Poster Board P5-054

0702 THE STABILIZING EFFECT OF TRASYLOL ON PLATELET MEMBRANES

H.D.Reuter, Medizinische Universitätsklinik Köln-Lindenthal, 5 Köln 41, F.R.Germany

The proteinase inhibitor Trasylol^{R}(2000 U/ml) in vitro inhibits aggregation of human platelets induced in citrated plasma by 2 and 4 µM/ml adrenaline significantly ($p < 0.01$) by 61.3±14.0% and 61.8±15.1% (mean + S.D.), respectively. Aggregation induced by 4 µM/ml ADP was inhibited significantly ($p < 0.01$) by 24.6±7.6% while aggregation induced by 2 µg/ml collagen was inhibited by only 7.2±5.0% (n.s.). In adrenaline- and ADP-induced aggregation, first phase was inhibited slightly while there was strong inhibition of the second phase which indicates release reaction. The varying extent of inhibition obtained by the aggregation inducers adrenaline, ADP, and collagen may reflect the varying degree of replacement of aggregation inducers from the platelet membrane by the competitive inhibitor Trasylol. The inhibition of retraction (x = 66.6%) also reflects inhibition of the release of platelet constituents. Trasylol because of its cationic properties can bind to the negatively charged platelets thus influencing the membrane-bound enzyme adenylate cyclase which catalizes the formation of cyclic AMP. Cyclic AMP results in activating a platelet protein kinase which in turn phosphorylates a membrane protein thus stabilizing the platelet membrane.

P5-055

0703 SYNERGISM BETWEEN ADRENALINE AND ADENINE NUCLEOTIDES IN PRODUCING PLATELET AGGREGATION RESPONSES

B. Oppenheim and M.B.H. Youdim
Technion-Israel Institute of Technology, Haifa, Israel
Faculty of Medicine, Department of Pharmacology

Recently we have shown that 5'-adenylylimidodiphosphate (AIP), a structural analogue of ATP, causes a transient aggregation of human blood platelets similar to that produced by 5-hydroxytryptamine (5-HT) (Brit. J. Pharmacol. 1979, in press). In addition AIP strongly inhibits the second phase of aggregation induced by adrenaline (A), noradrenaline, ADP and irreversible 5-HT when such a response is obtained. However, it does not affect collagen response, indicating that AIP is an inhibitor of release I (i.e. release is reversible. Like 5-HT, the aggregation to AIP can be enhanced by pretreatment (30-60 sec.) with low (0.1-0.5 µM) non-aggregating concentrations of A, but without exhibiting a second phase of aggregation. The synergistic effect of A (but not isoproterenol, 10-100 µM) was also observed with ATP and ADP. ATP by itself does not produce an aggregation response but it causes a 5-HT like response after preincubation with A. The potentiating effects of A on aggregation responses are selectively prevented by phentolamine (10 µM) but not by proparanolol (10 µM). The results suggest an α-adrenergic mediated effect.

P5-056

0704 HUMAN PLATELET AGGREGATION INDUCED BY THE SYNTHETIC ENDOPEROXIDE ANALOGUE U-46619 IS INDEPENDENT FROM SECRETION, PROSTAGLANDIN PRODUCTION AND EXTRACELLULAR CALCIUM.

G. Di Minno*, L. Bianchi, G. de Gaetano and M.J. Silver, Mario Negri Institute, Milan, Italy and Cardeza Foundation and Pharmacol.Dept., Thomas Jefferson Univ., Philadelphia, Pa., USA

U-46619 is a stable analogue of cyclic prostaglandin endoperoxides which induces human platelet aggregation independently from nucleotide secretion. We studied platelet aggregation, ^{14}C-5 HT release and malondialdehyde (MDA) production induced by this compound in stirred or unstirred platelet-rich plasma (PRP) samples from 11 healthy volunteers. Each subject was tested both before and 90 min after aspirin ingestion (500 mg). The threshold aggregating concentration (TAC) of U-46619 ranged between 240 and 900 nM. Aggregation was maximal between 30 and 60 min after venepuncture and was concentration-dependent (60-7,200 nM). At concentrations below the TAC, U-46619 induced primary reversible aggregation without detectable ^{14}C-5 HT release. At TAC or higher concentrations aggregation and release proceeded as parallel events. Neither MDA production nor intracellular LDH loss could be detected in any of the tested situations. Aspirin ingestion did not modify the above pattern of platelet responses. In unstirred samples ^{14}C-5 HT release occurred to the same extent as in stirred platelet suspensions. Addition to citrated PRP of Na_2-EDTA did not affect either aggregation or release. It is suggested that aggregation and secretion may be independent, parallel responses of platelet activation by U-46619 and do not require either extracellular calcium or activation of endogenous arachidonic acid metabolism. (Supported by the Italian CNR and NIH).