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LC-UV/MS methods for the analysis of aroylhydrazone pro-chelator and its active substance: Utilization in an *in vitro* bioactivation and a pilot pharmacokinetic study

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Salicylaldehyde isonicotinoyl hydrazone (SIH) is an iron chelator with low toxicity and strong cytoprotective properties. However, it has a short biological half-life. Boronyl salicylaldehyde isonicotinoyl hydrazone (BSIH) is its pro-drug, synthesized to overcome this drawback. Moreover the concept of a pro-drug provides a possibility to focus therapeutic effect only to tissues suffering from oxidative stress and thus prevents possible iron deprivation often caused by former iron chelators. Analyses were performed on Zorbax Bonus-RP column. A mobile phase composed of EDTA, NaH₂PO₄, methanol and acetonitrile was utilized for LC-UV measurements. Aqueous part of mobile phase was replaced by ammonium formate for LC-MS analyses. The methods were validated for determination of SIH and BSIH in buffer and cell medium and BSIH in plasma. LC UV method was utilized in *in vitro* activation experiment of BSIH with H₂O₂ and LC-MS assay was used to estimate basic pharmacokinetic (PK) parameters of BSIH in rats. BSIH has been found to be more stable in the tested media as compared to SIH. Its significant conversion to SIH by H₂O₂ was also observed *in vitro*. PK parameters calculated in this study show improved elimination half-life of BSIH prior to SIH. The results of this study suggest that the prochelation is a promising strategy for further development of the aroylhydrazone cytoprotective agents.

Biography

Jan Bures has completed his MSc at the Faculty of Pharmacy, Charles University in Prague, Czech Republic. Currently, he is a postgraduate student in the field of Pharmaceutical analysis, first author or co-author of 8 poster presentations on scientific conferences and first author of three lectures presented on PhD/student scientific conferences at Faculty of Pharmacy. His research is focused on bioanalysis of iron chelators using LC-UV/MS.

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