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MULTIMECHANISTIC ANTIFIBROTIC EFFECT OF IRON CHELATORS: IMPLICATIONS OF INFLAMMATORY AND FIBROGENIC MEDIATORS

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Background & Aim: Iron overload is one of mechanisms by which HCV causes oxidative stress that may contribute to liver fibrosis and carcinogenesis. The therapeutic benefit of adding iron chelators to treatment regimen of HCV patients are warranted because: firstly, clinical data reported that excess iron deposits are found in the liver samples from about 20% of HCV-positive patients. Secondly, hepatic iron load enhances the levels of eukaryotic initiation factor 3, which is essential for HCV translation. Through an international joint project entitled investigating the coagulation profiles and the role of iron in patients with hepatitis C virus (HCV): impact of iron chelators in attenuating thrombosis and liver fibrosis, we investigated the potential antifibrotic effects of different iron chelators, and the underlying mechanisms through studying different oxidative stress, inflammatory and fibrotic markers.

Methods: Liver fibrosis was induced using concanavalin A (Con A; 15 mg/kg/w for six weeks, iv) and rats were treated with iron chelators (deseferoxamine, defriprone or defrasirox) three times per week for six weeks. Histopathology and iron homeostasis pathway were elucidated. Then different oxidative stress, inflammatory and fibrosis markers were assessed such as hydroxyproline, TGF-beta, alpha-SMA, CD4, NF-kB, TNF-alpha, iNOS, COX-2, IL6 and INF-γ.

Results: Collectively, it was found that iron chelators possess potent antifibrotic effects due to their antioxidant and anti-inflammatory properties as well as maintenance of iron homeostasis.

Conclusion: The present project may open a new scenario for the clinical usefulness of iron chelators in treatment of liver fibrosis associated conditions in the future.