

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. SHIRKHEKAR, 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

Development of a pMDI Formulation Containing Budesonide

E. ROBINS*, G. BROUET AND S. PRIOLKAR

Direction Technique, Valois SAS, Route des Falaises, 27100 Le Vaudreuil, France

A hydrofluoroalkane (HFA) based budesonide formulation was developed so that 220 µg of budesonide per shot would exit the valve over 200 doses. This formulation was designed to be physically and chemically stable and it would give reproducible aerosol performances¹⁻⁴. The stability of the resulting metered dose inhaler was also evaluated under accelerated storage conditions (40°/75%RH) up to 6 mo. The aim was also to match the innovator Pulmicort® CFC (chlorofluorocarbon) product in terms of *in vitro* performances.

MATERIALS AND METHODS

Excipients selected for evaluation were polyethylene glycol 300 (at levels of 0.15 to 5% w/w, supplied by

Fluka, France) and ethanol (at levels of 0.2 to 2% w/w, supplied by Prolabo, France)⁴. The amount of micronised budesonide (supplied by Aarti Healthcare Ltd, India) introduced into the formulation vessel was such that the appropriate dose of budesonide would be delivered to the patient. Pressurised metered dose inhalers (pMDIs) were prepared by introducing the HFA budesonide suspension formulation as a one step filling process, through a metering valve previously crimped onto a standard anodised aluminium canister (supplied by Presspart, Great-Britain).

To evaluate the homogeneity of the dispersion by visual inspection, formulations were filled into glass bottles. Promising formulations were evaluated with regard to drug stability upon storage, delivered dose uniformity (DDU) over 10 actuations at 28.3 l/min and particle size distribution using a Next Generation Impactor at 30 l/min.

*For correspondence

E-mail: emmanuelle.robins@valois.com

Valve types and materials combined with various actuator outlet orifice diameters were also evaluated. A first set of results was obtained with a DF30/50 RCU valve having polyacetal plastic components and nitrile rubber and thermoplastic elastomer gaskets combined with a 0.7 mm outlet orifice diameter actuator. A second set of results was obtained with a DF316/50 RCU valve with polyacetal plastic components and nitrile rubber and thermoplastic elastomer gaskets combined with a 0.5 mm outlet orifice diameter actuator.

RESULTS AND DISCUSSION

DDU results obtained with a DF30/50 valve fitted with a 0.7 mm outlet orifice diameter actuator are shown in (fig. 1) and those obtained with a DF316/50 valve fitted with a 0.5 mm outlet orifice diameter actuator are shown in (fig. 2). DDU data is summarised in Table 1 and conforms to the current FDA MDI/DPI guidance document for Dose Uniformity. Fine Particle Fraction (FPF) results are summarised in Table 2.

During this study, PEG 300 at levels less than 0.5% w/w was found to ensure good product performances and valve functioning throughout the MDI units' life. There was no sign of valve sticking. Ethanol at levels less than 1% w/w helped dissolution of the PEG300 without causing significant solubilisation of budesonide, which could lead to problems of chemical degradation. The level of ethanol selected also helped to decrease the propensity for rapid formation of coarse flocks. This formulation was readily re-dispersible and avoided irreproducible dosing of the drug. The stable suspension of particulate budesonide

was aided by employing a mixture of HFA propellants closely matching the density of the micronised budesonide.

Valois offers a fully developed budesonide HFA formulation. It includes a suspension formulation stable for at least 6 mo under 40°/75%RH storage conditions, together with the selected appropriate valve, canister and actuator.

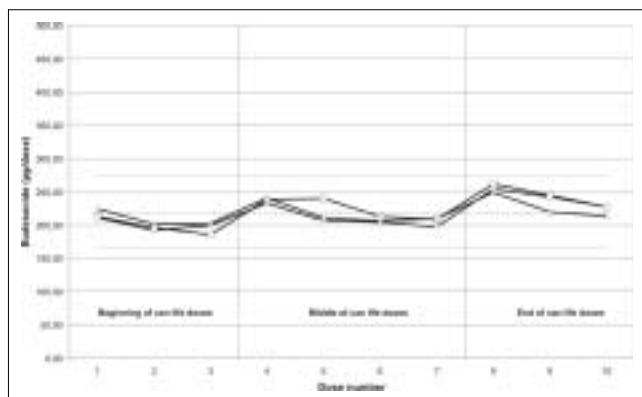


Fig. 1: Delivered dose uniformity of the formulations with DF30/50 valve

Delivered dose uniformity of the formulations at T 0 (—◇—), T 3 mo (—□—) and T 6 mo (—△—) under accelerated storage conditions using a 0.7 mm actuator fitted on a DF30/50 valve

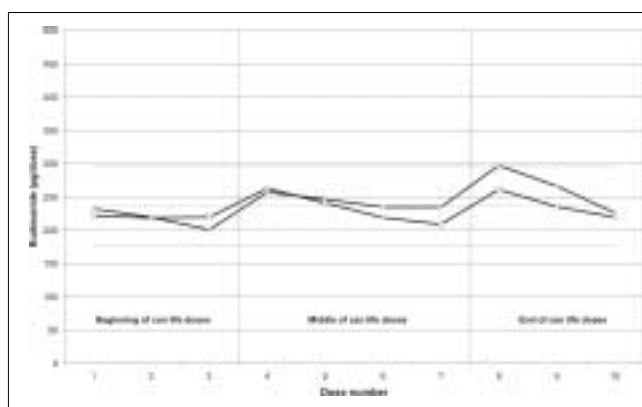


Fig. 2: Delivered dose uniformity of the formulation with a DF316/50 valve

Delivered dose uniformity of the formulation at T 0 (—□—) and T 3 mo under accelerated storage conditions (—◇—) using a 0.5 mm actuator fitted on a DF316/50 valve

TABLE 1: DELIVERED DOSE UNIFORMITY THROUGH CAN LIFE DEPENDING ON USED VALVE TYPE AND OUTLET ORIFICE SIZE OF THE ACTUATOR

	DF30 valve (n=10) 0.7 mm actuator	DF316 valve (n=2) 0.5 mm actuator
T0	217±22 µg	208±23 µg
T3 (40° /75%RH)	223±25 µg	223±20 µg
T6 (40° /75%RH)	218±15 µg	Not determined

TABLE 2: AERODYNAMIC PARTICLE SIZE DISTRIBUTION DEPENDING ON USED VALVE TYPE AND OUTLET ORIFICE SIZE OF THE ACTUATOR

	DF30 valve (n=3) 0.7 mm actuator		DF316 valve (n=2) 0.5 mm actuator		Pulmicort CFC (n=3) as supplied actuator	
	FPF (%)	MMAD (µm)	FPF (%)	MMAD (µm)	FPF (%)	MMAD (µm)
T0	17±2	5.06±0.02	19±2	5.06±0.05	14±1	5.46±0.11
T3 (40° /75%RH)	16±1	5.28±0.03	18±1	5.29±0.11	Not determined	
T6 (40° /75%RH)	14±2	5.36±0.04	Not determined		Not determined	

ACKNOWLEDGEMENTS

The authors would like to thank Presspart for supplying the canisters.

REFERENCES

1. Purewal T, Formulation of metered dose inhalers, Metered dose inhalers technology, Buffalo Grove: Interpharm Press; 1998; 1-8.

2. Atkins P, Baker PN, Mathiesen D, The design and development of inhalation drug delivery systems. Pharmaceutical Inhalation Aerosol Technology. New York: Marcel Dekker; 1992; 168-71.
3. Vervaet C, Byron PR. Drug-surfactant-propellant interactions in HFA-formulations. Int J Pharm, 1999; 186:13-30.
4. Hickey AJ, Lenfant C. editors. Inhalation aerosols, Physical and Biological Basis. 2nd ed. Lung Biology in Health and Disease 2007; 221.

26 October, 2007

Indian J. Pharm. Sci., 2007, 69 (5): 722-724
