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Trigonella foenum-graecum seed extract, 4-hydroxyisoleucine and metformin stimulate proximal insulin signaling and increases expression of glycogenic enzymes and GLUT2 in HepG2 cells

Nikita Naicker
University of KwaZulu-Natal, South Africa

Fenugreek (*Trigonella foenum-graecum*) is globally recognized for its medicinal properties and hypoglycaemic effects. The seed extractas well as its active compound, 4-hydroxyisoleucine (4-OH-lle), have been shown to reduce hyperglycaemia insulin resistance. The mechanism by which this occurs has not been investigated in human liver cells (HepG2) in comparison to the anti-hyperglycaemic drug, metformin. We investigated the effect of fenugreek aqueous seed extract (FSE), 4-OH-lle and metforminin human hepatoma HepG2 cellsrelative to insulin as a positive control. Cells were treated with FSE and 4-OH-lle at 10 ng/ml and 100 ng/ml under normoglycaemic (5 mM glucose) and hyperglycaemic (30 mM glucose) conditions for 72 h. Tyrosine phosphorylation of insulin receptor-β (IR-β), protein kinase B (Akt) and glycogen synthase kinase-3α/β (GSK-3α/β) was determined by western blotting. Gene expression of sterol regulatory element binding protein 1c (SREBP1c), glucose transporter 2 (GLUT2), glycogen synthase (GS) and glucokinase (GK) was evaluated by qPCR and supernatant glucose levels were measured using the Picollo Biochemistry Analyser. Under normo- and hyperglycaemic conditions, FSE, 4-OH-lle, insulin (100 ng/ml) and metformin (2 mM) caused a significant increase in tyrosine phosphorylation of IR-β, Akt and GSK-3α/β. Glucose uptake, however, was most significantly increased in FSE treated cells during normo-and hyperglycaemic conditions. FSE induced the most significant changes in downstream insulin signaling, GS, GK, SREBP1c and GLUT2 expression as compared to 4-OH-lle, metformin and insulin. Also, FSE significantly increased glucose uptake. Collectively, these findings provide a mechanism by which FSE exerts anti-hyperglycaemic effects similar to metformin and insulin occurs via enhanced insulin signaling, gene expression and increasing glucose uptake.

Biography

Nikita Naicker has completed her undergraduate degree in Biomedical Sciences, Honours degree in Medical Biochemistry and Masters in Medical Science (Medical Biochemistry) from the University of KwaZulu Natal (UKZN). She is currently in her first year of PhD at UKZN. She has currently submitted a manuscript to the *Journal of Phytomedicine*.

nikita.naicker@gmail.com

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