Population pharmacokinetics of oral ivermectin in venous plasma and dried blood spots in healthy volunteers

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The anthelminthic ivermectin is receiving new attention as it is being repurposed for new indications such as mass drug administrations for the treatment of scabies or in malaria vector control. As its pharmacokinetics are still poorly understood, we aimed to characterize the population pharmacokinetics of ivermectin in plasma and dried blood spots (DBS), a sampling method better suited to field trials, with special focus on the influence of body composition and enterohepatic circulation.; We performed a clinical trial in twelve healthy volunteers who each received a single oral dose of 12 mg ivermectin, and collected peripheral venous and capillary DBS samples. We determined ivermectin concentrations in plasma and DBS by liquid chromatography tandem mass spectrometry using a fully automated and scalable extraction system for DBS sample processing. Pharmacokinetic data were analyzed using nonlinear mixed effects modeling.; A two-compartment model with a transit absorption model, first-order elimination, and weight as an influential covariate on central volume of distribution and clearance best described the data. The model estimates (inter-individual variability) for a 70 kg subject were: apparent population clearance 7.7 (25%) L/h, and central and peripheral volumes of distribution 89 (10%) L and 234 (20%) L, respectively. Concentrations obtained from DBS samples were strongly linearly correlated (r; 2; = 0.97) with plasma concentrations, and on average 30% lower.; The model accurately depicts population pharmacokinetics of plasma and DBS concentrations over time for oral ivermectin. The proposed analytical workflow is scalable and applicable to the requirements of mass drug administrations.
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