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Diosmetin pharmacokinetic following diosmin oral administration in man; A new study on an old product with controversial pharmacokinetic findings in the past

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Several flavonoids are used in therapy with a wide range of indications; almost all are of natural origin and many products are employed in the popular medicine from long time. Diosmin is widely used to treat vascular diseases like hemorrhoids, lymphedema, chronic venous insufficiency, and varicose veins where it plays a beneficial role improving vascular and blood rheology. Like many other flavonoids diosmin is completely degraded by the intestinal bacteria and the aglycone, diosmetin, is systemically absorbed. Due to low concentrations attained also by diosmetin in blood, pharmacokinetic studies have been quite limited in early times, putting under discussion the availability of such molecules, and only in the last years, mainly thanks to mass spectrometry, data on systemic absorption have been obtained. Unfortunately the results have been very contrasting with measured levels going from a few ng/ml conjugated diosmetin (following oral administration of diosmin 400 – 600 mg) to several 100 ng/ml (for the same dose administered) of diosmetin itself. In the present study the results obtained with a highly specific HPLC-MS/MS method (employing a deuterated internal standard) in combination with selective enzymatic degradation methods are reported. Concentrations of free diosmetin were below LLOQ (50 pg/ml) while conjugated diosmetin, almost all as glucuronide, reached levels up to 10 ng/ml. Contamination of enzymes commonly used for flavonoid deconjugation proved to be a relevant source of unreliable results as well the dietary intake of similar flavonoid or their metabolites. In conclusions it has been proven that an adequate diosmetin pharmacokinetic can be determined and potential reasons of the past controversial data have been elucidated.

Biography

A.Iordachescu graduated in chemistry from the University of Bucharest in 2005. In 2010 she specialized in biostatistics from the same university and from 2010 until now she follows her doctoral study, at the same Institute, focused on chiral separation. She is working since 2006 in the pharmacokinetic laboratory of Pharma Serv Int'l as analyst specialized in mass-spectrometry. Development of new bio-analytical methods, often chiral, optimization of samples preparation techniques and implementation of regulatory rules are the main tasks.

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