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Research Article

Effect of Grewia Gum as a Suspending Agent on Ibuprofen Pediatric Formulation

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Abstract. The purpose of this work was to evaluate the potential of grewia gum (GG) as a suspending agent in pharmaceutical oral formulation using ibuprofen as model drug. Ibuprofen pediatric suspension (25 mg/5 mL) was formulated with grewia gum (0.5% *w/v*) as the suspending agent. Similar suspensions of Ibuprofen containing either sodium carboxymethylcellulose (Na-CMC) or hydroxymethylpropylcellulose (HPMC) were also produced. The suspensions were evaluated for ease of redispersion, sedimentation, rheological properties, and the effect of aging on the rheological properties at 25°C. The particle size and particle size distributions of the dispersed solute were determined. The redispersion time was 19, 11, and 0.5 min, respectively, for formulation containing Na-CMC, HPMC, and GG .The sedimentation volumes were 0.05, 0.05, and 0.125 mL, respectively, for Na-CMC, HPMC, and GG . Viscosities of suspensions at spindle speed of 25 rpm were of the order: GG>HPMC>Na-CMC when freshly prepared and of the order: HPMC>GG>Na-CMC within 6 months of storage. The particles size was 72.72, 73.82, 81.93, and 83.41 μm, respectively, for suspensions containing Na-CMC, ibuprofen alone, HPMC, and GG. Greatest hysteresis was observed in formulation containing HPMC. All the formulations were stable. It was our conclusion that the difference in the physicochemical properties of ibuprofen pediatric formulations was influenced more by the suspending agent used in the formulations than the drug. GG combined better redispersion with minimal changes in viscosity on storage compared to Na-CMC and HPMC as suspending agent. Thus GG may serve as a good suspending agent requiring no further aid in suspension redispersibility.

KEY WORDS: grewia gum; oral pharmaceutical formulations; physicochemical properties; potential suspending agent.

INTRODUCTION

Non-adherence to medications can lead to unsuccessful therapy, prolonged treatment course, and increased healthcare cost. For pediatric patients, the ease of medication administration and the palatability of medications are important determinants for adherence to a treatment regimen (1,2). Majority of the medications used in pediatric patients are not labeled for pediatric use. As a result, there is a lack of dosage formulations appropriate for use in pediatric patients and clinicians often have to rely on adult formulations such as tablets and capsules. However, younger pediatric patients are either not willing or unable to swallow these dosage forms (3). Furthermore, these dosage forms do not provide adequate flexibility in dosing for the pediatric patient. Most medications used in pediatric patients are dosed based on their body weight or body surface area. Oral liquid formulations are, therefore, preferred due to their flexibility in dosing (4). An oral liquid formulation may be a solution or a suspension (5). In pharmaceutical solution preparations, the solute is dissolved in the solvent to form a homogenous one-phase system; while in suspensions, the solute is dispersed in a continuous medium. In both formulations, water is the most widely used vehicle. This is not surprising since it is a physiological fluid of the human body (5).

If the drug is insoluble or poorly soluble in a suitable solvent then formulation of suspension is usually required. In preclinical studies, poorly soluble drugs are usually administered orally to experimental animals as suspensions (6). The challenge of suspension formulation concerns sedimentation, caking, and resuspension (5). A suspension should not settle rapidly, it should be sufficiently fluid to flow easily under the condition of administration. As a suspension is energetically unstable, the particles that have settled tend to interact to form a cake or hard crystalline network. It is required that suspensions are formulated such that caking is minimized and so that the particles that have settled may be readily redispersed upon shaking (5). In a pharmaceutical suspension, a suspending agent helps the drug stay suspended thereby reducing caking at the bottom of the preparation. Consistency of the solute throughout the suspending medium is facilitated with the drug or solute staying suspended in the continuous phase, with the benefit that consistent withdrawal

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of uniform doses is possible. One of the properties of a well-formulated suspension is that it should easily be resuspended by the use of moderate agitation. A good suspension should allow for easy withdrawal of uniform and accurate doses throughout the period of medication. Sodium carboxymethylcellulose is commonly used as suspending agent in the pharmaceutical industry (7). Some natural polymers have found uses as suspending agents (8–18), as binders and sustained-release matrix in tablet formulations (19–24), as film coating agent (25), thickeners in cosmetics, and in food (26).The research into and use of natural materials in pharmaceutical formulations, particularly in developing countries will continue to be relevant because of local accessibility, natural abundance, cost effectiveness, and eco-friendliness compared to synthetic and semi-synthetic excipients.

Grewia gum is a polysaccharide derived from the inner stem bark of the edible plant *Grewia mollis*, Juss (family Tiliaceae). The plant is a savanna shrub that grows wildly but is usually cultivated (27). The leaves and bark of the plant contain mucilage (28). In Nigeria, the dried and pulverized inner stem bark is used as a thickening agent in some local dishes (29). The binding effect of *Grewia mollis* gum has been investigated on salicylic acid as a model drug. It was demonstrated that grewia gum has a good binding property (30). Some scientists (31) also investigated the effect of the gum on the mechanical properties of paracetamol tablet formulation using the density measurements and compression equations of Heckel and Kawakita as assessment parameters. Grewia gum was found to improve the fluidity of paracetamol granulation compared to polyvinylpyrrolidone. Okafor and Chukwu (32) found that the gum might find application in film coating of tablets, capsules, and granules. Recent work on the gum proved that the gum is a good film coating agent for core tablets that may be soft, bitter, or have objectionable odor and or taste and need to be masked with minimal or no effects on the tablets physicochemical properties (33).

Until this time, no report of the effect of grewia gum as a suspending agent has been found in literatures. It has been shown that the type of suspending agents rather than the physical characteristics of the drug appear to have the main influence on the physical stability of suspensions (6). The purpose of this work was to study the effect of grewia gum as a suspending agent on ibuprofen pediatric formulation in comparison to commercial analog sodium carboxymethylcellulose and hydroxymethylpropylcellulose. Ibuprofen was chosen as a useful non-steroidal anti-inflammatory agent that its formulation as a suspension could be beneficial in children that cannot swallow tablets.

MATERIALS AND METHOD

Ibuprofen (IB100 lot SE 0196, Spectrum Chemicals, NJ, US), Hydroxypropylmethylcellulose K100M, sodium carboxymethylcellulose (lot 93627 type 7MF PH, Passaic, NJ, Hercules), sodium lauryl sulphate (Spectrum Chemicals, Gardena, CA, USA).Grewia gum powder was procured from Jos main market, Nigeria.

Extraction of Grewia Gum

The extraction method developed by Ogaji (34) in our laboratory was used. Briefly, a 100 g gum was dispersed in 2 L Millipore water and was heated at 80°C for 1 h in the presence of 10 g sodium chloride. The dispersion was allowed to stand for 24 h and the supernatant was decanted. The supernatant was centrifuged at 3,445 rpm for 30 min. The gum was extracted from the mucilage with the aid of ethanol 96%. The extraction process was repeated until a whitish gum was obtained. The gum was dried in the oven at 50°C for 24 h to obtain a loss of drying of 2.8%.

Suspension

A pediatric ibuprofen suspension to deliver a dose of 25 mg/5 mL was formulated. A 5.0 g powder of the grewia gum (GG) to give 0.5% *w/v* was weighed and dispersed in 500 mL of demineralized water and allowed to stand for 12 h. Ibuprofen powder was sifted through sieve 45 and dispersed in about 200 mL of demineralized water, premixed with sodium lauryl sulphate as the wetting agent. The dispersed ibuprofen suspension was transferred to the bulk mixture and the content was mixed together using Lightnin® 316 stainless steel high efficiency axial flow impeller (Lightin®, model LIOU8, NJ, USA) for 30 min to ensure uniform mix. The volume was made up to 1,000 mL with demineralized water. The pH of the suspension was adjusted to 5–5.0 with citric acid monohydrate. Two replicate of ibuprofen suspensions were prepared, each containing 0.5% *w/v* of hydroxymethyl propyl cellulose (HPMC) and sodium carboxymethylcellulose (Na-CMC) as suspending agents.

Rheological Evaluation

A 600 mL of the suspension was transferred to 1,000-mL beaker and this portion was used for rheological studies. The viscosity of the suspension was determined using Brookfield DV-III+Digital Rheometer interfaced with Rheocal software (Brookfield Engineering, Mildborro, MA, USA) using vane RV2 spindle at eight variable speeds of 25, 50, 75,100,125,150, 200, and 250 rpm at 0.5-, 1- and 4-min interval. Viscosity, torque, and shear stress of the suspension as the average of five determinations were assessed within 24 h (D1) and 48 h (D2) of preparation. Subsequently, the evaluation was carried out every other week for 6 months. To also understand the elastic hysteresis of the materials the rheological evaluation was carried out at different shear rates (0–250 rpm) and intervals (0.5, 1, and 4 min). The results are the average of five determinations at 25°C.

Sedimentation Volume

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 noted as the volume occupied by the dispersed solids. A change in sedimentation volume was recorded daily until there was no visible change in volume in any of the samples. The results are the average of three determinations.

Time to Redisperse Study

The ease of redispersibility of the suspensions was quantitatively evaluated using a method devised in our laboratory. A 600 mL of the suspension was transferred to a 1,000 mL measuring cylinder and the suspension was allowed to stand for 24 h for sedimentation to take place. The Ligtnin® mixer was gently lowered into the suspension on a leveled surface. The mixer blade base was immersed and positioned at the center of the suspension at all times. The position of the base of the blade was maintained at 6.5 cm above the base of the suspension. The suspension was agitated at 500 rpm for 30 s. After each agitation, visual examination of the suspension was made to identify particles that were not dispersed. The exercise continued until there were no visible lumps at the base of the suspension. The time taken before the sediment was completely redispersed was calculated from the number of agitations required to achieve the redispersion. The displayed result was the average of determinations on four samples and was taken as the redispersion time.

Photomicrograph

A drop of the suspension was smeared on a microscope slide and viewed on the Nikkon eclipse microscope (model ME 600, Nikkon, Melville, NY, USA) fitted with Linksystem software. The live image was captured on the computer LCD.

Particle Size and Size Distribution

Standard bench laser diffraction instrument (Model: mastersizer®S.v2.18, Malvern Instruments Ltd, Malvern, UK) fitted with lens 300RF that measures size range of 0.05–880 μm was used to assess the particle size distribution of the suspensions. To analyze the measurement data polydisperse model was chosen and 3D (Fraunhofer) presentation was selected. The mastersizer was first aligned and the background measurement was taken. The sample was introduced into the small volume sample dispersion unit, which was connected to sample dispersion controller .The sample dispersion controller was set at stirring speed of 5,000 rpm to disperse the sample. Enough sample was introduced to produce at least an obscuration of 10% and the bar color turns green. The experiment was repeated for samples containing HPMC or Na-CMC as well as a dispersion of ibuprofen powder (IBU).The result obtained was the mean of ten determinations.

RESULTS AND DISCUSSION

General Description

Esthetic looking pediatric suspension of ibuprofen was produced in all the formulations. The physical appearance of GG suspension compares very well with similar preparations of pediatric ibuprofen formulations using either Na-CMC or HPMC as the suspending agent. The pH of the formulations was 5–5.5.

Sedimentation Volume and Redispersibility

That a suspended dispersed solute in a continuous medium will settle is a matter of time. The characteristics of both the dispersed and continuous phases are important in the rate and extent of this phenomenon. Dense particles (due to gravity) and conversely low viscosity (low resistance to movement of solute) of continuous medium will aid fast settling. On the other hand, less dense and more viscous medium will favor longer suspension of the solute in the medium without aggregating. It is recognized that the viscosity of the continuous phase is determined by the concentration of the suspending agent. In this study the concentration of the suspending agents was kept at 0.5%, similar to the use level of one of the innovators, Na-CMC (35). One concentration level was chosen because of the understanding that there is a linear relationship between viscosity and concentration of polymeric suspending agent (36). Table I shows the sedimentation volume and the time to redisperse of the ibuprofen formulations using suspending agents at 0.5% *w/v*. Twenty-four hours after formulation, the redispersion time for these suspensions was respectively 19, 11, and 0.5 min for formulation containing Na-CMC, HPMC, and GG as suspending agent. Ibuprofen formulations containing Na-CMC and HPMC exhibited increase in redispersion time with storage. More time was required to redisperse formulation with Na-CMC than the corresponding formulation with HPMC. On the other hand, formulation of Ibuprofen pediatric suspension with GG required a constant redispersion time of 0.5 min over the study period. The

Table I. Some Properties of Ibuprofen Pediatric Suspension

	Time to redisperse (min)			Sedimentation volume (mL)		
	HPMC	Na-CMC	GG	HPMC	Na-CMC	GG
Day						
1	11±0.50	19±0.40	0.5±0.06	5±0.10	4.5±0.30[a]	12±0.10[b]
6	17±0.20	35±0.06	0.5±0.05	5±0.25	5±0.30[a]	12±0.10[b]
20	23±0.05	45±0.20	0.5±0.05	5±0.10	5±0.25[a]	12±0.25[b]
34	23±0.40	45±0.50	0.5±0.00	5±0.20	5±0.00	12±0.15
48	ND	ND	ND	5±0.00	5±0.10	12±0.20
62	25±0.20	46±0.00	0.5±0.04	4.5±0.00	4.5±0.20	12.5±0.00

[a] 15 mL cloudy above this volume
[b] 55 mL cloudy above this volume

redispersion time was generally of the order of GG<HPMC< Na-CMC-containing formulations. While redispersion is one of the recognized quality attributes of pharmaceutical suspensions, its evaluation has been qualitative and subjective (11,16,37,38). The present effort at quantitative determination was to make the evaluation more objective when comparing a new suspending agent with established one. Easily redispersed sediments in a suspension allow withdrawal of uniform doses. Patients or their representative with the same effort will require less time to achieve complete redispersion of ibuprofen suspension containing GG as the suspending agent compared to those with either HPMC or Na-CMC.

The sedimentation volumes of the formulations are also shown in Table I. Twenty-four hours after preparation the formulation containing HPMC had a sedimentation volume of 5.0 mL. The corresponding volume for formulations Na-CMC and GG were respectively 4.5 and 12.0 mL. The sedimentation values were respectively 4.5, 4.5, and 12.5 mL for formulations containing HPMC, Na-CMC, and GG. Generally, the sedimentation volume of the suspensions was of the order: HPMC<Na-CMC<GG containing formulations. In formulations with CMC and GG, there were dispersed particles above the core solute sediment making the suspension turbid and cloudy. On the contrary, that containing HPMC had clear supernatant continuous phase. It seemed that the formulation containing GG was characteristically flocculated in the secondary minimum forming a loosely bound structure and the flocs retaining their structures to make it possible for easy redispersion whereas there seem to be a coagulation in the primary minimum in the Na-CMC and HPMC suspensions probably resulting from a reduction in zeta potential to a point where attractive force predominate and particles settle forming a dense mass, making redispersion difficult. Since it is inevitable that suspensions will settle down over time due to gravitational forces, it is a desirable quality that the sediments are easily redispersed with minimal agitation. The more the sedimentation volume, the more easily a suspension can be redispersed and GG formulation exhibited both characteristics. Generally, the order of sedimentation volume was $GG > Na - CMC = HPMC$. The result suggests with GG as a suspending agent in ibuprofen formulation other additives like silicon dioxide will not be necessary to achieve a good redispersibility profile unlike the case with suspensions containing either Na-CMC or HPMC.

In certain dispersions, the solid particles are held together by van der Waals forces in a loose, open structure known as flocculate or flocs (5). If the floc is supported in an open structure by the dispersion medium, it does not settle appreciably. The final volume of sediment is a characteristic of the suspension and it can be used as measure of the extent of flocculation. The sedimentation ratio is the ratio of the final volume of the sediment to its original volume (5). In the case of these ibuprofen formulations, the sedimentation ratios were respectively 12.5%, 4.5%, and 4.5% for GG-, HPMC-, and Na-CMC-containing formulation. Small sedimentation ratio is an indication that the particles sediment to a compact mass in which the interparticulate forces may be strong to cause caking (5,39). There were about thrice interparticulate forces in either Na-CMC or HPMC containing formulation than in GG containing formulation. This suggests that caking of ibuprofen suspension is thrice more likely in formulation containing either Na-CMC or HPMC than with GG as suspending agent.

Rheological Evaluation

Viscosity affects the ease with which a suspension is withdrawn for administration. The less viscous suspension tends to pour more easily than the more viscous ones. Rheological study can help us gain insight into the structure of a system. The majority of viscosity measurements are made at the quality control level and consist of a single data point using one spindle at one speed and this is a good bench mark for decision making in a production setting. However, many fluids exhibit characteristic change in viscosity with a change in applied force that cannot be captured with single viscosity measurement. Figures 1, 2, and 3 show the effect of shear rate and aging on the viscosity of ibuprofen formulations. When freshly prepared the viscosities were 187, 152, and 145 cP with the spindle speed of 25 rpm (shear rate of 188 s^{-1}) respectively with GG, HPMC, and Na-CMC as the suspending agent. At higher speed of 200 rpm (1,500 s^{-1}), the corresponding values were respectively 67.2, 177.6, and 136.68 cP for formulation containing GG, HPMC, and Na-CMC. The viscosity of formulation containing GG decreased with increase in shear rate and is typical of a pseudoplastic shear thinning. The viscosity of the formulations decreased with storage. Unlike that with GG, formulations with either Na-CMC or HPMC showed decrease in viscosity at lower shear rates. As the shear rate was increased, a point was reached that the viscosity increased with increase in shear rate. This is typical of a shear-thickening system. When freshly prepared, the formulation with GG had the highest viscosity, followed by that with HPMC irrespective of the spindle speed or shear rate. The order of viscosity, however, changed with storage of the suspension and the formulation with HPMC exhibited the highest viscosity, followed by that with GG at the constant temperature of 25°C. It was also observed that after 6 months of storage GG containing suspension began to show increases in viscosity at higher shear rates of 200–250 rpm (1,875 s^{-1}) similar to that with Na-CMC (100 rpm) or HPMC (75 rpm). It is probable that with longer storage, the pattern of viscosity with shear rate may be similar for all formulations. One of the qualities of a good suspension is pourability (40). A suspension must not be too viscous to pour freely from the orifice of the bottle or to flow through a syringe needle neither should it be too viscous to flow through pipes if it has to be transported through pipes during processing. Formulation with GG demonstrated decrease in viscosity with shear stress. This is of advantage when such a suspension is passed through pipes during

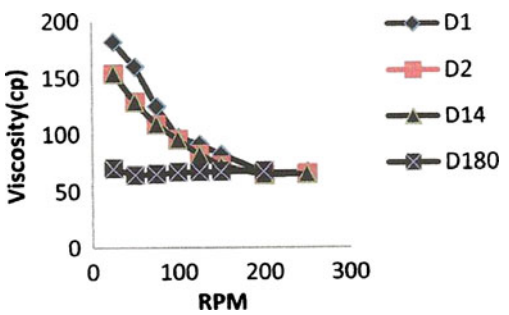

Fig. 1. Effect of shear rate and aging on the viscosity of ibuprofen containing GG as the suspending agent

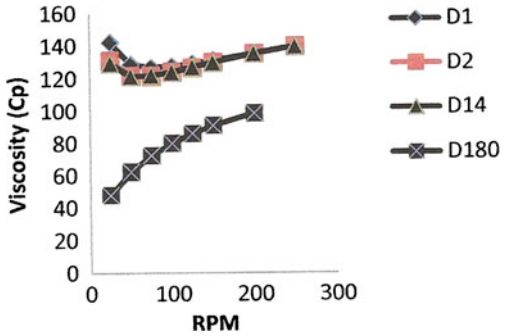

Fig. 2. Effect of shear rate and aging on the viscosity of ibuprofen containing Na-CMC as the suspending agent

manufacture and packaging. On the other hand, formulation with Na-CMC and HPMC may require special attention to assure smooth flow through pipes.

Effect of Aging on Rheological Properties of Suspension

Nowadays, in the age of technology, it is hardly practiced to make extemporaneous medicines only as when needed. Pharmaceutical products are now mass produced in pharmaceutical factories and are distributed for consumption. This process of distribution and use may continue throughout the shelf life of the medicine which may last up to 36 months in the case of most liquid preparations. Sequel to this, the rheological information that is obtained during manufacture may not always be the same throughout product's shelf life. Figures 1, 2, and 3 showed the effect of storage on the viscosity of the ibuprofen suspensions. Within 14 days of storage, for example, the viscosity of suspension containing GG dropped from 187 to 153.6 cP at 25 rpm (188 s^{-1}) and from 67.2 to 64.60 cP at 200 rpm (1,500 s^{-1}). The viscosity drop was sharper at lower shear rate than at higher shear rate. This decrease in viscosity was typical of all the ibuprofen pediatric formulations but Na-CMC-containing suspension showed highest decrease in viscosity on storage. A formulation with rapidly decreasing viscosity may suggest instability in the structure of the system and may be objectionable to the patient even if no detrimental changes have taken place. Such formulations may pour more quickly than the patient had experienced during the previous usage.

Elastic Hysteresis of Ibuprofen Suspensions

Hysteresis refers to systems which have memory and the effect of current input (or stimulus) to the system are not all felt at the same instant. Such a system may exhibit path dependence or rate-independent memory (41). These phenomena occur in magnetic, ferromagnetic, and ferroelectric as well as in elastic materials, in which a lag occurs between application and removal of a force and its subsequent effect. In rheology, this is typical of thixotropic fluids Fig. 4 shows the effect of increasing the shear rate from 50 to 250 rpm, then at either 0.5, 1.0, or 4 min decreased from 250 to 50 rpm on the viscosity of ibuprofen suspension. At either 0.5- or 1-min intervals of ramping up and ramping down to starting point, no changes were observed in the viscosities of formulations containing either GG or Na-CMC. The formulations with HPMC, however, had different viscosities when the shear stress was ramped up and returned to the starting point at 0.5-min interval. Hysteresis is an intrinsic property of a material. This was most likely to be due to the presence of HPMC in the preparation than the solute or the dispersion medium. The observation may be due to a number of factors such as difference in energy requirement between loading and unloading, internal friction within the material and a thermal exchange with the environment. Hysteresis is usually more pronounced when the loading and unloading is done more quickly than when done slowly. In general formulation containing HPMC showed more distinct hysteresis than those containing either GG or Na-CMC. Such effects may or may not be reversible; some thixotropic fluids, if allowed to stand undisturbed for a while, will regain their initial viscosity, while others never will (42).

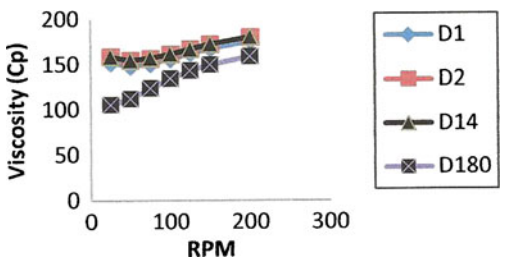

Fig. 3. Effect of shear rate and aging on the viscosity of ibuprofen containing HPMC as the suspending agent

Particle Size and Particle Size Distribution

Particle size distributions by volume of ibuprofen formulations are shown Table II. The volume of the particles was 72.59, 73.82, 83.41, and 85.821 μm respectively for suspensions containing Na-CMC, IBU, HPMC, and GG while the modal distributions were respectively 53.67, 54.90, 61.08, and 62.87. In order to quantify the degree of skewness of a

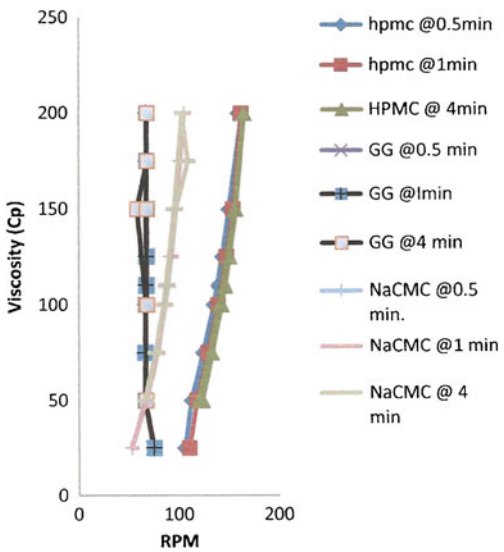

Fig. 4. Effect of shear rate and interval on the viscosity of ibuprofen suspension

Table II. Particle Size Distribution of Ibuprofen Pediatric Suspension Formulations

Description	HPMC	Na-CMC	GG	IBU
ASTM derived diameter (μm)				
D[4,3]	83.41±2.1	72.59±0.18	85.82±2.0	73.80±0.95
D[3, 2]	25.96±0.37	22.49±0.05	24.52±0.28	21.33±0.25
D[2, 1]	1.31±0.0	1.45±0.01	1.49±0.05	1.34±0.01
D[1, 0]	0.48±0.0	0.54±0.0	0.56±0.0	0.52±0.01
Distribution moments				
Volume	83.41±2.1	72.59±0.18	85.82±2.0	73.8±0.95
Standard deviation	61.36±1.61	56.91±0.27	66.9±2.7	60.10±0.45
Skewness	1.44±0.03	1.64±0.02	1.61±0.08	1.76±0.03
Kurtosis	2.14±0.18	3.02±0.08	2.90±0.3	3.60±0.09
Modal size (μm)	61.08±0.73	53.67±0.04	62.87±0.5	54.90±0.83
Distribution percentile (μm)-volume				
10%	25.22±0.42	20.43±0.11	23.8±0.54	19.69±0.09
20%	36.33±0.63	30.24±.08	36.24±0.75	30.19±0.27
50%	65.89±1.48	56.07±0.06	66.75±0.94	56.28±0.87
80%	123.20±3.70	106.16±0.15	125.39±2.00	106.64±2.00
90%	169.35±5.13	150.15±0.21	176.91±4.85	154.69±1.70

particle distribution, the interquartile coefficient of skewness can be determined from the relationship (43):

$$\text{IQCS} = (C - A) - \frac{A - B}{C - A} + (A - B)$$

Where A is the median diameter and B and C are the lower and upper quartile points in a cumulative frequency distribution curves. In these formulations, the skewness values were 1.61 and 1.44, respectively, for GG and HPMC containing formulations while the corresponding value for Na-CMC and IBU were, respectively, 1.64 and 1.76 a normal distribution would return a value of zero. On the other hand Kurtosis, K, helps to quantify the symmetry of a particle size distribution and its value is obtained from the relationship (44):

$$\text{kurtosis} = \frac{\sum_{i=1}^{N} \left(Y_i - \overline{Y}\right)^4}{(N-1)s^4}$$

where $\overline{Y}$ is the mean, s is the standard deviation, and N is the number of data points. These values were found to be 2.9, 2.1, and 3.0 respectively for formulation with GG, HPMC, and Na-CMC. The skewness and kurtosis are moderate and the values suggest a Weibull distribution profile. As one moves away from the center, the decay depends on the value of the shape parameters in this type of profile (44).

The photomicrograph of the suspensions is shown in Fig. 5. The solute particles were more clustered in formulation with HPMC than those in Na-CMC and GG. The clustering of the particles may offer greater resistance to flow than the less clustered. This might probably have accounted for the observed higher viscosity in HPMC containing formulation. This observation is more likely to be more of influence of the suspending agent than the characteristics of the drug (6).

In conclusion, formulation of ibuprofen suspension have been made containing GG as the novel suspending agent and analog agents (HPMC or Na-CMC), were prepared under the same experimental conditions for comparison purpose. Well-flocculated ibuprofen suspensions were successfully made using these agents. The study showed that incorporation of GG as the suspending agent resulted in a suspension with a good sedimentation volume combined with ease of redispersibility. These parameters which are desired of good suspension were superior in formulation with GG than with either HPMC or Na-CMC. Ibuprofen suspension formulations exhibited changes in viscosity with aging and the extent of these changes

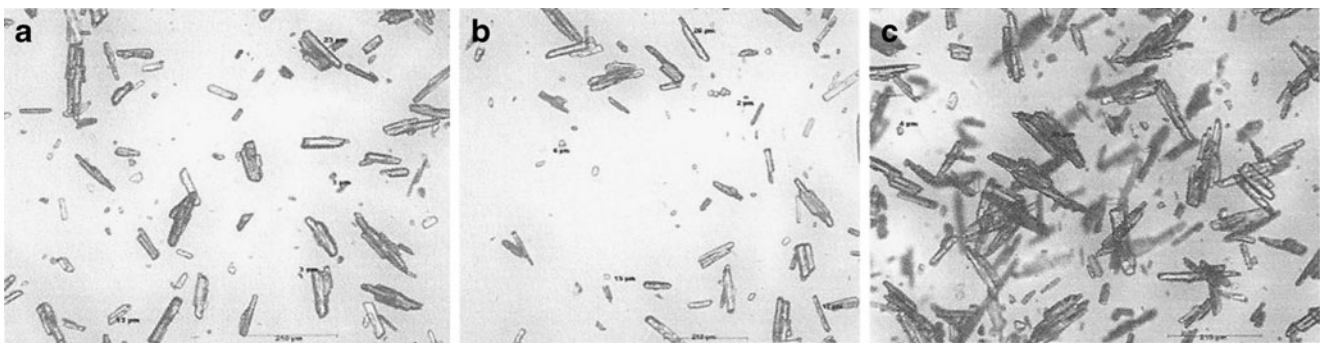

Fig. 5. Photomicrograph of ibuprofen suspension containing **a** Na-CMC **b** Grewia **c** HPMC

depended on the type of suspending agent incorporated. Ibuprofen pediatric formulation containing GG as the suspending agent combined high sedimentation volume with easy of redispersion to make it an ideal suspension. Moreover, this formulation experienced moderate changes in viscosity on storage. The type of suspending agent, rather than the physical characteristics of the drug, appeared to exert the main influence on the physical stability of suspensions.

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Conflicts of Interest None.

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