Antidiabetic activities of cucurbitane triterpenoids from the fruits of *Momordica charantia* in streptozotocin-induced diabetic mice

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Improvement of insulin sensitivity can be effective against uncontrolled type 1 as well as type 2 diabetes. Because insulin sensitizers have limitations, there is growing interest in development of new bioactive agents. This study investigated how new cucurbitane-type triterpenoids isolated from the fruits of *Momordica charantia* affected insulin sensitivity both in vitro and in vivo, and the underlying mechanisms.

Four compounds (C1-C4) isolated from an ethanol extract of *M. charantia* enhanced glucose uptake in C2C12 myotubes via insulin receptor substrate-1 (IRS-1) and protein kinase B (Akt). The most potent, compound 2 (C2), significantly increased activation of insulin receptor substrate-1 (IRS-1) and downstream signaling pathway, thus subsequent glucose transporter 4 (GLUT4) translocation. Intravenous administration of C2 to normal and streptozotocin-induced diabetic mice resulted in significant blood glucose-lowering and glycogen-storage effects through the IRS-1 signaling pathway in skeletal muscle but not adipose and liver tissues, indicating that C2 improves hyperglycemia by increasing glucose uptake into skeletal muscle.

These findings suggest the new cucurbitane-type triterpenoids may be useful for the prevention and management of diabetes by improving insulin sensitivity and glucose homeostasis.