AIM: Anticonvulsant activity assessment using Maximal Electroshock Method (MES) in rats

REFERENCE:

1) M.N. Gosh Common Laboratory Animals, Fundamentals of Experimental Pharmacology, Fifth Edition, 2011
2) Kulkarni S.K., Handbook of experimental pharmacology, New Delhi: Vallabh Prakashan, 2014.

INTRODUCTION

Epilepsy, a complex neurological condition characterized by recurrent seizures, affects millions worldwide. To explore potential treatments, researchers turn to animal models that replicate seizure activity. Among these models, the **maximal electroshock (MES) method** stands out. By inducing convulsions in laboratory rats, MES mirrors the tonic-colonic phases observed in human epilepsy. In our study, we narrow our focus to **phenytoin**, a widely used antiepileptic drug. Before embarking on this investigation, a solid grasp of antiepileptic pharmacology is essential. Let's delve into the intricacies of this experiment.

REQUIREMENTS:

Apparatus: Electro-convulsometer, corneal electrode (apply 150 mA current for 0.2 sec), stopwatch

Animal: Rat (150-200 gm)

Drugs: phenytoin (Dose 25 mg/kg; prepare a stock solution containing 5 mg/ml of drug and inject 0.5 ml/100g body weight of the animal).

PRINCIPLE:

- **Maximal Electroshock (MES)**: This method simulates grand mal epilepsy in animals.
- **MES Convulsions Phases**:

1. **Tonic Flexion**: Initial phase with muscle stiffness.
2. **Tonic Extensor**: Follows tonic flexion, characterized by extension of limbs.
3. **Clonic Convulsion**: Repetitive muscle contractions.
4. **Stupor**: A period of altered consciousness.
5. **Recovery or Death**: Outcome after convulsions.

- **Anticonvulsant Activity Assessment**:

1. A substance is considered anticonvulsant if it reduces or abolishes the tonic extensor phase of MES convulsions.

2. Phenytoin is a known antiepileptic drug.

OBSERVATION TABLE:

Control group

SR. NO.	Body weight (g)	Treatment	Time (sec) in various phases of convulsion				
			Flexion	Extensor	Clonus	Stupor	Recovery / death
1		Control					
2							
3							
4							
5							
6							
Mean							

Test group

SR. NO.	Body weight (g)	Treatment	Time (sec) in various phases of convulsion				
			Flexion	Extensor	Clonus	Stupor	Recovery / death
1		Phenytoin					
2							
3							
4							
5							
6							
Mean							

INFERENCE:

Control group

SR. NO.	Body weight (g)	Treatment	Time (sec) in various phases of convulsion				
			Flexion	Extensor	Clonus	Stupor	Recovery / death
1	150	Control	4	15	6	127	Recovery
2	165		5	13	6	119	Recovery
3	156		6	14	5	124	Recovery
4	180		4	12	4	115	Recovery
5	195		3	9	3	110	Recovery
6	170		4	13	4	117	Recovery
Mean			4.3	12.6	4.6	118.6	

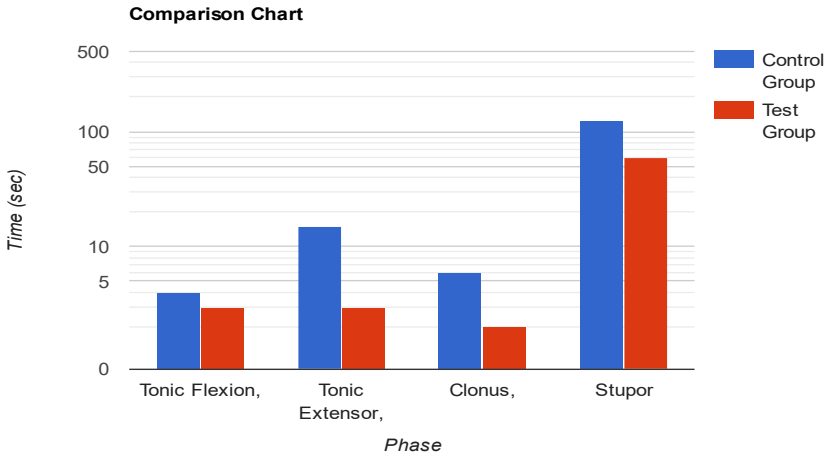
Test group

SR. NO.	Body weight (g)	Treatment	Time (sec) in various phases of convulsion				
			Flexion	Extensor	Clonus	Stupor	Recovery / death
1	155	Phenytoin	3	3	2	60	Recovery
2	165		3	4	3	58	Recovery
3	175		2	3	2	52	Recovery
4	185		3	2	2	48	Recovery
5	195		2	3	3	45	Recovery
6	170		3	4	2	56	Recovery
Mean			2.6	3.16	2.3	53.16	

*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:



PROCEDURE:

1. **Animal Preparation and Grouping**:

- Weigh and number the rats.
- Divide them into two groups, each consisting of 6 rats:
  - **Control Group**: This group will not receive any drug treatment.
  - **Test Group (Phenytoin)**: This group will receive phenytoin as the antiepileptic drug.

2. **Electroshock Application and Observation**:

- Properly hold the rat and place corneal electrodes on the cornea.
- Apply the prescribed current to induce maximal electroshock (MES).
- Note the different stages of convulsions:
  - **Tonic Flexion**: Initial muscle stiffness.
  - **Tonic Extensor Phase**: Extension of limbs.
  - **Clonic Convulsions**: Repetitive muscle contractions.
  - **Stupor**: Altered consciousness.
  - **Recovery or Death**: Outcome after convulsions.
- Record the time (in seconds) spent by the animal in each phase.
- Repeat the procedure with other animals in the control group after inducing the Drug.

3. **Phenytoin Administration**:

- Inject phenytoin intraperitoneally (I.P.) to a group of 6 rats in the test group.

- Wait for 30 minutes to allow phenytoin to take effect.

4. **Repeat Electro-Convulsions**:

- Subject the animals in the test group to electro-convulsions as described in step 2.
- Observe any reduction in the duration of the tonic extensor phase of MES-induced convulsions.
- Document any abolition of the tonic extensor phase due to phenytoin treatment.

RESULTS:

1. **Control Group**:
- Rats subjected to maximal electroshock (MES) without any drug intervention.
- Observed MES-induced convulsions, including tonic flexion, tonic extensor, clonus convulsion, stupor, and recovery or death.
2. **Drug Treatment Group (Phenytoin)**:
- Administered phenytoin intraperitoneally (I.P.) to rats.
- Noted the effect on MES-induced convulsions.
- **Observations**:
  - **Reduced Tonic Extensor Phase**: Phenytoin significantly reduced the duration of the tonic extensor phase.
  - **Anticonvulsant Activity**: Phenytoin demonstrated anticonvulsant properties by suppressing the most severe phase of convulsions.
3. **Comparison**:
- Compared results between control and drug treatment groups.
- Phenytoin's efficacy in reducing MES-induced convulsions validates its antiepileptic potential.

CONCLUSION:

- Phenytoin holds promise as an effective antiepileptic agent.
- Further studies are warranted to explore its mechanisms of action and safety profile.