

Hypoglycemic Effects of *Gynura procumbens* Fractions on Streptozotocin-induced Diabetic Rats involved Phosphorylation of GSK3 β (Ser-9) in Liver.

Abstract

Gynura procumbens, a medicinal plant locally known as Sambung nyawa, is widely used traditionally in South East Asia as a remedy to alleviate symptoms of various ailments including diabetes mellitus. Previous investigators reported that the ethanol plant extract was hypoglycemic in streptozotocin (STZ)-induced diabetic rats and suggested the blood glucose-reducing effect could be due to *G. procumbens* mimicking insulin effects. Our present study aimed to reevaluate the hypoglycemic effect(s) of *G. procumbens* and to ascertain the involvement of glycogen synthase kinase (GSK3), a key component of insulin biosignaling in the plant activity. A cell-based assay showed that the three *G. procumbens* fractions tested did not exhibit anti-GSK3 activities. Oral administrations of hexane, ethyl acetate, n-butanol fractions of *G. procumbens* (250 mg/kg b.w.) and Glibenclamide (5 mg/kg b.w.) for 14 days in STZ-induced diabetic rats reduced blood glucose levels by 29.7%, 60.1%, 33.5% and 61.7% ($p < 0.05$), respectively compared to diabetic control. Liver glycogen contents were elevated ($p < 0.05$), following administration of the three fractions of *G. procumbens* in diabetic rats when analysed after 14 days of treatment. Western blot analysis also showed GSK3 β in the liver of *G. procumbens* fractions-treated and Glibenclamide-treated animals were phosphorylated at Ser-9. The above findings indicated that the hypoglycemic action of *G. procumbens* fractions resulted in the inactivation of GSK3 β in liver of diabetic rats. Since *G. procumbens* fractions did not exhibit GSK3 inhibitory properties, it is possible that the hypoglycemic action of the fractions observed here could be due to direct or indirect effects on upstream components of the insulin biosignaling pathway.