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Mechanistic Insights into the Role of Vitamin D as a Key Modulator of Insulin Sensitivity

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Vitamin D deficiency significantly increases insulin resistance and type 2 diabetes risk, yet the precise underlying pathways remain incompletely understood. This mechanistic analysis represents a focused component of a comprehensive review article derived from PubMed database literature published between 1995-2021 using keywords: vitamin D, insulin resistance, diabetes, glucose metabolism, and related terms. Findings from animal experiments, human clinical trials, and in vitro studies were evaluated to elucidate key pathways through which vitamin D enhances insulin sensitivity. Vitamin D modulates insulin sensitivity through multiple interconnected mechanisms including upregulation of insulin-sensitising hormones such as adiponectin and leptin, enhancement of insulin receptor expression through calcitriol-VDR-RXR complex formation and binding to vitamin D response elements in insulin receptor gene promoters, amplification of PI3K-dependent insulin signalling pathways through insulin receptor substrate protein phosphorylation, modulation of FoxO1 expression which serves as a critical negative regulator in insulin signalling cascades, upregulation of glucose transporter GLUT1 and GLUT4 expression and translocation through SIRT1 activation pathways, and maintenance of optimal intracellular calcium concentrations essential for insulin- mediated glucose uptake processes. These coordinated mechanisms demonstrate vitamin D's role as a key modulator of glucose homeostasis through direct effects on hormone secretion, receptor expression, intracellular signalling pathways, and cellular glucose transport systems. The multi-targeted approach of vitamin D action provides mechanistic foundation for supplementation strategies in preventing insulin resistance and suggests significant therapeutic potential for managing metabolic disorders through restoration and maintenance of adequate vitamin D status.

Keywords: Diabetes, Glucose Metabolism, Insulin Sensitivity, Vitamin D

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