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ANTIAGGREGATING POTENCY OF E-TYPE PROSTAGLANDINS IN HUMAN AND RABBIT PLATELETS

Gennadi KOBZAR, Vilja MARDLA, Ivar JÄRVING, Madis LÕHMUS, Aino VAHEMETS, Nigulas SAMEL, Ülo LILLE. E-TÜÜPI PROSTAGLANDIINIDE ANTIAGREGATIIVNE TOIME INIMESE JA KÜÜLIKU VERELIISTAKUTELE

Геннадий КОБЗАРЬ, Вилья МАРДЛА, Ивар ЯРВИНГ, Мадис ЛЫХМУС, Айно ВАХЕМЕТС, Нигулас САМЕЛЬ, Юло ЛИЛЛЕ. АНТИАГРЕГАЦИОННОЕ ДЕЙСТВИЕ ПРОСТАГЛАНДИНОВ Е-ТИПА НА ТРОМБОЦИТЫ ЧЕЛОВЕКА И КРОЛИКА.

Prostaglandin E_1 (PGE_1) is a potent inhibitor of platelet aggregation [1]. It acts on the same or similar with prostacyclin receptor sites [2]. We studied a number of E-type prostaglandins (PGEs) extracted from ram seminal vesicles to gain information on the relationship between their chemical structure and antiaggregating potency as well as to compare the effect of PGEs on human and rabbit platelets.

The action of PGEs was tested on platelet-rich plasma of the two species according to the method of Born [3]. Aggregation was induced by adenosine 5'diphosphate (ADP). Relative antiaggregating potencies of PGEs studied are shown in the Table.

Relative potency of PGEs in inhibiting ADP-induced platelet aggregation in platelet rich plasma from human and rabbit. Results are calculated from IC_{50} for each prostaglandin. The value of IC_{50} for PGE_1 in both human and rabbit platelets is 40 nmol/l

Platelets	PGE_1	5,6-dihydro PGE_3	5,6-*trans* PGE_2	PGE_2	PGE_3	1a, 1b-dihomo PGE_2
Human	1	1.48	0.49	0.0013	0.017	0.0023
Rabbit	1	0.53	0.17	0.00067	0.002	0.00002

Of PGEs, the recently isolated 5,6-dihydro PGE_3 [4] proved to be the most potent inhibitor of human platelet aggregation, being 1.5 times as strong as PGE_1. PGE with a 5,6-*trans* double bond (5,6-*trans* PGE_2) is also rather effective, only two times less potent than PGE_1 on human platelets and about six times less potent on rabbit platelets. PGEs with 5,6-*cis* double bond, viz. PGE_2, PGE_3, and 1a, 1b-dihomo PGE_2 are considerably weaker inhibitors of platelet aggregation than PGEs with 5,6-single or 5,6-*trans* double bonds.

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Potencies of PGEs on human platelets differ from those on rabbit ones. This is the most noticeable for 1a, 1b-dihomo PGE_2. Except PGE_1, all PGEs are more potent on human platelets than on rabbit. Rank order of potency for PGEs is also different in both species. On human platelets 5, 6-dihydro PGE_3 is the most potent and PGE_2 has the lowest potency, whereas on rabbit platelets PGE_1 is the most potent and 1a, 1b-dihomo PGE_2 is the weakest inhibitor of platelet aggregation. These facts indicate a difference between human and rabbit platelet rich plasma.

Thus, it was shown in this work that of E-type PGs the most effective inhibitor of aggregation on human platelets is 5, 6-dihydro PGE_3; effective inhibitors of platelet aggregation of E-type prostaglandins contain a single or a *trans* double but not a *cis* double bond between the fifth and sixth carbons; human and rabbit platelet rich plasma have different sensitivity to E-type prostaglandins.

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