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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

# Microemulsion of Lamotrigine for Nasal Delivery

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Epilepsy is a neurological disorder which requires quick management of seizures in order to avoid the risk of permanent brain damage. Intranasal administration allows transport of drugs to the brain circumventing BBB, thus providing a unique feature and better option to target drugs (for example lamotrigine) to the brain with quick onset of action in case of emergencies such as epilepsy. We have already reported microemulsion (ME) of lamotrigine for nasal delivery<sup>1</sup>. Further, previous studies on ME of tamoxifen citrate (hydrophobic drug) have demonstrated a dramatic increase in solubility with micellar and ME despite poor solubility of drug in oily phase<sup>2</sup>. This finding can be utilized in formulation of nasal ME of hydrophobic drugs. Improved solubilization by virtue of ME can be exploited to accommodate higher drug concentration per unit nasal ME as nasal anatomy pose severe constraints on volume of formulation to be administered. This can aid reduction of dosage volume of nasal ME ultimately resulting in high patient compliance. The objective of present study was to evaluate the role of ME components in solubilization of lamotrigine. Ascertaining the role of ME components would create better understanding of the system for further formulation development.

## MATERIALS AND METHODS

Formulation components are listed in Table 1 with equilibrium solubility data. ME and micelles (MI) were formulated using surfactant - cosurfactant mixtures, Solutol HS 15 and Transcutol P in the ratio of 1:2 and Solutol HS 15: soluphor P in the ratio of 1:1, with and without oil phases, respectively. Solubilization

by ME and MI was determined by adding excess of lamotrigine and concentration of solubilized drug was determined by UV spectrophotometry (307 nm) after 48 h of equilibration.

## RESULT AND DISCUSSION

The observed solubilization capacity of ME and MI systems was much lower than the predicted solubility calculated from the summation of contribution of each component of the system (Table 2). Furthermore the improvement in solubilization capacity of ME over MI was not high in relation to the equilibrium solubility data for lamotrigine in the three oil phases. Also the solubilization capacity of the ME did not increase with

**TABLE 1: FORMULATION COMPONENTS AND EQUILIBRIUM SOLUBILITY OF LAMOTRIGINE**

	Formulation components (mg/ml $\pm$ SE)	Lamotrigine solubility
Oily phases	Capmul MCM	45.13 $\pm$ 0.1821
	Peceol	18.04 $\pm$ 0.3564
	Captex 355	0.93 $\pm$ 0.1245
Surfactant	Solutol HS 15	67.06 $\pm$ 0.7189
Co surfactants	Transcutol P	133.39 $\pm$ 0.7726
	Soluphor P	13.46 $\pm$ 0.3834
Aqueous phase	Water	0.17 $\pm$ 0.678

**TABLE 2: COMPARISON OF PREDICTED AND OBSERVED SOLUBILIZATION CAPACITIES OF ME AND MI**

Oil phase	Concentration of oily phase (% w/w)	Solubility (mg/ml) Predicted	Solubilization (mg/ml $\pm$ SE) capacity observed
Capmul MCM	3.5	68.32	34.01 $\pm$ 0.034
	8.5	70.67	34.07 $\pm$ 0.9596
Peceol	3.5	67.38	29.87 $\pm$ 0.685
	7	68.1	30.02 $\pm$ 0.1555
Captex 355	3.5	66.78	28.57 $\pm$ 0.1619
	5	66.79	28.55 $\pm$ 0.448
Micelles	-	66.75	26.33 $\pm$ 0.125

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increase in concentration of the oil phase irrespective of solubility in oil.

Solubilization capacity of ME of lamotrigine was significantly lower than predicted. Moreover no appreciable difference was seen in solubilization capacity of MI and ME formulation. This observation though contrary to our previous study with tamoxifen, where marked increase in solubilization was observed, was in accordance with reports on steroid ME<sup>3</sup>. Though the oil phase is known to play a significant role in generation of the interface it may not always play a major role in drug solubilization. Moreover, cosurfactants may affect the micelle structure<sup>3</sup> thereby causing significant reduction in solubilization by MI and ME despite high solubility of drug in cosurfactant. The decreased solubilization of lamotrigine by ME compared to the predicted could be due to interaction of the drug with ME components. This however needs to be explored and confirmed. However adequate solubilization was observed to enable design of ME

[5 mg lamotrigine per actuation (100 µl)] for nasal delivery.

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## REFERENCES

1. Shende AJ, Devarajan PV. Microemulsion based nasal mucoadhesive sprays of lamotrigine. Seventh International Symposium on Advances in Technology and Business Potential of New Drug Delivery System: Mumbai; February, 2007.
2. Thakker K. Development of Novel Drug Delivery Systems. M. Pharm Thesis: University of Mumbai; 2006.
3. Malcomson C, Lawrence M. J Pharm Pharmacol 1993;45:141.

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