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0705 INHIBITION OF THROMBIN-, EPINEPHRINE- AND COLLAGEN-INDUCED PLATELET AGGREGATION BY α_1-ACID GLYCOPROTEIN

P. Andersen[X] and C. Eika, Hem.Res.Lab., Ullevål Hospital, Oslo, Norway.

α_1-Acid glycoprotein (α_1-acid GP) isolated from human plasma was found to inhibit thrombin-induced aggregation of washed human platelets (0.05 NIH U/ml final conc.), and inhibition was complete with physiological concentrations of α_1-acid GP (1.0-1.5 g/l final conc.). The inhibitory effect seemed to occur immediately on thrombin addition, thus similar to the effect of heparin previously observed. As opposed to heparin, however, α_1-acid GP did not affect spontaneous platelet aggregation. Furthermore, α_1-acid GP (in optimal conc.) reduced the combined inhibitory effect of heparin and antithrombin III on thrombin-induced platelet aggregation, thus consistent with the previous findings using heparin thrombin clotting time.

Snyder and Coodley (1976) found α_1-acid GP to inhibit platelet aggregation induced by epinephrine and adenosine diphosphate in platelet-rich plasma. As we also found α_1-acid GP to inhibit collagen-induced platelet aggregation, α_1-acid GP may possibly act as an inhibitor of the release reaction though fairly high concentrations (10 mg/ml final conc.) was needed for complete inhibition.

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0706 TACHYPHYLAXIS IN HUMAN BLOOD PLATELETS INDUCED BY VARIOUS AGONISTS AND THE EFFECT ON RESPONSE TO OTHER AGONISTS

P.A. Ruggles and M.C. Scrutton, Dept. Biochem., King's College, London, U.K.

Tachyphylaxis of human platelets to ADP, adrenaline, thrombin, 5-HT and vasopressin (VP) was induced by preincubation of stirred citrated PRP with an agonist concentration which induced primary reversible aggregation. The effect was demonstrable within 2 mins. after addition of some of the agonists and persisted for at least 30 mins. The extent of tachyphylaxis showed a positive correlation with agonist concentration used to induce the initial reversible response. Partial agonists at the ADP (2',3'-dialcohol ADP) or α-adreno-(clonidine) receptors did not induce significant tachyphylaxis to subsequent addition of the full agonist. In most instances platelets made tachyphylactic to a given agonist showed an unchanged or enhanced response to all other agonists including arachidonate. However tachyphylaxis to ADP, 5HT or thrombin was associated with an attenuated response to collagen. Furthermore tachyphylaxis to thrombin also caused attenuation of the response to VP and arachidonate. Induction of tachyphylaxis to VP, or addition of oxytocin (an inhibitor of aggregation induced by VP) had no effect on the response to thrombin. Thus the region of the thrombin receptor responsible for induction of tachyphylaxis to this agonist is not identical with that at which VP interacts. If stimulus-response coupling involves a common pathway for most agonists these data suggest that development of tachyphylaxis depends on events which preceed the effect of the agonists on this common pathway.

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0707 PLATELET ADHESION TO COLLAGEN IS INHIBITED BY 5'-ADENOSINE DIPHOSPHATE BUT UNAFFECTED BY CELL SHAPE

F.A. Meyer*, Z. Weisman and M.M. Frojmovic, Weizmann Institute of Science, Rehovot, Israel

The effect of ADP on the adhesion of rabbit platelets to collagen from unstirred suspensions has been investigated. Reduced binding was seen at ADP concentrations sufficient for platelets in PRP suspensions to undergo shape change (>10^{-8}M). However, shape change per se was not involved. The time dependence of the effect of ADP on platelet shape and on platelet adhesion did not correlate. Also reduced adhesion still occurred if shape change was prevented e.g. by treatment with 1 µM PGE_1 or with fixatives. Washed platelet preparations in spite of being fully shape-changed also adhered less well in the presence of ADP. As expected platelets whose shape was changed without ADP being involved, e.g. by a cold exposure treatment, displayed normal binding to collagen.

ADP binding to the platelet per se is not sufficient, since reduced adhesion to collagen is seen only some time after binding has taken place. Also AMP blocked the effect of ADP on platelet adhesion if added before but not after ADP. The time dependent event that occurs is likely to be local since reduced platelet adhesion was seen with fixed platelets. It is unlikely to result from the conversion of ADP to ATP. Although ATP does inhibit adhesion, it does so only at much higher concentrations and then only after a lag period similar to that seen with ADP.

Our findings imply that some of the agents reported to reduce platelet adhesion to collagen may do so by causing ADP to be released from the platelet.

Surface shape and chemistry