Ayurveda, one of the ancient sciences of life, is practiced for attaining complete health. It is not merely a kind of antiquated medicine. It is a science based upon the observation of living beings and their actual response and reactions to their environment. More than a medical system, Ayurveda is a way of life, a way of cooperating with nature and living in harmony with her. The main aim of Ayurveda is prolongation of healthy life and prevention of diseases\(^1\).

Every science has an objective and Ayurveda is not an exception. The objective of Ayurveda is the maintenance of metabolic equilibrium of the human psycho-somatic state and the restoration of the same to normalcy, when disturbed\(^2\). It provides integrated approach to preventing and treating illness through life style interventions and natural therapies.

Around 5000 years B.C. Rigveda and Atharvaveda contain many hymns on diseases and their treatment by various plants and other materials. Systemic utility of herbs will be found in the Rigveda-Ousadhi Sukta (10.97.1-23) and also in Atharvaveda (8.7.1-8 and 11.6.16-17). At that time plants were also used as Mani (amulet) to ward off evil spirits. Vedic literature explained the mode of drug action due to its inherent powder (Veerya)\(^3\). It was long ago when Ayurvedic fundamentals and its eight clinical specialties were documented in the Ayurvedic literatures\(^{25, 26}\). Initially Dravyaguna shastra was not mentioned as a separate branch of Ayurveda. But all the treatises contain elaborate descriptions about the herbs, their properties and indications. Charaka identified the necessity of complete knowledge on herbs and their utility in therapeutics. Charaka opined that a deadly poison can become a very good medicine if it is administered properly i.e. used in proper dosage, in proper manner and in the proper stage of the diseases\(^4\).

The uses of poison have been recorded in ancient Ayurvedic classic since long long ago. Acharya Charaka has elaborately mentioned various poisoning, symptoms and its management\(^5\). Acharya Sushruta has classified categorically the various sources of poison and described accordingly\(^6\). The poisonous plants reported in ancient scriptures of Ayurveda are being still practiced widely in a number of diseases after proper Shodhana (purificatory procedures). Ayurvedic physicians successfully employed these drugs after proper Shodhana (processing) known as Samaskara. The
Concept of Shodhana was mentioned for the first time in Charaka Samhita in the context of Danti Dravanti Kalpadhyaya. To reduce the ‘Vikasi’ property of Danti root, Charaka mentioned a specific Samaskara by Agni. Acharya Vagbhata also mentioned the Shodhana of plant drugs in detail in the context of Bhallataka Rasayana and Amrita Bhallataka. The concept of Shodhana in Ayurveda is not only a process of purification/detoxification but also a purificatory procedure to enhance the potency and efficacy of the drug. It is reported that Aconite (Vatsanabha) purified by cow’s urine is converted to cardiac stimulant, whereas raw Aconite is cardiac depressant.

The classification of poison is based on certain basic criteria like origin, base, properties, potency etc. Some of the Ayurvedic classics and texts in medieval period have classified all the poisons into two categories as MahaVisha and Upavisha basing on their toxicity and potency. Upavisha are the group of drugs which were less toxic in nature and not so lethal but produce certain toxic symptoms on consumption or administration. The symptoms produced in the body due to Upavisha are less toxic, less severe, usually not life threatening and their toxicity can be controlled by therapeutic measures. The ancient scholars of Ayurveda considered the drug Kupeelu as one of the Upavisha.

Kupeelu (Nux-vomica) is also described as a lethal poison and a cure for demonic possession in the KITAB AL-SUMMAM, an Arabian book of poison, which dates back to the 9th Century. Use of nux-vomica spreads rapidly from Asia to North Africa and subsequently to the Western World. Nux-vomica was introduced into Europe in the 15th century as a cattle poison. Member of strychnos genus were also used by Amazonian Indians as arrowhead poisons, or curare, which are highly toxic to the blood stream. Gradually it becomes a very popular ‘murder weapon’ which is believed to have killed an unknowable number of people, especially during the 19th century. It is believed that many men met their ends via strychnine but murder was never suspected. Main toxic alkaloids present in seeds are Strychnine and Brucine.

Kupeelu was not reported in the ‘Brihat Trayee’ texts of Ayurveda. Its uses in Ayurveda were recorded from the period of “Brinda Madhava” (9th A.D.). The drug Visamusti was mentioned in the English translation of Brinda’s Siddha Yoga edited by P.V.Tiwari, while describing ‘Vatavyadhi chikitsa’. Later it was mentioned by different authors with a number of synonyms. Synonyms like Visatinduka, Kupeelu,
Visamusti etc., indicate toxic nature of this tree. The other parts like leaf, bark, wood, and root are also used in the therapeutics. Though the plant is described under the ‘Upavisa Vargas’ (sub poisonous group)\textsuperscript{13}, its seeds have been used successfully in different formulations to combat different diseases after proper Samaskara known as Shodhana\textsuperscript{14}. The seeds are mainly used as aphrodisiac, appetizer, anti-periodic, digestive, purgative, and stimulant. Further the seeds are also used in anemia, asthma, bronchitis, intermittent & malarial fever and in weakness of extremities \textsuperscript{15}. It is claimed in the ancient manuscripts of Ayurveda that the ‘Visha’ becomes ‘Amrita’ after logical use and the physicians of Ayurveda successfully employed this drug in a number of diseases after proper purification in some specific media\textsuperscript{16}. Shodhita Kupeelu is also claimed to be a potent drug in countering old age problems and specially recommended during senility as Rasayana (antioxidant) \textsuperscript{17}. The plant is also found to have analgesic & anti-inflammatory \textsuperscript{18}, anti-oxidant \textsuperscript{19}, anti-tumor \textsuperscript{20}, anti-snake venom \textsuperscript{21}, anti-diarrhoeal \textsuperscript{22} and hepato-protective \textsuperscript{23} activities when studied in animal models.

While going through various literatures it is revealed that specific media is used for Shodhana of particular substances. Studies have also shown that the toxic substances present in the plant drug are transferred into the media during the Shodhana process rendering the drug nontoxic\textsuperscript{24}.

Searching through various research journals, text books of Ayurveda and different search engines reveals that very few works have been reported on the Shodhana aspect of Kupeelu. Even The Ayurvedic Pharmacopoeia of India does not provide details regarding this drug. A few folklore purificatory methods are also followed traditionally in some parts of India. Though these methods are cost effective and time saving, but there is no scientific research regarding the Shodhana methods. Keeping all these facts in mind, the present research work has been planned by carrying out various Shodhana processes of Kupeelu seeds to evaluate the impact of Shodhana on its Pharmacognostical, Analytical and Pharmacological parameters.

AIMS AND OBJECTIVES:

The present study has been planned to accomplish the following aims & objectives:
• To carry out a conceptual study related to visa, drug Kupeelu and role of different media used for Shodhana from the available literatures on Ayurveda, modern and other systems of medicine.
• To carry out Shodhana of Kupeelu seeds as mentioned in different Ayurvedic texts & literatures.
• To study the pharmacognostical characters along with phytochemical analysis of the Kupeelu seeds both before and after purification.
• To assess the acute toxicity, analgesic & anti-inflammatory activity of the test drugs having highest and lowest percentage of strychnine & brucine respectively.

HYPOTHESIS:
The present research work has been planned with the following two hypotheses:

➢ Null hypothesis:
Shodhana process has no relevance on purifying the Kupeelu seeds.

➢ Alternate hypothesis:
The Shodhana treatment will successfully remove the toxic alkaloids from raw Kupeelu rendering the Shodhita Kupeelu relatively less toxic in prescribed dose.

REVIEW OF PREVIOUS WORK:
A few research works carried out on Shodhana aspects of Kupeelu in Ayurvedic, Unani and Modern field are compiled here.

A. Studies in Ayurveda:


B. *Studies in Unani*:


C. *Studies in Modern medicine*:


MATERIALS AND METHODS:

This study has been carried out by incorporating following phases:

1. Conceptual study
2. Pharmacognostical study
3. Pharmaceutical study
4. Analytical study
5. Pharmacological study
6. Discussion
7. Summary & Conclusion

1. CONCEPTUAL STUDY:

In this phase, available data regarding concept of Visha & Upavisha, the drug Kupeelu, and role of media in Shodhana were compiled from various Ayurvedic, Unani, Homeopathic, and modern literatures were critically analyzed and presented in a systematic manner.

2. PHARMACOGNOSTICAL STUDY:

This phase of the study deals with the collection of Kupellu fruits from its natural habitat and identification through macroscopic and microscopic examination. The Pharmacognostical study has been carried out in following phases as per the standard protocol:

- Macroscopic study of the raw seeds
- Microscopic study (T.S) of the raw seeds
- Histochemical tests by using different chemicals
- Microscopic & organoleptic study of powder characters of the raw & purified seeds

Powder microscopic characters of the purified samples were compared to that of the raw Kupeelu seed and the observations were mentioned accordingly.

3. PHARMACEUTICAL STUDY:

In this phase of the study, an attempt has been made to validate the different Shodhana procedures of Kupeelu with various media like Gomutra (cow urine), Godugdha (cow milk), Goghrita (cow ghee), Kanji (sour gruel), Eranda taila (castor oil), Ardraka swarasa (fresh ginger juice) and water as control.
To provide a high degree of accuracy to the Shodhana procedures, validation of each process was carried out in three different batches following the standard procedures, and the results were documented accordingly. The precaution, observation and result of each Shodhana process were cited accordingly. Shodhana of Kupeelu seeds were carried out by following ten methods.

1) **Shodhana with Gomutra** (cow urine)
2) **Shodhana with Godugdha** (cow milk)
3) **Shodhana with Goghrita** (cow ghee)
4) **Shodhana of Kupeelu** with successive two media –first *Gomutra* (cow urine) followed by *Godugdha* (cow milk)
5) **Shodhana of Kupeelu** consecutively with *Gomutra* (cow urine), *Godugdha* (cow milk) and *Goghrita* (cow ghee)
6) **Shodhana with Eranda taila**
7) **Shodhana with Kanji** (sour gruel)
8) **Shodhana with Ardraka swarasa**
9) **Shodhana with R.O water**
10) **Shodhana with boiling water**

**4. ANALYTICAL STUDY:**

In this phase of the study, the physicochemical analysis and preliminary phytochemical investigation of raw and different *Shodhita Kupeelu* samples were carried out following the standard procedures and results obtained, were compared to observe the impact of Shodhana processes. Quantitative estimation of strychnine & brucine in all the *Shodhita* samples had been executed by H.P.T.L.C. and were compared to that of the raw drug.

**5. PHARMACOLOGICAL STUDY:**

In this phase of the study an attempt was made for the first time to evaluate the impact of two Shodhana procedures on LD50 values, analgesic & anti-inflammatory activities of the Kupeelu seeds. For this purpose, *Kanji* purified Kupeelu seeds and *Gomutra-Godugdha-Goghrita* (A.F.I approved method) purified seeds were selected for the study and the results were compared to the raw seeds.
6. DISCUSSION:
   In this chapter, the facts of conceptual study and the observations with results of pharmacognostical, pharmaceutical, analytical and pharmacological studies have been discussed and interpreted accordingly.

7. SUMMARY AND CONCLUSION:
   The whole study has been summarized in this chapter and possible conclusions based on obtained results and observations, have been drawn.
REFERENCES:

4. Ibidem (ref.1), Su. 1/26.
5. Ibidem (ref. 1), Chi. 23.


25. Ibidem (ref.8), Su. 1/5.

26. Ibidem (ref.2), Su. 1/7.

27. Ibidem (ref.13), 24/7-8.

