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Liv.52-induced Modification of Barbiturate Hypnosis in Albino Rats

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Liv.52 administration for sufficiently prolonged period in patients with liver diseases as well as in laboratory animals with experimentally induced hepatic damage has been shown to protect the liver and also to improve its structure and function[1-3,6]. The exact mechanism of this protective effect of Liv.52 in hepatic disorders is not known; however, it appears likely that the chronic administration of Liv.52 may affect hepatic enzymes metabolizing drugs. Since barbiturate-induced hypnosis is known to be affected by several factors,[4] it was thought to be of interest to study the effect of Liv.52 administration in rats on pentobarbitone and barbitone-induced hypnosis in rats. As pentobarbitone is metabolized mainly in the liver and barbitone is practically completely excreted through kidneys, both were selected for the present study.

MATERIALS AND METHODS

Fifty adult male healthy albino rats (225-280 g) were used for the study. They were divided into two equal groups of twenty five each. Fifteen rats from each group received Liv.52, 0.5 ml/100 g body weight orally and the remaining ten from each group acting as control were given water in equal volume for thirty days. At the end of the thirty days' treatment one group was subjected to pentobarbitone (30 mg/kg IP) induced hypnosis and the other group of barbitone (100 mg/kg IP) induced hypnosis.

The person who performed the sleeping time test was unaware of the treatment given to the rats. Sleeping time was considered as the interval between the loss and regain of the righting reflex. The results were statistically analysed by 't' test.

Table 1

Group	No. of rats	Pentobarbitone sleeping time in minutes (Mean ± SE)	Significance
Control	10	57.7 ± 6.6	–
Liv.52	15	34.93 ± 6.7	$p<0.05$

Table 2

Group	No. of rats	Barbitone sleeping time in hours and minutes (Mean ± SE)	Significance
Control	10	6 hrs, 17 mins. ± 21.2	–
Liv.52	15	6 hrs, 24 mins. ± 23.6	Insignificant

Barbitone induced hypnosis was not all affected by Liv.52 treatment.

Liv.52 treated group had significant ($p<0.05$) reduction in pentobarbitone induced sleeping time. In this group four rats were only sedated, they had no loss of righting reflex.

COMMENTS

The results show that chronic administration of Liv.52 in rats has significantly and selectively reduced pentobarbitone induced hypnosis whereas barbitone-induced hypnosis was not affected at all. In case of pentobarbitone sleeping time, it is of interest and importance to note that four Liv.52-treated rats had no loss of righting reflex, they were only sedated. Drug-induced modification in barbiturate-induced hypnosis can result either due to the alterations in barbiturate metabolism and excretion or due to the central effects of the drug concerned. In the present study prolonged

administration of Liv.52 might have caused the stimulation of hepatic microsomal enzymes. This in turn would enhance metabolism of pentobarbitone leading to hastened termination of its hypnotic effect. Interference with excretion of barbiturates at the renal levels has been ruled out since barbitone (which is mainly excreted by the kidneys) induced hypnosis was without any effect by Liv.52. Thus it appears that Liv.52 chronic administration accelerates pentobarbitone metabolism by stimulating hepatic microsomal enzymes, which may be responsible for the observed reduction in pentobarbitone sleeping time.

Liv.52 is clinically used for its beneficial effects in hepatic disorders. It is of interest to study whether this beneficial effect of Liv.52 is through stimulation of microsomal enzyme systems.

SUMMARY

Chronic Liv.52 administration in rats significantly reduced pentobarbitone-induced hypnosis whereas barbitone-induced hypnosis was not affected. It appears likely that this effect of Liv.52 may be due to stimulation of hepatic microsomal enzymes metabolizing pentobarbitone.

REFERENCES

1. Joglekar, G. V., Chitale, G. K. and Balwani, J. H., Protection by indigesnous drugs against hepatotoxic effects of carbon tetrachloride in mice. *Acta Pharmacol. et Toxicol.* (1963) : 20, 73.

2. Karandikar, S. M., Joglekar, G. V., Chitale, G. K. and Balwani, J. H., Protection by Indigenous Drugs against Hepatotoxic effects of Carbon tetrachloride. *Acta Pharmacol. et Toxicol.* (1973) : 20, 274.

3. Patrao, S., Observations on Liv.52. *J. Ind. Med. Prof.* (1957): 4.

4. Sethy, V. H. and Sheth, U. K., Factors affecting barbiturate sleeping time. *Ind. J. Med. Sci.* (1968): 22, 507.

5. Sheth, S. C., Northover, B. J., Tibrewala, N. S., Warerkar, U. R. and Karande, V. S., Therapy of cirrhosis of liver and liver damage with an indigenous drug – Experimental and clinical studies. *Ind. J. Paediat.* (1960): 27, 204.

6. Sule, C. R., Sathe, P. M., Koshy, M.C. and Deshpande, M. S., Ascites due to liver deficiency treated with an indigenous drug. *The Ind. Practit.* (1955): 9, 357.