Exploring Strategies to Treat NASH: Beneficial Effect of YHK on Metal-Induced Oxidative Damage of Hepatocytes and Lysosomal Fraction

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It has been shown that metals undergo redox cycling and there is an increasing literature suggesting the role of free radical generation and oxidant injury in the pathogenesis of NASH. The aim of the present study was to test a natural hepatoprotective compound, which has recently shown to decrease transaminase level in HCV patients, on metal-induced liver injury. Hepatocytes were isolated from Wistar rats by collagenase perfusion method and cultured as such and also with a-linolenic acid (LNA)-bovine serum albumin （BSA）.Hepatocytes were taken cultured in with graded dilution of YHK (Kyotsu, Tokyo, Japan) sample (100mg/ml and 200mg/ml) or sylibin (100mg/ml) dissolved in dimethyl sulfoxide 10min before the addition of metallic salts (iron,copper and vanadium). Lysosomal fraction were prepared to carry out lysosome fragility test by measuring b-galactosidase activity and lactate dehydrogenase leakage and oxidative damage tests in the presence of hydrophilic and lipophilic free radical generators. Quenching activity by DPPH was also assessed. Either YHK and sylilbin showed a significant protective effect against all challenge metal irons, as expressed by the half inhibition concentration (IC50) of the compound against lipid peroxidation and MDA formation. However, YHK seemed to be more effective than sylibin in Fe-induced peroxidative damage ($p<0.05$). Both test compounds, irrespective of the concentration, significantly reduced the LDH and b-galactosidase concentration in lysosomal fractions. As compared to untreated lysosomal fractions challenged with the two peroxide radicals generators, either YHk and sylibin exerted a significant protection. Both compounds showed a comparably significant DPPH radical-scavenging activity. These data support the potential clinical application of this novel natural compound in clinical practice.