Academic Sciences Asian Journal of Pharmaceutical and Clinical Research

Vol 5, Issue 4, 2012 ISSN - 0974-2441

Research Article

EVALUATION OF VARIOUS NATURAL SUSPENDING AGENTS FOR ITS SUSPENDING BEHAVIOUR USING PARACETAMOL AS MODEL DRUG FOR SUSPENSION

NAGARGOJE SUDAM*, BAWASKAR MANISH, MAHAJAN RITESH, PATIL SACHIN,M.P.RATNAPARKHI, CHAUDHARI SHILPA

Marathwada Mitra Mandal's college of pharmacy, Thergaon, Pune.Email: shilpapchaudhari78@yahoo.com

Received:2 August 2012, Revised and Accepted:7 September 2012

ABSTRACT

Many Excipients are currently available as a suspending agent. The purpose of this study is to search for cheap and effective natural Excipients that can be used as an effective alternative for the formulation of pharmaceutical suspensions. The study was aimed with firstly to compare between the flocculating behaviour of ocimum basilicum mucilage, tomato powder and tragacanth, secondly comparison between there suspending properties. For this all the three suspending agent were subjected to physicochemical study and evaluated for its flocculating and suspending properties. Suspensions of paracetamol were prepared and compared with different concentrations (0.5%, 1%, 1.5% and 2% w/v) of *ocimum basilicum* mucilage, tomato powder and tragacanth gum. Their sedimentation profile, pH, and rheological behaviour were compared. The ocimum basilicum mucilage was found to be a superior suspending agent than tomato powder and is comparable to tragacanth. Studies indicate that the mucilage from *ocimum basilicum* seeds may be used as a pharmaceutical adjuvant and as a suspending agent at 2%w/v, depending on its suspending ability and the stability of the resulting suspension.

Keywords: suspending agents, sedimentation volume, rheology, Flocculation, tomato powder, ocimum basilicum mucilage.

INTRODUCTION

A pharmaceutical suspension is a coarse dispersion in which insoluble solid particles are dispersed in a liquid medium, 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. A major challenge to formulation of suspensions is that of physical stability. The solid insoluble drug separates from the vehicle and settles to the bottom. It is desirable that such a formulation re-suspend easily upon shaking. Settling and aggregation may result in the formation of cakes that are difficult to re-suspend. Redispersibility of insoluble drug substance is therefore a critical requirement in the evaluation of suspensions. It is also a critical requirement that the drug in suspension be homogeneously mixed and remain both physically and chemically stable during the shelf life of the formulation. This is important because of the need to dispense a fairly uniform and accurate dose of the medicament.[1-3]

Mucilage's are polysaccharide macro molecules that dissolve more or less upon contact with water and form colloidal solutions. In recent years, plant gums and mucilage's have evoked tremendous interest due to their diverse application in pharmacy in the formulation of both solid and liquid dosage forms as thickeners, water retention agents,emulsion stabilizers, suspending agents, binders and film formers.[4] Suspending agents are(i) inorganic materials, (ii) synthetic compounds, or (iii) polysaccharides. Natural gums like Acacia, Tragacanth, Khaya, Karaya belong to the latter group.[5] Gums have been wildly used as tablet binders, emulgents and thickeners in cosmetics and suspensions as film-forming agents and transitional colloids. Mucilage are widely employed in the pharmacy as thickeners, suspending agents, emulsifying agents, binders and film formers. With the increase in demand for natural Excipients, it has been necessary to explore the newer sources of gums to meet the industrial demands. There are reports about the successful use of *Buteamonospermama, Albizia zygia gum* and *Leucaena eucocephala* seed gum as suspending agent.

In this study, the suspending properties of *ocimum basilicum* mucilage and spray dried tomato powder was compared with tragacanth as suspending agents for paracetamol suspension at a concentration of 0.5 %, 1 %, 1.5 %,2%w/w. The evaluation parameters were appearance, viscosity, rheology, sedimentation volume, redispersdibility, and flocculation studies.

MATERIALS AND METHODS

Paracetamol and spray dried tomato powder are gift samples provided by centaur Pharmaceuticals Ltd, Pune and Anmol dehydration Pvt. Ltd. Ahmadabad, Gujarat, India respectively. All the other solvents, reagents used were of Pharmacopoeial and analytical grade. The Seeds of *ocimum basilicum* were purchased from local market.

Extraction of the Mucilage[7, 8]

The extraction of mucilage from basil seeds was performed by modifying the method given in S.H. Hosseini- Parvar et al., 2010. The basil seeds were soaked and swelled in distilled water at 68 ± 1 ^{0}C and a water/seed ratio of 65:1. The mixture was stirred with a lab stirrer (Remi motor, Remi electrotechnik Ltd.) until the seeds were completely swelled (4 hrs agitation, 500 rpm). The swelled seeds were passed through a high speed homogenizer at 6000 rpm (Remi motor, Remi electotechnik Ltd.) to separate the gum layer from the seed surface. Then the total mixture is squeezed manually by hand through (40#) muslin cloth so that seeds get separated from gum and then gum was treated with acetone to remove any soluble impurities. The precipitated OBM separated, vacuum dried in vacuum oven (Lab Hosp, Mumbai; with vacuum pump of capacity 50Lt/min, vacuum 0.005 Torr, Atharva Vacuum Technologies Pvt. Ltd.) at 30-40 ^{0}c, powdered and passed through sieve (80#), then stored in tightly closed containers under dry and cool conditions.

Flocculation studies[9, 10]

For studying flocculation/coagulation processes jar test is widely used. The flocculant dye solutions were agitated for mixing for about 15-20 minutes. After the mixing the beakers were kept in safe place for sedimentation. The solutions were allowed for sedimentation for 20 minutes. The different concentrations of flocculants were taken in the range of 5-20mg/L. At regular intervals and definite intervals the supernatant solution was taken out, decanted, centrifuged and analysed spectrphotometrically. The concentrations of dye were analysed using UV-Vis spectrophotometer at wavelength 664 nm for Methylene blue. The test was done at room temperature.

The % dye removal was calculated from initial concentration (c_0) and final concentrations (c_e) of test solutions.

% dye removal = $\frac{co-ce}{c0} \times 100$

Preparation of Paracetamol Suspension

Compound tragacanth powder (1.0 g) and 0.75 g of paracetamol were triturated together with 20 ml of water to form a smooth paste. Sucrose (5 gm) and vanillin (1gm) were added gradually with constant stirring to above solution. After that preservatives like methyl and propyl paraben were added. The mixture was transferred into a 100 ml volumetric flask, made up to volume with distilled water and then shaken vigorously for 2 min (thus making 1.0 %w/v of the gum in the preparation). The procedure was repeated using 0.5, 1.5 and 2.0%w/v of tragacanth powder. The above procedure was repeated with tomato powder and *ocimum basilicum* mucilage.

EVALUATION OF SUSPENSION

Rate of separation[11]

The rate of separation of the suspensions were determined by keeping 50 ml portion of each suspensions in stoppered measuring cylinder and stored undisturbed at room temperature. The separation of clear liquid was noted at intervals of 7 d. The sedimentation volume, F (%), was then calculated using the following equation

F = 100Vu/Vo

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

Redispersion[12]

Fixed volume of each suspension (50 ml) was kept in calibrated tubes which were stored at room temperature for various time intervals (5, 10, 25 days). At regular interval of 5 d, one tube was removed and shaken vigorously to redistribute the sediment and the presence of deposit if any was recorded.

Rheological Study[13]

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

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

The viscosity (in poise) of the samples was determined at 25° C using the Brookfield viscometer, model DV-II+PRO (Brookfield Laboratories, Massachusetts) at 20 revolutions/min (Spindle no.18). All determinations were made in at least triplicate and the results obtained are expressed as the mean values.

Determination of the pH of the suspensions[13]

The pH of each of the prepared suspension was measured using pH meter (Equiptronics Digital pH meter) , 10 ml of each suspension was poured into four calibrated tubes, which were stored at room temperature.

Degree of flocculation[13, 14]

Potassium dihydrogen phosphate was added as a deflocculating agent. The degree of flocculation (β) was assessed by comparing the ultimate sedimentation volume ($F\alpha$) with control formulations in which no flocculating agent was added.

Degree of flocculation, $\beta = F / F\alpha$

Where, F is the ultimate flocculation height in the flocculated system and, $F\alpha$ is the ultimate sedimentation height in deflocculated system

RESULT AND DISCUSSION

The mucilage obtained from seeds of ocimum basilicum was subjected to physicochemical characterization results of which are given in table 1.

Table 1 Results of physicochemical characterisation of suspending agent:

Test	*Ocimum basilicum*	*Tragacanth*	*Tomato powder*
Solubility	Slightly soluble in water, practically insoluble in ethanol, acetone, ether and chloroform.	Slightly soluble in water, insoluble in ethanol, acetone and ether	Slightly soluble in water, insoluble in ethanol and ether
Swelling Index:			
a)In 0.1 N HCl	3.4	2.5	2.3
b)In Phosphate buffer pH 7.4	3.3	2.4	2.2
c)In Distilled water	3.6	2.8	2.6
pH	6.32	5.4	5.8
Viscosity (cp)	1.89	1.36	1.18
Bulk density (gm/ml)	0.600	0.44	0.54
Tapped density (gm/ml)	0.767	0.47	0.51
Compressibility Index (%)	14.54	29.11	28.18
Hausner ratio	1.152	1.41	1.32
Angle of repose (in degrees)	23.8	21.77	24.78

Flocculation is very important in case of pharmaceutical suspensions. The plot in fig.1 shows % dye removal (methylene blue) versus concentration of Flocculants used. It was observed that with increase in concentration of flocculants (*ocimum basilicum* mucilage, gum Tragcanth and tomato powder) %dye removal was increased up to certain level, above that there was decrease in dye removal as concentration of flocculants increases. The maximum dye removal was found to be 45% at 10mg/L concentration of mucilage. At lower concentration of flocculants in suspension caused larger amount of dye particles to aggregate and settle this is due to polymer bridging during flocculation. At higher concentrations of flocculants in dye solution particle settling was disturbed, which may be due to increase in repulsive energy between flocculants and dye solution. The results of flocculation studies reveals that flocculation ability of *ocimum basilicum* mucilage was more than gum Tragcanth, while Tomato powder was having less flocculation ability as per figure1.

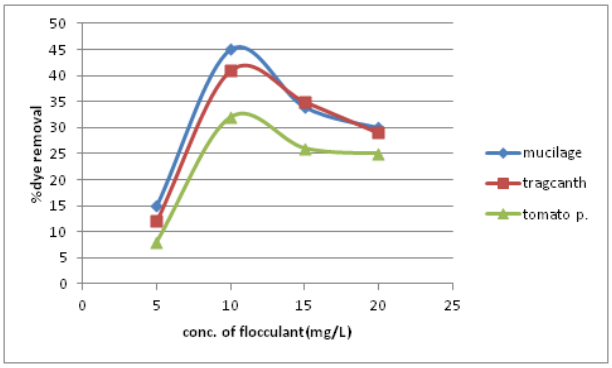

Figure 1: effect of concentration of flocculants on % dye removal

To evaluate the suspending properties of the mucilage, Paracetamol suspension formulation containing: either *Ocimum basilicum* mucilage, *Tragacanth or Tomato powder* as the suspending agent in the concentration range of 0.5 to 2% w/v was prepared. The preparations were evaluated based on their sedimentation profile, flow rate, rheology, pH.

It is quite known that the better is the suspending medium the lesser the rate of sedimentation. Suspensions are routinely evaluated for their suspending property. To evaluate the suspending properties of the mucilage, suspensions were prepared with fixed concentration of paracetamol but with varying concentration of test mucilage (0.5 to 2.0%w/v) as well as tragacanth and spray dried tomato powder. As the concentration of the suspending agent increases sedimentation volume and viscosity of the suspensions increased. There was faster rate of sedimentation of dispersed particles in suspensions containing 0.5% and 1% w/v of suspending agent. However the suspensions prepared with 2% suspending agent the change in sedimentation volume was minimum throughout of study. During study of 7 days rate of sedimentation was higher during first 2 days. (Table 2 and 3).

Table 2: Determination of flow rate and viscosity of suspension

Suspending agents	Concentration (%w/v)	Flow rate (ml/sec)	Viscosity (cp)
Tragacanth	0.5	1.23	105
	1	1	128
	1.5	0.82	141
	2	0.74	160
Tomato Powder	0.5	1.65	81
	1	1.42	95
	1.5	1.24	108
	2	0.89	128
Ocimum bacilicum mucilage	0.5	1.15	220
	1	1.02	265
	1.5	0.85	310
	2	0.72	Too viscous

Table 3: Determination of Sedimentation volume (%) using different concentration of suspending agents:

Time	Tragacanth				Tomato Powder				*Ocimum Mucilage*			
	0.5	**1**	**1.5**	**2**	**0.5**	**1**	**1.5**	**2**	**0.5**	**1**	**1.5**	**2**
½ hr	100	100	100	100	100	100	100	100	100	100	100	100
6 hr	64	67	69	72	75	78	81	85	58	61	62	100
1 day	42	44	46	48	73	76	78	82	45	52	60	100
2 days	41	43	45	47	64	68	70	70	40	51	58	100
3 days	40	42	44	47	42	45	48	50	40	49	55	100
4 days	39	42	42	45	38	41	44	42	39	48	55	99
5 days	38	39	41	44	37	40	42	42	38	48	52	98
6 days	37	39	41	42	33	35	37	39	38	48	52	98
7 days	36	38	41	42	32	35	37	39	38	48	52	98

Table 4: Determination of pH of formulations using different concentration of suspending agents:

Conc.(%)	Tragacanth	Tomato powder	Ocimum mucilage
0.5	7.19	5.65	6.01
1	7.35	5.75	6.09
1.5	7.45	5.84	6.15
2	7.48	5.98	6.22

Table 5 :Degree of flocculation of prepared formulation

Suspending agents	Concentration (%w/v)	Degree of flocculation
Tragacanth	0.5	1.90
	1	2.40
	1.5	4.30
	2	5.21
Tomato Powder	0.5	1.72
	1	2.81
	1.5	3.78
	2	4.40
Ocimum basilicum mucilage	0.5	1.80
	1	3.03
	1.5	4.88
	2	5.11

The rheological studies of the suspensions prepared with *ocimum basilicum* mucilage, gum tragacanth and tomato powder shows that the suspensions are pseudo plastic in their nature and their viscosity decreases with increase in rate of shear, which is an essential property in the formulation of suspension. Flow rate also decreases with increase in concentration of suspending agent.

Since the suspension produces sediment on storage it must be readily dispersible so as to ensure the uniformity of the dose. If sediment remains even after shaking vigorously for specified time, the system is described as caked. The prepared formulations containing ocimum basilicum mucilage and tragacanth easily redisperse after shaking no deposit observed. While formulations of tomato powder shows caking phenomenon.

The change in the pH of suspensions prepared with different concentrations of *ocimum basilicum mucilage*, tomato powder and *gum* tragacanth were recorded, formulations stored at room temperature. The pH of all the suspensions was found to be between 5.6- 7.5.

A comparison of Degree of Flocculation (β-values) for suspensions prepared with *ocimum basilicum* mucilage, gum tragacanth and tomato powder shows a slight higher values at the 1.5 and 2% w/v level for *ocimum basilicum* mucilage then tragacanth and Tomato

powder. These observations show that *ocimum basilicum* is a better suspending agent than tomato powder.

CONCLUSION

The formulations containing *ocimum basilicum* mucilage showed consistent superiority over tomato powder-containing formulations in terms of sedimentation volume ratio. The Results were comparable yet better than with that formulations containing Tragacanth as suspending agent. *Ocimum basilicum* mucilage and tragacanth -containing suspension formulations are more easily redispersed when compared with tomato powder-containing formulations. *Ocimum basilicum* mucilage may provide a suitable alternative to existing synthetic Excipients as suspending agent in pharmaceutical suspensions, providing a more readily available and affordable option in the countries where it is found growing abundantly, wild or cultivated. The maximum dye removal obtained at 10mg/L of mucilage conc. So the mucilage was having flocculating properties but not as an effective flocculant for removal of dye compared to other reported flocculants.

ACKNOWLEDGEMENT

The Authors are thankful to Dr. M. J. Patil, principal, Marathwada Mitra Mandal's College of pharmacy for providing the facilities for the present work.

REFERENCES

1. Martin A., Swarbrick J., Cammarata A., Physical Pharmacy, Lea and Febiger, Philadelphia and London, 1993, 4th ed., 477-511.
2. Banker S.G., Rhodes C.T., Modern Pharmaceutics, Marcel Dekker, Inc., New York, 1998, 3rd ed.,311
3. Bummer P.M., Remington: The Science and Practice of Pharmacy, Philadelphia College of Pharmacy and Science, 2005, 21st ed., 280.
4. Anroop B, Bhatnagar S.P, Ghosh B and Versha P. "Studies on *Occimum gratissimum* seed mucilage: evaluation of suspending properties," Indian J Pharm Sci., 2005; 67(2): 206-209.
5. Trease G E and Evans WC. In Pharmacognosy (4th Edition); 1996: pp. 196 – 210.
6. Pal S, Chakrborty S K, Banerjee A, Mukharji B. "Search of anticancer drugs from Indian Medicinal Plants (Ayurvedic, Unani, etc)", Indian J Med Res., 1968;56 : 445-55.
7. Koocheki A, Taherian AR, Bostan A, Studies on the steady shear flow behaviour and functional properties of *Lepidium perfoliatum* seed gum, food research international 2011:1-11
8. Hosseini- parvar SH, Matia- merino L, Goh K..K.T, Mortazavi S.A., steady shear flow behaviour of gum extracted from *ocimum basilicum L.* seed: effect of concentration And temperature journal of food engineering 2010;101:236-243
9. Mishra A, Bajpai M. The flocculation performance of *Tamarindus* mucilage in relation to removal of vat and direct dyes, bio tech,2006;97:1055-1059
10. Samantaroy S., Mohanty AK, Mishra A., Removal of hexavalent chromium by kendu fruit gum dust. J. Appl. Polym. Sci. 1997; 66: 1485-1494.
11. Mann A.S., Jain N.K., Khrya M.D., Evaluation of suspending properties of *Cassia tora* mucilage on sulphadimide suspension, Asian J. Exp. Sci., 2007,21(1), 63-67.
12. Sepulveda E., Saenz C., Aliaga E., Extraction and characterization of mucilage in opuntia Spp., J. of Arid Enviro., 2007, 68, 534-545.
13. Kumar R., Patil M. B., Patil S. R., Paschapur., Mahesh S., "Evaluation of Abelmoschus Esculentus Mucilage as Suspending Agent in Paracetamol Suspension." Int. J. PharmTech Research, 2009, 1(3), 658-665.
14. Jerald E., Dosi S., Raj A., Application of hibiscus leaves mucilage as suspending agent, Ind. J.Pharm. Edu. Res., 2007, 41(4).
15. Zatz JL. Applications of gums in pharmaceutical and cosmetic suspensions. Ind Eng Chem Prod Res Dev 1984; 23: 12-16
16. Lachman L., Lieberman H. A., Kanig J. L., Theory and Practice of Industrial Pharmacy, 3rdEd., Varghese Publishing House, Mumbai, 1987,3rd ed., 497-499
17. Jafar M., Aejaz A., "Studies on Ready mix Suspension of Ampicillin Trihydrate Development**,** characterization and in vitro evaluation" Int.J. Pharm. And Pharmaceutical Sci., 2010, 2(2), 110.