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Metabolism and function of myo-inositol and inositol phospholipids.

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Abstract

Alterations in the level of dietary inositol can significantly influence the concentration of free inositol and inositol-containing phospholipid in the circulation and in selected mammalian tissues and cells. The 1-stearoyl 2-arachidonyl molecular species that commonly predominates in cellular phosphoinositides may be of considerable importance for the functioning of these phospholipids in biological membranes. Retailoring reactions subsequent to the de novo biosynthesis of PI involving the acylation of lyso(1-acyl) PI allow for the preferential enrichment of this phospholipid in arachidonic acid. The impaired release of plasma lipoprotein, increased fatty acid mobilization from adipose tissue, and enhanced fatty acid synthesis in liver have all been implicated as causative factors in the hepatic triacylglycerol accumulation occurring with experimental inositol deficiency. The severe intestinal lipodystrophy that develops in female gerbils consuming inositol-deficient diets is likely mediated by a reduced synthesis of PI and the associated impairment of chylomicron assembly and secretion. Membrane PI can potentially regulate enzyme activities and transport processes as well as providing a source of free arachidonic acid for production of the eicosanoids. There has been mounting evidence recently to indicate that an accelerated turnover of the phosphoinositides may play a key role in mediating cellular responses to external stimuli. The transient rise of phosphoinositide-derived 1,2-diacylglycerol in stimulated cells may serve as a signal for the transmembrane control of protein phosphorylation by activating protein kinase C. Receptor occupancy also elicits the phosphodiesterase-catalyzed release of the second messenger inositol 1,4,5-trisphosphate, which appears to provide for the mobilization of calcium from internal stores. Subnormal levels of free inositol and inositol phospholipid, as found in the nerves of animals with experimental diabetes and in sciatic nerves removed postmortem from diabetic patients, have been implicated in the impaired nerve conduction of human diabetics. Patients with renal failure exhibit a dramatic hyperinositolemia that may have clinical significance. Nutritional intervention may offer an approach for counteracting abnormalities in inositol and inositol phospholipid profiles and associated physiological responses in certain disease states