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# Development of new biomarkers and early prognosis for drugs causing hepatotoxicity through different metabolomic approaches

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## Abstract

Hepatotoxicity (from hepatictoxicity) implies chemical-driven liver damage. Drug-induced liver injury is a cause of acute and chronic liver disease.The liver plays a central role in transforming and clearing chemicals and is susceptible to the toxicity from these agents. Certain medicinal agents, when taken in overdoses and sometimes even when introduced within therapeutic ranges, may injure the organ. Other chemical agents, such as those used in laboratories and industries, natural chemicals (e.g., microcystins) and herbal remedies can also induce hepatotoxicity. Chemicals that cause liver injury are called hepatotoxins.

Drug-induced hepatotoxicity is a potentially fatal adverse effect and the leading cause of acute liver failure in most of the countries. The liver can be affected directly, in a dose-dependent manner, or idiosyncratically, independently of the dose, and therefore unpredictable. Currently, hepatotoxicity is a diagnosis of exclusion that physicians should suspect in patients with unexplained elevation of liver enzymes. Therefore, new diagnostic biomarkers are necessary to improve the prognosis of hepatotoxicity. Although several biomarkers have been found through various analytical and genetic approaches, none of them have been able to display enough specificity and sensitivity, so new approaches are needed. Targeted metabolomics aims to analyze a set of pre-selected metabolites from biologically relevant metabolic pathways. The triple quadrupole mass spectrometry (QqQ-MS) based multiple reaction monitoring (MRM) technique is the most widely approach used for targeted metabolomics, and features high selectivity and sensitivity, good reproducibility and wide dynamic range in quantitative analysis. In this sense, metabolomics approaches using sophisticated instruments like LC-MS/MS is a strongly and promising emerging field which is achieved from biofluids collected through minimally invasive procedures (either SPE or LLE or Ppt or ABE), can obtain early biomarkers of toxicity, which may constitute specific indicators of hepatotoxicity. These biomarkers can be mainly identified and qualified in rat but also for humans, several biomarkers will be described and will be validated, followed by future (pre-) clinical routine application. Liquid chromatography separation and positive/negative ion polarity switching based MS detection, and is able to acquire data from multiple types of biological samples such as bacteria, cultured mammalian cells, animal tissues and biofluids (e.g., serum and urine). Finally, the MRM Analyzer software can automatically process the generated large-scale data set with high efficiency.

**Key words:** Multiple reactions monitoring; metabolomics; hepatotoxicity; quadrupole mass spectroscopy

## Biography

Nalini kanta Sahoo is currently working as Professor & H.O.D in MLR Institute of Pharmacy. Also he is advisor for NFPS and Trans Integra Healthcare Ltd. He serves as Research scientist for Vision science research, Malaysia. Recently he is awarded best professor in Pharmacy for ITAP 2018 Awards conducted by Tutor pride. He obtained his Doctoral degree in 2015 from Siksha ?O? Anusandhan University, Bhubaneshwar. He has to his credit nearly 35 publications of good scientific merit. He is a member on the Editorial boards of around 40 national and international journals. He is a subject expert for two private institutes and a Q.A. expert for Chegg Pvt. Ltd., USA. He taught subjects like Advanced Pharmaceutical Analysis, Inorganic chemistry, Modern Analytical Techniques, Validation and Quality assurance and Drug Regulatory Affairs at the graduate and post graduate levels. As a teacher, he is quite industrious, dedicated and exhibited notable merit in his academic responsibilities. After serving Yalamarty Pharmacy College till 2014, he joined M.N.R. College of Pharmacy, Medak. Earlier after his graduation, joined Shilpa Medicare Pvt.Ltd.Raichur, Karnataka and worked as a Q.C. Executive for one year during 2005 and 2006. In his Ph.D. program Dr.Nalini kanta developed newer Liquid chromatographic methods for estimating some important drugs in formulations and biological fluids. This study was of significant value, as these methods can be adopted by analytical laboratories for routine estimation of these drugs in dosage forms and for bioavailability and bioequivalence studies. Thus, during his nearly twelve years of service in colleges and industry, he acquired good skills in the analysis of various drugs in formulations and in biological matrices especially by adopting Liquid chromatography and LC-MS techniques. Dr.Nalini kanta is familiar with handling of modern analytical instruments including Spectrophotometers. HPLC, LC-MS, FTIR etc. Dr.Nalini kanta has good communication and inter-personal skills. With his good research experience, he can successfully carry out various research programs in an analytical division.


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