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, HbA1c, 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 LCHRMS 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.