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On the Differences Between Ouabain and Digitalis Glycosides

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Abstract

Digoxin and digitoxin are widely used in the treatment of heart diseases. The exact mechanism of action of these drugs has remained an enigma. Ouabain has become the standard tool to investigate the mode of action of cardiotonic steroids, and results with ouabain are regarded as generally valid for all cardiac glycosides. However, there are marked differences between the effects of ouabain and digitalis glycosides. Ouabain has a different therapeutic profile from digitalis derivatives. Unlike digitalis glycosides, ouabain has a fast onset of action and stimulates myocardial metabolism. The inotropic effect of cardiotonic steroids is not related to inhibition of the Na-K-ATPase. Ouabain and digitalis derivatives develop their effects in different cellular spaces. Digitalis glycosides increase the intracellular calcium concentration by entering the cell interior and acting on the ryanodine receptors and by forming transmembrane calcium channels. Ouabain, by activation of the Na-K-ATPase from the extracellular side, triggers release of calcium from intracellular stores via signal transduction pathways and activates myocardial metabolism. These data no longer support the concept that all cardiotonic steroids exhibit their therapeutic effects by partial inhibition of the ion-pumping function of the Na-K-ATPase. Hence, it is suggested that this deeply rooted dogma be revised.

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