

# Indian Journal of Pharmaceutical Sciences

## Scientific Publication of the Indian Pharmaceutical Association

Indexed in Ind MED, EMBASE/Excerpta Medica, International Pharmaceutical Abstracts, Chemical Abstracts.

Volume 69

Number 5

September-October 2007

### CONTENTS

#### REVIEW ARTICLES

- Recent Trends in Drug-Likeness Prediction: A Comprehensive Review of *In Silico* Methods**  
R. U. KADAM AND N. ROY 609-615
- Biodegradable Polymers: Which, When and Why?**  
V. B. KOTWAL, MARIA SAIFEE, NAZMA INAMDAR AND KIRAN BHISE 616-625

#### RESEARCH PAPERS

- Strong Cation Exchange Resin for Improving Physicochemical Properties and Sustaining Release of Ranitidine Hydrochloride**  
S. KHAN, A. GUHA, P. G. YEOLE, AND P. KATARIYA 626-632
- Novel Co-Processed Excipients of Mannitol and Microcrystalline Cellulose for Preparing Fast Dissolving Tablets of Glipizide**  
S. JACOB, A. A. SHIRWAIKAR, A. JOSEPH, K. K. SRINIVASAN 633-639
- Formulation and Optimization of Directly Compressible Isoniazid Modified Release Matrix Tablet**  
M. C. GOHEL, R. K. PARIKH, M. N. PADSHALA, K. G. SARVAIYA AND D. G. JENA 640-645
- Effect of Casting Solvent and Polymer on Permeability of Propranolol Hydrochloride Through Membrane Controlled Transdermal Drug Delivery System**  
T. E. G. K. MURTHY AND V. S. KISHORE 646-650
- Preparation of Mucoadhesive Microspheres for Nasal Delivery by Spray Drying**  
MAHALAXMI RATHANANAND, D. S. KUMAR, A. SHIRWAIKAR, RAVI KUMAR, D. SAMPATH KUMAR AND R. S. PRASAD 651-657
- Effect of Polymers on Crystallo-co-agglomeration of Ibuprofen-Paracetamol: Factorial Design**  
A. PAWAR, A. R. PARADKAR, S. S. KADAM AND K. R. MAHADIK 658-664
- Synthesis and Antimicrobial Evaluation of Some Novel 2-Imino-3-(4'-carboxamido pyridyl)-5-Arylidene-4-Thiazolidinones and their Brominated Derivatives**  
P. MISHRA, T. LUKOSE AND S. K. KASHAW 665-668
- Measurement of Urine and Plasma Oxalate with Reusable Strip of Amaranthus Leaf Oxalate Oxidase**  
NISHA SHARMA, MINAKSHI SHARMA, V. KUMAR AND C. S. PUNDIR 669-673

#### SHORT COMMUNICATIONS

- Simultaneous HPLC Estimation of Omeprazole and Domperidone from Tablets**  
LAKSHMI SIVASUBRAMANIAN AND V. ANILKUMAR 674-676
- Isolation and Evaluation of Fenugreek Seed Husk as a Granulating Agent**  
AMELIA AVACHAT, K. N. GUJAR, V. B. KOTWAL AND SONALI PATIL 676-679
- Synthesis and *In Vitro* Efficacy of some Halogenated Imine Derivatives as Potential Antimicrobial Agents**  
A. K. HALVE, DEEPTI BHADAURIA, B. BHASKAR, R. DUBEY AND VASUDHA SHARMA 680-682
- Simultaneous Spectrophotometric Estimation of Atorvastatin Calcium and Ezetimibe in Tablets**  
S. S. SONAWANE, A. A. SHIRKHEDKAR, R. A. FURSULE AND S. J. SURANA 683-684
- High Performance Thin Layer Chromatographic Estimation of Lansoprazole and Domperidone in Tablets**  
J. V. SUSHEEL, M. LEKHA AND T. K. RAVI 684-686
- Antimicrobial Activity of *Helicteres isora* Root**  
S. VENKATESH, K. SAILAXMI, B. MADHAVA REDDY AND MULLANGI RAMESH 687-689
- Synthesis and Antibacterial Activity of 2-phenyl-3,5-diphenyl (substituted) -6-aryl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]thiazoles**  
S. K. SAHU, S. K. MISHRA, R. K. MOHANTA, P. K. PANDA AND MD. AFZAL AZAM 689-692

- Simultaneous Estimation of Aceclofenac, Paracetamol and Chlorzoxazone in Tablets**  
G. GARG, SWARNLATA SARAF AND S. SARAF 692-694
- Reverse Phase High Performance Liquid Chromatography Method for Estimation of Ezetimibe in Bulk and Pharmaceutical Formulations**  
S. K. AKMAR, LATA KOTHAPALLI, ASHA THOMAS, SUMITRA JANGAM AND A. D. DESHPANDE 695-697
- Synthesis and Antiinflammatory Activity of N-Aryl Anthranilic Acid and its Derivatives**  
J. K. JOSHI, V. R. PATEL, K. PATEL, D. RANA, K. SHAH, RONAK PATEL AND RAJESH PATEL 697-699
- RP-HPLC Method for the Determination of Atorvastatin calcium and Nicotinic acid in Combined Tablet Dosage Form**  
D. A. SHAH, K. K. BHATT, R. S. MEHTA, M. B. SHANKAR AND S. L. BALDANIA 700-703
- Determination of Etoricoxib in Pharmaceutical Formulations by HPLC Method**  
H. M. PATEL, B. N. SUHAGIA, S. A. SHAH AND I. S. RATHOD 703-705

#### Proceedings of the Symposium on Advances in Pulmonary and Nasal Drug Delivery, October 2007, Mumbai

- Albumin Microspheres of Fluticasone Propionate Inclusion Complexes for Pulmonary Delivery**  
A. A. LOHADE, D. J. SINGH, J. J. PARMAR, D. D. HEGDE, M. D. MENON, P. S. SONI, A. SAMAD AND R. V. GAIKWAD 707-709
- Design and Development of Thermoreversible Mucoadhesive Microemulsion for Intranasal Delivery of Sumatriptan Succinate**  
R. S. BHANUSHALI AND A. N. BAJAJ 709-712
- Preparation and Characterization of Chitosan Nanoparticles for Nose to Brain Delivery of a Cholinesterase inhibitor**  
BHAVNA, V. SHARMA, M. ALI, S. BABOOTA AND J. ALI 712-713
- Poloxamer Coated Fluticasone Propionate Microparticles for Pulmonary Delivery; *In Vivo* Lung Deposition and Efficacy Studies**  
D. J. SINGH, J. J. PARMAR, D. D. HEGDE, M. D. MENON, P. S. SONI, A. SAMAD, AND R. V. GAIKWAD 714-715
- Sustained Release Budesonide Liposomes: Lung Deposition and Efficacy Evaluation**  
J. J. PARMAR, D. J. SINGH, D. D. HEGDE, M. D. MENON, P. S. SONI, A. SAMAD AND R. V. GAIKWAD 716-717
- Generation of Budesonide Microparticles by Spray Drying Technology for Pulmonary Delivery**  
S. R. NAIKWADE AND A. N. BAJAJ 717-721
- Microemulsion of Lamotrigine for Nasal Delivery**  
A. J. SHENDE, R. R. PATIL AND P. V. DEVARAJAN 721-722
- Development of a pMDI Formulation Containing Budesonide**  
E. ROBINS, G. BROUET AND S. PRIOLKAR 722-724
- Development of a pMDI Formulation Containing Salbutamol**  
E. ROBINS, G. WILLIAMS AND S. PRIOLKAR 724-726
- Aqua Triggered *In Situ* Gelling Microemulsion for Nasal Delivery**  
R. R. SHELKE AND P. V. DEVARAJAN 726-727
- In vivo* Performance of Nasal Spray Pumps in Human Volunteers By SPECT-CT Imaging**  
S. A. HAZARE, M. D. MENON, P. S. SONI, G. WILLIAMS AND G. BROUET 728-729
- Nasal Permeation Enhancement of Sumatriptan Succinate through Nasal Mucosa**  
S. S. SHIDHAYE, N. S. SAINDANE, P. V. THAKKAR, S. B. SUTAR AND V. J. KADAM 729-731
- Formulation Development of Eucalyptus Oil Microemulsion for Intranasal Delivery**  
N. G. TIWARI AND A. N. BAJAJ 731-733

# Isolation and Evaluation of Fenugreek Seed Husk as a Granulating Agent

AMELIA AVACHAT\*, K. N. GUJAR, V. B. KOTWAL AND SONALI PATIL

Sinhgad College of Pharmacy, Off Sinhgad Road, Vadgaon (BK.), Pune - 411 041, India

**In the present study a relatively simple method for the separation of husk from the seeds of *Trigonella-foenum graecum* (fenugreek) was developed. The entire seeds were subjected to size reduction followed by successive extractions with chlorinated hydrocarbons to separate the husk from the 'core and oily portion' to yield about 40%w/w of the husk. The dried husk was further powdered to 180 - 250  $\mu$ . It was characterized for various physicochemical parameters including swelling index, particle size distribution and flow properties. Use of fenugreek husk as a binding/granulating agent in solid dosage forms was also investigated. Diclofenac sodium and paracetamol were the model drugs of choice for optimizing the binding properties of husk in tablets using fenugreek husk dispersion, comparing the results against starch paste. Friability, hardness, disintegration, weight variation and dissolution were**

---

**\*For correspondence**

E-mail: amavachat@yahoo.com

**the parameters of comparative studies. Fenugreek husk dispersion was found to be superior over starch paste, on the basis of the selected parameters. The maximum concentration required of the husk as a binding agent was 4-5% of the dosage form, which is relatively low as compared to starch.**

**Key words: Fenugreek husk, swelling index, granulating agent, tablets**

The plant, *Trigonella-foenum graecum* Linn. (Leguminosae)<sup>1</sup> 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 uses like gastroprotective, antiurolithiatic<sup>2</sup>, hypoglycemic<sup>3</sup>, diuretic, anti dandruff agent, antiinflammatory agent and as antioxidant. Mucilage of various seeds has been used as granulating and binding agent due to its non-toxicity, low cost, free availability, emollient and non irritating nature<sup>4,5</sup>. Isolation of mucilage from fenugreek seeds has been reported, but is a tedious and time-consuming process. Reported methods have isolated its mucilage from the seeds by maceration using water followed by precipitation<sup>6</sup>. In the present study an economically viable and a simple method for the separation of husk from fenugreek seeds was developed. Looking at the ability of the husk to form a mucilage, the possibility of using it as a binding/granulating agent and release retardant material in solid dosage forms was also explored.

Fenugreek seeds were procured from Yucca Enterprises, paracetamol and diclofenac sodium were obtained as gift samples from Sunij Pharmaceuticals, Ahmedabad. All other chemicals and solvents were of analytical reagent grade.

For isolation of husk, seeds of *Trigonella-foenum graecum* were initially size reduced to 1000–1500  $\mu$  using a Hammer mill. These were then treated with various chlorinated hydrocarbons like chloroform, carbon tetrachloride, methylene chloride and other organic solvents. It was observed that chloroform and methylene chloride are better solvents and were used for experimental work. These 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  $\mu$ . The milled material was passed through 60 # sieve

to get the husk of particle size less than 250  $\mu$ . Size reduction was done to increase the surface area and swelling capacity.

The husk powder was evaluated for Swelling index<sup>7</sup>, flow properties and particle size distribution. The swelling index is the volume in milliliter occupied by 1 g of a material, including any adhering mucilage, after it has swollen in aqueous liquid for 4 h.

One gram of powder was placed in a 25 ml ground-glass-stoppered cylinder graduated over a height of about 120 to 134 mm in 5 ml divisions. The powder was moistened with 1 ml of ethanol (96%), water was added up to 25 ml and the cylinder was closed. It was shaken vigorously every 10 min for 1 hour and then allowed to stand for 3 h. The volume occupied by the powder was measured, including any adhering mucilage. Three tests were carried out at the same time. Swelling index was calculated from the mean of the three tests<sup>8</sup>. The dried and powdered fenugreek husk was also characterized and evaluated for various physicochemical properties such as Angle of repose, Carr's compressibility index and Particle size distribution<sup>9-11</sup> (Tables 1 and 2).

Paracetamol and diclofenac sodium were used as model drugs for evaluating fenugreek husk powder as binder (Table 3). Binder solution was prepared by hydrating the given amount of fenugreek husk powder in minimum quantity of water for 15 min to form a paste-like mass (dispersion). Granules of both drugs were prepared by wet granulation method using fenugreek husk paste and were compared against granules prepared by using starch paste as a standard binding agent. Other excipients like lactose, magnesium stearate, talc and aerosil were added as diluent and lubricants, respectively. The prepared granules were evaluated for particle size distribution and flow properties like angle of repose and Carr's compressibility index (Tables 1 and 2).

The tablets were compressed using 6-station rotary

**TABLE 1: PHYSICO-CHEMICAL PROPERTIES OF FENUGREEK HUSK POWDER, PARACETAMOL AND DICLOFENAC SODIUM GRANULES**

Parameters	Fenugreek husk powder	Result			
		Paracetamol granules		Diclofenac Sodium granules	
		Fenugreek Husk	Starch	Fenugreek Husk	Starch
Angle of Repose	21.3°	20.35°	35.22°	23.35°	25.54°
Density: Tapped (g/cc)	0.886	0.68 g/cc	0.52 g/cc	0.58 g/cc	0.72 g/cc
Untapped (g/cc)	0.806	0.75 g/cc	0.62 g/cc	0.64 g/cc	0.88 g/cc
Carr's compressibility index	9.029%	9.37%	16.10%	10.21%	18.37%
Swelling index (ml)	4.5	-	-	-	-

**TABLE 2: SIEVE ANALYSIS OF FENUGREEK HUSK POWDER, PARACETAMOL AND DICLOFENAC SODIUM GRANULES**

Sieve no.	Fenugreek husk powder	% Weight retained			
		Paracetamol granules		Diclofenac sodium granules	
		Fenugreek Husk	Starch	Fenugreek Husk	Starch
12 <sup>#</sup>	--	--	--	1.63	20.10
25 <sup>#</sup>	--	27.85	22.10	46.43	30.2
60 <sup>#</sup>	--	51.21	60.8	39.13	17.5
85 <sup>#</sup>	47.8	6.45	6.8	5.65	9.8
100 <sup>#</sup>	32.2	5.71	5.8	3.26	0.6
120 <sup>#</sup>	12.7	2.7	0.8	0.54	9.7
Below 120 <sup>#</sup>	7.3	6.08	3.7	3.36	12.10

<sup>#</sup>indicates the sieve used for evaluation

**TABLE 3: FORMULATION OF PARACETAMOL AND DICLOFENAC SODIUM TABLETS**

Paracetamol Tablets			Diclofenac Sodium Tablets		
Ingredients	A (mg)	B (mg)	Ingredients	A (mg)	B (mg)
Paracetamol	500	500	Diclofenac Sodium	100	100
Starch (diluent)	53	23	Fenugreek husk paste	8	--
Starch for paste	--	60	Starch for paste	--	16
Fenugreek husk paste	30	--	Lactose	46	38
Magnesium stearate	4	4	Magnesium stearate	3	3
Talc	8	8	Talc	3	3
Aerosil 200	5	5			
Total weight per tablet	600	600		160	160

Formulation A - granulated using fenugreek husk paste, Formulation B - granulated using starch paste

**TABLE 4: PROPERTIES OF TABLETS**

Parameters	Result			
	Paracetamol tablets		Diclofenac Sodium tablets	
	Fenugreek husk	Starch	Fenugreek husk	Starch
Weight / tab (mg)	600	600	160	160
Diameter (mm)	12.6	12.6	8	8
Thickness (mm)	4.5	4.3	2.8	2.8
Hardness (kg/cm <sup>2</sup> )	6-7	5	5-6	5-6
Friability (%)	0.7	1.3	0.5	0.6
Disintegration time (min)	5	7	5	5
Weight variation	Passes	Passes	Passes	Passes
Avg.% dissolution in 30 min using PO4 buffer pH6.8 (50 rpm) using App-1	86.5	90.3	92.8	91.1

tablet machine, using 12.5 mm flat-faced beveled edge punches for paracetamol tablets. Diclofenac sodium tablets were compressed using 8 mm flat-faced beveled edge punches. The tablets were evaluated for various standard parameters<sup>12</sup> (Table 4).

Chloroform and methylene chloride proved to be

better solvents for the separation of husk from the crushed seeds. Successive extractions produced higher yields. The yield of husk obtained from the seeds was around 40% w/w. Swelling capacity of the studied material and viscosity building ability of husk was favorable for it to be a good candidate as a granulating agent.

The granules prepared using the husk powder were comparable in various physical properties to those prepared using starch paste as a binder. The advantage of fenugreek husk over starch as a binding agent was that it could be used as a cold binder whereas starch has to be heated.

The tablets prepared with 5% of fenugreek husk showed more hardness as compared to those prepared with starch paste. These tablets also showed better properties in terms of friability and disintegration time specifically in case of paracetamol tablets, because capping is a problem frequently observed during high-speed compaction and further processing of paracetamol tablets. Comparable properties in diclofenac sodium tablets were also observed as compared to those made using starch paste. These properties were observed at a relatively much lower concentration of the binder as can be seen from the formula (Table 3).

The disintegration and dissolution time of both the tablets was comparable to the tablets prepared with starch paste as a binder which indicates that fenugreek husk is a better binder for paracetamol tablets since it has minimized the capping tendency without adversely affecting the properties which are crucial for therapeutic efficacy.

Fenugreek husk can easily be separated and subsequently powdered from the seeds by simple techniques. The particles can be easily hydrated and dispersed in water at room temperature in a very short time. The granules prepared of the suitable drugs with relatively lower proportion of the fenugreek husk paste (dispersion) as compared to traditional starch paste had better flow and compressibility. The compressed tablets complied with quality parameters as per official specifications.

Thus the aqueous dispersion of fenugreek husk was found to be a better granulating agent, being food article, devoid of toxicity and economic too, along

with an ability to give desired attributes to the dosage form. Fenugreek husk studies are further going to explore its role in drug delivery systems including its release retardant properties and mucoadhesive nature.

## ACKNOWLEDGEMENTS

The authors are thankful to Sinhgad College of Pharmacy for providing the facilities for carrying out the research project.

## REFERENCES

1. Trease GE, Evans MC, editors. Textbook of Pharmacognosy, 15<sup>th</sup> ed., Balliere, Tindall: London; 2002.
2. Ahsan SK, Tariq M, Ageel AM, Al-yahya MA, Shah AH. Effect of *Trigonella-foenum-graecum* and *Ammi majus* on calcium oxalate urolithiasis in rats. *J Ethnopharmacol* 1989;26:249-54.
3. Abdul-Barry JA, Abdul-Hassan IA, Al-Hakein MH. Hypoglycaemic and antihyperglycaemic effects of *Trigonella foenum-graecum* leaf in normal and alloxan-induced diabetic rats. *J Ethnopharmacol* 1997;58(3):149-55.
4. Baveja SK, Rao KV, Arora J. Examination of natural gums and mucilages as sustaining materials in tablet dosage forms, Part 2. *Indian J Pharm Sci* 1989;51:115-118.
5. Baveja SK, Rao KV, Arora J. Examination of natural gums and mucilages as sustaining materials in tablet dosage forms. *Indian J Pharm Sci* 1988;50:89-92.
6. Kulkarni GT, Gowthamarajan K, Rao BG, Suresh B. Evaluation of binding properties of *Plantago ovata* and *Trigonella foenum graecum* mucilages. *Indian drugs* 2002;39(8):422-425.
7. Gohel MC, Patel MM, Amin AF. Development of modified release Diltiazem HCL tablets using composite index to identify optimal formulation. *Drug Develop Ind Pharm* 2003;29(5):565-74.
8. British Pharmacopoeia, Vol.II, Her Majesty's stationary office for the Department of Health; 3<sup>rd</sup> ed., London; 2000.
9. Anderson NR, Banker GS. Tablets. In: Lachman L, Liberman HA, Kanig JL, editors. *The Theory and Practice of Industrial Pharmacy*. 3<sup>rd</sup> ed. Mumbai; Varghese Publication House; 1991. p. 27, 297, 320.
10. Aulton ME. *Pharmaceutics: The science of dosage form design*. 2<sup>nd</sup> ed. Churchill Livingstone: Edinburgh; 2002.
11. Martin A. *Physical Pharmacy: Physical Chemical principles in the Pharmaceutical Sciences*. 4<sup>th</sup> ed. Lippincott William and Wilkins: USA; 2002.
12. *Indian Pharmacopoeia*, Vol. II, Govt. of India, Ministry of Health and Family Welfare, The Controller of Publications: New Delhi; 1996.

Accepted 4 October 2007

Revised 24 March 2007

Received 27 December 2005

Indian J. Pharm. Sci., 2007, 69 (5): 676-679