**ABSTRACT**

The pathogenesis of hepatic ischemia/reperfusion (I/R) is mediated through the generation of oxidative and nitrosative stress-induced cell injury. Hence, the present study was designed to evaluate the hepatoprotective effect of quercetin (QR) compared to N-acetylcysteine (NAC) against hepatic I/R injury in rats and to assess iNOS, eNOS and NOSTRIN protein expressions, as a possible mechanism of its hepatoprotective effect. Hepatic ischemia was surgically performed by occlusion of hepatic pedicle (hepatic artery, portal vein, bile duct) that supplies the left and medial lobes (approximately 70% of the total liver mass), for 30 minutes with a vascular clamp followed by releasing the clamp and the liver was reperfused for 30 minutes. QR-pretreatment increased eNOS protein expression with simultaneous decrease in iNOS and NOSTRIN protein expressions. It also decreased serum aspartate aminotransferase (AST), alanine aminotransferases (ALT) and hepatic myeloperoxidase (MPO) activities. In addition, it restored the depleted content of reduced glutathione (GSH) and decreased malondialdehyde (MDA) and nitric oxide (NO) levels. A notable finding is that QR alleviated I/R-induced histopathological changes. The present study illustrates the hepatoprotective effect of quercetin compared to N-acetylcysteine against ischemia/reperfusion-induced liver injury by inhibiting oxidative stress and by modulating iNOS, eNOS and NOSTRIN protein expressions.