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Assessment of the suspending properties of *Cordia gheraf Gum* on Paracetamol suspension

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Abstract

Some excipients are currently available for the formulation of pharmaceutical suspensions. The purpose of this study is to search for cheaper and effective natural excipients that can be used as an effective alternative for the formulation of pharmaceutical suspension. The suspending properties of *Cordia gheraf* (family Boraginaceae) were evaluated comparatively with those of compound tragacanth, Acacia and gelatin at concentration range of 0.5 – 4.0% w/v in Paracetamol suspension. Characterization tests were carried out on purified *Cordia gheraf* pulp. Sedimentation volume (%), rheology and particle size analysis were employed as evaluation parameters. The values obtained were used as basis for comparison of the suspending agents studied. *Cordia gheraf* pulp is safe for use as a suspending agent in human and pet foods based on the levels of use, which are comparable to the use levels of other suspending agents. *Cordia gheraf* pulp (2.5%w/v) produced a comparable suspending ability as 4%w/v compound tragacanth. Also, the suspending ability of all the materials was found to be in the order: *Cordia gheraf* > Compound tragacanth gum > *Acacia* gum > Gelatin. At all concentrations employed, Cordia gheraf pulp had the strongest suspending ability relative to the other materials. The results suggest that, due to the high viscosity of *Cordia gheraf* pulp, its pulp can be a stabilizer of choice when high viscosity is desired. It can also serve as a good thickening agent in both pharmaceutical and food industries. Studies indicate that the pulp of *Cordia gheraf* may be used as a pharmaceutical adjuvant and as a suspending agent at 4%w/v, depending on its suspending ability and the stability of the resulting suspension.

Key words: *Cordia gheraf*, suspending agents, rheology, degree of flocculation and sedimentation volume.

Introduction

Gums are widely employed in the pharmacy as thickeners, suspending agents, emulsifying agents, binders and film formers. With the increase in demand for natural gums, it has been necessary to explore the newer sources of gums to meet the industrial demands. India, due to its geographical and environmental positioning has traditionally been a good source for such products among the Asian countries [1]. A pharmaceutical suspension, like other disperse systems, is thermodynamically unstable, thus, making it necessary to include in the dosage form, a stabilizer or suspending agent which reduces the rate of settling and permits easy redisperse of any settled particulate matter both by protective colloidal action and by increasing the consistency of the suspending medium. Suspending agents may be (i) inorganic materials, (ii) synthetic compounds, or (iii) polysaccharides. Natural gums like Acacia, Tragacanth, Khaya, Karaya and *Cordia gheraf* pulp belong to the latter group [2]. Gums have been wildly used as tablet binders, emulgents and thickeners in cosmetics and suspensions as film-forming agents and transitional colloids. Seed gums are important agrochemical used in various industries worldwide. The growing industrial utility of these gums in the field of paper, textile, petroleum recovery and pharmaceutical industries has resulted in an impetus in India for intensified research on new sources of gums and their modified products. *Cordia gheraf* pulp derived from the seeds of *Cordia gheraf* is a common herbaceous annual occurring weed throughout India [3]. Although, some work had already been carried out on gums as excipients; it seems that no work has been done on the suitability of *Cordia gheraf* pulp as a suspending agent in Paracetamol suspension as compared to the relatively common natural agents as *Acacia*, tragacanth and gelatin, using sedimentation volume, rheology and particle size analysis as assessment parameters. *Cordia* pulp is safe for use as a suspending agent in human and pet foods based on the levels of use of *Cordia* pulp, which are comparable to the use levels of other suspending agents [4].

Materials and Methods

The materials used include Paracetamol (fine powder), gelatin, benzoic acid, and amaranth solution (Merck,), Acacia gum powder (S.D. Fine, Mumbai), compound Tragacanth powder (Merck). The seed sample had earlier been identified and authenticated in the herbarium Department of Botany, Chandrasekhar Azad Agriculture University, Kanpur (Uttar.Pradesh). About 5 kg of fresh immature fruit of *Cordia gheraf* were collected from a Durjapur village local market of Kanpur district. After removal of the seeds, the fresh immature fruits were sliced, homogenized and extracted with cold water containing 1% (w/v) sodium metabisulphate [5]. The gum was dried at 50^{o} C for 8 hr, pulverized using blender, hydrated in double strength chloroform water for 5 days with intermittent stirring, then strained through a piece of muslin cloth. The gum was precipitated from solution using acetone. The precipitated gum was filtered, washed with diethyl either, and then dried in a hot air oven at 45^{o}C. The dried mass was powdered and stored in an airtight container. 1%w/v solution of the crude gum in cool distilled water was subjected to some characterization tests [6].

Preparation of Paracetamol Suspensions

Compound Acacia gum (0.5 g) and 10 g of Paracetamol were triturated together with 20 ml of Raspberry syrup to form a smooth paste. Benzoic acid solution (2 ml) and 1 ml of amaranth

solution were added gradually with constant stirring and then mixed with 50 ml of chloroform water double strength. The mixture was transferred into a 100 ml amber bottle, made up to volume with distilled water and then shaken vigorously for 2 min (thus making 0.5% w/v of the gum in the preparation). The procedure was repeated using 1.0, 1.5, 2.0, 2.5, 3.0, 3.5 and 4.0% w/v of compound tragacanth powder. The above procedure was repeated with tragacanth powder, gelatin and *Cordia gheraf* pulp.

Phytochemical Examination

Preliminary tests were performed to confirm the nature of mucilage obtained. The chemical tests that were conducted are: Ruthenium red test, Molisch test, test for reducing sugars and Ninhydrin test are shown in Table 1.

Table -1: Phytochemical screening of mucilage of *Cordia gheraf* pulp

S.No.	Tests	Observations
1.	Test for Carbohydrates (Molisch's test)	+ ve
2.	Test for Tannins (Ferric chloride test)	- ve
3.	Test for proteins (Ninhydrin test)	- ve
4.	Test for alkaloids (Wagner's test)	- ve
5.	Test for glycosides **(**Keller – Killaini test)	- ve
6.	Test for mucilage (Ruthenium red test)	+ ve
7.	Test for flavonoid (Shinoda test)	- ve
8.	Test for reducing sugar (Felhing's test)	- ve
9.	Mounted in 95% alcohol	Transparent angular masses under microscope
10.	Mounting in the iodine	No blue colored particles (starch absent)
11.	Test with cupric –tartaric solution	Red precipitate is observed
12.	Warming with 5M sodium hydroxide	A brown color is observed
13.	Test for chlorides(silver nitrate test)	- ve
14.	Test for sulphate (barium chloride test)	- ve

Determination of the Suspension Properties:

Particle Size Analysis

After shaking, 10 ml of each sample was separately transferred into 200 ml cylinder. Distilled water (150 ml) was then added, mixed, and 10 ml aliquot was removed at a distance of 10 cm below the surface of the mixture and at 1, 5, 10, 15, 20, 25 and 30 min. This was transferred into an evaporating dish and evaporated to dryness in an oven at 105^{o} C and the residue weighed. The particle diameter (d in cm) was then calculated using the Stoke's equation (Patel *et al*., 1986):

$$d = \frac{18\eta h}{(\rho s - \rho 0)} gt$$

where, h is the distance of fall of the particle (cm), t is the time (s), ρ is the viscosity of the dispersion medium (poise), $\rho s - \rho 0$ is the density gradient between the dispersed particles and the liquid (gcm^{-3}) and g is the gravitational constant (cms^{-2}).

Table - 2: Effect of type and concentration of suspending agents on the flow rate and viscosity of suspensions

Suspending agents	Concentration (%w/v)	Flow rate ml s-1	Viscosity (poise)
Cordia gheraf gum	3.0	0.96	2.85
	3.5	Too viscous	Intermediate
Tragacanth powder	3.0	1.35	1.26
	3.5	1.12	1.32
Acacia Gum	3.0	1.42	0.91
	3.5	1.26	0.85
Gelatin	3.0	1.74	0.27
	3.5	1.44	0.24

Determination of the pH of the suspensions

The pH of each of the prepared suspension was measured using pH meter (Merck Digital) at weekly intervals for 4weeks for ease of redispersibility, 10 ml of each suspension was poured into four calibrated tubes, which were stored at room temperature for 1, 2, 3 and 4 weeks. At the end of each storage period, each tube was shaken at constant moderate rate of 30 shake/min. the time (s) taken to redisperse the sedimented suspension was recorded.

Table- 3: Physicochemical characterization of *Cordia gheraf* gum

S.No.	Parameters	Observation
1.	Solubility	Slightly soluble in water, practically insoluble in alcohol, chloroform and acetone. Forms thick gel in water
2.	pH (1% w/v solution)	6.5
3.	Ash value	6.58%
4.	True density	2.6 g/dl
5.	Tapped density	0.65 g/cc
6.	Description	Powder: dark brown colored granular powder
7.	Angle of repose	26.25

Degree of Flocculation

The degree of flocculation was determined following the equation $\beta = F/F\alpha$, where F is the ultimate sedimentation volume in the flocculated suspension and $F\alpha$ is the ultimate sedimentation volume in the deflocculated suspension [7].

Sedimentation Volume:

Each suspension (50 ml) was stored in a 50ml measuring cylinder for 7 days at 35^{o}C. Observations were made at every hr for 7 hr and then every 24 hr for 7 days. The sedimentation volume, F (%), was then calculated using the following equation (Banker and Rhodes 1998): $F = 100Vu/Vo$ where, Vu is the ultimate volume of the sediment and Vo is the original volume of the of suspension.

Table-4: Degree of flocculation (β) of various suspending agents

Suspending agent	Concentration(% w/v)	Degree of flocculation(β)2
Cordia gheraf gum	1	1.95 + 0.39
	2	2.96+ 0.48
	3	4.59 + 0.59
	4	5.43 + 0.29
Tragacanth powder	1	2.08 + 0.84
	2	2.38 + 0.64
	3	4.47 + 0.25
	4	5.19 + 0.25
Gelatin	1	3.13 + 0.18
	2	3.53 + 0.49
	3	3.85 + 0.66
	4	4.60 + 0.19
Acacia Gum	1	2.13 + 0.18
	2	3.23 + 0.29
	3	3.95 + 0.36
	4	4.00 + 0.19

Table - 5: Values of Sedimentation volume (%) of suspension using different concentration of suspending agents.

Suspending agent	Concentration %w/v	Time (Hours)							
		0	1	2	3	4	5	6	7
Cordia gheraf gum	0	100	43	42	41	40	40	40	40
	3.0	100	86	84	82	78	77	75	75
	3.5	100	100	100	100	100	100	100	100
Tragacanth powder	3.0	100	87	84	81	78	67	64	62
	3.5	100	92	89	84	80	75	70	68
Acacia Gum	3.0	100	82	79	74	68	65	61	57
	3.5	100	87	84	77	72	68	64	62
Gelatin	3.0	100	78	66	61	57	52	48	45
	3.5	100	80	77	72	68	61	58	55
Suspending agent	**Concentration %w/v**	**Time (days)**							
		1	2	3	4	5	6	7	
Cordia gheraf gum	0	38	36	33	31	29	27	27	
	3.0	72	70	67	61	58	58	58	
	3.5	100	100	100	100	100	100	100	
Tragacanth powder	3.0	60	57	55	53	53	53	53	
	3.5	65	63	61	59	59	58	58	
Acacia Gum	3.0	55	52	50	48	48	47	47	
	3.5	60	58	56	54	54	54	54	
Gelatin	3.0	42	40	38	36	34	34	34	
	3.5	53	51	48	46	44	44	44	

Rheology:

The time required for each suspension sample to flow through a 10 ml pipette was determined and the apparent viscosity ($\eta\alpha$ in mls^{-1}) was calculated using the equation:

$$\text{Flow Rate} = \eta\alpha = \frac{\text{Volume of Pipette (ml)}}{\text{Flow time Seconds}}$$

The viscosity (in poise) of the samples was determined at 25° C using the Brookfield Synchro-electric viscometer; model LV DV (Brookfield) at 30 revolutions/min (Spindle#4). All determinations were made in at least triplicate and the results obtained are expressed as the mean values [8].

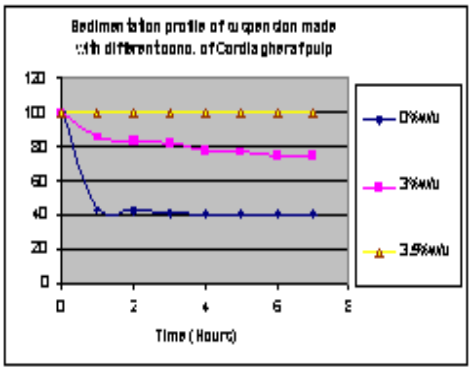
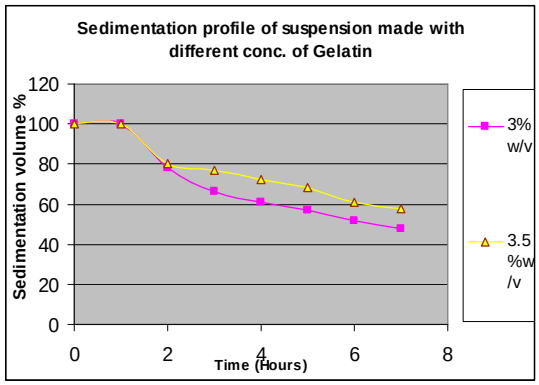


Fig.1



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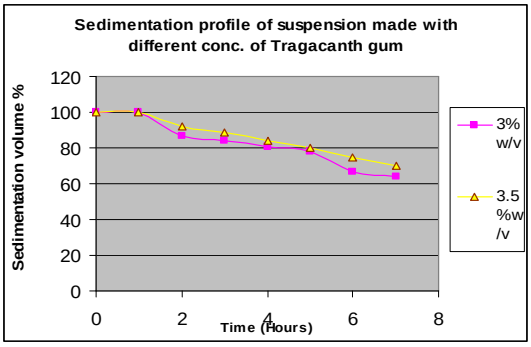

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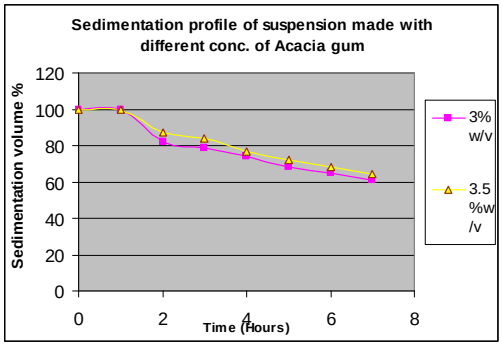
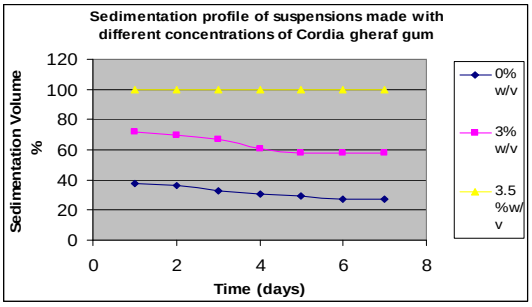


Fig.4



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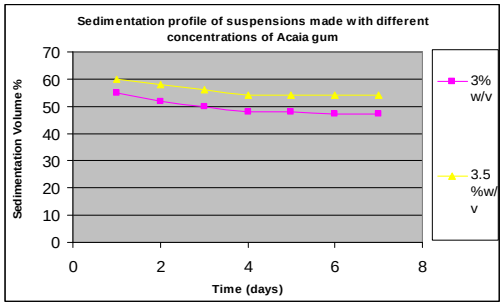

Fig.6

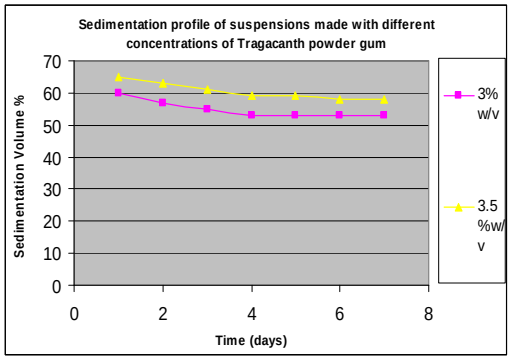

Fig.7

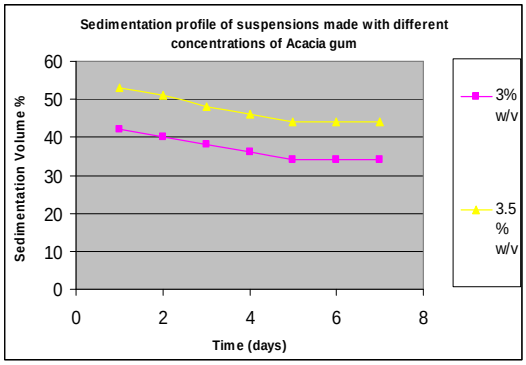

Fig.8

Results and Discussion

The effects of the type and concentration of the suspending agents on sedimentation volume, flow rate, viscosity and particle size are as shown in Tables 1 and 2. Phytochemical tests carried out on *Cordia gheraf* pulp confirmed the absence of alkaloids, anthraquinones and carbohydrates in accordance with the belief that gums do not contain carbohydrates, but complex acids built up of less common sugar. A Paracetamol suspension formulation was prepared in batches containing *Cordia gheraf* pulp, compound tragacanth, *Acacia* or gelatin (concentration range of 0 – 4% w/v at 0.5 w/v intervals). The preparations were assessed based on their sedimentation volume, viscosity, and flow rate and particle size analysis. The results showed that sedimentation volume, viscosity and particle size were found to be directly proportional to the concentration of the suspending agents. The reverse was the case for the flow rate. The sedimentation volume profile of the suspensions prepared with *Cordia gheraf gum*, Tragacanth powder, Gelatin and Acacia gum are shown in figure 1, 2, 3, 4, 5, 6, 7 and 8 respectively. Inverse proportionality was observed between the storage time on one hand and sedimentation volume on the other. All the formulations were observed to obey the Stoke's law (Equation 4) when subjected to particle size analysis. The suspending ability of the suspendants (as evaluated by the above assessment parameters) were in the order of *Cordia gheraf* gum> Compound Tragacanth > *Acacia* > Gelatin (except for the flow rate in which the reverse order was the case). Thus *Cordia gheraf* pulp appeared to exhibit the best suspendability of all the materials investigated. In fact, 3.5%w/v of this pulp produced suspension of optimal properties which compared favorably with the suspension containing 4%w/v compound tragacanth, a traditional suspending agent.

Conclusion

In view of these properties, pulp of *Cordia gheraf gum* can be employed as stabilizer and thickener of choice when high viscosity is desired especially in cosmetic, pharmaceutical and food industries. The binding and emulsifying properties of the gum are being studied.

Future Perspectives

The present investigation is a primary platform to indicate the suitability of *Cordia gheraf* gum as a suspending agent. The work can further be extended for evaluation of its suitability as disintegrating agent, gelling agent, emulsifying agent and other similar pharmaceutical

applications considering the easy and ample availability of the plant. The work can go a long way to evaluate herbal pharmaceutical excipients.

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