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FORMULATION AND EVALUATION OF NORFLOXACIN SUSPENSION USING FENUGREEK HUSK AS A NATURAL SUSPENDING AGENT

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ABSTRACT

The present study aims to utilize effective natural excipient that can be used as an alternative for the formulation of pharmaceutical suspensions. Since no significant work has been done on fenugreek husk as a suspending agent, an attempt has been made to study the suspending property of fenugreek husk by formulating suspension of Norfloxacin. The fenugreek husk was extracted from the seeds of Trigonella foenum graecum. Norfloxacin was selected as a model drug due to its potent antimicrobial activity and is effective in the treatment of urinary tract infections, gonococcal urethritis and infectious diarrhea. The suspensions were prepared by using different concentration (0.25, 0.5 and 0.75% w/v) of fenugreek husk powder as suspending agent. These developed formulations were evaluated for sedimentation volume, redispersibility, pH measurement, viscosity measurement, particle size, drug content determination and in-vitro dissolution rate profile. Norfloxacin suspension formulated using 0.5% w/v of fenugreek husk and a blend of propylene glycol and glycerin exhibited good sedimentation rate (F=1) and easy redispersibility. Dissolution rate profile revealed that 100% drug release was achieved at the end of 40 minutes.

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Key words: Fenugreek seed husk, Norfloxacin, suspension, suspending agent.

INTRODUCTION

Oral route of drug administration is most widely used among all routes of drug administration. Suspensions though have to undergo dissolution are still advantageous over solid dosage forms as disintegration step is absent and the drug is ready for solubility in the gastro-intestinal medium[1].

The plant, *Trigonella-foenum graecum Linn.* (Leguminosae) is an aromatic annual herb. Various parts of fenugreek, mainly its leaves and seeds

have been widely used in the Indian food. It has several cosmetic and medicinal values like gastroprotrective, antiurolithiatic, hypoglycemic, diuretic, anti dandruff agent, anti-inflammatory agent and as antioxidant[4]. Mucilages are most commonly used adjuvant in pharmaceutical preparations. They consist of sugar and uronic acid units. They swell in water and form a gel. They possess variety of pharmaceutical properties such as emulsifying, gelling and suspending agents. No significant work has been reported on Fenugreek seed mucilage. Hence, the present study was aimed at proving the potential utility of this mucilage as a suspending agent[5].

Norfloxacin, 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid, is a synthetic antibacterial fluoroquinolone[2]. Quinolones belongs to synthetic class of antimicrobial agents with potent antimicrobial activity which are effective orally and parentally for a wide variety of infectious diseases. It is effective in the treatment of urinary tract infections, gonococcal urethritis and infectious diarrhea[3]. A number of patients especially pediatric and geriatrics have difficulty in swallowing solid dosage forms. Therefore, a liquid dosage form of norfloxacin is needed. Since norfloxacin is a solid and is slightly soluble in water, a suspension dosage form is the most suitable if the product is physically and chemically stable[1].

MATERIALS AND METHODS

Norfloxacin was obtained as a gift sample from Smruthi Organic Limited, Solapur, India. Fenugreek seeds were purchased from local market. Propylene glycol and glycerin were purchased from RFCL Limited, New Delhi, India. Methyl paraben, Propyl paraben and Aspartane were purchased from S.D Fine Chemicals, Mumbai, India. All other solvents and chemicals used were of AR/LR grade.

OBJECTIVES

The present study was performed with following objectives

a) Isolation of fenugreek husks from seeds of trigonella foenum graecum.
b) To check drug-excipients interaction studies.
c) Formulation of norfloxacin suspensions.
d) Evaluation of formulated suspensions.

ISOLATION OF FENUGREEK HUSKS

For isolation of husk, seeds of *Trigonella foenum graecum* were initially size reduced to 1000-1500 µ using a Hammer mill. The crushed seeds were soaked in chloroform for 15 min. By decantation, the crushed seeds were separated into husk and core that contains oily portion. Successive extractions with chloroform removed the traces of oily portion and core. The separated husk was air dried and subjected to size reduction by using Hammer mill to 180-250 µ. The milled material was finally passed through 60 # sieve to get the husk powder[6].

FORMULATION OF NORFLOXACIN SUSPENSION

Norfloxacin suspension was prepared according to formula given in Table 1. Fenugreek husk powder was taken in a mortar and pestle, to which preservatives were added and triturated with a small quantity of water to make a paste. The norfloxacin was mixed with co-solvents like glycerin and propylene glycol. The drug solution was added slowly to the above dispersion and triturated for 15-20 minutes. Then colouring agent (methyl orange) dissolved in water and flavouring agent (mentha oil) were added and mixed in suspension. Volume made up with water and homogenized.

Table 1: Composition of Norfloxacin suspension

Ingredients	Formulation Code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Norfloxacin (g)	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Fenugreek husk (g)	0.25	0.25	0.25	0.5	0.5	0.5	0.75	0.75	0.75
Propylene glycol (ml)	10	-	5	10	-	5	10	-	5
Glycerin (ml)	-	10	5	-	10	5	-	10	5
Methyl paraben (mg)	6	6	6	6	6	6	6	6	6

Propyl paraben (mg)	2	2	2	2	2	2	2	2	2
Aspartame (mg)	100	100	100	100	100	100	100	100	100
Mentha oil (ml)	1	1	1	1	1	1	1	1	1
Methyl orange (mg)	1	1	1	1	1	1	1	1	1
Purified water (q.s)	100	100	100	100	100	100	100	100	100

EVALUATION STUDIES

Sedimentation volume: Sedimentation volume (F) is a ratio of the final or ultimate volume of sediment (Vu) to the original volume of sediment (VO) before settling. It can be calculated by following equation.

$$F = V u / V0$$

Where, Vu = final or ultimate volume of sediment

V0 = original volume of suspension before settling[7].

Redispersibility: The bottles containing suspension were held up right between the fingers and rotated clockwise upside down through 180^0 in a semicircular path and back in the anti-clock wise direction (one cycle). This process was repeated continuously until the sediment was completely redispersed[8].

Determination of viscosity: The viscosity of suspension was determined by DVII+ Brookfield viscometer using adequate amount of sample.

pH determination: The pH of the developed formulations was measured by using digital P^H analyzer ELICO INDIA (Model LI 613)[3].

Drug content: 2ml of (25 mg equivalent of the drug) 0f the suspension was measured accurately and transferred into 100ml volumetric flask and the volume made with 0.1N Hcl. From this, 5ml of the sample was transferred to 100ml volumetric flask and made up the volume with 0.1N Hcl. Further from the above solution, 5ml sample was diluted to 25ml in a volumetric flask using 0.1 N Hcl. The absorbance of the resultant was measured at 277.5nm on a UV-Visible spectrophotometer (Shimadzu 1700) using 0.1N Hcl as a blank.

Particle size measurement: The particle size distribution of Norfloxacin 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 were counted and their size was determined.

***In-vitro* drug dissolution studies:** The dissolution of formulated suspension(10 ml equivalent to 125 mg of drug) was carried out using dissolution apparatus (LAB INDIA DISSO 8000). 900ml of 0.1N Hcl was used as a dissolution media. The USPXXXIII Type I apparatus was adjusted to 100 rpm and the temperature was maintained at 37°±0.5°C. 2ml of aliquots were withdrawn at the time intervals of 10 minutes and replaced with the fresh dissolution medium. The aliquots were transferred into 25ml volumetric flask and made up the volume with 0.1N Hcl. The absorbance was measured at 277.5nm using UV-Visible spectrophotometer (Shimadzu1700) against 0.1N Hcl as a blank.

Drug-polymer compatibility studies: The Compatibility studies of drug, polymer and the mixture of both drug and polymer were carried out using Fourier Transform Infrared Spectrophotometer (Shimadzu FT-IR 8400-S) in the range of 400-4000cm^{-1} by KBr disc method.

RESULTS AND DISCUSSION

Fenugreek husk powder was isolated and the suspension of Norfloxacin using the same was formulated as a suspending agent in the concentration range between 0.25 -0.75 % w/v. From the developed formulations (F1-F9), the F1, F2 and F4 were found to be disturbed within one day. So, they were not evaluated for the further parameters. The sedimentation rate of other formulations was observed for 7 days and the results are indicated in Figure 1. Of the developed formulations, F6 and F7 were found to be stable and dispersed at the end of 7 days.

Fig.1 Sedimentation rate volume of the developed suspensions

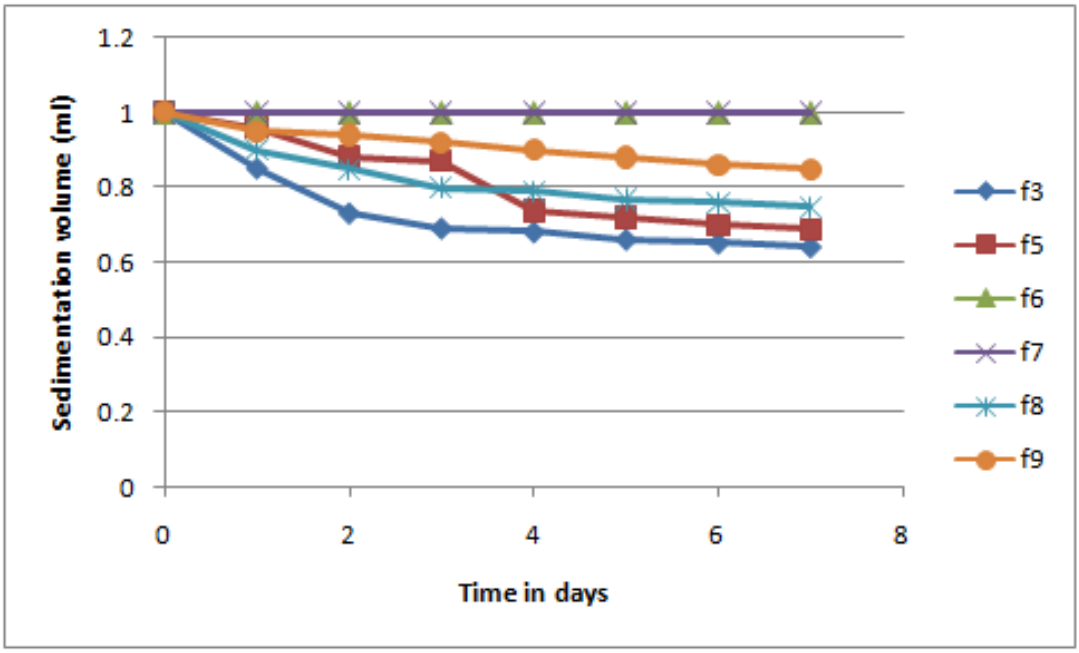
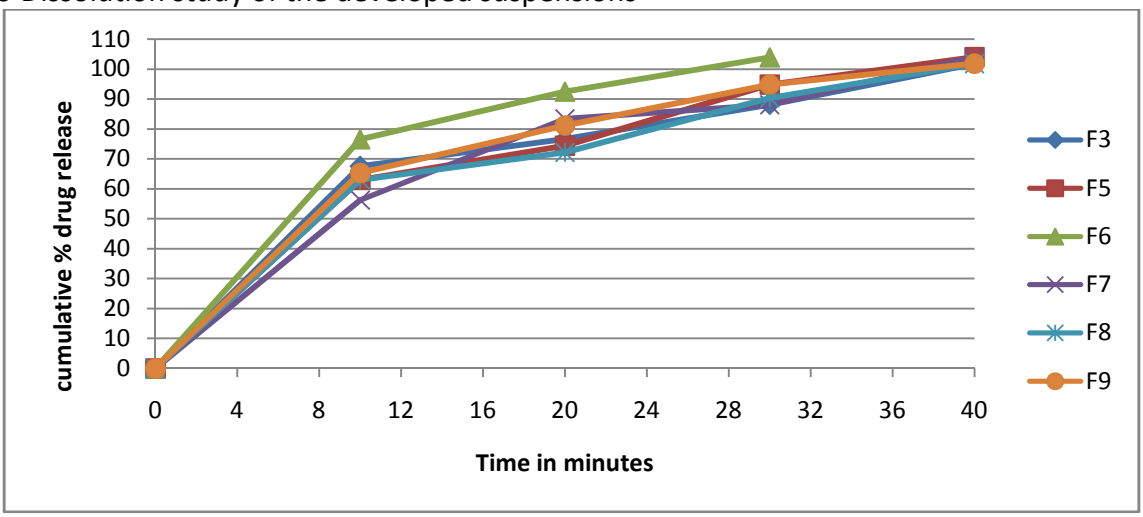


Fig.2 *In vitro* Dissolution study of the developed suspensions



Formulations F6 and F7 (optimized batch) were further evaluated for their particle size. The average size of the particle in the formulation F6 and F7 was found to be 25.98±14.53 µm and 27.39±13.91 µm respectively.

Rheological study of the developed formulations revealed that as the RPM increases viscosity decreases, confirming the shear thinning nature of the suspension. The drug content of all the formulations was in the range of 95.7-99.6% and the pH of all the formulation was found to be in the range of 7.07-7.39 (Table 2). Dissolution study was performed using 0.1N Hcl. The study was revealed that 100% drug release was obtained at the end of 40 minutes.

Table 2: pH, viscosity and drug content analysis of the developed suspensions

Formulations	pH	Viscosity		Drug content (%)
		100 RPM	50 RPM	
F3	7.03	2.78	6.3	96.1
F5	7.07	3.71	7.5	98.7
F6	7.30	8.36	17.3	99.2
F7	7.36	5.81	11.6	99.6
F8	7.26	3.3	7.6	98.4
F9	7.22	5.4	11.9	99.3

Drug-polymer compatibility studies are done to evaluate interaction between drug and polymer. The IR spectra of Norfloxacin, fenugreek seed husk powder and mixture of both drug and polymer are indicated in the Figures (3-5) below. The IR spectra of Norfloxacin has shown characteristic peaks at 1452.72 cm^{-1} indicating C=C stretch, 786.90 cm^{-1} indicating C(out of plane), 1612.38 cm^{-1} indicating C=O stretch, 1352.01 cm^{-1} indicating tertiary C-N stretch, 2974.03 cm^{-1} indicating C-H aliphatic stretch, 3459.27 cm^{-1} indicating N-H(secondary) stretch, 1091.63 cm^{-1} indicating C-F stretch and 3311.55 cm^{-1} indicating OH stretch are the major peaks of the drug. The IR spectra of Fenugreek seed husk powder has shown characteristic peaks at 3426.98 cm^{-1} indicating primary N-H stretch, 2939.37 cm^{-1} indicating C-H aliphatic stretch and 1671.88 cm^{-1} indicating C=O (carboxylic acid) stretch. The physical mixture also showed the characteristic peaks of pure drug indicating that there were no interaction between the drug and the husk powder.

Fig.3 IR spectrum of Norfloxacin

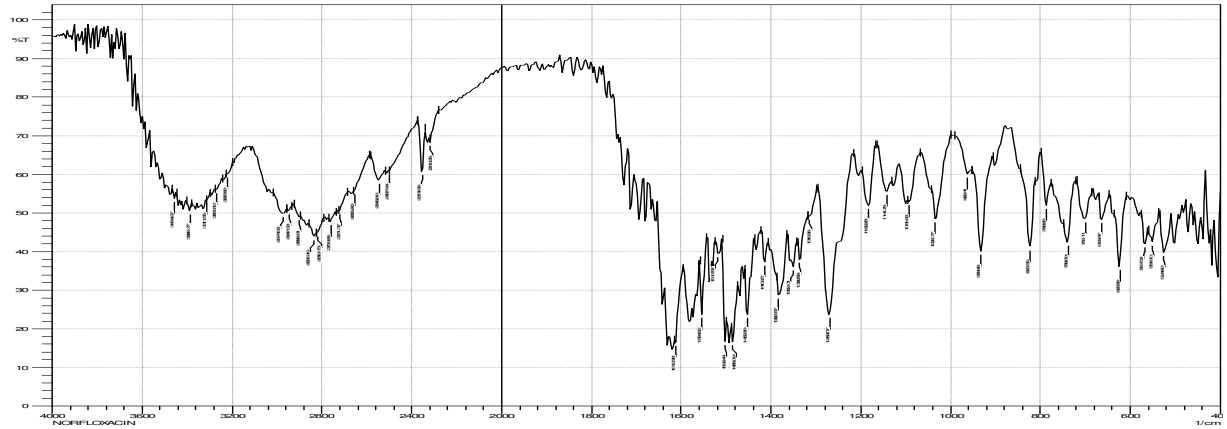


Fig.4 IR spectrum of Fenugreek seed husk

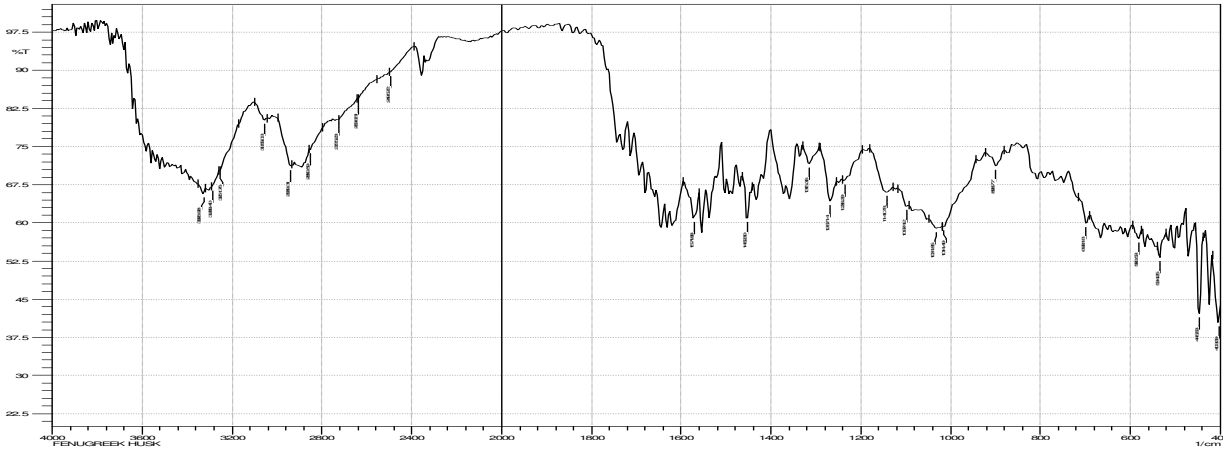
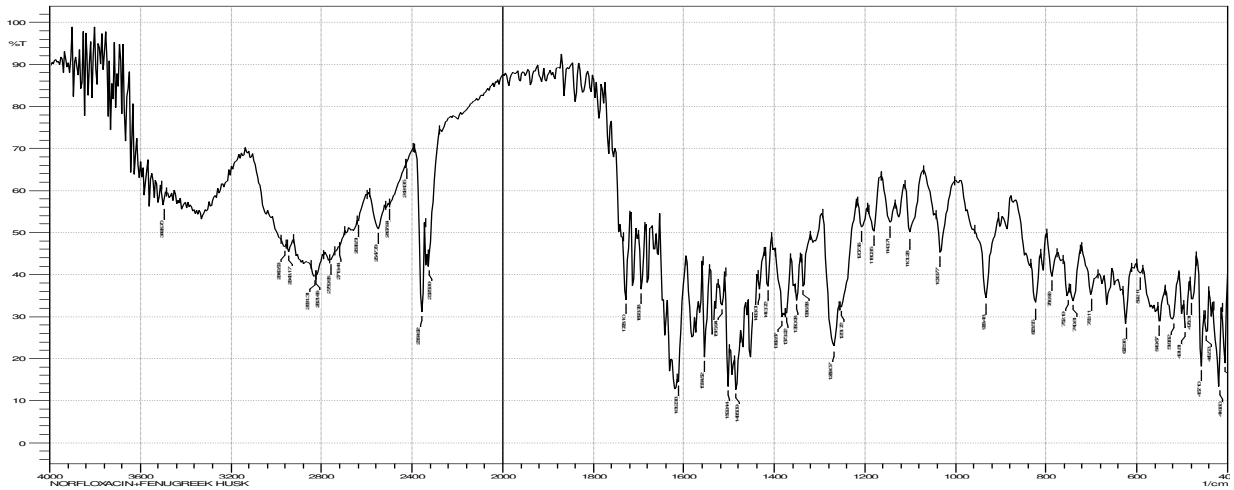


Fig.5 IR spectrum of Norfloxacin + fenugreek seed husk



CONCLUSION

The present study was carried out to check the suspending property of fenugreek husk and impact of viscosifier on the formulation. Norfloxacin was selected as model drug and fenugreek husk was used as suspending agent in different concentration of 0.25%, 0.5%, and 0.75% w/v. From all the developed formulations, F6 was selected as the ideal formulation as it produced a stable, redispersible, flocculated suspension with all the features of an ideal suspension. Hence by considering, all above evaluation parameters it can be concluded that fenugreek husk powder used in the concentration of 0.5% w/v was proving as good suspending agent with the blend of propylene glycol and glycerin as a better viscosifier in the formulation of Norfloxacin suspension.

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