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Sphingosine 1-phosphate mediated suppression of leptin secretion in rat adipocytes.

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Sphingosine 1-phosphate is a metabolite of complex sphingolipids that acts as both a second messenger and as a high-affinity ligand for cell surface receptor. Since the possible involvement of sphingosine 1-phosphate has not been investigated in adipocyte, we examined the response of intracellular calcium ($[Ca^{2+}]_i$) and intracellular cAMP ($[cAMP]_i$) and the effect of sphingosine 1-phosphate on adipocyte function using rat primary adipocyte. 3 and 30 microM S1P significantly inhibited insulin mediated leptin secretion for 24 hours in adipocyte. S1P obviously increased $[Ca^{2+}]_i$ and $[cAMP]_i$ in a dose-dependent manner, interestingly but show distinct dose profiles which half-maximum effective concentrations (EC50) of SPP was about 30nM and 30uM respectively. Pertussis toxin, a G(i) protein inhibitor, significantly attenuated the elevation of $[Ca^{2+}]_i$ induced by S1P, however potentiated the elevation of $[cAMP]_i$. 30 microM U73122 (phospholipase C inhibitor) completely blocked S1P-induced $[Ca^{2+}]_i$, but did not affects in $[cAMP]_i$. pretreatment with 10uM GF109203X significantly attenuated S1P-mediated $[cAMP]_i$. Since known that EDG receptors are not coupled to Gs, It is considered that the distinct effects of SPP was mediated through a G(i)protein coupled membrane receptor and a PLC-independent / PKC-sensitive adenylyl cyclase responsible for SPP induced $[cAMP]_i$ generation, may be involved in inhibition of leptin secretion by insulin.