

Quantitation of Mevinolic acid in human plasma by HPLC

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Simple and precise high-performance liquid chromatographic(HPLC) assay developed and validated for the determination of a HMG-Co A reductase inhibitor, lovastatinTM and its active metabolite(Mevinolinic acid) in human plasma. The internal standard and analyte were extracted solid phase extraction using Sep-Pak Cartridge. Samples were analyzed by reversed-phase HPLC using Capcell-Pak C18 column with ultraviolet detection at 238 nm. The quantitation limit of mevinolinic acid was 2ng/ml and the calibration curve was linear over range of 0.002-0.05 µg/ml ($r^2 > 0.99$). In human plasma, intra- and inter-assay accuracy ranged from 97.07 to 103.33% and 98.72 to 104.53%, respectively. The average recoveries were similar(80%) for mevinolinic acid and methylmevinolinic acid. The method described has been successfully applied to the quantification of mevinolinic acid in about 1000 human plasma samples over six-month period.

[PD4-6] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

MICROBORE HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC ANALYSIS OF LOVASTATINIC ACID IN HUMAN SERUM WITH COLUMN-SWITCHING

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A fully automated semi-microbore high performance liquid chromatographic method using triple column switching was developed for the analysis of lovastatinic acid, an active metabolite of lovastatin from human serum samples obtained after oral administration of lovastatin tablet. Serum samples (120 µl) were directly injected onto a Capcell pak MF ph-1 column (20 x 4.0 mm I.D.) where lovastatinic acid was separated from serum components and lovastatinic acid fraction was transferred into an intermediate column (35 x 2.0 mm I.D.) using 5 % acetonitrile in phosphate buffer (30 mM, pH 6.86) for deproteinization and concentration. The main separation was performed on a semi-microbore C18 column (250 x 1.5 mm I.D.) using linear gradient elution with solvent A (5 % acetonitrile in phosphate buffer (30 mM, pH 6.86)) and solution B (70 % acetonitrile in 0.2 % phosphoric acid). The method showed excellent sensitivity (limit of quantitation : 2 ng/ml) and good precision(C.V. 8.2 %), and shortened total analysis time per serum sample (55 min). The calibration curve was linear (r^2 0.999) over the concentration range 2-100 ng/ml. The applicability of the assay method was proved in the bioequivalence test of two commercial lovastatin tablets.

[PD4-7] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

The Contents of Preservations in Commercial Drugs

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This study was performed to analyze the content of preservatives in commercial drugs. 159 of drugs kinds were collected from 1998. 1 to 1999. 12 in Seoul area.

The results were as follows :

1. Paraben mixtures (methyl paraben and propyl paraben) were used in most cases. (90 a 159 samples)
2. In case of methyl and propyl paraben being used, capsules showed a higher concentration than any other shape of drugs.
3. The sum of paraben (methyl paraben and propyl paraben) concentration was 0.06~0.28% in creams, 0.03~0.11% in syrups, 0.111% in suppositories 0.02~0.054% in ophthalmics solutions, 0.051~0.15% injections, 0.15~5.32mg/cap in capsules and 0.08~0.12% in solutions.

[PD4-8] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Chiral separations of β -blockers by HPLC using (S)-(+)-TBMB-COOH

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The fluorescent chiral derivatizing agent, (S)-(+)-TBMB carboxylic acid was applied for highly sensitive HPLC analysis of enantiomeric β -blockers. Racemic β -blockers were derivatized with (S)-TBMB-COCl in pyridine-CH₃CN solution and subjected to normal phase silica column HPLC for the separations of the derived diastereomeric di-(S)-TBMB-carboxylated β -blocker derivatives.

Optically pure (S)-TBMB-COCl was synthesized and its CH₃CN solution was successfully used for the determination of the optical purities of β -blockers as their diastereomeric di-(S)-TBMB derivatives without any racemization. Optimum reaction conditions, reaction time, temperature and the concentration of (S)-TBMB-COCl, and HPLC conditions were examined using a normal phase silica column(4.6×250mm). The eluents were monitored by fluorescent detection at Ex. 310nm and Em. 380nm and the detection limits of (S)-TBMB-derivatized β -blockers were 0.1 pmole on column.

In this study, we have successfully demonstrated for the chiral separations of various β -blockers by normal phase HPLC using fluorescent chiral derivatization agent, (S)-(+)-TBMB-COOH, and the extension of the present method is underway.

[PD4-9] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Studies on the Chiral Separation Mechanism of Amine Moiety Drugs using chiral CBH column

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Enantioseparation of chiral drugs are sometimes laborious and time-consuming study and the chiral stationary phase is very expensive. Therefore, if the prediction of chiral separation of the drug is possible by their 3-dimensional molecular structure, it is certain that will be a very useful tool in studying the chiral separation of drugs and separation mechanism of chiral stationary phases. Especially, all beta blockers have chiral center in their molecule and most of them are marketed as racemic mixtures. It has been well documented that the single enantiomers of beta blocking agents, as well as several other drugs, differ largely in their pharmacodynamic and pharmacokinetic profiles. (S)-propranolol is more than 100 times potent in blocking beta receptors than the corresponding (R)-enantiomer. In this study, eleven of the most popular beta-blockers and some other drugs which have very similar structure with amine moieties were chosen as model drugs.

Firstly, in order to study the prediction of the chiral separation of some amine moiety drugs, influence on enantioselective retention of several mobile phase parameters, e. g., types of organic modifier, i.e., 2-propanol, acetonitrile, concentration of organic modifier, mobile phase buffer pH,