

# Abstract

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## Chromium supplementation enhances insulin signalling in skeletal muscle of obese KK/HIJ diabetic mice.

Chen WY, Chen CJ, Liu CH, Mao FC.

Department of Veterinary Medicine, National Chung Hsing University, Taichung, Taiwan.

**AIM:** Chromium is an essential nutrient required for glucose and lipid metabolism. Laboratory and clinical evidences indicate that chromium supplementation may improve insulin sensitivity by enhancing intracellular signalling. Considerable evidence suggests that serine phosphorylation of insulin receptor substrate 1 (IRS1) at 307 residue (IRS1-Ser307) inhibits insulin signalling and results in peripheral insulin resistance. Therefore, we investigated whether chromium-associated insulin action was mediated by modulation of IRS1-Ser307 phosphorylation.

**METHODS:** Male KK/HIJ mice (genetically obese and insulin resistant) were supplemented daily with chromium-containing milk powder or placebo for 7 weeks. In analysing functionally characterized insulin resistance, the changes of blood biochemicals, inflammatory factors and insulin signalling molecules in skeletal muscle were analysed.

**RESULTS:** Using KK mice model, we demonstrated that daily supplementation of trivalent chromium-containing milk powder reduced serum levels of glucose, insulin and triglycerides, and improved glucose and insulin tolerance. Mechanistic study showed that chromium supplementation activated postreceptor insulin signalling such as increasing IRS1, IRS1 tyrosine phosphorylation, p85alpha regulatory subunit of phosphatidylinositol 3-kinase and glucose transporter 4 expression, stimulating Akt activity, downregulating c-Jun N-terminal kinase (JNK) activity and decreasing IRS1 ubiquitination and insulin resistance-associated IRS1 phosphorylation (IRS1-Ser307) in skeletal muscle. In addition, chromium supplementation attenuated pro-inflammatory cytokine expression in both blood circulation and skeletal muscle.

**CONCLUSION:** Our data suggest that chromium-containing milk powder supplementation can provide a beneficial effect in diabetic subjects by enhancing insulin signalling in skeletal muscle. The improvement in insulin signalling by chromium was associated with the decreased IRS1-Ser307 phosphorylation, JNK activity and pro-inflammatory cytokine production.

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