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Research Article

Preparation and Evaluation of Diclofenac Suspension by using Trigonella Foenum Graecum Mucilage as suspending agent

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ABSTRACT
The purpose to perform this is to study is to prepare and evaluate a novel and effective suspending agent from natural source that can be utilized as a better alternative for traditional suspending agent. In the first step the extraction of mucilage as a suspending agent from theseeds of Trigonella foenum graecum followed by steps involving testing of the mucilage obtained which include solubility testing, phytochemical testing, swelling index determination, preparation of diclofenac suspension (blank), sedimentation volume determination, measurement of viscosity, and flow rate determination. The result of study showed that the mucilage extraction of fenugreek seeds had potential as suspending agent. It contains carbohydrates, alkaloids, proteins and amino acid. The fenugreek seeds mucilage as a suspending agent shows highest sedimentation volume as collate with acacia, tragacanth and diclofenac only.

Keywords: Diclofenac suspension, Natural suspending agent, Trigonella foenum-graecum, Mucilage as a suspending agent

INTRODUCTION
A pharmaceutical suspension is heterogeneous thermodynamically unstable biphasic system consist of dispersion of a solid material (dispersed phase) in a liquid (continuous phase).[1-2] Suspensions are thermo labile biphasic liquid dosage forms in which the solid particles are dispersed uniformly distributed in outer or external phase with the suspending action of suspending agent and are prepared by application of mechanical stirring.[3] As dispersion system suspension are unstable system stabilized and make stable by adding suitable single or combination of suspending agents. [4-5]
When the water is added in the mucilage by dissolve little or more they form colloidal solutions. The tremendous interest evoked due to multiple application of plant mucilage's and gums in the formulation of both solid as well as liquid dosage forms as binders, suspending agents, water retention agents, emulsion stabilizers, and film formers.[6] A number of mucilages and gums have been used as suspending agent in various pharmaceutical suspension formulations. There are reports about the successful use of Isapgol mucilage[7], Tamarind Seed Polysaccharide[8], okra gums[9], Cassia tora Mucilage[10], Trigonella foenum graecum Mucilage[11], Abelmoschus Esculentus Mucilage[12] and Albizia zygia gum[13] as suspending agent.
The leaflets of Trigonella foenum graecum are tripartite, toothed an oval and flat with a narrower base with green color[14]. In the various food dishes of Indian origin consist of fenugreek seeds are a common and vital ingredient, it is used as whole as well as in the powdered form in the vegetable dishes, pickles, and spice mixture for various purposes[15-16].

Diclofenac
Diclofenac is 2-[2-(2, 6-dichloroanilino) phenyl] acetic acid, most frequently prescribed and commonly used anti-inflammatory agent. It is mainly used in treating a variety of acute and chronic pain and inflammatory conditions, like Dysmenorrhea, fever and headache. Its chemical structure is as in Figure1

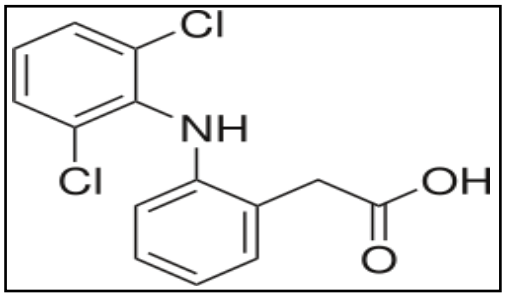

Fig.1: Diclofenac chemical structure

MATERIALS AND METHODS

Materials

Diclofenac were obtained as gift sample. Trigonella foenum-graecum seed was collected from the local market of Pune, Acacia, Benzoic acid, Tragacanth, (Loba Chemie, Mumbai). All other solvents used for experiment were of analytical grade.

Methods

Extraction of Mucilage as a suspending agent from Trigonella foenum graecum (Seed):

First size of seeds of Trigonella foenum graecum was reduced using ball mill. To prepare slurry of the crushed seeds of Trigonella foenum graecum were soaked in distilled water for about half day and then boiled in water bath. Then slurry was cooled and allows unwanted material to settling down. Upper portion was collected. The concentrated of collected portion were prepared by kept on water bath and allow to cool. Then with continuous shaking acetone was added in concentrated portion. The formed precipitate was separated and collected then dried at room temperature for a whole day. The dried material was size reduced to a powered form and transfer on sieve no. 60. The powder is kept in desiccators for removal of remaining moisture and used for further evaluation[19-20].

Evaluation of mucilage

Determination of Swelling Index:

The 0.5 gm of isolated powdered mucilage of seeds of Trigonella foenum graecum was taken in glazed porcelain dish. The distilled water (10ml) was put in powdered mucilage. Then mucilage- water mixture were stirred and allowed to stand for 60 minutes. After 60 minutes the remaining water in glazed porcelain dish was separated. The weight increase of the isolated mucilage was measured. By using above measurements the swelling index a calculated by using following equation,

$$\text{Swelling Index \% (SI)} = \frac{(W2 - W1)}{W1} \times 100 \quad \text{---------- (1)}$$

Where

W1= Weight of compact at time '0'W2= Weight of compact t at time't'

Phyto-chemical screening of mucilage

To screen and confirm the nature of mucilage obtained preliminary tests were performed. The various phto chemical screening are perform by conducting Molisch's test for detection of Carbohydrates, Ninhydrin test for detection of proteins, Wagner's test for detection of alkaloids, Ruthenium red test for detection of mucilage, Iodine test for detection of starch, Shinoda test for detection of flavonoids, Keller-Killaini test for detection of glycosides, Felhing's test for detection of reducing sugar and Ferric chloride test for detection of Tannins.

Preparation of diclofenac suspension

Accurately weighed 1 g of compound tragacanth powder and 1 g of diclofenac were triturated together with 20 ml of water to form a smooth paste. After that preservative 0.1% w/v benzoic acid were added with constant stirring to above solution. The mixture of all above was added into a volumetric flask with 100 ml size and with vigorous shaking for 5 minutes, volume make up with distilled water (1.0% w/v). The procedure was repeated using 0.5%, 1.5% and 2.0% w/v of tragacanth powder. The above procedure was repeated with 0.5%, 1%, 1.5% and 2.0% w/v acacia and Trigonella foenum graecum mucilage. Diclofenac suspension was prepared as per formula given in Table 1.

Table 1: Formulation of Diclofenac suspension

Compound	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Diclofenac(gm)	1	1	1	1	1	1	1	1	1	1	1	1
Compound tragacanth powder (gm)	0.5	1	1.5	2	--	--	--	--	--	--	--	--
Acacia (gm)	--	--	--	--	0.5	1	1.5	2	--	--	--	--
Mucilage (gm)	--	--	--	--	--	--	--	--	0.5	1	1.5	2
Benzoic acid (gm)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Pineapple flavor (ml)	1	1	1	1	1	1	1	1	1	1	1	1
Distilled water q.s (ml)	100	100	100	100	100	100	100	100	100	100	100	100

Evaluation

1. pH:

The digital p^H meter is used for measurement of pH for all of the developed formulations.

2. Sedimentation volume[2]

The sedimentation volume of all preparation is calculated by using the following equation,

$$F = \frac{Hu}{Ho} \quad \text{.....2}$$

Where,

F is Sedimentation volume

Hu is ultimate or final height of sediment as suspension settles,

Ho is original or initial height of suspension.

3. Redispersibility

50 ml fixed volume of all preparation was put remains in calibrated tubes, were stored at room temperature for 1, 5, 10, 15, 20, 30, 45 days time intervals. One calibrated tube was removed at regular interval and vigorously shaken for sediment to redistribute and if any presence of deposit was recorded.

4. Flow rate

The flow rate (F) of each formulated suspension was determined by counting time taken for 20 ml sample of formulation to flow through a 20 ml pipette and by using the following equation:

$$F = \frac{\text{Volume of pipette (ml)}}{\text{Flow time (sec)}} \quad \text{.....3}$$

5. Determination of viscosity

The Brookfield viscometer was used with 100 rpm for measurement of viscosity of all formulations. Viscosity of each formulation was measured three times and the mean value is calculated.

6. Effect of temperature

The effect of temperature in the range of 30°c to 60°c was analyzed on viscosity of all formulations.

RESULTS AND DISCUSSION

Mucilage Evaluation

The swelling index of mucilage was found to be 38% after 60 minutes. The result shows increased swelling index was found with time. The swelling index value is increased it's becauseof the directly proportional relationship weight gain by mucilage and rate of hydration. So as the concentration of mucilage increase the increase in swelling index observed.

Mucilage phyto-chemical screening

The result of various chemical test on mucilage performed for analysis of composition confirms the absence of glycosides, flavanoids, reducing sugar, starch and tannins. The chemical test of mucilage with ruthenium red showed red coloration which gives confirmation of the mucilage. Mucilage with Molisch's reagent develops the violet ring at the junction of two liquids gives confirmation about presence of carbohydrates. The phyto-chemical screening outcomes ofmucilage are given in Table 2

Table 2: Outcome of Phytochemical screening of mucilage

Sr. No	Identification test	Name of test	Observation
1	Test for Carbohydrates	Molisch's test	Positive
2	Test for proteins	Ninhydrin test	Negative
3	Test for alkaloids	Wagner's test	Positive
4	Test for mucilage	Ruthenium red test	Positive
5	Test for starch	Iodine test	Negative
6	Test for flavonoids	Shinoda test	Negative
7	Test for glycosides	Keller-Killaini test	Negative
8	Test for Tannins	Ferric chloride test	Negative

Evaluation of suspensionpH determination

All formulation shows the pH in the range of 6.89 – 7. 16. All determined pH for all formulation is summarized in Table 3 and represented in Figure 2.

Table 3: pH profile for all formulation of suspensions

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
pH	6.89	6.99	7.01	7.19	6.91	7.16	7.1	6.98	6.90	6.94	7.16	7.12

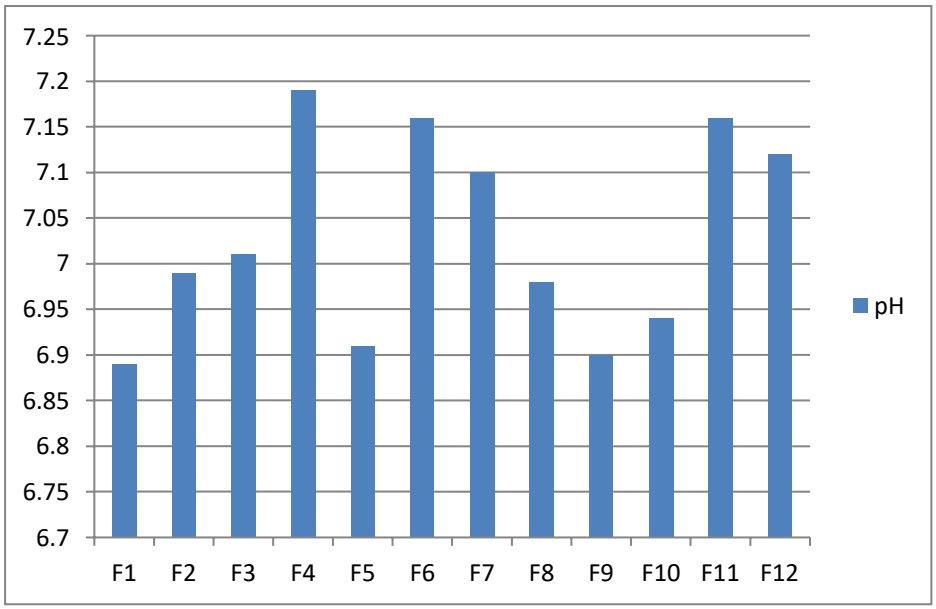

Fig.2: pH of all formulation of suspensions

Sedimentation volume

Initially sedimentation volume of all formulation was observed high value but shows low value on end of 7 days. The comparative values of Sedimentation Volume for all formulation are summarized in Figure 3. Formulation with high concentration of suspending agent was found to be stable and easily redispersed even after 45 days. The higher values of sedimentation value at faster rate are observed in formulation with the low concentration of suspending agent as comparison to the formulation with higher amount of suspending agent.

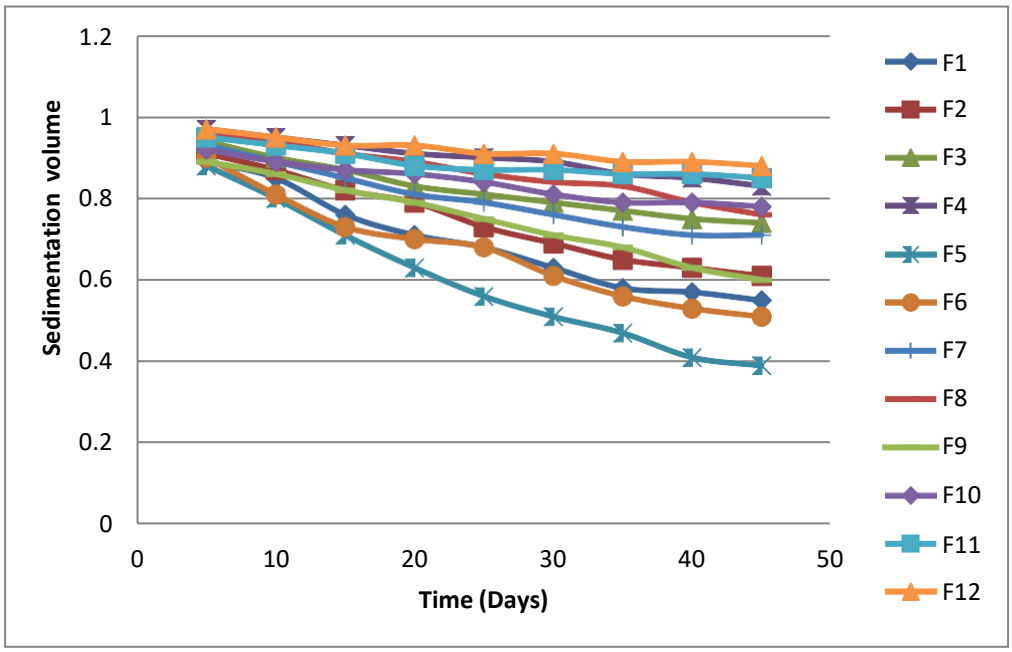

Fig.3: Comparative sedimentation volume profile of all formulation of suspensions

Redispersibility

Suspension formulation is called as caked if the settled particle remains as sediment even on vigorous shaking of formulation. Upon evaluation after 45 days all the formulated suspension was easily redispersible on maximum 13 shaking which all are summarized in Table 4. The formulated suspension with less amount of suspending agent shows easy as well as faster redispersion than the suspension formulation with high amount of suspending agent. This may due to high viscosity of suspensions with high amount of suspending agent.

Table 4: Redispersibility of all Formulation of suspension

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
No. of shaking for complete dispersion	5	6	8	13	6	8	10	15	5	7	10	12

Flow rate:

The flow rate was formulated suspension with low amount of suspending agent shows high flow rate as compared to formulated suspension with high amount of suspending agent. The value of flow rate is increases from higher to lower amount of suspending agent in formulation. The flow rate of formulation in the range of 0.015-0.038 and are summarized in the Table 5.

Table 5: Flow rate of all Formulation of suspension

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Flow rate	0.035	0.031	0.027	0.024	0.038	0.035	0.032	0.030	0.028	0.023	0.019	0.015

Determination of viscosity:

As increase in the rpm the viscosity of all formulation was shows decreased value of viscosity which indicate shear thinning nature of suspension. The viscosity values of all formulation have been summarized in table 6.

Table 6: Viscosity of all Formulation of suspension

Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Viscosity	0.027	0.032	0.035	0.040	0.023	0.028	0.033	0.037	0.027	0.033	0.036	0.044

Effect of temperature

The gradual rise in temperature of the suspension shows reduction in the viscosity for allformulation.

CONCLUSION

The mucilage extracted from Trigonella foenum graecum has the potential as a suspending agent at various concentrations and can be used as a pharmaceutical excipient. The increases in concentration of suspending agent in suspension lead to increase in the viscosity of formulation which attributes to reduce the sedimentation rate and plays crucial rule for increasing stability of the suspension.

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