. A similar reconstituted suspension without suspending agent also was left to stand for fourteen days and the volume (V∞) of its sediment was recorded. The degree of flocculation (β) was calculated using equation.[3]

$$\text{Degree of flocculation } (\beta) = \frac{Vu}{V\infty} \quad \text{(Equation 3)}$$

Where Vu is the ultimate sediment volume of the flocculated suspension and V∞ is the ultimate sediment volume of the deflocculated suspension.

Viscosity

Viscosity of each batch of the paracetamol suspension was determined at 1 min, 5 min, 10 min, 15 min, 20 min, 30 min and 60 min using a digital viscometer (model NDJ-1S, Shandong, China) at 30 rpm. A 50 mL of each formulation was transferred into the viscometer cup and after one minute, viscosity was determined using rotor 3 spindle.[7]

Dissolution rate profile

The dissolution rate was carried out using the BP apparatus II (Hanson Research SR6 dissolution tester) in 900 mL phosphate buffer at pH of 6.8 for sixty minutes at 37 $\pm$ 0.5^0C and 25 rpm. A 5 mL of each batch of the reconstituted suspension equivalent to 125 mg of paracetamol was introduced careful into the bottom of the apparatus using a 5 mL syringe. Samples of 5 mL were drawn at specified intervals for analysis and were replenished by an equivalent amount of the phosphate buffer. The samples were filtered, diluted with phosphate

buffer and absorbance measured using UV spectrophotometer (Metertech SP-8001, Taiwan) at 245 nm.[6] All results were made in duplicate and were expressed as mean values.

RESULTS

Some Physicochemical Properties of Reconstituted Paracetamol Suspension

Sedimentation volume and rate

Figure 1 shows the results of the sedimentation volume ratio of formulations of paracetamol prepared with three samples of okra gum and tragacanth gum. There was rapid settling within the first ten (10) minutes after which it became gradual and almost no observable settling noticed after thirty (30) minutes. Formulations containing okra gum undersize 355 µm and tragacanth undersize 180 µm showed the fastest settling rate and slowest settling rate respectively. Generally, formulations containing smaller particle size (undersize 180 µm) of the gums exhibited high sedimentation volume and low sedimentation rate.

Redispersibility

Table 2 shows the number of inversions required to achieve redispersibility of sedimented batches of paracetamol suspensions containing different particle sizes of okra and tragacanth gums as suspending agents over a period of two weeks. Formulations containing gums with particle size of undersize 180 µm yielded suspensions that were easily redispersed as indicated by lowest number of inversions. Generally, the number of inversions increased as the particle size of the gum increased with particle size of undersize 355 µm having the highest number of inversions.

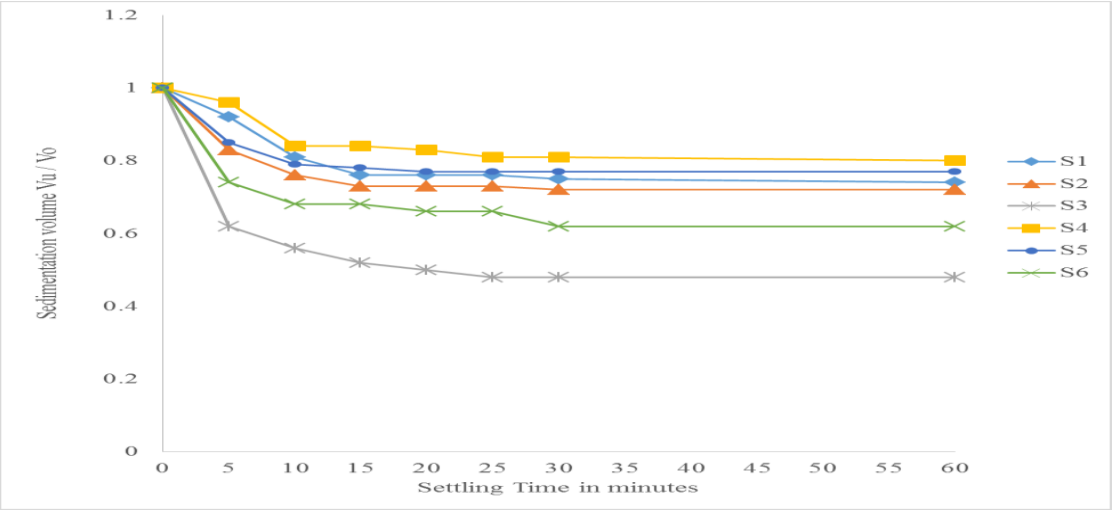

Figure 1: Sedimentation volume of paracetamol suspensions containing suspending agents of different particle sizes.

Table 2: Redispersibility of samples of paracetamol pediatric suspensions.

Formulation	Number of inversions required for dispersion
S1	7
S2	9
S3	10
S4	11
S5	14
S6	13

Degree of flocculation

The flocculation behavior of the paracetamol suspension formulations containing the three samples of okra and tragacanth gums over a period of two weeks was shown on Table 3. Among the three samples, formulations containing gums with particle size of under 180 µm yielded suspensions with higher degree of flocculation. Generally, the degree of flocculation increased as the particle size of the gum decreased. The suspension formulations containing tragacanth gum had higher degree of flocculation as compared to those with okra gum.

Table 3: Degree of flocculation of samples of paracetamol pediatric suspensions.

Formulation	Degree of flocculation
S1	8.5
S2	7
S3	6
S4	14.5
S5	13
S6	11

Viscosity profile

Figure 3 shows the viscosity profile of paracetamol suspensions containing the three samples of okra and tragacanth gums as suspending agents. It was observed that one minute after reconstitution, the viscosity of five formulations was less than 100 mpa.s except for the suspension formulation containing tragacanth gum of particle size of undersize 180 µm which had a viscosity of 550 mpa.s. The paracetamol suspension formulations containing okra fractions and tragacanth undersize 180 µm had gradual increase in viscosity and remained relatively stable towards the end of the one hour period while viscosity of formulations containing tragacanth undersize 250 µm and undersize 355 µm increased rapidly from 44 mpa.s to 1261 mpa.s within the one hour period.

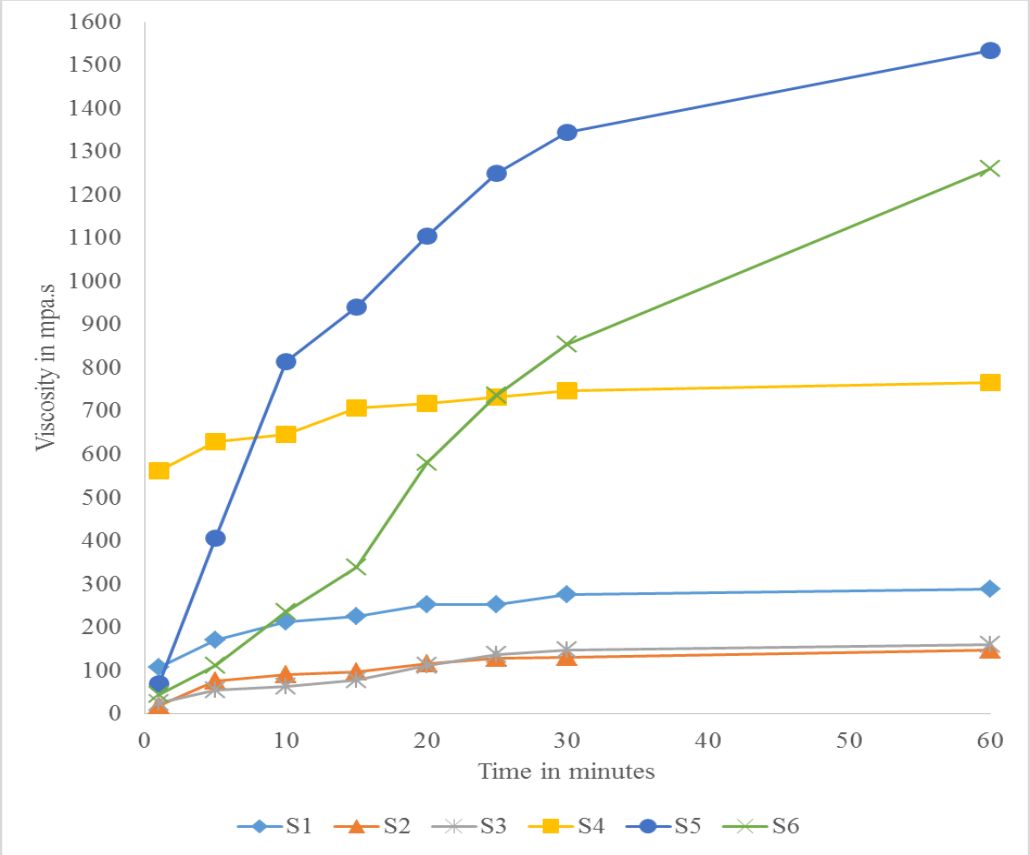

Figure 2: Viscosity profiles of batches of paracetamol suspensions containing suspending agents of different particle sizes.

Dissolution rate profile

The drug release profiles of the suspension formulations containing the three samples of okra and tragacanth gums were shown in Figure 4. It was observed that within thirty (30) minutes, all suspensions had released more than 90% of the drug content. The suspension formulation containing okra gum of particles of undersize 180 µm had the highest cumulative release of 98.7% of the drug. The suspension formulation containing tragacanth gum of particles of undersize 355 µm had the lowest cumulative release 92.8% of the drug. It took 2-4 minutes for the suspension formulations to release 50% of the drug and 6-10 minutes for the suspension formulations to release 80% of the drug content.

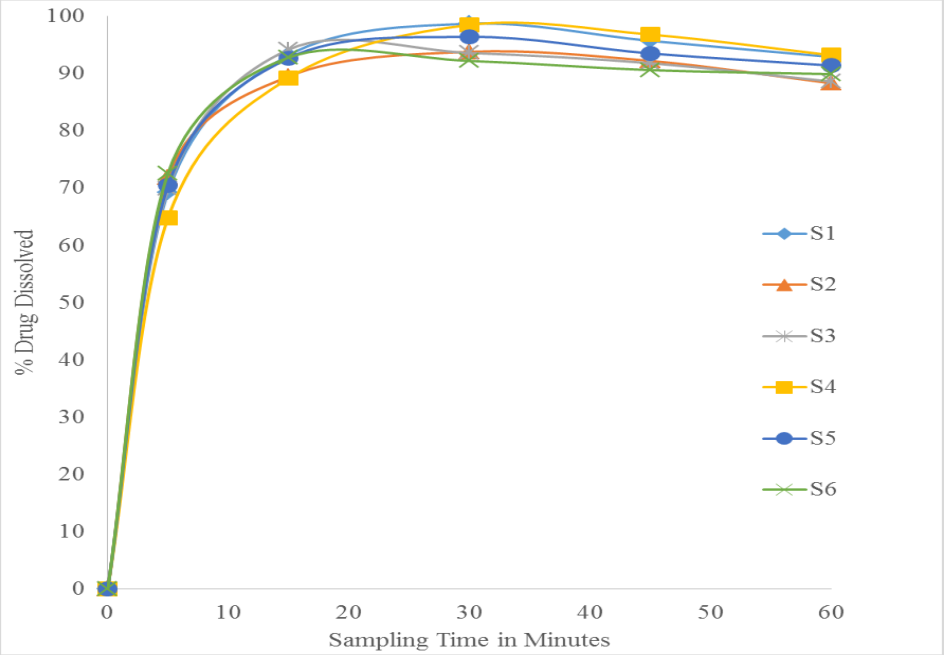

Figure 3: Dissolution rate profiles of batches of paracetamol suspensions containing suspending agents of different particle sizes.

DISCUSSION

All suspension formulations settled down to a differing extent. The sedimentation volume at five minutes was 0.92, 0.83 and 0.62 for batches of paracetamol suspension containing okra gum particles of undersize 180, 250 and 355 µm respectively. The same formulations except for the difference in the sizes of the okra gum having different sedimentation volume means that the sedimentation volume of a suspension is affected by the particle size of the gum all other things being equal. This means that particle size of the gum should not be taken for granted in ascertaining the quality of a dry suspension formulation as demonstrated by this result.

It was also noted that the sedimentation volume depended on the type of gum used as tragacanth at the same particle size had different effect on the suspension than okra gum as suspending agent. Rapid settling within the first ten minutes was possibly due to inadequate viscosity of the suspensions which offered less resistance to movement of the dispersed drug particles.[8] Generally, the sedimentation volume of all suspensions were of the order tragacanth undersize 180 µm > okra undersize 180 µm > tragacanth undersize 250 µm > okra undersize 250 µm > tragacanth undersize 355 µm > okra undersize 355 µm.

The sedimentation volume was inversely related to particle size of the suspending agent. This was probably do to the fast dispersion of the smaller particles and acting fast enough to suspend the paracetamol particles in the dispersion while the larger particles required more time to do so. This would also mean that over time, the sedimentation volume profile should be similar for all the sizes.

The paracetamol suspensions settled over time and it was important that the ease of redispersibility was assessed by counting number of gentle inversions required to form homogeneous suspensions. Paracetamol suspensions containing suspending agents with particles undersize 180 µm were easily redispersed and this was possibly due to their high sedimentation volume. Paracetamol suspensions containing suspending agents with particles undersize 355 µm had highest number of inversions possibly due to their low sedimentation volume and formation of a hard sediment that required more inversions to completely redisperse the drug particles. This observation indicated that ease of redispersibility was sensitive to particle size of the suspending agent. In addition, paracetamol suspensions containing tragacanth gum particles undersize 250 µm and 355 µm formed more viscous dispersions overtime thus made it a little bit difficult to resuspend the drug particles with minimal agitation.

Number of inversions were lowest with paracetamol suspensions containing suspending agents with particles undersize 180 µm and increased as particle size of the suspending agents increased. Generally, suspensions containing okra gum had slightly lower number of inversions because the suspensions were less viscous than suspensions containing tragacanth gum at the same concentration of suspending agent. Ease of redispersion of all suspensions were of the order okra undersize 180 µm > okra undersize 250 µm > okra undersize 355 µm > tragacanth undersize 180 µm > tragacanth undersize 250 µm > tragacanth undersize 355 µm.

Paracetamol suspensions containing suspending agents with particles undersize 180 µm had highest degree of flocculation because they had the highest sedimentation volume. Suspending agents with particles undersize 180 µm were able to quickly form viscous suspension within the first few minutes after reconstitution. As viscosity of the suspensions increased, the terminal settling velocity decreased and the dispersed drug particles settled at a slower rate and remained dispersed for a longer time yielding paracetamol suspensions with higher degree of flocculation. Suspending agents of particles undersize 355 µm hydrated

slowly forming inadequate initial viscosity resulting to low sedimentation volumes and thus low degree of flocculation implying that the suspensions were less stable.

The viscosity at five minutes was 171 mpa.s, 77mpa.s, and 54 mpa.s for paracetamol suspensions containing okra gum particles of undersize 180, 250 and 355 µm respectively. The same formulations except for the difference in the sizes of the okra gum having different viscosities means that the viscosity of a suspension is affected by the particle size of the gum all other things being equal. This means that particle size of the gum should not be taken for granted in ascertaining the quality of a dry suspension formulation as demonstrated by this result. Viscosity is important for both patient's acceptance of a product, its easy of withdrawal from the container and packaging and should be considered as part of the quality attributes of a suspension.

Viscosity of the suspensions increased over time as the suspending agents particles continued to hydrate and swell. Different particle sizes of gums had different rates of hydration and swelling thereby resulting in different viscosities. Paracetamol suspensions containing gum particles undersize 180 µm had gradual change in viscosity and viscosity remained relatively constant towards the end of the one hour period. This is an important attribute for reconstitutable suspensions where it is desirable to achieve a steady viscosity for ease of administration.

The percent of drug dissolved by the samples at thirty minutes was 98.7%, 93.8% and 93.6% for paracetamol suspensions containing okra gum particles of undersize 180, 250, and 355 µm respectively. Paracetamol suspensions containing suspending agents with particles of undersize 355 µm were less viscous and the drug dissolved quickly compared to paracetamol suspensions containing suspending agents with particles of undersize 180 µm which were more viscous and the drug dissolved at a slower rate. All suspensions had released more than 90% of the drug at thirty minutes. Although there is no official specifications for the amount of drug to be released from a suspension at specified time, releasing more than 90% of the drug at thirty minutes is very satisfactory. Conventional tablets that can release 84% of the active pharmaceutical ingredient into the dissolution medium within 40 minutes pass the USP requirements.

CONCLUSSION

Oral reconstitutable paracetamol suspensions containing different particle sizes of okra gum and tragacanth gum as suspending agents were formulated successfully. The evaluated physicochemical properties were characteristic of the type and particle size of the suspending agent used. The same formulations except for the difference in the sizes of the okra gum having different physicochemical properties means that the physicochemical properties of a suspension are affected by the particle size of the gum all other things being equal. There was a trend that smaller particle size of a suspending agent yielded suspensions with better profile of physicochemical properties irrespective of the suspending agent used. The results implies that when formulating a dry suspension, particle size of the suspending agent is critical as it affects the physicochemical properties of the suspension.

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REFERENCES

1. Gbenga LB, Oluwabunmi A. Suspending properties of natural gums extracted from *Abelmoschus esculentus* pod and *Chrysophyllum albidium* fruit. African Journal of Pharmacy and Pharmacology, 2015; 9(10): 321-326.
2. Kundu S, Patil VA, Srinivasan G, Borkar N. Controlled release suspension: A Review. International Journal of Pharmaceutical Innovations, 2012; 2(4): 1-18.
3. Kadiri JO, Okafor I.S. Evaluation of the suspending property of grewia gum in metronidazole suspension. Nigerian Journal of Pharmaceutical Research, 2010; 8(1): 247-254.
4. Venugopal NK, Abhilash M. Study of hydration kinetics and rheological behavior of guar gum. International Journal of Pharma Sciences and Research (IJPSR), 2010; 1(1): 28-39.
5. Farooq U, Malviya R, Sharma KP. Extraction and characterization of okra mucilage as pharmaceutical excipient. Academic Journal of Plant Sciences, 2013; 6(4): 168-172.
6. Venkateswarlu K, Chnadrasekhar KB, Ramachandra R. Development and in-vitro evaluation of reconstitutable suspension of flucloxacillin. Marmara Pharmaceutical Journal, 2016; 20(3): 280-287.
7. Ogaji IJ, Omachi J, and Iranloye T. Effect of *Adansonia digitata* gum on some physicochemical properties of paracetamol pediatric suspension

formulations. International Journal of Research in Pharmacy and Science, 2012; 2(2): 75-83.

8. Ogaji IJ, and Hoag WS. Effect of grewia gum as a suspending agent on ibuprofen pediatric formulation. American Association of Pharmaceutical Scientists Pharm Sci Tech, 2011; 12(2): 507-513.