

Assessment of Co-Processed Composites of Cissus-Acacia and Cissus-Guar Gums as Suspending Agents in Metronidazole Benzoate Suspension

Kenneth Chinedu Ugoeze and Harriet Uwhuetume Oyagiri

Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Port Harcourt, Nigeria.

ABSTRACT

The study evaluated various co-processed hydrophilic polymer composites derived from cissus gum (CG) and acacia gum (CAG), cissus gum and guar gum (CGG) and CG, acacia gum (AG) and guar gum (GG) alone at varying concentrations as suspending agents in the formulation of metronidazole benzoate (MTZB) suspensions. Suspensions containing MTZB, 200 mg/5ml was formulated using 1.5, 2.0 and 3.0 % w/v of either CG, AG, GG, CAG or CGG. The suspensions were evaluated considering sedimentation volume, flow rate, viscosity, pH, freeze-thaw test and redispersibility. The results showed that all the hydrophilic polymers employed yielded enhanced properties of the suspensions following the increase in their respective concentrations leading to enhanced viscosities, reduced flow rates and increased sedimentation volumes with the best outcomes observed as CGG>GG>CG>CAG>AG>Control ($p < 0.05$) for sedimentation volume; CGG>CG>GG>AG>CAG>Control ($p < 0.05$) for viscosity and CGG>GG>CG>CAG>AG>Control for flow rate ($p < 0.05$). Very stable pH was recorded with CG at all the concentrations studied, followed by the CGG, especially at the early days following their preparations. There was no changes in the particle sizes of the MTZB in the products formulated with the CG following the freeze-thaw test ($p > 0.05$). Other batches exhibiting stable particle sizes after freeze-thaw test were got with 2.0 % w/v of AG, 2.0 % w/v of GG and 2.0 % w/v of CGG ($p > 0.05$). The batch containing 3.0 % w/v of CGG and the control batch had their p -values = 0.05. These results may be indication that stable suspensions of the MTZB may be obtained with 2.0 % w/v of these hydrophilic polymers. The ease of redispersibility of the MTZB suspensions were in the order GG < CG < CGG < CAG < AG < Control. The best co-processed hydrophilic polymer were those prepared with CG and GG.

Keywords: Co-processed composites, Cissus gum, acacia gum, guar gum, suspending agent, metronidazole benzoate, suspension.

INTRODUCTION

The application of a natural polymer as pharmaceutical additive is increasing daily. They have basic advantages of low cost, safety issues, availability, bio-degradable, etc. There are varieties of these with varied characteristics [1, 2]. Polymers are macromolecules encompassing great numbers of repeated monomers bonded through a chemical procedure described as polymerization. They are classified as either natural or synthetic. The natural polymers are obtained from plants or animals. Plant-based polymers are found in plant parts like stem, seed, root or tubers and include the polysaccharides [3-5]. Developments in polymer science have led to the progress of novel drug delivery systems. Some polymers are obtained from natural resources and then chemically modified for various applications, while

others are chemically synthesized and used. A large number of natural and synthetic polymers are available [6]. Natural polymeric excipients can be applied in various formulations such as solid, liquid and semi-solid dosage forms where they act as disintegrates, binders, film formers, matrix formers, release modifiers, thickeners, stabilizers, emulsifiers, suspending agents, sweetener and mucoadhesives agents [1]. Pharmaceutical suspensions consist of coarse dispersions of insoluble solids in a liquid medium. Such suspensions are biphasic and thermodynamically unstable. They are heterogeneous systems consisting of two phases, a solid dispersed in a liquid and the particulate dispersions are of colloidal dimension, or as two-phase systems consisting of finely divided solids (internal phase) dispersed uniformly in a liquid medium (external phase) [7]. The internal phase of suspensions contains the pharmaceutical active ingredient (API) which is an insoluble solid in the given liquid medium and having a particle size range of 0.05 to 5 μm . This is maintained uniformly throughout the vehicle with the aid of a single or combination of suspending agent(s) [8]. The external phase is generally aqueous in some instances or may be an organic or oily liquid for non-oral use. Dosage forms officially categorized as suspensions are designated as such if they are not included in other more specific categories of suspensions such as oral suspensions, or topical suspensions. Some are prepared ready for use while others are prepared as solid mixtures intended for reconstitution just before use with an appropriate vehicle and such are designated as oral suspensions [9]. To achieve a pharmaceutically acceptable, thermodynamically stable suspension formulation, it is pertinent that a stabilizer or suspending agent be added to the dosage form. This will help to maintain a uniform dispersion of particles by the formation of a physical barrier around the particles which would prevent aggregation and enhance the consistency of the continuous phase thereby preventing the rapid settling of the particles that would have led to the formation of a closely packed sediment which may prevent the removal of an accurate dose of the formulation from its container [10-12]. Natural polysaccharides are one of the most commonly used suspending agents and examples include acacia, guar gum, agar, xanthan gum and tragacanth. Other suspending agents frequently used include semi-synthetic polysaccharides such as carmellose sodium, sodium carboxymethylcellulose; clays and synthetic agents [13, 14]. Plant gums and mucilages have been used as suspending agents because they lead to an increase in the viscosity of a suspension which in turn causes a reduction in the rate of sedimentation of drug particles or other in-diffusible powders [15-17]. Besides their usage as suspending agents, plant gums have been widely used in the pharmaceutical sector as thickeners, disintegrants, binders, emulsifying agents and film formers [18-20]. Hydrophilic polymers with improved properties can be developed through co-processing. Co-processing is a new approach employed to adjust excipient functionality without losing its basic properties while enhancing it with innovative properties. This has been feasible by handling the parent excipient with additional excipient. New excipients emerging through co-processing has often exhibited improved flow properties, compressibility, disintegration and dissolution of solid dosage forms, enhancement of gelling or viscosity control properties which is brought about by value-added hydration and swelling capacity of the new excipient, etc. Obtaining new excipients with these enhanced characteristics has always been the drive for of co-processing in pharmaceutical technology [21-28].

The aim of the current study was to evaluate the suspending properties of a new co-processed hydrophilic polymers derived from cissus-acacia and cissus-guar gums. The processing and characterization of the co-processed hydrophilic polymers based on cissus, acacia and guar gums has been reported [29].

MATERIALS AND METHODS

Materials

The following reagents were used as procured: Sodium metabisulphite (Merck), acetone (JHD, China), guar gum (Qualikems, India), acacia (J.T Baker, USA), metronidazole benzoate (MTZB) (Aarey Drugs, India), propyl paraben (Sigma-Aldrich, USA).

Methods

Procurement of Cissus populnea stems and processing of cissus gum

The procurement of *Cissus populnea* stem and the processing of cissus gum has been documented [29].

Processing of co-processed hydrophilic polymers composites of cissus, acacia and guar gums

This was carried out according the methods reported by Ugoeze and Ameh, 2021 [29]. The new co-processed powders were obtained by combining cissus gum (CG) with acacia gum (AG) or guar gum (GG) [29]. Using the formula in Table 1, two batches of co-processed hydrophilic polymers each containing 20.0 % w/w of CG with 80.0 % w/w of either AG or GG were developed. The separate quantities of the respective hydrophilic polymers amounting to 100.0 % in each batch was homogenized and dispersed in 55.0 ml of deionized water to form a smooth slurry. It was precipitated with acetone, and dried to a constant weight in a desiccator loaded with silica gel, pulverized and classified with 180 µm sieve. The co-processed hydrophilic polymers composites were coded as CAG (cissus-acacia gum) and CGG (cissus-guar gum).

Table 1: Development of the co-processed hydrophilic polymers containing CG and AG or CG and GG [29].

Polymer	Composition (%w/w)
Cissus-Acacia (CAG) gums composites	
CG	20.0
AG	80.0
Cissus-Guar (CGG) gums composites	
CG	20.0
GG	80.0

Table 2: Formulation of metronidazole benzoate (MTZB) suspension

Ingredient	Batch			Control
	Concentration (% w/v)			
CG or AG or GG or CAG or CGG	1.5	2.0	3.0	0.00
Metronidazole benzoate (MTZB)	4.0	4.0	4.0	4.0
Propyl paraben	0.05	0.05	0.05	0.05
Dist. Water, q. s.	100.0	100.0	100.0	100.0

The suspensions containing metronidazole benzoate (MTZB) (200 mg/5 ml) was formulated using either cissus (CG), acacia (AG), guar (GG), co-processed

hydrophilic polymer composites of cissus-acacia (CAG) or cissus-guar (CGG) gums in the concentrations of 1.5, 2.0 and 3.0 (w/v) of respectively with the batch serving as a control containing no hydrophilic polymer (Table 2). An amount of 8.0 g of MTZB powder was blended with the respective amount of the hydrophilic polymer in each batch, adding 0.1 g of propyl paraben. Distilled water was added in bits with dispersion to make a smooth paste and further until it was pourable. The mixture was transferred into an amber coloured glass container and made up to 200.0 ml. Each batch was prepared in triplicate. They were stored at ambient temperature for evaluation in terms of sedimentation volume, rheological studies (flow rate), viscosity, freeze-thaw and redispersibility. The evaluations lasted for 28 days.

Evaluation of MTZB suspensions

Sedimentation volume

A 50.0 ml of each batch of suspensions prepared was placed in different 50 ml glass measuring cylinders for 4 weeks at ambient temperature. The initial volume was recorded for each batch immediately after preparation. The sedimentation volume, H_t on each day was noted for 7 days and later, on weekly basis for the next 3 weeks. The rate of sedimentation S_r (%) was calculated using the following formula [30]:

$$S_r (\%) = \frac{H_t}{H_o} \dots\dots\dots (1)$$

Rheology (flow rate)

The time required for 10.0 ml of each batch of MTZB suspension to flow through a 10.0 ml glass pipette was noted at weekly interval for 4 weeks. The flow rate was determined using the following formula [30]:

$$\text{Flow rate} = \text{Volume of preparation/Flow time} \dots\dots\dots (2)$$

Viscosity measurement

The viscosity of the respective batch of metronidazole benzoate suspension was determined with a Brookfield viscometer (DV2T, Brookfield Engineering Laboratories, Massachusetts, USA) using spindle #62 at 12 revolutions per minute (rpm) for 2 min at 27.5°C [16].

pH of Suspensions

The initial pH of the respective suspensions were recorded at the first day, later, it was evaluated weekly for 4 weeks using a pH meter (Ultrameter II, 6PFC E; Myron L, UK).

Freeze-thaw test

The particle size of the dispersed phase of the respective batches of the suspensions was determined with a photomicrograph microscope ((Model XSZ-107BN, Zenithlabo, USA) fitted with a Phenix Micro Image Analysis Software (PHMIAS 2006 Ver. 2.0). Later, each batch was subjected to a freeze-thaw assessment by refrigerating a sample of the respective batches for 24 h and then allowing it to thaw at room temperature for 24 h. The respective samples were exposed to the temperature (approximately 45°C) for 24 h and later kept at ambient temperature for 24 h. The particle size of the respective samples were re-assessed for any possible significant particle size changes using a photomicrograph microscope [16, 31].

Redispersibility tests

After 4 weeks, the various batches of the metronidazole benzoate suspensions were redispersed simultaneously by shaking the respective measuring cylinders containing the products in a particular pattern and taking note of the number of shakes when a complete redispersion of the sedimented products got fully redispersed which tallies to the redispersibility number for the respective batch. The lower the redispersible number, the more redispersible the suspension is assumed to be [9, 16].

Statistical analysis

The figures were presented as a mean $\pm$ standard deviation (SD). One-way analysis of variance (ANOVA) was performed followed by Fisher's Least Significant Difference (LSD) post hoc test to determine the level of significance.

RESULTS AND DISCUSSION

Sedimentation volume

Figures 1-3 show the effect varying concentrations of CG, AG and GG on the sedimentation volume of MTZB suspension. Generally, sedimentation volume was observed to increase with corresponding increase in each level of concentration of the respective polymers evaluated in the order GG > CG > AG > Control ($p < 0.05$). Higher concentrations of each polymer, 2-3 % w/v resulted to more consistent sedimentation volumes which stabilized within the first to 4th day in most of the formulations with GG still providing the best result. Figures 4-6 represent the effect of type and concentration of co-processed composite polymers of CG, AG and GG in comparison with similar concentration of them alone. At all the concentrations studied, the order of highest sedimentation volumes got were as CGG > GG > CG > CAG > AG > Control ($p < 0.05$). The co-processed composite derived from CG and AG had poor performance, though, with improvement from AG alone.

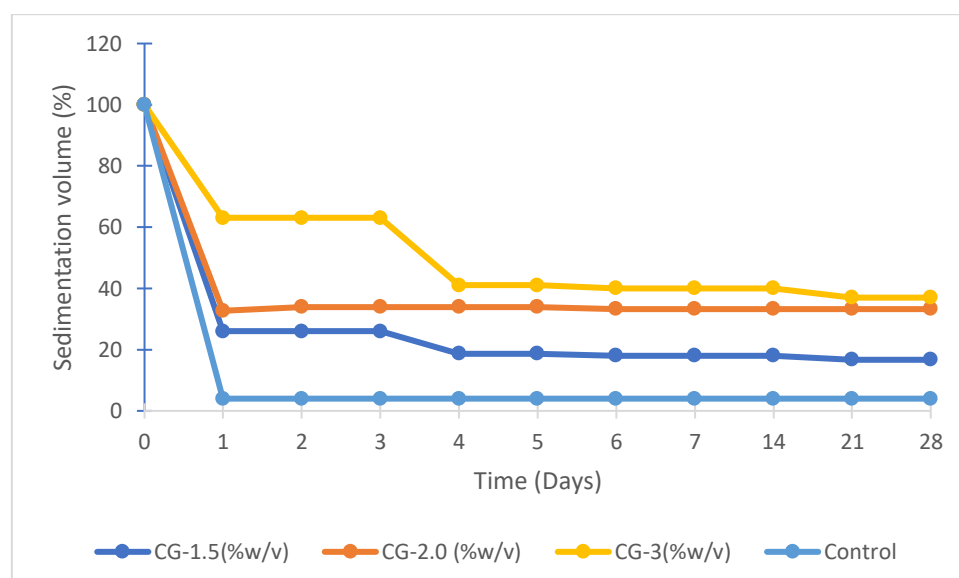


Figure 1: Mean sedimentation volume for the various metronidazole benzoate suspension prepared with varying concentrations of CG compared with the control.

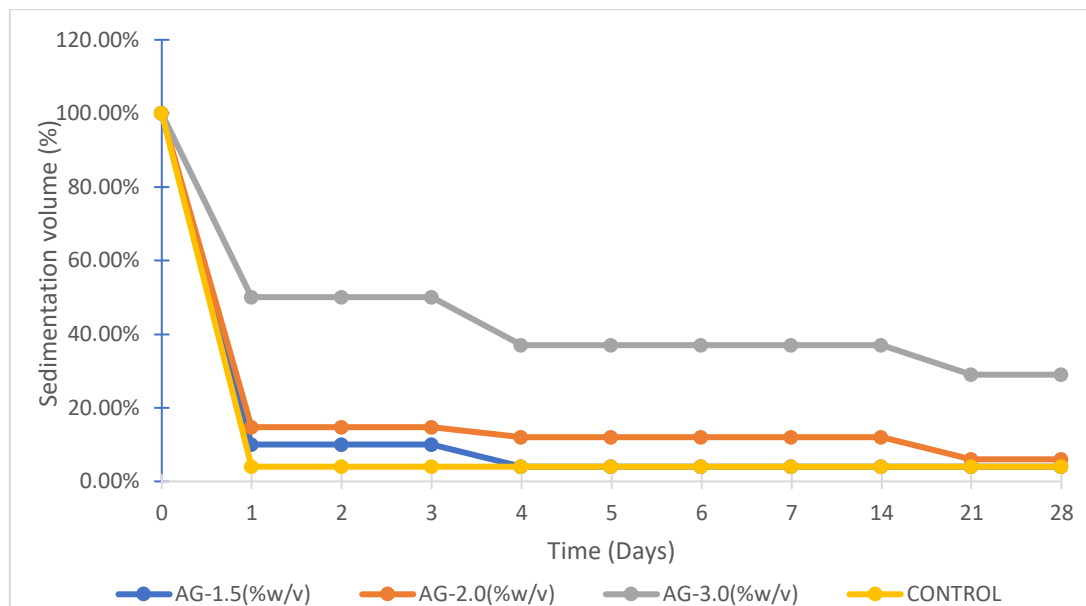


Figure 2: Mean sedimentation volume for the various metronidazole benzoate suspension prepared with varying concentrations of AG compared with the control.

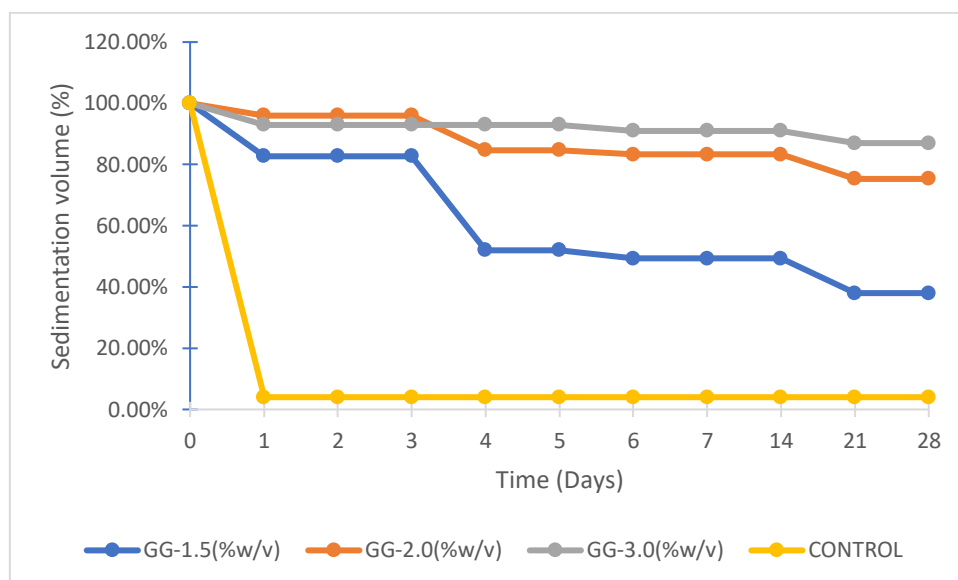


Figure 3: Mean sedimentation volume for the various metronidazole benzoate suspension prepared with varying concentrations of GG compared with the control

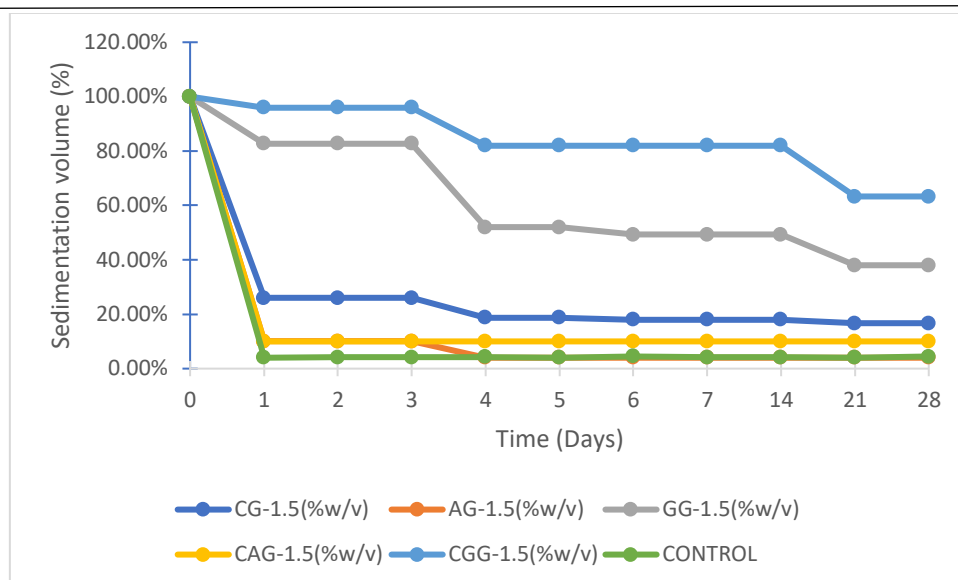


Figure 4: Comparison of the mean sedimentation volumes of 1.5 % w/v of various hydrophilic polymers

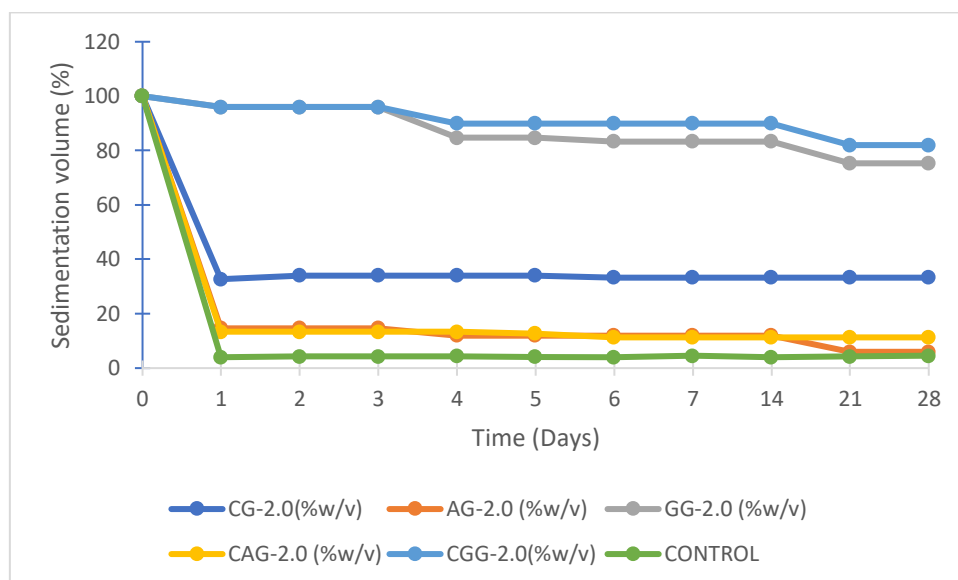


Figure 5: Comparison of the mean sedimentation volumes of 2.0 % w/v of various hydrophilic polymers

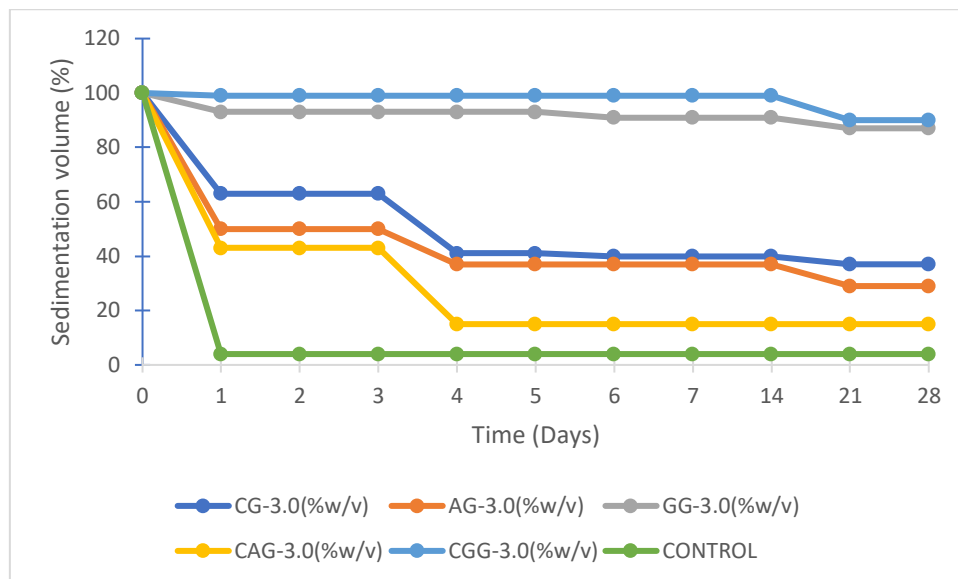


Figure 6: Comparison of the mean sedimentation volumes of 3.0 % w/v of various hydrophilic polymers

Flow rate

Figures 7-9 show that effect of type and varying concentrations of CG, AG and GG on the flow rate of MTZB suspensions. It was observed that flow rate was inversely proportional to the concentration of the polymer in each polymer type and concentration, showing that formulations exhibiting higher viscosities will manifest lower flow rate. Fairly consistent flow pattern was recorded in each case, however, lowest best result occurred in the order GG>CG>AG>Control. Further results showing the effect of type and concentration of polymer on the flow rate of MTZB suspensions are presented in Figures 10-12 for the co-processed polymer composites in comparison with CG, AG and GG alone in their concentration levels of 1.5, 2.0 and 3.0 % w/v respectively. At all the concentrations of the co-processed polymer composites in comparison with their single constituents the best results were in the order CGG>GG>CG>CAG>AG>Control. In most instances, the co-processed polymer obtained with CG and AG offered poor outcomes.

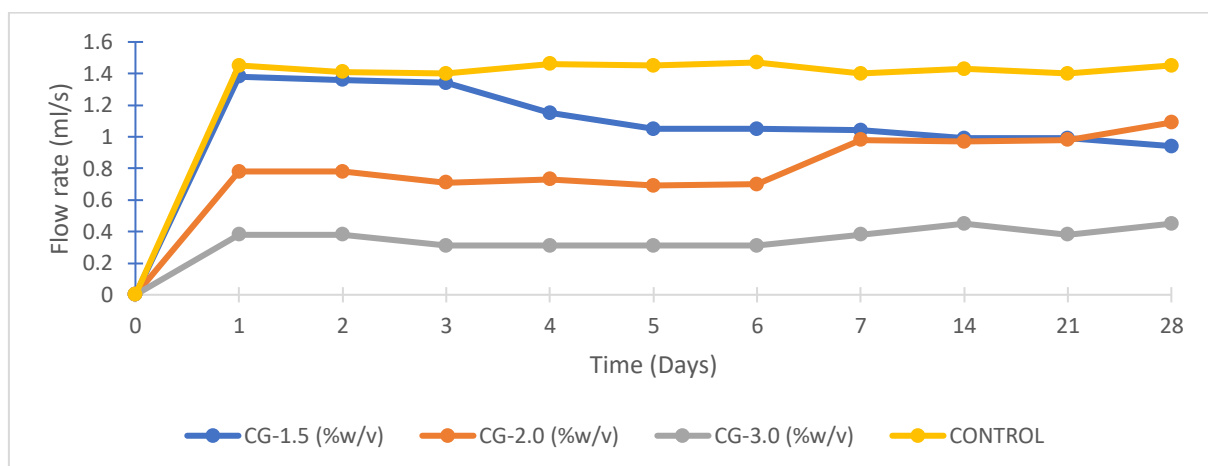


Figure 7: Mean flow rate of metronidazole benzoate suspension prepared with varying concentrations of CG

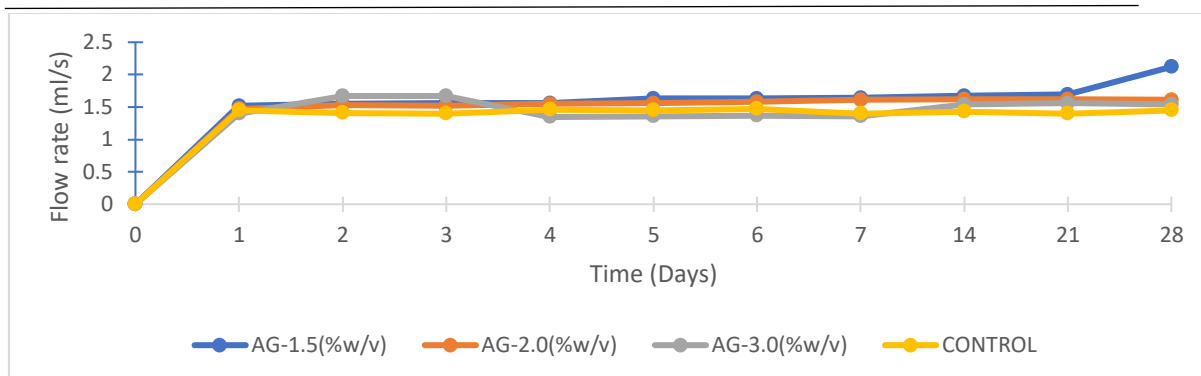


Figure 8: Mean flow rate of metronidazole benzoate suspension prepared with varying concentrations of AG

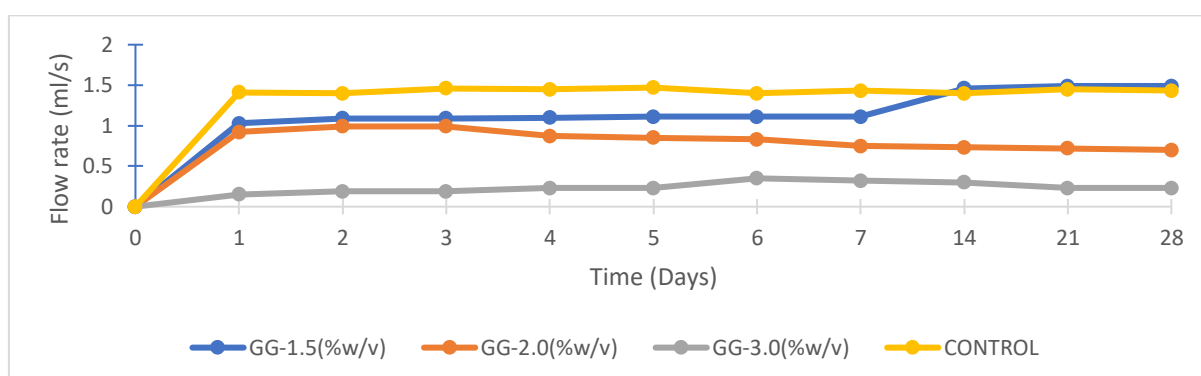


Figure 9: Mean flow rate of metronidazole benzoate suspension prepared with varying concentrations of GG

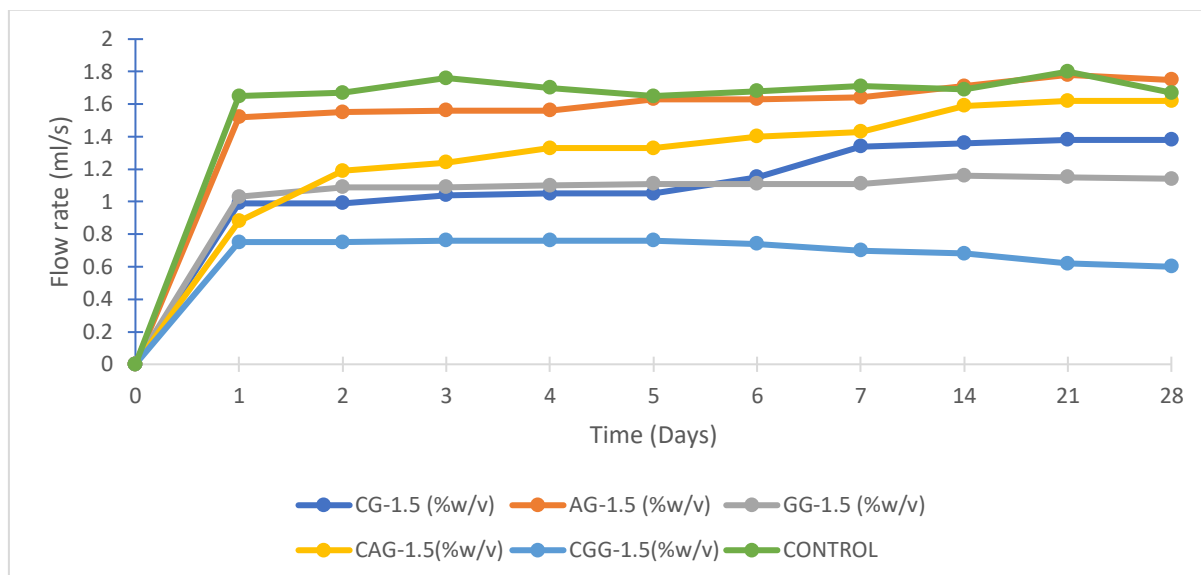


Figure 10: Mean flow rate of metronidazole benzoate suspensions prepared with 1.5%w/v of varying hydrophilic polymers

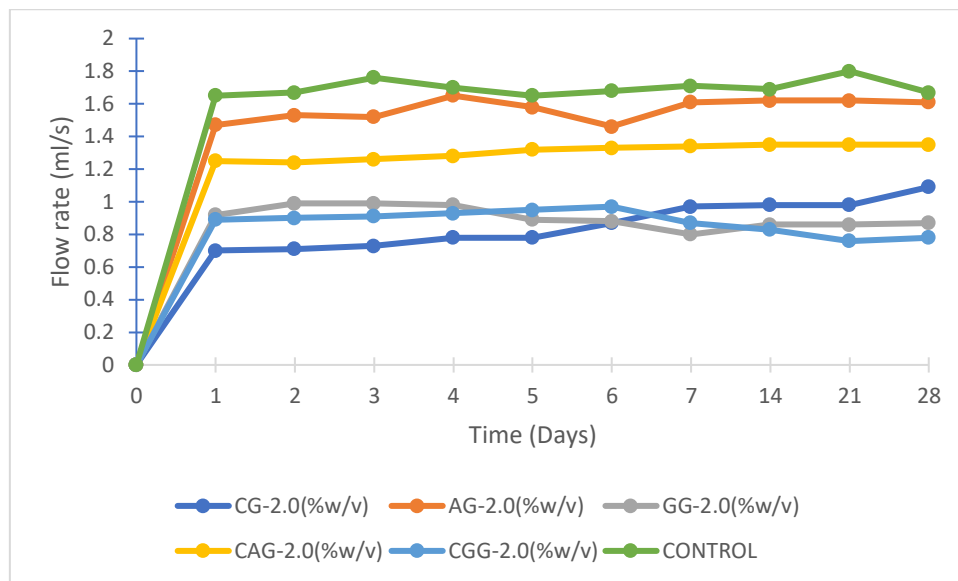


Figure 11: Mean flow rate of metronidazole benzoate suspensions prepared with 2.0 %w/v of varying hydrophilic polymers

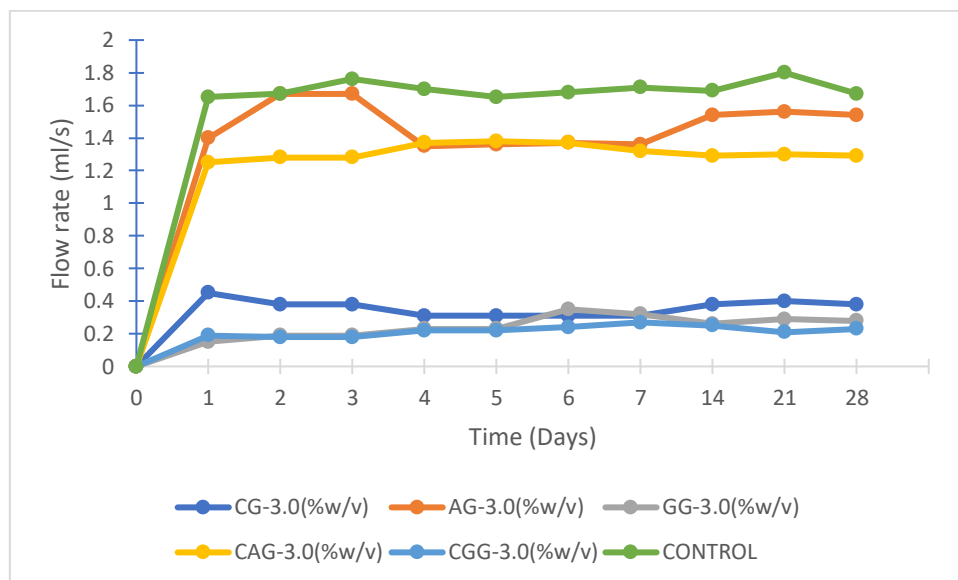


Figure 12: Mean flow rate of metronidazole benzoate suspensions prepared with 3.0 %w/v of varying hydrophilic polymers

Viscosity of MTZB suspensions

The viscosities of the MTZB suspensions prepared with varying concentrations of CG, AG, GG and their co-processed composites. The records obtained were presented in Figures 13-15. Generally, viscosity increased with the respective increase in the concentration of the respective hydrophilic polymers studied. In terms of the ability of the respective polymers used to yield high viscosity in MTZB suspension at the various concentrations employed in the formulation, $CGG > CG > GG > AG > CAG > \text{Control}$ ($p < 0.05$). The high viscosity impact of CG tends to be lost in its combination with AG.

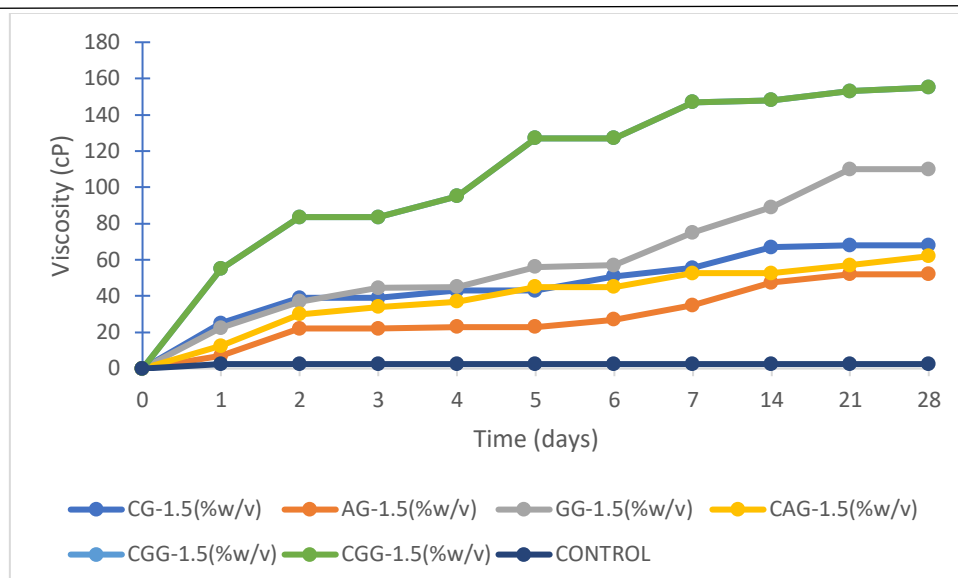


Figure 13: Mean viscosity of metronidazole benzoate suspensions prepared with 1.5 % w/v of varying hydrophilic polymers

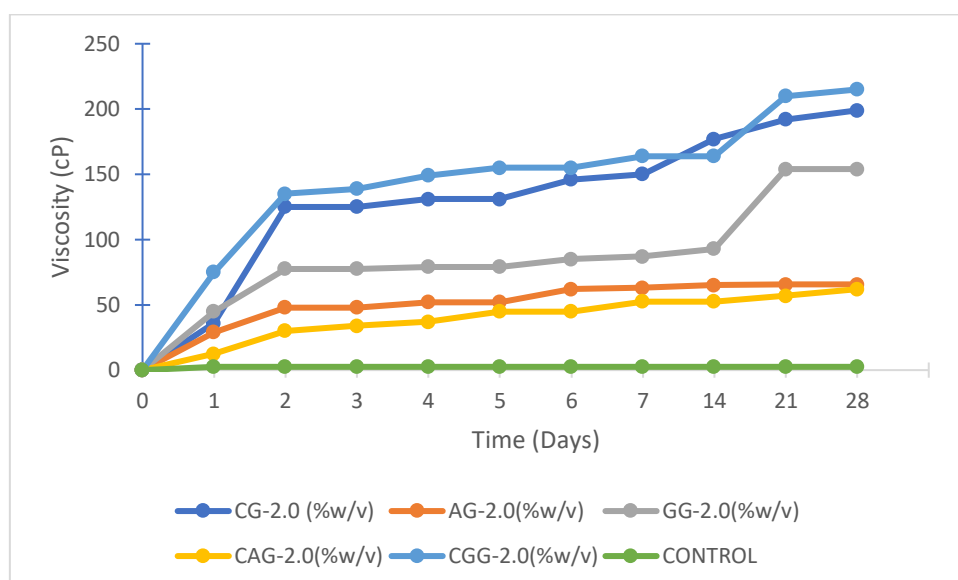


Figure14: Mean viscosity of metronidazole benzoate suspensions prepared with 2.0 % w/v of varying hydrophilic polymers

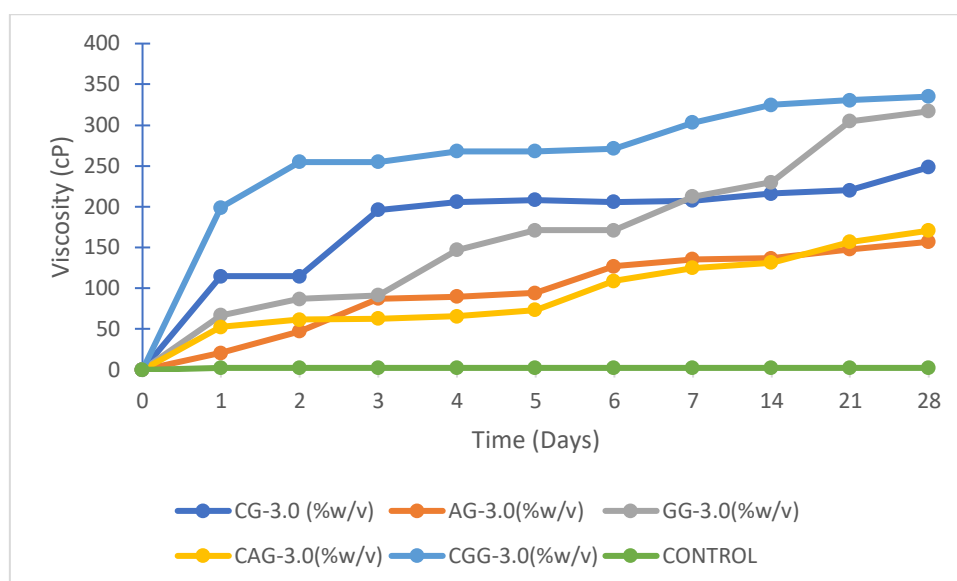


Figure15: Mean viscosity of metronidazole benzoate suspensions prepared with 3.0 % w/v of varying hydrophilic polymers

pH of MTZB suspensions

The records obtained from the monitoring of the pH of the various MTZB suspensions were presented in Tables 3-5. Table 3 shows the pH of MTZB suspensions prepared with varying concentrations of CG and AG. For the products prepared with 1.5, 2.0 and 3.0 % w/v of CG exhibited stable pH within the period of 4 weeks ($p < 0.05$) while those prepared with similar concentrations of AG exhibited inconsistent and varying pH within the 4 weeks of studies. Also, Table 4 presents the pH of MTZB suspensions prepared with varying concentrations of GG and CAG as recorded with 4 weeks. Those prepared with 1.5 -3.0 % w/v of GG exhibited stable pH within the first 3 days after preparation ($p < 0.05$) and became inconsistent till the 4th week ($p > 0.05$) while the products formulated with the co-processed composites of CG and AG (CAG) at all the concentrations studied exhibited stable pH within the first 3 days after preparation ($p > 0.05$) and began to show unstable pH through the other days of the studies ($p < 0.05$). Further, Table 5 shows the readings obtained for the pH of the MTZB suspensions prepared with varying concentrations of CGG. It showed that within all the concentrations studied, the pH was stable within the first 2-3 days after preparation ($p > 0.05$) and exhibited sharp drop in pH which was not consistent through the remaining period of the studies ($p < 0.05$). The batch of formulation that served as the control contained no hydrophilic polymer. Record showed that its pH was stable through the period of 4 weeks. This may be an indication that the instability in pH recorded in some of the formulations may be attributed to those hydrophilic polymers or it may be related to their concentrations.

Table 3: pH of MTZB suspensions prepared with varying concentrations of CG and AG.

Days	Hydrophilic polymer /Concentration (% w/v)						
	CG-1.5	CG-2.0	CG-3.0	AG-1.5	AG-2.0	AG-3.0	Control
0	7.00±0.0	7.02±0.0	7.07±0.0	6.30±0.0	5.57±0.06	5.43±0.06	7.03±0.0
	1	2	6	0			6
1	7.01±0.0	7.01±0.0	7.08±0.0	6.27±0.0	5.58±0.07	5.38±0.03	7.04±0.0
	1	1	4	5			6
2	7.01±0.0	7.02±0.0	7.08±0.0	6.19±0.0	6.28±0.03	6.29±0.03	7.04±0.0
	1	2	3	1			6
3	7.04±0.0	7.08±0.0	6.89±0.1	6.21±0.0	6.31±0.01	6.29±0.03	7.01±0.0
	5	4	0	2			1
4	7.08±0.0	7.05±0.0	7.01±0.0	6.03±0.0	6.20±0.01	6.19±0.01	7.01±0.0
	3	5	2	6			1
5	7.01±0.0	7.03±0.1	6.93±0.1	6.03±0.0	6.18±0.03	5.68±0.03	7.04±0.0
	2	1	1	6			6
6	7.05±0.0	7.02±0.0	6.86±0.0	6.13±0.0	5.69±0.01	9.13±0.06	7.00±0.0
	5	2	6	6			0
7	7.04±0.0	7.01±0.0	6.96±0.0	6.09±0.0	6.13±0.06	5.69±0.01	7.01±0.0
	4	2	7	1			1
14	7.05±0.0	7.01±0.0	6.90±0.1	6.87±0.0	5.89±0.01	5.61±0.01	7.10±0.0
	5	2	0	6			0
21	7.05±0.0	7.01±0.0	6.93±0.1	6.89±0.0	5.89±0.01	5.61±0.02	7.10±0.0
	3	2	1	1			0
28	7.07±0.0	7.02±0.0	6.91±0.1	6.88±0.0	5.88±0.03	5.60±0.01	7.10±0.0
	2	2	0	3			0

Table 4: pH of MTZB suspensions prepared with varying concentrations of GG and CAG.

Days	Hydrophilic polymer /Concentration (% w/v)						
	GG-1.5	GG-2.0	GG-3.0	CAG-1.5	CAG-2.0	CAG-3.0	Control
0	8.67±0.0	9.27±0.0	9.33±0.0	7.50±0.1	7.47±0.06	7.01±0.01	7.03±0.0
	6	6	6				6
1	8.68±0.0	9.29±0.0	9.22±0.0	7.57±0.0	7.52±0.04	7.01±0.02	7.04±0.0
	3	2	3	6			6
2	8.69±0.0	9.29±0.0	8.39±0.0	7.57±0.0	7.49±0.02	6.93±0.06	7.04±0.0
	2	2	2	6			6
3	8.69±0.0	8.30±0.0	8.39±0.0	7.55±0.0	6.83±0.06	6.89±0.01	7.01±0.0
	1	1	2	5			1
4	9.03±0.0	8.30±0.0	9.39±0.0	7.47±0.0	6.85±0.08	6.93±0.06	7.01±0.0
	6	1	2	6			1
5	9.02±0.0	8.89±0.0	9.39±0.0	7.57±0.0	6.51±0.02	6.95±0.06	7.04±0.0
	7	2	1	6			6
6	8.78±0.0	9.13±0.0	9.17±0.0	7.47±0.0	6.61±0.02	6.73±0.06	7.00±0.0
	3	6	6	6			0
7	9.07±0.0	8.81±0.0	9.14±0.0	7.53±0.0	6.63±0.06	6.73±0.06	7.01±0.0
	6	1	6	6			1
14	7.61±0.0	8.51±0.0	8.82±0.0	7.47±0.0	6.58±0.04	6.63±0.11	7.10±0.0
	1	1	8	6			0
21	7.60±0.0	8.51±0.0	8.81±0.0	7.47±0.1	6.21±0.01	6.83±0.04	7.10±0.0
	6	1	1	4			0
28	7.57±0.0	8.50±0.0	8.80±0.0	7.47±0.0	6.63±0.06	6.73±0.06	7.10±0.0
	2	1	1	6			0

Table 5: pH of MTZB suspensions prepared with varying concentrations of CGG.

Days	Hydrophilic polymer /Concentration (% w/v)			
	CGG-1.5	CGG-2.0	CGG-3.0	Control
0	9.07±0.06	9.07±0.06	9.12±0.08	7.03±0.06
1	9.07±0.06	9.07±0.05	9.11±0.09	7.04±0.06
2	9.07±0.46	9.08±0.04	9.11±0.09	7.04±0.06
3	7.57±0.06	8.59±0.02	7.68±0.03	7.01±0.01
4	7.61±0.02	7.72±0.03	7.67±0.05	7.01±0.01
5	7.67±0.06	7.67±0.06	7.67±0.05	7.04±0.06
6	7.85±0.05	7.69±0.01	7.67±0.06	7.00±0.00
7	7.88±0.03	7.67±0.06	7.63±0.11	7.01±0.01
14	7.83±0.11	7.68±0.04	7.68±0.04	7.10±0.00
21	7.88±0.03	7.68±0.04	7.69±0.06	7.10±0.00
28	7.88±0.03	7.69±0.01	7.69±0.01	7.10±0.00

Freeze-thaw test

The records got from the freeze-thaw test are presented in Table 6. It showed that the products formulated with all the concentrations of CG studied exhibited no changes in the particle size of MTZB, hence, were not affected adversely by the freeze-thaw procedures ($p > 0.05$). Other batches of MTZB suspensions that exhibited non-particle size alterations following the freeze-thaw test were that containing 2.0 % w/v of AG, 2.0 % w/v of GG and 2.0 % w/v of CGG ($p > 0.05$). The batch containing 3.0 % w/v of CGG and those of the control batch had their p -values = 0.05. These results may be indication that stable suspensions of the MTZB may be obtained if formulated with 2.0 % w/v of these hydrophilic polymers since. Freeze-thaw test has been one of the simple ways to determine the stability of pharmaceutical disperse systems as it aids to ascertain the extent of stability exercised by drug particles when formulation is exposed very low or elevated temperatures. At low temperature, solubility of the polymeric materials is reduced and could lead to aggregation. At elevated temperature, the viscosity of the system is reduced, causing increased particulate motion and collisions. These complex activities result to several forms of particle deformation or rearrangements [31, 32].

Table 6: Effect of the type and concentration of hydrophilic polymer on the mean particle size before and after freeze-thaw tests.

Hydrophilic polymer	Conc. (% w/v)	Particle size (µm)		P-value
		Before freeze-thaw test	After freeze-thaw test	
CG	1.5	4.99±0.05	4.87±0.18	0.405
	2.0	5.18±0.20	5.13±0.26	0.718
	3.0	5.78±0.09	5.78±0.09	1.000
AG	1.5	4.92±0.05	5.83±0.16	0.000
	2.0	5.01±0.05	5.07±0.15	0.652
	3.0	5.11±0.03	6.58±0.32	0.000
GG	1.5	12.30±0.26	11.65±0.41	0.000
	2.0	10.77±0.32	11.16±0.29	0.100
	3.0	12.69±0.34	13.17±0.21	0.002
CAG	1.5	8.69±0.05	6.58±0.07	0.000
	2.0	8.59±0.09	6.77±0.08	0.000
	3.0	8.81±0.10	6.55±0.04	0.000
CGG	1.5	6.28±0.07	5.62±0.07	0.000
	2.0	6.68±0.22	6.42±0.11	0.075
	3.0	7.45±0.05	7.88±0.09	0.005
Control	-	5.67±0.06	8.79±0.06	0.005

Redispersibility

The mean number of shakes applied to ascertain the ease of redispersibility of the various MTZB suspensions are presented in Table 7. The values were in the order GG < CG < CGG < CAG < AG < Control.

Table 7: Effects of hydrophilic polymer types and their concentration on the redispersibility of MTZB suspensions.

Concentration of polymer (% w/v)	Numbers of shakes to re-disperse a sedimented preparation					
	CG	AG	GG	CAG	CGG	Control
0.0 (control)	-	-	-	-	-	56.0±1.0
1.5	23.0±1.0	32.0±1.0	15.0±1.0	25.0±1.0	20.0±1.0	-
2.0	14.0±1.0	20.0±1.0	11.0±1.0	15.0±1.0	17.0±1.0	-
3.0	6.0±1.0	12.67±0.5	2.0±1.0	6.0±1.0	7.67±0.5	-

A good hydrophilic polymer should be able to produce sufficient swelling or gelling as its concentration increases, an indication of their ability to take up water and retain it [33, 34]. Enhanced viscosity of disperse system like suspension affects the rheology of the formulation. This would reduce flow rate as well retard the rate of sedimentation of the dispersed phase. Reduction in sedimentation rate will further affect the pattern of packing of the sediments and further affect the redispersibility of the formulated suspension [35, 36]. Hydrophilic polymers such as cissus gum, acacia and guar gums as well their co-processed composites demonstrated enhanced viscosities as their concentrations were increase from 1.5 -3.0 % w/v in the respective formulations of the MTZB suspensions. This gave room for the desirable sedimentation volumes and flow rates as well as redispersibility recorded in the batches indicated in this report.

SUMMARY AND CONCLUSION

The study evaluated various co-processed hydrophilic polymer composites derived from CG, AG and GG and their non-co-processed forms at varying concentrations as suspending agents in the formulation of MTZB suspensions. The studies showed that all the hydrophilic polymers employed yielded enhanced properties of the suspensions following the increase in their respective concentrations which led to enhanced viscosities, reduced flow rates and increased sedimentation volumes with the best outcomes observed as CGG>GG>CG>CAG>AG>Control ($p < 0.05$) for sedimentation volume; CGG>CG>GG>AG>CAG>Control ($p < 0.05$) for viscosity and CGG>GG>CG>CAG>AG>Control for flow rate ($p < 0.05$). Very stable pH was recorded with CG at all the concentrations studied, followed by the CGG, especially at the early days following their preparations. There was no changes in the particle sizes of the MTZB in the products formulated with the CG following the freeze-thaw test ($p > 0.05$). Other batches exhibiting stable particle sizes after freeze-thaw test were got with 2.0 % w/v of AG, 2.0 % w/v of GG and 2.0 % w/v of CGG ($p > 0.05$). The batch containing 3.0 % w/v of CGG and those of the control batch had their p -values = 0.05. These results may be indication that stable suspensions of the MTZB may be obtained if formulated with 2.0 % w/v of these hydrophilic polymers. The ease of redispersibility of the MTZB suspensions were in the order GG < CG < CGG < CAG < AG < Control. The co-processing of CG with either AG or GG generated new hydrophilic polymers useful as suspending agents following their ability to impart higher viscosity leading to reduced flow rate of suspensions all which enhances the

sedimentation volume of disperse systems such as a suspension. The inconsistencies in pH in some of the products may be attributed to the presence of the various hydrophilic polymers since the controls batches exhibited stable pH all through the studies. The best co-processed hydrophilic polymer were those prepared with CG and GG.

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