## Quercetin Nanoparticles and Their Hypoglycemic Effect in a CD1 Mouse Model with Type 2 Diabetes Induced by Streptozotocin and a High-Fat and High-Sugar Diet

**Authors :** Adriana Garcia-Gurrola, Carlos Adrian Peña Natividad, Ana Laura Martinez Martinez, Alberto Abraham Escobar Puentes, Estefania Ochoa Ruiz, Aracely Serrano Medina, Abraham Wall Medrano, Simon Yobanny Reyes Lopez

Abstract: Type 2 diabetes mellitus (T2DM) is a metabolic disease characterized by elevated blood glucose levels. Quercetin is a natural flavonoid with a hypoglycemic effect, but reported data are inconsistent due mainly to the structural instability and low solubility of quercetin. Nanoencapsulation is a distinct strategy to overcome the intrinsic limitations of quercetin. Therefore, this work aims to develop a quercetin nano-formulation based on biopolymeric starch nanoparticles to enhance the release and hypoglycemic effect of guercetin in T2DM induced mice model. Starch-guercetin nanoparticles were synthesized using high-intensity ultrasonication, and structural and colloidal properties were determined by FTIR and DLS. For in vivo studies, CD1 male mice (n=25) were divided into five groups (n=5). T2DM was induced using a high-fat and high-sugar diet for 32 weeks and streptozotocin injection. Group 1 consisted of healthy mice fed with a normal diet and water ad libitum; Group 2 were diabetic mice treated with saline solution; Group 3 were diabetic mice treated with glibenclamide; Group 4 were diabetic mice treated with empty nanoparticles; and Group 5 was diabetic mice treated with quercetin nanoparticles. Quercetin nanoparticles had a hydrodynamic size of 232  $\pm$  88.45 nm, a PDI of 0.310  $\pm$  0.04 and a zeta potential of -4  $\pm$  0.85 mV. The encapsulation efficiency of nanoparticles was  $58 \pm 3.33$  %. No significant differences (p = > 0.05) were observed in biochemical parameters (lipids, insulin, and peptide C). Groups 3 and 5 showed a similar hypoglycemic effect, but quercetin nanoparticles showed a longer-lasting effect. Histopathological studies reveal that T2DM mice groups showed degenerated and fatty liver tissue; however, a treated group with guercetin nanoparticles showed liver tissue like that of the healthy mice group. These results demonstrate that quercetin nano-formulations based on starch nanoparticles are effective alternatives with hypoglycemic effects.

**Keywords:** quercetin, diabetes mellitus tipo 2, in vivo study, nanoparticles

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