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Hepatoprotective action of prostaglandin A(2) analogs under CCl(4)-induced liver injury in vitro.

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Aim: The cytoprotective effects of six novel synthetic prostaglandin A(2) analogs against carbon tetrachloride (CCl(4)) as a toxic agent were studied with isolated rat liver hepatocytes in vitro. Results: It was found that hepatocytes treatment with CCl(4) induced: (i) a significant increase of lactic dehydrogenase (LDH) release from cytoplasm; (ii) leakage of glutamate dehydrogenase (GDH) and acid phosphatase from mitochondria and lysosomes, respectively; (iii) 10-fold increase of trien conjugates formation; and (iv) a reduction of free SH-groups by 50%. Prostanoids U-26, U-9 and U-34 decreased cytotoxic index of CCl(4) on average by 1.5-2.0 times and were more effective than PGI(2), the well-known hepatoprotector of prostanoids type. The protective action of the prostanoids was not a cAMP- or Ca(2+)-dependent process. However, prostanoids U-26, U-9 and U-34 normalized intracellular content of SH-groups, reduced trien conjugates formation by 60-80% and strongly prevented enzyme leakage through cellular membranes. They were also able to inhibit CCl(4) effects via decreasing cytochrome P(450)2E1 activity. Conclusion: The results obtained demonstrate that prostanoids provide cytoprotective effects on liver hepatocytes through the prevention of lipid peroxidation of the plasma and the cellular membranes and maintenance of their barrier function.