

# Acute Toxicity Study of White and Black Gunja Pericarps (*Abrus precatorius*)

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## Abstract

**Aim:** *Abrus precatorius* Linn. (Fabaceae) pericarps are used for the treatment of sciatica and alopecia which comprises the toxic protein and alkaloids, abrine, trigonelline, choline, and hypaphorine. *Ayurveda* urges the use of *Abrus* pericarps after the *Shodhana* process (detoxification). The current study was aimed at performing the *Shodhana* process, *Swedana* (boiling) of *A. precatorius* pericarps using cow's milk, and *Kanji* (sour gruel) as a medium and to evaluate the acute toxicity of pericarps before and after detoxification in cow's milk and *Kanji*. **Materials and Methods:** The acute toxicity study was carried out as per organization for economic cooperation and development guidelines 425. In acute toxicity study, the intraperitoneal dose (0.5, 1, and 2 mg/kg) of *Ashodhita* (unprocessed) and *Shodhita* (processed) white and black varieties of pericarps of *A. precatorius* was administered to 30 groups in a single dose, and general behavior, adverse effects, and mortality were determined up to 72 h. **Results and Discussion:** In acute toxicity, *Ashodhita* white and black varieties of pericarps of *A. precatorius* were found toxic, whereas neither mortality nor any significant alteration in behavior was observed in black varieties of pericarps of *Shodhita A. precatorius*, while some mortality and alteration in behavior were observed in white varieties of pericarps of *Shodhita A. precatorius*. **Conclusion:** The white varieties of pericarps are more toxic than black varieties of *A. precatorius*. It was also found that *Shodhana* in *Kanji* is more effective than cow's milk.

**Key words:** *Abrus precatorius*, intraperitoneal, *Kanji*, pericarps, *Shodhita*

## INTRODUCTION

Toxicology is the essential perspective of pharmacology that deals with the adverse impact of the bioactive substance on existing organisms earlier to the use of drug or chemical in clinical use. As per the Organization for Economic Co-operation and Development (OECD) guidelines, in the direction to stabilize the safety and efficacy of a new drug, toxicological studies are necessary for animals such as mice, rat, guinea pig, dog, rabbit, and monkey under many conditions of the drug. Toxicological studies help to build decision whether an innovative drug should be approved for clinical use or not. OECD 401, 423, and 425 do not support the use of drug clinically without its clinical trial as well as toxicity investigations. Depending on the duration of drug showing to animals, toxicological studies may be three types such acute, subacute, and chronic toxicological studies. Acute toxicity studies are the most characteristic of the toxicity or safety

evaluations. It is usually defined as the adverse effects of a drug or substance that results either from a single exposure or from multiple exposures in a short period of time (usually <24 h).<sup>[1]</sup> *Abrus precatorius* Linn. (Fabaceae) usually known as crabs' eye, Indian liquorice, is a woody twining found almost in all parts of India, ascending to an altitude of 3500 ft. Three varieties of *A. precatorius* (black, white, and red) commonly found throughout the tropics. All three varieties of pericarps of *A. precatorius* enclose with toxic chemical constituents such as abrin, abrusic acid, choline, urease, hypaphorine,

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and much more alkaloids and steroidal oils.<sup>[2,3]</sup> The thought of *Shodhana* in *Ayurveda* not only includes the process of purification/detoxification of physical as well as chemical impurities but also covers the minimization of side effects and enhancing the healing efficacy of the purified drugs.<sup>[4-6]</sup> The Ayurvedic Pharmacopoeia of India details *Shodhana* of *A. precatorius* pericarps, which leads to its purification by various methods. The present research article is deal with the detoxification process of the pericarps and comparative evaluation of the acute intraperitoneal toxicity of *Ashodhita* and *Shodhita A. precatorius* pericarps.

## MATERIALS AND METHODS

### *Shodhana* in cow's milk and *Kanji*

The *Shodhana* of white and black *A. precatorius* pericarps was performed by *Swedana* process (boiling in *Dola-Yantra*) in cow's milk and *Kanji* for 6 and 3 h, respectively. When *Shodhana* process was completed, the *Shodhita* pericarps of both varieties were washed with warm water and kept for shade drying.<sup>[2]</sup>

### Experimental animals

Acute toxicity test was performed as per the OECD guidelines 425.<sup>[7]</sup> Experiments were performed using Swiss strain albino mice of either sex weighing between 25 g and 30 g. Animals were acclimatized for 1 week before using them, and before experimentation, the animals were kept fasting overnight. The animals were randomly divided into 30 groups each containing six mice. The animals were housed in polypropylene cages, in a temperature-controlled environment ( $23 \pm 2^\circ\text{C}$ ). Lighting was controlled to supply 12 h of light and 12 h of dark for each 24 h period. Each cage was identified by a card. The mice were fed with standard laboratory animal prescribed food with water *ad libitum*.

### Preparation of drug sample

The white and black *Ashodhita* and *Shodhita A. precatorius* pericarp powder were weighed and dissolved in 100 mL of distilled water and macerated in the cold water and kept overnight for extraction. On the next day, the material was then centrifuged and supernatant obtained was diluted with water as required for per kg body weight of mice as per three different doses, i.e., 0.5, 1, and 2 mg/kg body weight.

### Drug administration

The mice were fasted 3 h before dosing (only food was withheld for 3 h but not water). Following the period of fasting, animals were weighed and test sample was administered intraperitoneal at a dose of 0.5, 1.0, and 2.0 mg/kg. The foods were suspended for 2 h after the administration of the drug.

The treated mice were observed after 2 h intervals for 24 h. The effect of the test drugs on the mice was scored with the use of 9° with a scale of 0–8. Scoring was performed at the time of peak effect. The base score below and above 4 was a subnormal response and the base score for the abnormal sign was 0–8 and 4 for the normal sign.<sup>[8]</sup>

## RESULTS

CNS activity and acute toxicity screening of *A. precatorius* shown in Tables 1-12.

**Table 1: Effect of *Ashodhita* white pericarps of *A. precatorius* on behavioral test in mice**

CNS activity	Screening	Results
Awareness	Alertness	Slight CNS depression This depression was directly related to the dose of test drug
	Visual placing	No change in animal response when placed in different positions
	Stereotypy	No effect was seen
Mood	Grooming	Unaffected
	Restlessness	Absent in the unaffected mice
	Irritability	Aggressiveness
Motor activity	Fearfulness	Absent
	Spontaneous activity and reactivity	Sluggish, dose related
	Touch response	Present
CNS excitation	Pain response	Present
	Tremors	Absent
	Convulsions	Absent at 0.5 and 1 mg/kg but present at 2.0 mg/kg
Posture	Body posture	No effect
Muscle tone	Limb tone	Elongated
	Body tone	Tail both are dose related
Reflexes	Pinna	Absent
	Corneal	Absent
Autonomic	Pupil size	No effect
	Salivation	No effect
	Body temperature	No change

(Contd...)

**Table 1: (Continued)**

CNS activity	Screening	Results
	Skin color	Slight brown at the site of injection
	Heart rate	Decreased
	Respiratory rate	Decreased

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius***Table 2: Effect of milk *Shodhita* white pericarps of *A. precatorius* on behavioral test in mice**

CNS activity	Screening	Results
Awareness	Alertness	No change
	Visual placing	No effect
	Stereotypy	No effect
Mood	Grooming	No effect
	Restlessness	Absent
	Irritability	Slight excitation
	Fearfulness	Absent
Motor activity	Spontaneous activity and reactivity	No effect
	Touch response	Present
	Pain response	Present
CNS excitation	Tremors	Absent
	Convulsions	Absent
Posture	Body posture	No effect
Muscle tone	Limb tone	No effect
	Body tone	No effect
Reflexes	Pinna	Present
	Corneal	Present
Autonomic	Pupil size	No effect
	Salivation	No effect
	Body temperature	No change
	Skin color	Slight brown
	Heart rate	Decreased
	Respiratory rate	Decreased

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius***Table 3: Effect of *Kanji Shodhita* white pericarps of *A. precatorius* on behavioral test in mice**

CNS activity	Screening	Results
Awareness	Alertness	No change
	Visual placing	No effect
	Stereotypy	No effect
Mood	Grooming	No effect

**Table 3: (Continued)**

CNS activity	Screening	Results
	Restlessness	Absent
	Irritability	Absent
	Fearfulness	Absent
Motor activity	Spontaneous activity and reactivity	No effect
	Touch response	Present
	Pain response	Present
CNS excitation	Tremors	Absent
	Convulsions	Absent
Posture	Body posture	No effect
Muscle tone	Limb tone	No effect
	Body tone	No effect
	Reflexes	Pinna
	Corneal	Present
Autonomic	Pupil size	No effect
	Salivation	No effect
	Body temperature	No change
	Skin color	Slight brown
	Heart rate	Decreased
	Respiratory rate	Decreased

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius***Table 4: Effect of *Ashodhita* black pericarps of *A. precatorius* on behavioral test in mice**

CNS activity	Screening	Results
Awareness	Alertness	Slight CNS depression This depression was directly related to the dose of test drug
	Visual placing	No change in animal response when placed in different positions
	Stereotypy	No effect was seen
Mood	Grooming	Unaffected
	Restlessness	Absent in the unaffected mice
	Irritability	Aggressiveness
	Fearfulness	Absent
Motor activity	Spontaneous activity and reactivity	Sluggish
	Touch response	Present
	Pain response	Present

(Contd...)

**Table 4: (Continued)**

CNS activity	Screening	Results
CNS excitation	Tremors	Absent
	Convulsions	Absent
Posture	Body posture	No effect
Muscle tone	Limb tone	Elongated
	Body tone	Tail
Reflexes	Pinna	Absent
	Corneal	Absent
Autonomic	Pupil size	No effect
	Salivation	No effect
	Body temperature	No change
	Skin color	Slight brown
	Heart rate	Decreased
	Respiratory rate	Decreased

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius*

**Table 5: Effect of milk *Shodhita* black pericarps of *A. precatorius* on behavioral test in mice**

CNS activity	Screening	Results
Awareness	Alertness	No change
	Visual placing	No effect
	Stereotypy	No effect
Mood	Grooming	No effect
	Restlessness	Absent
	Irritability	Absent
	Fearfulness	Absent
Motor activity	Spontaneous activity and reactivity	No effect
	Touch response	Present
	Pain response	Present
CNS excitation	Tremors	Absent
	Convulsions	Absent
Posture	Body posture	No effect
Muscle tone	Limb tone	No effect
	Body tone	No effect
Reflexes	Pinna	Present
	Corneal	Present
Autonomic	Pupil size	No effect
	Salivation	No effect
	Body temperature	No change
	Skin color	Slight brown
	Heart rate	Decreased
	Respiratory rate	Decreased

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius*

**Table 6: Effect of *Kanji Shodhita* black pericarps of *A. precatorius* on behavioral test in mice**

CNS activity	Screening	Results
Awareness	Alertness	No change
	Visual placing	No effect
	Stereotypy	No effect
Mood	Grooming	No effect
	Restlessness	Absent
	Irritability	Slight excitation
	Fearfulness	Absent
Motor activity	Spontaneous activity and reactivity	No effect
	Touch response	Present
	Pain response	Present
CNS excitation	Tremors	Absent
	Convulsions	Absent
Posture	Body posture	No effect
Muscle tone	Limb tone	No effect
	Body tone	No effect
Reflexes	Pinna	Present
	Corneal	Present
Autonomic	Pupil size	No effect
	Salivation	No effect
	Body temperature	No change
	Skin color	Slight brown
	Heart rate	Decreased
	Respiratory rate	Decreased

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius*

## DISCUSSION

The method of *Shodhana* includes boiling the pericarps in cow's milk and *Kanji*, which requires removing the toxin. The toxins notified to be present in *Abrus* pericarps comprise a toxic abrin, lectin, glucoside abruccic acid, abrine, choline, and hypaphorine. The contents found in cow's milk comprise milk proteins, casein, lactose, fatty acid, lipoprotein, and xanthine oxidase. *Kanji* (pH 3.4) being acidic in character may aid the extraction of alkaloids such as abrine, choline, and hypaphorine, along with other chemical constituents from *A. precatorius* pericarps. When *Abrus* pericarps are mixed with cow's milk and *Kanji* furthermore heated, the above-mentioned toxins might be removed by one of the mechanisms: The first mechanism, i.e. the heat given to the method might denature the toxic phytoconstituents. The alkaloids in the pericarps might form a combined with one of the components of the milk and *Kanji* moreover hence get removed. The steroidal oil might become eradicated in the fatty acid part of the milk and *Kanji*, which itself is an emulsion. These conclusions suggest

**Table 7:** CNS activity and acute toxicity screening of *Ashodhita* white pericarps of *A. precatorius*

Screening	Dose of pericarps		
	0.5 mg	1.0 mg	2.0 mg
Awareness			
Alertness	3	3	3
Visual placing	3	2	3
Stereotypy	3	3	2
Mood	3		
Grooming	3	3	3
Restlessness	3	3	3
Irritability	3	3	3
Fearfulness	3	3	2
Motor activity			
Spontaneous activity and reactivity	3	3	2
Touch response	3	3	3
Pain response	3	3	3
CNS excitation	3		
Tremors	3	3	1
Convulsions	3	2	2
Posture	3		
Body posture	3	3	2
Muscle tone	3		
Limb tone	3	3	3
Body tone	3	3	3
Reflexes	3		
Pinna	3	3	3
Corneal	3	3	2
Autonomic	3		
Pupil size	3	3	3
Salivation	3	3	2
Body temperature	3	3	1
Skin color	3	3	2
Heart rate	3	2	2
Respiratory rate	3	2	1

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius*

that the said method of *Shodhana* as explained in *Ayurveda* is proficient of removing the toxin and holding the efficacy at the same time. The white and black *A. precatorius* pericarps were processed in cow's milk and *Kanji* and subjected to acute toxicity studies.<sup>[2]</sup> In this study, *Shodhana* of white and black pericarps was done through *Swedana* process, mentioned in *Ayurvedic* classics texts.<sup>[9-11]</sup> The aqueous extract of white and black *Ashodhita* and *Shodhita A. precatorius* pericarps was given intraperitoneal route at three different doses levels (0.5, 1, and 2 mg/kg). The observations were taken on the neurological behavior autonomic studies. The injected mice

**Table 8:** CNS activity and acute toxicity screening of milk *Shodhita* white pericarps of *A. precatorius*

Screening	Dose of pericarps		
	0.5 mg	1.0 mg	2.0 mg
Awareness			
Alertness	4	4	3
Visual placing	4	4	3
Stereotypy	4	4	3
Mood			
Grooming	4	4	4
Restlessness	4	4	4
Irritability	4	3	2
Fearfulness	4	4	4
Motor activity			
Spontaneous activity and reactivity	4	4	4
Touch response	4	4	4
Pain response	4	4	3
CNS excitation			
Tremors	4	4	3
Convulsions	4	4	4
Posture			
Body posture	4	4	4
Muscle tone			
Limb tone	4	4	4
Body tone	4	4	3
Reflexes			
Pinna	4	4	4
Corneal	4	4	4
Autonomic			
Pupil size	4	4	3
Salivation	4	4	4
Body temperature	4	4	4
Skin color	4	3	3
Heart rate	4	4	3
Respiratory rate	4	4	3

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius*

were observed after 2 h intervals for 24 h. The effect of the all tested drugs on the mice was scored with the use of 9° with a scale of 0–8. Scoring was performed at the time of peak effect. The base score below and above 4 was the subnormal response, and the base score for the abnormal sign was 0–8 and 4 for the normal sign. In the CNS activity including awareness (alertness), mood (irritability), motor activity (reactivity), CNS excitation (convulsion), and autonomic responses (skin color, heart, and respiratory rate), considerable variations were observed in *Ashodhita*, milk, and *Kanji Shodhita* white and black varieties of *A. precatorius*. Overall effects have

**Table 9:** CNS activity and acute toxicity screening of *Kanji Shodhita* white pericarps of *A. precatorius*

Screening	Dose of pericarps		
	0.5 mg	1.0 mg	2.0 mg
Awareness			
Alertness	4	4	4
Visual placing	4	4	3
Stereotypy	4	4	4
Mood			
Grooming	4	4	4
Restlessness	4	4	4
Irritability	4	4	3
Fearfulness	4	4	4
Motor activity			
Spontaneous activity and reactivity	4	4	4
Touch response	4	4	3
Pain response	4	4	4
CNS excitation			
Tremors	4	4	4
Convulsions	4	4	3
Posture			
Body posture	4	4	4
Muscle tone			
Limb tone	4	4	4
Body tone	4	4	4
Reflexes			
Pinna	4	4	4
Corneal	4	4	3
Autonomic			
Pupil size	4	4	4
Salivation	4	4	4
Body temperature	4	3	3
Skin color	4	4	4
Heart rate	4	4	3
Respiratory rate	4	4	4

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius***Table 10:** CNS activity and acute toxicity screening of *Ashodhita* black pericarps of *A. precatorius*

Screening	Dose of pericarps		
	0.5 mg	1.0 mg	2.0 mg
Awareness			
Alertness	3	3	3
Visual placing	3	3	2
Stereotypy	3	2	2

(Contd...)

**Table 10:** (Continued)

Screening	Dose of pericarps		
Mood			
Grooming	3	3	3
Restlessness	3	3	4
Irritability	3	3	2
Fearfulness	4	4	3
Motor activity			
Spontaneous activity and reactivity	3	3	3
Touch response	3	3	2
Pain response	3	3	3
CNS excitation			
Tremors	3	3	3
Convulsions	3	3	2
Posture			
Body posture	4	3	3
Muscle tone			
Limb tone	3	4	3
Body tone	3	4	2
Reflexes			
Pinna	4	4	2
Corneal	3	3	2
Autonomic			
Pupil size	3	3	3
Salivation	3	3	3
Body temperature	3	2	2
Skin color	3	3	3
Heart rate	3	3	2
Respiratory rate	3	2	1

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius*

**Table 11:** CNS activity and acute toxicity screening of milk *Shodhita* black pericarps of *A. precatorius*

Screening	Dose of pericarps		
	0.5 mg	1.0 mg	2.0 mg
Awareness			
Alertness	4	4	4
Visual placing	4	4	4
Stereotypy	4	4	4
Mood			
Grooming	4	4	4
Restlessness	4	4	4
Irritability	4	4	4
Fearfulness	4	4	4

(Contd...)

Table 11: (Continued)

Screening	Dose of pericarps		
	0.5 mg	1.0 mg	2.0 mg
Motor activity			
Spontaneous activity and reactivity	4	4	4
Touch response	4	4	4
Pain response	4	4	4
CNS excitation			
Tremors	4	4	4
Convulsions	4	4	4
Posture			
Body posture	4	4	4
Muscle tone			
Limb tone	4	4	4
Body tone	4	4	4
Reflexes			
Pinna	4	4	4
Corneal	4	4	4
Autonomic			
Pupil size	4	4	4
Salivation	4	4	4
Body temperature	4	4	3
Skin color	4	4	4
Heart rate	4	4	3
Respiratory rate	4	4	4

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius*Table 12: CNS activity and acute toxicity screening of *Kanji Shodhita* black pericarps of *A. precatorius*

Screening	Dose of pericarps		
	0.5 mg	1.0 mg	2.0 mg
Awareness			
Alertness	4	4	4
Visual placing	4	4	4
Stereotypy	4	4	4
Mood			
Grooming	4	4	4
Restlessness	4	4	4
Irritability	4	4	4
Fearfulness	4	4	4
Motor activity			
Spontaneous activity and reactivity	4	4	4
Touch response	4	4	4
Pain response	4	4	4

(Contd...)

Table 12: (Continued)

Screening	Dose of pericarps		
	0.5 mg	1.0 mg	2.0 mg
CNS excitation			
Tremors	4	4	4
Convulsions	4	4	4
Posture			
Body posture	4	4	4
Muscle tone			
Limb tone	4	4	4
Body tone	4	4	4
Reflexes			
Pinna	4	4	4
Corneal	4	4	4
Autonomic			
Pupil size	4	4	4
Salivation W	4	4	4
Body temperature	4	4	4
Skin color	4	4	4
Heart rate	4	4	4
Respiratory rate	4	4	4

CNS: Central nervous system, *A. precatorius*: *Abrus precatorius*

been summarized in Tables 1-12. The present study conducted as per the OECD guidelines 423 revealed that *Ashodhita A. precatorius* (white and black) was found toxic [Tables 1, 4, 7, 10] but both varieties of purified pericarps of *A. precatorius* did not produce any mortality throughout the study period of 14 days [Tables 2, 3, 5, 6, 8, 9, 11, and 12].<sup>[12]</sup> On the basis of the present study, it was concluded that white and black varieties of *Ashodhita A. precatorius* were found toxic, whereas a white variety of milk *Shodhita A. precatorius* at the dose level of 2 mg/kg found mild toxic as compared to *Kanji Shodhita*. However, the both pericarps of milk and *Kanji Shodhita A. precatorius* are suitable for medicinal purposes at a dose level of 1 mg/kg as compared to *Ashodhita* varieties of *A. precatorius* pericarps with respect to their neurological behavior and autonomic behavior. These findings were suggested that the said method of *Shodhana* as explained in *Ayurveda* is proficient of removing the toxin and holding the efficacy at the same time. The studies also suggest that the white variety is more toxic than black varieties of pericarps of *A. precatorius*.

## CONCLUSION

Acute toxicity study is an essential test in the toxicological investigation of unexplored materials. LD<sub>50</sub>, although not considered as a biological, is the sign of the acute toxicity. The before-mentioned study also serves to give information about the

doses that should be chosen for following studies. No mortality and adverse effect was recognized in the experimental animals during the period for white and black varieties of *Shodhita A. precatorius*, while *Ashodhita A. precatorius* pericarps produce a toxic effect in the animal. It is also interesting to note that the more reduction in toxicity was observed in *Kanji Shodhita A. precatorius*. It is also concluded that white varieties of pericarps are more toxic than black varieties of *A. precatorius*. A chronic toxicity study of the doses utilized in traditional drug should be moreover carried out to evaluate the long-term safety of both varieties of *A. precatorius* pericarps.

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