

## Effects of Nanoencapsulated Echinacea purpurea Ethanol Extract on the Male Reproductive Function in Streptozotocin-Induced Diabetic Rats

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**Abstract :** Diabetes mellitus (DM) is a major health problem that affects patients' life quality throughout the world due to its many complications. It characterized by chronic hyperglycemia with oxidative stress, which impaired male reproductive function. Fibroblast growth factor 21 (FGF21) is a metabolic regulator that is required for normal spermatogenesis and protects against diabetes-induced germ cell apoptosis. Echinacea purpurea ethanol extract (EE), which contain phenolic acid and isobutylamide, had been proven to have antidiabetic property. Silica-chitosan nanoparticles (Nano-CS) has drug delivery and controlled release properties. This study aims to investigate whether silica-chitosan nanoparticles encapsulated EE (Nano-EE) had more ameliorating male infertility by analyzing the effect of testicular FGF21. The Nano-EE was characterized before used to treatment the diabetic rat model. Male Sprague-Dawley (SD) rats were obtained and divided into seven groups. A group was no induced Streptozotocin (STZ), marked as normal group. Diabetic rats were induced into diabetes by STZ (33 mg/kg). A diabetic group was no treatment with sample (diabetic control group), and other groups were treatment by Nano-CS (465 mg/kg), Nano-EE (93, 279, 465 mg/kg), and metformin (Met) (200 mg/kg) used as reference drug for 7 weeks. Our results indicated that the average nanoparticle size and zeta potential of Nano-EE were 2630 nm and -21.3 mV, respectively. The encapsulation ratio of Nano-EE was about 70%. It also confirmed the antioxidative activity was unchanged by comparing the DPPH and ABTS scavenging of Nano-EE and EE. In vivo test, Nano-EE can improve the STZ induced hyperglycemia, insulin resistance, and plasma FGF21 levels. Nano-EE has increased sperm motility, mitochondria membrane potential (MMP), plasma testosterone level, and reduction of abnormal sperm, nitric oxide (NO), superoxide production as well as reactive oxygen species (ROS). In addition, in plasma antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase (SOD) was increased whereas pro-inflammatory cytokines TNF- $\alpha$ , and IL-1 $\beta$  were decreased. Further, in testis, protein content of FGF21, PGC-1 $\alpha$ , and SIRT1 were improved. Nano-EE might improve diabetes-induced down-regulation of testicular FGF21 and SIRT1/PGC-1 $\alpha$  signaling hence maintain spermatogenesis.

**Keywords :** diabetes mellitus, Echinacea purpurea, reproductive dysfunction, silica-chitosan nanoparticles

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