

Targeting obesity with Cucurbitacins: Role of JAK-STAT signaling pathway

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Obseity epidemic is swiftly sweeping across the world with currently 600 million individuals obese and 1.9 billion adults overweight. JAK-STAT signaling regulates adipose tissue development and physiology at transcriptional level. Cucurbitacin compounds have been classified as inhibitors of JAK-STAT. In this study, we have analyzed the therapeutic potential of novel cucurbitacins in reducing obesity and related metabolic dysfunctions. We monitored the effects of several cucurbitacins on adipogenesis and glucose uptake in fat cells. Selected cucurbitacins were found to be potent inhibitors of adipogenesis. In diet induced obese mice model, inhibitory effects of cucurbitacins on fat depots were observed with significant reduction in visceral obesity. Increase in adiponectin and reduction in leptin and TNF- α concentration were also detected in mice. Cucurbitacins mediated these effects by reducing JAK-STAT signaling in visceral fat and muscles of mice. Cucurbitacins also enhances insulin signaling in obesity induced insulin resistant mice muscles by reducing serine phosphorylation of IRS-1 and JAK activity and enhancing activity of AKT/PKB and AMPK. Potential of cucurbitacins in targeting energy expenditure was assessed through reduction in weight of brown fat and gene expression of UCP-1. Improvement in dyslipidemia was also evident. In conclusion, our results suggest that cucurbitacins are potential therapeutic compounds for combating obesity and related metabolic complications.

Biography

Munazza Murtaza is currently pursuing her PhD in Molecular Medicines from International Center for Chemical and Biological Sciences, Karachi, Pakistan. Her Bachelor's degree was in Clinical Laboratory Sciences with specialization in molecular diagnostics techniques. She along with her colleagues is involved in targeting therapeutic aspects of metabolic syndrome, obesity and diabetes through natural or synthetic plant extracts and compounds.

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