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CONTENTS

REVIEW ARTICLES

- Cholesteryl Ester Transfer Protein: A Potential Target for the Treatment of Coronary Artery Disease**
HARSHA PATEL, JIGNA SHAH, SUNITA PATEL AND I. S. ANAND 735-740
- Properties and Formulation of Oral Drug Delivery Systems of Protein and Peptides**
A. SEMALTY, MONA SEMALTY, R. SINGH, S. K. SARAF AND SHUBHINI SARAF 741-747

RESEARCH PAPERS

- Fabrication and Evaluation of Asymmetric Membrane Osmotic Pump**
C. S. CHAUHAN, M. S. RANAWAT AND P. K. CHOUDHURY 748-752
- Studies of Disintegrant Properties of Seed Mucilage of *Ocimum gratissimum***
RAVIKUMAR, A. A. SHIRWAIKAR, ANNIE SHIRWAIKAR, S. LAKHSHMANA PRABU, R. MAHALAXMI, K. RAJENDRAN AND C. DINESH KUMAR 753-758
- Simultaneous Spectroscopic Estimation of Ezetimibe and Simvastatin in Tablet Dosage forms**
S. J. RAJPUT AND H. A. RAJ 759-762
- Formulation and Optimization of Carbamazepine Floating Tablets**
D. M. PATEL, N. M. PATEL, N. N. PANDYA AND P. D. JOGANI 763-767
- Effects of *Medicago sativa* on Nephropathy in Diabetic Rats**
M. S. MEHRANJANI, M. A. SHARIATZADEH, A. R. DESFULIAN, M. NOORI, M. H. ABNOSI AND Z. H. MOGHADAM 768-772
- Development of Hospital Formulary for a Tertiary Care Teaching Hospital in South India**
R. J. D'ALMEIDA, LEELAVATHI D. ACHARYA, PADMA G. M. RAO, J. JOSE AND RESHMA Y. BHAT 773-779
- Simultaneous Spectrophotometric Estimation of Rosiglitazone Maleate and Glimepiride in Tablet Dosage Forms**
ANJU GOYAL AND I. SINGHVI 780-783
- Preparation, Characterization and Antimicrobial Activity of Acrylate Copolymer Bound Amoxicillin**
J. S. PATEL, H. R. PATEL, N. K. PATEL AND D. MADAMWAR 784-790
- Haematitic Evaluation of *Lauha Bhasma* and *Mandura Bhasma* on HgCl₂-Induced Anemia in Rats**
P. K. SARKAR, P. K. PRAJAPATI, A. K. CHOUDHARY, V. J. SHUKLA AND B. RAVISHANKAR 791-795
- RPHPLC Method for the Estimation of Glibenclamide in Human Serum**
S. D. RAJENDRAN, B. K. PHILIP, R. GOPINATH AND B. SURESH 796-799
- 2D QSAR of Arylpiperazines as 5-HT_{1A} Receptor Agonists**
URMILA J. JOSHI, SONALI H. TIKHELE AND F. H. SHAH 800-804
- Antiproliferative and Cancer-chemopreventive Properties of Sulfated Glycosylated Extract Derived from *Leucaena leucocephala***
AMIRA M. GAMAL-ELDEEN, H. AMER, W. A. HELMY, H. M. RAGAB AND ROBA M. TALAAT 805-811

SHORT COMMUNICATIONS

- Simultaneous Derivative and Multi-Component Spectrophotometric Determination of Drotaverine Hydrochloride and Mefenamic Acid in Tablets**
P. P. DAHIVELKAR, V. K. MAHAJAN, S. B. BARI, A. A. SHIRKHEDKAR, R. A. FURSULE AND S. J. SURANA 812-814
- Design and Synthesis of Substituted 2-Naphthylxyethylamines as Potential 5-HT_{1A} Antagonists**
URMILA J. JOSHI, R. K. DUBE, F. H. SHAH AND S. R. NAIK 814-816
- Diuretic Activity of *Lagenaria siceraria* Fruit Extracts in Rats**
B. V. GHULE, M. H. GHANTE, P. G. YEOLE AND A. N. SAOJI 817-819
- Determination of Racecadotril by HPLC in Capsules**
S. L. PRABU, T. SINGH, A. JOSEPH, C. DINESH KUMAR AND A. SHIRWAIKAR 819-821
- Novel Spectrophotometric Estimation of Frusemide Using Hydrotropic Solubilization Phenomenon**
R. K. MAHESHWARI, S. DESWAL, D. TIWARI, N. ALI, B. POTHEN AND S. JAIN 822-824
- In Vivo* Pharmacokinetic Studies of Ibuprofen**
ABHA DOSHI AND S. G. DESHPANDE 824-827
- Protective Effect of *Tamarindus indica* Linn Against Paracetamol-Induced Hepatotoxicity in Rats**
B. P. PIMPLE, P. V. KADAM, N. S. BADGUJAR, A. R. BAFNA AND M. J. PATIL 827-831
- Simultaneous Estimation of Atorvastatin Calcium and Amlodipine Besylate from Tablets**
P. MISHRA, ALKA GUPTA AND K. SHAH 831-833
- Development and Validation of a Simultaneous HPTLC Method for the Estimation of Olmesartan medoxomil and Hydrochlorothiazide in Tablet Dosage Form**
N. J. SHAH, B. N. SUHAGIA, R. R. SHAH AND N. M. PATEL 834-836
- Orodispersible Tablets of Meloxicam using Disintegrant Blends for Improved Efficacy**
P. V. SWAMY, S. H. AREEFULLA, S. B. SHIRSAND, SMITHA GANDRA AND B. PRASHANTH 836-840
- Spectrophotometric Method for Ondansetron Hydrochloride**
SRADHANJALI PATRA, A. A. CHOUDHURY, R. K. KAR AND B. B. BARIK 840-841
- HPTLC Determination of Artesunate as Bulk Drug and in Pharmaceutical Formulations**
S. P. AGARWAL, A. ALI AND SHIPRA AHUJA 841-844
- Simultaneous Spectrophotometric Estimation of Metformin and Repaglinide in a synthetic mixture**
J. R. PATEL, B. N. SUHAGIA AND B. H. PATEL 844-846
- Synthesis and Antiinflammatory Activity of Substituted (2-oxochromen-3-yl) benzamides**
V. MADDI, S. N. MAMLEDESAI, D. SATYANARAYANA AND S. SWAMY 847-849
- Evaluation of Hepatoprotective Activity of Ethanol Extract of *Prosopium acerifolium* Ster Leaves**
S. KHARPATE, G. VADNERKAR, DEEPTI JAIN AND S. JAIN 850-852
- New Antihistaminic Agents: Synthesis and Evaluation of H1-Antihistaminic actions of 3-[(N,N-Dialkylamino)alkyl]-1,2,3,4-tetrahydro-(1H)-thioquinazolin-4(3H)-ones and Their oxo Analogues**
M. B. RAJU, S. D. SINGH, A. RAGHU RAM RAO AND K. S. RAJAN 853-856

Novel Spectrophotometric Estimation of Frusemide Using Hydrotropic Solubilization Phenomenon

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Maheshwari, *et al.*: Spectrophotometric Estimation of Frusemide

A novel, safe and sensitive method of spectrophotometric estimation in ultraviolet region has been developed using 0.5 M ibuprofen sodium solution as hydrotropic solubilizing agent for the quantitative determination of frusemide, a poorly water-soluble diuretic drug in tablet dosage form. Frusemide shows maximum absorbance at 330 nm. Beer's law was obeyed in the concentration range of 20 to 100 µg/ml. Ibuprofen sodium does not absorb above 300 nm. Commonly used tablet excipients and ibuprofen sodium did not interfere in spectrophotometric estimation. Results of the analysis were validated statistically and by recovery studies. Using 0.5 M ibuprofen sodium solution for analysis of two different tablet formulations of frusemide, the percent label claims and percent recoveries estimated were close to 100 with low values of standard deviation, percent coefficient of variation and standard error.

Key words: Frusemide, hydrotrophy, ibuprofen sodium, spectrophotometry

Increasing the aqueous solubility of insoluble and slightly soluble drugs is of major importance. Various techniques have been employed to enhance the aqueous solubility of poorly water-soluble drugs. Hydrotropic solubilization is one of them. The term hydrotrophy has been used to designate the increase in solubility in water of various substances due to the presence of large amounts of additives. Sodium salicylate, sodium benzoate, urea, nicotinamide, sodium citrate and sodium acetate are the most common examples of hydrotropic agents¹⁻¹⁵. Maheshwari has analyzed various poorly water-soluble drugs using hydrotropic solubilization phenomenon viz. ketoprofen¹, frusemide⁴, cefixime⁵, salicylic acid¹, tinidazole⁶ and amoxicillin⁷. Maheshwari *et al.*, have developed various analytical techniques employing hydrotropic solubilisation phenomenon to analyze poorly water-soluble drugs like hydrochlorothiazide⁸, aceclofenac⁹ and ofloxacin¹⁰.

Various organic solvents such as methanol, chloroform and dimethyl formamide, have been employed for solubilization of poorly water-soluble drugs to carry out spectrophotometric analysis. Drawbacks of organic solvents include their higher cost, toxicity and pollution. Hydrotropic solution may be a proper choice to preclude the use of organic solvents.

Frusemide (4-chloro-N-furfuryl-5-sulphamoylanthranilic

acid) is a widely used diuretic drug. In the preliminary solubility studies there was more than 105 fold enhancement in the solubility of frusemide in 0.5 M ibuprofen sodium solution. Therefore, it was thought worthwhile to employ this hydrotropic solution to extract out the drug from fine powder of tablets to carry out spectrophotometric estimation.

There is broad scope for hydrotropic agents in quantitative estimations of other poorly water-soluble drugs. Shimadzu UV/Vis recording spectrophotometer (Model UV160A) with 1 cm matched silica cell was employed. Frusemide was obtained from M/s Alkem Lab Ltd, Mumbai. All other chemicals were of analytical grade.

For the preparation of 0.5 M ibuprofen sodium solution, 10 g of sodium hydroxide was dissolved in 200 ml of distilled water. Ibuprofen (51.6 g) was added little at a time and stirred to dissolve. After complete addition of ibuprofen, the pH was adjusted to remain between 7.5 to 8.0 with sodium hydroxide to assure the complete neutralization of ibuprofen. Then the volume was made up to 250 ml with distilled water.

For the preparation of a calibration curve, 100 mg of the drug was dissolved in 10 ml of 0.5 M ibuprofen sodium solution and diluted up to 100 ml with distilled water. The standard solution (1000 µg/ml) was further diluted with distilled water to obtain

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TABLE 1: RESULTS OF ANALYSIS OF FRUSEMIDE TABLET FORMULATIONS

Amount of drug in tablet powder taken (mg)	Amount found (mg)		Percentage estimated	
	Formulation 1	Formulation 2	Formulation 1	Formulation 2
100	97.36	99.11	97.36	99.11
100	98.59	98.86	98.59	99.86
100	101.30	98.22	101.30	98.22

Formulation 1 is Lasix, Aventis Pharma Limited, Ankleshwar and Formulation 2 is Frusenex-100 of Geno Pharmaceuticals Limited, Goa

TABLE 2: STATISTICAL EVALUATION OF ANALYSIS OF TABLETS

Tablet formulation	Mean % estimation	Standard deviation	%coefficient of variation	Standard error
1	99.08	2.016	2.035	1.164
2	98.73	0.458	0.464	0.264

Formulation 1 is Lasix, Aventis Pharma Limited, Ankleshwar and Formulation 2 is Frusenex-100 of Geno Pharmaceuticals Limited, Goa.

TABLE 3: RESULTS OF RECOVERY STUDIES OF TABLET FORMULATION WITH STATISTICAL EVALUATION

Tablet formulation	Drug present in preanalysed tablet powder(mg)	Pure drug added (mg)	% recovery estimated*(mean±SD)	% coefficient of variance	Standard error
1	100	20	98.33±1.231	1.252	0.711
	100	40	98.76±0.813	0.823	0.469
2	100	20	99.30±0.922	0.928	0.532
	100	40	97.58±1.008	1.033	0.582

Formulation 1 is Lasix, Aventis Pharma Limited, Ankleshwar and Formulation 2 is Frusenex-100 of Geno Pharmaceuticals Limited, Goa. *(n=3).

20, 40, 60, 80 and 100 µg/ml. Absorbances were noted against respective reagent blanks to plot the calibration curve.

In the preliminary solubility studies the solubility of frusemide was determined in distilled water and 0.5 M ibuprofen sodium solution at 27±1°. Enhancement in the solubility of frusemide in 0.5 M ibuprofen sodium solution was more than 105 folds (as compared to its solubility in distilled water).

Analysis of tablet formulation of frusemide by the proposed method was done by a method in which two different marketed tablet formulations of frusemide were used. Twenty tablets of frusemide from formulation 1 (Lasix, Aventis Pharma Limited, Ankleshwar) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 100 mg of frusemide was transferred to a 100.0 ml of volumetric flask containing 10 ml of 0.5 M ibuprofen sodium solution. The flask was shaken for about 5 min to solubilize the drug and the volume was made up to mark with distilled water. The solution was filtered through Whatmann filter paper No 41. The filtrate was diluted appropriately with distilled water and was analyzed on UV spectrophotometer against reagent blank. Drug content of tablet formulation was then calculated (Table 1). Tablet formulation 2 (Frusenex-100, Geno Pharmaceuticals Limited, Goa) was treated in the same way.

Recovery studies were performed adding pure drug in the preanalysed tablet powder and following the same method of analysis. All types of analysis were performed in triplicate. Percent label claims estimated by the proposed method were 99.08±2.016 and 98.73±0.458 (Table 2), which were near to 100, indicating the accuracy of the proposed method. Low values of standard deviation, percent coefficient of variation and standard error further validated the proposed method. Percent recoveries ranged from 97.58±1.008 to 99.30±0.922 (Table 3). All these values were very close to 100. Also the values of standard deviation, percent coefficient of variation and standard error were satisfactorily low. This further confirmed the accuracy, reproducibility and validity of the proposed method.

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