



Metabolomics to Analyze the Therapy and Adverse Effect of Glycyrrhizin Capsules Towards Liver Cancer

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SUMMARY. The diagnosis and therapy of liver carcinoma remain to be very challenging. Metabolomics technology was employed to search the potential biomarkers of liver carcinoma, and used to evaluate the therapeutic efficiency and adverse effects of glycyrrhizin capsules. Blood was taken from 20 healthy volunteers and 40 patients with liver carcinoma. Among them, 20 patients have been given one glycyrrhizin capsule one day. *In vitro* incubation system was used to determine the inhibition of glycyrrhizin towards the metabolism of clopidogrel. The level of amino acid Asparagine (Asn) significantly increased in the blood obtained from the patients with liver carcinoma. The treatment with glycyrrhizin capsule significantly prevented the elevation of Asn in the blood. The adverse effect of glycyrrhizin capsule was determined through evaluating the inhibition of glycyrrhizin towards human liver microsomes (HLMs)-catalyzed clopidogrel metabolism. Glycyrrhizin inhibited about 40% activity of clopidogrel metabolism ($p < 0.05$). In conclusion, metabolomics has been successfully applied to find the clinical biomarkers for the therapy of glycyrrhizin capsules towards liver carcinoma, and explain the possible adverse effects of glycyrrhizin capsules.

RESUMEN. El diagnóstico y tratamiento del carcinoma de hígado siguen siendo muy difíciles. En este trabajo se empleó la tecnología metabolómica para buscar los biomarcadores potenciales de carcinoma de hígado y se utiliza para evaluar la eficacia terapéutica y los efectos adversos de las cápsulas de glicirricina. Se extrajo sangre de 20 voluntarios sanos y 40 pacientes con carcinoma de hígado, a 20 de los cuales se les suministró una cápsula de glicirricina. El sistema de incubación *in vitro* se utilizó para determinar la inhibición de la glicirricina hacia el metabolismo de clopidogrel. El nivel de asparagina (Asn) aumentó significativamente en la sangre obtenida de los pacientes con carcinoma de hígado. El tratamiento con cápsulas de glicirricina impidió significativamente la elevación de Asn en sangre. El efecto adverso de la glicirricina se determinó mediante la evaluación de la inhibición de la glicirricina hacia microsomas hepáticos humanos (HLM) que catalizan el metabolismo de clopidogrel, comprobando que glicirricina inhibió la actividad de alrededor del 40% del metabolismo de clopidogrel ($p < 0,05$). En conclusión, la metabolómica se ha aplicado con éxito para encontrar los biomarcadores clínicos para la terapia de cápsulas de glicirricina en carcinoma hepático y explicar los posibles efectos adversos de las mismas.

KEY WORDS: adverse effects, biomarkers, diagnosis, glycyrrhizin capsules, metabolomics.

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