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A similar order was observed also in the cytotoxicity. Mutagenic and cytotoxic potencies of these α -hydroxy N-nitrosamines in V79 cells were well correlated not only with those of model compounds, α -acetoxy and α -hydroperoxy N-nitrosamines, but with their alkylating ability measured by alkylation of thiophenol. The mutagenic activity of the α -hydroxy N-nitrosamines in V79 cells was shown to be in parallel with that in Salmonella typhimurium TA1535 and with that of N-nitrosodialkylamines in V79 cells after metabolic activation by rat hepatocytes. The results obtained here supported further that the α -hydroxy N-nitrosamine is the active species in the metabolic activation of carcinogenic and mutagenic N-nitrosodialkylamines.

Metabolism of N-Nitrodialkylamines

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[8th International Meeting on N-Nitroso Compounds (Banff, Canada, September, 1983) で発表]

In vitro and in vivo metabolism of N-nitramines were investigated to compare their mode of action with that of N-nitrosamines. N-Nitrodibutylamine and N-nitrodiethylamine were incubated with rat liver microsomes and hepatocytes, and the products were analyzed by HPLC and GLC. The in vitro metabolic pattern of these N-nitramines was quite similar to that of the corresponding N-nitrosamines except that N-nitromonoalkylamines (produced by α -hydroxylation) were isolated and characterized in the incubation with the N-nitrodialkylamines. Seven N-nitramines including glucuronides were isolated and identified from urine of rats given N-nitrodibutylamine, which were produced by ω , ω -1, and α oxidations of the N-nitramine. The in vivo metabolic pattern of N-nitrodibutylamine was also similar to that of N-nitrosodibutylamine, except that N-nitromonobutylamine (a product of α -hydroxylation) was isolated and characterized.

N-Nitramines were mutagenic to E. coli WP2 hcr^- but not to S. typhimurium TA1535. N-Nitrodibutylamine and N-nitrodiethylamine were mutagenic only in the presence of hepatic microsomes, while N-nitromonobutylamine and N-nitromonoethylamine were direct mutagens. Thus, the N-nitrodialkylamine is also metabolically activated to a mutagen through α -hydroxylation.

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