Use of nanotechnology in restoring glucose homeostasis in type 2 diabetes mellitus *in vivo* model

Recently, metabolic disorders are increasing at an alarming rate and one such example of metabolic disorder is type 2 diabetes mellitus (T2DM). Unregulated gluconeogenesis in T2DM results in increased hepatic glucose output and that causes fasting and postprandial hyperglycaemia. Extensive proofs have shown that downregulation of the key rate-limiting enzyme phosphoenolpyruvate carboxykinase-1 (PCK-1) of gluconeogenesis improved glucose homeostasis *in-vivo*.

In the present study, Scientists at National Agri Food Biotechnology Institute (NABI), Mohali have synthesized and characterized liver-specific stearic acid conjugated octaarginine (StA-R8) functionalized 4arm-2K-PEG amineylated graphene oxide nano sheets (GPR8) for the delivery of siRNA against PCK-1 in T2DM C57BL/6 mice. Scientists found that a single dose of intravenous administration of siRNA (3mg/kg BW) conjugated to GPR8 (GPR8: PCK-1siRNA (3mg/kg BW) conjugate) in an optimised N/P ratio exploited as a therapeutic nano-formulation maintained glucose homeostasis for nearly 4 weeks in T2DM mice model.

Efficient silencing of PCK-1 in T2DM liver tissue increased the phosphorylation of serine-256 of FOXO-1 thus showed a marked decrease in hepatic gluconeogenesis. Gluconeogenesis control and consequently glucose output from the liver furthermore partially enhanced liver and muscle insulin sensitivity results in the stimulation of the insulin/AKT-2 signaling pathway which indirectly restored glucose homeostasis in the treated T2DM group. Our therapeutic nano-formulation also improved glycogen storage in the liver and membrane translocation of Glut-4 in the muscle of treated T2DM group. In conclusion, GPR8: PCK-1siRNA (3mg/Kg BW) restored glucose homeostasis by controlling the hepatic glucose production and improved peripheral insulin sensitivity as a consequence of reduced hyperglycemia. Thus, offered an alternative strategy for the therapeutics for T2DM.

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