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Exploring the compartmental pharmacokinetics and bio-distribution of donepezil hydrochloride

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Donepezil hydrochloride is a potent, acetylcholinesterase inhibitor used for the treatment of Alzheimer's disease. The objective of this study was to explore the compartmental pharmacokinetics and tissue distribution studies of donepezil after intravenous administration in Wistar rats. A simple HPLC-PDA assay method was developed and validated for rapid determination of Donepezil hydrochloride, a potent acetylcholinesterase inhibitor in rat plasma and tissues. Solid-phase extraction method has been optimized using Loratadine as an internal standard (IS). Chromatographic separation was detected on Waters Nova-Pak C18 column (3.9×150 mm, 5 µm) using isocratic mobile phase of acetonitrile and ammonium formate (pH 6.4; 0.01M, 62:38 v/v) at flow rate of 1 ml/min. All validation parameters were performed as per the guidelines of bioanalytical method validation. Weighted linear regression analysis was also performed on the calibration data. The method was successfully applied for exploring the compartmental pharmacokinetics and tissue distribution studies of Donepezil after intravenous bolus administration at dose of 5 mg/kg in Wistar rat. Experimental plasma concentration-versus-time profiles were fitted to compartmental pharmacokinetic models. One, two and three-compartment models were tested to characterize the pharmacokinetic parameters and statistically model was validated. Tissue distribution studies were also performed to assess the bio-distribution studies. These parameters were analyzed for statistical significance by unpaired Student's t-test. All validation parameter results were within the acceptable range described in guidelines. The method showed linearity in the concentration range of 50-5000 ng/mL with LOD of 20 ng/mL and LLOQ of 50 ng/ml. The mean absolute recoveries were found to be 79.86±1.55% for Donepezil. Three-compartmental micro model was fitted to the plasma concentration-versus-time profiles and it was statistically validated by Akaike information criterion (AIC), Schwarz Bayesian criteria (SBC) and regression coefficient. Tissue distribution results showed that Donepezil was well distributed in highly perfused tissues.

Biography

Sunil Kumar Dubey has been working in the area of clinical pharmacology, pharmacokinetics of racemic drugs (especially focused on CNS drug candidates) and also on designing nanocarriers like polymeric nanoparticles, micelles and polymersomes, etc. for effective drug delivery. He also has expertise in the field pharmacokinetic and pharmacodynamic parameters modeling and simulation. He has been working in the thrust areas of CNS. His commitment to work and capability to successfully completing independent projects is reflected from his projects taken and international peer-reviewed publications.

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