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Protective role of intravenous macelignanagainst unilateral hind limb ischemia-reperfusion injury in a murine model

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Ischemia-reperfusion injury (I/RI) is a complex pathological process in which tissue damage caused by oxygen deprivation is further aggravated upon reoxygenation. This study aimed to investigate the protective effects and underlying mechanisms of macelignan in an experimental rat model of unilateral hind limb I/RI. Rats were divided into five experimental groups: control, sham, I/RI, and two treatment groups receiving intravenous macelignan either before ischemia (M1) or after ischemia (M2). Ischemia was induced by clamping the unilateral femoral artery for 3 hours, followed by a 3-hour reperfusion period. Macelignan was administered intravenously at a dose of 15 mg/kg: 60 minutes before ischemia in the M1 group and at the onset of reperfusion in the M2 group. Blood and tissue samples were collected for biochemical and histopathological analyses.Significant differences were observed among the groups in serum levels of alanine aminotransferase, creatinine, lactate dehydrogenase, and creatine phosphokinase-3 ($P<0.05$). Total antioxidant status (TAS) was significantly higher and total oxidant status (TOS) was significantly lower in the drug-treated groups compared to the I/RI group ($P<0.05$). Serum nitric oxide levels were significantly reduced in the M1 group ($P=0.022$). Tissue TOS and oxidative stress index (OSI) levels also differed significantly among the groups ($p<0.001$). Tissue caspase-3 levels were highest in the I/RI group and lowest in the drug-treated groups ($P=0.006$). Tumor necrosis factor-alpha (TNF-α) levels were significantly lower in the M2 group compared to the I/RI group ($P=0.004$). Our findings suggest that macelignan has a promising protective effect against I/RI induced musculoskeletal tissue damage in rats.

Keywords: Macelignan, Anwuligan, *Myristica fragrans*, nutmeg, acute hind limb ischemia-reperfusion injury.