Determination of Atorvastatin and Its Metabolites from Human Plasma by High Performance Liquid Chromatography-Mass Spectrometry

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Atorvastatin is being used for the treatment of lipoprotein metabolism disorders such as high serum cholesterol. Atorvastatin is administered in its active acid form and gives very low plasma concentrations (ng/ml levels). Liver metabolism produces two active hydroxy metabolites, 2-OH-Atorvastatin and 4-OH-Atorvastatin.

A simple and sensitive high performance liquid chromatographic method with MS detection (HPLC-MS) for the determination of atorvastatin and its metabolites from plasma was developed and validated. Liquid-liquid extraction was used for extracting atorvastatin and its metabolites from plasma. Ethylacetate was used as extraction solvent. The chromatographic separation of atorvastatin, metabolites and Rosuvastatine (IS) was carried out using reverse phase Zorbax Eclipse XDB-C8 column (150x4.6 mm, 5μm) with mobile phase of Acetonitrile:Acetic acid (%1) 60/40 (v/v). The flow rate of mobile phase was 0.3 ml/min, injection volume was 10 μl. The mass spectrometric parameters were optimized to obtain maximum sensitivity at unit resolution. Atmospheric pressure ionization-electrospray mode(API-ES) was used at positive ionization. Data was collected by monitoring Selected Ion Mode (SIM). The ions used to quantify were selected as m/z 559.20 for atorvastatin, m/z 575.10 for hydroxymetabolites and m/z 482.10 for IS. The calibration curve was linear within the concentration range 1-50 ng/ml. The limit of quantification was 1 ng/ml with good accuracy and precision. The stability was assessed under a variety of conditions and found that appropriate for the quantification. The method developed can be used for bioequivalence and pharmacokinetic studies.

References