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## 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

# Nasal Permeation Enhancement of Sumatriptan Succinate through Nasal Mucosa

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Sumatriptan succinate is a 5-HT<sub>1</sub> receptor agonist used in the treatment of migraine. It is administered orally, in doses of 25, 50 or 100 mg as a single dose, nasally in doses of 10 or 20 mg and also

subcutaneously, as two 6 mg doses within twenty four hours. Low oral bioavailability (15%) due to high first-pass metabolism<sup>1,2</sup> justifies a need of nasal drug delivery. To improve the nasal retention time of sumatriptan succinate it has been formulated as *in situ* mucoadhesive gel<sup>3</sup>. The objective of this work was to improve the nasal bioavailability of sumatriptan

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**TABLE 1: RESULTS OF PERMEATION STUDIES OF SUMATRIPTAN SUCCINATE THROUGH SHEEP NASAL MUCOSA**

Formulations containing	Permeation coefficient* mg. cm/min	Flux* mg/cm <sup>2</sup> min	Enhancement ratio
No penetration enhancer	0.002652±0.000276	0.008593±0.001129	
1% EDTA	0.00273±0.000213	0.008868±0.000916	1.029
0.1% Tween 80	0.002881±0.000129	0.009326±0.000628	1.055
1% Bile salts	0.003114±0.000106	0.010078±0.000584	1.08
1% SLS	0.005348±0.000781	0.017303±0.000647	1.717

\*Each value represents mean ±S.D

succinate by increasing its nasal retention time as well as the nasal permeation. Nasal permeation of sumatriptan succinate was improved by using different penetration enhancers such as SLS, Tween 80, bile salts and EDTA.

## MATERIALS AND METHODS

### HPLC method development for analysis of sumatriptan succinate for nasal formulation:

The evaluation of permeation studies was carried out by HPLC method using phosphate buffer (pH 3): methanol (80:20) as mobile phase using a reverse phase column.

### Preparation of mucoadhesive nasal gel of sumatriptan succinate<sup>4</sup> and evaluation:

The gel containing drug, Pluronic F127 (18% w/v), 1% propylene glycol and Carbopol 934P (0.3% w/v) was prepared. To this solution, different penetration enhancers (EDTA 1% w/v, Tween 80 0.1% v/v, SLS 1% w/v and bile salt 1% w/v) were added separately to form different formulations. The formulation was studied for the gelation temperature<sup>5</sup> and mucoadhesive strength<sup>6</sup>.

### In vitro permeation studies:

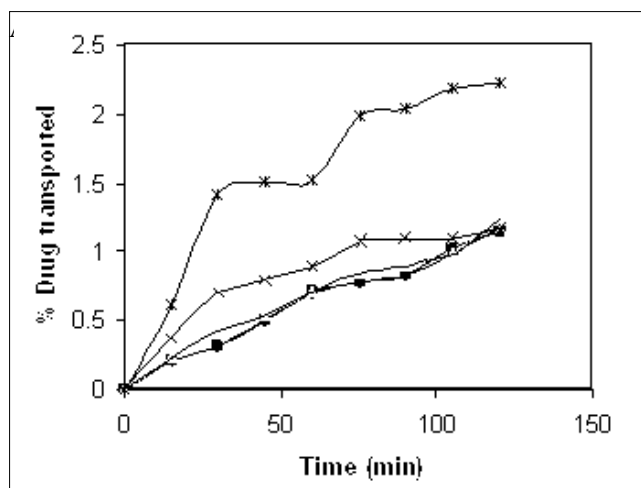
The nasal mucosa was separated from underlying muscular and part of the connective tissue with forceps and scissors. The fresh tissue was kept at 34° in phosphate buffered saline (PBS) pH 6.4 upon removal. Mucosa was used within 45 min of separation. Franz diffusion cell was used for this purpose. Receptor compartment contained 21 ml of pH 6.4 phosphate buffer while donor compartment was filled with 3 ml distilled water. The solution was placed in donor compartment and aliquots were removed at time intervals of 15, 30, 45, 60, 75, 90, 105, 120 min from the receptor compartment while the solution was being stirred continuously using magnetic stirrer, replacing it with fresh medium each time. The experiment was carried out at 34°. The amount of drug permeated was assayed using HPLC

method of analysis. The graph of %drug permeated v/s time was plotted and flux, permeability coefficient and enhancement ratio was determined.

## RESULTS AND DISCUSSION

For HPLC analysis, the mixture of phosphate buffer pH 3 and methanol in three different proportions were tried, to resolve the peak of sumatriptan succinate from peaks of protein impurities. The mobile phase containing phosphate buffer pH 3: methanol (80:20) produced satisfactory result with good resolution of drug peak and showed good linearity in the range 5-80 µg/ml ( $y = 85244x$ ;  $r^2 = 0.9986$ ).

Clear transparent mucoadhesive solution was formed with viscosity sufficiently low to administer in the nasal cavity with the help of dropper. The viscosity of the formulation was increased as temperature of the solution increased with gelation at nasal cavity temperature (34°). The mucoadhesive strength of the formulation was found to be 10.5 g, which is sufficient to improve the retention time of solution at nasal mucosa.



**Fig. 1: Effect of various penetration enhancers on permeation of sumatriptan succinate through nasal mucosa**  
The graphs represent the following: Formulation without penetration enhancer (-○-), with 1% EDTA (-■-), with 0.1% Tween 80 (-▲-), with 1% Bile salt (-×-), with 1% SLS (-\*-)

penetrate though the nasal mucosa without permeation enhancer but low permeation was observed due to low Log P value of 0.93. When 1% EDTA and 0.1% Tween 80 was used in formulation these was no significant increase in the permeation of sumatriptan succinate when tested by student's t-test while formulation containing 1% bile salts showed slight increase in the permeation. The permeation was found to increase two times with 1% SLS with enhancement ratio of 1.72.

It may be concluded that nasal mucosa delivery of sumatriptan succinate could be good alternative when formulated in the *in situ* mucoadhesive gel. This mucoadhesive gel showed satisfactory mucoadhesive strength and gelation temperature. It was found that use of penetration enhancer was required to achieve permeation through nasal mucosa and SLS was found to be the most effective among various penetration

enhancers tried.

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