AIM: Study of effect of hepatic microsomal enzyme inducers on the phenobarbitone sleeping time in mice.

REFERENCE:

1) Medhi Band Prakash A, Introduction to Experimental Pharmacology, Practical Manual of Experimental and Clinical Pharmacology. Jaypee Brothers Medical Publishers (P) Ltd. First Edition, 2010
2) M.N. Gosh Common Laboratory Animals, Fundamentals of Experimental Pharmacology, Fifth Edition, 2011
3) Kulkarni S.K., Handbook of experimental pharmacology, New Delhi: Vallabh Prakashan, 2014.

INTRODUCTION:

The study investigates how hepatic microsomal enzyme inducers affect phenobarbitone-induced sleep duration in mice. These inducers enhance liver enzyme activity, particularly the cytochrome P450 system, impacting drug metabolism. Hepatic microsomal enzyme inducers activate liver oxidative enzymes, altering drug metabolism. When administered alongside another drug, the duration of action may decrease due to enhanced metabolism. By understanding these interactions, we gain insights into drug efficacy and safety.

REQUIREMENTS:

Animal: Mice(20-25 g)

Apparatus: Mice cages, stopwatch

Drugs: Phenobarbitone sodium (Dose: 50 mg/kg i.p, once a day for 5 days)

Pentobarbital sodium (Dose: 45 mg/kg i.p.)

PRINCIPLE:

The hepatic microsomal enzyme system, primarily involving cytochrome P450 enzymes, plays a crucial role in the metabolism of various drugs, including barbiturates like phenobarbitone. Enzyme inducers such as phenylbutazone or rifampicin enhance the activity of these enzymes, leading to an increased rate of drug metabolism. In this experiment, the effect of enzyme induction is assessed by measuring the duration of sleep induced by phenobarbitone in mice. A shortened sleeping time after pre-treatment with an enzyme inducer indicates accelerated metabolism and clearance of phenobarbitone due to enhanced microsomal enzyme activity. This study helps in understanding drug interactions and the impact of enzyme inducers on drug pharmacokinetics.

PROCEDURE:

1. Weigh and number the animals. Divide them into Two groups, each comprising of at least 6 mice.
2. Prepare a stock solution containing 5 mg/ml of the drug and inject 1 ml/100g of body weight of animal. Prepare fresh solution everyday
3. To the First group inject Phenobarbitone once daily for 5 days. To second group inject distilled water, similarly for 5 days.
4. Prepare a stock solution containing 4.5 mg/ml of the drug and inject 1 ml/100g of the body weight of animal.
5. One hour after the last dose of phenobarbitone on the 5th day, inject pentobarbital to both the groups.
6. Note the onset and duration of sleep due to pentobarbital in both the groups.

OBSERVATION TABLE:

Sr no.	Body wt. (gm)	Treatment	Onset of action(min.)	Duration of action (min.)	% reduction in sleep time
Group 1 (Pentobarbital Treated group)					
1					
2					
3					
4					
5					
6					
Mean					
Group 2 (Phenobarbitone + Pentobarbital treated group)					
1					
2					
3					
4					

5					
6					

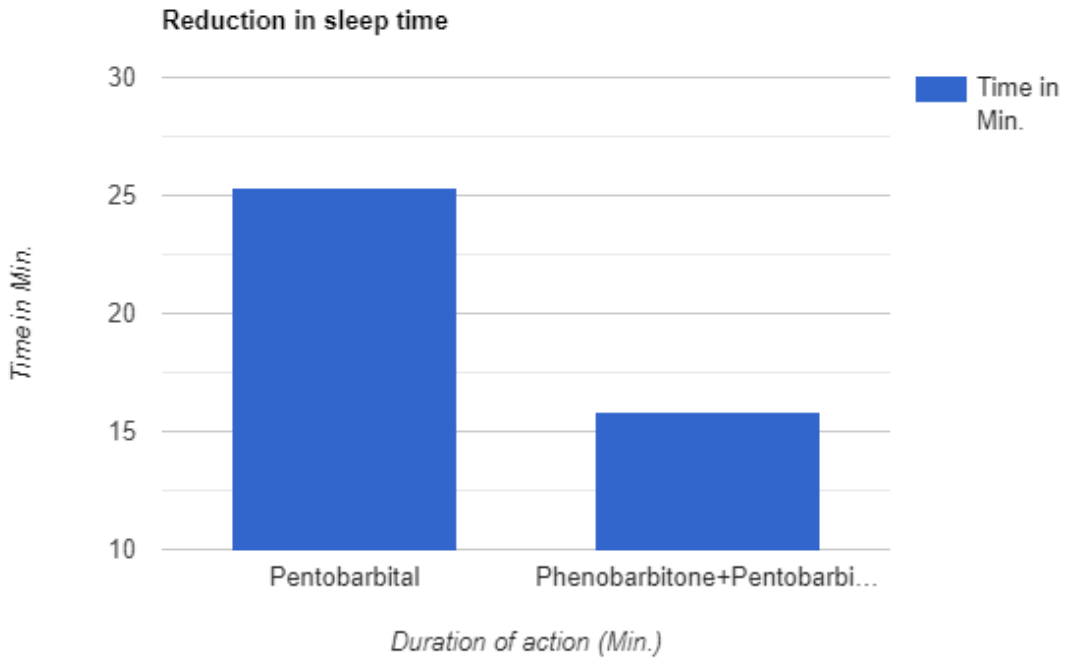
INFERENCE:

Sr no.	Body wt. (gm)	Treatment	Onset of action(min.)	Duration of action (min.)	% reduction in sleep time
Group 1 (Pentobarbital Treated group)					
1	20	Distilled water for 5 days followed by Pentobarbital (45mg/kg i.p on 5th day)	10	25	**37.5**
2	22		12	25	
3	23		9	28	
4	24		8	26	
5	21		8	25	
6	22		10	23	
Mean			9.5	25.33	
Group 2 (Phenobarbitone + Pentobarbital treated group)					
1	24	Phenobarbitone 50mg/kg i.p for 5 days followed by Pentobarbital (45mg/kg i.p on 5th day)	8	15	
2	21		10	17	
3	22		9	16	
4	24		11	15	
5	22		10	16	
6	20		8	16	
Mean			9.33	15.83	

*Observation table after completion of the experiment can be downloaded by clicking tab (RJPT SimLab)

DISCLAIMER: "The results provided here are only for reference or comparison purposes. Students are expected to perform the experiment and record their actual observations."

GRAPH:



RESULT:

The average sleeping time in the control group (Group 1), which received only pentobarbital after 5 days of distilled water, was **25.33 minutes**. In contrast, the experimental group (Group 2), which was pretreated with phenobarbitone (a hepatic microsomal enzyme inducer), showed a significantly reduced average sleeping time of **15.83 minutes**. This indicates a **~37.5% reduction** in sleeping time due to prior administration of the enzyme inducer. The decreased duration of pentobarbital-induced sleep in Group 2 suggests enhanced hepatic metabolism of pentobarbital owing to induction of liver microsomal enzymes by phenobarbitone.