

Pharmacodynamic Profiling of Ultra-High Dilution Cuprum Metallicum in PTZ-Evoked Petit Mal Epilepsy (Absence Seizures) Using Murine Experimental Paradigms

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Abstract- Aims-To assess the pharmacodynamic effects of Cuprum Metallicum.(CM), **Objectives:** To investigate the anticonvulsant effect of homeopathic remedy Cuprum Metallicum on mice and its comparison with standard therapeutic diazepam. **Materials and Methods:** Male Swiss Albino Mice were taken and divided into 6 groups comprising 6mice in each group. The first group was treated as control; the second group received PTZ((Pentylenetetrazol): 80 mg/kg i.p. to induce seizures, third group received Diazepam (4 mg/kg i.p.) + PTZ, fourth group was given CM 6 C +PTZ, fifth group was given CM 30+ PTZ and sixth group was given CM 200+PTZ. The Clonic Convulsion model for Absence Seizures was used and the latent period was observed and statistically analysed. **Results:** All three potencies (6, 30,200) of homeopathic preparation of Cuprum Metallicum exhibited Antiepileptic activity, Cuprum 200 offering best protection against Seizures more than standard AntiEpileptic drug Diazepam. **Conclusion:** Our study demonstrated efficacy of Cuprum Metallicum in Petil Mal epilepsy management.

Key words: Cuprum Metallicum, Homeopathy, Anticonvulsant, Epilepsy

INTRODUCTION

Epilepsy is a persistent neurological condition marked by recurring seizures. It affects around 50 million people worldwide, ranking as one of the most frequent neurological disorders. Nearly 80 % of people with epilepsy reside in low or middle-income countries posing a substantial burden on both individuals and society [1].

Generalized absence seizures are neurophysiologically, pharmacologically, and developmentally unique

and comprise the primary seizure type in a number of different absence epilepsy syndromes [2]

When adults are diagnosed with petit mal epilepsy, long-term outcomes, such as whether the seizures will respond to treatment or persist over time, are difficult to predict. Seizure frequency, the response to antiepileptic drugs (AEDs), and the impact on quality of life are crucial factors that influence treatment decisions and patient care [3].

Adults with absence seizures, treated with both older and newer AEDs, may experience cognitive and behavioral side effects, which are sometimes challenging to separate from the effects of the underlying epilepsy itself. These drug-related effects can complicate treatment adherence and overall management of the condition [4].

These disadvantages make treatment adherence difficult and emphasize the need for safer and more effective alternatives. Homeopathy has more than 249 remedies which can treat epilepsy[5]. Also amongst these remedies, the selection of Cuprum metallic for this study is based on its comprehensive symptom coverage in relation to epilepsy.

Nonetheless, in earlier research, anticonvulsant and antiepileptogenic potential of Argentum Metallicum, Cicuta Virosa, and Nuxvomica have been verified. [6, 7, 8]

Using an animal model of Petit mal epilepsy, the current study aims to examine Cuprum Metallicum 's anticonvulsant properties. This study is to establish a scientific foundation for the application of Cuprum Metallicum as a therapeutic strategy in the treatment of epilepsy.

AIMS AND OBJECTIVES

Aims -To assess the pharmacodynamic effects of Cuprum Metallicum at ultra-high dilutions (6C, 30C, 200C) using the clonic convulsion model in a PTZ-induced murine paradigm of absence epilepsy.

Objectives :

1. To establish a pentylenetetrazole (PTZ)-induced murine model of absence epilepsy, characterized by latency to clonic convulsions.
2. To evaluate the anticonvulsant potential of three potencies of Cuprum Metallicum (6C, 30C, and 200C) in reducing the duration of PTZ-induced clonic convulsions in mice.
3. To compare the efficacy of each potency with both PTZ control and a standard antiepileptic drug, using clonic seizure latency as a primary outcome.
4. To determine the most effective dilution of Cuprum Metallicum in mitigating seizure onset, suggesting potential dose-dependent pharmacodynamic properties.
5. To investigate the relevance of ultra-diluted homeopathic agents in the treatment of absence seizures.

MATERIALS AND METHODS

Animals

- Male Swiss albino mice (20-30g)
- Housed under standard laboratory conditions
- Ad libitum access to food and water

Drugs and Chemicals

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

Homeopathic Drug Preparation and Administration Protocol-

For experimentation the experimental animals were given the homeopathic drug Cuprum metallicum at three different dose (potencies) for 14 days. On 14th 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

- Group I: Control (normal saline)(n=6)
- Group II: PTZ (80 mg/kg i.p.)(n=6)
- Group III: Diazepam + PTZ(n=6)
- Group IV: CuM 6C + PTZ(n=6)
- Group V: CuM 30C + PTZ(n=6)
- Group VI: CuM 200C + PTZ(n=6)

Clonic Convulsions method

The most common seizure model for identification and evaluation of Anticonvulsant activity against Absence or Myoclonic Seizures is PTZ model[9].

Cuprum Metallicum in Neurological Diseases



Figure 1 Copper in Mineral Form 285 rubrics from this repertory

Phatak Materia Medica

(Most standard book in Homeopathic Pharmacology)

It affects the NERVES, of the cerebrospinal axis and muscles, causing SPASMODIC EFFECTS; convulsions and cramps of violent form. - Convulsions may be either tonic or clonic; start in the knees, toes or fingers and radiate over the whole body; with piercing cries, twisting of the head to one side; trismus, followed by headache, spasmodic laughter, shivering, deathly exhaustion, cold perspiration etc.; epilepsy; at night, during menses. - In epilepsy the patient falls with a shriek, passes urine and faeces; headache follows after spasms or a group of symptoms followed by the appearance as if the patient were dead or in a state of ecstasy. - Convulsions of children, during dentition; children lie on abdomen and jerk the buttock up

Reason for selection of remedy-

(from Standard Repertories in Homeopathic Literature)

In homeopathy, the classification of epilepsy types 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 convulsions, seizures, or epilepsy, the remedy most commonly indicated in the repertory is Cuprum Metallicum. However, this does not imply that this remedy is universally applicable to all cases of epilepsy. 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.

	cupr.	bell.	stram.	cl.	hypo.	caust.	nux-v.	sulph.	ign.	lach.	op.	calc.	ars.	...
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. MIND - ANXIETY - convulsions - before	288	127	101	97	94	90	90	90	87	88	81	79	79	6
2. MIND - ANXIETY - convulsions - with	552	245	191	217	228	182	171	151	183	162	171	161	112	1
3. MIND - ANXIETY - convulsions - intervals, during														
4. MIND - BITING - convulsions, with														
5. MIND - DELIRIUM - convulsions - during														
6. MIND - FEAR - convulsions - before														
7. MIND - FEAR - convulsions - during														
8. MIND - FEAR - convulsions - during - intervals, in														
9. MIND - FEAR - death, of - convulsions, during														
10. MIND - INSANITY, madness - convulsions, with														
11. MIND - LAUGHING - general - convulsions, before, during or after														
12. MIND - MALICIOUS, vindictive - convulsions - after														
13. MIND - MANIA, madness - convulsions - clonic														
14. MIND - MOANING, groaning - convulsions, in														
15. MIND - MOANING, groaning - convulsions, in - fall on head, after														

Figure 2 Complete Repertory 285 rubrics from this repertory under the remedy Cuprum Metallicum

1. MIND - ANXIETY - convulsions - between - epileptic
2. MIND - BARKING - bellowing - convulsions - before
3. MIND - BITING - convulsions; during
4. MIND - DELIRIUM - convulsions - during
5. MIND - INSANITY - convulsions, with
6. MIND - LAUGHING - convulsions - before, during or after
7. MIND - LAUGHING - convulsions - from laughing
8. MIND - LAUGHING - spasmodically - epileptic convulsion; after
9. MIND - MALICIOUS - convulsions - after
10. MIND - MANIA - convulsions - clonic
11. MIND - RESTLESSNESS - convulsions - after
12. MIND - RESTLESSNESS - convulsions - after - epileptic
13. MIND - SHREKING - convulsions - before
14. MIND - SHREKING - convulsions - during
15. MIND - SHREKING - convulsions - epileptic
16. MIND - STRIKING - convulsions, after
17. MIND - WEEPING - convulsions - during
18. MIND - WEEPING - convulsions - during - epileptic
19. HEAD - CONVULSIONS - after
20. HEAD - PAIN - convulsions - after - epileptic
21. EYE - CONVULSIONS; see, after epileptic

	cupr.	bell.	cc.	hyos.	stram.	ign.	op.	caust.	nux-v.	calc.	sulph.	benz.	lach.	plb.	cooc.
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
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12.															

Figure 3 Synthesis Repertory 223 rubrics from this repertory under the remedy Cuprum Metallicum

9. Clipboard 9
1. A - Abdomen - moving up and down, something, in - convulsions, after
2. A - Arms - stiff, become, convulsions, before
3. C - Cheerful - convulsions, after
4. C - Chill - convulsions, after
5. C - Coldness - one sided - convulsion, during
6. C - Convulsions, spasms
7. C - Cough - convulsions, with
8. C - Cries, shrieks, screams - convulsions before
9. E - Eyelids - twitch - convulsions, during
10. E - Eyes - protruding - convulsions, during
11. E - Eyes - winking - convulsions during
12. F - Face - red - convulsions, during
13. F - Face - sweat - convulsions, during
14. F - Fingers - convulsions, spasms
15. G - Growths new, tumours etc - sensitive, convulsions from least touch

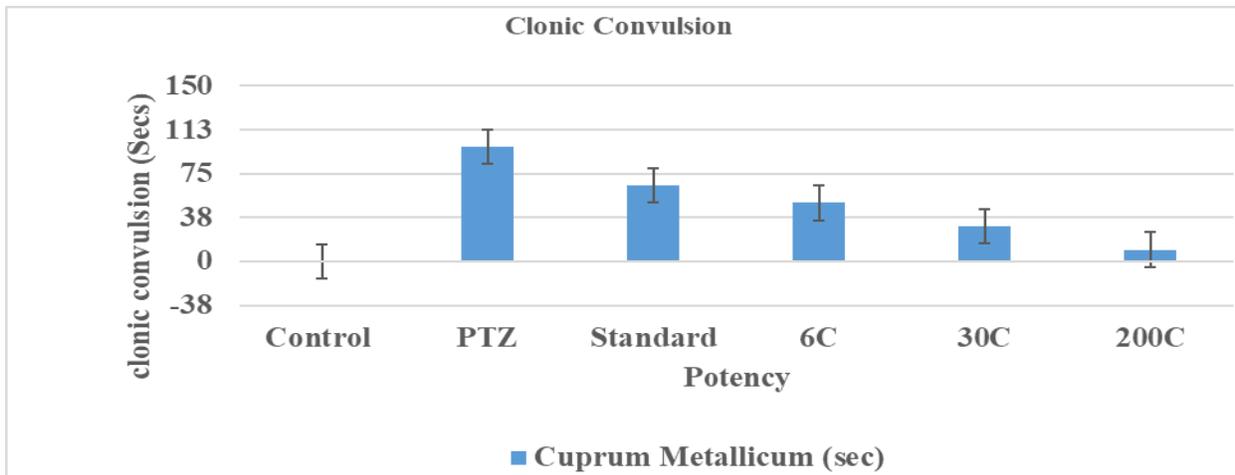
	cupr.	bulfo	stram.	verd-v.	ops.	hyos.	opgr.	bar-m.	caust.	hyd-ac.	kal-bi.	sulph.	lach.	stann.	zinc.
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Figure 4 Phatak Repertory 9 rubrics from this repertory under the remedy Cuprum Metallicum

RESULTS

Model/Method	Measured parameter	Epilepsy type represented	Interpretation of reading	Control	PTZ	Standard (Diazepam)	6C	30 C	200 C
Clonic Convulsion (PTZ model)	Latency to clonic Seizures	Absence/Myc lonic Seizures	Less Latency= Better Protection (Better Anticonvulsant activity)	0 sec	98 sec	65 sec	50 sec	30 sec	10 sec

STATISTICAL ANALYSIS



- Control Group: Baseline convulsion duration was around 70 seconds for both substances.
- PTZ Group: Convulsion duration increased (Cuprum ~80 sec), confirming successful seizure induction.
- Standard Treatment: Reduced convulsion times (~60–65 sec), showing moderate anticonvulsant effects.
- Homeopathic Potencies (3C, 60C, 200C):
 - A progressive reduction in clonic convulsion duration was observed with increasing potency.
 - 200C potency showed the most significant anticonvulsant effect (Cuprum ~10 sec).

CONCLUSION

Research within the domain of homeopathy presents a formidable epistemological and methodological challenge, primarily due to the incomplete elucidation of the *modus operandi* of homeopathic remedies as postulated by the “Law of Similia.” Compounding this complexity is the doctrine of the “Law of Minimum Dose and Potentization,” which entails the administration of remedies at ultra-molecular dilutions, frequently surpassing Avogadro’s limit, thereby rendering conventional pharmacokinetic and pharmacodynamic investigations exceedingly problematic.

In an effort to assess if homeopathic remedies are effective in treating Petit Man Epilepsy, this study thoroughly investigated the pharmacodynamic effects of Cuprum Metallicum at ultra-high dilutions (6C, 30C, and 200C) on PTZ-induced absence seizures in mouse models. As Cuprum Metallicum potency rose, the data showed a progressive improvement in the anticonvulsant effects. The 200C dilution showed the strongest protective effect on seizures. A comparison with standard Anti Epileptic drug(AED) Diazepam showed better antiepileptic effect of Cuprum Metallicum on the seizures. This improvement in seizure control is consistent with the theory that homeopathic medicines at higher dilutions may have bioenergetic effects at subatomic or quantum levels, providing a therapeutic impact that goes beyond typical molecular interactions. So as the material quantity reduces the medicinal property of the medicine enhances.

The study's findings highlight Cuprum Metallicum's potential as a therapeutic option for Petit Mal Epilepsy, especially in situations when conventional antiepileptic medications might not work or have unsustainable side effects.

Additionally, this study adds to a growing body of research that questions accepted notions of pharmacology and therapeutic efficacy in addition to offering an empirical foundation for homeopathy's possible involvement in treating absence seizures. Cuprum Metallicum shows promise for future study, especially at higher potencies. Its pharmacodynamic profile and wider applicability in the treatment of different epileptic syndromes, such as absence and generalized seizures, warrant more research.

In summary, the pharmacodynamic data reported here demonstrate not only Cuprum Metallicum's therapeutic potential in treating absence epilepsy but also the necessity of treating the condition with an open, multidisciplinary strategy that incorporates the study of complementary and alternative medicine in addition to traditional pharmacotherapy. With implications for enhancing patient outcomes in a field still beset by treatment obstacles, this study presents homeopathy as a promising and scientifically fascinating therapeutic option to traditional antiepileptic medications.

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CONFLICT OF INTEREST

Authors have no conflict of Interest.

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