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Published in:
Resveratrol 2014

Publication date:
2014

Document version
Final published version

Citation for pulished version (APA):
Radko, Y., Christensen, K. B., & Christensen, L. P. (2014). Preparative-scale isolation of resveratrol metabolites from human urine. In Resveratrol 2014: 3rd International conference of resveratrol and health (pp. 44). [SO-09]

2014
RESVERATROL

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SO-09 Preparative-scale isolation of resveratrol metabolites from human urine
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The metabolite profile of biofluids from humans and rats after oral intake of trans-resveratrol (t-RES) have shown that the absorption of t-RES is very high but is rapidly cleared from the circulation. The resveratrol metabolites encountered in human urine after oral administration of t-RES or its predominant form in plant-derived foods (trans-resveratrol-3-O-β-D-glucoside) includes t-RES sulfates, glucuronides and conjugates of dihydroresveratrol. Although, the systemic bioavailability of t-RES seems to be low, the accumulation of t-RES and potentially bioactive t-RES metabolites in epithelial cells may contribute to the health-promoting effects of this nutraceutical. However, little is known about the bioactivity of t-RES metabolites, which is probably due to the limited accessibility of these metabolites. t-RES metabolites are usually produced by chemical synthesis but the yields are low. In order to explore the bioactivity of t-RES metabolites in vitro and in preclinical trials a method for preparative isolation of t-RES metabolites from human urine after oral intake of a t-RES-containing dietary supplement was developed. The urine was pre-treated by using solid-phase extraction to give a brown oily residue, which was separated using a combination of different chromatographic methods resulting in the isolation of several t-RES metabolites in preparative-scale including trans-resveratrol-3-O-sulfate, trans-resveratrol-3,5-O-disulfate, trans-resveratrol-3,4'-O-disulfate, trans-resveratrol-3-O-β-D-glucuronide and dihydroresveratrol conjugates such as dihydroresveratrol-3-O-β-D-glucuronide. The structures of the isolated metabolites were elucidated by NMR and LC-DAD-MS/MS. The present method enables the isolation of t-RES metabolites in relative large quantities for testing in preclinical trials and is a good alternative to chemical synthesis of conjugate metabolites of t-RES and dihydroresveratrol. The method is reliable, reproducible, and is relatively easy to apply and may also find use to reveal and isolate hitherto unknown or not fully characterized t-RES metabolites in human urine, which may help to shed light on the metabolism of t-RES in humans and thus its health-promoting effects.