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Research Article

INVESTIGATION OF THE EMULSIFYING AND SUSPENDING POTENTIAL OF CASHEW TREE GUM IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Cashew gum was investigated as a potential emulsifying and suspending agent in pharmaceutical formulations. The microbial quality of the purified gum was higher than the crude gum. Both crude and purified gum (20 – 50 % w/v) showed no antimicrobial activity against a number of pathogenic bacteria and fungi tested. The emulsifying property of the purified gum was investigated by preparation of emulsions using different classes of oils and employing the wet and dry gum methods. The ratio of oil to water to gum needed for the preparation of stable primary emulsions was determined. All the primary emulsions prepared creamed readily on dilution. The stability of paraffin oil emulsions was assessed and reduction in creaming was attempted through homogenization, addition of a surfactant and a thickening agent. Addition of a small quantity of Tween 80 (0.0125 – 0.015 % v/v) which is greater than the critical micelle concentration of the surfactant stabilised the emulsions. Homogenisation and addition of xanthan gum, a thickening agent, had no marked stabilising effect. The suspending property of the gum was investigated by assessing the sedimentation volume, flow rate and ease of redispersibility of zinc oxide suspensions, compared to those prepared with xanthan gum. Cashew gum produced flocculated zinc oxide suspensions with clear supernatant, fast sedimentation, low sedimentation volume and greater ease of redispersibility. The suspending ability of cashew gum was however; lower than that of xanthan gum.

Keywords: Cashew gum, Xanthan gum, Suspensions, Emulsions, Tween 80, Crude and purified gum

INTRODUCTION

Gums are complex polysaccharides with high molecular mass and may be classified as acidic (tragacanth, albizia, acacia), neutral (asparagus gum, plantago seed gum) or basic. Natural gums are known to be either acidic or neutral as there are no naturally-occurring basic gums [1]. Natural gums have the advantage of being hydrophilic, relatively inexpensive, generally non-toxic, and biodegradable and with wide pharmaceutical applications. Natural gums are, however, more susceptible to microbial contamination, uncontrolled hydration, batch to batch variation and prone to viscosity reduction upon storage, than synthetic gums [2].

Natural gums have been employed successfully as emulsifying and suspending agents in various pharmaceutical formulations [3-9]. Other applications of gums include the use as adhesives or binders [10, 11], drug release modifiers [12] and as film coatings [13] in tablet formulations. Commercially useful natural gums are obtained from sources as diverse as marine (alginate, agar, carrageenan), seed (guar gum, locust bean, amylose), tree exudates (acacia, khaya, albizia, tragacanth), animal origin (chondroitin sulphate, chitin, chitosan) and microbial (dextran, xanthan, emulsan). To make up for the limited availability and higher cost of some of these commercial gums, efforts have been made to find cheaper alternative naturally-occurring gums that have desirable, and possibly, enhanced pharmaceutical applications.

Natural gums of varying sources have recently been evaluated for their suspending and emulsifying applications. The mucilage extracted from the kernels of *Irvingia gabonensis* has been evaluated for its potential emulsifying and suspending properties [3, 4, 6]. One study showed that Irvingia mucilage at lower concentrations was a better suspending and emulsifying agent than acacia and tragacanth [4]. *Cissus rufescence* stem gum when used at concentrations of 0.6 to 1.0 % w/v produced highly flocculated zinc oxide suspensions with enhanced redispersibility [5]. Also, at concentrations above 0.75 % w/v, cissus gum produced liquid paraffin emulsion with minimal separation. *Leucaena leucocephala* seed gum, when used at different concentrations, demonstrated acceptable suspending ability in zinc oxide suspensions [7]. The purified gum extracted from the tubers of *Ferula gumosa* was found to reduce surface and interfacial tension of soybean oil emulsions [8]. Shear thinning emulsions were produced which showed overall stability over a six month period. The mucilage from the pods of *Abelmoschus esculentus* was found to possess better suspending ability than tragacanth, but comparable activity to sodium carboxymethyl cellulose, in paracetamol suspensions [9].

Cashew gum is the exudates obtained from the stem bark of the cashew tree (*Anacardium occidentale* Linn, family: Anacardiaceae), and are produced in the epithelial cells of the plant. The gum fluid produced in an infected or wounded cashew tree dries up by evaporation of water on reaching the external environment [14]. Cashew gum is a complex polysaccharide of high molecular mass which on hydrolysis yields L-arabinose, L-rhamnose, D-galactose and glucuronic acid. The chemical composition and structure of cashew gum has been extensively evaluated [15-17].

This paper investigates the emulsifying and suspending potential of cashew tree gum obtained from Ejura Cashew Plantation in the Ashanti Region of Ghana. The work is an extension of our earlier report on the physicochemical and tablet binding properties of cashew tree gum [11].

MATERIALS AND METHODS

Materials

Cashew gum was collected from Ejura cashew plantation as natural exudates of the stem bark of *Anacardium occidentale* Linn (family, Anacardiaceae) at Ejura, Ghana, after authentication by the curator of the plantation. The gum was selected, cleaned, purified, milled and screened as previously described [11]. Nutrient agar, macConkey agar, mannitol salt agar, cetrimide agar, sabouraud plus streptomycin agar, bismuth sulphite agar, zinc oxide, glycerine, castor oil, paraffin oil and peppermint oil were obtained from the chemical store of the Department of Pharmaceutics, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana. Distilled water was freshly prepared. The test microorganisms used were *Staphylococcus aureus* NCTC 10788, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* NCTC 102662, *Klebsiella* and *Candida albicans* ATCC 10231 (Stocks of Pharmaceutical Microbiology laboratory, KNUST, Ghana). The bacterial strains were grown and maintained on nutrient agar at 37 °C, while the yeast *Candida albicans* was grown and maintained on Sabouraud's dextrose agar at 30 °C.

Microbial quality of gum

The total aerobic viable count and fungal (yeast and mould) count of crude and purified cashew gum were determined by the pour-plate method [18]. In determining the presence of pathogenic bacteria in the gums, crude and purified cashew gum (0.1 g) were dissolved separately in 10 ml of sterile water and 1ml of the mucilage was inoculated into a previously stabilised MacConkey agar, mannitol salt agar, cetrimide agar, Sabauraud plus streptomycin agar and bismuth sulphite agar. The inoculated agars were incubated at 37 °C for 48 hours and growth of specific organisms depending on the selective media that was used was read as present or not present. All the experiments were done in triplicate.

Antimicrobial activity of gum

Purified and crude cashew gum (20 – 50 % w/v) was prepared separately in distilled water and the antimicrobial activity determined against *E. coli, Staph. aureus, Candida albicans, Klebsiella*, and *Pseudomonas aeruginosa* using the cup plate method. The plates were observed for any zones of inhibition after incubation for 48 hours. All experiments were duplicated.

Preparation of primary emulsions

Different ratios of oil, water and gum were investigated to determine the most stable primary emulsions of castor oil (fixed oil), paraffin oil (mineral oil) and peppermint oil (volatile oil). The castor oil, paraffin oil and peppermint oil emulsions investigated contained 12.5 – 33.3 %, 14.3 – 33.3 % and 20.0 – 35.7 % cashew gum, respectively. The emulsions were prepared by employing the wet gum and dry gum techniques of emulsion formation. For the wet gum method, the specified amount of water was added to the purified gum and triturated in a glass mortar. The oil was added drop-wise to the hydrocolloid solution and triturated till the hearing of a cracking sound to form the primary emulsion. For the dry gum method, the stated amount of oil was triturated with the gum followed by drop-wise addition of water till the hearing of a cracking sound. The primary emulsions prepared were observed for consistency and phase separation.

Stabilization of emulsions

Paraffin oil emulsions containing 20 % w/v cashew gum were prepared using the wet gum method. One hundred milliliters (100 ml) of paraffin oil emulsion was transferred into a domestic blender and homogenized for 3 minutes. Stabilization of 100 ml paraffin oil emulsions was further attempted by addition of a thickening agent (xanthan gum: 40 ml, 0.025 – 0.5 % w/v) and a surfactant (Tween 80: 15 ml, 0.0025 - 0.05 % v/v) followed in each case by homogenization in a domestic blender for 3 min. The emulsions were transferred into plain bottles, covered and stored at room temperature for observation.

Preparation of zinc oxide suspensions

The suspending potential of cashew gum was investigated by incorporating different amounts of the gum in zinc oxide suspensions. The suspending property of cashew gum was compared to that of xanthan gum, a standard suspending agent for peroral preparations. Zinc oxide powder (sifted through sieve 0.177 mm and levigated with glycerine) was used to prepare suspensions containing 0.1, 0.2, 0.3, 0.4, 0.5, 1.0, 2.0, 3.0 and 4.0 % w/v cashew gum and 0.1, 0.2, 0.3, 0.4 and 0.5 % w/v xanthan gum. All the suspensions were preserved with 0.2 % sodium benzoate.

Evaluation of suspensions

Zinc oxide suspensions prepared with cashew gum and xanthan gum were evaluated for their sedimentation profile, rheological behaviour and ease of redispersion. Each suspension (50 ml) was stored in a 50 ml measuring cylinder for 42 days at room temperature and observed hourly for 6 h and then every 72 h for 42 days. The sedimentation volume, S (%), of each suspension was calculated using the equation: $S = 100\ Vu/Vo$, where Vu is the ultimate volume of the sediment and Vo is the original volume of the suspension. The time required for each suspension to flow through a 10 ml pipette was determined and the flow rate or apparent viscosity ($\eta\alpha\ mls^{-1}$) was calculated using the equation: Flow rate = volume of suspension (ml) /flow time (s). The flow rates of freshly prepared and stored suspensions were determined. Fifty millilitres of each suspension was stored, undisturbed, in 50 ml measuring cylinders at room temperature for 42 days. After the storage period, the suspensions were shaken to redistribute the sediment, and the presence of deposits and cakes, if any, was recorded and the ease of redispersibility was assessed.

RESULTS AND DISCUSSIONS

Microbial quality and antimicrobial potential of cashew gum

Table 1 shows the microbial quality of crude and purified cashew gum. The microbial quality of the gums was assessed to determine their acceptability for use as pharmaceutical excipients in oral formulations. The total viable aerobic count and fungal count of the purified cashew gum was lower than that of the crude gum. Both the crude and purified forms of the gum did not contain *E. coli, Pseudomonas aeruginosa* or pathogenic Staphylococci. However, *Salmonella spp.* was found in the crude gum but not the purified gum. Microbial quality of purified cashew gum was satisfactory and met the European Pharmacopoeia [18] requirements of microbiological quality of pharmaceutical preparations while the crude gum did not meet the requirement. The current study has shown than purification has marked influence on microbial quality of cashew gum. Our earlier study had demonstrated that purification has marked effect on the physicochemical properties of cashew gum such as moisture content, insoluble matter, pH, viscosity and metallic ion content [11]. Purification is thus an important process in gum production as it reduces the microbial load, debris, and other extraneous material in natural gums.

Crude and purified cashew tree gums were tested for their antimicrobial activity against bacteria, and fungi. Both crude and purified cashew gum, at concentrations of 20 – 50 % w/v, presented no activity against *E. coli*, *S. aureus*, *Klebsiella spp.*, *Pseudomonas aeruginosa* and *Candida albicans,*. The results are in agreement with a recent study which reported no activity against all nine microorganisms tested except a weak activity observed against *Saccharomyces cerevisiae* [14]. These researchers attributed the low antimicrobial activity of the purified cashew gum to the possible removal of anacardic acid present in the crude gum during purification. However, in the present study no antimicrobial activity was observed in the crude and purified cashew gum at the concentrations investigated. Thus, anacardic acid may not be present in adequate amounts in the crude gum studied or that it may not be the only compound responsible for the antimicrobial activity of cashew gum.

Table 1: Comparison of microbial quality of crude and purified cashew gum

Parameter/Organism	Gum type	
	Crude cashew gum	**Purified cashew gum**
Total viable aerobic count	4.7×10^3 cfu/g	1.0×10^3 cfu/g
Fungal count	550 cfu/g	< 100 cfu/g
Pathogenic Staphylococci	Present	Absent
Salmonella spp.	Present	Absent
Pseudomonas spp.	Absent	Absent
E. coli	Absent	Absent

Emulsifying potential of gum

Different ratios of oil, water and cashew gum were used in the preparation of primary emulsions of castor oil, paraffin oil and peppermint oil. Table 2 shows the optimal ratio of oil to water to gum required for the preparation of stable primary emulsions of castor oil, paraffin oil and peppermint oil. The primary emulsion of peppermint oil formed was rather unstable, and broke down on

standing after a short time. The wet gum method produced better and more stable castor oil and paraffin oil primary emulsions while the dry gum method produced only stable primary emulsions of paraffin oil. All the primary emulsions formed exhibited massive creaming when they were diluted with water; there was therefore the need to stabilise them to minimise the incidence of creaming.

Table 2: Composition of stable primary emulsions prepared with cashew gum using the wet gum technique

Type of oil	Composition of emulsion (% v/v)		
	Oil	Water	Gum
Castor oil	54.5	27.3	18.2
Paraffin oil	50.0	30.0	20.0
*Peppermint oil	40.0	26.7	33.3

*Relatively less stable primary emulsion formed

Table 3: Effect of incorporation of Tween 80 on stability of paraffin oil emulsions

Concentration of Tween 80 (% v/v)	Effect on emulsion formed
0.0025 – 0.01	Marked creaming
0.0125 – 0.015	Stable emulsion with minimal creaming
0.018 – 0.050	Separation into 3 layers with marked creaming

Creaming, unlike cracking, is a reversible process as the emulsion is readily reformed after shaking the container. However, creaming of emulsions makes the pharmaceutical product aesthetically unacceptable. Creaming of emulsions occur when the dispersed phase is lighter than the continuous phase. Techniques such as homogenisation, addition of a thickening agent or reduction of the interfacial tension with a surfactant are commonly used to reduce creaming in emulsions. Homogenisation ensures the distribution of the gum (stabilizer) over the surface of the dispersed phase particles, thus reducing particle coalescence. Inclusion of thickening agents in the continuous phase of emulsions produces non-Newtonian systems that will have a high residual or zero shear viscosity [19]. Surfactants will reduce the interfacial tension between the phases as well as form a barrier between the phases against coalescence.

At 20 % w/v cashew gum concentration, the paraffin oil emulsions continued to exhibit marked creaming after homogenisation. Also, addition of 40 ml of 0.025 – 0.5 % w/v xanthan gum followed by homogenisation, did not have any marked effect on the level of creaming of the emulsions. Table 3 shows the influence of addition of different concentrations of Tween 80 on the stability of paraffin oil emulsions formulated with cashew gum. Tween 80 is a nonionic surfactant with specific gravity of 1.07, critical micelle concentration (CMC) of 13 – 15 mg/l and micelle molecular weight of 76 kDa [20]. Addition of Tween 80 to paraffin oil emulsions followed by homogenisation produced interesting observations. When Tween 80 (15 ml) was added at concentrations < 0.0125 % v/v and 0.018 - 0.050 % v/v, the extent of creaming of the paraffin oil emulsions was rather enhanced. However, addition of Tween 80 (15 ml) at a concentration range of 0.0125 – 0.015 % v/v caused a marked reduction in creaming of the emulsions. Thus, a critical amount of Tween 80, greater than its critical micelle concentration, was required to reduce creaming in paraffin oil emulsions. Concentrations of Tween 80 above the CMC will cause aggregation of the molecules into micelles. This will protect the oil globules from the aqueous phase leading to the formation of a relatively stable emulsion system.

Suspending potential of gum

The suspending potential of cashew gum was assessed in comparison to that of xanthan gum in zinc oxide suspensions at concentrations of 0.1 - 0.5 % w/v. The parameters which were assessed were sedimentation volume, flow rate or apparent viscosity and ease of redispersion. Table 4 shows the flow rate of zinc oxide suspensions formulated with cashew gum and xanthan gum as suspending agents. On the whole, an increase in gum concentration resulted in decreased flow rate and hence an increase in apparent viscosity of the suspension. Thus, the apparent viscosity of cashew gum formulated suspensions was lower than that of xanthan gum at the same concentration. Xanthan gum showed a more consistent reduction in flow rate with increase in concentration than cashew gum. The change in apparent viscosity of cashew gum with increase in concentration was less than that of xanthan gum. Figure 1 depicts the flow rate of freshly prepared cashew gum formulated suspensions and after storage for 42 days at room temperature. There was little or no difference between the flow rates of the two suspensions hence the apparent viscosity of the freshly prepared suspension remained largely unchanged after storage for 42 days at room temperature Viscosity is an essential characteristic of suspensions as a good suspension should remain fluid long enough for an accurate dose of a drug to be taken but should regain its original viscosity within a short period of time. Thus, thixotropic suspensions that are viscous on storage but would lose their consistency and become fluid on shaking are preferable.

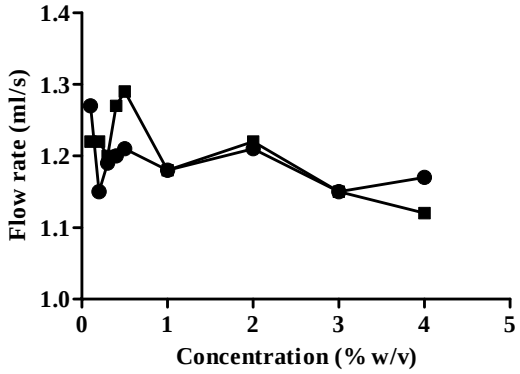

Fig. 1: The flow rate `of freshly prepared and stored zinc oxide suspensions prepared with cashew gum as suspending agent. Type of suspension: □ = freshly prepared suspension; ■ = stored suspension

Table 4: The flow rate of zinc oxide suspensions prepared with cashew gum and xanthan gum as suspending agents

Gum concentration (% w/v)	Flow rate (ml/s)	
	Cashew gum	Xanthan gum
0.10	1.27	1.05
0.20	1.15	1.06
0.30	1.19	1.02
0.40	1.20	0.98
0.50	1.21	0.89
1.00	1.18	ND
2.00	1.21	ND
3.00	1.15	ND
4.00	1.17	ND

ND = Not determined

Tables 5 and 6 show the sedimentation volume of zinc oxide suspensions prepared with xanthan gum and cashew gum, respectively, when stored for 42 days at room temperature. In both suspension formulations, the sedimentation volume showed a consistent decrease over the first 6 h, after which it remained the same or reduced marginally from the 3rd to the 42nd day. For most of the suspensions there was marked reduction in sedimentation volume upon storage from 6 h to the 3rd day. The rate of sedimentation of dispersed particles in the cashew gum formulated suspensions was faster than that of xanthan gum suspensions. At all

concentrations, the sedimentation volume were considerably lower for cashew gum suspensions compared to xanthan gum suspensions. For most of the suspensions, the minimum sedimentation volume was attained by the 15th day of storage.

Table 5: The sedimentation volume (% v/v) of zinc oxide suspensions prepared with xanthan gum as suspending agent

Gum concentration (% w/v)	Sedimentation volume (% v/v)														
	Time (h)							Time (day)							
	0	1	2	3	4	5	6	3	9	15	21	27	33	39	42
0.1	100	76	62	58	54	50	46	42	42	42	42	42	42	42	42
0.2	100	80	66	64	60	58	54	48	48	48	48	48	48	48	48
0.3	100	80	76	70	67	64	50	54	54	54	54	54	54	54	54
0.4	100	84	84	80	74	68	64	56	55	55	55	55	55	55	55
0.5	100	90	90	84	78	74	70	58	58	58	58	57	57	57	57

Table 6: Sedimentation volume (% v/v) of zinc oxide suspensions prepared with cashew gum as suspending agent

Gum concentration (% w/v)	Sedimentation volume (% v/v)														
	Time (h)							Time (day)							
	0	1	2	3	4	5	6	3	9	15	21	27	33	39	42
0.1	100	44	34	31	28	26	24	20	20	20	20	20	20	20	20
0.2	100	48	40	34	30	26	23	21	21	21	21	21	21	21	20
0.3	100	50	42	36	34	26	24	20	19	19	19	18	18	18	18
0.4	100	53	45	38	33	28	24	20	19	19	18	18	18	18	18
0.5	100	55	48	41	36	29	24	20	19	18	18	18	18	18	18
1.0	100	62	57	48	40	31	26	20	20	19	19	19	19	19	19
2.0	100	63	58	50	47	30	26	22	21	21	21	21	21	21	21
3.0	100	66	61	54	49	33	30	26	26	25	25	25	25	25	25
4.0	100	68	62	56	50	34	34	30	29	29	29	28	28	28	28

Table 7 shows the extent of redispersibility of cashew gum and xanthan gum suspensions on shaking after storage for 42 days at room temperature. Before redispersion, the supernatant was clearer in cashew gum suspensions than in xanthan gum suspensions. Zinc oxide suspensions containing 0.1 – 2 % w/v cashew gum were easily redispersed on shaking, but those containing 3 – 4 % w/v formed cakes which were redispersed with some difficulty. There was faster rate of sedimentation and tighter packing of suspended particles in the cashew gum suspensions which lead to caking of the sediment at higher concentrations of the gum. The addition of a deflocculating agent may reduce the fast rate of sedimentation of the cashew gum formulated suspensions. With xanthan gum only the 0.5 % concentration dispersed with a little difficulty upon shaking. The clear supernatant formed on storage, the faster rate of sedimentation and the greater ease of redispersibility of the cashew gum formulated suspensions are characteristic of flocculated suspensions. Xanthan gum formulated zinc oxide suspensions also exhibited the characteristics of flocculated suspensions with clear supernatant on storage, fast sedimentation, and higher sedimentation volume and easy to redisperse. This study shows that cashew gum has the potential to act as a suspending agent in pharmaceutical formulations but its suspending ability is lower than that of xanthan gum.

Table 7: Redispersibility on shaking of zinc oxide suspensions prepared with cashew gum and xanthan gum as suspending agents

Gum concentration (% w/v)	Extent of redispersion	
	Cashew gum	Xanthan gum
0.10	Easily redispersed	Easily redispersed
0.20	Easily redispersed	Easily redispersed
0.30	Easily redispersed	Redispersed on vigorous shaking
0.40	Easily redispersed	Redispersed on vigorous shaking
0.50	Easily redispersed	Redispersed on vigorous shaking
1.00	Easily redispersed	ND
2.00	Easily redispersed	ND
3.00	Cake formed, redispersed on vigorous shaking	ND
4.00	Cake formed, redispersed on vigorous shaking	ND

ND = Not determined

CONCLUSION

Cashew gum has been shown to possess emulsifying and suspending properties in pharmaceutical formulations. Emulsions formulated with cashew gum exhibits marked creaming which can be stabilised by incorporation of small quantities of Tween 80. When used at concentrations of 0.1 – 2.0 % w/v, cashew gum produces flocculated suspensions with clear supernatant, fast sedimentation, low sediment volume and demonstrable ease of redispersibility. However, the suspending ability of cashew gum is lower than that of xanthan gum, a reference suspending agent.

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