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Master Thesis Defense

Entitled

IN VITRO INVESTIGATION OF THE EFFECT OF CAMEL MILK PROTEINS AND ITS FRACTIONS ON INSULIN RECEPTOR FUNCTION

By
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Abstract

Camel milk has been reported to have anti-diabetic properties in many in vitro and in vivo studies but the molecular basis of such beneficial properties are still elusive. Recently, camel milk whey proteins (CMWPs) have been shown to positively affect the activity of the human insulin receptor (hIR) in cell lines. In this study, we profiled crude CMWPs and their hydrolysates as well as camel milk lactoferrin (CMLF) for their pharmacological and functional effects on hIR activity and its downstream signaling in both human embryonic kidney (HEK293) and hepatocarcinoma (HepG2) cell lines. For this, bioluminescence resonance energy transfer (BRET) technology was used to assess hIR activity in live cells and the phosphorylation status of the downstream protein kinase B (Akt) and the extracellular signal-regulated kinases (ERK1/2) was also analyzed in parallel. Moreover, glucose uptake was examined in order to link our data to more integrated cell response and to the hypoglycemic effects of camel milk. Our data clearly demonstrate the biological activity of CMWPs, their hydrolysates, and CMLF, by promoting Akt and ERK1/2 phosphorylation in both HEK293 and HepG2 cells. In addition, our BRET assay confirmed the positive pharmacological action of CMWPs and their hydrolysates on hIR activity in a dose-dependent manner. More interestingly, the combination of CMWPs and their hydrolysates with insulin revealed an allosteric modulation of hIR that was drastically abolished by the competitive hIR-selective peptide antagonist S691. This clearly demonstrates the implication of hIR activation in the effects of CMWPs and their hydrolysates. Finally, such effects on BRET data and kinase phosphorylation were nicely correlated with an increase in glucose uptake in HepG2 cells. Our data reveal the pharmacological effects of camel milk proteins on hIR activity and function. This provides for the first time the molecular basis of the anti-diabetic properties of camel milk that was unknown until now.

Keywords: Camel milk, Diabetes, Insulin receptor, Insulin, Glucose