Suven Research Publications in 2010

1. Biomed Chromatogr. 2010 Nov;24(11):1159-67.

Liquid chromatography tandem mass spectrometry method for the quantification of sarpogrelate, a selective 5-HT(2A) receptor antagonist, in plasma: application to a pre-clinical pharmacokinetic study.

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Abstract

A simple LC-MS/MS method was developed and validated for the estimation of sarpogrelate in 50□µL of rat plasma. The analyte and internal standard (IS) were extracted from rat plasma by acetonitrile precipitation and they were separated on a reversed-phase C8 column with gradient program. The MS acquisition was performed with multiple reaction monitoring mode using m/z 430.2 to m/z 135.0 for analyte and m/z 448.2 to m/z 285.3 for IS. The calibration curves were linear over the range of 1-1000□ng/mL with the correlation coefficient greater than 0.999. With dilution integrity up to 20-fold, the upper limit of quantification was extendable up to 15,000□ng/mL. The method was successfully applied to the analysis of rat plasma samples after single dose oral administration of sarpogrelate at 5□mg/kg to rats for the determination of its pharmacokinetics. Following oral administration the maximum mean concentration in plasma (C(max), 11514□ng/mL) was achieved at 0.25□h (T(max)) and the area under curve (AUC0-24) was 11051 ± 3315□ng□h/mL. The half-life ($t_{1/2}$) and clearance (Cl) were 2.9 ± 1.1 □h and 490 ± 171□mL/h/kg, respectively. We believe that development of a method in rodent plasma would facilitate the ease of adaptability of sarpogrelate in human plasma.

PMID: 20954206 [PubMed - indexed for MEDLINE]

2. Bioorg Med Chem Lett. 2010 Aug 1;20(15):4440-3. Epub 2010 Jun 12.

Synthesis and pharmacological evaluation of aryl aminosulfonamide derivatives as potent 5-HT(6) receptor antagonists.

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Abstract

A series of novel aryl aminosulfonamides was designed and synthesized as 5-HT(6) receptor ligands. Many compounds screened in a functional reporter gene based assay displayed potent antagonistic activity with Kb values in the range of 0.02-10nM. The lead compound 11m exemplified in this series showed good ADME surrogate properties, acceptable pharmacokinetic profile and is active in animal models of cognition like novel object recognition test and Morris water maze. The compound was selected for detailed profiling.

PMID: 20594839 [PubMed - indexed for MEDLINE]

3. J Chromatogr Sci. 2010 Feb;48(2):100-3.

High-performance liquid chromatographic method for the separation of enantiomeric gatifloxacin.

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Abstract

A high-performance liquid chromatographic method has been developed in normal-phase conditions for the separation of enantiomeric gatifloxacin, (+/-) 1-cyclopropyl-6-fluoro-8-methoxy-7-(3-methylpiperazin-1-yl)-4-oxo-quinoline-3-carboxylic acid, an antibiotic in bulk drug. The method involved the use of an amylose-based Chiralpak AD-H (150 mm x 4.6 mm, 5 microm) column using a mobile phase system containing n-hexane-ethanol-diethylamine (85:15:0.1% v/v). The conditions affording the best resolution were found by selection and variation of the mobile-phase compositions and the differences in separation capability of the method is noted. Relative standard deviation of retention times and peak areas were better than 0.2% and 0.4%, respectively, for precision. Gatifloxacin sample solution and mobile phase are found to be stable for at least 48 h.

PMID: 20109285 [PubMed - indexed for MEDLINE]

4. Biomed Chromatogr. 2010 Jan;24(1):39-48.

Quantification of acetylcholine, an essential neurotransmitter, in brain microdialysis samples by liquid chromatography mass spectrometry.

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Abstract

Chemical neurotransmission has been the subject of intensive investigations in recent years. Acetylcholine is an essential neurotransmitter in the central nervous system as it has an effect on alertness, memory and learning. Enzymatic hydrolysis of acetylcholine in the synaptic cleft is fast and quickly metabolizes to choline and acetate by acetylcholinesterase. Hence the concentration in the extracellular fluid of the brain is low (0.1-6 nm). Techniques such as microdialysis are routinely employed to measure acetylcholine levels in living brain systems and the microdialysis sample volumes are usually less than 50 microL. In order to develop medicine for the diseases associated with cognitive dysfunction like mild cognitive impairment, Alzheimer's disease, schizophrenia and Parkinson's disease, or to study the mechanism of the illness, it is important to measure the concentration of acetylcholine in the extracellular fluid of the brain. Recently considerable attention has been focused on the development of chromatographic-mass spectrometric techniques to provide more sensitive and accurate quantification of acetylcholine collected from in-vivo brain microdialysis experiments. This review will provide a brief overview of acetylcholine biosynthesis, microdialysis technique and liquid chromatography mass spectrometry, which is being used to quantitate extracellular levels of acetylcholine

PMID: 19877295 [PubMed - indexed for MEDLINE]

5. **African Journal of Basic & Applied Sciences 2 (5-6): 128-134, 2010**

Safety Evaluation of Sibutramine in Wistar Rats

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Abstract: Sibutramine is a novel anti-obesity drug, acts pharmacologically as both serotonin and nor-adrenalin reuptake inhibitor. Inhibitory effect of sibutramine on body weight and food intake was studied extensively and however, very sparse information available on toxicity concerns. Therefore the present study was designed to assess the toxicological properties of sibutramine. Male and female wistar rats were divided into groups of five rats each for main study and three rats each for toxicokinetic study and were gavaged with 0, 10, 30 and 100 mg/kg/day sibutramine for 7 days. During and at the end of the treatment period various toxicological parameters were studied. Toxicokinetic was performed on day 1 and 7. Significant reduction in body weight was observed in male and female Wistar rats at 30 and 100 mg/kg/day. Food intake was significantly decreased in both sexes at first 3 days in all dose levels and only in high dose at day 5. Reduction in reticulocytes count was observed in all treated rats and serum cholesterol was also decreased at 100 mg/kg/day sibutramine. Decreased peritoneal fat mass, small size spleen and thymus were observed on gross pathological examination during terminal sacrifice. No major treatment related histopathological changes were observed up to the high dose. In conclusion that there was no adverse effect of sibutramine up to 30 mg/kg/day in Wistar rats.