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Rapid and sensitive quantification of rosmarinic acid in human plasma by LC-MS/MS: Application to a clinical pharmacokinetic study

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Rosmarinic acid (RA) is contained in various Lamiaceae herbs used commonly as culinary herbs. Although RA has various potent physiological actions, little is known on its bioavailability. Several Studies shown that rosmarinic acid targets new blood vessel formation (angiogenesis) that plays a pivotal role in various life threatening pathological conditions for instance, cancer, age-related macular degeneration, Alzheimer's disease, chronic inflammatory diseases such as arthritis, dermatological diseases such as psoriasis, telangiectasis, pyogenic granuloma, seborrheic dermatitis and acne. A simple, precise and rapid LC/ MS/MS method was developed and validated for the quantification of rosmarinic acid in human plasma using Irbesartan as the internal standard (IS). The method involves solid phase extraction of rosmarinic and the IS using Hi-Purit HLB cartridge (30 cc/1 mg, National chromatography, Inc) from 0.250 mL human plasma. A Kinetex HILIC (50×4.6 mm, 2.6 μm particle size) analytical column was used for the chromatographic separation under isocratic conditions. The mobile phase consists of Acetonitrile: 2 mM ammonium acetate with 0.2% Formic acid (50:50 v/v). The parent>product ion transitions for Rosmarinic acid (m/z=359.00>160.90) and the IS (m/z=427.1>193.30) were monitored on a AB-SCIEX 4000 Qtrap mass spectrometer, operated in the multiple reaction monitoring negative ion mode. The method was validated over the concentration range of 2.137-2279.104 ng/mL for rosmarinic acid, with a total chromatographic run time of 3.5 min. Acceptable precision and accuracy were obtained for the concentrations used to prepare the standard curves. The applicability of the method will be demonstrated by a pharmacokinetic study involving a single ascending dose study (48 healthy human subjects), a multiple ascending dose study (32 healthy human subjects) and a cross over study (24 healthy human subjects) under fasting condition to establish the bioavailability parameters on the formulation, CANSSUFIVE* Nuvastatic.

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