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FORMULATION AND COMPARISON OF SUSPENDING PROPERTIES OF DIFFERENT NATURAL POLYMERS USING PARACETAMOL SUSPENSION

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ABSTRACT

The present study aims to search for a cheap and effective natural excipient that can be used as an effective alternative for the formulation of pharmaceutical suspensions. So in this research suspending properties of different natural polymers were evaluated comparatively with each other .Tamarind seed polysaccharide, Tragacanth, Acacia and Gelatin at concentration range of 1 – 4.5%w/v are used to prepare paracetamol suspension. Characterization tests were carried out on each of polysaccharide. Sedimentation volume (%), rheology and particle size analysis were employed as evaluation parameters. The values obtained there from, were used as basis for comparison of the suspending agents studied. Results shown that the suspending ability of all the materials was found to be in the specific order: Compound Tragacanth gum > Acacia gum > Gelatin > tamarind seed polysaccharide. At all concentrations employed, compound Tragacanth gum had the strongest suspending ability relative to the other materials. The findings of the results suggest that, due to the high viscosity of compound tragacanth gum, it 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.

Key Words: natural polysaccharide, suspending Agents, sedimentation volume, rheology, particle Size.

INTRODUCTION

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 redispersion of any settled particulate matter both by protective colloidal action and by increasing the consistency of the suspending medium. Suspending agents are (i) inorganic materials, (ii) synthetic compounds, or (iii) polysaccharides. Natural gums like Acacia, Tragacanth, Khaya, and Karaya gum come under this category of polysaccharide [(1-3)]. Gums have been wildly used as tablet binders, emulgents and thickeners in cosmetics and suspensions as film-forming agents and transitional colloids. In this study, above mentioned four polymers viz. tragacanth gum, gum acacia, tamarind gum and gelatin were studied as suspending agent in paracetamol suspension as compared to the relatively common suspending agents of inorganic and synthetic category, using sedimentation volume, rheology and particle size analysis as assessment parameters. As reported, tragacanth is the dried gummy exudation from *Astragalus gummifer* and other species of *Astragalus* [(2)]. The gum is obtained through injury to the stem and is accumulated in the pith and medullary rays. In general, for most of the gums absorption of water causes the gum to swell and exude through the incision. Most of the gums consist of the calcium,

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magnesium and potassium salts of bassoric acid, known as bassorin. Most of them have been reportedly used as a suspending agent for insoluble powder, an emulsifying agent for oils, resin and a binding agent. Whereas, gelatin is derived from animal skin and is polysaccharide in nature which shows good suspending property. Paracetamol was chosen as a model drug for this investigation [1,3] because it is a typical representative of practically insoluble drugs which would require a suspending agent to be prepared as a liquid dosage form.

MATERIALS AND METHODS

The materials used include paracetamol (fine powder), gelatin, benzoic acid BP, and amaranth solution, chloroform water and raspberry syrup BP (RANKEM limited, New Delhi), Acacia gum powder, compound tragacanth powder (central drug house (P) LTD, New Delhi). Tamarind gum was extracted from the seed of *Tamarindus indica*.

Isolation of gum from Tamarind Seed: The crushed seeds of *Tamarindus indica* were soaked in water for 24 h, boiled for 1 h, and kept aside for 2 h for the release of gum into water. The soaked seeds were taken and squeezed in a muslin bag to remove marc from the filtrate. Then, to the filtrate, equal quantity of absolute ethyl alcohol was added to precipitate the gum. The gum was separated by filtration. The marc was not discarded but it was sent for multiple extractions with decreasing quantity of extracting solvent, i.e., water with the increase of number of extractions. The isolation was continued until the material was free of gum. The separated gum was dried in hot air oven at temperature 40°C. The dried gum was powdered and stored in airtight containers at room temperature [4, 5].

Preparation of suspension: For preparation of paracetamol suspensions, polysaccharide powder (individually 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 1ml 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 polysaccharide powder [4-6].

Sedimentation Volume: Each suspension (50 ml) was stored in a 50 ml-measuring cylinder for 7 days at 35°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:

$$F = 100Vu/Vo$$

(Equation 1)

Where, Vu is the ultimate volume of the sediment and Vo is the original volume of the suspension.

Rheology: The time required for each suspension sample to flow through a 10 ml pipette was determined and the apparent viscosity (one gm per cm per sec) was calculated using the equation:

Flow rate = Volume of pipette (ml) /Flow time (s)

(Equation 2)

The viscosity (in poise) of the samples was determined at 25°C using the Brookfield Synchro-lectric viscometer, model LVF (Brookfield Laboratories, Massachusetts) at 30 revolutions per min (Spindle #4). All determinations were made in at least triplicate and the results obtained are expressed as the mean values [7-11].

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 °C and the residue weighed. The particle

diameter (d in cm) was then calculated using the Stokes equation[7,10-14]:

$$d = 18 \acute{\eta} h / (\gamma_s - \gamma_0) gt$$

(Equation 3)

Where, h is the distance of fall of the particle (cm), t is the time (s), $\acute{\eta}$ is the viscosity of the dispersion medium (poise), $(\gamma_s - \gamma_0)$ is the density gradient between the dispersed particles and the liquid (g cm^{-3}) and g is the gravitational constant (cm s^{-2}) [15-17].

RESULTS

The effects of the type and concentration of the suspending agents on sedimentation volume, viscosity and particle size can be enumerated with the help of tables given below (Table 1- 4).

Table - 1: Values of Sedimentation volume (%) of suspension using different concentration of Tamarind Gum.

Sedimentation Volume (%)

Time (h)									Time (days)						
0	0	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1	100	67	56	50	46	40	39	39	39	39	38	36	36	36	35
2	100	68	53	52	47	43	44	42	41	40	39	40	37	37	38
3	100	70	50	61	53	50	46	49	48	46	46	44	44	43	43
4	100	82	77	79	64	62	60	57	56	54	51	50	49	49	48
5	100	91	83	80	74	70	69	65	64	63	63	62	60	57	55
7	100	97	89	83	81	77	71	71	68	68	67	67	67	66	66

Table - 2: Values of Sedimentation volume (%) of suspension using different concentration of Gum Acacia.

Sedimentation Volume (%)

Time (h)									Time (days)						
0	0	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1	100	63	50	49	45	42	38	38	36	39	36	34	32	30	28
2	100	65	52	51	43	43	42	40	40	40	36	38	37	39	
3	100	71	52	60	58	55	54	43	44	46	38	44	44	44	37
4	100	88	78	78	68	62	58	55	55	54	41	50	49	40	39
5	100	93	81	79	74	73	69	68	67	63	48	48	47	44	44
7	100	96	95	93	93	92	92	92	86	73	73	73	70	70	70

Table 3: Values of Sedimentation volume (%) of suspension using different concentration of Gelatin.

Sedimentation Volume (%)

Time (h)									Time (days)						
0	0	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1	100	47	47	46	46	46	46	45	45	45	44	44	44	43	43
2	100	50	57	57	57	57	52	50	48	48	46	42	42	42	41
3	100	53	68	64	57	57	56	56	56	56	56	56	56	56	53
4	100	69	72	75	77	76	75	65	74	71	73	73	73	73	72

5	100	78	80	79	79	79	78	78	76	76	75	75	75	75	75
7	100	96	95	93	90	88	87	87	83	83	83	83	83	84	83

Table 4: Values of Sedimentation volume (%) of suspension using different concentration of Tragacanth.

Time (h)	Sedimentation Volume (%)							Time (Days)						
0	0	1	2	3	4	5	6	7	1	2	3	4	5	6	7
1	100	43	42	42	42	42	38	38	30	30	30	30	30	29	28
2	100	49	47	47	47	47	42	40	38	38	36	32	32	32	31
3	100	50	48	48	47	47	46	43	40	40	38	38	38	37	37
4	100	58	56	55	55	55	55	50	50	43	43	43	43	43	42
5	100	61	60	60	60	60	60	59	56	56	56	56	55	55	55
7	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

A suspension containing Paracetamol as model drug was prepared in batches containing tamarind gum, compound tragacanth, acacia and gelatin as suspending agents (in the concentration range of 1,2,3,4,5,7% w/v). The preparations were evaluated on the basis of their sedimentation volume, flow rate, viscosity, and particle size analysis.

Flow rate at higher concentrations of each suspending agent shows the fact that Tragacanth Gum has very poor flow rate in formulated suspension using paracetamol as model drug (Table5)

Table 5: Effects of the type and concentration of suspending agents on the flow rate of paracetamol suspensions

Suspending Agent	Conc. (%w/v)	Flow Rate (ml s^{-1})
Tragacanth Gum	5	Too Viscous
	7	Extremely Viscous
Acacia Gum	5	0.73
	7	0.88
Gelatin	5	1.32
	7	1.57
Tamarind Gum	5	1.90
	7	1.94

Inverse proportionality was thus obtained between sedimentation volume and flow rate. The flow rate was found to obey the following order Tamarind gum > Gelatin > gum Acacia > Tragacanth gum. The results also illustrated the fact that the sedimentation volume, viscosity and particle size (except the flow rate) were found to be directly proportional to the concentration of the suspending agent. Inverse

proportionality was noticed between time for sedimentation and sedimentation volume.

DISCUSSIONS:

As demonstrated by all the parameters evaluated, Tamarindus indica seed gum possesses least potential as a candidate to act as suspending agent as compared to Gelatin, Gum Acacia and Gum Tragacanth. The present study also indicates the fact that Tamarind Gum cannot be used as stabilizer and thickener of choice when products of low viscosity grade are desired to be employed especially in cosmetic, pharmaceutical and food industries. All the studies also reveal the fact that Tragacanth gum has a very high potential to be used as suspending agent, stabilizer and thickener in pharmaceutical formulations in varying range of concentrations. The other two i.e. Gelatin and gum Acacia show better chances to be used but, not as prominent as that of Tragacanth gum. Thus, it can be predicted on the basis of all previous studies and present research work that though all gums possess characteristics to act as suspending agent but, suspending ability may differ. The study also illustrates that though gums may act as suspending agent, there are other natural polymers like Gelatin which possess significant suspending property when formulated in form of suspension.

Conclusions:

The results show the fact that sedimentation volume, viscosity and particle size were found to be directly proportional to the concentration of the suspending agents. The reverse case has been reported on flow rate parameter. 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 3) when subjected to particle size analysis. The suspending ability of the suspendants (as evaluated by the above assessment parameters) were in the order of Tragacanth gum > Gum Acacia > Gelatin > Tamarind gum. Thus, Tragacanth gum appeared to exhibit the best suspendability of all the materials which were under investigation.

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