# Oral supplementation of diabetic mice with propolis restores the proliferation capacity and chemotaxis of B and T lymphocytes towards CCL21 and CXCL12 by modulating the lipid profile, the pro-inflammatory cytokine levels and oxidative stress.

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## Abstract:

BACKGROUND: Type 1 diabetes mellitus (T1D) is a chronic autoimmune disease caused by the selective destruction of pancreatic  cells, followed by hyperglycemia, oxidative stress and the subsequent extensive impairment of immune cell functions, a phenomenon responsible for the development of chronic diabetic complications. Propolis, a natural bee product that is extensively used in foods and beverages, significantly benefits human health. Specifically, propolis exerts antioxidant, anti-inflammatory and analgesic effects that may improve diabetic complications. To further elucidate the potential benefits of propolis, the present study investigated the effect of dietary supplementation with propolis on the plasma cytokine profiles, free radical levels, lipid profile and lymphocyte proliferation and chemotaxis in a streptozotocin (STZ)-induced type I diabetic mouse model. METHODS: Thirty male mice were equally distributed into 3 experimental groups: group 1, non-diabetic control mice; group 2, diabetic mice; and group 3, diabetic mice supplemented daily with an ethanol-soluble derivative of propolis (100 mg/kg body weight) for 1 month. RESULTS: First, the induction of diabetes in mice was associated with hyperglycemia and significant decreases in the insulin level and the lymphocyte count. In this context, diabetic mice exhibited severe diabetic complications, as demonstrated by a significant decrease in the levels of IL-2, IL-4 and IL-7, prolonged elevation of the levels of pro-inflammatory cytokines (IL-1, IL-6 and TNF-) and reactive oxygen species (ROS) and altered lipid profiles compared with control non-diabetic mice. Moreover, antigen stimulation of B and T lymphocytes markedly reduced the proliferative capacity and chemotaxis of these cells towards CCL21 and CXCL12 in diabetic mice compared with control mice. Interestingly, compared with diabetes induction alone, treatment of diabetic mice with propolis significantly restored the plasma cytokine and ROS levels and the lipid profile to nearly normal levels. Most importantly, compared with untreated diabetic mice, diabetic mice treated with propolis exhibited significantly enhanced lymphocyte proliferation and chemotaxis towards CCL21 and CXCL12. CONCLUSION: Our findings reveal the potential immuno-modulatory effects of propolis, which acts as a natural antioxidant to enhance the function of immune cells during diabetes.

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