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## Postictal neuromuscular deficits: Experimental investigation of the therapeutic potential of *Plumbum metallicum*

Avishkar Zagday, Vinay Upadhyay

### ABSTRACT

**Background:** Conventional antiepileptic treatments frequently fail to address postictal neuromuscular impairments, which include motor incoordination and muscle weakness, which are typical following epileptic episodes. This study uses a Pentylene tetrazole (PTZ) induced mouse seizure paradigm to assess the therapeutic potential of *Plumbum metallicum*, a homeopathic medicine, in reducing these impairments. **Aim and Objectives:** This study aims to evaluate the therapeutic potential of *Plumbum metallicum* in mitigating postictal neuromuscular deficits using a PTZ-induced murine seizure model. Motor coordination was assessed via the rotarod test, comparing the effects of *Plumbum metallicum* at 6C, 30C, and 200C potencies with diazepam and PTZ-only groups. **Materials and Methods:** Male albino Wistar mice were divided into six groups (n=6/group): Control, PTZ-only, Diazepam+PTZ, and three groups receiving *Plumbum metallicum* at 6C, 30C, and 200C potencies prior to PTZ administration. Treatments were given chronically for 14 days. Motor coordination was measured by Rota Rod test and statistical analysis by Dunnett's test and one-way ANOVA. **Results:** *Plumbum metallicum* improved rotarod performance in a dose-dependent way. When compared to the PTZ group, the 200C potency had statistically significant neuroprotective and motor-enhancing benefits, but the 6C potency exhibited little or even negative effects. Performance in the 200C group was similar to that of the diazepam-treated group, indicating similar effectiveness in fostering postictal motor recovery. **Conclusion:** The results indicate that *Plumbum metallicum* has a potency-dependent impact, with 200C showing the greatest effectiveness in alleviating postictal motor impairments. This is consistent with homeopathic principles, which indicate that larger potencies have more therapeutic potential. The study lays the groundwork for future clinical and mechanistic investigations into *Plumbum metallicum's* function in post-seizure recovery and emphasizes its potential as a neurotherapeutic agent.

**Keywords:** Seizure recovery, Homeopathic potency, Rodent behavior, Motor dysfunction, Rotarod performance.

### INTRODUCTION

The postictal period is referred to as the period after a seizure has occurred and is associated with various physiological and behavioral symptoms [1]. Postictal syndrome (PIS) is characterized by clinical, biological, electroencephalographic (EEG) and, possibly, brain imaging signs immediately following the termination of the epileptic ictal discharge [2]. Conventional pharmacological treatments focus primarily on seizure control but often neglect postictal motor dysfunction and neuromuscular recovery. There is growing interest in medical sciences including homeopathy, which may offer adjunctive benefits in seizure management and neuromuscular rehabilitation. *Cuprum metallicum*, a homeopathic preparation derived from copper, has shown promise in experimental models of seizures. For example, studies using pentylene tetrazole (PTZ)-induced seizure paradigms in mice suggest that ultra-high dilutions of *Cuprum metallicum* can modulate seizure activity and improve neuromuscular recovery [3]. In addition to mineral-based homeopathic remedies, several botanical agents have demonstrated neuropharmacological activities relevant to epilepsy and postictal neuromuscular function. *Fumaria officinalis* Linn., for instance, has been evaluated for its muscle relaxant and CNS depressant properties in experimental animals, showing significant effects that support its anticonvulsant potential [4]. Similarly, the aqueous extract of *Thuja occidentalis* Linn. has exhibited anxiolytic, nootropic, anticonvulsant, and motor coordination benefits in animal models, including PTZ-induced seizures [5]. Furthermore, *Ficus benghalensis* root extracts also display anticonvulsant and neuromuscular-stabilizing properties [6]. These findings underscore the potential of integrating homeopathic interventions for a multimodal neurotherapeutic approach. Contemporary neuropharmacological research stresses the importance of addressing not only seizure activity but also the functional restoration of motor coordination and muscle strength postictally. Electrophysiological studies and behavioral assays have been instrumental in advancing this understanding [7,8]. This research study evaluates the role of *Plumbum metallicum* in

managing postictal neuromuscular deficits, using diazepam as the standard antiepileptic drug for comparison. Drawing on experimental and integrative medicine research, it aims to promote innovative, holistic strategies for improving outcomes in seizure disorders.

### Reason for selection of remedy

In homeopathy, postictal neuromuscular deficit is not explicitly referenced within the repertory. Instead of prescribing based on a specific diagnosis, homeopathic treatment focuses on the individualized symptoms presented by the patient. This approach stands in contrast to conventional medicine, which typically prescribes treatments based solely on the diagnosed condition. In homeopathy, remedies are selected based on their ability to match the patient's overall symptom profile. For cases involving conditions such as postictal neuromuscular deficit the remedy most commonly indicated in the repertory is *Plumbum metallicum*. However, this does not imply that this remedy is universally applicable to all cases of postictal neuromuscular deficit. It represents the nearest similimum — a remedy that most closely matches the patient's individual symptom presentation. Also given below are the Repertory Sheets of the remedy and the rubrics covering the remedy for rubrics like Seizures, Convulsion and Epilepsy.

This study aims to evaluate the efficacy of *Plumbum metallicum* in mitigating postictal neuromuscular deficits in a pentylenetetrazole (PTZ)-induced murine seizure model by assessing motor recovery through the rotarod performance test and comparing its therapeutic effects at different potencies (6C, 30C, and 200C) against both PTZ controls and a diazepam-treated group.

## MATERIALS AND METHODS

### Animals

Adult albino Wistar male mice (100-150 g) were used for this study. The animals were housed at  $24 \pm 2^\circ\text{C}$  and relative humidity  $55 \pm 5$  with 12:12 h light and dark cycle. They had a free access to food and water ad libitum. The animals were acclimatized for a period of 7 days before the study.

### Ethical Approval

The experimental protocol was approved by the Institutional Animal Ethics Committee of SMBT College of Pharmacy, Nashik. (Registration no: 1329/PO/Re/S/10/CCSEA).

### Drugs and Chemicals

- PTZ (Pentylenetetrazol): 80 mg/kg i.p. to induce seizures
- Plumbum metallicum: Homeopathic preparations (6C, 30C, and 200C potencies)
- Diazepam: Standard anticonvulsant (4 mg/kg i.p.)

### Homeopathic Drug Preparation and Administration Protocol

For experimentation the experimental animals were given the homeopathic drug *Plumbum metallicum* at three different dose (potencies) for 14 days. On 14<sup>th</sup> Day PTZ was given to the experimental animals and readings were noted. After readings the animals were sacrificed and brain was extracted for essays.

Initially, an acute administration protocol was attempted in which the homeopathic dilutions were administered shortly before PTZ injection on the same day. However, this acute intervention failed to elicit anticonvulsant activity, as animals displayed no significant delay in seizure onset. In response, and consistent with the laws of Drug proving and the Theory of chronic disease management, a chronic

dosing protocol was adopted. This allowed for potential systemic modulation and subtle energetic imprinting over time.

### Experimental Design

Number of mice in each group- 6

Gender- All Male.

- Group I: Control (normal saline)
- Group II: PTZ (80 mg/kg i.p.)
- Group III: Diazepam + PTZ
- Group IV: Plu M(*Plumbum Metallicum*) 6C + PTZ
- Group V: Plu M 30C + PTZ
- Group VI: Plu M 200C + PTZ

Total number of mice- 36

### Behavioural Test- Rota Rod Test

The rotarod test is a behavioral assessment method used in animal studies to evaluate motor coordination, balance, and learning by measuring how long a rodent can stay on a rotating rod before falling.

#### Purpose:

The rotarod test is used to assess the effects of drugs, genetic manipulations, or injuries on motor function in rodents.

#### Procedure:

Rodents are placed on a rotating rod, which can be set to rotate at a constant speed or accelerate.

The time the animal can stay on the rod (latency to fall) is recorded. The test can be used to assess motor coordination, balance, and motor learning.

#### Applications:

Evaluating the effects of drugs on motor coordination. Assessing motor deficits in animal models of neurological disorders.

- Higher fall time = Better motor performance.
- Shorter fall time = Impaired coordination or muscle weakness.

**Advantages:** Simple and objective method for assessing motor function. Widely used in preclinical research.

**Disadvantages:** The test may not be sensitive to subtle motor deficits. The test can be stressful for animals.

#### Statistical Analysis

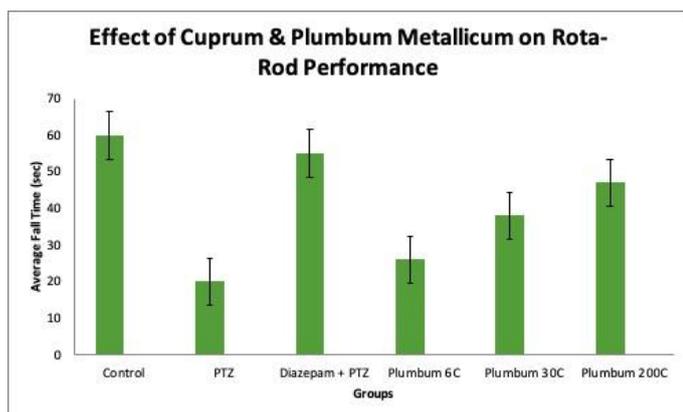
All the data were shown as mean  $\pm$  standard error of the mean. Statistical analysis was performed with one-way ANOVA followed by Dunnett's test.

## RESULTS

*Plumbum* shows dose-dependent improvements in Rota Rod performance (Table 1). 200C potency demonstrate significant neuroprotective or motor-enhancing effects. Low potencies (3C) may initially worsen coordination, possibly due to aggravating effects or insufficient stimulation. *Plumbum* counteracts motor deficits, with highest efficacy at 200C potency (Figure 1). This remedy could support traditional use of this homeopathic agent in treating motor coordination disorders.

**Table 1:** Rota Rod performance

Group	Avg Fall Time (Second)
Control	60
PTZ	20
Diazepam + PTZ	55
Plumbum 6C	26
Plumbum 30C	38
Plumbum 200C	47



**Figure 1:** Effect of *Plumbum metallicum* on Rota-Rod Performance

## DISCUSSION

This study demonstrates that *Plumbum metallicum* enhances motor coordination in a dose-dependent fashion, with the 200C potency exhibiting the most pronounced improvement in Rota Rod performance. These results corroborate earlier assertions of Plumbum's neuroprotective or motor-enhancing properties, especially in situations that impair coordination [3,6-8]. The 6C potency, which is expected to exert a physiological stimulation due to its relatively higher material content, did not produce effects comparable to the 200C potency. According to the 'Organon of Medicine' in homeopathy, the higher the potency, the lesser the material substance, yet the greater the medicinal effect. By this reasoning, one might expect 6C to show stronger physiological effects, particularly in the presence of pronounced pathology. However, the findings suggest that *Plumbum metallicum* is a nearer simulum to this pathology.

The noticeable improvement at 200C raises the possibility that highly potentized Plumbum may activate regulatory pathways that enhance neuromuscular performance. Further research is needed to confirm these findings and clarify the biological basis of these effects.

## CONCLUSION

This study shows that *Plumbum metallicum* has a potential effect on postictal neuromuscular impairments in a PTZ-induced mouse model of tonic-clonic seizures, as measured by rotarod performance. The results show a potency-dependent therapeutic impact, with the 200C dilution generating the greatest improvement in motor coordination and endurance after seizures. While lesser potencies, such as 3C, had no or even transiently negative effects, greater potencies (especially 200C) indicate a considerable neuroprotective and motor-rehabilitative potential.

A comparison with diazepam highlights *Plumbum metallicum*'s significance in promoting motor recovery during the postictal period. These findings back up its longstanding usage in homeopathy to treat motor coordination deficits and give experimental justification for its use into holistic, complementary seizure control techniques. Further

research into its molecular processes and long-term effects is required to enhance its translational application.

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## Conflict of interest

The authors declared no conflict of interest.

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None declared.

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