Aim: Study of Effect of Hepatic Microsomal Enzyme Inducers on the Phenobarbitone Sleeping Time in Mice

Reference: Thomas N Thompson, Curtis D Klaassen, The Effects of Hepatic Microsomal Enzyme Inducers on the Pharmacokinetics of Ouabain after Portal and Systemic Administration to Rats, Journal of Pharmacy and Pharmacology, Volume 47, Issue 12A, December 1995, Pages 1041–1047, https://doi.org/10.1111/j.2042-7158.1995.tb03294.x

Introduction:

Hepatic microsomal enzyme inducers are compounds that enhance the activity of liver enzymes, particularly the cytochrome P450 enzyme system. These inducers can increase the metabolism of various drugs, thereby affecting their pharmacokinetic and pharmacodynamic properties. This study investigates how enzyme inducers alter the duration of phenobarbitone-induced sleep in mice.

Materials and Equipment:

- Animals: Healthy adult mice (20-30 g)

- Drugs and Chemicals:

- Phenobarbitone sodium (standard hypnotic agent)
- Enzyme inducers (e.g., phenobarbital, rifampicin)
- Saline solution (control)

- Equipment:

- Animal housing and handling equipment
- Syringes and needles
- Stopwatch
- Weighing balance

Method:

1. Animal Preparation:

- Acclimatize mice to the laboratory environment for at least one week before the experiment.
- Divide mice into three groups of six animals each:

- Control group (saline solution)

- Phenobarbitone group (enzyme inducer-treated)

- Rifampicin group (enzyme inducer-treated)

2. Pre-treatment with Enzyme Inducers:

- Administer the enzyme inducer (phenobarbital or rifampicin) to the respective groups intraperitoneally (i.p.) for seven consecutive days. Use saline for the control group.

- Typical doses:

- Phenobarbital: 80 mg/kg/day

- Rifampicin: 50 mg/kg/day

3. Phenobarbitone Administration:

- On the eighth day, administer phenobarbitone sodium (50 mg/kg, i.p.) to all groups.

4. Monitoring and Recording:

- Place the mice in individual cages immediately after phenobarbitone administration.

- Observe and record the onset and duration of sleep for each mouse. Sleep is defined as the loss of the righting reflex (inability to return to a normal upright position when placed on their back).

- Record the time from phenobarbitone injection to the onset of sleep and the total sleeping time (time until the mouse regains the righting reflex).

Observations:

Record the following data for each group:

- Time to onset of sleep (minutes)

- Duration of sleep (minutes)

Observations: The average time to onset of sleep and the duration of sleep for each group of mice can be represented in the following table:

Group	Time to Onset of Sleep (min)	Duration of Sleep (min)
Control	10 ± 2	120 ± 10
Phenobarbital	8 ± 1	60 ± 5
Rifampicin	9 ± 1	65 ± 7

Note: This table is only for reference, actual results depend on your practice in laboratory.

Interpretation of Results:

Control Group: The control group, which received saline solution, had an average onset of sleep at 10 minutes and slept for about 120 minutes.

Phenobarbital Group: Mice pre-treated with phenobarbital, an enzyme inducer, showed a reduced duration of sleep (approximately 60 minutes). This indicates enhanced metabolic activity due to enzyme induction, leading to faster clearance of phenobarbitone from the system.

The onset of sleep occurred slightly earlier compared to the control group, averaging 8 minutes.

Rifampicin Group: Similar to the phenobarbital group, mice pre-treated with rifampicin also had a reduced sleeping time (approximately 65 minutes), confirming the enzyme-inducing effects of rifampicin. The onset of sleep in this group was at 9 minutes on average.