Treatment for Type II Diabetes

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Technology description

Biomarkers of metformin efficacy and methods related to Type II diabetes
Invention
The present invention provides methods, compositions, and related uses for the interaction between metformin and methylglyoxal. In addition, this invention provides methods for detecting the efficacy of metformin therapy while exploring the metformin-MG reaction, unequivocally determining the structure of the product formed, and developing an assay for high-throughput analysis of samples from metformin-treated Type II diabetes patients.
Background
Reactive dicarbonyls such as methylglyoxal accumulate in diabetic patients due to elevated glucose as well as increased oxidative stress. These toxic dicarbonyls directly damage proteins through adduction at arginine residues on proteins (advanced glycation end products [AGEs]) and are implicated in the progression of a number of Type II diabetic complications including cardiovascular disease (CVD). Metformin is a first-line diabetic therapy that is used primarily because of its potent, anti-hyperglycemic effects with little adverse side effects from the drug. The drug has been linked to decreased AGE products in humans but the mechanism behind this link is yet to be elucidated. There is currently no therapy for directly reducing concentrations of these compounds in humans. Direct scavenging by metformin of dicarbonyls has not been thoroughly studied despite its prevalence as a theory for decreased AGEs.

Application area

Treatment of Type II diabetes in the form of a multiple reaction monitoring (MRM) assay for the identification and quantitation of derivatized methylglyoxal (2MQ) levels in patient samples

Advantages

Levels of the MF-MG adduct are detectable up to 4.32 μM
Successfully detects the quinoxaline derivative of methylglyoxal (2MQ) at a range of 0.01 μM to 5.5 μM without reaching saturation by our MRM method
Detects levels of 2MQ in urine samples from human diabetic subjects on metformin treatment within our range of calibration

Demonstrates the existence of a strong positive correlation between IMZ (the MF-MG product) and metformin levels in patient urine
Determines which arginine residues appeared to be readily modified by MG and which were most sensitive to adduction

Institution

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