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UHPLC-MS/MS analysis of samples from *in vitro* and *in vivo* studies of a novel iron chelating anti-cancer agent - DpC

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Cancer has been ranked among top causes of death worldwide. Generally, cancer is difficult to treat pharmacologically mainly due to the heterogeneity of these diseases and their resistance against currently established antineoplastics. Therefore, new anti-cancer drugs are needed. Di(2-pyridyl)ketone-4-cyclohexyl-4-methyl-3-thiosemicarbazone (DpC) is a novel iron chelator currently under advanced preclinical development as an anti-cancer drug. As to promote these investigations from preclinical to clinical phase, basic pharmacokinetic (PK) data on this compound need to be determined.

Aim of this work was to develop an UHPLC-MS/MS method for analysis of DpC in biological materials and utilize it to monitor the cellular uptake of the compound by breast carcinoma cells (MCF-7) and describe pharmacokinetic parameters of DpC in rats.

Combination of protein precipitation and liquid-liquid extraction of DpC from biological materials followed by UHPLC-ESI-QqQ-MS/MS analysis (Shimadzu Nexera coupled with Shimadzu LCMS 8030) was used in this work. An Acquity BEH C18 column with mobile phase consisting of aqueous ammonium formate with EDTA and acetonitrile in a gradient mode were utilized. This method was validated according to FDA guidelines for determination of DpC in plasma and MCF-7 cells. Our study suggests that cellular uptake of DpC might be influenced by active transport. Application of this method to analysis of plasma taken from PK study allowed for estimation of basic pharmacokinetic parameters of DpC.

The UHPLC-MS/MS developed in this study will be further optimized and utilized in a future excretion study.

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Biography

Vit Sestak has started his PhD studies at Charles University, Czech Republic two years ago. Aim of his work is development of bioanalytical LC-MS methodologies for analysis of novel antineoplastic agents. Vit is currently working on determining PK characteristic of thiosemicarbazone iron chelators. Being in the second year of his PhD course, he has published 2 papers in journals with impact factor.

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