1: Biomed Chromatogr. 2007 Jun 22; [Epub ahead of print]

Quantification of tenatoprazole in rat plasma by HPLC: validation and its application to pharmacokinetic studies.

Nirogi R, Kandikere V, Mudigonda K, Bhyrapuneni G.

Pharmacokinetics and Drug Metabolism, Discovery Research, Suven Life Sciences Ltd, Serene Chambers, Road No. 7, Banjara Hills, Hyderabad 500034, India.

A simple, reliable HPLC method with UV detection (295 nm) in rat plasma was developed and validated for quantification of tenatoprazole, a novel proton pump inhibitor, which is in clinical trials. Following a single-step liquid-liquid extraction, the analyte and internal standard were separated using an isocratic mobile phase on a reverse phase C(18) column. The lower limit of quantitation was 20 ng/mL, with a relative standard deviation of less than 10%. A linear dynamic range of 20-6000 ng/mL was established. This HPLC method was validated with between-batch and within-batch precision of 2.9-6.3 and 1.4-5.8%, respectively. The between-batch and within-batch accuracy was 95.1-104.1 and 92.4-101.0%, respectively. This validated method is simple and repeatable enough to be used in pharmacokinetic studies. Copyright (c) 2007 John Wiley & Sons, Ltd.

PMID: 17590865 [PubMed - as supplied by publisher]

2: Biomed Chromatogr. 2007 Jun 21; [Epub ahead of print]

Quantification of pramipexole in human plasma by liquid chromatography tandem mass spectrometry using tamsulosin as internal standard.

Nirogi RV, Kandikere V, Shrivastava W, Mudigonda K, Maurya S, Ajjala D.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road No. 5, Avenue 7, Banjara Hills, Hyderabad 500034, India.

A high-performance liquid chromatography/electrospray ionization tandem mass spectrometry method was developed and validated for the quantification of pramipexole in human plasma. Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reverse-phase column and analyzed by MS/MS in the multiple reaction monitoring mode using the respective [M + H](+) ions, m/z 212/152 for pramipexole and m/z 409/228 for the IS. The method exhibited a linear dynamic range of 200-8000 pg/mL for pramipexole in human plasma. The lower limit of quantification was 200 pg/mL with a relative standard deviation of less than 8%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 3.5 min for each sample made it possible to analyze more than 200 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 (c) 2007 John Wiley & Sons, Ltd.

PMID: 17583880 [PubMed - as supplied by publisher]


Novel base catalysed rearrangement of sultone oximes to 1,2-benzisoxazole-3-methane sulfonate derivatives.
A new process for the preparation of 1,2-benzisoxazole-3-methanesulfonates and 4-oximino-2,3-dihydrobenzoxathin-2,2-dioxides (sultone oximes) is described. These compounds are important intermediates for the preparation of zonisamide, an anti-convulsant drug.

PMID: 17555607 [PubMed]


Chromatography-mass spectrometry methods for the quantitation of statins in biological samples.

Nirogi R, Mudigonda K, Kandikere V.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

The 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase inhibitors, more commonly known as 'statins', are a novel class of drugs widely used for the treatment of hypercholesterolaemia in patients with established cardiovascular disease as well as those at high risk of developing atherosclerosis. Published chromatographic-mass spectrometric methods for the quantification of presently available seven statins, atorvastatin, simvastatin, lovastatin, pravastatin, fluvastatin, rosuvastatin and pitavastatin are reviewed. High performance liquid chromatography (HPLC) in combination with tandem mass spectrometry (MS/MS) is the analytical technique of choice for the quantification of statins in biological samples. This review envisages that most of the methods used for quantification of statins are in plasma and they are suitable for therapeutic drug monitoring of these drugs.

Publication Types:
Review

PMID: 17433599 [PubMed - indexed for MEDLINE]


Quantitative determination of galantamine in human plasma by sensitive liquid chromatography-tandem mass spectrometry using loratadine as an internal standard.

Nirogi RV, Kandikere VN, Mudigonda K, Maurya S.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. Ramakrishna_nirogi@yahoo.co.in

A simple, rapid, sensitive, and selective liquid chromatography-tandem mass spectrometry method is developed and validated for the quantitation of galantamine, an acetylcholinesterase inhibitor in human plasma, using a commercially available compound, loratadine, as the internal standard. Following liquid-liquid extraction, the analytes are separated using an isocratic mobile phase on a reverse-phase C18 column and analyzed by mass spectrometry in the multiple reaction monitoring mode using the respective (M+H)+ ions, m/z 288 to 213 for galantamine and m/z 383 and 337 for the internal standard. The assay exhibit a linear dynamic range of 0.5-100 ng/mL for galantamine in human plasma. The lower limit of quantitation is 0.5 ng/mL, with a relative standard deviation of less than 8%. Acceptable precision and accuracy are obtained for concentrations over the standard curve range. A run time of 2.5 min for each sample makes it possible to analyze more than 400 human plasma samples per day. The validated
method is successfully used to analyze human plasma samples for application in pharmacokinetic, bioavailability, or bioequivalence studies.

Publication Types:
  Validation Studies

PMID: 17425139 [PubMed - indexed for MEDLINE]


Quantification of pseudoephedrine in human plasma by LC-MS/MS using mosapride as internal standard.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S, Komarneni P.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road 7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive and rapid high-performance liquid chromatography/positive ion electrospray tandem mass spectrometry (LC-MS/MS) method was developed and validated for the quantification of pseudoephedrine in human plasma using mosapride as internal standard. Following solid-phase extraction, the analytes were separated using an isocratic mobile phase on a reverse-phase column and analyzed by MS/MS in the multiple-reaction monitoring mode using the respective [M + H](+) ions, m/z 166/148 for pseudoephedrine and m/z 422/198 for the IS. The method exhibited a linear dynamic range of 2-1000 ng/mL pseudoephedrine in human plasma. The lower limit of quantification was 2 ng/mL with a relative standard deviation of less than 9% for pseudoephedrine. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. The total chromatographic run time of 2 min for each sample made it possible to analyze 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.

Publication Types:
  Evaluation Studies

PMID: 17230461 [PubMed - indexed for MEDLINE]


Quantification of fexofenadine in human plasma by liquid chromatography coupled to electrospray tandem mass spectrometry using mosapride as internal standard.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S, Komarneni P.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A rapid high-performance liquid chromatography/positive ion electrospray tandem mass spectrometry method was developed and validated for the quantification of fexofenadine in human plasma using mosapride as internal standard. Following solid-phase extraction, the analytes were separated using an isocratic mobile phase on a reverse-phase column and analyzed by MS/MS in the multiple reaction monitoring mode using the respective [M+H]+ ions, m/z 502/466 for fexofenadine and m/z 422/198 for the IS. The method exhibited a linear dynamic range of 1-500 ng/mL for fexofenadine in human plasma. The lower limit of quantification was 1 ng/mL with a relative standard deviation of less than 5% for fexofenadine. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. The total chromatographic run time of 2 min for each sample made it possible to analyze
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.

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Publication Types:
Validation Studies

PMID: 17221908 [PubMed - indexed for MEDLINE]


Effect of food on bioavailability of a single oral dose of clopidogrel in healthy male subjects.

Nirogi RV, Kandikere VN, Mudigonda K.

Biopharmaceutical Research, Suven Life Sciences Ltd., Hyderabad, India. ramakrishna_nirogi@yahoo.co.in

OBJECTIVE: The present study aimed at investigating the effects of concomitant food intake on the bioavailability of a single oral dose of clopidogrel (CAS 113665-84-2). METHODS: Clopidogrel was given under two conditions separated by a 14-day washout period: fasted and fed (after a standardized high fat breakfast). Concentrations of clopidogrel in plasma were quantified by a validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) with positive ion electro-spray ionization using multiple reaction monitoring (MRM). Pharmacokinetic parameters such as Cmax, Tmax, AUC0-t, AUC0-inf and t1/2z were estimated using a noncompartmental model. RESULTS: The pharmacokinetic parameters were significantly affected by food intake. Specifically, Cm, and AUC0-inf of clopidogrel increased 6.1-fold and 9.2-fold, respectively, in the fed condition compared to the fasted condition. The t1/2 increased from 2.5 h in the fasted state to 5.0 h in the fed state. The limit of quantification was 5 pg/mL for plasma clopidogrel analysis. CONCLUSION: Food substantially enhanced the bioavailability of clopidogrel in healthy subjects.

Publication Types:
Randomized Controlled Trial

PMID: 17220050 [PubMed - indexed for MEDLINE]


Quantification of trandolapril and its metabolite trandolaprilat in human plasma by liquid chromatography/tandem mass spectrometry using solid-phase extraction.

Nirogi RV, Kandikere VN, Shrivastava W, Mudigonda K.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A sensitive high-performance liquid chromatography/electrospray ionization tandem mass spectrometry (MS/MS) method was developed and validated for the simultaneous quantification of trandolapril and its metabolite trandolaprilat in human plasma using ramipril as an internal standard. Following solid-phase extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase column and analyzed by MS/MS in the multiple reaction monitoring mode using the respective [M-H]- ions, m/z 429/168 for trandolapril, m/z 401/168 for trandolaprilat and m/z 415/166 for the internal standard. The method exhibited a linear dynamic range of 20-10,000 pg/mL for both trandolapril and trandolaprilat in human plasma. The lower limit of quantification was 20 pg/mL for both trandolapril and its metabolite.
Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 2.0 min for each sample made it possible to analyze 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.

PMID: 17117442 [PubMed - indexed for MEDLINE]


A simple and rapid HPLC/UV method for the simultaneous quantification of theophylline and etofylline in human plasma.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Ajjala DR.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive and selective high performance liquid chromatography (HPLC) method with ultraviolet detection (272 nm) was developed and validated for the simultaneous quantification of theophylline and etofylline in human plasma. Following rapid sample preparation, the analytes and internal standard (hydrochlorothiazide) were separated using an isocratic mobile phase on a reverse phase C18 column. The lower limit of quantification was 100 ng/mL for both theophylline and etofylline with a relative standard deviation of less than 6%. A linear dynamic range of 100-10,000 ng/mL for both theophylline and etofylline was established. This HPLC method was validated with between-batch precision of 2.2-6.0 and 1.4-3.7% for theophylline and etofylline, respectively. The between-batch accuracy was 94.3-98.0 and 95.4-98.2%, respectively. Stability of theophylline and etofylline in plasma was excellent, with no evidence of degradation during sample processing (autosampler) and 30 days storage in a freezer. This validated method is simple and rugged enough to be used in pharmacokinetic studies.

PMID: 17110179 [PubMed - indexed for MEDLINE]


Liquid chromatographic-electrospray tandem mass spectrometric method for the quantification of nimodipine in human plasma.

Nirogi RV, Kandikere VN, Maurya S, Mudigonda K, Boosi R.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Banjara Hills, Hyderabad, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive and rapid liquid chromatography/electrospray ionization tandem mass spectrometry (LC-MS/MS) method was developed and validated for the quantification of nimodipine, a calcium channel blocker, in human plasma. Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reverse phase C18 column and analyzed by MS in the multiple reaction monitoring mode using the respective [M + H]+ ions, m/z 419/343 for nimodipine and m/z 409/228 for the IS. The assay exhibited a linear dynamic range of 0.2-50 ng/mL for nimodipine in human plasma. The lower limit of quantification was 200 pg/mL with a relative standard deviation of less than 8%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 3 min for each sample made it possible to analyze more than 250 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.

PMID: 17069421 [PubMed - indexed for MEDLINE]
Simultaneous quantification of fexofenadine and pseudoephedrine in human plasma by liquid chromatography/tandem mass spectrometry with electrospray ionization: method development, validation and application to a clinical study.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S, Komarneni P.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500 034, India. ramakrishna_nirogi@yahoo.co.in

To support the pharmacokinetic and bioavailability study of a once-daily fexofenadine/pseudoephedrine combination, a high-performance liquid chromatography/positive ion electrospray tandem mass spectrometry (HPLC/ESI-MS/MS) method for the simultaneous quantification of fexofenadine and pseudoephedrine was developed and validated with 500 microL human plasma using mosapride as an internal standard (IS). Following solid-phase extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase column and analyzed by MS/MS in the multiple reaction monitoring mode using the respective [M+H]+ ions, m/z 502/466 for fexofenadine, m/z 166/148 for pseudoephedrine and m/z 422/198 for the IS. The method exhibited linear dynamic ranges of 1-500 ng/mL and 2-1000 ng/mL for fexofenadine and pseudoephedrine, respectively, in human plasma. The lower limits of quantification were 1 and 2 ng/mL with a relative standard deviation of less than 10% for fexofenadine and pseudoephedrine, respectively. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. The total chromatographic run time was 2 min and more than 400 human plasma samples could be analyzed in one day by running the system overnight. The method is precise and sensitive enough for its intended purpose. Copyright 2006 John Wiley & Sons, Ltd.

Publication Types:
  Evaluation Studies
  Validation Studies

PMID: 16969767 [PubMed - indexed for MEDLINE]

Quantification of oxcarbazepine and its active metabolite 10-hydroxycarbazepine in human plasma by high-performance liquid chromatography.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Aijala DR.

Biopharmaceutical Research, Suven Life Sciences Ltd., Hyderabad, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive and selective high-performance liquid chromatography (HPLC) method with ultraviolet detection (230 nm) was developed and validated for the quantification of oxcarbazepine (CAS 28721-07-5), a new antiepileptic drug, and its active metabolite 10-hydroxycarbazepine (CAS 29331-92-8) in human plasma. Following solid-phase extraction, the analytes and internal standard (zaleplon, CAS 151319-34-5) were separated using an isocratic mobile phase on a reverse phase C18 column. The lower limit of quantification was 50 ng/mL for oxcarbazepine and 100 ng/mL for 10-hydroxycarbazepine with a relative standard deviation of less than 10%. A linear dynamic range of 50 to 5000 ng/mL for oxcarbazepine and of 100 to 10000 ng/mL for 10-hydroxycarbazepine was established. This HPLC method was validated with between-batch precision of 0.8 to 8.6% and 3.2 to 7.5% for oxcarbazepine and 10-hydroxycarbazepine respectively. The between-batch accuracy was 94.0 to 102.4% and 95.4 to 105.6%, respectively. Stability of oxcarbazepine and 10-hydroxycarbazepine in plasma was excellent, with no
evidence of degradation during sample processing (autosampler) and 30 days storage in a freezer. This validated method is sensitive, simple and repeatable enough to be used in pharmacokinetic studies.

Publication Types:
Clinical Trial

PMID: 16927533 [PubMed - indexed for MEDLINE]


Liquid chromatographic tandem mass spectrometry method for the quantification of miglitol in human plasma.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S, Boosi R, Yerramilli A.

Biopharmaceutical Research, Suven Life Sciences Ltd, Hyderabad, India. ramakrishna_nirogi@yahoo.co.in

A rapid, sensitive and accurate liquid chromatography-tandem mass spectrometry (LC-MS/MS) method was developed and validated for the quantification of miglitol (CAS 72432-03-2), an alpha-glucosidase inhibitor, in human plasma using gabapentin (CAS 60142-96-3) as internal standard (IS). Following protein precipitation, the analytes were separated using an isocratic mobile phase on a reversed phase phenyl column and analyzed by MS in the multiple reaction monitoring mode using the respective [M+H]+ ions, m/z 208/146 for miglitol and m/z 172/154 for the IS. The assay exhibited a linear dynamic range of 100-6000 ng/mL for miglitol in human plasma. The lower limit of quantification was 100 ng/mL with a relative standard deviation of less than 5 %. Acceptable precision and accuracy were obtained for concentrations over the standard curve ranges. The average absolute recoveries of miglitol and the IS from spiked plasma samples were 40.5 +/- 2.7 and 47.1 +/- 2.9 %, respectively. A run time of 2.5 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. The miglitol plasma concentration profile could be obtained for pharmacokinetic study. The observed maximum plasma concentration (Cmax) of miglitol (100 mg oral dose) is 1740 ng/mL, time to observed maximum plasma concentration (tmax) is 3.5 h and elimination half-life (t(1/2)) is 2.5 h.

PMID: 16821643 [PubMed - indexed for MEDLINE]


Quantification of tizanidine in human plasma by liquid chromatography coupled to tandem mass spectrometry.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500 034, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive and rapid high-performance liquid chromatography/positive ion electrospray tandem mass spectrometry (MS/MS) method was developed and validated for the assay of tizanidine in human plasma. Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase column and analyzed by MS/MS in the selected reaction monitoring mode. The assay exhibited a linear dynamic range of 50-5000 pg/mL for tizanidine in human plasma. The lower limit of quantification was 50 pg/mL with a relative standard deviation of less than 13%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 2.5 min for each
Quantification of metaxalone in human plasma by liquid chromatography coupled to tandem mass spectrometry.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Shrivastava W, Datla PV.

Biopharmaceutical Research, Suven Life Sciences, Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A simple, rapid, sensitive, and selective liquid chromatography-tandem mass spectrometry (MS) method was developed and validated for the quantification of metaxalone, a skeletal muscle relaxant, in human plasma using galantamine as internal standard (IS). Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reverse phase C18 column and analyzed by MS in the multiple reaction monitoring mode using the respective \([M+H]^{+}\) ions, \(m/z\) 222/161 for metaxalone and \(m/z\) 288/213 for the IS. The assay exhibited a linear dynamic range of 50-5000 microg/L for metaxalone in human plasma. The lower limit of quantification was 50 microg/L with a relative standard deviation of less than 10%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 2.5 min for each sample made it possible to analyze 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.

Publication Types:
Evaluation Studies

PMID: 16810637 [PubMed - indexed for MEDLINE]


Quantification of cephalosporin antibiotic cefditoren in human plasma by high-performance liquid chromatography.

Nirogi RV, Kandikere VN, Shrivastava W, Mudigonda K.

Biopharmaceutical Research, Suven Life Sciences Ltd., Hyderabad, India. nvsrk@suven.com

A simple, sensitive and selective high-performance liquid chromatography (HPLC) method with ultraviolet detection (305 nm) was developed and validated for quantification of cefditoren (CAS 104145-95-1), a broad-spectrum orally administered cephalosporin in human plasma. Following solid-phase extraction using Waters Oasis SPE cartridges, the analyte and internal standard (hydrochlorothiazide, CAS 58-93-5) were separated using an isocratic mobile phase of 0.03 % trifluoro acetic acid buffer / acetonitrile (81/19, v/v) on reverse phase Waters symmetry C18 column. The lower limit of quantification was 50 ng/mL, with a relative standard deviation of less than 4%. A linear range of 50 to 5000 ng/mL was established. This HPLC method was validated with between-batch and within-batch precision of 0.5 to 3.7 % and 0.5 to 2.5%, respectively. The between-batch and within-batch accuracy was 96.9 to 103.8% and 97.5 to
102.3%, respectively. Stability of cefditoren in plasma was excellent, with no evidence of degradation during sample processing (autosampler) and 30 days storage in a freezer. This validated method is sensitive, simple and repeatable enough to be used in pharmacokinetic studies.

PMID: 16724518 [PubMed - indexed for MEDLINE]


High-throughput quantification of perindopril in human plasma by liquid chromatography/tandem mass spectrometry: application to a bioequivalence study.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S, Komarneni P.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500 034, India.

A simple, sensitive and rapid high-performance liquid chromatography/positive ion electrospray tandem mass spectrometry method was developed and validated for the quantification of perindopril in human plasma. Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase column and analyzed by mass spectrometry in the multiple reaction monitoring mode using the respective [M+H](+) ions, m/z 369/172 for perindopril and m/z 417/234 for the internal standard. The method exhibited a linear dynamic range of 0.1-100 ng/mL for perindopril in human plasma. The lower limit of quantitation was 0.1 ng/mL with a relative standard deviation of less than 6.1%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 2.0 min for each sample made it possible to analyze more than 450 human plasma samples per day. The validated method has been successfully used to analyze human plasma samples for application in pharmacokinetic, bioavailability and bioequivalence studies. Copyright (c) 2006 John Wiley & Sons, Ltd.

Publication Types:
Validation Studies

PMID: 16715478 [PubMed - indexed for MEDLINE]


Quantification of zolpidem in human plasma by high-performance liquid chromatography with fluorescence detection.

Nirogi RV, Kandikere VN, Shrivasthava W, Mudigonda K.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road 7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A simple, reliable HPLC method with fluorescence detection (excitation 320 and emission 388 nm) was developed and validated for quantitation of zolpidem in human plasma. Following a single-step liquid-liquid extraction, the analyte and internal standard (quinine) were separated using an isocratic mobile phase on a reversed-phase C(18) column. The lower limit of quantitation was 1.8 ng/mL, with a relative standard deviation of less than 5%. A linear dynamic range of 1.8-288 ng/mL was established. This HPLC method was validated with between-batch and within-batch precision of 1.7-4.8 and 1.2-2.3%, respectively. The between-batch and within-batch accuracy was 95.3-100.4 and 95.5-102.7%, respectively. Frequently coadministered drugs did not interfere with the described methodology. Stability of zolpidem in plasma was excellent, with no evidence of degradation during sample processing (autosampler) and 30 days storage in a freezer. This validated method is simple and repeatable enough to be used in Pharmacokinetic studies.
Publication Types:
  Research Support, Non-U.S. Gov't

PMID: 16703647 [PubMed - indexed for MEDLINE]


Quantification of clopidogrel in human plasma by sensitive liquid chromatography/tandem mass spectrometry.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S, Boosi R.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500 034, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive and rapid high-performance liquid chromatography/positive electrospray ionization tandem mass spectrometry method was developed and validated for the assay of clopidogrel in human plasma. Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase column and analyzed by mass spectrometry in the multiple reaction monitoring mode using the respective [M+H](+) ions, m/z 322/212 for clopidogrel and m/z 264/154 for the internal standard. The assay exhibited a linear dynamic range of 5-6000 pg/mL for clopidogrel in human plasma. The lower limit of quantification was 5 pg/mL with a relative standard deviation of less than 8%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 2.5 min for each sample made it possible to analyze 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 (c) 2006 John Wiley & Sons, Ltd.

PMID: 16637000 [PubMed - indexed for MEDLINE]


Liquid chromatography/negative ion electrospray tandem mass spectrometry method for the quantification of fluvastatin in human plasma: validation and its application to pharmacokinetic studies.

Nirogi RV, Kandikere VN, Shrivastava W, Mudigonda K, Datla PV.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500 034, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive and rapid high-performance liquid chromatography/negative ion electrospray tandem mass spectrometry method was developed and validated for the assay of fluvastatin in human plasma. Following solid-phase extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase column and analyzed by mass spectrometry in the multiple reaction monitoring mode using the respective [M-H]- ions, m/z 410/348 for fluvastatin and m/z 480/418 for the internal standard. The assay exhibited a linear dynamic range of 2-500 ng/mL for fluvastatin in human plasma. The lower limit of quantification was 2 ng/mL with a relative standard deviation of less than 5%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 1.5 min for each sample made it possible to analyze 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 2006 John Wiley & Sons, Ltd.

PMID: 16541405 [PubMed - indexed for MEDLINE]
Development and validation of a sensitive liquid chromatography/electrospray tandem mass spectrometry assay for the quantification of olanzapine in human plasma.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S, Boosi R, Yerramilli A.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive and rapid liquid chromatography/electrospray ionization tandem mass spectrometry (LC-ESI-MS/MS) method was developed and validated for the quantification of olanzapine, atypical antipsychotic drug, in human plasma using loratadine as internal standard (IS). Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reverse phase C18 column and analyzed by MS in the multiple reaction monitoring mode using the respective \([M+H]^+\) ions, m/z 313/256 for olanzapine and m/z 363/337 for the IS. The assay exhibited a linear dynamic range of 0.1-30 ng/mL for olanzapine in human plasma. The lower limit of quantification was 100 pg/mL with a relative standard deviation of less than 10%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. The average absolute recovery of olanzapine from spiked plasma samples was 85.5+-1.9%. A run time of 2.0 min for each sample made it possible to analyze 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.

Publication Types:
  Validation Studies

PMID: 16504450 [PubMed - indexed for MEDLINE]

Simultaneous quantification of atorvastatin and active metabolites in human plasma by liquid chromatography-tandem mass spectrometry using rosuvastatin as internal standard.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Maurya S, Boosi R, Anjaneyulu Y.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road 7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A simple, sensitive, selective and rapid liquid chromatography-tandem mass spectrometry (LC-MS/MS) method was developed and validated for the quantification of atorvastatin and its active metabolites ortho-hydroxyatorvastatin and para-hydroxyatorvastatin in human plasma using rosuvastatin as internal standard (IS). Following simple liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase C18 column and analyzed by MS in the multiple reaction monitoring mode using the respective \([M+H]^+\) ions, m/z 559/440 for atorvastatin, m/z 575/466 for ortho-hydroxyatorvastatin, m/z 575/440 for para-hydroxyatorvastatin and m/z 482/258 for the IS. The assay exhibited a linear dynamic range of 0.1-20 ng/mL for atorvastatin and its two metabolites in human plasma. The lower limit of quantification was 100 pg/mL with a relative standard deviation of less than 8%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. The average absolute recoveries of atorvastatin, ortho-hydroxyatorvastatin, para-hydroxyatorvastatin and the IS from spiked plasma samples were 54.2 +/- 3.2, 50.1 +/- 3.8, 65.2 +/- 3.6 and 71.7 +/- 2.7%, respectively. A run time of 2.5 min for each sample made it possible to analyze more than 300 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 2006 John Wiley & Sons, Ltd.
Simultaneous quantification of cilostazol and its primary metabolite 3,4-dehydrocilostazol in human plasma by rapid liquid chromatography/tandem mass spectrometry.

Nirogi RV, Kandikere VN, Shukla M, Mudigonda K, Shrivasthava W, Datla PV, Yerramilli A.

A simple, rapid, sensitive and selective liquid chromatography/electrospray tandem mass spectrometry method was developed and validated for the simultaneous quantification of cilostazol and its primary metabolite 3,4-dehydrocilostazol in human plasma using mosapride as an internal standard. The method involves a simple one-step liquid-liquid extraction with a diethyl ether and dichloromethane mixture (7:3). The analytes were chromatographed using an isocratic mobile phase on a reversed-phase C18 column and analyzed by mass spectrometry in the multiple reaction monitoring mode using the respective [M+H]+ ions, m/z 370/288 for cilostazol, m/z 368/286 for 3,4-dehydrocilostazol and m/z 422/198 for the internal standard. The assay exhibited a linear dynamic range of 5-2,000 ng/mL for cilostazol and 5-400 ng/mL for 3,4-dehydrocilostazol in human plasma. The lower limit of quantitation was 5 ng/mL for both cilostazol and its metabolite. Acceptable precision and accuracy were obtained for concentrations over the standard curve ranges. A run time of 2.5 min for each sample made it possible to analyze more than 400 human plasma samples per day. The validated method has been successfully used to analyze human plasma samples for application in pharmacokinetics, bioavailability or bioequivalence studies.

Quantification of faropenem in human plasma by high-performance liquid chromatography.

Nirogi RV, Kandikere VN, Shrivastava W, Mudigonda K.

A simple, sensitive and specific high-performance liquid chromatography (HPLC) method with ultraviolet detection (315 nm) was developed and validated for quantitation of faropenem (CAS 106560-14-9), the newest addition to the group of beta-lactam antimicrobials, in human plasma. Following solid-phase extraction using Waters Oasis SPE cartridges, the analyte and internal standard (hydrochlorothiazide, CAS 58-93-5) were separated using an isocratic mobile phase of 10 mmol/L acetate buffer (pH adjusted to 7.0 with dilute acetic acid) /methanol / triethyl amine (70/30/0.03, v/v/v) on reverse phase Waters symmetry C18 column. The lower limit of quantitation was 200 ng/mL, with a relative standard deviation of less than 2 %. A linear range of 200 to 25000 ng/mL was established. This HPLC method was validated with between-batch and within-batch precision of 1.6 to 2.3 % and 0.4 to 1.6 %, respectively. The between-batch and within-batch bias was -3.1 to 5.3 % and -6.0 to 1.5 %, respectively. Frequently coadministered drugs did not interfere with the described methodology. The stability of faropenem in plasma was excellent, with no evidence of degradation during sample processing (autosampler) and 30 days storage in a freezer. This validated method is sensitive, simple and repeatable enough to be used in pharmacokinetic studies.
A simple, sensitive and rapid high-performance liquid chromatography/electrospray ionization tandem mass spectrometry method was developed and validated for the assay of amlodipine in human plasma. Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reverse-phase C18 column and analyzed by MS in the multiple reaction monitoring mode using the respective [M+H]+ ions, m/z 409/238 for amlodipine and m/z 409/228 for the IS. The assay exhibited a linear dynamic range of 50-10,000 pg/mL for amlodipine in human plasma. The lower limit of quantification was 50 pg/mL with a relative standard deviation of less than 8%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 1.5 min for each sample made it possible to analyze 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. The observed maximum plasma concentration (Cmax) of amlodipine (2.5 mg oral dose) was 1425 pg/mL, time to observed maximum plasma concentration (Tmax) was 8.1 h and elimination half-life (T(1/2)) was 50.1 h. Copyright 2006 John Wiley & Sons, Ltd.

A simple, sensitive and rapid high-performance liquid chromatography/electrospray ionization tandem mass spectrometry method was developed and validated for the assay of granisetron in human plasma. Following liquid-liquid extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase C18 column and analyzed by MS in the multiple reaction monitoring mode using the respective [M+H]+ ions, m/z 313/138 for granisetron and m/z 409/228 for the IS. The assay exhibited a linear dynamic range of 0.1-20 ng/mL for granisetron in human plasma. The lower limit of quantification was 100 pg/mL with a relative standard deviation of less than 5%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. A run time of 2.0 min for each sample
made it possible to analyze 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 2006 John Wiley & Sons, Ltd.

Publication Types:
  Validation Studies

PMID: 16389637 [PubMed - indexed for MEDLINE]


Quantitation of zopiclone and desmethylzopiclone in human plasma by high-performance liquid chromatography using fluorescence detection.

Nirogi RV, Kandikere VN, Mudigonda K.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road 7, Banjara Hills, Hyderabad 500034, India. ramakrishna_nirogi@yahoo.co.in

A simple, reliable HPLC method using fluorescence detection (excitation 307 and emission 483 nm) was developed and validated for simultaneous quantitation of zopiclone and its metabolite desmethylzopiclone in human plasma. Following a single-step liquid-liquid extraction, the analytes and internal standard (zaleplon) were separated using an isocratic mobile phase on a reversed-phase C18 column. The lower limit of quantitation was 3 ng/mL for zopiclone and 6 ng/mL for desmethylzopiclone with a relative standard deviation of less than 5%. A linear dynamic range of 3-300 ng/mL for zopiclone and of 6-500 ng/mL for desmethylzopiclone was established. This HPLC method was validated with between-batch precision of 1.7-4.2% and 3.2-7.5% for zopiclone and desmethylzopiclone respectively. The between-batch accuracy was 99.4-111.5% and 101.6-104.8% for zopiclone and desmethylzopiclone, respectively. Frequently coadministered drugs did not interfere with the described methodology. Stability of zopiclone and desmethylzopiclone in plasma was excellent, with no evidence of degradation during sample processing (autosampler) and 30 days' storage in a freezer. This validated method is simple and repeatable enough to be used in pharmacokinetic studies. Copyright 2005 John Wiley & Sons, Ltd.

Publication Types:
  Validation Studies

PMID: 16292747 [PubMed - indexed for MEDLINE]


Rapid quantification of gabapentin in human plasma by liquid chromatography/tandem mass spectrometry.

Ramakrishna NV, Vishwottam KN, Koteswara M, Manoj S, Santosh M, Chidambara J, Sumatha B, Varma DP.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A simple, sensitive and rapid liquid chromatography/tandem mass spectrometry (LC-MS/MS) method was developed and validated for the quantification of gabapentin, a new antiepileptic drug, in human plasma using its structural analogue, 1,1-cyclohexane diacetic acid monoamide (CAM) as internal standard. The method involved a simple protein precipitation by means of acetonitrile followed by a rapid isocratic elution with 10mM ammonium formate buffer/acetonitrile (20/80, v/v, pH 3.0) on Waters Symmetry C(18 reversed phase chromatographic column and analyzed by mass spectrometry in the multiple reaction
monitoring mode. The precursor to product ion transitions of m/z 172→154 and m/z 200→182 were used to measure the analyte and the IS, respectively. The assay exhibited a linear dynamic range of 40-10000 ng/mL for gabapentin in human plasma. The limit of detection and lower limit of quantification in human plasma were 10 and 40 ng/mL, respectively. Acceptable precision and accuracy were obtained for concentrations over the standard curve ranges. A run time of 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.

PMID: 16112830 [PubMed - indexed for MEDLINE]


High-performance liquid chromatography method for the quantification of entacapone in human plasma.

Ramakrishna NV, Vishwottam KN, Wishu S, Koteshwara M, Chidambara J.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A simple, sensitive and selective HPLC method with UV detection (315 nm) was developed and validated for quantitation of entacapone in human plasma, the newest addition to the group of antiparkinsonian agents. Following a single-step liquid-liquid extraction (LLE) with ethyl acetate/n-hexane (30/70, v/v), the analyte and internal standard (rofecoxib) were separated using an isocratic mobile phase of 30 mM phosphate buffer (pH 2.75)/acetonitrile (62/38, v/v) on a reverse phase C18 column. The lower limit of quantitation was 25 ng/mL, with a relative standard deviation of less than 8%. A linear range of 25-2500 ng/mL was established. This HPLC method was validated with between-batch and within-batch precision of 2.2-4.2% and 1.7-7.8%, respectively. The between-batch and within-batch accuracy was 98.7-107.5% and 97.5-106.0%, respectively. Frequently coadministered drugs did not interfere with the described methodology. Stability of entacapone in plasma was excellent, with no evidence of degradation during sample processing (autosampler) and 30 days storage in a freezer. This validated method is sensitive, simple and repeatable enough to be used in Pharmacokinetic studies.

Publication Types:
Clinical Trial
Research Support, Non-U.S. Gov't

PMID: 16009606 [PubMed - indexed for MEDLINE]


Rapid quantification of nebivolol in human plasma by liquid chromatography coupled with electrospray ionization tandem mass spectrometry.

Ramakrishna NV, Vishwottam KN, Koteshwara M, Manoj S, Santosh M, Varma DP.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A simple, sensitive and rapid liquid chromatographic/electrospray ionization tandem mass spectrometric method was developed and validated for the quantitation of nebivolol in human plasma. The method involved a simple single-step liquid-liquid extraction with diethyl ether/dichloromethane (70/30). The analyte was chromatographed on Waters symmetry C18 reversed-phase chromatographic column by isocratic elution with water:acetonitrile:formic acid (30:70:0.03, v/v) and analyzed by mass spectrometry in
the multiple reaction monitoring mode. The precursor to product ion transitions of m/z 406.4-151.5 and m/z 409.1-228.1 were used to measure the analyte and the internal standard (I.S.), respectively. The chromatographic runtime was 2 min and the weighted (1/x2) calibration curves were linear over the range 50-10,000 pg/mL. 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 10 and 50 pg/mL, respectively. The within- and between-batch accuracy and precision were found to be well within acceptable limits (<10%). The analyte was stable after three freeze-thaw cycles (deviation <10%). The average absolute recoveries of nebivolol and tamsulosin, used as an internal standard, from spiked plasma samples were 73.4+/-3.7 and 72.1+/-2.0%, respectively. The assay method described here was applied to study the pharmacokinetics of nebivolol.

PMID: 16006083 [PubMed - indexed for MEDLINE]


High-performance liquid chromatography method for the quantification of pantoprazole in human plasma.

Ramakrishna NV, Vishwottam KN, Wishu S, Koteshwara M.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A sensitive and selective HPLC method with UV detection (290 nm) was developed and validated for quantitation of pantoprazole, proton-pump inhibitor, in human plasma. Following a single-step liquid-liquid extraction with methyl tert-butyl ether/diethyl ether (70/30, v/v), the analyte and internal standard (zonisamide) were separated using an isocratic mobile phase of 10mM phosphate buffer (pH 6.0)/acetonitrile (61/39, v/v) on reverse phase Waters symmetry C18 column. The lower limit of quantitation was 20 ng/mL, with a relative standard deviation of less than 4%. A linear range of 20-5000 ng/mL was established. This HPLC method was validated with between-batch and within-batch precision of 1.3-3.2% and 0.7-3.3%, respectively. The between-batch and within-batch bias was -0.5 to 8.2 % and -2.5 to 12.1%, respectively. This validated method is sensitive and repeatable enough to be used in pharmacokinetic studies.

Publication Types:
Validation Studies

PMID: 16005696 [PubMed - indexed for MEDLINE]


Liquid chromatography/electrospray ionization mass spectrometry method for the quantification of valproic acid in human plasma.

Ramakrishna NV, Vishwottam KN, Manoj S, Koteshwara M, Santosh M, Chidambara J, Kumar BR.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A simple, sensitive and rapid liquid chromatography/electrospray ionization mass spectrometry (LC/ESI-MS) method was developed and validated for the quantification of valproic acid, an antiepileptic drug, in human plasma using benzoic acid as internal standard (IS). Following solid-phase extraction, the analytes were separated using an isocratic mobile phase on a reversed-phase C18 column and analyzed by MS in the single ion monitoring mode using the respective [M-H]- ions, m/z 143 for valproic acid and m/z 121 for the IS. The assay exhibited a linear dynamic range of 0.5-60 microg/mL for valproic acid in human
plasma. The lower limit of quantification was 500 ng/mL with a relative standard deviation of less than 10%. Acceptable precision and accuracy were obtained for concentrations over the standard curve range. The average absolute recoveries of valproic acid and the IS from spiked plasma samples were 96.1 +/- 4.2 and 95.6 +/- 2.7%, respectively. A run time of 4.5 min for each sample made it possible to analyze more than 250 human plasma samples per day. The validated method has been successfully used to analyze human plasma samples for application in pharmacokinetic, bioavailability and bioequivalence studies. Copyright (c) 2005 John Wiley & Sons, Ltd.

PMID: 15954179 [PubMed - indexed for MEDLINE]


Sensitive liquid chromatography-tandem mass spectrometry method for quantification of hydrochlorothiazide in human plasma.

Ramakrishna NV, Vishwottam KN, Manoj S, Koteshwara M, Wishu S, Varma DP.
Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A simple, rapid, sensitive and specific liquid chromatography-tandem mass spectrometry method was developed and validated for quantification of hydrochlorothiazide (I), a common diuretic and anti-hypertensive agent. The analyte and internal standard, tamsulosin (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 reversed-phase column (Waters symmetry C18) with a mobile phase of 10 mm ammonium acetate-methanol (15:85, v/v) using a Glas-Col Multi-Pulse Vortexer. The mass transitions m/z 296.1 solidus in circle 205.0 and m/z 407.2 solidus in circle 184.9 were used to measure I and II, respectively. The assay exhibited a linear dynamic range of 0.5-200 ng/mL for hydrochlorothiazide in human plasma. The lower limit of quantitation was 500 pg/mL, with a relative standard deviation of less than 9%. Acceptable precision and accuracy were obtained for concentrations over the standard curve ranges. A run time of 2.5 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. (c) 2005 John Wiley & Sons, Ltd.

Publication Types:
Validation Studies

PMID: 15856489 [PubMed - indexed for MEDLINE]


Rapid, simple and highly sensitive LC-ESI-MS/MS method for the quantification of tamsulosin in human plasma.

Ramakrishna NV, Vishwottam KN, Manoj S, Koteshwara M, Wishu S, Varma DP.
Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A simple, rapid, sensitive and specific liquid chromatography-tandem mass spectrometry method was developed and validated for quantification of tamsulosin (I), a highly selective alpha1-adrenoceptor antagonist used for the treatment of patients with symptomatic benign prostatic hyperplasia. The analyte
and internal standard, mosapride (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 Waters symmetry C18 column with a mobile phase of 0.03% formic acid-acetonitrile (30:70, v/v). The protonated analyte was quantitated in positive ionization by multiple reaction monitoring with a mass spectrometer. The mass transitions m/z 409.1 solidus in circle 228.1 and m/z 422.3 solidus in circle 198.3 were used to measure I and II, respectively. The assay exhibited a linear dynamic range of 0.1-50.0 ng/mL for tamsulosin in human plasma. The lower limit of quantitation was 100 pg/mL with a relative standard deviation of less than 10%. Acceptable precision and accuracy were obtained for concentrations over the standard curve ranges. A run time of 2.0 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. (c) 2005 John Wiley & Sons, Ltd.

PMID: 15828055 [PubMed - indexed for MEDLINE]


Validated liquid chromatographic ultraviolet method for the quantitation of Etoricoxib in human plasma using liquid-liquid extraction.

Ramakrishna NV, Vishwottam KN, Wishu S, Koteshwara M.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A simple, sensitive and specific HPLC method with UV detection (284 nm) was developed and validated for quantitation of Etoricoxib in human plasma, the newest addition to the group of nonsteroidal anti-inflammatory drugs-a highly selective cyclooxygenase-2 inhibitor. Following a single-step liquid-liquid extraction with diethyl ether/dichloromethane (70/30, v/v), the analyte and internal standard (Zaleplon) were separated using an isocratic mobile phase of water/acetonitrile (58/42, v/v) on reverse phase Waters symmetry C(18) column. The lower limit of quantitation was 5 ng/mL, with a relative standard deviation of less than 20%. A linear range of 5-2500 ng/mL was established. This HPLC method was validated with between- and within-batch precision of 4.1-5.1% and 1.1-2.4%, respectively. The between- and within-batch bias was -3.8-4.7% and -0.6-9.4%, respectively. Frequently coadministered drugs did not interfere with the described methodology. Stability of Etoricoxib in plasma was >90%, with no evidence of degradation during sample processing (autosampler) and 30 days storage in a freezer. This validated method is sensitive and simple with between-batch precision of <6% and was used in pharmacokinetic studies.

Publication Types:
Validation Studies

PMID: 15664353 [PubMed - indexed for MEDLINE]


High-performance liquid chromatography method for the quantification of rabeprazole in human plasma using solid-phase extraction.

Ramakrishna NV, Vishwottam KN, Wishu S, Koteshwara M, Kumar SS.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com
A simple, sensitive and selective HPLC method with UV detection (284 nm) was developed and validated for quantitation of rabeprazole in human plasma, the newest addition to the group of proton-pump inhibitors. Following solid-phase extraction using Waters Oasis trade mark SPE cartridges, the analyte and internal standard (Pantoprazole) were separated using an isocratic mobile phase of 5 mM ammonium acetate buffer (pH adjusted to 7.4 with sodium hydroxide solution)/acetonitrile/methanol (45/20/35, v/v) on reverse phase Waters symmetry C(18) column. The lower limit of quantitation was 20 ng/mL, with a relative standard deviation of less than 8%. A linear range of 20-1000 ng/mL was established. This HPLC method was validated with between- and within-batch precision of 2.4-7.2% and 2.2-7.3%, respectively. The between- and within-batch bias was -1.7 to 2.6% and -2.6 to 2.1%, respectively. Frequently coadministered drugs did not interfere with the described methodology. Stability of rabeprazole in plasma was excellent, with no evidence of degradation during sample processing (autosampler) and 3 months storage in a freezer. This validated method is sensitive, simple and repeatable enough to be used in pharmacokinetic studies.

Publication Types:
Research Support, Non-U.S. Gov't
Validation Studies

PMID: 15664352 [PubMed - indexed for MEDLINE]


Validation and application of a high-performance liquid chromatography—tandem mass spectrometry assay for mosapride in human plasma.

Ramakrishna NV, Vishwottam KN, Manoj S, Koteshwara M, Chidambara J, Varma DP.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

A simple, rapid, sensitive and specific liquid chromatography-tandem mass spectrometry method was developed and validated for quantification of mosapride (I), a novel and potent gastroprokinetic agent that enhances the upper gastrointestinal motility by stimulating 5-HT(4) receptor. The analyte and internal standard, tamsulosin (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 reversed-phase Waters symmetry C(18) column with a mobile phase of 0.03% formic acid-acetonitrile (10:90, v/v). The protonated analyte was quantitated in positive ionization by multiple reaction monitoring with a mass spectrometer. The mass transitions m/z 422.3 →198.3 and m/z 409.1 →228.1 were used to measure I and II, respectively. The assay exhibited a linear dynamic range of 0.5-100.0 ng/mL for mosapride in human plasma. The lower limit of quantitation was 500 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 2.0 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 (c) 2005 John Wiley & Sons, Ltd.

Publication Types:
Validation Studies

PMID: 15654725 [PubMed - indexed for MEDLINE]


Simple, sensitive and rapid LC-MS/MS method for the quantitation of cerivastatin in human plasma—application to pharmacokinetic studies.
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 10 pg/mL with a relative standard deviation of less than 15%. Acceptable precision and accuracy were obtained for concentrations over the calibration curve ranges (0.01-10 ng/mL). Sample analysis time of 2 min 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]


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


Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road #7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

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

Ramakrishna NV, Vishwottam KN, Puran S, Manoj S, Santosh M, Koteshwara M.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

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 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 assay method described here could be applied to study the pharmacokinetics of lacidipine.

PMID: 15282762 [PubMed - indexed for MEDLINE]

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

Ramakrishna NV, Vishwottam KN, Puran S, Koteshwara M, Manoj S, Santosh M.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

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 proton 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.

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

Ramakrishna NV, Vishwottam KN, Puran S, Manoj S, Santosh M, Wishu S, Koteshwara M, Chidambara J, Gopinadh B, Sumatha B.

Biopharmaceutical Research, Suven Life Sciences Ltd., Serene Chambers, Hyderabad 500 034, India. nvsrk@suven.com

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.

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

Ramakrishna NV, Vishwottam KN, Wishu S, Koteshwara M.

Biopharmaceutical Research, Suven Life Sciences Ltd, Serene Chambers, Road # 7, Banjara Hills, Hyderabad 500034, India. nvsrk@suven.com

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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