

Differential proteomic analysis in the progression of aristolochic acid nephropathy in mice using the FD- LC–MS/MS method

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Introduction

The fluorogenic derivatization-liquid chromatography-tandem mass spectrometry (FD-LC-MS/MS) method has been extensively applied to proteomics analysis from cells to tissue homogenates due to efficient, sensitive, reproductive properties^{1,2,3}. Aristolochic acid nephropathy (AAN) is a well-known nephritis which might progress into end-stage renal disease. This study aimed to investigate the biomarkers in the progression of AAN without any specific indicators for diagnosis using a proteomics method with FD-LC–MS/MS.

Materials and Methods

The C3H/He female mice were given *ad libitum* aristolochic acid (AA)-distilled water (0.5 mg/kg/day) and distilled water for 56 days in the AA and normal groups, respectively. The mice were sacrificed on 0, 14, and 28 days after 56-day administration of AA/distilled water. The kidneys were made into sections for histological examination and homogenate for proteomics study, including fluorogenic derivatization with 7-chloro-N-[2-(dimethylamino) ethyl]-2,1,3-benzoxadiazole-4-sulfonamide (DAABD-Cl), followed by high-performance liquid chromatography analysis with flurescence detection and then identified by LC-MS/MS with a MASCOT database searching system.

Results and Discussion

The renal damage, including cell infiltration, fibrosis, tubular atrophy, was certainly induced in the AA- group mice under histological examination. The number of altered peaks between normal and AA groups on 0, 14 and 28 days after administration of AA/distilled water were 16, 54, and 24, respectively. In terms of functions, these identified proteins could categorized into anti-oxidant effect, extracellular matrix regulation, inflammations, apoptosis, oncogenesis, and ATP synthesis.

Conclusion

AA-induced proteins were found in the current proteomics study with FD-LC–MS/MS. According to the results, we could further understand the pathological mechanisms in the progression of AAN.

Bibliography

¹Imai et al., Towards clinical proteomics analysis. Biomed. Chromato., 2011, 25, 59-64.

- ² Ichibangase *et al.*, An FD- LC- MS/MS proteomic strategy for revealing cellular protein networks: A conditional superoxide dismutase 1 knockout cells, *PLoS One*, 2012, 7, e45483.
- ³ Lin *et al.*, Proteomics analysis of altered proteins in kidney of mice with aristolochic acid nephropathy using the fluorogenic derivatization–liquid chromatography–tandem mass spectrometry method. *Biomed.Chromato.*, 2017, e4127.