

A BIOCHEMICAL METHOD FOR ASSESSING THE NEUROTOXIC EFFECTS OF MISONIDAZOLE IN THE RAT

G. P. ROSE, A. J. DEWAR AND I. J. STRATFORD*

From the Shell Toxicology Laboratory (Tunstall), Sittingbourne Research Centre, Kent ME9 8AG.

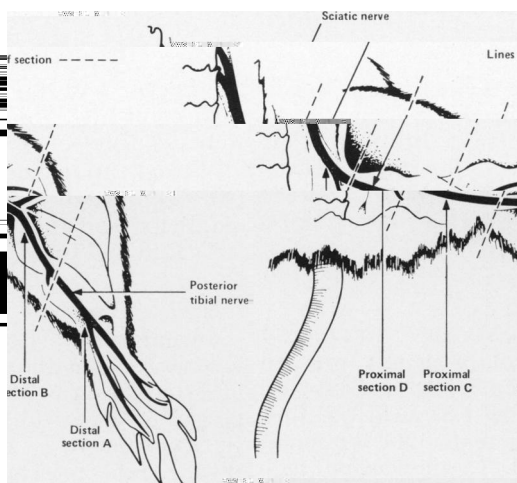
*and the *Institute of Cancer Research, Royal Marsden Hospital, Radiobiology Unit.*

Received 20 May 1980 Accepted 11 September 1980

Summary.—A proven biochemical method for assessing chemically induced neurotoxicity has been applied to the study of the toxic effects of misonidazole (MISO) in the rat. This involves the fluorimetric measurement of β -glucuronidase and β -galactosidase activities in homogenates of rat nervous tissue. The tissues analysed

in vivo changes can occur after treatment

METHODS



diluted standard was added 1 ml 0.1M

The fluorescence was measured as described above. β -Galactosidase activity was expressed

as μg methylumbelliferone liberated/h/mg (wet weight).

(b) β -Glucuronidase.—A 0.5ml aliquot of

polypropylene tube and diluted with 0.5 ml of 0.1M sodium acetate buffer (pH 4.5). A

0.1ml aliquot of 1mM methylumbelliferone

sidase activities in distal sections of the sciatic/posterior tibial nerve of male Wistar rats

180

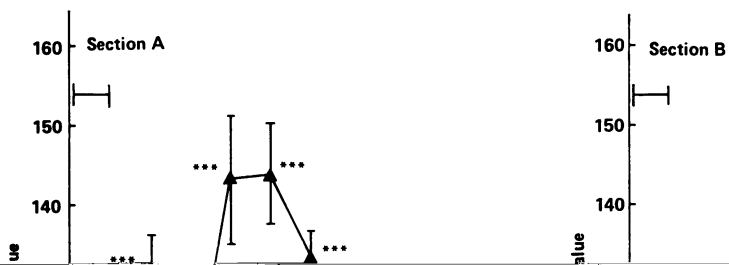


TABLE III.—*Effect of increasing doses of MISO on the β -glucuronidase and β -*

galactosidase activities in the triaeminal

ganglia of male Wistar rats

Enzyme activity expressed as

μ g of methylumbelliferone

TABLE V.—*Effect of increasing doses of MISO on the β -glucuronidase and β -*

galactosidase activities in the cerebellum

of male Wistar rats

Enzyme activity expressed as

μ g of methylumbelliferone

TABLE IV.—*Effect of the subacute administration of MISO on the β -glucuronidase and*

by large increases in β -glucuronidase tive methods such as behavioural or func-

degeneration, V: β -glucuronidase. *Biochem. J.*, **52**, 659.

and function appraisal of misonidazole-induced neurotoxicity, in the rat. *Workshop on Neurotoxic*

KAPLAN, M. L. & MURPHY, S. D. (1972) Effect of

Properties of Misonidazole and Other Radiosensi-

acrylamide on rota-rod performance and sciatic

tizers, Ludwig Inst., Sutton. U.K.

nerve β -glucuronidase activity of rats. *Toxicol. Appl. Pharmacol.*, **22**, 259.

LEQUESNE, P. M. (1975) Neuropathy due to drugs.

SAUNDERS, M. I., DISHE, S., ANDERSON, P. & FLOCKHART, I. R. (1978) The neurotoxicity of misonidazole and its relationship to dose, half-life

delphia: Saunders. p. 1263.

(Suppl. III). 268.

MCCAMAN, R. E. & ROBINS, E. (1959) Quantitative biochemical studies of Wallerian degeneration in

SCHARER, K. (1972) Selective alterations of Purkinje cells in the dog after oral administration of high