Effect of emetine treatment on tissue transaminase activity

Although emetine is used extensively in the treatment of amoebiasis its administration is complicated by its myocardial toxicity. Many attempts have been made to correlate its toxicity with changes in metabolic processes (Deitrich & Heim, 1956; Marino & Magliulo, 1961; Chang, Ynan & others, 1966; Appelt & Heim, 1968; Chatterjee, Roy & others, 1970) and in this context we have recently investigated the effects of emetine on tissue transaminase activities in rats.

Male wistar rats, 80–100 g, were divided into two groups of equal average weight. The diet was that reported by Chatterjee, Roy & others (1970, 1971). Rats of one group were treated with emetine hydrochloride (0·2 mg 100 g^{-1} day^{-1}, s.c.) for 10 days. The emetine-treated group were pair-fed with those of control group. After the experimental period the animals were killed and bled from the hepatic vein. Liver, heart, muscle and kidneys were removed, blotted dry and weighed. A 1% homogenate of each tissue was prepared and used for the assay of glutamic-aspartic (Tonhazy, White & Umbreit, 1950) and glutamic-alanine (Chatterjee, Jamdar & Ghosh, 1966) transaminase activities.

Table 1. *Effect of emetine on transaminase activities of different tissues.*

Group	Transaminase activity* Liver		Heart		Muscle		Kidney	
	Gl-Asp	Gl-Al	Gl-Asp	Gl-Al	Gl-Asp	Gl-Al	Gl-Asp	Gl-Al
Pair-fed control	2·58±0·27 (6)	0·27±0·03 (6)	4·88±0·29 (6)	0·10±0·04 (6)	1·24±0·14 (6)	0·15±0·06 (6)	1·83±0·03 (5)	0·16±0·02 (4)
Emetine-treated	1·77±0·23 (6) $P<0·05$	0·08±0·04 (6) $P<0·005$	4·42±0·16 (6)	0·13±0·04 (6)	1·13±0·19 (6)	0·17±0·04 (6)	1·82±0·07 (6)	0·15±0·03 (5)

The values are means ± s.e.
* μmol of keto-acid produced mg^{-1} tissue (wet weight) h^{-1} at 37°.
The figures in the parentheses indicate the number of animals.

The results (Table 1) demonstrate that emetine treatment reduced the activity of both glutamic-aspartic and glutamic-alanine transaminases of liver. The fact that the reduction in the liver transaminase activity after emetine treatment was not brought about by a diminution in the free amino-acid level seemed evident from the enhanced free amino-acid nitrogen concentrations of liver in emetine-treated rats (Chatterjee & others, 1971). Grollman (1966, 1968, 1970; Beller (1968) and Jondorf & Szapary (1968) have demonstrated impairment of tissue protein synthesis after emetine treatment. Chatterjee & others (1970) also suggested a diminished protein breakdown occurred in emetine-treated animals in addition to reduced protein synthesis. So, one factor contributing to the diminished activity of transaminases in liver of emetine-treated rats may be the presence of reduced amount of enzyme protein. A similar reduction in the amount of liver enzyme synthesizing ascorbic acid in emetine-treated rats has been suggested recently (Chatterjee, Datta & Ghosh, 1972). But, the transaminase activity of heart, muscle and kidney was not altered by emetine treatment although there could be reduction in the synthesis of proteins in such tissues. It appears therefore that emetine does not show a general depressing effect on the synthesis *in vivo* of apoprotein of transaminases. For example, emetine treatment appeared to affect the synthesis of liver transaminases, while the same treatment appeared to have no effect on the amount of apoprotein of transaminases in other tissues, such as, heart, muscle and kidney.

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Effect of some lipid-soluble derivatives of amphetamine on amphetamine levels in rat brain

Jonsson & Gunne (1972) observed that amphetamine levels in brain after injection of (+)-amphetamine into rats were higher when the rats had been pretreated with fenfluramine. Jonsson (1972) showed that fenfluramine, norfenfluramine, and *N*-(2-benzoyloxyethyl) norfenfluramine inhibited the *para*-hydroxylation of amphetamine. The lipid-soluble character of the drugs seemed to be a factor in the inhibition but two other lipid-soluble derivatives of amphetamine (4-chloroamphetamine and 4-chloromethamphetamine) were unable to block the *para*-hydroxylation of amphetamine, a finding that led Jonsson to propose that both lipid-solubility and an unoccupied *para* position on the ring were requirements for inhibition.

We have compared 2-chloro, 3-chloro-, and $\beta\beta$-difluoro-amphetamine, which are lipid-soluble derivatives with an unoccupied *para* position, fenfluramine, 4-chloroamphetamine and 3-trifluoromethyl-α-methylbenzylamine, the next lower homologue of norfenfluramine, on amphetamine levels in tissues.

Male albino Wistar rats, 130–155 g, were given (+)-amphetamine sulphate (SKF) (5 mg kg^{-1}, i.p.) to which (+)-[^{3}H] amphetamine sulphate (New England Nuclear) had been added to give a specific activity of 2 μCi mg^{-1}. Two h later, the rats were decapitated, and the brain, liver, and whole blood were immediately removed. Amphetamine levels were measured by extraction of the radioactive amine from