

Abstract

Hepatotoxicity is an intricate process, particularly in the context of liver diseases, often aggravated by gut microbiota dysbiosis. The gut-liver axis has been regarded as a key idea in liver health. It indicates that changes in gut flora caused by various hepatotoxicants can affect the balance of the gut's microflora, which may lead to increased dysbiosis and intestinal permeability. As a result, bacterial endotoxins would eventually enter the bloodstream and liver, causing hepatotoxicity and inducing inflammatory reactions. Many treatments, including liver transplantation and modern drugs, can be used to address these issues. However, because of the many side effects of these approaches, scientists and medical experts are still hoping for a therapeutic approach with fewer side effects and more positive results. The current work examined the hepatoprotective potential of two probiotic strains, *Lactobacillus rhamnosus* + *Saccharomyces boulardii*, against hepatotoxicity in mice induced by thioacetamide. Mice (60) were divided into 08 groups. Group III, IV and V are positive control groups, which were given Silymarin, *Lactobacillus rhamnosus* + *Saccharomyces boulardii*, Silymarin+ *Lactobacillus rhamnosus* + *Saccharomyces boulardii* respectively. Group II was administrated with thioacetamide (TAA) for two weeks to induce hepatotoxicity and then after two weeks, mice (25) were further divided into four subgroups IIA, IIB, IIC and IID, treated with TAA, Silymarin, *Lactobacillus rhamnosus* + *Saccharomyces boulardii*, Silymarin+ *Lactobacillus rhamnosus*+*Saccharomyces boulardii* respectively. The biochemical analysis showed a higher level of biomarkers i.e., ALAT (256.4 ± 4.7 U/L), ASAT (538.4 ± 7.0 U/L), AFP (93.0 ± 3.2 ng/ml), ALP (414.0 ± 6.0 U/L), LDH (1013.4 ± 5.2 U/L), GGT (51.0 ± 2.0 U/L), Total bilirubin (9.20 ± 0.1 mg/dL), MDA (11.0 ± 0.2 mmol/l), TNF- α (48.6 ± 2.1 pg/ml), IL-6 (33.2 ± 1.20 pg/ml), TGF- β 1 (33.2 ± 1.6 ng/ml) and low levels GSH (2.6 ± 0.1 umol/l), Catalase (99.2 ± 3.1 mmol/l), GPx (102.0 ± 2.2 U/L) and SOD (107.0 ± 4.8 U/ml), in the group that received TAA, indicating that the mice had developed hepatotoxicity. But lower biomarker levels i.e., ALAT (141.20 ± 5.20 U/L), ASAT (538.4 ± 7.0 U/L), AFP (57.82 ± 1.51 ng/ml), ALP (245.0 ± 6.7 U/L), LDH (557.6 ± 7.9 U/L), GGT (33.0 ± 1.21 U/L), Total bilirubin (6.7 ± 0.1 mg/dL), MDA

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(6.2 ± 0.1 mmol/l), TNF- α (33.0 ± 1.0 pg/ml), IL-6 (20.4 ± 0.9 pg/ml), TGF- β 1 (19.6 ± 1.2 ng/ml) and higher levels of GSH (4.8 ± 0.1 μ mol/l), Catalase (154.0 ± 3.2 mmol/l), GPx (145.4 ± 3.7 U/L) and SOD (130.6 ± 4.4 U/ml) were observed in treatment group with Silymarin+ Lactobacillus rhamnosus+ Saccharomyces boulardii. The liver from the TAA-treated group's histological examination revealed hyperplasia of Kupffer cells, a damaged central vein, and persistent inflammation. But in the treatment group with Silymarin+ Lactobacillus rhamnosus+ Saccharomyces boulardii, almost normal features of liver with normal central vein and normal hepatocytes were observed. It is concluded that Silymarin+ Lactobacillus rhamnosus+ Saccharomyces boulardii has great hepatoprotective potential in the prevention and treatment of hepatotoxicity.

Keywords: Hepatotoxicity, Silymarin, Thioacetamide (TAA), Probiotics, Lactobacillus rhamnosus, Saccharomyces boulardii