

ABSTRACT

Diabetes mellitus is characterized by an uncontrolled increase in blood glucose. The use of medicinal plant extracts is very promising as an alternative treatment for diabetes mellitus since they show fewer side effects compared to conventional drugs. The performance of an extract can also be improved by combining it with other extracts that have similar activity. The aim of this study was to combine the leaf extracts of *Coccinia grandis* and *Blumea balsamifera* and test their antioxidant and antidiabetic properties through the mechanism of reducing oxidative stress. The extraction process was carried out by the maceration method with 70% ethanol as the solvent. The extracts were assayed using several methods in order to determine their specific and non-specific characteristics. The *in vitro* antioxidant assays were carried out spectrophotometrically. The antioxidant synergistic effect of the combination of *C. grandis* and *B. balsamifera* extracts was calculated based on the combination index (CI) value. The antidiabetic assay *in vivo* was carried out in groups of diabetic rats induced by streptozotocin (65 mg/kg b.w.) and nicotinamide (110 mg/kg b.w.). Each group was given glibenclamide (4.5 mg/kg b.w.), *C. grandis* extract (300 mg/kg b.w.), *B. balsamifera* extract (150 mg/kg b.w.), extract combinations with a ratio of 1:1 (combination 1), 1:3 (combination 2), and 3:1 (combination 3). The treatment was administered every day for 28 days. The levels of fasting blood glucose and body weight of diabetic rats were measured every week. Meanwhile, the levels of malondialdehyde and antioxidant enzymes, pancreatic histology, and insulin expression were measured on day-29th. The results showed that the extracts have a variation of phytochemical content. The combination of *C. grandis* and *B. balsamifera* extracts showed a potent antioxidant activity. It was revealed that the reducing power and the radical scavenging activity of the combined extract increased as the concentration of *B. balsamifera* extract increased. The antioxidant synergistic effects of the combination were shown at a low concentration ratio. The combination of *C. grandis* and *B. balsamifera* leaf extracts reduced fasting blood glucose levels while increasing body weight in diabetic rats. The combined extracts also significantly lowered the malondialdehyde level and increased the levels of superoxide dismutase and catalase in comparison to the diabetic rat group. Furthermore, the combined extracts exhibited β -cells regeneration in the pancreas of diabetic rats. The enhancement of insulin expression was also observed in diabetic rats treated with combined extracts. Among all the combinations, combination 2 showed the greatest effect, indicating a synergistic effect occurred.

Keywords: Antidiabetic, *B. balsamifera*, combination, *C. grandis*, synergism.