Abstract

SAPK-JNK pathway performs a significant role in the pathogenesis of type 2 diabetes. *Balanites aegyptiaca* (BA) is used as an anti-diabetic agent in folk medicine however; its hypoglycemic mechanism is not fully elucidated. The current study aimed to evaluate the effect of crude extract, butanol, and dichloromethane fractions from BA on the stress-activated protein kinase/c-Jun N-terminal kinase (SAPK-JNK) pathway in experimental diabetic rats. Six groups of male Wistar rats were included: normal control, diabetic, diabetic rats treated with crude, butanol or dichloromethane fraction from BA (50 mg/kg BW) and diabetic rats treated with gliclazide as a reference drug for one month. Our results suggested a protective role of treatment of diabetic rats with BA against oxidative stress-induced SAPK-JNK pathway. Moreover, BA treatment produced a reduction in plasma glucose, HbA_{1c}, lactic acid, lipid profile, malondialdehyde levels and produced an increase in insulin, reduced glutathione levels, catalase and superoxide dismutase activities compared with untreated diabetic rats. Moreover, it decreased apoptosis signal-regulating kinase 1, c-Jun N-terminal kinase 1, protein 53 and increased insulin receptor substrate 1 in rat pancreas while it increased glucose transporter 4 in rat muscle. Analysis of BA extracts by LC-HRMS revealed the presence of different saponins with reported hypoglycemic effect. In conclusion, BA exerted hypoglycemic, hypolipidemic, insulinotropic and antioxidant effects. Additionally, it reduced apoptosis in pancreatic β-cells and increased glucose uptake in muscle. These results suggest that the hypoglycemic effect of BA is due to the inhibition of the SAPK-JNK pathway.

Key words: *Balanites aegyptiaca*, Diabetes, SAPK-JNK pathway, Oxidative stress, Apoptosis