

A natural compound ameliorates hepatic steatosis through regulation of lipid metabolism *in vitro*

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Abstract:

Non Alcoholic Fatty Liver Disease (NAFLD) is the most common liver disorder, characterized by an accumulation of lipid droplets (LDs) in approximately 5% of hepatocytes. This is a reversible condition that may evolve in more severe and irreversible pathologies such as non-alcoholic steatohepatitis (NASH), cirrhosis and hepatocellular carcinoma [1,2]. Lipophagy and lipolysis play a key role in the balance between lipid storage and utilization.

In my thesis project, I am studying a natural compound purified from the leaves of *Glycyrrhiza glabra*, which is able to stimulate the AMP-activated protein kinase (AMPK) and protein kinase PKA, two key regulators of lipid metabolism [1,2].

We use HepG2 cells as an *in vitro* model of steatotic hepatocytes by administering oleate and palmitate to induce LDs accumulation. The effect of this natural compound on lipid catabolism, considering relevant pathways including lipophagy and lipolysis, will be evaluated by western blot analysis and by quantifying the number and the volume of LDs through fluorescence microscopy.

Our results suggest that the protective effect of this compound may involve the activation of lipolysis in a PKA-dependent manner and of lipophagy in an AMPK-dependent manner. Further studies are ongoing to deeply understand the mechanism of action of this compound and the crosstalk between lipolysis and lipophagy in this context.

[1] Mastoridou, E.M.; Goussia, A.C.; Kanavaros, P.; Charchanti, A.V. Involvement of Lipophagy and Chaperone-Mediated Autophagy in the Pathogenesis of Non-Alcoholic Fatty Liver Disease by Regulation of Lipid Droplets. *Int. J. Mol. Sci.* **2023**, *24*, 15891.

[2] Kim, J.-H.; Sim, H.A.; Jung, D.Y.; Lim, E.Y.; Kim, Y.T.; Kim, B.J.; Jung, M.H. *Poria cocos* Wolf Extract Ameliorates Hepatic Steatosis through Regulation of Lipid Metabolism, Inhibition of ER Stress, and Activation of Autophagy via AMPK Activation. *Int. J. Mol. Sci.* **2019**, *20*, 4801.