

TITLE

Quantitation of donepezil and its active metabolite 6-O-desmethyl donepezil in human plasma by a selective and sensitive liquid chromatography-tandem mass spectrometric method

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A sensitive and selective LC-MS/MS assay for the simultaneous determination of donepezil (D) and its pharmacologically active metabolite, 6-O-desmethyl donepezil (ODD) in human plasma is developed using galantamine as internal standard (IS). The analytes and IS were extracted from 500 μ L aliquots of human plasma via solid phase extraction on Waters Oasis HLB cartridges. Chromatographic separation was achieved in a run time of 6.0 min on a Waters Novapak C18 (150 mm x 3.9 mm, 4 μ m) column under isocratic conditions. Detection of analytes and IS was done by tandem mass spectrometry, operating in positive ion and multiple reaction monitoring (MRM) acquisition mode. The protonated precursor to product ion transitions monitored for D, ODD and IS were at m/z 380.1 \rightarrow 91.2, 366.3 \rightarrow 91.3 and 288.2 \rightarrow 213.2 respectively. The method was fully validated for its selectivity, interference check, sensitivity, linearity, precision and accuracy, recovery, matrix effect, ion suppression/enhancement, cross specificity, stability and dilution integrity. A linear dynamic range of 0.10-50.0 ng mL⁻¹ for D and 0.02-10.0 ng mL⁻¹ for ODD was evaluated with mean correlation coefficient (r) of 0.9975 and 0.9985 respectively. The intra-batch and inter-batch precision (%CV) across five validation runs (LLOQ, LQC, MQC, HQC and ULOQ) was less than 7.5 % for both the analytes. The method was successfully applied to a bioequivalence study of 10 mg donepezil tablet formulation in 24 healthy Indian male subjects under fasting condition.

Biography

Dr. Bhavin kumar patel has completed his PhD at the age of 31 from School of science, Gujarat University, is currently working as a Senior Research Scientist-I (project manager) in BA Research India Ltd. Authored Eight Scientific Papers in Reputed International Journals along with Mr. Naveen Sharma, Dr. (Mrs.) Mallika Sanyal and Dr. Pranav S. Shrivastav.