

**Mass Spectrometry based approaches for the study of drug delivery and biodistribution: Applications in drug discovery and development programs**

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The main scope of targeted therapies is the efficient delivery of the drug in the tissue of interest. Mass Spectrometry is a robust bioanalytical technique that can provide useful information towards the development of targeted therapies. One paradigm of this approach is the design and evaluation of gemcitabine based peptide conjugates. Gemcitabine, a drug with established efficacy against a number of solid tumors, has therapeutic limitations due to its rapid metabolic inactivation. Our aim was the development of an innovative strategy to produce metabolically stable analogues of gemcitabine that could also be selectively delivered to cancer cells based on cell surface expression of receptors that are over-expressed in cancer cells. The Gonadotropin Releasing Hormone-Receptor (GnRH-R) is targeted in the presented study as a cancer specific target. Novel bioanalytical methodologies (LC-MS/MS) were developed to monitor the balance of active/inactive metabolites resulting from the gemcitabine prodrugs in order to further elucidate the mechanism of action of selected compounds. Another example of interest in which Mass Spectrometry plays a crucial role, is the evaluation of the levels of doxorubicin in blood, in hepatocellular cancer patients that have been chemoembolized with polymeric microspheres. This type of administration aims to achieve higher and more sustained levels of doxorubicin in the liver along with less peripheral toxicity.

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