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 Disintegrate Properties of Seed Mucilage of Ocimum gratissimum
RAVIKUMAR, A. A. SHIRWAIKAR, ANNIE SHIRWAIKAR, S. LAKSHMHANA PRABU, R. MAHALAXMI, K. RAJENDRAN AND C. DINESH KUMAR 753-758

In Vivo Pharmacokinetic Studies of Produgs of Ibuprofen
ABHA DOSHI AND S. G. DESHPANDE 824-827

Effect 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
C. S. CHAUHAN, M. S. RANAWAT AND P. K. CHOUDHURY 748-752

Evaluation of Hepatoprotective Activity of Ethanol Extract of Psorospermum acerifolium Ster Leaves
S. SWAMY 847-849

New Antihistaminic Agents: Synthesis and Evaluation of H1-Antihistaminic Activities of 3-
[(N,N-Dialkylamino)alkyl]-1,2,3,4-tetrahydropyridines and Their oxo Analogues
S. KHARPATE, G. VADNERKAR, DEEPTI JAIN AND S. JAIN 850-852

Simultaneous Spectrophotometric Estimation of Ezetimibe and Simvastatin in Tablet Dosage forms
S. J. RAJPUT AND H. A. RAJ 759-762

Pharmaceutical Formulations
B. SURESH 796-799

Simultaneous Spectrophotometric Determination of Drotaverine Hydrochloride and Mefenamic Acid in Tablets
M. J. PATIL 827-831

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

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
C. S. CHAUHAN, M. S. RANAWAT AND P. K. CHOUDHURY 748-752

Evaluation of Hepatoprotective Activity of Ethanol Extract of Psorospermum acerifolium Ster Leaves
S. SWAMY 847-849

New Antihistaminic Agents: Synthesis and Evaluation of H1-Antihistaminic Activities of 3-
[(N,N-Dialkylamino)alkyl]-1,2,3,4-tetrahydropyridines and Their oxo Analogues
S. KHARPATE, G. VADNERKAR, DEEPTI JAIN AND S. JAIN 850-852

Simultaneous Spectrophotometric Estimation of Ezetimibe and Simvastatin in Tablet Dosage forms
S. J. RAJPUT AND H. A. RAJ 759-762

Pharmaceutical Formulations
B. SURESH 796-799

Simultaneous Spectrophotometric Determination of Drotaverine Hydrochloride and Mefenamic Acid in Tablets
M. J. PATIL 827-831

Hydrotropic Solubilization Phenomenon
R. K. MAHESHWARI, S. DESWAL, D. TIWARI, N. ALI, B. POTHEN AND S. JAIN 822-824

SHORT COMMUNICATIONS

Simultaneous Derivative and Multi-Component Spectrophotometric Determination of Drotaverine Hydrochloride and Mefenamic Acid in Tablets
M. J. PATIL 827-831

Synthesis and Design of Substituted 2-Naphthoxyethylenamines as Potential 5-HT1A Antagonists

Simultaneous HPTLC Method for the Estimation of Glibenclamide in Human Serum
P. MISHRA, ALKA GUPTA AND K. SHAH 831-833

HPTLC Determination of Artesunate as Bulk Drug and in Pharmaceutical Formulations
P. MISHRA, ALKA GUPTA AND K. SHAH 831-833

Simultaneous Spectrophotometric 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

Preparation, Characterization and Antimicrobial Activity of Acrylate Copolymer Bound Amoxicillin
J. S. PATEL, H. R. PATEL, N. K. PATEL AND D. MADAMWAR 784-790

Evaluation of Lacha Bhasma and Mandura Bhasma for Improved Efficacy
ABHA DOSHI AND S. G. DESHPANDE 824-827

5HT1 Receptor Agonists
URMILA J. JOSHI, SONALI H. TIKEHE 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. TALAT 805-811

Evaluation of Hepatoprotective Activity of Ethanol Extract of Pitsporum acerifolium Styer Leaves
S. KHPARTE, 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 spectrophotometric method, atorvastatin, amlodipine

Atorvastatin calcium (ATVC), [(βR,δS)-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 HPLC4,5 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 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 absorbivity 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 4.8864×10⁴ l/mol.cm. at 246 nm. Molar absorptivity values for amlodipine at 246 nm and 360 nm were 1.5988×10⁴ l/mol.cm. and 7.3014×10³ l/mol.cm, respectively. The method employs solving of simultaneous equations using Cramer’s rule and matrices. The simultaneous equations formed were,

\[ A_{1} = 0.0422 C_{X} + 0.0281 C_{Y} \quad (1) \]
\[ A_{2} = 0.0128 C_{Y} \quad (2) \]

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 | AMLB |
| 5 | 5 | 427.00 | 282.60 | 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
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


TABLE 3: RECOVERY STUDY OF ATORVASTATIN CALCIUM AND AMLODIPINE BESYLATE

<table>
<thead>
<tr>
<th>Tablet</th>
<th>Tablet component</th>
<th>Label claim (mg/tab)*</th>
<th>Amount added (mg/10 tab)*</th>
<th>Percent recovery ± SD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipikind-Am</td>
<td>ATVC</td>
<td>10</td>
<td>10</td>
<td>100.17±0.5857</td>
</tr>
<tr>
<td></td>
<td>AMLB</td>
<td>5</td>
<td>5</td>
<td>99.82±0.1892</td>
</tr>
<tr>
<td>Avas-Am</td>
<td>ATVC</td>
<td>10</td>
<td>10</td>
<td>100.11±0.2871</td>
</tr>
<tr>
<td></td>
<td>AMLB</td>
<td>5</td>
<td>5</td>
<td>99.75±0.2528</td>
</tr>
</tbody>
</table>

*Average of six determinations