باللغة الانجليزية:

Apoptosis signal-regulating kinase 1 (ASK1), a redox-sensor mitogen-activated protein kinase kinase kinase (MAPKKK) that activates p38 MAPK pathways in oxidative stress-induced hepatotoxicity in D-galactosamine/lipopolysaccharide (D-GalN/LPS) model, is a key central pathway in which specific targeting of ASK1 deactivation is of a great therapeutic potential. We tested the effect of silibinin and vitamin E in curative and prophylactic manner of treatment on the negative modulators of ASK1, thioredoxin1 (Trx1), thioredoxin reductase1 (TrxR1), and the protein phosphatase (PP5), whereas they have previously proven to have hepatoprotective effect. Either curative or prophylactic silibinin and vitamin E groups significantly decreased ASK1 and p38 MAPK levels through increasing the gene expression of Trx1, TrxR1, and PP5 to reduce the oxidative stress as demonstrated by decreasing the levels of NADPH oxidase 4 (NOX4), TBARS and conjugated diene with a concomitant increase in the levels of GSH, CAT, and SOD. These results were confirmed by histopathology examination which illustrated progressive degenerative changes of hepatocytes such as hydropic degeneration, vacuolation, pyknosis, karyolysis, and loss of architecture of some cells in D-GalN/LPS treatment, and these features were alleviated with silibinin and vitamin E administration. In conclusion, silibinin and vitamin E decreased ASK1-p38 MAPK pathway through deactivating the upstream signalling ASK1 molecule via increasing the levels of Trx1 and TrxR1 as well as the PP5 to alleviate in D-GalN/LPS induced hepatotoxicity.

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