遊離肝細胞における薬物代謝のモデル系；メタロポルフィリン錯体によるシクロヘキセンの酸化

桜井　弘*，旗谷　裕紀子*，五郎丸　毅，松浦　博*

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A Model System for Drug Metabolism in Isolated Hepatocytes; Oxidation of Cyclohexene by Metalloporphyrin Complexes

Hiromu SAKURAI*, Yukiko HATAYA*, Tsuyoshi GOROMARU and Hiroshi MATUURA*

ABSTRACT: Althoug many chemical models for cytochrome P450-dependent monooxygenases have been advanced, no models for the isolated hepatocytes have been reported. We now reported that an Mn (TPP)-$NaBH_4$-O_2 system containig a crown ether mimics cyclohexene oxidation in isolated rat hepatocytes. In a typical chemical experiment, Mn (TPP) Cl, dibenzo-18-crown-6 and cyclohexene were dissolved in benzene and $NaBH_4$ was added to start the reaction under a 100 % oxygen atmosphere at 20℃. In experiments using isolated rat hepatocytes, a mixture of hepatocytes and cyclohexene was incubated by gentle stirring at 37℃ under an O_2/CO_2 gas mixture for 30 min. After incubation, the oxygenated products were extracted and analyzed by GLC methods and mass spectrometry. Cyclohexene oxide, cyclohexanone, 2-cyclohexene-1-o1 and cyclohexanol were detected as products in the oxidation of cyclohexene by model systems. The distribution of products in cyclohexene oxidation by the Mn (TPP)-$NaBH_4$-crown ether-O_2 system is quite for model systems giving four oxidation products, being sililar to that in reactions by isolated rat hepatocytes rather than in reaction by cytochrome P450 systems.

抄録　チトクローム P450 酸化酵素の化学モデルに関しては多くの研究があるが、遊離肝細胞のモデルは報告されていない。著者らはクラウンエーテルを含む Mn (TPP)-$NaBH_4$-O_2 系と遊離肝細胞でのシクロヘキセンの酸化について比較検討した。シクロヘキセンの酸化生成物シクロヘキセンオキシド，シクロヘキサノン，2-シクロヘキセン-1-オール及びシクロヘキサノールの4種の生成比より Mn (TPP)-$NaBH_4$-クラウンエーテル-O_2 系は遊離肝細胞のモデルとなりうることが判明した。

* Faculy of Pharmaceutical Sciences, University of Tokushima. 徳島大学薬学部