Biochem Biophys Res Commun. 2006 Mar 10;341(2):357-62. Epub 2006 Jan 19.

Synthetic heteroprostanoids of A- and E-types as novel non-comprehensive inhibitors of adenylyl cyclase in rat hepatocytes.

Hubich AI, Zheldakova TA, Chernikhova TV, Koroleva EV, Lakhvich FA, Sholukh MV.

Belarussian State University, Minsk, Belarus. Hubich_Oksana@tut.by

Treatment of rat hepatocyte plasma membranes with five novel synthetic heteroprostanoids of A- and E-types significantly decreased basal activity of adenylyl cyclase. Inhibition of forskolin-stimulated activity of the enzyme was seen as well. The maximal effective concentration for all substances tested was found at approximately 5x10(-6)-1x10(-5) M. The values of half maximal concentration (IC50) for all prostanoids were at the region of 0.7-1.1 microM. Prostanoids belonging to cyclopentenone group A (U-39, U-26) were less active than analogs of 11-deoxy-PGE1 (TA-227, TA-280, and TA-239). The strongest inhibitory effect of adenylyl cyclase activity (more than 3 times) was determined in the presence of prostanoid TA-227 possessing hydrophobic 15-phenyl ring and isoxazol group in omega-chain. The investigation of AC activity in the presence of different concentrations of prostanoids and varying concentrations of Mg x ATP has demonstrated that a non-comprehensive mechanism with particular effect takes place in case of AC inhibition by the heteroprostanoids.