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Binding and Internalization of Platelet-activating Factor 1-O-Alkyl-2-acetyl-*sn*-glycero-3-phosphocholine in Washed Rabbit Platelets*

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AGEPC (platelet-activating factor) is a phospholipid chemical mediator which exhibits potent biological activities in a variety of cells as well as tissues. It structure has been characterized as 1-*O*-alkyl-2-acetyl-*sn*-glycero-3-phosphocholine. The structural specificity for the biological effects of AGEPC on target cells has suggested the presence of specific receptor(s) for this lipid on the membrane. Actually specific binding of AGEPC has been reported in various cells and tissue as well as in membrane preparations and it was presumed to represent binding to specific receptor(s) on the surface membrane. In this communication, the binding profile of AGEPC (platelet-activating factor) to washed rabbit platelets was investigated through the use of structural analogs of AGEPC, e.g. U 66985, which specifically suppressed AGEPC biological activities on rabbit platelets. This interaction of AGEPC with platelets could be divided into three different components termed A, B and C. Component A was considered as one of high affinity ($Kd = 0.5 \times 10^{-9}$ M) and with a low capacity (about 400 sites/platelet). The binding of AGEPC to component A was reversible and was blocked by the inhibitory analogs of AGEPC. This was considered to be the AGEPC receptor site(s). Component B was irreversible in nature and was presumed to be associated with internalization of AGEPC. The latter process was sensitive to the structural inhibitors. Component C was not affected by the inhibitors and probably represented a nonspecific binding to the lipid layer of the membrane. The binding profile of lysoGEPC, a biologically inactive and non-inhibitory analog of AGEPC was observed to consist of a single component and was (also) unaffected by the inhibitors.

Internalization of AGEPC into rabbit platelets was further examined by the BSA extraction method which was originally developed by Mohandas *et al.* (J. Biol. Chem. **257**, 6537—6543 (1982)). AGEPC was instantly taken up by the cell and internalized into its membrane, where it remained and was not released into cytosol. The internalization of AGEPC was suppressed by pretreating the cells with AGEPC analogs.

In platelets desensitized to AGEPC, no down regulation of the receptor site(s) was observed. The internalization of AGEPC in the desensitized cells was clearly enhanced and this was obvious even in the presence of the AGEPC inhibitor(s). Even in the presence of the inhibitors, effective internalization of AGEPC was also evident in thrombin-

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treated cells. These results suggested that the internalization of AGEPC was irreversibly enhanced in the platelets which were activated by AGEPC itself as well as by thrombin.