

ISAPGOL MUCILAGE AS A POTENTIAL NATURAL SUSPENDING AGENT

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ABSTRACT

Mucilage can be used to suspend insoluble substances in liquids and it helps in preventing sedimentation due to its colloidal nature and viscosity. The inclusion of stabilizer or suspending agent in the pharmaceutical suspension 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. The present study deals with isolation of a natural pharmaceutical excipient from the seeds of *Plantago ovata* which can be used as an effective suspending agent. The compatibility between the drug and isolated mucilage powder was found to be good by the I.R spectral studies. Suspensions of Nimesulide were prepared and the properties were compared with that of a marketed product. The sedimentation was observed for 7 days. The sedimentation behavior of formulation F3 was found to be similar with that of the marketed product. All the formulations were redispersed uniformly without any deposits. The average size of the particles in the suspension was found to be 36.3 μm and the minimum and maximum particle size were 14.7 & 67.4 μm respectively. The drug content of all the formulations was in the range of 96-99.3%. The rheological study confirmed the shear thinning nature of the suspension. The present study confirms that isapgol mucilage powder can be used as an effective suspending agent in oral liquid formulations. But utilizing the same in large scale manufacturing needs to be studied in future.

KEYWORDS: Nimesulide, Isapgol mucilage powder, Suspending agent, *Plantago ovata*

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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 medium¹. The precision of each dose of a pharmaceutical suspension depends on the homogeneity of the dispersion and the volume removed for administration. The influence of formulation and package-related factors can be easily controlled during development². In practice, suspensions are usually redispersed by shaking. Suspended solids may slowly separate on standing but are easily redispersed³.

Plant Mucilage are pharmaceutically important polysaccharide with wide range of applications such as thickening, binding, disintegrating, suspending, emulsifying, stabilizing, and gelling agents. They have been also used as matrices for sustained and control release drugs⁴. Mucilage because of its colloidal nature and viscosity can be used to suspend insoluble substances in liquids and help in preventing sedimentation⁵. Nimesulide is a non steroidal anti-inflammatory drug having half-life 1.56 to 4.95 hr which requires frequent dosing to maintain plasma concentration⁶. Various works have been reported with respect to usage of Nimesulide for pediatric purpose^{7, 8}. The purpose of this study was to isolate a natural pharmaceutical excipient which can be used as an effective suspending agent in the formulation of pharmaceutical suspensions. Mucilage was extracted from the seeds of *Plantago ovata* and used as a suspending agent in Nimesulide suspension. The prepared suspension was compared with that of a marketed product and evaluated for various parameters like sedimentation volume, rheology and particle size analysis as assessment parameters.

MATERIALS

Nimesulide was obtained as a gift sample from Panacea Biotech, Lalru, Punjab. Isapgula seeds were procured from local market, Bangalore. Citric acid, methyl paraben, propyl paraben and vanillin flavor were purchased from S.D. Fine Chemicals, Mumbai, India. All other reagents used were of AR grade

EXPERIMENTAL METHOD

Isolation of mucilage from *Plantago ovata* seed

The *Plantago ovata* seeds were soaked in distilled water for 48 hours and then boiled for 10 minutes. The resulting mass was squeezed through muslin cloth. To the filtrate an equal volume of acetone was added to precipitate the mucilage. The isolated mucilage was dried in an oven at 40⁰C for 2 hours, powdered, passed through sieve No. 80 and stored in a desiccator^{9, 10}.

Mucilage powder characterization

The bulk density and tap density of the ispagol mucilage powder were determined using tap density tester (USP) ED – 1020 (Electro lab). Also the flow properties of the powder were also found.

Drug-Excipient interaction studies

The pure drug sample and the physical mixture of drug & mucilage powder in the ratio 1:1 were subjected to I.R spectral studies using FTIR spectrophotometer (FTIR 8400 S, Shimadzu, Japan).

Formulation of suspension

The required quantity of ispagol mucilage powder was taken in a mortar. A small quantity of water was added and the mucilage was allowed to soak for 15 min. To this 500 mg of Nimesulide was added and triturated to form a paste. The preservatives, methyl and propyl paraben, citric acid, and flavor vanillin was added and further triturated to form a homogenous mixture. The mixture was transferred to a calibrated bottle and the volume was made up using sufficient quantity of water.

Evaluation of suspension

Sedimentation Volume: The 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:

$$F = V_u/V_o$$

Where, V_u is the ultimate volume of the u sediment and V_o is the original volume of the suspension.

Rheological Behavior: The viscosity of the prepared and marketed suspensions was determined using Brookefield's viscometer (Model DV II). The viscosity values were determined at 10, 12, 20, 30, 50, 60 and 100 rpm at 25°C using spindle No. 2. The All determinations were made in triplicate and the results obtained are expressed as the mean values.

Particle size analysis: The particle size distribution in the suspension was determined using optical microscope (Olympus LITE image). The suspensions were mixed thoroughly and a drop of the suspension was taken on a slide and spread into a thin film. A total of 100 particles are counted and their minimum, maximum and average particle size is determined.

Redispersion: Fixed volume of each suspension (50 ml) was kept in calibrated tubes which were stored at room temperature for 45 days. At regular interval of 5 days, one tube was removed and shaken vigorously to redistribute the sediment and the presence of deposit if any was recorded.

Drug content: Amount equivalent to 50mg of drug was taken, volume made up to 50ml with acetone, vortexed, filtered, diluted suitably with acetone and the drug content was estimated using UV-VIS spectrophotometer (UV-1601, Shimadzu) at 450 nm¹¹.

Stability studies: The prepared formulations were stored in accelerated storage condition of $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ RH for a period of 45 days and observed for changes in physical appearance and drug content¹².

RESULTS AND DISCUSSION

The results of powder analysis are shown in **Table 1**. The extracted mucilage powder was found to be free flowing. The compatibility between the drug and isolated mucilage powder was found to be good by the I.R spectral studies which are indicated in (**Fig.1, 2**). Suspensions of Nimesulide were prepared using ispagol mucilage powder as suspending agent in various concentrations (**Table 2**). The properties of the prepared suspension were compared with that of a marketed product. The sedimentation was observed for 7 days. The sedimentation behaviors of the formulations are indicated in **Fig. 3**. The formulation F3 was found to be the formulation with close comparison to the marketed product. All the formulations were redispersed uniformly without any deposits. This formulation was further evaluated for its rheological properties and particle size distribution (**Fig. 4**). The average size of the particles in the suspension was found to be 36.3 μm and the minimum and maximum particle size were 14.7 & 67.4 μm respectively. The drug content of all the formulations was in the range of 96-99.3%. The suspensions were stable in accelerated storage conditions and the drug content does not vary to larger extent during the period of study. Also there was no change in the physical appearance of the formulations. The rheological study of the formulation F3 indicated that as the rpm increases the viscosity decreases, confirming the shear thinning nature of the suspension. The present study suggests that ispagol mucilage powder can be used as an effective suspending agent in oral liquid formulations and it can be a good alternative to synthetic suspending agents. The feasibility of isolation of mucilage powder in large scale needs to be studied in future.

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Table 1: Mucilage Powder Characterization

Parameters	Observed values
Bulk Density	0.24 g/ml
Tap density	0.363 g/ml
Carr's index	19.11%
Hausner's ratio	1.23
Angle of repose	13°
Average particle size	185µm

Table 2: Formulation of Nimesulide Suspension

Ingredients (in mg)	Formulation Code			
	F1	F2	F3	F4
Nimesulide	500	500	500	500
Isapghol mucilage powder	250	500	750	1000
Citric acid	200	200	200	200
Methyl paraben	150	150	150	150
Propyl paraben	100	100	100	100
Vanillin flavor	5	5	5	5
Purified water Q.S to ml	50	50	50	50

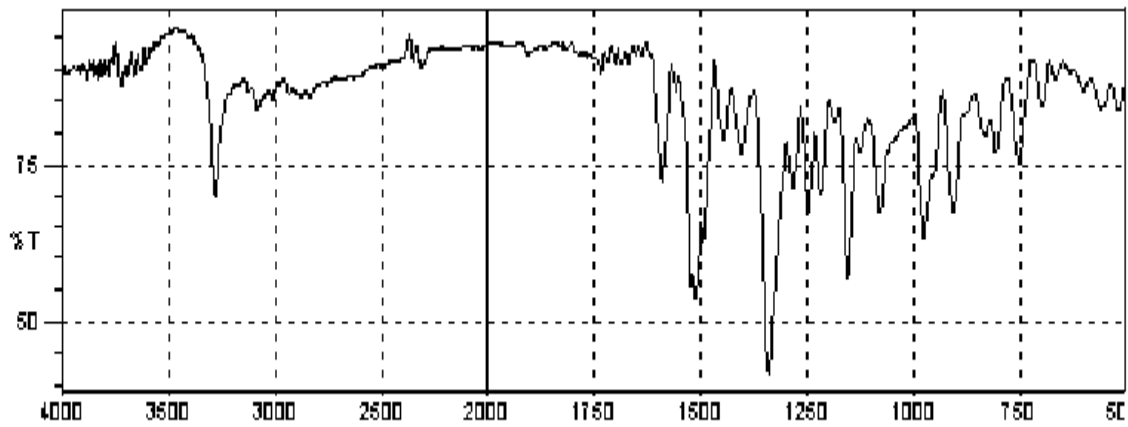


Fig 1: I.R.Spectra of Isapgol mucilage powder with Nimesulide

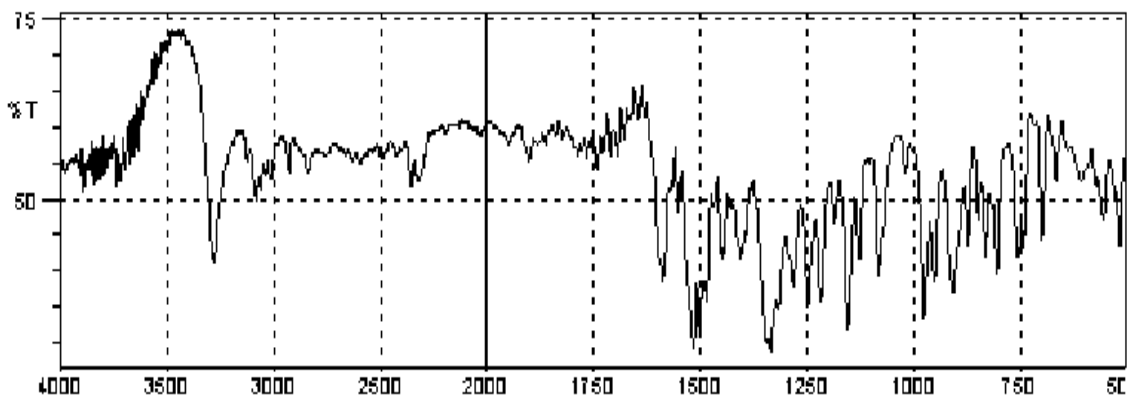


Fig 2: I.R.Spectra of pure drug Nimesulide

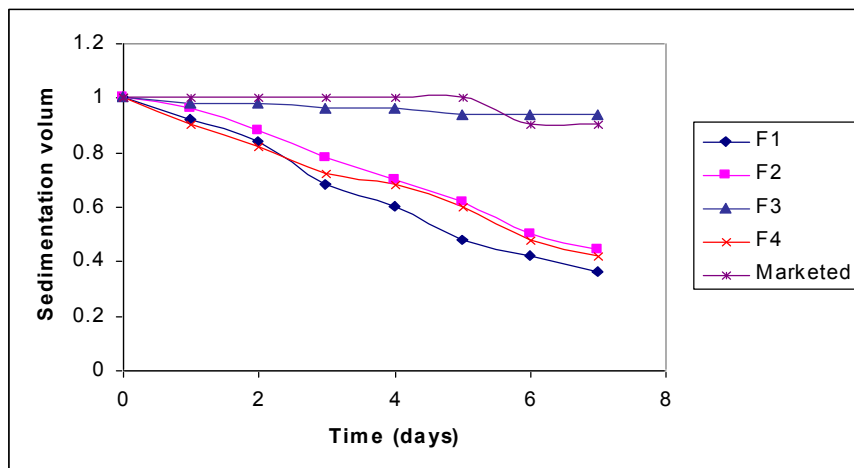


Fig 3: Sedimentation volume of different formulations

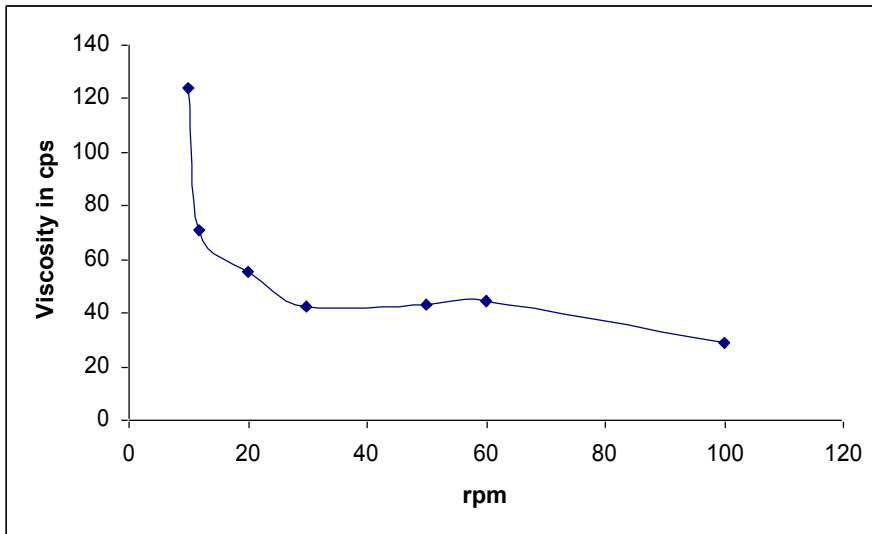


Fig 4: Viscosity of suspension (F3) at different rpm

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