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Título	Method Development And Validation Of Ursodiol And Its Major Metabolites In Human Plasma By HPLC-Tandem Mass Spectrometry
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Resumo	Background: Ursodeoxycholic acid (UDCA) and its metabolites tauroursodeoxycholic acid (TUDCA) and glycoursodeoxycholic acid (GUDCA) have been the subject of several pharmacological studies. The objective of this study was to develop an innovative method of quantification by HPL-tandem mass spectrometry (LC-MS/MS), with a lower cost and suitable, for application in bioequivalence studies. Methods: The procedure involved liquid–liquid extraction for quantification of UDCA/ GUDCA and precipitation extraction for TUDCA, using deuterated substances as internal standards (ISs) and Phenomenex Luna 250×4.6 mm 5µ C18 100A column. The mobile phase used was acetonitrile/ammonium acetate 30 mM (420: 580 v/v pH 7) for UDCA, acetonitrile/ ammonium acetate 10 mM/ammonium hydroxide (400:600: 0.5 v/v/v pH 9) for GUDCA, and acetonitrile/ammonium acetate 10 mM (570: 430 v/v pH 7) for TUDCA. Ions were monitored by the electrospray ion source (ESI) mass spectrometer, operating in a negative ionization mode. Compound determination was performed by LC-MS/MS system using a calibration curve of 15–10,000 ng/mL for UDCA/GUDCA and 5–500 ng/mL for TUDCA. The method was developed and validated according to the Brazilian National Health Surveillance Agency (ANVISA) of Brazil norms harmonized with the main international guidelines as a prerequisite for conducting in vivo study in human volunteers. Results: The method did not present matrix effect and residual effect, showing to be selective for studied molecules, with adequate accuracy and precision. In addition, the method was considered sensitive presenting a coefficient of variation less than 20% for the lower limit of quantification of each compound.

	Conclusion: This method can be applied in bioequivalence studies to determine ursodiol and its metabolites reproducibly, simply, and effectively with the use of readily accessible analytical materials and instrumentation.
Fomento	