Suven Research Publications in 2004

1. J Pharm Biomed Anal. 2004 Nov 15; 36(3):505-15.

Simple, sensitive and rapid LC-MS/MS method for the quantitation of cerivastatin in human plasma--application to pharmacokinetic studies.

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A simple and sensitive liquid chromatography-tandem mass spectrometry method was developed and validated for estimation of cerivastatin (I) in human plasma, a potent hydroxy-methylglutaryl-coenzyme A reductase inhibitor. The analyte and internal standard (atorvastatin, II) were extracted by liquid/liquid extraction with diethyl ether/dichloromethane (70/30, v/v). The chromatographic separation was performed on reverse phase Xterra ODS column with a mobile phase of water/acetonitrile (30/70, v/v) with 0.03% formic acid. The protonated analyte was quantitated in positive ionization by multiple reaction monitoring with a mass spectrometer. The mass transitions m/z 460.4 --> 356.3 and 559.2 --> 440.3 were used to measure I and II, respectively. The lower limit of quantitation was 10pg/mL with a relative standard deviation of less than 15%. Acceptable precision and accuracy were obtained for concentrations over the calibration curve ranges (0.01-10ng/mL). Sample analysis time of 2min for each sample made it possible to analyze a throughput of more than 400 human plasma samples per day. The assay can be used to analyze human plasma samples to support phase I and II clinical studies.
Publication Types:
Comparative Study

PMID: 15522524 [PubMed - indexed for MEDLINE]

2: J Chromatogr B Analyt Technol Biomed Life Sci. 2004 Oct 5;809(2):243-9.

Quantitation of tadalafil in human plasma by liquid chromatography-tandem mass spectrometry with electrospray ionization.

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A simple, rapid, sensitive and specific liquid chromatography-tandem mass spectrometry method was developed and validated for quantitation of tadalafil (I) in human plasma, a new selective, reversible phosphodiesterase 5 inhibitor. The analyte and internal standard (sildenafil, II) were extracted by liquid-liquid extraction with diethyl ether/dichloromethane (70/30, v/v) using a Glas-Col Multi-Pulse Vortexer. The chromatographic separation was performed on reverse phase Xterra MS C18 column with a mobile phase of 10mM ammonium formate/acetonitrile (10/90, v/v, pH adjusted to 3.0 with formic acid). The protonate of analyte was quantitated in positive ionization by multiple reaction monitoring with a mass spectrometer. The mass transitions m/z 390.4 --> 268.0 and m/z 475.5 --> 58.3 were used to measure I and II, respectively. The assay exhibited a linear dynamic range of 10-1000 ng/mL for tadalafil in human plasma. The lower limit of quantitation was 10 ng/mL with a relative standard deviation of less than 15%. Acceptable

precision and accuracy were obtained for concentrations over the standard curve ranges. Run time of 1.2 min for each sample made it possible to analyze a throughput of more than 400 human plasma samples per day. The validated method has been successfully used to analyze human plasma samples for application in pharmacokinetic, bioavailability or bioequivalence studies. Copyright 2004 Elsevier B.V.
Publication Types:
Research Support, Non-U.S. Gov't

PMID: 15315772 [PubMed - indexed for MEDLINE]

3: J Mass Spectrom. 2004 Jul; 39(7):824-32.

Simple, sensitive and rapid liquid chromatographic/electrospray ionization tandem mass spectrometric method for the quantification of lacidipine in human plasma.

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A simple, sensitive and rapid liquid chromatographic/electrospray ionization tandem mass spectrometric method was developed and validated for the quantification of lacidipine in human plasma using its structural analogue, amlodipine, as internal standard (IS). The method involves a simple single-step liquid-liquid extraction with tert-butyl methyl ether. The analyte was chromatographed on an Xterra MS C(18) reversed-phase chromatographic column by isocratic elution with 20 mM ammonium acetate buffer-acetonitrile (10:90, v/v; pH 6) and analyzed by mass spectrometry in the multiple reaction monitoring mode. The precursor to product ion transitions of m/z 456.4 --> 354.4 and m/z 409.3 --> 238.3 were used to measure the analyte and the I.S., respectively. The chromatographic run time was 1.5 min and the weighted (1/x(2)) calibration curves were linear over the range 0.1-25 ng ml(-1). Lacidipine was sensitive to temperature in addition to light. The method was validated in terms of accuracy, precision, absolute recovery, freeze-thaw stability, bench-top stability and re-injection reproducibility. The limit of detection and lower limit of quantification in human plasma were 50 and 100 pg ml(-1), respectively. The within- and between-batch accuracy and precision were found to be well within acceptable limits (<15%). The analyte was stable after three freeze-thaw cycles (deviation <15%). The average absolute recoveries of lacidipine and amlodipine (IS) from spiked plasma samples were 51.1 +/- 1.3 and 50.3 +/- 4.9%, respectively. The assay method described here could be applied to study the pharmacokinetics of lacidipine.

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4: J Chromatogr B Analyt Technol Biomed Life Sci. 2004 Sep 25; 809(1):117-24.

Selective and rapid liquid chromatography-tandem mass spectrometry assay of dutasteride in human plasma.

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A simple, rapid, sensitive and specific liquid chromatography-tandem mass spectrometry method was developed and validated for quantification of dutasteride (I), a potent and the first specific dual inhibitor of 5alpha-reductase, in human plasma. The analyte and internal standard

(finasteride (II)) were extracted by liquid-liquid extraction with diethyl ether/dichloromethane (70/30, v/v) using a Glas-Col Multi-Pulse Vortexer. The chromatographic separation was performed on a reverse phase Xterra MS C18 column with a mobile phase of 10 mM ammonium formate/acetonitrile (15/85, v/v, pH adjusted to 3.0 with formic acid). The protonated analyte was quantitated in positive ionization by multiple reaction monitoring with a mass spectrometer. The mass transitions m/z 529.5 --> 461.5 and m/z 373.3 --> 317.4 were used to measure I and II, respectively. The assay exhibited a linear dynamic range of 0.1-25.0 ng/mL for dutasteride in human plasma. The lower limit of quantitation was 100 pg/mL with a relative standard deviation of less than 15%. Acceptable precision and accuracy were obtained for concentrations over the standard curve ranges. A run time of 1.2 min for each sample made it possible to analyze a throughput of more than 400 human plasma samples/day. The validated method has been successfully used to analyze human plasma samples for application in pharmacokinetic, bioavailability or bioequivalence studies.
Publication Types:
Research Support, Non-U.S. Gov't

PMID: 15282101 [PubMed - indexed for MEDLINE]

5: J Chromatogr B Analyt Technol Biomed Life Sci. 2004 Jun 5; 805(1):13-20.

Liquid chromatography-negative ion electrospray tandem mass spectrometry method for the quantification of tacrolimus in human plasma and its Bioanalytical applications.

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A simple, rapid, novel and sensitive liquid chromatography-tandem mass spectrometry method was developed and validated for quantification of tacrolimus (I) in human plasma, a narrow therapeutic index, potent macrolide immunosuppressive drug. The analyte and internal standard (tamsulosin (II)) were extracted by liquid-liquid extraction with t-butylmethylether using a Glas-Col Multi-Pulse Vortexer. The chromatographic separation was performed on reverse phase Xterra ODS column with a mobile phase of 99% methanol and 1% 10mM ammonium acetate buffer. The deprotonate of analyte was quantitated in negative ionization by multiple reaction monitoring (MRM) with a mass spectrometer. The mass transitions m/z 802.5-->560.3 and m/z 407.2-->151.9 were used to measure I and II, respectively. The assay exhibited a linear dynamic range of 0.05-25ng/ml for tacrolimus in human plasma. The lower limit of quantitation was 50pg/ml with a relative standard deviation of less than 20%. Acceptable precision and accuracy were obtained for concentrations over the standard curve ranges. Run time of 2min for each sample made it possible to analyze a throughput of more than 400 human plasma samples per day. The validated method has been successfully used to analyze human plasma samples for application in comparative bioavailability studies. The tacrolimus plasma concentration profile could be obtained for pharmacokinetic study. The observed maximum plasma concentration (C(max)) of tacrolimus (5mg oral dose) is 440pg/ml, time to observed maximum plasma concentration (T(max)) is 2.5h and elimination half-life (T(1/2)) is 21h.

PMID: 15113534 [PubMed - indexed for MEDLINE]

6: J Chromatogr B Analyt Technol Biomed Life Sci. 2004 Apr 5; 802(2):271-5.

Quantitation of Valdecoxib in human plasma by high-performance liquid chromatography with ultraviolet absorbance detection using liquid-liquid extraction.

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A simple, sensitive and specific HPLC method with UV detection (210 nm) was developed and validated for quantitation of Valdecoxib in human plasma, the newest addition to the group of non-steroidal anti-inflammatory drugs-a highly selective cyclooxygenase-2 inhibitor. The analyte and an internal standard (Rofecoxib) were extracted with diethyl ether/dichloromethane (70/30 (v/v)). The chromatographic separation was performed on reverse phase ODS-AQ column with an isocratic mobile phase of water/methanol (47/53 (v/v)). The lower limit of quantitation was 10 ng/ml, with a relative standard deviation of <20%. A linear range of 10-500 ng/ml was established. This HPLC method was validated with between-batch and within-batch precision of 1.27-7.45 and 0.79-6.12%, respectively. The between-batch and within-batch bias was 0.74-7.40 and -0.93 to 7.70%, respectively. Frequently coadministered drugs did not interfere with the described methodology. Stability of Valdecoxib in plasma was excellent, with no evidence of degradation during sample processing (autosampler) and 30 days storage in a freezer. This validated method is suitable for bioequivalence studies following single dose in healthy volunteers.

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