## REVERSIBILLTY OF LIVER FIBROSIS WITH INTEGRATED CHINESE AND WESTERN MEDICINE

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Aim: To explore the possibility of reverting HBV-related hepatic fibrosis and cirrhosis with traditional Chinese medicine (TCM).

Methods: An herbal recipe (Cpd. 861) was used as the antifibrotic agents. Four clinical trials on 156 patients with HBV-related fibrosis and cirrhosis were carried out, including a randomized, double-blinded, placebo controlled clinical trial with 49 HBV patients. Liver biopsies before and after treatment were assessed with Scheuer and Chevallier's scoring system.  $CCl_4$  and human albumin immune injury rat hepatic fibrosis models, cultured hepatic stellate cells (HSC) was used. Total and type I, III, IV collagen content of liver were measured, mRNA for collagen I, III, IV, transforming growth factor- $\beta$  (TGF- $\beta$ ), matrix metalloproteinase (MMP1, MMP2), tissue inhibitor of metalloproteinase (TIMP) in liver tissue were also detected. Serum and liver tissue collagenase activity was determined. Histopathological study of liver specimen was investigated.

Results: (1) In HBV patients, after six months treatment with oral Cpd. 861, the reversion rate of fibrosis was 78% in S2, 82% in S3 (precirrhotic stage) and 75% in S4 (cirrhosis). The result was demonstrated by the randomized clinical trial. (2) Total and type I, III, V collagen in animal liver were significantly reduced after treatment, whereas quantitation of mRNA for collagen I, III, V and TGF- $\beta$  were also markedly suppressed in liver tissue and cultured HSC, suggesting suppression of fibrogenesis. At the same time, serum and liver tissue collagenase activity (latent and active) were enhanced significantly by Cpd. 861, while mRNA for MMP1 in cultured HSC and collagenase activity in the supernatant were both increased. mRNA for TIMP1 was significantly suppressed, indicating the enhancement of matrix degradation after Cpd. 861 treatment.

Conclusions: (1) Liver fibrosis and early cirrhosis due to HBV infection in man could be definitely reversed by TCM treatment of Cpd. 861. (2) The mechanism leading to reversal of fibrosis was due to suppression of fibrogenesis, and the concurrent enhancement of matrix degradation. Suppression of TIMP also plays an important role. (3) Herbal Cpd. 861 could affect both initiation and perpetuation of HSC.