**delta-Iodolactones decrease epidermal growth factor-induced proliferation and inositol-1,4,5-trisphosphate generation in porcine thyroid follicles--a possible mechanism of growth inhibition by iodide.**

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**Source**
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**Abstract**

delta-Iodolactone (6-iodo-8,11,14-eicosatrienoic delta-lactone, delta-IL), an iodinated derivative of arachidonic acid, has been shown to be synthesized in thyroid tissue and to inhibit thyroid cell proliferation. It is discussed as a potential mediator of the autoregulatory pathway of iodide in cyclic adenosine-3',5'-monophosphate (cAMP)- and thyrotropin (TSH)-independent growth. We therefore further localized the action of iodide and of delta-IL in isolated porcine thyroid follicles. Epidermal growth factor (EGF) and 12-O-tetradecanoylphorbol-13-acetate (TPA) dose dependently stimulated thyroid cell proliferation, which could be inhibited by staurosporin (0.1-10 nmol/l). Iodide (2.5-40 mumol/l) as well as delta-IL (0.5-2 mumol/l) also dose dependently inhibited EGF- and TPA-induced proliferation. As the calcium ionophor A23187 (100 pmol/l) completely abolished the inhibitory effects of iodide and of delta-IL, this may indicate a mechanism of delta-IL at or proximal to the calcium-dependent activation of protein kinase C. The growth inhibitory effect was restricted to delta-iodolactones when delta-IL was compared to 6-iodo-8,11,14,17-eicosatetraenoic delta-lactone and 5-iodo-7,10,13,16,19-docosapentaenoic gamma-lactone. It could not be prevented with propylthiouracil and therefore deiodination and a different iodide action is unlikely. Inositol-1,4,5-trisphosphate (IP3) and cAMP were measured in extracts from isolated porcine thyroid follicles stimulated with EGF (10 ng/ml) or TSH (1.0 U/l) revealing comparable kinetics in IP3 generation, while cAMP formation was only stimulated by TSH. delta-Iodolactone (2 mumol/l) only decreased EGF-induced IP3 formation, whereas TSH-induced IP3 and cAMP formation was unchanged.(ABSTRACT TRUNCATED AT 250 WORDS)