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The Molecular Basis of the Anti-Diabetic Properties of Camel Milk

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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 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 hIR and its key downstream signaling proteins, 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 and their hydrolysates, by promoting hIR, 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. Finally, such effects on BRET and kinase phosphorylation were nicely correlated with an increase in glucose uptake in HepG2 cells. This clearly demonstrates the implication of hIR activation in the effects of CMWPs and their hydrolysates. 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.

Recent Publications

1. Ali A, Palakkott A, Ashraf A, Al Zamel I, Baby B, Vijayan R, and Ayoub MA*. Positive Modulation of Angiotensin II Type 1 Receptor-Mediated Signalling by LVV-Hemorphin-7. Front. Pharmacol. 10:1258. doi: 10.3389/fphar.2019.01258.
2. Ayoub MA*, Palakkott A, Ashraf A, and Iratni R. The Molecular Basis of the Anti-Diabetic Properties of Camel Milk. Diabetes Res Clin Pract. 2018 Nov 16;146:305-312
3. Riccetti L, Yvinec R, Klett D, Gallay N, Combarnous Y, Reiter E, Simoni M, Casarini L, and Ayoub M.A*. Human Luteinizing Hormone and Chorionic Gonadotropin Display Biased Agonism at the LH and LH/CG Receptors. zScientific Reports. 2017 Apr 19; 7(1):940
4. Ayoub M.A*. Small molecules targeting heterotrimeric G proteins. Eur J Pharmacol. 2018 Mar 6; 826:169-178
5. Ayoub M.A*, Crépieux P, Koglin M, Parmentier M, Pin J.P, Poupon A, Reiter E, Smit M, Steyaert J, Watier H, and Wilkinson T. Antibodies Targeting G Protein-Coupled Receptors: Recent Advances and Therapeutic Challenges. MAbs. 2017 Jul; 9(5):735-741

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