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Evaluation of the Suspending Properties of a Novel Hydrophilic Biopolymer Derived from the Tubers of *Ipomoea batatas* on Sulphamethoxazole Suspension

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Authors' contributions

This research was carried out in collaboration between both authors. Author UKC conceived the work. Both authors designed the study, wrote the protocol and interpreted the data. Both authors anchored the bench work and managed the literature search, performed the data/statistical analysis. Author UKC produced the initial draft under the supervision of author NN. Both authors read and approved the final manuscript.

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ABSTRACT

Aims: This work examines a novel hydrophilic biopolymer, *I-polygel* derived from *Ipomoea batatas* tubers (Convolvulaceae) as a suspending agent in sulphamethoxazole suspension using acacia and tragacanth respectively as comparing standards.
Methods: Aqueous suspensions of sulphamethoxazole containing 1, 2, 4 or 5% w/v of *I-polygel,* acacia or tragacanth respectively were prepared and evaluated using sedimentation volume, rheology, viscosity, free-thaw cycle and redispersibility tests.
Results: Sedimentation volume was proportional to the concentrations of suspending agents across the preparations with the suspensions containing *I-polygel* exhibiting more consistency: *I-polygel* > acacia > tragacanth > control (P = 0.000). The flow rates were inversely proportional to the concentrations of the respective suspending agents whereas the reverse was the case with viscosity. There was no impediment to the flow of the suspensions at the concentrations of the

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suspending agents employed. The suspensions containing *I-polygel* indicated higher viscosities in all the concentrations: *I*-polygel > acacia > tragacanth > control (*P* = 0.000). There was no significant particle size increase before and after the freeze-thaw cycle test, showing that sulphamethoxazole may be stable in the presence *I-polygel*, acacia and tragacanth. All the preparations containing *I-polygel* was redispersed with the minimal shear stress: *I-polygel* < acacia < tragacanth < control (*P* = 0.000).

Conclusion: The application of a newly developed hydrophilic polymer, *I-polygel* as a suspending agent in comparison to acacia and tragacanth in the formulation of sulphamethoxazole suspensions yielded a more consistent and stable suspension with statistically proven higher sedimentation volume, better rheological properties, higher viscosities and ease of redispersion of suspension with minimal shear stress.

Keywords: Hydrophilic biopolymer; I-polygel; Ipomoea batatas; acacia; tragacanth; suspension; sulphamethoxazole.

1. INTRODUCTION

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) [1]. 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 aid of a single or combination of suspending agent(s) [2]. 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 [3]. 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 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 [4-6]. 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 [7,8]. 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 [9]. Besides their usage as suspending agents, plant gums have been widely used in the pharmaceutical sector as thickeners, binders, emulsifying agents and film formers [10].

Sulphamethoxazole (SMX) is a sulphonamide antibacterial agent [11]. It is an odourless, slightly bitter- after-taste and white powder that is very slightly soluble in water which would require a suspending agent to be formulated into a liquid dosage form. This property, therefore, makes it suitable for the evaluation of the suspending property of a new suspending agent [12-14].

The purpose of this study was to evaluate the suspending properties of a hydrophilic biopolymer, *I-polygel* (IP) obtained from the tubers of *Ipomoea batatas* [15-18] on sulphamethoxazole suspension using some biopolymers, acacia (AC) and tragacanth (TG) for comparison. The processing and characterization of *I-polygel have* been documented [19].

2. MATERIALS AND METHODS

2.1 Materials

The following materials were used as procured and includes: sodium hydroxide (Tianye chemicals, China), acacia, (J.T. Bakers, USA), tragacanth (Chemical & Instrument, India), sodium hypochlorite (3.5% w/v) (Multipros, Nigeria), ethanol, acetone (Sigma, USA), sulphamethoxazole (Indo Pharma, India).

2.2 Methods

2.2.1 Preparation of a novel hydrophilic biopolymer derived from *Ipomoea batatas* tubers *(I-polygel)*

This was prepared as described by Ugoeze et al. [19]. The fibre obtained after de-starching the milled tubers of *Ipomoea batatas was* dried at 60℃ and pulverised. A 500 g of this was submerged in enough 3.50% w/v sodium hypochlorite and kneaded for 10 min. This was washed severally with distilled water till the pH became neutral. It was covered with 96% ethanol and slurried for 5 min, dried at 60℃ and classified with sieve 60. A 100 g of this was blended with 250 ml of 3.0% w/v sodium hydroxide and precipitated with acetone. It was dried in a desiccator and passed through a 250 µm sieve.

2.2.2 Preparation of sulphamethoxazole (SMX) *suspension*

Different batches of SMX suspensions were formulated and contains either *I-polygel* (IP), acacia (AC) or tragacanth (TG) in concentrations of 1, 2, 4 and 5% w/v respectively (Table 1). Accurate amounts of the respective suspending agents and 2.0 g of SMX were homogenised and 0.05 g of benzoic acid was added and blended. Purified water was added and blended until the mixture became pourable. It was transferred into a 50 ml glass measuring cylinder. The mortar was rinsed and the volume of the preparation was made up to 50 ml with deionized water. The measuring cylinder was shaken for proper mixing of its content. Each batch was prepared in triplicate. The products were kept on a flat surface at ambient temperature for evaluation. The studies lasted for 10 days. The quality of the respective batches of preparations was evaluated using the sedimentation volume, rheological studies (flow rate), viscosity, freeze-thaw cycle and redispersibility tests.

2.2.3 Evaluation of SMX suspensions

2.2.3.1 Sedimentation volume

The initial volume, V_o was recorded for each batch of SMX suspension immediately after preparation. The sedimentation volume, V_t at any given period was also recorded on daily basis for ten days. The respective percentage sedimentation volume (*F*) was calculated using the equation [20]:

$$F = [Vt/Vo]\, X\, 100 \quad (1)$$

2.2.3.2 Rheology (flow rate)

The time required for 10 ml of each batch of SMX suspension to flow through a 10 ml glass pipette was determined and the apparent viscosity (*nα* in mls^{-1}) was calculated using the equation:

$$Flow\ rate\ (n\alpha) = Volume\ of\ pipette\ (ml)/ Flow\ time\ (sec) \quad (2)$$

2.2.3.3 Viscosity measurement

The viscosity of each batch of SMX suspension was determined with a Brookfield viscometer (DV2T, Brookfield Engineering Laboratories, Massachusetts, USA) using spindle #62 at 12 rpm for 5 min at 27.5℃. Determinations were carried out in triplicates.

2.2.3.4 Freeze-thaw test

The particle size of the dispersed phase of the respective batches of SMX suspensions was determined in a photomicrograph microscope ((Model XSZ-107BN, Zenithlabo, USA) using a Phenix Micro Image Analysis Software (PHMIAS 2006 Ver. 2.0). Each batch of the preparations was then subjected to a freeze-thaw testing by refrigeration for 24 h and then allowing it to thaw at room temperature for 24 h. The samples were then placed in a higher temperature (approximately 45℃) for 24 h and then kept at room temperature again for 24 h. The samples were later analysed for significant particle size changes using a photomicrograph microscope [21,22].

2.2.3.5 Redispersibility tests

After the 10^{th} day of the storage, the respective batches of the preparations were shaken in a clockwise direction with a uniform swinging movement. The number of times of swirling for

Table 1. Formula for the preparation of SMX suspension

Ingredients	Batch				Control
	Concentrations (% w/v)				
IP or AC or TG	1.00	2.00	4.00	5.00	0.00
Sulphamethoxazole (SMX)	4.00	4.00	4.00	4.00	4.00
Benzoic acid	0.10	0.10	0.10	0.10	0.10
Water (mL) to	100.00	100.00	100.00	100.00	100.00

the sediments to redisperse to produce a homogeneously mixed suspension was noted.

2.2.4 Statistical analysis

All statistical analysis of data was carried out using the IBM SPSS Statistics 20 software. A significant difference was considered where *P*-values were less than 0.05 and vice versa.

3. RESULTS AND DISCUSSION

3.1 Sedimentation Volume

The results of the studies on the effect of type and concentration of various suspending agents on the sedimentation volume of the batches of SMX suspensions are presented in Figs. 1-3 and Table 2. There was rapid sedimentation within the 1st day after the formulation after which a very gradual sedimentation was observed up to the 4th day after which there was almost no observable decrease in sedimentation volume. Generally, sedimentation volume was observed to be proportional to the concentration of suspending agents across the three polymers studied with the suspensions containing IP exhibiting more consistency than all other suspensions in terms of sedimentation volume. All the formulations were observed to obey the Stokes law [20]. The results could be summarized as follows: IP > AC > TG > Control (P = 0.000).

3.2 Flow Rate and Viscosity

The results of the effect of type and concentration of suspending agent on the flow rate (rheology) and viscosity of SMX suspensions are presented in Table 3. The flow

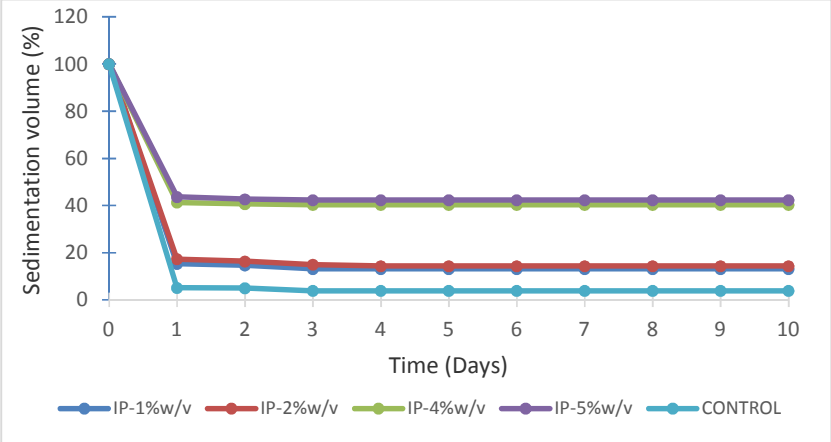

Fig. 1. Effect of concentration of IP on the sedimentation volume of SMX suspension

Table 2. Effect of concentration of suspending agents on the mean sedimentation volume

Concentration (%w/v)	Sedimentation volume (%)			
	I-polygel (IP)	Acacia (AC)	Tragacanth (TG)	Control
0.0 (control)	-	-	-	4.13±0.49
1.0	13.50±0.80	5.83±0.29	5.18±0.19	-
2.0	14.90±1.07	7.05±0.38	5.64±0.22	-
4.0	40.46±0.32	11.88±0.53	7.22±0.10	-
5.0	42.50±0.42	12.23±0.41	7.35±0.19	-

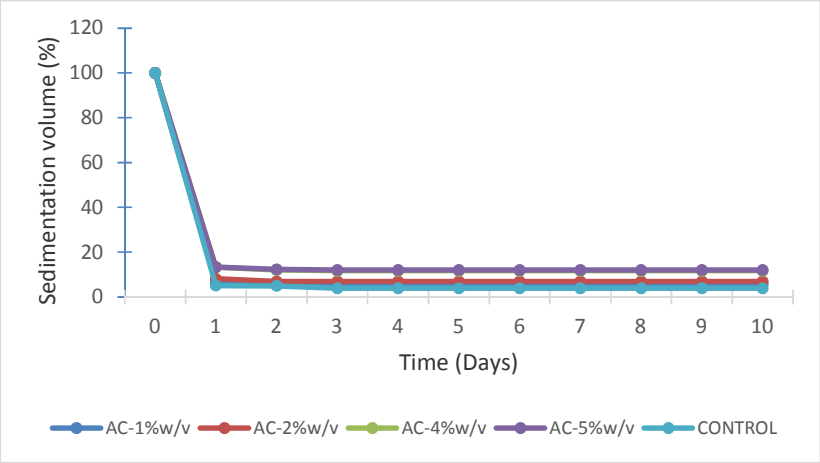

Fig. 2. Effect of concentration of AC on the sedimentation volume of SMX suspension

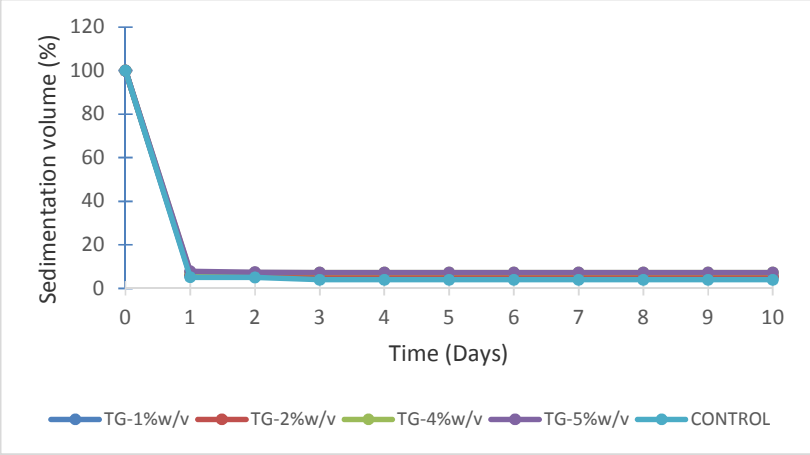

Fig. 3. Effect of concentration of TG on the sedimentation volume of SMX suspension

rate was inversely proportional to the concentration of the respective polymers whereas the reverse was the case with viscosity. However, there was no impediment to flow of the suspensions at the concentrations of the suspending agents employed. A good suspension ought to possess an enhanced viscosity at minor shear and low viscosity at high shearing rate so as to enable flow when agitated to enable pourability of the preparation from its container [23]. The general results of rheological studies show that the suspensions containing IP at all the concentrations tested indicated higher viscosities. In summary, the order of viscosity was: IP > AC > TG > Control (P = 0.000).

3.3 Freeze-thaw cycle test

The findings on the mean particle sizes of the various batches of suspensions prepared from various suspending agents before and after the freeze-thaw test show that there was no significant particle increase in the various formulations (Table 4). This shows the stability of SMX in the presence of the polymers used for this studies.

3.4 Redispersibility Test

Table 5 presents the number of shakes applied to achieve the redispersibility of the sedimented SMX suspension prepared with IP, AC and TG respectively. This number was lowest in the SMX suspensions formulated with IP and it was observed to decrease with the increasing concentration of the polymer, though, statistically, these apparent increase has no significant effect on the redispersibility of the preparations formulated with IP as observed (P = 0.788), showing that the concentration of IP as

low as 1%w/v could also offer a great ease of redispersibility of SMX suspension. However, a reverse trend was observed in the products prepared with AC and TG respectively as the number of shakes applied before the complete redispersion of the SMX suspension was proportional to the concentration of the suspending agent. Among the suspending agents studied, it was observed that IP yielded a product that was most readily redispersed. The ease of redispersion of sedimented products therefore, could be presented as follows: IP < AC < TG < Control (P = 0.000).

Table 3. Effect of the type and concentration of suspending agent on the flow rate and viscosity of SMX suspensions

Suspending agent	Concentration (% w/v)	Mean flow rate (ml/s)	Mean viscosity (cP)
I-polygel (IP)	1.00	2.35±0.01	14.75±0.35
	2.00	2.30±0.03	44.50±0.71
	4.00	2.24±0.02	61.50±0.71
	5.00	2.23±0.02	67.00±0.71
Acacia (AC)	1.00	2.37±0.03	10.75±1.06
	2.00	2.31±0.01	12.81±0.43
	4.00	2.29±0.03	27.70±0.28
	5.00	2.26±0.03	62.15±0.49
Tragacanth(TG)	1.00	2.42±0.01	7.75±0.35
	2.00	2.38±0.06	17.75±0.35
	4.00	2.36±0.01	21.50±0.71
	5.00	2.34±0.04	29.85±0.21
Control	0.00	2.48±0.06	5.90±0.14

Table 4. Effect of the type and concentration of suspending agents on particle size before and after freeze-thaw test

Suspending agent	Concentration (%w/v)	Particle size (µm)		*P*-value
		Before freeze-thaw test	After freeze-thaw test	
I-polygel (IP)	1.00	2.118±1.98	2.120±2.52	0.055
	2.00	2.122±1.37	2.125±1.43	0.004
	4.00	1.985±0.57	1.990±0.60	0.001
	5.00	1.985±0.58	1.990±0.60	0.001
Acacia (AC)	1.00	1.985±0.57	1.990±0.60	0.001
	2.00	2.298±1.50	2.300±1.51	0.014
	4.00	2.182±1.14	2.185±1.15	0.006
	5.00	2.182±1.13	2.185±1.15	0.006
Tragacanth (TG)	1.00	1.400±0.62	1.405±0.66	0.000
	2.00	1.968±1.01	1.970±1.05	0.001
	4.00	1.819±0.78	1.820±0.80	0.000
	5.00	1.651±0.57	1.655±0.59	0.000
Control	0.00	2.401±1.01	2.405±1.04	0.027

Table 5. Effect of concentration of suspending agent on the redispersibility of SMX suspensions

Concentration (%w/v)	Number of shakes to re-disperse product			
	I-Polygel	Acacia	Tragacanth	Control
0.0 (control)	-	-	-	105±13.23
1	3.33±0.58	24.33±1.15	35.00±5.00	-
2	2.67±0.58	26.67±1.53	44.00±2.65	-
4	2.33±0.58	29.00±2.65	48.00±2.00	-
5	1.33±0.58	39.00±12.29	50.00±4.00	-

4. CONCLUSION

The application of a newly developed hydrophilic polymer, *I-polygel* as a suspending agent in comparison to acacia and tragacanth in the formulation of sulphamethoxazole suspensions yielded a more consistent and stable suspension with statistically proven higher sedimentation volume, better rheological properties, higher viscosities and ease of redispersion of suspension with minimal shear stress. *I-polygel,* therefore could serve as a better suspending agent in formulating a stable sulphamethoxazole suspension than acacia and tragacanth.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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