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The effects of N,N,N-trimethyl chitosan chloride-superoxide dismutase conjugate (TMC-SOD) on carbon tetrachloride-induced acute liver failure and hepatic fibrosis in mice

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Abstract: Cu, Zn-SOD was chemically modified with N,N,N-trimethyl chitosan chloride derivatives (TMC) to yield a polymer–enzyme conjugate TMC-SOD in our early study that demonstrated superior therapeutic effect to native SOD. The present work projects the protection afforded by TMC-SOD against severe hepatic damage induced by CCl_4 on the basis of biochemical assessment confirmed by histopathological examination. The acute liver injury of TMC-SOD group was significantly lessened. The development of CCl_4-induced acute liver failure altered the redox state with a decreased hepatic GSH and increased formation of lipid per oxidative products, which were partially normalized by treatment with TMC-SOD or TMC+SOD. In the study of hepatic fibrosis, the results showed that TMC-SOD markedly attenuated the mRNA expression of TGF-β1, MMP-2 and collagen-I. Moreover, Western blots of tissue homogenates revealed that the protein expression of TGF-β1 was substantially reduced also by TMC-SOD treatment. Histological and hepatic hydroxyproline examination revealed that TMC-SOD significantly arrested the progression of hepatic fibrosis. The results support that TMC-SOD is a promising agent for the treatment of hepatic fibrosis. Therefore, the administration of TMC-SOD may be an optional therapeutic and preventive measure against oxidative stress-induced liver injury and hepatic fibrosis.

Keywords: Cu, Zn-superoxide dismutase; chitosan; N,N,N-trimethyl chitosan chloride derivatives; acute liver failure; TGF-β1