Abstract

Hyperlipidemia is a commonly widespread, multifactorial, prolonged, metabolic, and progressive liver abnormality affecting many people globally. While various standard hypolipidemic drugs are being utilized to alleviate the indications of hyperlipidemia, their long-term administration frequently leads to substantial adverse effects. Therefore, supportive and alternative therapies sourced from plant-based materials have proven beneficial in alleviating hyperlipidemia symptoms with negligible side effects. This research evaluates the antihyperlipidemic activity of milk thistle extract loaded basil seed hydrogel in combating hepatic hyperlipidemia induced by a high-fat diet (HFD) in mice. Hyperlipidemia was developed in swiss albino mice by feeding a HFD that was formulated by combining 1% cholesterol along with 25% lard into the standard diet. After 10 weeks, biochemical tests revealed elevated levels of cholesterol, LDL, triglycerides, IL-6, TNF-α, ASAT, ALP, and MDA, as well as a lower level of HDL in comparison to the control group, confirming the induction of the disease. Hyperlipidemia-induced groups were treated with a standard drug (15 mg/kg), basil seed hydrogel (50 mg/kg), milk thistle extract (100 mg/kg), and milk thistle extract conjugated silver nanoparticles (100 mg/kg) for 4 weeks. Sixty mice were distributed into twelve groups. Groups II, IV, V, VI, and VII served as positive control groups and were administered with standard drug (ST), basil seed (BS) hydrogel, milk thistle (MT) extract, a combination of BS and MT and a synergistic combination of BS hydrogel with MT extract nanoparticles, correspondingly. A HFD was given to Group III for ten weeks in order to cause hyperlipidemia. Afterward, the 30 mice in this group were further separated into six subgroups: IIIA, IIIB, IIIC, IIID, IIIE, and IIIF. These subgroups were treated with HFD alone, ST, BS hydrogel, MT extract, a combination of BS and MT, and BS with MT nanoparticles (BS+MTNPs), respectively. Through biochemical and histological studies, the anti-hyperlipidemic potential of these biomaterials was assessed at the end of the 14th week experiment. Lipid profile markers (HDL, LDL, total cholesterol, triglycerides), inflammatory markers (IL-6, TNF-alpha), oxidative stress markers (SOD, catalase, GSH, MDA), liver function markers (GGT, ALP, AST), metabolic markers (C-peptide, HbA1c), and a renal function marker (urea) were included in the biochemical examinations. In the HFD group, GGT (96.6 ± 3.0 U/L), ALP (343.4 ± 9.4 U/L), TNF-α

(170.9 ± 4.9 pg/mL), IL-6 (284.2 ± 5.5 pg/mL), ASAT (148.0 ± 4.2 U/L), LDL (156.8 ± 6.0 mg/dL), urea (61.8 ± 2.9 mg/dL), MDA (19.4 ± 0.2 nmol/L), cholesterol (316.4 ± 11.0 mg/dL), triglycerides (174.0 ± 2.2 mg/dL), and HbA1c (12.0 ± 0.5%) were all significantly elevated compared to the control group. Conversely, GSH (5.9 ± 0.4 µmol/L), HDL (29.2 ± 1.4 mg/dL), SOD (76.4 ± 2.5 U/mL), catalase activity (0.6 ± 0.1 mmol/mL), and C-peptide (0.5 ± 0.1 ng/mL) were significantly decreased in the HFD group relative to controls. In the BS + MTNPs (T) group, levels of GSH (15.4 ± 1.1 µmol/L), SOD (169.2 ± 12.4 U/mL), catalase activity (4.1 ± 0.1 mmol/mL), C-peptide (4.1 ± 0.1 ng/mL), and HDL (56.2 ± 2.2 mg/dL) were all significantly increased compared to the HFD group. Conversely, significant reductions were observed in GGT (55.0 ± 1.7 U/L), ALP (170.4 ± 6.4 U/L), TNF-α (63.8 ± 2.0 pg/mL), IL-6 (102.0 ± 4.1 pg/mL), ASAT (57.4 ± 3.2 U/L), LDL (76.2 ± 1.4 mg/dL), urea (30.8 ± 2.6 mg/dL), MDA (6.6 ± 0.2 nmol/L), cholesterol (158.0 ± 4.0 mg/dL), triglycerides (121.8 ± 1.6 mg/dL), and HbA1c (7.4 ± 0.2%) relative to the HFD group. Hepatic cell edema and disruption of normal liver lobule structure are caused by acute microvesicular steatosis and fat deposition in the hepatic tissue of the HFD group. This results in central vein congestion, sinusoidal constriction, and nuclear displacement. In addition, severe inflammatory cell infiltration shows both chronic liver inflammation and liver damage, which impairs hepatic function. However, the administration of hydrogel derived from basil seeds combined with milk thistle extract nanoparticles in a synergistic manner significantly enhanced liver structure by reducing fat deposition, hepatocyte swelling, and inflammation, consequently restoring a healthy hepatic structural organization and function. It has been established that the synergistic combination of milk thistle extract nanoparticles and basil seed hydrogel has a great deal of hepatoprotective potential in reducing liver damage induced by a high-fat diet.

Key words: Hyperlipidemia, High-fat diet, Statin, Milk thistle, Basil seed, Hydrogel