Title	発癌性ジアルキルニトロサミンの代謝活性体の化学
Sub Title	
Author	望月, 正隆(Mochizuki, Masataka)
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.71- 71
Abstract	
Notes	抄録
Genre	Technical Report
URL	http://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000031-0071

発癌性ジアルキルニトロサミンの代謝活性体の化学*

望 月 正 隆

Carcinogenic alkylating agents containing nitrogen-nitrogen bonds are suspected of causing human cancer. They alkylate specific positions of DNA, damage genetic informations and initiate carcinogenesis. Amoung them, *N*-nitroso compounds are the most important. They appear in our environment as foods, beverages, cosmetics, and so on, and are known to be formed in digestive tracts by reactions between amines in foods or drugs, and nitrite produced from nitrate in saliva. Nitrosodialkylamines require activation through metabolism, since they are stable and their reactivity are low in contrast to unstable and reactive nitrosoamides. Metabolic hydroxylation at the α-position of *N*-nitroso group was postulated as the mechanism of the activation. α-Acetoxy and α-hydroperoxy *N*-nitrosamines were synthesized as models of α-hydroxy *N*-nitrosamines and they were proved to be convertible easily to α-hydroxy *N*-nitrosamines. α-Hydroxy *N*-nitrosamines were finally synthesized, and their chemical and biological properties were investigated. All the properties of α-hydroxy *N*-nitrosamines satisfy requirements as the active species in the metabolic activation of carcinogenic nitrosodialkylamines. They are unstable in neutral aqueous solution but more stable in weakly acidic aqueous solution. They decompose by releasing aldehydes and formed alkylating species, which are able to alkylate various nucleophiles as water, thiophenol, amino acids and deoxyribonucleosides. They are potent mutagens without metabolic activation in microbial and mammalian cells. Thus, α-hydroxy *N*-nitrosamines are proved to be the active species in metabolic activation of carcinogenic nitrosodialkylamines. Further work remained in this field are the mechanism of formation of α-hydroxy *N*-nitrosamines from nitrosodialkylamines, and the mechanism of the decomposition of α-hydroxy *N*-nitrosamines to alkylating species. From these investigation it will be possible to regulate the carcinogenesis by *N*-nitroso compounds and also by alkylating carcinogens, and then to open a way to prevent human cancer.

* 本報告は薬学研究の進歩 研究成果報告集, 2, 1—13 (1986) に発表