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The effects of tanshinone II-A on the liver proteome in hyperlipidemia rats by iTRAQ

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Objective: To observe the changes of proteome in the livers of hyperlipidemia rat and study the effects of Tanshinone II-A on them by the method of iTRAQ, in order to seek a new treatment to prevent and cure hyperlipidemia on molecular level.

Methods: Wistar rats (45 males) were randomly divided into three groups: control group, model group and treatment group. The rats in model group and treatment group were fed with high fat diet, while control group were fed with normal diet. The rats in treatment group were treated with Tanshinone II A (Sulfotanshinone Sodium Injection, intraperitoneal injection), 20mg/kg/rat per day, and the rats in control group and model group were treated with normal saline (intraperitoneal injection). The content of TG, TC, HDL-C and LDL-C in serum were detected by automatic biochemical analyzer. The change of liver structure and lipid deposition were detected by oil red staining method. The total protein was separated and extracted from livers in each group. After enzymatic hydrolysis, the protein was marked with ITRAQ, and used for liquid phase separation by SHIMADZU LC-20AB liquid phase system and SHIMADZU LC-20AD nanoliter liquid high performance liquid chromatograph. Then the peptides were analyzed by series ESI mass spectrometry. To search for peptide mass fingerprinting in the protein database and identify peptide/ proteins by Mascot 2.3.02 software.

Result: The levels of TC and LDL-C increased while the levels of HDL-C decreased significantly in model group, compared with control group. Oil red staining indicated that obvious lipid deposition was formed in the liver cells in model rats. Compared with model group, the levels of HDL-C increased in treatment group, and TC, LDL-C levels decreased significantly. Proteomics analysis was shown that in model group 312 proteins increased compared with control group, such as Apolipoprotein, Carboxylesterase etc. While 173 proteins decreased, such as 7-dehydrocholesterol reductase, low density lipoprotein receptor related protein, 3- glyceraldehyde phosphate dehydrogenase etc. In treatment group 106 proteins increased and 146 proteins decreased. The opposite trend was shown in treatment group compared with model group.

Conclusion: Tanshinone II A could prevent hyperlipidemia by up-regulating the proteins such as Apolipoprotein, Carboxylesterase etc.. while down-regulating the proteins such as 7-dehydrocholesterol reductase, low density lipoprotein receptor related protein, 3- glyceraldehyde phosphate dehydrogenase etc.

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