

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 6

November-December 2007

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
- Haematonic 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 Prodrugs 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

Simultaneous Estimation of Atorvastatin Calcium and Amlodipine Besylate from Tablets

P. MISHRA*, ALKA GUPTA AND K. SHAH

Department of Pharmaceutical Sciences, Dr. H. S. Gour Vishwavidyalaya, Sagar - 470 003, India

Mishra, *et al.*: Simultaneous Estimation of Atorvastatin and Amlodipine

The present communication deals with the development of a new, simple, specific, sensitive, rapid and economical procedure for simultaneous estimation of atorvastatin calcium and amlodipine besylate in a combined dosage form. The method is based on the native ultraviolet absorbance maxima of the two chemotherapeutic agents. As both compounds do not interact chemically in methanol, two wavelengths 246 nm for atorvastatin calcium and 360 nm for amlodipine besylate were used. Both the drugs obeyed Beer's law in the concentration range that was employed in the method.

Key words: Simultaneous estimation, UV spectrometric method, atorvastatin, amlodipine

Atorvastatin calcium (ATVC), [(β R, δ S)-2-(4-fluorophenyl)- β , δ -dihydroxy-5-(1-methylethyl)-3-phenyl-4[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid calcium salt¹⁻³ is a lipid lowering agent, acting through the inhibition of HMG Co-A reductase. It is used in hypercholesterolemia. Several methods for its estimation using HPLC^{4,5} and HPTLC⁶ are reported.

Amlodipine besylate(AMLB), [3-ethyl-5-methyl (4RS)-

2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-methyl-1-dihydropyridine-3,5-dicarboxylate benzenesulfonate⁷⁻⁹. Amlodipine besylate is a calcium channel blocker, which is used as an antihypertensive agent. It is official in EP¹⁰ and BP¹¹. A number of spectrophotometric¹²⁻¹⁷ and HPLC¹⁸⁻²⁰ methods are reported in the literature for the estimation of AMLB, both individually as well as in combination with other drugs other than ATVC.

Fixed dose combination containing ATVC and AMLB are available only in the market as tablets. To our knowledge no simultaneous method for their determination are reported. In this communication we report a new UV-spectrophotometric method

*For correspondence

E-mail: glatrg@rediffmail.com

GLA Institute of Pharmaceutical Research,
200/1, Yugal Niwas, Raman Reti, Vrindaban, Mathura

for simultaneous determination of atorvastatin and amlodipine in tablets, which is simple, rapid, selective and precise.

A GBC Cintra-10 double beam UV/Vis spectrophotometer (Australia) equipped with 10 mm matched quartz cells was used in the present investigation. Methanol (AR) (Qualigens) was used in the present study. Drug samples of ATVC received from M/s Zydus Medica, Ahmedabad and AMLB from M/s IPCA Laboratories Ltd., Mumbai were used as such without further purification.

ATVC and AMLB, accurately weighed (100 mg each), were dissolved separately in 100 ml of methanol. Two milliliters of the above solutions were diluted separately to 20 ml with methanol in volumetric flask to give 100 µg/ml working standard solutions. These working standard solutions were further diluted 20 µg/ml. These dilutions were scanned in the UV region.

ATVC showed absorption maximum at 246 nm whereas AMLB showed absorption peaks at 237 and 360 nm. ATVC has no absorbance at 360 nm. Two wavelengths selected for the formation of simultaneous equations were 246 nm and 360 nm. Both the drugs showed linearity range of 5-30 µg/ml at the selected wavelengths respectively. The absorptivity for the two drugs is presented in Table 1, while (fig. 1) represents the overlain spectra of both the drugs.

Molar absorptivity value as determined for ATVC was found to be 4.8864×10^4 l/mol.cm. at 246nm. Molar

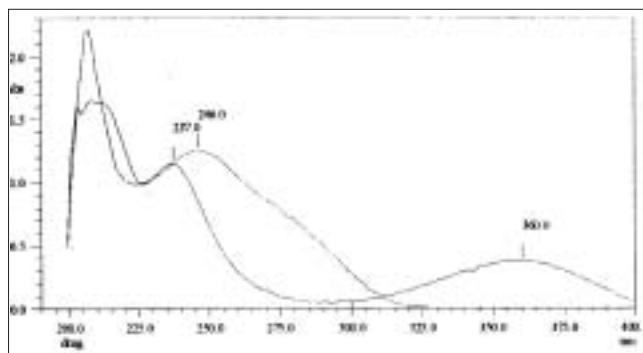


Fig. 1: Overlain Spectra of atorvastatin calcium and amlodipine besylate

absorptivity values for amlodipine at 246 nm and 360 nm were 1.5988×10^4 l/mol.cm. and 7.3014×10^3 l/mol.cm, respectively. The method employs solving of simultaneous equations using Cramer's rule and matrices. The simultaneous equations formed were, At 246 nm, $A_1 = 0.0422 C_X + 0.0281 C_Y \dots 1$ and at 360 nm, $A_2 = 0.0128 C_X \dots 2$, where A_1 and A_2 are absorbances of sample solution at 246 nm and 360 nm respectively. C_X and C_Y are the concentrations of ATVC and AMLB, respectively.

Two commercial formulations, Lipikind-Am (Mankind) and Avas-Am (Micro Labs) were purchased from a local pharmacy. The average weight of each tablet (before and after removing coating) was calculated using 20 tablets. Ten tablets were powdered finely in a glass mortar after removing the coating. Powdered sample equivalent to 100 mg of ATVC and 50 mg of AMLB of coated tablet was taken in 30 ml of methanol and shaken well to dissolve the drugs and transferred quantitatively to 100 ml volumetric flask after filtering through Whatman filter paper. The volume was then made up. Further dilutions were then accordingly made so that the final concentration lie between workable limit of 5-30 µg/ml. Absorbances of these solutions were measured at 246 nm and 360 nm and concentrations of these two drugs in the sample were calculated using Eqns. 1 and 2. Results are reported in Table 2.

To study accuracy, reproducibility and precision of

TABLE 1: ABSORPTIVITY VALUES FOR ATORVASTATIN CALCIUM AND AMLODIPINE BESYLATE

Concentration (µg/ml)	Absorptivity at 246 nm		Absorptivity at 360 nm	
	ATVC	AMLB	ATVC	AMLB
5	5	427.00	280.60	130.00
10	10	420.10	282.40	130.90
15	15	420.13	281.40	130.40
20	20	424.35	284.70	127.45
25	25	423.64	281.28	126.32
30	30	422.43	281.20	127.43
Mean		422.94	281.93	128.75

TABLE 2: STATISTICAL ANALYSIS FOR ATORVASTATIN CALCIUM AND AMLODIPINE BESYLATE

Tablet	Tablet component	Label claim* (mg/tab)	Amount found (mg/tab)*	SD*	% RSD*	SE*
Lipikind-Am	ATVC	10	9.9615±0.0541	0.0677	0.6796	0.0276
	AMLB	5	5.0012±0.0086	0.0109	0.2179	0.0044
Avas-Am	ATVC	10	9.9637±0.0448	0.0562	0.5640	0.0229
	AMLB	5	4.9861±0.0217	0.0272	0.5455	0.0110

*Average of six determinations

TABLE 3: RECOVERY STUDY OF ATORVASTATIN CALCIUM AND AMLODIPINE BESYLATE

Tablet	Tablet component	Label claim (mg/tab)*	Amount added (mg/10 tab)*	Percent recovery \pm SD*
Lipikind-Am	ATVC	10	10	100.17 \pm 0.5857
	AMLB	5	5	99.82 \pm 0.1892
Avas-Am	ATVC	10	10	100.11 \pm 0.2871
	AMLB	5	5	99.75 \pm 0.2528

*Average of six determinations

the proposed methods, recovery studies were carried out by the addition of known amount of pure drug to the pre-analyzed sample of the tablet powder and the mixture was analyzed for the drug content using proposed method. Results of recovery studies were found to be satisfactory Table 3.

The proposed method for simultaneous estimation of ATVC and AMLB dosage forms were found to be simple, accurate, economical and rapid. In this method, the values of coefficient of variation were satisfactorily low and recovery was close to 100 % for both the drugs. Hence, it can be employed for routine analysis in quality control laboratories.

ACKNOWLEDGEMENTS

The authors thank the Head of the Department for providing necessary facilities, and Zydus Medica, Ahmedabad, and IPCA Laboratories Ltd., Mumbai, for providing the gift samples of ATVC and AMLB, respectively. One of the authors (AG) thanks the All India Council of Technical Education (AICTE), New Delhi for providing financial assistance in the form of fellowship.

REFERENCES

- Mehley RW, Bersot TP. Drug therapy for hypercholesterolemia and dyslipidemia. *In*; Hardman JG, Limbird LE, Gilman AG, editors. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 10th ed. New York: McGraw Hill; 2001. p. 971.
- Budavari S, editor. The merck index: An encyclopedia of chemicals, drugs and biologicals. 13th ed. Merck Research Laboratories, Division of Whitehouse Station, NJ: Merck and Co., Inc; 2001. p. 148.
- Sweetman SC, editor. Martindale: The complete drug reference, 34th ed. London: Royal Pharmaceutical Society of Great Britain; 2005. p. 868.
- Manoj K, Shanmugapandiyam P, Anbazhagan S. RP-HPLC method for simultaneous estimation of atorvastatin calcium and aspirin from capsule formulation. *Indian Drugs* 2004;41:284.
- Erturk S, Akta ES, Ersoy L, Ficicioglu S. An HPLC method for the determination and its impurities in bulk drug and tablets. *J Pharm Biomed Anal* 2003;33:1017-23.
- Yadav SS, Mhaske DV, Kakad AB, Patil BD, Kadam SS, Dhaneshwar SR. A simple and sensitive HPTLC method for the determination of content uniformity of atorvastatin calcium tablets. *Indian J Pharm Sci* 2005;67:182.
- Budavari S, editor. The merck index: An encyclopedia of chemicals, drugs and biologicals, 13th ed. Merck Research Laboratories, Division of Whitehouse Station, NJ: Merck and Co. Inc; 2001. p. 86.
- Oates JA, Brown NJ. Antihypertensive agents and drug therapy of hypertension. *In*; Hardman JG, Limbird LE, Gilman AG, editors. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 10th ed. New York: McGraw Hill; 2001. p. 871.
- Sweetman SC, editor. Martindale: The complete drug reference, 34th ed. London: Royal Pharmaceutical Society of Great Britain; 2005. p. 862.
- European Pharmacopoeia, 4th ed. Strassburg, Cedex 1, European Directorate for the Quality of Medicine Council of Europe: France; 2002. p. 639.
- British Pharmacopoeia, Vol. 1, London: Her Majesty's Stationary Office; 2004. p. 125.
- Gohil K., Trivedi P, Molvi KJ. Spectrophotometric method for amlodipine besylate in bulk and in tablet dosage forms. *Indian J Pharm Sci* 2005;67:376.
- Topale PR, Gaikwad NJ, Tajane MR. Simultaneous UV-spectrophotometric estimation of losartan potassium and amlodipine in tablet. *Indian Drugs* 2003;40:119.
- Prabhakar AH, Giridhar R. Spectrophotometric method for the determination of amlodipine besylate in pure form and in tablets. *Indian Drugs* 2002;39:204.
- Jain HK, Agrawal RK. Spectrophotometric methods for simultaneous estimation of amlodipine besylate and lisinopril in tablets. *Indian Drugs* 2000;37:196.
- Surekha A, Khopade, Jain NK. Difference spectrophotometric estimation of amlodipine besylate. *Indian Drugs* 2000;37:351.
- Sethi PD, editor. Quantitative Analysis of Drugs in Pharmaceutical Formulations, 3rd ed. New Delhi: CBS Publishers and Distributors; 1997. p. 373.
- Rao JR, Kadam SS, Mahadik KR. RP-HPLC determination of amlodipine and benazepril hydrochloride in tablets. *Indian Drugs* 2002;39:378.
- Gowri N, Vaidhyalingam V, Shantha A. Simultaneous estimation of amlodipine and benazepril from tablets by RP-HPLC. *Indian Drugs* 2002;39:532.
- Avadhanulu AB, Srinivas JS, Anjaneyulu A. RP-HPLC Determination of Amlodipine besylate in drug and its pharmaceutical dosage forms. *Indian Drugs* 1996;33:36.

Accepted 16 December 2007

Revised 30 May 2007

Received 12 July 2006

Indian J. Pharm. Sci., 2007, 69 (6): 831-833