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EXCRETION OF DIETHYLCARBAMAZINE (DEC) IN HUMAN URINE AND ITS RELATIONSHIP TO URINARY pH[1,2]

by

Alasdair Breckenbridge
Department of Pharmacology and Therapeutics
University of Liverpool
Liverpool
England

Over the past three years, a series of investigations on the clinical pharmacology of diethylcarbamazine (DEC) has been carried out as a collaborative study between the Department of Pharmacology and Therapeutics, University of Liverpool, the Liverpool School of Tropical Medicine and the Centre for Onchocerciasis Research, Tamale, Ghana.

Utilizing gas-liquid chromatographic techniques, plasma and urine concentrations of DEC and DEC N-oxide (its main metabolite, which may also be therapeutically active) have been measured in patients with onchocerciasis, in human volunteers and in experimental animals. In man, unlike the rat, approximately 40% of DEC is excreted unchanged in urine. Because of the physico-chemical properties of DEC, however, urine pH influences the rate and extent of its urine excretion. In volunteers whose urine was rendered acid with ammonium chloride, some 62% of DEC was excreted unchanged. When the urine was rendered alkaline with sodium bicarbonate, only 5% was excreted unchanged. There was a corresponding change in the kinetics of DEC as measured by plasma half life which doubled when the urine was rendered alkaline. The implications of this work are that under alkaline urine conditions, accumulation of DEC may predispose to toxicity, but under acidic urine conditions a therapeutically effective plasma concentration may not be maintained. By careful manipulation of urine pH small doses of DEC may be administered, thus decreasing the body load of the drug and reducing the cost of therapy. These suggestions are currently under investigation in Tamale. This pH dependence may be of great practical importance since it is known that diet can influence urine pH. With a largely vegetable diet, a more alkaline urine is formed, while when animal protein constitutes a substantial part of the diet, urine tends to be acid. These observations may be relevant in several forms of filariasis in which DEC is used.

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[1] These studies received financial assistance from the Filariasis Component of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.

[2] The work described in this document is discussed in greater detail in an article of the journal Clinical Pharmacology and Therapeutics (in press)

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