ABSTRACT

The rising prevalence of diabetes, obesity and their interconnected metabolic complications has heightened the need for therapeutic agents with diverse and synergistic mechanisms of action. This study synthesized silver nanoparticles using the ethanolic extract of *Boerhavia diffusa* L. (EBdAgNPs) and its antidiabetic and antiobesity efficacy through both *in vitro* and *in vivo* experimental models. FTIR, XRD, SEM-EDX, zeta potential analysis and UV-visible spectroscopy were used to analyze the EBdAgNPs. These results verified that the EBdAgNPs exhibit stability, a spherical morphology, a crystalline structure and reducing and capping properties. The *in vitro* assays revealed strong antioxidant potential and significant inhibition of α-amylase, α-glucosidase, protein glycation, glucose diffusion and pancreatic lipase activities. The *in vivo* studies conducted in albino rat models of diabetic, obese and obesity-associated diabetes treated with EBdAgNPs demonstrated improvements in fasting blood glucose, lipid profile, liver and kidney function markers and hematological parameters. Antioxidant enzyme activities were restored, and weight gain was attenuated in obesity models. Gene expression analysis by RT-qPCR demonstrated the normalization of PPAR-α and PPAR-γ levels, alongside a significant reduction in RBP4 expression, suggesting enhanced lipid oxidation, suppression of adipogenesis and improved insulin sensitivity. The synergistic interplay between the phytochemical constituents of *B. diffusa* and the nanoscale delivery of silver nanoparticles contributed to alleviating oxidative stress, modulating key metabolic enzymes and restoring both glucose and lipid homeostasis. Collectively, these results position EBdAgNPs as an efficient multifunctional therapeutic approach for the management of diabetes, obesity and associated metabolic disorders.

Keywords: *Boerhavia diffusa* L., Silver nanoparticles, Antidiabetic activity, Antiobesity activity, Biochemical biomarkers