The aim of this study was to evaluate the role of γ-lipoic acid (γ-LA) on oxidative damage and inflammation that occur in endothelium of aorta and heart while constant consumption of high-fructose corn syrup (HFCS). The rats were randomly divided into three groups with each group containing eight rats. The groups include HFCS, HFCS + γ-LA treatment, and control. HFCS was given to the rats at a ratio of 30% of F30 corn syrup in drinking water for 10 weeks. γ-LA treatment was given to the rats at a dose of 100 mg/kg/day orally for the last 6 weeks. At the end of the experiment, the rats were killed by cervical dislocation. The blood samples were collected for biochemical studies, and the aortic and cardiac tissues were collected for evaluation of oxidant-antioxidant system, tissue bath, and pathological examination. HFCS had increased the levels of malondialdehyde, creatine kinase MB, lactate dehydrogenase, and uric acid and showed significant structural changes in the heart of the rats by histopathology. Those changes were improved by γ-LA treatment as it was found in this treatment group. Immunohistochemical expressions of tumor necrosis factor α and inducible nitric oxide synthase were increased in HFCS group, and these receptor levels were decreased by γ-LA treatment. All the tissue bath studies supported these findings. Chronic consumption of HFCS caused several problems like cardiac and endothelial injury of aorta by hyperuricemia and induced oxidative stress and inflammation. γ-LA treatment reduced uric acid levels, oxidative stress, and corrected vascular responses. γ-LA can be added to cardiac drugs due to its cardiovascular protective effects against the cardiovascular diseases.