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A novel and sensitive UPLC-MS/MS method for simultaneous analysis of four components of Socheongryong-tang tablet in humans: Method development and application to pharmacokinetic study

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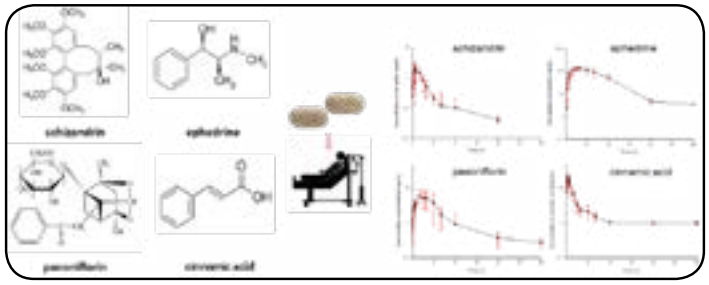
The aim of this study is to develop a novel UPLC-MS/MS (Ultra performance liquid chromatography- tandem mass spectroscopy) method for simultaneous analysis of schizandrin, ephedrine, paeoniflorin, and cinnamic acid as constituents of Socheongryong-tang tablet in human plasma. These four components were separated using 0.01% (v/v) aqueous formic acid and methanol as a mobile phase by gradient elution at a flow rate of 0.3 mL/min with a HALO-C_{18} column (2.1 mm×100 mm, 2.7 µm particle size). Quantitation was performed on a triple quadrupole mass spectrometer employing electrospray ionization technique, operating in multiple reaction monitoring mode. Mass transitions were m/z 432.9 → 384.1 for schizandrin, 165.8 → 148.1 for ephedrine, 525.0 → 449.2 for paeoniflorin, 146.8 → 102.9 for cinnamic acid, and 340.0 → 324.0 for papaverine as internal standard. Liquid-liquid extraction and protein precipitation with ethyl acetate-methanol (1:2, v/v) were used in the sample extraction to obtain these four components. Chromatograms showed high resolution, sensitivity, and selectivity with no interference by plasma constituents. Calibration ranges of schizandrin, ephedrine, paeoniflorin, and cinnamic acid in human plasma were 0.02 to 8 ng/mL, 0.5 to 200 ng/mL, 0.2 to 80 ng/mL, and 1 to 400 ng/mL, respectively, and displayed excellent linearity with correlation coefficients greater than 0.99. For all four components, both intra- and inter-day precisions (CV%) were less than 5.99%. The accuracy was 99.35-103.30% for schizandrin, 98.48-104.38% for ephedrine, 97.06-103.34% for paeoniflorin, and 99.97-104.36% for cinnamic acid. The analytical method developed in this study satisfied the criteria of international guidance. It could be successfully applied to pharmacokinetic studies of schizandrin, ephedrine, paeoniflorin, and cinnamic acid after oral administration of Socheongryong-tang tablet to humans.



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Biography

YongBok Lee received his PhD Degree in Pharmaceutics from Seoul National University, Republic of South Korea. He is currently a Professor of the College of Pharmacy at Chonnam National University, Republic of South Korea. His research interests are focused on the lymphatic delivery of immunosuppressants and the application of population PK/PD models associated with genetic differences in drug transporters and enzymes. He has won many prestigious awards and honors including the KSPs Progress Prize and Academic Prize, the KFDC Academic Prize, the CNU Yongbong Academic Prize and the MEST official commendation.

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