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Ga-mi-Yuk-Mi-Jihwang-Tang Ameliorates LPS-injected acute Liver Injury via Regulation of Sirtuin6 in Inflammasome Triggered-pyroptosis Using Mice Model

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Excessive endogenous endotoxin, especially lipopolysaccharide (LPS) reflux from gastrointestinal (GI) tract to the liver tissue is one of the most serious reasons of severe and acute liver injury which is mainly mediated by Kupffer cell activations. However, there is no clear molecular clues to explain the exact pathophysiological mechanism and effective drugs available till nowadays. We aimed to comprehend the pathophysiological features of LPS-induced liver injury and evaluate the efficacies of potential therapeutic drug, Ga-mi-Yuk-Mi-Jihwang-Tang (GYM), which is composed of herbal plants. GYM remarkably caused to normalize hepatic inflammation and oxidations against LPS-induced liver injury by evidence of serum liver enzymes, histopathological analysis, both hepatic protein and gene expression levels of pro-inflammatory cytokines, nitric oxide levels, and hepatic tissue levels of reactive oxygen species (ROS) levels, malondialdehyde (MDA), and 4-hydroxyneoneal, respectively. To assess molecular events in the hepatic tissue, we further found hepatic Sirtuin6 (Sirt6) levels were considerably depleted by LPS injection with aberrant alterations of Nrf2/HO-1 signaling pathways, whereas administration with GYM notably exerted to normalize these abnormalities. Our results exhibited that GYM would be one of target drug to diminish hepatic inflammation as well as oxidative stress by regulation of hepatic Sirt6 levels.

Key words: Hepatic inflammation, oxidative stress, herbal medicine, Inflammasome, Sirtuin6

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