WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 14, Issue 24, 720-729. Research Article ISSN 2277–7105

EVALUATION OF THE ANTIDOTAL POTENTIAL OF HEM GAIRIKA (RED OCHRE) AGAINST ARKA KSHEERA (CALOTROPIS SPP. LATEX)-INDUCED TOXICITY IN ALBINO MICE

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Article Received on 16 Nov. 2025,
Article Revised on 06 Dec. 2025,
Article Published on 15 Dec. 2025,

https://doi.org/10.5281/zenodo.17950372

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How to cite this Article: Dr. Mamata Adhao[1]*, Dr. Abhijit Kawale[2] (2025). Evaluation of the Antidotal Potential of Hem Gairika (Red Ochre) Against Arka Ksheera (calotropis spp. Latex)-Induced Toxicity in Albino Mice. World Journal of Pharmaceutical Research, 14(24), 720–729.

ABSTRACT

Background: *Arka* (Calotropis gigantea/procera), classified as an *Upavisha* (moderately toxic herb), possesses toxic latex (*Arka Ksheera*) containing potent cardiac glycosides. Hem Gairika (Red Ochre), traditionally described in Ayurvedic texts like *Rasajalanidhi*, is recognized for its detoxifying properties and has been suggested as a potential antidote for Ark (Calotropis) poisoning. **Objectives:** To experimentally evaluate the antidotal effect of Hem Gairika in an in vivo animal model of Arka Ksheera toxicity. **Materials and Methods:** Latex of *Calotropis spp.* was collected and used to induce toxicity in Swiss albino mice. Hem Gairika was procured, purified using *Goghrita* (cow ghee), and administered orally in two doses (19.5 mg/kg and 39 mg/kg). Mice were divided into four groups: Control, Arka toxicity only and two treatment groups with Hem Gairika at different doses. Animals were monitored for 15 days post-dosing. Parameters such as body temperature, convulsions, pupil dilation, survival rate and other toxic symptoms were recorded and statistically analyzed using one-way ANOVA, Dunn's test, and Chi-square test. **Results:** Arka Ksheera produced significant toxic effects including convulsions, salivation, dilated pupils, and increased mortality. Administration of Hem Gairika, especially at the higher dose, significantly delayed the onset of convulsions ($p < 0.01$), pupil dilation ($p < 0.0001$) and improved survival rates although the latter was not statistically significant ($p > 0.05$).

Reduction in symptoms like salivation and irregular respiration was observed in the treated groups. **Conclusion:** The study provides preliminary evidence supporting the antidotal role of Hem Gairika in mitigating acute toxicity caused by Arka Ksheera.

KEYWORDS: Arka Ksheera, Hem Gairika, Upavisha, Antidote, Albino mice.

INTRODUCTION

Agadtantra, known as Ayurvedic toxicology, is a specialized branch of traditional Indian medicine that focuses on identifying and managing harmful effects caused by various natural or artificial substances in the body. This discipline is vital not only for the prevention of poisoning but also for the development of effective treatment strategies. Within this framework, certain plant-based agents are classified under ***Upavisha*** - a category of moderately toxic herbs that can pose health risks under inappropriate use or exposure.[1,2]

One such plant is ***Arka*** (Calotropis gigantea *and* Calotropis procera), a commonly found shrub across India with recognized applications in both therapeutic and spiritual practices. Although frequently used in Ayurvedic formulations. *Arka* is inherently toxic. Its milky latex, known as *Arka Ksheera*, contains potent **cardiac glycosides** such as **uscharin, calotropin, calotoxin**, and **calactin**, which can irritate the skin on contact and cause blisters and inflammation. Ingesting the latex in excessive amounts may lead to serious systemic symptoms like **vomiting, convulsions, excessive salivation, diarrhoea, abdominal cramps**, and in extreme cases, death.[3,4]

Traditional preparations like ***Mahavishgarbha Taila, Dhanvantara Ghrita***, and ***Arka Lavana*** often incorporate *Arka* as a core ingredient, underlining its widespread therapeutic usage. However, due to the plant's toxic nature, accidental exposure or misuse intentional or unintentional can lead to poisoning.[5] Despite its widespread use and known toxicity, standardized treatment protocols for ***Arka* (Calotropis) poisoning** are still underdeveloped.

Classical Ayurvedic texts offer various ***Vishaghna Dravyas*** (antidotal substances) to manage toxic effects. One such remedy, described in ***Rasajalanidhi***, is ***Hem Gairika*** (*Red Ochre*), a naturally occurring mineral composed of alumina silicate and iron oxide.[6] Once processed through purification methods using cow's ghee (*Goghrita*) and cow's milk (*Godugdha*)**.** *Hem Gairika* is applied both externally and orally to mitigate the harmful effects of *Arka Ksheer* (latex). Apart from its detoxifying role, this mineral has been traditionally used in managing a

range of conditions such as **skin diseases, ulcers, bleeding disorders, urticaria, and inflammatory conditions**, indicating its broad therapeutic spectrum. Given the increased use of Arka in herbal medicine and the possibility of accidental poisoning, coupled with the limited availability of scientifically validated antidotes, a deeper evaluation of **Hem Gairika's antidotal potential** is warranted. Its **cost-effectiveness, easy accessibility, and historical relevance** make it suitable for further investigation.[7-9]

This study aims to explore and validate the effectiveness of ***Hem Gairik* in countering the toxic effects of *Arka***, thereby aligning ancient Ayurvedic principles with modern approaches to toxicology.

OBJECTIVES

To experimentally evaluate the antidotal efficacy of Hem Gairik Churna in mitigating the toxic effects of Ark (Calotropis spp.) of Ark Poisoning in Abino Mice.

MATERIALS AND METHOD

Drug Collection

a. *Arka Ksheer* (latex of *Calotropis*) was sourced from the herbal garden of the institute by collecting the latex from fresh leaves and stored in a clean glass container.
b. *Hem Gairik* (haematite) was procured from the local market and processed into powder form (Churna) in the Rasashastra department of the home institution.

Drug Authentication

Both substances were authenticated by the faculties from the Department of Dravyaguna of Bhausaheb Mulak Ayurved Mahavidyalay Nandanvan, Nagpur.

Preparation of *Arka Ksheer*

The latex of Calotropis was obtained directly from the plant by plucking the leaves and collecting the exudate in a glass container.

Shodhana (Purification) of *Hem Gairik*

Purification of *Hem Gairik* was carried out using *Goghrita* (cow ghee) as per classical guidelines.[10]

Animal experiment was conducted in the pharmacology laboratory of Priyadarshini J. L. College of Pharmacy at a CPCSEA New Delhi - approved facility (Registration No. 648/PO/ERe/S/02/CPCSEA), following all ethical guidelines established by the Institutional Animal Ethics Committee (IAEC).

Animal Experimentation

1. Selection of animals

- Healthy young adult Swiss Albino mice were selected for the study. The female mice were nulliparous and non-pregnant. At the start of dosing, each animal was between 8 to 12 weeks of age, and their body weights were maintained within ±20% of the average weight i.e.25-30gm.
- Housing and Feeding Conditions:Animals were housed under controlled conditions with room temperature maintained at 22 ± 3°C. Relative humidity levels were kept between 30% and 70%, with a target range of 50–60%, except during routine cleaning procedures.[11]

Table-1: **Selection and dosing of Animals.**

Animal species	Albino mice
Strain	Swiss albino
Source of animal	College of pharmacy
Average wt of mouse	25-30 gm

No of mice	6 in each groups
Age of mice	6-8 weeks
Sex of mice	50% males & 50% females
Diet	Pelleted feed
Room temperature	22-26^{0}C.
Vehicle used	Distilled water
Period of acclimatization	7 days
Dosing	Arkaksheer and Hem Gairik were given by Oral route.

1. Preparation of animals

The animals were randomly selected, individually marked for identification, and housed in their cages for five days prior to dosing to allow acclimatization to laboratory conditions.

Dose Calculation for Albino Mice

To determine the appropriate dose for albino mice, a standard human-to-mouse conversion factor of 0.0026 was applied. This conversion allows extrapolation of human doses to mice, following the formula:

Dose for mice = Human dose × 0.0026

Arka Sheer Dose Calculation

The reported fatal dose of *Arka Sheer* in humans is approximately 500 mg/kg. Using the established conversion factor, the estimated fatal dose for albino mice is calculated as:

- Mouse dose = 500 mg/kg × 0.0026 = 1.3 mg

To express this on a per-kilogram basis for mice weighing approximately 30 grams:

- Per kg dose in mice = 1.3 mg × 30 = 39 mg/kg

Hem Gairik Dose Calculation

The therapeutic dose range of *Hem Gairik* in humans is between 250 mg and 500 mg. Applying the same conversion factor:

- Mouse dose range = 250 mg × 0.0026 to 500 mg × 0.0026 = 0.65 mg to 1.3 mg

On a per-kilogram basis for a standard 30 g mouse:

- Low dose (Dose I) = 0.65 mg × 30 = 19.5 mg/kg
- High dose (Dose II) = 1.3 mg × 30 = 39 mg/kg

These doses are in accordance with values reported in the *Ayurvedic Pharmacopoeia of India.*[12]

Procedure of Animal experimentation

- The drug samples were prepared as suspensions by thoroughly mixing them with distilled water to ensure uniformity.
- Both *Arka Ksheer* and *Hem Gairika* were administered via the oral route.
- Following administration, animals were closely monitored for any signs of toxicity, behavioral changes, or mortality over the initial 24-hour period, and observations continued daily for a duration of 7 to 15 days.
- A preliminary toxicity assessment was initially conducted for *Arka Ksheer*.
- The body weight of each animal was recorded prior to dosing, and the required amount of *Arka Ksheer* and *Hem Gairika* was calculated based on individual weight.
- The potentially toxic compound and the antidote were both administered orally.
- Post-administration, animals were observed intensively for the first 24 hours and routinely monitored for up to 7 to 15 days for any delayed toxic effects.[13]

Table 2: Grouping of Animals.

Sr. no	Group	No of mice
1	Control	6
2	Acute toxicity of Arkaksheer	6
3	Hem Gairik (Dose 1) + Arkaksheer	6
4	Hem Gairik (Dose 2) + Arkaksheer	6

Parameters

Change in temperature, Appearance of convulsions, Dilatation of pupils, Survival period, (death), Salivation, Lacrimation, Drowsiness, Irregular respiration, Tachycardia.

OBSERVATIONS AND RESULTS

1. Changes in Body Temperature

Intergroup comparisons of changes in rectal temperature were performed using Dunn's Multiple Comparison Test. A statistically significant elevation in body temperature was observed between Group-1 and Group-2 (mean difference = 1.80; $Z = 2.898$; $p = 0.0038$), and between Group-1 and Group-3 (mean difference = 0.85; $Z = 2.338$; $p = 0.0194$). The comparison between Group-1 and Group-4 did not reach statistical significance ($p = 0.517$). Further, Group-2 vs Group-3 (mean difference = 0.95; $p = 0.0154$) and Group-2 vs Group-4 (mean difference = 1.36; $p = 0.0057$) demonstrated statistically significant differences. No significant change was observed between Group-3 and Group-4 ($p = 0.1395$). These findings

indicate that temperature alterations were predominantly higher in Groups 2 and 3 compared to the control.

2. Time of Onset of Convulsions

A one-way ANOVA revealed a highly significant difference in the time of appearance of convulsions among the treatment groups ($F = 16.10$; $p = 0.0002$) Subsequent Dunn's post hoc analysis, demonstrated no significant difference between Group-2 and Group-3 ($p = 0.08719$). However, convulsions appeared significantly later in Group-4 when compared with both Group-2 (mean difference = 24.33; $p = 0.0062$) and Group-3 (mean difference = 23.5; $p = 0.0062$), indicating a delayed onset of convulsive activity in Group-4.

3. Time of Onset of Pupillary Dilation

A highly significant difference in the latency to pupillary dilation was observed among groups ($F = 78.47$; $p < 0.0001$).

Post hoc comparisons indicated no statistical difference between Group-2 and Group-**3** ($p = 1.000$). However, Group-4 exhibited a markedly delayed onset of pupillary dilation compared with both Group-2 (mean difference = 35.9; $p < 0.001$) and Group-3 (mean difference = 35.7; $p < 0.0001$).

This demonstrates a significantly prolonged latency for pupillary effects in Group-4.

4. Survival and Mortality Analysis

Comparison of survival proportions across groups using the **Chi-square test** did not reveal statistically significant differences ($\chi^2 = 6.0516$; $p = 0.124$). Although variations in survival rates were observed descriptively (100% in Group-1 vs. 33.3–67.7% in treated groups), these differences were not statistically meaningful.

5. Clinical Signs and Symptoms

The distribution of clinical signs among groups was compared using the Chi-square test .A statistically significant association was observed for salivation ($\chi^2 = 12.6000$; $p = 0.020$) and twitching ($\chi^2 = 9.4827$; $p = 0.015$).

Irregular respiration demonstrated a highly significant association ($\chi^2 = 16.7143$; $p = 0.003$). No significant associations were observed for tachycardia, drowsiness, locomotor activity, lacrimation, or lethargy ($p > 0.05$).

These results indicate that autonomic and neuromuscular signs (salivation, twitching, respiratory irregularities) were more prominently affected in the treatment groups.

DISCUSSION

This study aimed to evaluate the antidotal efficacy of *Hem Gairika* against *Arka Ksheera* (latex of *Calotropis*) toxicity using an in vivo mouse model. Based on Ayurvedic literature and classical toxicology principles, *Arka* is classified as an *Upavisha*, a group of moderately toxic herbs, while *Hem Gairika* is recognized in classical texts such as *Rasajalanidhi* for its detoxifying and haemostatic properties.[14-16]

Experimental findings demonstrated that *Arka Ksheera* induced a clear toxic response in albino mice, including convulsions, dilated pupils, excessive salivation, and increased mortality rates. The latency to appearance of toxic symptoms (e.g., convulsions and pupil dilation) was significantly delayed in the group treated with higher doses of *Hem Gairika*, indicating a protective or antidotal effect. While mortality was reduced in the treated groups, the survival difference was not statistically significant, potentially due to the limited sample size.

The significant differences observed in physiological parameters, such as temperature regulation, convulsion onset, and pupil dilation, suggest that *Hem Gairika* exerts a mitigating effect on the acute toxicity induced by *Arka*. Group 4 (high-dose *Hem Gairika*) consistently performed better in delaying toxic symptoms and improving survival than Group 2 (Arka only) and Group 3 (low-dose *Hem Gairika*). Parameters like irregular respiration, salivation, and muscular twitching also showed statistically significant improvements in the treated groups, particularly at higher doses.

These findings are aligned with the classical Ayurvedic hypothesis that *Hem Gairika*, when properly purified through *Shodhana* processes, acts as a *Vishaghna Dravya* (antidotal substance). Its properties such as absorbent action, astringency, and cooling potency likely contribute to stabilizing systemic effects caused by the glycoside-induced toxicity of *Calotropis* latex.

One of the strengths of this study is its integration of classical Ayurvedic principles with modern experimental pharmacology, supported by detailed drug authentication, proper dose calculation using human-to-animal conversion, and standardized analytical evaluation based on *Ayurvedic Pharmacopoeia of India* protocols. The use of ethical animal experimentation under IAEC guidelines also enhances the study's credibility.

However, certain limitations need to be acknowledged The sample size per group (n=6) may not provide strong statistical power for some endpoints, particularly mortality. Only two dosage levels of *Hem Gairika* were tested dose-ranging studies could provide a better understanding of its therapeutic window. The study duration was limited to 15 days longer observation might yield insights into chronic effects or delayed toxicity. Biochemical, histopathological, or molecular parameters were not evaluated to validate internal organ protection or mechanistic pathways.

CONCLUSION

This study provides preliminary yet compelling evidence supporting the antidotal efficacy of Hem Gairika against the acute toxicity of Arka Ksheera (latex of *Calotropis* spp.) in an in vivo mouse model. The findings demonstrate that Hem Gairika, particularly at higher doses, can significantly delay the onset of toxic symptoms such as convulsions, pupil dilation, and abnormal physiological responses, while also contributing to reduced mortality albeit without statistical significance due to the limited sample size.

The integration of traditional Ayurvedic principles with modern pharmacological methodology enhances the translational potential of this research. However, further studies with larger sample sizes, extended observation periods, multiple dosage levels, and inclusion of biochemical and histopathological analyses are warranted to fully elucidate the protective mechanisms and therapeutic scope of Hem Gairika.

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