

Is There Any Liver Anti-Fibrotic Effect of K-17.22? An Experimental Study with Immunohistochemical Analysis in A Rat Model

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1 F Marotta*, 2 Y Rahman-Shield, 3 E Minelli, 4E. Oliva, 2 P Safran, 5 M Harada, 1Hepato-GI Dept., S. Giuseppe Hosp., Milano, Italy; 2 SFJO & Labs., Paris, France; 3 WHO Centre for Traditional Medicine, State University, Milano, Italy; 4Angiology Post-Graduate School, Surg. Dept., Univ. of Siena, Italy, 5 MCH Hospital, Tokyo, Japan.

ABSTRACT ONLY

Liver fibrosis in chronic liver disease is not a simple deposition of excess but it implies a change in the type of matrix molecules. The problem in antifibrotics development is the toxicity and the therapeutic effects when used in clinical study. The aim of this study was to test a novel natural compound, which has been shown to significantly decrease GPT level in HCV-patients as well as exerting potent antioxidant properties, in a liver fibrosis model. 150 SD rats were allocated into 2 groups:

A) fibrosis model (0.2ml/kg CCL4 i.p. injection twice/week);

B) as A with diet added with K-17.22 50mg/kg (Kyotsu, Japan) while healthy rats served as control.

At sacrifice the liver was immediately removed and samples used for routine histology, hydroxyproline determination, Immuno-histochemical analysis of activated stellate cells and for Northern blot analysis of Tissue Inhibitor Metallo Proteinase-1 (TIMP-1) and α 2-procollagen mRNA. Blood routine biochemistry, Type IV collagen 7s and hyaluronic acid were measured as well. While serum level of type IV collagen 7s was not affected by liver fibrosis, the concentration of hyaluronic acid showed an over 20-fold increase in A group ($p<0.001$). However, such phenomenon was completely prevented by the administration of K-17.22 ($p<0.001$ vs A). Accordingly, GOT, GPT, ALP and Bilirubin increased level ($p<0.001$ vs healthy control) significantly improved in B group ($p<0.05$ vs A).

Group A showed an increased content of hydroxyproline (1190 ± 205 vs 343 ± 61 , $p<0.001$ vs control) which was significantly reduced by the concomitant supplementation with K-17.22 ($p<0.05$ vs A). The histological examination of liver in A group showed the typical features of diffuse fat deposition in hepatocytes, periportal fibrosis with elongation of fiber bundles around the portal area and some portal-portal bridging. An overt reduction of the above morphological features appeared in group B. K-17.22 significantly decreased the number of activated stellate cells and the expression and densitometric assessment of either TIMP-1 and α 2-procollagen mRNA ($p<0.05$). These data suggest that the present novel phytotherapeutic compound K-17.22 exerts a potent antifibrotic effect and further studies are awaited to corroborate its clinical potential.