

## The Gut-Liver Balance of Metformin



Metformin, a commonly prescribed drug for treating type 2 diabetes, remains an enigma even after decades of use. A recent review published in Trends in Pharmacological Sciences sheds light on how metformin interacts with the liver and gut to decrease circulating glucose levels.

The study, led by Professor Manuel Vázquez-Carrera, Faculty of Pharmacy and Food Sciences, University of Barcelona, the Institute of Biomedicine of the UB (IBUB), the Sant Joan de Déu Research Institute (IRSJD), and the Diabetes and Associated Metabolic Diseases Networking Biomedical Research Centre (CIBERDEM), explores how metformin works to reduce glucose production.

Type 2 diabetes is a metabolic disorder. It is characterised by excessive glucose levels in the bloodstream. This is typically due to the body's inadequate response to insulin or insufficient insulin production. Metformin is used to combat this by reducing blood glucose levels and improving peripheral circulation.

The liver is believed to be the primary site of metformin's action. However, recent findings confirm that metformin also significantly affects the gut. Prof Vázquez-Carrera explains that recent studies have focused on these two organs - the liver and the gut - because that is where metformin's actions appear most important.

The review highlights a recent discovery that metformin increases the levels of miRNA let-7 in the liver. This microRNA is involved in various physiological functions and is important in reducing hepatic glucose production, the main contributor to elevated glucose levels in patients with type 2 diabetes. Hence, it is possible to activate the expression of miRNA let-7 as a novel strategy for treating diabetes mellitus.

The effects of metformin on the intestine have also been explored. Another recent study shows that metformin activates the conversion of glucose to lactate and acetate in the intestine. These metabolites then reach the liver via the portal vein and initiate processes that further reduce hepatic glucose production. This interaction between the intestine and the liver establishes a connection that contributes to metformin's antidiabetic mechanism of action.

These recent findings and the review help unravel longstanding questions regarding metformin's specific mechanism of action and provide insights into how this drug reduces hepatic glucose production.

Source: University of Barcelona

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