Natural Compounds from Hatikana Extract Potentiate Antidiabetic Actions as Displayed by In Vivo Assays and Verified by Network Pharmacological Tools

ABSTRACT

Background. Hatikana is a traditional medicinal plant used to treat inflammation, urolithiasis, goiter, cancer, wounds and sores, gastrointestinal, tumor, tetanus, arthritis, hepatic damage, neurodegeneration, and other ailments. The goal of this study is to investigate the antidiabetic properties of Hatikana extract (HKEx) and to construct the effects of its natural constituents on the genes and biochemical indices that are connected with them. Methods. HKEx was evaluated using GC-MS and undertaken for a three-week intervention in fructose-fed STZ-induced Wistar albino rats at the doses of HKEx50, HKEx100, and HKEx200 mg/kg bw. Following intervention, blood serum was examined for biochemical markers, and liver tissue was investigated for the mRNA expression of catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD1) by RTPCR analysis. Most abundant compounds (oleanolic acid, 7α, 28-olean diol, and stigmasterol) from GC-MS were chosen for the network pharmacological assay to verify function-specific gene-compound interactions using STITCH, STRING, GSEA, and Cytoscape plugin cytoHubba. Results. In vivo results showed a significant ($P < 0:05$) decrease of blood sugar, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine kinase (CK-MB), and lactate dehydrogenase (LDH) and increase of liver glycogen, glucose load, and serum insulin. Out of three antioxidative genes, catalase (CAT) and superoxide dismutase (SOD1) were found to be few folds increased. Oleanolic acid and stigmasterol were noticed to strongly interact with 27 target proteins. Oleanolic acid interacted with the proteins AKR1B10, CASP3, CASP8, CYP1A2, CYP1A2, HMGB1, NAMPT, NFE2L2, NQO1, PPARA, PTGIR, TOP1, TOP2A, UGT2B10, and UGT2B11 and stigmasterol with ABCA1, ABCG5, ABCG8, CTSE, HMGCR, IL10, CXCL8, NR1H2, NR1H3, SLCO1B1, SREBF2, and TNF. Protein-protein interaction (PPI) analysis revealed the involvement of 25 target proteins out of twenty-seven. Cytoscape plugin cytoHubba identified TNF, CXCL8, CASP3, PPARA, SREBF2, and IL10 as top hub genes. Pathway analysis identified 31 KEGG metabolic, signaling, and immunogenic pathways associated with diabetes. Notable degree of PPI enrichment showed that SOD1 and CAT are responsible for controlling signaling networks and enriched pathways. Conclusion. The findings show that antioxidative genes have regulatory potential, allowing the HKEx to be employed as a possible antidiabetic source pending further validation.