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LIPOCALIN-2 AMELIORATES THE SIGNS AND OUTCOMES OF DIABETES MELLITUS IN AN ANIMAL MODEL

by

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Abstract

Lipocalin-2 (LCN2) is a new adipocytokine consisting of 198 amino acids. It is also referred to as neutrophil gelatinase-associated lipocalin, siderocalin, uterocalin, α1-microglobulin related protein, or 24p3. LCN2 belongs to a large group of transport proteins that are capable of carrying small and lipid soluble molecules in blood circulation. It has two membrane receptors, megalin/glycoprotein GP330, which binds human LCN2 and SLC22A17 or 24p3R, which forms complexes with mouse Lcn2 protein. LCN2 is encoded by a gene located at chromosome locus 9q34.11. LCN2 was initially isolated from neutrophil granules released at site of infection and inflammation in human and from mouse kidney cells. LCN2 kills bacteria by iron depletion during antibacterial innate immune response via sequestering bacterial ferric siderophores enterobactin (Ent). It has a protective role in infection, inflammation, injury and other forms of cellular stress. In addition, it is able to interact with and stabilize matrix metalloproteinase-9 in human neutrophils. Tissue localization and the effect of LCN2 were studied in streptozotocin-induced diabetic rats using morphological, physiological, biochemical and molecular biology techniques. We showed that LCN2 is co-localized with insulin in normal and diabetic pancreatic β-cells. In addition, LCN2 significantly reduced the plasma levels of AST, ALT, ALP, bilirubin, CHOL, TG, LDL, HDL and improved the levels of total protein after the onset of diabetes. LCN2 treatment decreased the plasma levels of BUN, Urea and LIPC in diabetic animals. Moreover, the levels of insulin, C-peptide, amylin and GIP were significantly increased in diabetic rats treated with LCN2. Furthermore, LCN2 showed a significant antioxidant activity by increasing GSH, SOD and CAT levels in pancreatic tissue of normal and diabetic animals, as well as their levels in the serum. In vitro observations show that LCN2 at a concentration of 10^{-8} M and 10^{-12} M caused large and significant increases in insulin release from the INS-1 rat insulinoma cell line.

In conclusion, LCN2 ameliorates the acute and chronic complications of diabetes mellitus and appears to be a promising adjuvant therapy in the management of DM.

Keywords: Diabetes mellitus, irisin, metabolic parameters, rat, hormones, electron microscopy.