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High-Performance Liquid Chromatography Method Appropriate for the Determination of Mycophenolic Acid in Renal Transplantation

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Abstract

Background: Mycophenolate mofetil and mycophenolate sodium, both produgs of the active metabolite mycophenolic acid, are immunosuppressive agents used in transplantation for the prevention of acute rejection. The inter-patient variability in mycophenolic acid exposure is wide compared with the therapeutic window. Therapeutic drug monitoring for mycophenolic acid levels in renal transplantation has been suggested to optimize outcomes by reducing rejection or drug related toxicities.

Aim: The aim of this study is to validate a simple, rapid and sensitive high-performance liquid chromatography method combined with protein precipitation for the determination of the concentration of mycophenolic acid in human plasma.

Method: HPLC analysis was carried out using the chromatographic system Agilent Technologies 1200 DAD. Precipitation of plasma proteins was performed by the addition of acetonitrile. Samples were injected manually and the compounds were separated on a Lichrosphere select B C18 analytical column (particle size 5μm). The mobile phase consisted of 5:55 (v/v) acetonitrile-buffer phosphate adjusted at pH 2.5, flow rate was 1.0mL/min and column temperature was kept at 30°C. Detection was performed at 215nm. Naproxen was used as

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internal standard. Inter-day and intra-day precision and accuracy were evaluated from the analysis of control samples (low QC of 1 μg/ml, medium QC of 5 μg/ml and high QC of 10 μg/ml) measured on five different days. The precision and accuracy of this HPLC assay were estimated.

Results: The proposed method showed appropriate linearity for mycophenolic acid (MPA) with correlation coefficient greater than ($r2 > 0.999$). The precision and accuracy of intra-day and inter-day of this HPLC assay is suitable for routine therapeutic drug monitoring applications. The Limit of Detection (LOD) and Limit of Quantification (LOQ) were found to be respectively 0.1 μg/ml and 0.4 μg/ml.

Conclusion: This HPLC-UV method for the determination of MPA concentration in human plasma is simple and suitable to be used for therapeutic monitoring. The method was intended to be applied in the analysis of human plasma from renal transplanted patients followed at the University Hospital Center "Mother Theresa" in Tirana, Albania.

Keywords: mycophenolic acid, HPLC method, renal transplantation