Title	Structural analogs of alkylacetylglycerophosphocholine inhibitory behavior on platelet activation
Sub Title	
Author	徳村, 彰(Tokumura, Akira) 本間, 浩(Honma, Hiroshi) Hanahan, Donald J.
Publisher	共立薬科大学
Publication year	1986
Jtitle	共立薬科大学研究年報 (The annual report of the Kyoritsu College of Pharmacy). No.31 (1986.) ,p.49- 49
JaLC DOI	
Abstract	
Notes	抄録
Genre	Technical Report
URL	https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000031-0049

Structural Analogs of Alkylacetylglycerophosphocholine Inhibitory Behavior on Platelet Activation*

Akira TOKUMURA, Hiroshi HOMMA and Donald J. HANAHAN**

徳村　彰, 本間　浩, Donald J. Hanahan

Platelet activating factor, a lipid mediator released from IgE-sensitized rabbit basophils has been identified as 1-*O*-alkyl-2-acetyl-*sn*-glycero-3-phosphocholine (AGEPC). Subsequent studies have revealed that this unique phospholipid has diverse biological effects on a variety of cells other than platelets. Much attention has been directed to the structure-activity relationships in activation of many types of cells by AGEPC, and these studies suggest the existence of specific binding sites (receptors) on the plasma membrane that are responsible for transducing a stimulatory signal within the cells. On the other hand, there is less information on the structure-activity relationships for inhibition by structural analogs on AGEPC-induced cell activation. Consequently, several analogs of AGEPC were investigated as potential selective inhibitors of AGEPC-induced activation of washed rabbit platelets. Two particular compounds, CV-3988 (*rac*-3-(N-n-octadecylcarbamoyloxy)-2-methoxypropy-2-thiazolioethyl phosphate) and U66985 (1-O-octadecyl-2-acetyl-*sn*-glycero-3-phosphoric acid-6-trimethylammoniumhexyl ester) emerged as particularly active and effective inhibitors. Aggregation and secretion profiles, as well as the degradation of inositol phospholipids and production of phosphatidic acid, were used as monitors of their inhibitory capabilities. U66985 was the most effective inhibitor, giving an IC_{50} value of $4.1\pm1.5\times10^{-6}$M against a challenge of 1×10^{-10}M AGEPC in the secretion assay. Phospholipid turnover was blocked completely at this inhibitor concentration. On the other hand, while CV-3988 was an effective inhibitor, a higher concentration was required and a more restricted range of activity was noted with an IC_{50} value of $5.9\pm1.3\times10^{-7}$M against a challenge of 1×10^{-10}M AGEPC in the secretion assay. While CV-3988 did indeed completely block the turnover of inositol phospholipids and phosphatidic acid formation, these effects were noted at a higher concentration than with U66985. On the basis of data obtained in desensitization experiments with AGEPC and U66985, it appears that each inhibitor occupies the same receptor site as the agonist, AGEPC. These results illustrate the usefulness of these AGEPC analogs in exploring the biochemical characteristics of the interaction of AGEPC with a cell.

* *J. Biol. Chem.*, **260**, 12710—12714 (1985)

** The University of Texas Health Science Center.