

# Metabolomics Used in Herb-Induced Liver Injury



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**Abbreviations:** MS: Mass Spectrometry; TCM: Traditional Chinese Medicine; NMR: Nuclear Magnetic Resonance; HILI: Herb-Induced Liver Injury; AA: Aristolochic Acid

## Introduction

Metabolomics [1]. As a formidable tool, is usually used to systematically assess the molecular responses of living systems to all external stimuli, characterize pathological states, diagnostic information and mechanistic insights into biochemical effects of drugs, based on global metabolite profiles in biological samples [2]. Mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy, two major analytical platforms, with visualization software, have driven forward the discipline of metabolomics. Traditional Chinese Medicine (TCM) with its focus on herbal use is popular and appreciated worldwide with increased tendency [3,4]. And treatment was perceived as fairly safe but discussions emerged more recently as to whether herb-induced liver injury (HILI) from herbal TCM is a major issue. The multi-component and multi-target nature of TCM makes toxicological research far more complex than that of chemical drugs. Looking for rapid and sensitive biological toxicity effect evaluation technology has become a major problem urgently to be solved in current TCM safety evaluation. Metabolomics can further be employed as a perfect approach to link the gap between TCM and molecular toxicology. We reviewed the applications of the metabolomics with two major analytical platforms for HILI researches.

## NMR-Metabolomics Used in HILI

NMR is one of the most commonly used technologies in metabolomics research, providing detailed information on the molecular structure and probing metabolite molecular dynamics and mobility [5]. Aconite is a very typical toxic Chinese medicine. Li et al. [6]. Using [1] H NMR for investigation of metabolites of Aconite on its toxicity in Westar rats. The 1H NMR spectral analyses were coincident with the results of serum biochemical parameters which mean the slight impairment of liver. The sub-acute toxicity of aristolochic acid (AA) was investigated by 1H NMR spectroscopic

by Pei Lab [7]. Slight liver lesion was observed in spectra of AA, a main component of Aristolochia and As arum, treated rats in time interval of 48-56 h and 96-104 h based on the increase of urinary turbine and decrease of 2-oxoglutarate, which was NMR marker of liver impairment.

## MS Metabolomics Used in HILI

The high selectivity of mass spectrometry with low-detection limits makes mass spectrometry an ideal tool for metabolomics applications. It is a sensitive tool that can be used to characterize, identify and quantify a large number of compounds in a biological sample where metabolites concentrations might cover a broad range of information with regard to disease path physiology [8,9], Zhao and her coworker [10]. Using LC-MS for investigation of metabolites of Tripterygium wilfordii on liver toxicity of Sprats analyzed and identified seven possible endogenous biomarkers, which were 6-phosphate glucosamine, lysophospholipid, tryptophan, guanidine acetic acid, 3-indole prop ionic acid, cortisone, and ubiquinone. The level changes of above metabolites indicated the related metabolism pathways were disordered. The toxic effect of total spooning had been established by using UPLC-MS. It was shown that there was obvious acute liver toxicity and accumulated one for saikosaponin Wang et al. [11,12].

Evaluated dynamic metabolomics changes of liver injury in rats caused by Polygonal multiflorum (PM) with LC-MS/MS-Q-TOF. Six potential biomarkers were screened through comparative analysis, including polyamide, Lysophosphatidylcholines (16:0), leukotriene A4, trans-tetra-dec-2-enoic acid, dihydrocortisol and 7 $\alpha$ -hydroxydehydroepiandrosterone, which are more sensitive than ALT and AST. It can reveal the dynamic mechanism of PM causing liver injury. Cui et al. [13]. Discovered that 55 metabolites distributed in 33 metabolic pathways were identified as being

significantly altered in *Dioscorea bulbiferous* Rhizome-treated rats using UPLC-Q-TOF/MS. Dong et al. [14]. revealed that Aconite Root produced serious heart and liver toxicity by analyzed the urinary metabolomics which was performed by UPLC-Q-TOF-Hamlin Westar rats, consistent with clinical biochemistry and histopathology. Furthermore, urine metabolomic profiling has provided 17 sensitive biomarkers, The rat urine after given *Fructus Conidia* were analyzed by UPLC/Q-TOF MS indicates that the extractor of *Fructose Conidia* has certain toxicity to the liver and kidneys [15].

## Conclusion

The metabolomics analysis were coincident with the results of classical toxicology study parameters, even more superiority to traditional technologies on the toxicological study of TCM with the abilities of dynamical monitoring the response of bio system and evaluating biological effects from the metabolic [6]. Due to the complexity of HILI mechanism, metabolomics is especially suitable on the hepatic toxicity study of traditional Chinese medicine.

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