Biochem. Pharmacol. 62, 2853-861 (2001).

Metabolic alterations by clofibric acid in the formation of molecular species of phosphatidylcholine in the liver of rats

Hiroki Mizuguchi[1], Naomi Kudo[2] (工藤なをみ), and Yoichi Kawashima[2] (川嶋洋一)

[1]Research Laboratories, Torii Pharmaceutical Co., Ltd., 2183-1, Teranosaku, Ohta, Sakura-shi, Chiba, 285-0808, Japan and [2]Faculty of Pharmaceutical Sciences, Josai University, 1-1, Keyakidai, Sakado, Saitama 350-0295, Japan

The mechanism by which p-chlorophenoxyisobutyric acid (clofibric acid) induces striking changes in the proportion of the molecular species of phsphatidylcholine (PC) in rat liver wa studies. Treatment of rats with clofibric acid strikingly increased the content of 1-palmitoyl-2-eleoyl-(16:0-18:1)PC, but decreased the contents of 1-palmitoyl-2-docosahexaenoyl(16:0-22:6)PC, 1-stearoyl-2-arachidonoyl(18:0-20:4)PC, and 1-stearoyl-2-linolepyl (18:0-18:2)PC; the drug did not change the content of 1-palmitoyl-2-arachidonpy-16:0-20:4)PC. We found that (i) the incorporation of [^{3}H]glycerol, which was injected intravenously, into 16:0-18:1diacylglycerol (DG) and 16:0-18:1 PC was increased markedly by clofibric acid feeding without changing the substrate specificity of CDP-choline:DG cholinephosphotransferase, (ii) the in vivo formation of 16:0-18:1 and 16:0-20:4PC from 1-16:0-[^{3}H]glycerophosphocholine(GPC), which was injected intraportally, was increased markedly by clofibric acid feeding, and (iii) The incorporation of [^{14}C]ethanolamine, which was intraperitoneally injected, into 16:0-22:6, 18:0-22:6 and 18:0-20:4 PC, was decreased by clofibric acid feeding; the extent of the decrease in 16:0-20:4 PC was less than that of 18:0-20:4 PC. It is concluded, therefore, that clofibric acid increased selectively the content and proportion of 16:0-18:1 PC by enhancing both the CDP-choline pathway and the remodelling of pre-existing PC molecule and that the drug kept the content of 16:0-20:4 PC unchanged by stimulating the remodelling of pre-existing PC molecule.