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Structure-Related Cytotoxicity and Anti-Heaptofibric Effect of Asiaticoside Derivatives in Rat Hepatic Stellate Cell Line, Hsc-T6

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Asiaticoside, a biologically active triterpenoid present in Centella asicatica, has been known to exert a variety of biological effect such as wound-healing, hepatoprotective, anti-inflammatory. In this study, we observed the effect of asiatic acid asiaticoside and its 16 derivatives on the cytotoxicity and the content of hydroxyproline in rat hepatic stellate cell line, HSC-T6 cell as a preliminary study for screening the anti-hepatofibrotic effect. The cytotoxicity of asiaticoside derivatives were varied depending on the structure from 5.5 μM of IC50 to no effect. The substitution of A-ring 2-OH to N=C was increased the cytotoxicity and keton group on C11 at C-ring was reduced it. The sugar moiety of the molecule dramatically reduced the cytotoxicty. The collagen synthesis judged by hydroxyproline content was inhibited to maximum 48% to no effect by asiaticoside derivatives. The anti-fibrotic effect of them was due to decrease the expression of Timp-1, Timp-2 and prolyl 4-hydroxylase α and β subunit, when we observed the mRNA levels of hepatic fibrosis related proteins by RT-PCR. However, the inhibition of collagen by asiaticoside derivatives was not shown any structural-activity relationship.

Keyword : asiaticoside derivatives, cytotoxicity, anti-hepatofibrotic effect