Amphibian skin peptide macrotympanain A1 powerfully reduces lipid accumulation in a cellular model of hepatic steatosis

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Macrotympanain A1 (MA1) is an amphibian skin peptide displaying significant anti-oxidant and anti-inflammatory abilities, which are useful for amphibian skin protection and health. Evidence suggests that amphibian skin peptides exert various biological effects also in mammalian cells. In this work, we demonstrate a lipid-lowering activity of MA1 in a cellular model of hepatic steatosis and begin to investigate a possible mechanism of action of MA1 on liver cells.

MA1 (FLPGLECVW) was synthetized using the standard method of solid phase peptide synthesis, which follows the Fmoc strategy. Rat hepatoma FaO cells were made steatotic by incubation with oleate/palmitate mixture for 3 h, and then exposed to 10 µg/mL MA1 for 24 h. The lipid extracts of cells were analysed by TLC and MALDI-TOF/MS. Expression of PPAR (Peroxisome Proliferator Activated Receptor) isoforms, that play an important role in lipid homeostasis, was evaluated by qPCR. MA1 effects on intracellular signal transduction pathways was evaluated by western blotting.

The results show that MA1 was able to significantly reduce the content of triacylglycerols and cholesterol-esters in steatotic cells, whereas the polar lipid profile was not altered.

The anti-steatotic effect of MA1 was associated with modulation of *Pparg* expression and of PI3K and ERK/MAPK signaling pathways.

Experiments are in progress in order to better understand the lipid lowering mechanisms triggered by MA1 on mammalian liver cells.

KEY WORDS: amphibian skin peptides, hepatic steatosis, signal transduction