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Abstract

Mycophenolic acid (MPA) is the active metabolite of the immunosuppressant drug mycophenolate mofetil (MMF), which is commonly prescribed after organ transplantation in conjunction with other immunosuppressants. MMF therapy is monitored to balance therapeutic efficacy with minimizing adverse effects associated with high serum concentrations. A LC-MS/MS method was developed for the quantitation of MPA and two additional metabolites, 7-O-mycophenolic acid glucuronide (MPAG) and mycophenolic acid acyl-glucuronide (AcMPAG), in serum using reverse-phase chromatography and multiple reaction monitoring (MRM) in positive electrospray ionization mode. Analytes were chromatographically resolved and the method was linear from 0.5 to 30.0 µg/ml MPA, 4.7 to 300 µg/ml MPAG, and from 0.5 to 30.0 µg/ml AcMPAG. Calibration curves for all analytes had $r \geq 0.990$. Intra- and inter-assay imprecision coefficients of variation (CVs) were ≤ 6.9% and ≤ 14.5%, respectively. No ion suppression or interferences were observed. The method compared favorably with an unaffiliated reference laboratory. Retrospective data analyses indicate interpatient differences in drug metabolism.