



**Ameliorative influence of *Euphorbia ammak* leaves
extract on streptozotocin-induced diabetes mellitus
via targeting specific immunological pathway in
mice**

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B.Sc., in Zoology & Chemistry, 2019

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Summary

Chronic hyperglycemia is a metabolic disorder defined by inadequate insulin secretion, impaired insulin action, or a combination of both, resulting in significant metabolic disturbances. If left unmanaged, uncontrolled diabetes can lead to severe complications, including coma and, in rare instances, death due to ketoacidosis or hyperosmolar syndrome (**Poznyak *et al.*, 2020**).

T2DM primarily stems from defective insulin secretion, where the production of insulin fails to meet the demands created by **IR**. The disposition index, which indicates the relationship between insulin sensitivity and secretion, is frequently low in T2DM patients, reflecting an inadequate capacity to enhance insulin production.

Research has underscored the involvement of inflammatory cytokines, including IL-1 β , IL-6, and TNF- α in T2DM. The activation of inflammatory signaling pathways, including NF- κ B, is also significant in the context of obesity and metabolic dysfunction, further impairing glucose metabolism (**Duncan & Schmidt, 2001**).

Oxidative stress plays a critical role in the pathogenesis of diabetes. Free radicals can inflict damage on cellular components, leading to tissue dysfunction and activating stress-sensitive signaling pathways. Biomarkers such as TC and MDA are utilized to evaluate oxidative stress in diabetic patients (**Chen *et al.*, 2020; Kang & Yang, 2020**).

The plasma lipid profile, which includes TC, TGs, LDL-C, VLDL-C, and HDL-C, is crucial in the pathophysiology of T2DM (**Kundu *et al.*, 2017**).

Euphorbia is a diverse genus comprising nearly 2,000 species within the Euphorbiaceae family (**Tebogo Mic *et al.*, 2020**). Historically, various Euphorbia species have been employed to treat conditions such as cancer and headaches, exhibiting pharmacological properties that include antiviral,

anticancer, antimicrobial, and antifungal effects (Villanueva *et al.*, 2015). Moreover, *Euphorbia hirta* has demonstrated a significant antidiabetic activity in various studies (Kumar *et al.*, 2010). Based on previous evidences, we hypothesize that *Euphorbia ammak* may possess antidiabetic properties.

This study examined the potential antidiabetic action of *Euphorbia ammak* ethanol extract using STZ-induced diabetic mice. The animals were divided into six groups: normal control, diabetic control, and treatment groups receiving the extract of *Euphorbia ammak* in low (250 mg/kg) and high (400 mg/kg) dosages over 21 days. Diabetes was induced by a single dose of STZ in diabetic control and treated groups, while the normal control group received citrate buffer. Treatment started three days post-STZ injection. Blood glucose, serum insulin levels (measured with ELISA kits), and plasma lipid profiles (TC, TGs, LDL-C, VLDL-C, HDL-C) were analyzed to assess hypoglycemic and antihyperlipidemic activities. Additionally, pancreatic mRNA expressions of cytokines (TNF- α , IL1- β , iNOS, MCP1 (CCL2), GLUT2) were measured by RT-PCR, and pancreatic (NF)- κ B p65 and TLR4 protein expressions were analyzed using Western Blotting technique. Oxidative stress parameters were also assessed.

The results indicated a significant reduction in blood glucose levels, NF- κ B p65, TLR4, and an improvement in lipid profiles, enhanced by reduced levels of inflammatory cytokines and GLUT2. The hypolipidemic effect was evident in the form of reduced TC, TGs, LDL-C, and VLDL-C. Serum insulin, GSH, and HDL-C levels also approached normoglycemic levels, demonstrating the considerable antidiabetic activity of *Euphorbia ammak* ethanol extract