INTRODUCTION:

The word concept literally means the idea of forming a perception with the help of past and present theories. For correct acquaintance with the topic matter, it is perpetually necessary to accumulate information from the past that helps to elucidate the facts and findings of the present and to form correct designing for the long term. The conceptual study could be a compilation of the review of the literatures relating to the topic matters and the theories mentioned in numerous classics with reference to the topic matters.

The toxic plants like Kupeelu, Vatsanabha, Bhallataka etc. are vividly reported in the versatile texts of Dravyaguna along with their different Shodhana procedures. The toxic results induced by these plants and their management are also mentioned within the numerous classics of Dravyaguna.

To properly perceive the subject matter of this study, it appears to be necessary to compile the ideas relating to, the Shodhana procedure mentioned in the classics of Ayurveda and also to review the literatures concerning the drug employed in the present study.

Plan of the Study:

The conceptual study has been carried out in 3 phases.

(1) Concept of Visha and Upavisha:

Concept of Visha and Upavisha have been compiled in this phase from various Ayurvedic classics.

(2) Concept of Shodhana & role of media:

In this part the concept concerning Shodhana procedures and various media i.e. Gomutra, Godugduh, Goghrita, Eranda taila, Ardraka swarasa and Kanji used in the present study for Shodhana of Kupeelu seeds have been compiled and interpreted accordingly.

(3) Drug review:

In this section, review of various Ayurvedic and modern literatures and revealed papers are allotted to collect information regarding the drug Kupeelu.
CONCEPT OF VISHA

- Any substance when enters the body causes vitiation of the healthy Dhatus or it may even destroy healthy person, it is known as Visha\(^1\).
- The Substance which causes Vishada to the World known as Visha\(^2\).
- The term Visha is used for the Vishada (Grief) producing - even to the Devatas\(^3\).
- Sarangadhara defined it as the substance which is Agnihuta pradhana, destroyer of life and Yogavahi in action\(^4\).

Derivation

The word Visha is derived from the root “विष ‘व्यास्तो” which means the one which prevades the whole body immediately after ingestion\(^5\).

Synonyms of Visha\(^3\),\(^4\)

1. **Ambu Sambhavata**: Because of its origin from Sea water, it is called Ambusambhava or Jala Sambhava.
2. **Paavakopamata**: The characteristic features of Visha are similar to Agni. It gives rise to Paittika Symptoms in the body and gets pacified with water, hence it is called Paavakopamata.
3. **Dvividha**: The poison is of two types Sthavara and Jangama and hence it is called Dvividha.
4. **Amritatwa**: The origin of poison as well as Amrita are same. If Visha is used in smaller and therapeutic doses, it work like Amrita & hence it is called Amritatwa.
5. **Visha**: As it causes Vishada (grief), it is known as Visha. Grief means pain and sorrow. As it is a material that causes bodily pain it is described as Visha.
6. **Vishanna**: Means that is given up, that is to be thrown away, that causes grievous and painful condition and also a material that resists and de-stabilizes the energy and causes pain, sorrow and dejection.
7. **Kshweda**: Kshweda is the one that causes Moha or fainting or unconsciousness.
8. **Garala**: That takes away the life.
9. **Vyaptau**: Which spreads very quickly on entering the system.
10. **Vishat**: “

    पवित्रिते पवित्रिते दुखिता चा विषत

    ” – (Vishnu purana) It encases all the bodily actions, causes delay for them, stops their movement encounter them,
causes tremors in them. It should be undressed as the one which agitates the stable dispositions of the body.

11. **Kakola**: Because it is as black in color as that of a crow.  
12. **Kalakuta**: The one that troubles and torture even Kala, the Yama.

**Mythological origin of Visha**

- **Charaka Samhita**: Long ago, when the ocean was churned by the Gods and demons for obtaining nectar, there arose a ferocious-looking person who was resplendent with aura having four fangs, long hairs and fiery eyes. The World became Vishada (Grief) at his sight because of which he was known as Visha or poison.  
- **Shusruta Samhita**: A Demon by name Kaitabha started obstructing in many ways during the time of creation of the Universe by Lord Brahma. The Devatas became very angry, which resulted in the production of a very dreadful person, who killed the demon Kaitabha. The anger increased profusely and created sadness or depression among the Gods resulting in the formation of Visha.
- **Astanga Samgraha / Astanga Hridaya**: When the Suras (Gods) and Asuras (Demons) churned the ocean of milk for the sake of obtaining nectar, a person having dreadful appearance, four teeth, brown hair and fiery eyes was born. Seeing him the whole world became grief-stricken, hence he was named as "Visha". He was cursed by Lord Brahma which made him to discard his real form and got resided in both Sthavara (plant) and Jangama (animal) substances. In Sthavara Visha it resides in ten Adhistanas (seats), In Jangama Visha it resides in sixteen Adhistanas (seats). Acharya Charaka also mentioned the Visha yonis (origin) as two types, one is Sthavara (Plant origin) another one is Jangama (Animal origin). The Sthavara Visha Adhistanas and their actions are as follows:

1. **Mula** (Root): Cramps in all the limbs, delirium, stupor  
2. **Patra** (Leaf): Yawning, cramps in all parts of the body and dyspnoea  
3. **Phala** (Fruit): Swelling of the testes, burning sensation in the body and aversion to food  
4. **Pushpa** (Flower): Vomiting, tympanitis, stupor  
5. **Twak** (Bark): Foul breath, roughness of the body, head ache, mucoid expectoration.
6. **Ksheera** (Milk): Frothing from the mouth, loose motions, heaviness of tongue\(^1\).

7. **Saara** (Pith): same as *Twak*\(^1\).

8. **Niryasa** (Exudate): same as *Twak*\(^1\).

9. **Dhatu** (Minerals): Pain in the heart, fainting and burning sensation in the palate\(^1\).


**General features of Sthavara Visha poisoning**

The *Sthavara Visha* (plant poison) produces fever (*Jvar*), hiccup (*Hikka*), tingling sensation in teeth (*Dantaharsa*), spasm in throat (*Gala graham*), frothy salivation with vomiting (*Phena Vamana*), anorexia (*Aruchi*), dyspnoea (*Swasa*) and fainting (*Murcha*)\(^15\).

The mode of action of *Visha Dravyas* inside the human body has been mentioned by *Vagbhata* in the following manner\(^16\),

1. By *Teekshna* and *Ushna* qualities it aggravates *Pitta* and *Rakta*.
2. By *Ruksha* quality it aggravates *Vata*.
3. By *Vishada* quality it causes obstruction of urges.
4. By *Sukshma* & *Vyavayi* quality it enters all the *doshas, dhatus and malas*.
5. By *Ashukari* quality it produces adverse reactions and kills the patient quickly.
6. *Laghu* quality makes it difficult to remove from body.
7. By *Avyakta rasa* it aggravates the Kapha.
8. By *Apaki* quality it does not go for digestion and surely kills the person who has consumed it.

**Visha Gunas**

Regarding the properties of *Visha*, there were differences in opinion among the Ayurvedic Scholars. The difference reflects not only in actual properties but also in the number of properties attributed to *Visha*. The details are mentioned below in a tabular form.

**Table 2.1: Properties of Visha as reported in various classical texts**

<table>
<thead>
<tr>
<th>Charaka(^17)</th>
<th>Susruta(^18)</th>
<th>Astanga Hridaya(^19)</th>
<th>Astanga Samgraha(^20)</th>
<th>Sarangadhara Samhita(^21)</th>
</tr>
</thead>
</table>
Due to its Vyavayi property, Visha spreads even before its digestion. Because of its Aasukari property it is very fast in action. Apaki is the most important quality of Visha due to which it doesn't get metabolized or gets digested in the body. Different Gunas and their attributed actions have been compiled and presented in a tabular form.

**Table 2.2: Guna attributed to Visha along with their systemic effects**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Visha Guna</th>
<th>Action in the Body</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Laghu&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Helps to do lekhana karma, causes lightness in the body.</td>
</tr>
<tr>
<td>2</td>
<td>Ruksha&lt;sup&gt;23&lt;/sup&gt;</td>
<td>Causes Stambhana, Kharatwa, Kathinatwa. Aggravate bodily Vayu and vitiates Rakta and Pitta.</td>
</tr>
<tr>
<td>3</td>
<td>Aasukari&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Spreads throughout the body very quickly proves fatal speedily</td>
</tr>
<tr>
<td>4</td>
<td>Vishada&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Removes moistness does not adhere to any tissue or part of the body</td>
</tr>
<tr>
<td>5</td>
<td>Vyavayi&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Quickly absorbed and spreads throughout the entire systems then gets digested.</td>
</tr>
<tr>
<td>6</td>
<td>Teekshna&lt;sup&gt;27&lt;/sup&gt;</td>
<td>Burning sensation, increases suppuration and secretions, unconsciousness, disintegration of limbs.</td>
</tr>
<tr>
<td>7</td>
<td>Vikasi&lt;sup&gt;28&lt;/sup&gt;</td>
<td>Spreads throughout the body in undigested state and produces looseness of joints and ligaments by separating Ojas from the Dhatu.</td>
</tr>
<tr>
<td>8</td>
<td>Sukshma&lt;sup&gt;29&lt;/sup&gt;</td>
<td>Enters the minute channels of the body.</td>
</tr>
<tr>
<td>9</td>
<td>Ushna&lt;sup&gt;30&lt;/sup&gt;</td>
<td>Helps in vrana pachana, liquefies the dhatu, causes fever, vitiates Rakta and Pitta.</td>
</tr>
<tr>
<td>10</td>
<td>Anirdisyarasa&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Does not possess any particular taste.</td>
</tr>
<tr>
<td>11</td>
<td>Apaki&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Does not get digested in the body and produces complication for longer time.</td>
</tr>
</tbody>
</table>
CONCEPT OF UPAVISHA

The classification of poisons 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\textsuperscript{35}.

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\textsuperscript{36}. There are different opinions among Ayurvedic scholars regarding, number of drugs in Upavisha group. Some texts have numbered them seven and some other as eleven etc. According to Rasatarangini they are as follows\textsuperscript{31},

1. Kupeelu (Strychnos nux-vomica Linn.)
2. Ahiphena (Papaver somniferum Linn.)
3. Jayapala (Croton tiglium Linn.)
4. Dhattura (Datura metel Linn.)
5. Bhanga (Cannabis sativa Linn.)
6. Gunja (Abrus precatorius Linn.)
7. Bhallataka (Semicarpus anacardium Linn.)
8. Arka ksheera (Calotropis gigantea Linn. R.Brown)
9. Snuhi ksheera (Euphorbis nerifolia Linn.)
10. Langali (Gloriosa superba Linn.)
11. Karavira (Nerium odorum Soland.)

According to Rasaratnasamucchaya, Upavishas are seven in number\textsuperscript{32}.

1. Langali (Gloriosa superba Linn.)
2. Visha musti (Strychnos nux-vomica Linn.)
3. Karavira (Nerium odorum Soland.)
4. Bhanga (Cannabis sativa Linn.)
5. Nilaka (Semicarpus anacardium Linn.)
6. Kanaka (Datura metel Linn.)
7. **Arka** (*Calotropis gigantea* Linn. R.Brown)

Different *Upavishas* and their doses have been compiled and presented in the below mentioned table,

Table 2.3: *Upavishas* at a glance

<table>
<thead>
<tr>
<th>Sanskrit name</th>
<th>Hindi name</th>
<th>English name</th>
<th>Major Alkaloids</th>
<th>Fatal Dose</th>
<th>Fatal Period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kupeelu</strong></td>
<td>Kuchala</td>
<td>Nux-vomica</td>
<td>Strychnine, Brucine</td>
<td>60 grains or one crushed seed</td>
<td>5 mints-4 hrs.</td>
</tr>
<tr>
<td><strong>Ahiphena</strong></td>
<td>Aphima</td>
<td>Opium</td>
<td>Codeine, morphine, papaverine</td>
<td>Opium-2g., morphine0.2g., codeine 0.5g.</td>
<td>6-12 hrs.</td>
</tr>
<tr>
<td><strong>Jayapala</strong></td>
<td>Jamalgota</td>
<td>Croton seeds</td>
<td>Crotin, cotonoside Oil-Tiglylo, crotonol</td>
<td>4 seeds or 1ml oil</td>
<td>6 hrs.-3 days</td>
</tr>
<tr>
<td><strong>Dattura</strong></td>
<td>Dattura</td>
<td>Thorne apple</td>
<td>Atropine, hyoscyamine, hyoscine</td>
<td>0.6-1 g. (100-125 seeds)</td>
<td>24 hrs.</td>
</tr>
<tr>
<td><strong>Bhanga</strong></td>
<td>Bhanga</td>
<td>Indian hemp</td>
<td>Cannabinol, canabidiol</td>
<td>10 g./kg. body wt.</td>
<td>Several days</td>
</tr>
<tr>
<td><strong>Gunja</strong></td>
<td>Ratti</td>
<td>Indian liquorice root</td>
<td>Abrin, Abraline</td>
<td>90-120 mg by injection.</td>
<td>3-5 days</td>
</tr>
<tr>
<td><strong>Bhallataka</strong></td>
<td>Bhilava</td>
<td>Marking nut</td>
<td>Bilwanol, Anacardiol</td>
<td>5-10 g.</td>
<td>12-24 hrs.</td>
</tr>
<tr>
<td><strong>Arka</strong></td>
<td>Aaka</td>
<td>Madar.</td>
<td>Uscharin, calatoxin</td>
<td>Uncertain</td>
<td>12 hrs.</td>
</tr>
<tr>
<td><strong>Snuhi</strong></td>
<td>Sehund</td>
<td>Common milk hedge</td>
<td>Euphorbin</td>
<td>Uncertain</td>
<td>Uncertain</td>
</tr>
<tr>
<td><strong>Langali</strong></td>
<td>Kalihari</td>
<td>Glory Lily</td>
<td>Colchicine</td>
<td>Uncertain</td>
<td>Uncertain</td>
</tr>
<tr>
<td><strong>Karavira</strong></td>
<td>Kenara</td>
<td>Oleander</td>
<td>Karabin, Neriodorin</td>
<td>15-20 g. of root</td>
<td>20-36 hrs.</td>
</tr>
</tbody>
</table>
REFERENCES (Concept of Visha & Upavisha):


6. Ibidem (ref. 2), Chi. 23/4-5.


10. Ibidem (ref. 3), Ka. 2/3-9.

11. Ibidem (ref. 3), Ka. 2/6.

12. Ibidem (ref. 3), Ka. 2/7.


15. Ibidem (ref. 2), Chi. 23/16.

16. Ibidem (ref. 8), Su. 40/13

17. Ibidem (ref. 2), Chi. 23/24.

18. Ibidem (ref. 3), Ka. 2/18.


20. Ibidem (ref. 8), Ut. 40/31.

21. Ibidem (ref.4)

22. Ibidem (ref. 3), Su. 46/526.

23. Ibidem (ref. 3), Su. 46/523.
24. Ibidem (ref. 3), Su. 46/531.
25. Ibidem (ref. 3), Su. 46/524.
26. Ibidem (ref. 3), Su. 46/530.
27. Ibidem (ref. 3), Su. 46/525.
28. Ibidem (ref. 3), Su. 46/531.
29. Ibidem (ref. 3), Su. 46/532.
30. Ibidem (ref. 3), Su. 46/522.
35. Ibidem (ref. 31), 24/6-8.
CONCEPT OF SHODHANA AND ROLE OF MEDIA

The Shodhana process described in various Ayurvedic Classics is not simply a process of separation or detoxification rather it increases the therapeutic efficacy of the drug also. Previous studies on Shodhana expose the fact that some kind of changes takes place in the purified drugs, which may be beneficial for therapeutic purposes.

When a raw material is processed with specifically mentioned drugs by means of churning, pounding, triturating etc. to eradicate toxic substances this process is known as Shodhana of that particular raw material.

Shodhana is a process of separation by which physical and chemical impurities get separated from the substances by treatment with various drugs.

It is a process by which blemishes are separated from the substance by means of pharmaceutical processing of Swedana, Mardana etc. with particular drugs.

This term indicates the Pharmaceutical process of various poisonous substances which are essential before administering drugs into a chemical as well as therapeutic purpose and this term is broadly used for Shodhana in Rasashastra like Vatsnabha, Kupeelu, Vijaya etc. in order to make them free from toxicity and suitable for the body. Shodhana is indicated for eliminating all such blemishes, toxic qualities and to induce certain valuable qualities too.

An impurity in a drug substance as defined by the International Conference on Harmonization (ICH) Guidelines is any component of the drug substance that is not the chemical entity defined as the drug substance and affects the purity of active ingredient or drug substances. Therefore any extraneous material present in the drug substance has to be considered an impurity even if it is totally inert or has superior pharmacological properties. Impurities in drug substance can be classified into the following categories:

- Organic impurities (process- and drug-related)
- Inorganic impurities
- Residual solvents

Organic impurities can arise during the manufacturing process and/or storage of the new drug substance. They can be identified or unidentified, volatile or nonvolatile, and include:

- Starting materials
By-products
> Intermediates
> Degradation products
> Reagents, ligands, and catalysts

Inorganic impurities can result from the manufacturing process. They are normally known, identified and include:
> Reagents, ligands and catalysts
> Heavy metals or other residual metals
> Inorganic salts
> Other materials (e.g., filter aids, charcoal)

Solvents are inorganic or organic liquids used as vehicles for the preparation of solutions or suspensions in the synthesis of a new drug substance. Since these are generally of known toxicity, the selection of appropriate controls is easily accomplished.

Impurities may occur either in natural form or sometimes added artificially. The artificial impurity is generally called as adulteration. In Rasashastra, the impurities are usually described as following types.

- **Naisargika** - physically occurring in natural form (natural).
- **Yougika** - added artificially (adulteration) or chemically occurring in natural form (physic-chemical)
- **Oupadhika** - Chemically occurring in artificial form (chemical)

In the context of Dravyaguna the impurities may be categorized as physical & chemical impurities.

- Physical impurities- Guggulu, Shilajit, Sarjarasa etc., containing stones, sand, sticks etc.
- Chemical impurities- Langali, Kupeelu, Vatsanabha, Bhallataka etc., contain poisonous ingredients.

**Objectives of Shodhana**:

Shodhana of various drugs are usually performed with a view to accomplish the following objectives,

- Elimination of physical and chemical impurities, which are not desired.
- Eradication or minimization of toxicity of the material.
Transformation of the hard and non-homogeneous material to soft, brittle, ductile and homogeneous material.

Induction of desired qualities.

Potentiation of therapeutic efficacy of the drug material.

Conversion of the material in suitable form for further processing.

Leads to unique and suitable physico-chemical changes.

For the direct therapeutic uses in some cases.

**Principles used in Shodhana**:

According to the need, different principles are adopted for the Shodhana of poisonous and non poisonous substances such as,

- **Swedana** (Boiling under liquid bath): The material is boiled in prescribed liquid media through Dola Yantra method e.g. Kupeelu Shodhana.

- **Bharjana** (Frying): The material is fried with specific liquid media on Mandagni e.g. Kupeelu Shodhana, Gairika Shodhana etc.

- **Nimajjana** (Dipping): The material is kept immersed in the prescribed liquid for specific period e.g. Kupeelu Shodhana, Vatsanabha Shodhana.

- **Prakshalana** (Washing): The material is washed with prescribed liquid to remove its physical impurities e.g. Godanti Shodhana.

- **Prithakikarana** (Separation): Physical impurities are removed manually e.g. Guggulu Shodhana.

- **Atapa Soshana** (Drying): The material is kept on fire or exposed to sun rays till its dryness e.g. Shilajatu Shodhana.

- **Mardana** (Trituration): The material is ground properly with prescribed drug for specific period. e.g. Parada Shodhana.

- **Bhavana** (Levigation): The material is triturated with prescribed liquid media for specific time period e.g. Kasis Shodhana.

- **Abhishek** (Sprinkling): The material is heated strongly and liquid media is sprinkled on it e.g. Mandura Shodhana.

- **Nirvapa** (Heating and Quenching): The red hot material is dipped into the prescribed liquid e.g. Rajat Shodhana.

- **Dhalana** (Melting and Quenching): At first the material is melted by intense heat and then poured into a liquid media e.g. Naga Shodhana.
- **Galana** (Melting and Straining): The solid material is melted first by heating and then filtered through a cloth e.g. *Gandhaka Shodhana*.
- **Achushana** (Absorption): Oily content of certain toxic material is minimized through different absorption means e.g. *Bhallataka Shodhana*.
- **Nirjalikarana** (Evaporation of water): Whole water content of the material is evaporated by heating e.g. *Sphatika Shodhana*.
- **Patana** (Sublimation): Through *patana yantra* the material is heated to convert into vapour from which the material is regained again by condensing e.g. *Parad Shodhana*.
- **Parishravana** (Straining): The solid material is dissolved in suitable liquid media and separated from insoluble impurities through straining e.g. *Navasadara Shodhana*.
- **Vilayana** (Elutriation): The material is firstly dissolved in prescribed liquid media and left as such for some time, then the upper part of the liquid containing the soluble drug material is decanted into another pot leaving behind the impurities in the bottom of first pot e.g. *Shilajatu Shodhana*.

**Impact of Shodhana process:**

Shodhana process has a great impact on the drugs selected for this purpose. Some kind of changes also take place which may be beneficial for therapeutic purposes like,

1. **Physical changes:**
   
   (a) **Elimination of physical impurities**: *Kampillaka* is separated from brick powder. *Guggulu* is separated from physical mixture. *Shilajatu* is separated from insoluble physical impurities.

   (b) **Reduction in hardness**: By repeated heating and quenching, hardness of the metals and minerals become less.

   (c) **Increase brittleness**: By repeated heating and quenching in liquid media, cracks are seen on the surface of metals and minerals and these become brittle.

   (d) **Reduction in particle size**: During *Nirvapa* process cracks develop on the surface of metals and minerals, and these are broken into coarse powder. In *Bhavana* process mass of the substance become powder in form.

2. **Chemical changes:**
(a) **Elimination of chemical impurities:** During *Shodhana* of native *Makshika* (*CuFeS₂*) impurities like arsenic get eliminated by heating.

(b) **Formation of chemical compounds:** *Lauha* when heated up to red hot reacts with atmospheric oxygen to form ferroso-ferric oxide, which is favorable to the body.

(c) *Makshika* when fried, sulphur (S) is eliminated and iron and copper part convert into oxide form.

(d) **Change into desired compound:** During *Shodhana* of *Tankana* and *Kankshi*, water portion is evaporated and desired chemical compound is formed.

(3) **Biological changes:**

The ultimate objective of these physico-chemical changes of the material is to increase its biological availability and to potentiate its biological efficacy. Reduction in particle size helps in absorption, smoothness leads to non-irritability, and all chemical changes make the material body friendly like *Shodhita Vatsanabha* (*Aconitum ferox* purified in cow urine) is converted into cardiac stimulant, where as crude *Vatsanabha* is claimed to be cardiac depressant, seeds of *Kupeeulu* (*Strychnos nuxvomica*) purified in cow milk show CNS depressant activity, pentabarbitone hypnosis potentiation, inhibited morphine induced catalepsy. *Anjana* purified in juice of *Bhringaraja* (*Eclipta alba*) is proved non-toxic to eyes in experimental animals⁸⁹.

**Media used for Shodhana:**

While going through various literatures it is revealed that specific media is used for *Shodhana* of particular substances. The media used for *Shodhana* also play a crucial role in either breaking down or transforming the toxic chemical constituents into their relatively nontoxic derivatives. Sometimes media acts like solvent and separate the substances from insoluble impurities like in *Guggulu Shodhana*⁷ or it removes toxic alkaloids from the drug completely or partially e.g., in *Vatsanabha Shodhana*⁶. Even there are some nontoxic medicinal plants also used in medicine after proper *Shodhana*. The drug *Kustha* (*Saussurea lappa* C.B.Clarke) is used in many *Ayurvedic* formulations which contains specific oil (sesquiterpenes) responsible for its pharmacological actions⁸⁹. However, only a certain quantity of this oil is required for therapeutic purposes and the excess quantity of oil is removed by boiling.
process. 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.

Here are some of the examples of media from various sources (animal, plant, mineral etc.) frequently used for Shodhana of certain plant drugs are mentioned below.

**Animal source:**
- **Gomutra** (cow urine) - e.g. roots of *Vatsanabha*¹¹
- **Godugdha** (cow milk) - e.g. seeds of *Kuppelu*¹²
- **Aja dugdha** (goat’s milk) - e.g. roots of *Vatsanabha*²¹
- **Goghrita** (cow ghee) - e.g. leaf of *Bhanga*²⁴
- **Gomaya** (cow dung) - e.g. seeds of *Kuppelu*⁹⁷

**Plant source:**
- **Narikela udaka** (coconut water) - e.g. fruits of *Bhallataka*¹³
- **Panchapallava Kwatha** - e.g. rhizome of *Vacha*¹⁴
- **Ardraka swarasa** (ginger juice) - e.g. latex of *Ahiphena*¹⁵
- **Triphala kwatha** (decoction of *Triphala*) - e.g. oleo-gum resin of *Guggulu*¹⁷
- **Kanji** (sour gruel) - e.g. seeds of *Gunja*¹⁹
- **Eranda taila** (castor oil) - e.g. seeds of *Kupeelu*²⁰
- **Chincha patra swarasa** - e.g. latex of *Snuhi*³³
- **Babul twak kwatha** - e.g. leaf of *Bhanga*²⁴
- **Apamarga kwatha** - e.g. seeds of *Nimbuka*²⁵

**From mineral source:**
- **Istika choorna** (brick powder) - e.g. fruits of *Bhallataka*¹⁸
- **Ushnodaka** (hot water) - e.g. fruits of *Bhallataka*²²
- **Churnodaka** (lime water) - e.g. roots of *Chitraka*¹⁶
- **Multani mitti** - e.g. seeds of *Kuppeelu*⁹⁷

**Different media used for Shodhana of Kupeelu seeds:**

While searching different texts it is observed that different media are used for Shodhana of Kupeelu seeds. Here in this section an attempt has been made to compile scientific research base information related to following media like,

- **Gomutra** (cow urine),
Cow urine therapy is capable of curing many curable and incurable diseases. Cow Urine Treatment and Research Center, Indore has conducted a lot of research over the past few years and reached the conclusion that it is capable of curing diabetes, blood pressure, asthma, psoriasis, eczema, heart attack, blockage in arteries, fits, cancer, AIDS, piles, prostrate, arthritis, migraine, thyroid, ulcer, acidity, constipation, gynecological problems, ear and nose problems and several other diseases.

The analysis of cow urine has shown that it contains nitrogen, sulphur, phosphate, sodium, manganese, carabolic acid, iron, silicon, chlorine, magnesium, melci, citric, titric, succinic, calcium salts, Vitamin A, B, C, D, E, minerals, lactose, enzymes, creatinine, hormones and gold. A person falls ill when there is deficiency or excess of these substances inside the body. Cow urine contains all of these substances, which are naturally present in the human body. Therefore consumption of cow urine maintains the balance of these substances and this helps cure incurable diseases.

**Guna-Karma of Gomutra:**

- **Rasa:** Katu-Tikta-Kashaya
- **Guna:** Tikshna, Laghu, Kshar
- **Virya:** Ushna
- **Dosaghnata:** Vata-Kapha shamaka
- **Therapeutic uses:** Shula, gulma, udara, anaha, kandu, akshi & mukha roga, kilasa, vata vyadhi, basti roga, kustha, kasa, swasa, shotha, kamla, pandu etc.

**Chemical composition of cow urine:**

1. Nitrogen (N₂, NH₂): Removes blood abnormalities and toxins, natural stimulant of urinary track, activate kidneys and it is diuretic.

2. Sulphur (S): Supports motion in large intestines, cleanses blood.
3. Ammonia (NH\textsubscript{3}): Stabilize bile, mucous and air of body. Stabilizes blood formation.

4. Copper (Cu): Controls built up of unwanted fats.

5. Iron (Fe): Maintains balance and helps in production of red blood cells & hemoglobin. Stabilizes working power.

6. Urea CO (NH\textsubscript{2})\textsubscript{2}: Affects urine formation and removal. Germicidal.

7. Uric Acid (C\textsubscript{5}H\textsubscript{4}N\textsubscript{4}O\textsubscript{3}): Removes heart swelling or inflammation. It is diuretic therefore destroys toxins.


11. Manganese (Mn): Germicidal, stops growth of germs, protects against decay due to gangrene.

12. Carbolic acid (HCOOH): Germicidal, stops growth of germs and decay due to gangrene.

13. Calcium (Ca): Blood purifier, bone strengthener, germicidal.


15. Vitamins A, B, C, D, and E: Vitamin B is active ingredient for energetic life and saves from nervousness and thirst, strengthens bones and reproductive ingredient for energetic life and saves from nervousness and thirst, strengthens bones and reproductive power.


17. Lactose (C\textsubscript{6}H\textsubscript{12}O\textsubscript{6}): Gives nourishment, strengthens heart, removes thirst and nervousness.

18. Enzymes: Make healthy digestive juices, increase immunity.

19. Water (H\textsubscript{2}O): Maintains fluidity of blood, maintains body temperature.

20. Hippuric acid (C\textsubscript{9}H\textsubscript{9}NO\textsubscript{3}): Removes toxins through urine.

21. Creatinine (C\textsubscript{4}N\textsubscript{3}H\textsubscript{5}O): Germicide.

22. Aurum Hydroxide (AuOH): It is germicidal and increases immunity power. AuOH is highly antibiotic and anti-toxic.
Patents of cow urine:

- **US Patent #6410059**: Cow urine distillate in a specific amount is scientifically proven to enhance the anti-microbial effects of antibiotic and antifungal agents.\(^{32}\) (US patent# 6410059 has been granted to Indian scientists for the invention on June 25, 2002). The invention relates to a novel use of cow urine as activity enhancer and availability facilitator for bioactive molecules, including anti-infective agents. The invention has direct implication in drastically reducing the dosage of antibiotics, drugs and anti-infective agent while increasing the efficiency of absorption of bio-active molecules, thereby reducing the cost of treatment and also the side-effects due to toxicity.

- **US Patents #6896907, #7235262**: Use of bioactive fraction from cow urine distillate (go-mutra) as a bio-enhancer of anti-infective, anti-cancer agents and nutrients\(^{33}\). The invention relates to a novel pharmaceutical composition comprising an effective amount of bio-active fraction from cow urine distillate as a bioavailability facilitator and pharmaceutically acceptable additives selected from anticancer compounds, antibiotics, drugs, therapeutic and nutraceutic agents, ions and similar molecules which are targeted to the living systems.

- **US Patent # 7297659**: Synergistic fermented plant growth promoting bio-control composition – produced from cow urine, neem, and garlic\(^{34}\). The present invention relates to a synergistic composition useful as plant and soil health enhancer, comprising urine, neem and garlic, individually or in all possible combinations, with the treatment showing it has the ability to stimulate accumulation of nutrients in the plant biomass, proliferation of plant growth promoting, phosphate solubilizing, abiotic stress tolerant and antagonists towards plant pathogenic fungi, control phytopathogenic fungi in the plants, and enhances the total phenolic contents of the plants.

NRRL B-30487, and NRRL-B 30488, individually or in all possible combinations, and optionally carrier, with each of the strains showing plant promotory activity, phytopathogenic fungi controlling activity, abiotic stress conditions tolerating capability, phosphate solubilization capability under abiotic stress conditions; further, a method of producing said composition thereof, and in addition, a method of isolating said bacterial strains from milk of the cow ‘Sahiwal’.

**Godugdha (cow milk)**

Indians believe that the cow milk is sacred, as well as the cow. They regard the cow as mother. Ayurveda considers that milk is helpful for the growth of the body and *Jeevan shakti*. It is having the similar properties like ‘Oja’ thereby it increases the same in the body. Amongst all the *Jeevaniya dravyas* milk is considered to be the best one and it is having the *Rasayana* properties.\(^9\)

**Guna-Karma of Godugdha:**\(^4\)

- **Rasa:** Madhura
- **Guna:** Guru, Snigdha
- **Virya:** Shita
- **Vipaka:** Madhura
- **Dosaghnata:** Vata-Pitta shamaka
- Pharmacological actions: *Jivaniya, Brimhaniya, Balya, Medhya, Vayasthapaniya, Sandhanakara, Rasayana, Vajikarana* etc.

**Composition of milk:**\(^4\)

The composition of milk varies from cow to cow and differs for the various breeds. However, commercial milks are a blend of many animals of many breeds and have the average compositions shown in this table.

**Table 2.4: Composition of different milk**

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Human</th>
<th>Cow</th>
<th>Goat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>1.2</td>
<td><strong>3.3</strong></td>
<td>3.4</td>
</tr>
<tr>
<td>Lactose</td>
<td>7.0</td>
<td><strong>4.8</strong></td>
<td>4.7</td>
</tr>
<tr>
<td>Fat</td>
<td>3.8</td>
<td><strong>3.8</strong></td>
<td>4.1</td>
</tr>
<tr>
<td>Ash (vitamins &amp; minerals)</td>
<td>0.21</td>
<td><strong>0.71</strong></td>
<td>0.77</td>
</tr>
<tr>
<td>Total solids</td>
<td>12.4</td>
<td><strong>12.8</strong></td>
<td>13.0</td>
</tr>
</tbody>
</table>
Various uses of cow milk in Ayurveda

1. **Milk with herbs:** Certain herbs with pungent and hot properties are processed with cow milk and used in children or in person with less strength. This serves three purposes,
   a. The herbal remedy gets the extra nutritional quality of milk
   b. The pungency and the strength of the herb is lowered. Thus the herbal formula is made suitable for patient with less strength.
   c. Milk acts as a fat and water soluble media for the active principles in the herb.

   **Example:** Garlic processed with milk, used in digestion problems.

2. **Cow milk in Ayurvedic medicated oils** – In processing many oils, where the oil is desired to have nourishing and rejuvenating effects, milk is added and processed along with oil and other herbs.

   This is especially beneficial in Ayurvedic medicated oils that are
   - used for massage against degenerative diseases like Osteoarthritis,
   - used to calm burning sensation,
   - used to heal nerve irritation and nerve pain.
   - used to nourish and strengthen muscles and ligaments.

   **Example:** Ksheerabala Taila.

   Most of the herbal oils, which are used for nasal instillation or for internal administration are processed along with milk.

3. **Shirodhara with Cow milk** – *Shirodhara* is a procedure, where continuous stream of liquid is directed uniformly over the forehead region. Milk is used in cases where *Vata* and *Pitta* are involved. This is generally used in cases of insanity, epilepsy, sleeplessness, burning sensation of the head and certain types of headache.\(^92\)

4. **Cow milk in Basti** – *Basti* is a *Panchakarma* procedure. Milk processed with herbs is used for *Basti* in *Raktarsha, Grahani, Pravahika, Kaphaja Atisara* etc., in Ayurveda.\(^93,94\)

5. **Cow milk for gargling:** To relieve burning sensation and to relieve oral ulcers.
Interesting note: sale of raw, unprocessed cow milk is an offence is USA.

Contraindication:

Following persons should not take cow milk,-

- Those who are allergic to cow milk.
- Who have Kapha imbalance symptoms.
- Who are obese.
- Who have severe low digestion power.

Goghrita (cow ghee)

The milk of cows is considered to possess the essence or sap of all plants and Ghee is the essence of milk. In India, Ghee has been so highly regarded for so many things, for so long, that one is slightly embarrassed to enter into this crowded river of praise. The ingestion of Ghee is like offering the finest of fuels into the fires of digestion-Agni. In accord with this, Ghee builds the aura, makes all the organs soft, builds up the internal juices of the body-Rasa, which are destroyed by aging and increases the most refined element of digestion-Shukra or Ojas, the underlying basis of all immunity and the “essence of all bodily tissues”. Ghee is known to increase intelligence--Dhi, refine the intellect-Buddhi and improve the memory-Smrti.

Although Ghee kindles or increases the digestive fire- Agni, on which all nutrition depends, it does so without aggravating Pitta- the elemental functioning of fire within the body. In fact, Ghee cools the body, essential in much of today’s world in which everything is overheating.

Ghee causes secretions and liquification in the dhatus-bodily tissues that dissolve wastes allowing the functional intelligences of the body-doshas to carry away toxins-ama. The ingestion of Ghee is used in Panchakarma specifically to first penetrate into and then dissolve ama in the dhatus, allowing the wastes to be then carried to the intestinal tract and then expelled.

It is traditionally considered, that the older Ghee, the better its healing qualities. 100-year-old Ghee is highly valued in India and fetches a very high price. Such Ghee was often kept in Temples in large vats and families often pass on aged Ghee to their next generation to be used as medicine.
Conceptual Study

Chapter 2

Shodhana of Kupeelu

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Guna-Karma of Goghrita43:
Rasa : Madhura
Guna : Guru, Snigdha, Mirdu
Veerya : Seeta
Vipaka : Madhura
Karma : Agnideepana, Anubhisyyandi, Ayushya, Balya, Cakshushya, Deepana,
Hridya, Kaantiprada, Medhya, Ojovardhaka, Rasayana, Ruchya,
Shleshmavardhana, Snehana, Shukravardhaka, Tejobalakara, Tvachya,
Vatapittaprasamana, Vayaasthapna, Vishahara, Virsya etc.

Chemical composition and analysis of Cow ghee as per modern chemical parameter is also important to know the utility of Ghee.

Composition of Ghee44:

Table 2.5: Composition of cow ghee

<table>
<thead>
<tr>
<th>Composition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy-K.cal</td>
<td>899.1</td>
</tr>
<tr>
<td>Carbohydrate % by mass</td>
<td>Nil</td>
</tr>
<tr>
<td>Fat % by mass</td>
<td>99.9</td>
</tr>
<tr>
<td>Protein % by mass</td>
<td>Nil</td>
</tr>
<tr>
<td>Vit-A</td>
<td>550µg.</td>
</tr>
<tr>
<td>Saturated Fat</td>
<td>67.33 g.</td>
</tr>
<tr>
<td>MUFA</td>
<td>29.17 g.</td>
</tr>
<tr>
<td>PUFA</td>
<td>3.45 g.</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>310mg.</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>97-98%</td>
</tr>
<tr>
<td>Diglycerides</td>
<td>0.25-0.40%</td>
</tr>
<tr>
<td>Monoglycerides</td>
<td>0.016-0.038%</td>
</tr>
<tr>
<td>Keto-acid glycerides</td>
<td>0.015-0.018%</td>
</tr>
<tr>
<td>Free fatty acids</td>
<td>0.1-0.44%</td>
</tr>
<tr>
<td>Phospholipids</td>
<td>0.2-1.0%</td>
</tr>
<tr>
<td>Sterols</td>
<td>0.22-0.41%</td>
</tr>
</tbody>
</table>
Uses of Ghee

1. For Body Massage-Abhyanga. Apply ghee all over the body, rubbing into head, chest, limbs, joints and orifices. This will bypass the digestive system and allow the qualities of Ghee to penetrate directly into the deeper tissues. It is said that 60% of what is placed on the skin is absorbed into the body. Western science has discovered that massaging the skin creates endorphins or peptides, which enhance the body’s immune system. Peptides are thought to be the vehicle that the mind and body use to communicate with each other, a literal chemistry of emotion. According to the *Charak Samhita*, regular Abhyanga slows the aging process.

2. Ghee is used in Purvakarma, (preparatory procedures of Panchakarma) where a small amount of Ghee is given to the patient to oleate the internal organs and “dissolves” the ama or toxic wastes in the tissues, allowing them to be carried to the digestive tract for elimination.

3. Ghee is used as a carrier or “yogavahi” for herbs and bhasmas because of its supreme penetrating qualities and thus ability to carry these substances deep into the dhatus or tissues.

4. One or two teaspoons first thing in the morning followed immediately with hot water will promptly produce a bowel movement. It will also warm the body quickly. Two spoonful of Ghee in warm (non-homogenized) milk before bedtime is soothing to the nerves and lubricates the intestines and facilitates a bowel movement in the morning.

5. Ghee is excellent for cooking and sautéing or stir-frying. Ghee has one of the highest flash points of all oils and is very difficult to burn. In India, it is said that food is incomplete without the use of Ghee.

6. Ghee is excellent for a gargle-gandush, to improve the health of the teeth and gums.

7. Ghee can be used as a bath oil. Take two tablespoons of Ghee and mix with several drops of an essential oil of your choice.

8. Ghee is excellent for scrapes and both chemical and heat or fire burns. Ghee can be used in the eyes for tiredness or fatigue.

9. Ghee is an exquisite facial moisturizer.

10. A few drops of ghee are placed in the nostrils to check the nosebleed. If this is done twice in a day, then headache can be relieved.
11. It is also used in hyperacidity, otalgia, debility due to chest injury, intoxication, syncope, headache, loss of memory, emaciation, mania / psychosis, intermittent fever, erysipelas, disorders due to poison, pain in female genital tract.

12. Cow ghee promotes memory, intellect, and power of digestion, semen, ojas, kapha and fat. It alleviates vata, pitta, toxic conditions, insanity, consumption and fever. It is the best of all the unctuous substances.

**Cow Ghee V/S Vegetable oil**

Marketing strategies force common Indians for switching their cooking media from Ghee to refined hydrogenated vegetable oil. This creates the confusion of blocking of our arteries and called as “THE FEAR OF CHOLESTEROL”. Cow ghee contains 62-67% saturated fat and a good amount of MUFA (Mono unsaturated fatty acids) which is most desirable for the health and this amount is more than that of vegetable oil. Cow ghee contains Linoleic acid which only found in cow ghee again a very essential fatty acid for proper growth of human body. Apart all of this cow ghee has some peculiar characteristics which are as follows.

During preparation of ghee, protein casein is removed. Animal studies show that casein elevates cholesterol. (Butter oil- IJCP July 1990) It contains natural vit A which keeps the outer lining of eye ball moist and prevent blindness. Its melting point is 35°C which is less than the normal human body temperature leading to its digestibility coefficient rate 96% which highest among the all edible oils. As other ingredients mixed with ghee as a vehicle (Anupana) reaches up to the cellular level because of its lipophilic nature. It contains beta-carotene and Vit E which are well-known antioxidants.

**Eranda taila (castor oil)**

Castor oil is a vegetable oil obtained from the seeds of *Ricinus communis* Linn. Castor oil (CAS number 8001-79-4) is a colorless to very pale yellow liquid with mild or no odor or taste. Its boiling point is 313 °C (595 °F) and its density is 961 kg/m³. It is a triglyceride in which approximately ninety percent of fatty acid chains are ricinoleic acid. Oleic and linoleic acids are the other significant components.
Ricinoleic acid, a monounsaturated, 18-carbon fatty acid, is unusual in that it has a hydroxyl functional group on the twelfth carbon. This functional group causes ricinoleic acid (and castor oil) to be unusually polar, and also allows chemical derivatization that is not practical with most other seed oils. It is the hydroxyl group which makes castor oil and ricinoleic acid valuable as chemical feed stocks. Compared to other seed oils which lack the hydroxyl group, castor oil commands a higher price.

Castor oil and its derivatives have applications in the manufacturing of soaps, lubricants, hydraulic and brake fluids, paints, dyes, coatings, inks, cold resistant plastics, waxes and polishes, nylon, pharmaceuticals and perfumes.

Sulfonated castor oil, also called sulfated castor oil, or Turkey Red Oil, is the only oil that completely disperses in water. It is made by adding sulfuric acid to pure castor oil. This allows easy use for making bath oil products. It was the first synthetic detergent after ordinary soap. It is used in formulating lubricants, softeners, and dyeing assistants.

The castor seed contains ricin, a toxic protein removed by cold pressing and filtering. However, harvesting castor plants is not without risk. Allergenic compounds found on the plant surface can cause permanent nerve damage, making the harvest of castor beans a human health risk. India, Brazil, and China are the major crop producers and the workers suffer harmful side effects from working with these plants. These health issues, in addition to concerns about the toxic byproduct (ricin) from castor oil production, have encouraged the quest for alternative sources for hydroxy fatty acid. Alternatively, some researchers are trying to genetically modify the castor plant to prevent the synthesis of ricin.

Guna-Karma of Eranda taila:
- Rasa: Madhura-Tikta-Katu
- Anurasa: Kasaya
- Guna: Tikshna, Picchila, Guru, Sukshma, Sara
- Virya: Ushna
- Vipaka: Madhura
- Karma: Deepana, Vrisya, Twachya, Vayasthapan, Shukra vishodhana etc.
Therapeutic uses: *Visama jwara, Hrid roga, Pristha & Guhya shula, Vatodara, Anaha, Gulma, Asthila, Katigraha, Vatarakta, Bibandha, Amavata, Shotha, Vidradhi* etc.

Chemical composition of Castor Oil and its Chemistry:  
- Castor Oil is unique among all fats and oils in that:
  - it is the only source of an 18-carbon hydroxylated fatty acid with one double bond
  - ricinoleic acid (12-Hydroxyoleic Acid) comprises approximately 90% of the fatty acid composition
  - product uniformity and consistency are relatively high for a naturally occurring material
  - it is a nontoxic, biodegradable, renewable resource

The remarkably constant composition of castor oil fatty acids is shown below:

- Ricinoleic acid: 89.50%
- Linoleic acid: 4.2%
- Oleic acid: 3.0%
- Stearic acid: 1.0%
- Palmitic acid: 1.0%
- Dihydroxystearic acid: 0.70%
- Linolenic acid: 0.30%
- Eicosanoic acid: 0.30%

The hydroxyl groups in castor oil account for a unique combination of physical properties:
- Relatively high viscosity and specific gravity
- Solubility in alcohols in any proportion
- Limited solubility in aliphatic petroleum solvents

The uniformity and reliability of its physical properties are demonstrated by the long-term use of castor oil as an absolute standard for viscosity. Because of its higher polar hydroxyl groups, castor oil is not only compatible with but will plasticize a wide variety of natural and synthetic resins, waxes, polymers and elastomers. Castor Oil also has excellent emollient and lubricating properties as well as a marked ability to wet and disperse dyes, pigments and fillers. In the form of its chemical derivatives, castor oil’s application versatility is further enhanced.
Uses of Castor Oil:

- **Castor oil in food**
  In the food industry, castor oil (food grade) is used in food additives, flavorings, candy (e.g., chocolate), as a mold inhibitor, and in packaging. Polyoxyethylated castor oil (e.g., Cremophor EL) is also used in the foodstuff industries.

- **Medicinal use of castor oil**
  The United States Food and Drug Administration (FDA) has categorized castor oil as "generally recognized as safe and effective" (GRASE) for over-the-counter use as a laxative, with its major site of action the small intestine. However, although it may be used for constipation, it is not a preferred treatment. Undecylenic acid, a castor oil derivative, is also FDA-approved for over-the-counter use on skin disorders or skin problems. Castor oil penetrates deep into the skin thanks to its molecular weight, which is low enough to penetrate into the stratum corneum. Castor Isostearate Succinate is a polymeric mixture of esters with Isostearic Acid and Succinic Acid used for skin conditioning, such as in shampoo, lipstick and lip balm. Ricinoleic acid is the main component of castor oil and it exerts anti-inflammatory effects. One study has found that castor oil decreased pain more than ultrasound gel or Vaseline during extracorporeal shockwave application. Therapeutically, modern drugs are rarely given in a pure chemical state, so most active ingredients are combined with excipients or additives. Castor oil, or a castor oil derivative such as Cremophor EL (polyethoxylated castor oil, a nonionic surfactant), is added to many modern drugs, including:
  - Miconazole, an anti-fungal agent;
  - Paclitaxel, a mitotic inhibitor used in cancer chemotherapy;
  - Sandimmune (cyclosporine injection, USP), an immunosuppressant drug widely used in connection with organ transplant to reduce the activity of the patient's immune system;
  - Nelfinavir mesylate, an HIV protease inhibitor;
  - Saperconazole, a triazole antifungal agent (contains Emulphor EL-719P, a castor oil derivative);
  - Xenaderm ointment, a topical treatment for skin ulcers is a combination of Peru balsam, castor oil, and trypsin.
- Aci-Jel (composed of ricinoleic acid from castor oil, with acetic acid and oxyquinoline), used to maintain the acidity of the vagina\textsuperscript{75}.

\begin{itemize}
  \item \textbf{Uses of castor oil in Traditional or folk medicines}
\end{itemize}

The use of cold pressed castor oil in folk medicine predates government medical regulations. Cold pressed castor oil is tasteless and odorless when pure. Uses include skin problems, burns, sunburns, skin disorders, skin cuts, and abrasions. Castor oil has also been used to draw out styes in the eye by pouring a small amount into the eye and allowing it to circulate around the inside of the eyelid. The oil is also used as a rub or pack for various ailments, including abdominal complaints, headaches, muscle pains, inflammatory conditions, skin eruptions, lesions, and sinusitis. A castor oil pack is made by soaking a piece of flannel in castor oil, then putting it on the area of complaint and placing a heat source, such as a hot water bottle, on top of it. This remedy was often suggested by the American psychic Edgar Cayce, given in many healing readings in the early mid-1900s. Castor oil has also been noted for its acne-healing abilities\textsuperscript{76}.

Castor oil has been used to induce childbirth in pregnant women, though it is not always effective in application. Castor oil, when ingested, triggers cramping in the bowel (making it an effective laxative). Thus, it is intended that such cramping extend to the uterus. In south Egypt, women use a large spoonful dosage of castor oil to prevent pregnancy for one year. It has also been claimed that castor promotes eyelash growth, however there's no supporting scientific data\textsuperscript{77}.

**Kanji (sour gruel)**

\textit{Kanji} or Sour gruel is water of boiled rice in the state of spontaneous fermentation\textsuperscript{80}. \textit{Kanji} is not only used extensively in Ayurveda for \textit{Shodhana} of certain minerals and plant drugs to reduce their toxic effects, but also it is administered in therapeutics.

**Guna-Karma of Kanji:**\textsuperscript{81}
- \textit{Guna: Tikshna, Laghu}
- \textit{Virya: Ushna}
- \textit{Dosaghnata: Vata-Kapha shamaka}
- \textit{Karma: Bhedana, Pachana, Jwaraghna, Shulaghna, Vasti shodhaka etc.}
• **Contraindication:** Shosa, Murcha, Bhrama, Mada, Kandu, Kustha, Raktapitta, Pandu, Raja yakshma, Kshata kshina, Shranta, Manda jwara etc. are some of the conditions where Kanji should not be given.

**Ardraka swarasa (ginger juice)**

Ginger of commerce or ‘Ardraka’ is the dried underground stem or rhizome of the plant, which constitutes one of the five most important major spices of India. Ginger, like cinnamon, clove and pepper, is one of the most important and oldest spices. It consists of the prepared and sun dried rhizomes which are either with the outer brownish cortical layers (coated or unscraped), or with outer peel or coating partially or completely removed.

Ginger requires a warm and humid climate. It is cultivated from sea level to an altitude of 1500 meters, either under heavy rainfall conditions of 150 to 300 cm or under irrigation. The crop can thrive well in sandy or clayey loam or lateritic soils.

**Guna-Karma of Ardraka:**

- **Rasa:** Katu  
- **Guna:** Guru, Tikshna, Ruksha  
- **Virya:** Ushna  
- **Vipaka:** Madhura  
- **Dosaghnata:** Vata-Kapha shamaka  
- **Karma:** Bhedana, Agnidipana, Pachana, Vrisya etc.

• **Contraindication:** The diseases like Kustha, Pandu, Mutrkriccha, Raktapitta, Vrana, Jwara, Daha etc. and in Grishma & Sarat ritu.

**Chemical constituents:**

The rhizome contains 1–4% essential oil and an oleoresin. The composition of the essential oil varies as a function of geographical origin, but the chief constituent sesquiterpene hydrocarbons (responsible for the aroma) seem to remain constant. These compounds include (-)-zingiberene, (+)-ar-curcumene, (-)-sesquiphellandrene, and β-bisabolene. Monoterpene aldehydes and alcohols are also present. The constituents responsible for the pungent taste of the drug and possibly part of its anti-emetic properties have been identified as 1-(3-methoxy-4-hydroxyphenyl)-5-hydroxyalkan-3-ones, known as [3–6]-, [8]-, [10]-, and [12]-gingerols (having a side-chain with 7–10, 12, 14, or 16 carbon...
atoms, respectively) and their corresponding dehydration products, which are known as shogaols.

It may be noted however that the composition given above may not be applicable to ginger produced in all the countries or region. For example inferior ginger may have excessive fiber for which they are valued at lower price. On steam distillation, dried, cracked and comminuted ginger yields 1.0 to 3.0 % of pale yellow, viscid oil. The oil possesses the aromatic odor but not the pungent flavor of the spice. The odor of the oil is quite lasting.

Ginger oleoresin is obtained by extraction of powdered dried ginger with suitable solvents like alcohol, acetone etc. Unlike volatile oil, it contains both the volatile oil and the non-volatile pungent principles for which ginger is so highly esteemed. Concentration of the acetone extract under vacuum and on complete removal of even traces of the solvent used, yields the so called oleoresin of ginger. Ginger oleoresin is manufactured on a commercial scale in India and abroad and is in great demand by the various food industries.

**Uses of Ginger:**

The aroma of ginger is pleasant and spicy and the flavor penetrating, slightly biting due to antiseptic or pungent compounds present in it, which makes it indispensable in the manufacture of a number of food products like ginger bread, confectionary, ginger ale, curry powders, soft drinks, vegetable, meat and fish curries, ginger cocktail, sauces etc. Ginger preserves and ginger candy prepared from green or fresh ginger is quite favorite of many and find great demand. A number of alcoholic beverages are prepared from ginger in foreign countries, such as ginger brandy, ginger wine, ginger beer etc.

According to the *Ayurvedic* and *Unani* system of medicine, ginger is considered to be carminative, stimulant and given in dyspepsia and flatulent colic. With honey and Basil leaves it acts as an excellent expectorant. Ginger oil is used as food flavorant, has pharmaceutical applications and to a limited extent in perfumery industries. Oleoresin has many applications identical to the spice itself.\(^\text{82}\)
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**KUPEELU (Strychnos nux-vomica Linn.)**

**History of nux-vomica as a deadly poison:**

Nux-vomica is 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 poison and it becomes a very popular murder weapon which is believed to have killed an unknowable number of people, especially during the 19th century. Strychnine, an indole found in the seeds, is a powerful central nervous system stimulant that competes with the inhibitory neurotransmitter glycine, producing an excitatory state with hyperreflexia, severe muscle spasm, and convulsions. Its principal action is to cause uncontrolled muscle contractions. In overdose, these lead to death from exhaustion or cardiac arrest. The muscle contractions can result in muscle tearing itself away from bone allowing the body to be twisted into normally impossible positions¹.

**Historic use of strychnine**

Strychnine was first isolated from the beans of *Strychnos ignatii* by Pierre Joseph Pelletier and Joseph Bienaimé Caventou in 1818. Scientists, who had been working with quinine, thought they would try to use it as another weapon against disease. Doctors experimented with it for years, trying it on everything from paralysis to constipation. No success over the next century proved that it was not helpful, but was instead extremely deadly for patients. The use of strychnine in the century following its discovery was relegated almost entirely to animal control and criminal behavior².

There are a number of reports of both fatal and non-fatal poisoning in Asia after the use of strychnine-based herbal remedies. These all mention the rapidity of onset of symptoms and the need for prompt, aggressive treatment. Strychnine is one of the principle murder poisons both in fiction and in fact. In Victorian times it was a major part of rat poison, which was available, no
questions asked, from most shops. The pre-death convulsions it causes are called tetanic because they look like tetanus, a disease that was endemic in the inner cities at the time. It is believed that many men met their ends via strychnine but murder was never suspected.

From the late 19th century, when it became much more tightly controlled, murder by strychnine became the province of the medical profession. A number of users of strychnine attribute in the talk about 'Medical Murderers'. Until very recently strychnine was still in use as a mole poison. The UK government lost its appeal against having to enforce new EU legislation on the use of strychnine based poisons to kill pests. The UK government was concerned about the 3000 licensed mole catchers who, until this ruling, could use strychnine in their work.

This use to poison moles cost a life as recently as 1934. Ethel Major used strychnine, which her gamekeeper father had for pest control, to murder her husband. His death was attributed to ‘status epilepticus’, a condition producing prolonged seizure with convulsions, and she had mistakenly put some leftover food scraps out for a neighbor’s dog which died as a result. The police were able to do a post mortem examination of the dog and obtain evidence of the presence of strychnine which gave them grounds for exhuming the husband.

It is sometimes said that Venetian ladies used *Strychnos nux-vomica* as the ‘inheritance plant’. There is no evidence for this use. There was an ‘inheritance powder’ which has been shown to be arsenic used as a way of speeding the acquisition of the family silver. Madame Toffana, who, in the 17th Cen., was accused of being responsible for 600 deaths mostly undertaken by women she had trained, used a paste containing arsenic. This was sold as a cosmetic but women who had the benefit of Madame Toffana’s training knew how to apply it to more deadly purposes.

**Introduction of nux-vomica in Ayurveda:**

*Kupeelu* was not reported in the ‘Brihat Trayee’ texts of Ayurveda. However, *Vishamustika* is mentioned by *Susruta* in the *Surasadi ganä* but it is not botanically identified as *S.nux-vomica*. *Dalhana* also mentioned it as *Raja Nimba*. 
It’s uses in Ayurveda was 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.

Some scholars opine that the drug Vishamusti quoted by Kaiyadeva (15th A.D.) may be the nux-vomica. Afterward the drug Kupellu has been botanically identified as Strychnos nux-vomica (Linn.) by the Ayurvedic scholars as well as the Botanists and being used in many formulations.

Though the plant is described under the ‘Upavisha Vargas’ (semi poisonous group), it has been used successfully in the management of several diseases after proper Samaskar, called Shodhana (purificatory measures). Review of literature indicates that the word ‘Kupeelu’ was first time reported for this plant in Abhidhana Ratnamala (Sadrasa Nighantu) probably during the 12th-13th Century A.D. On the other hand, European countries started using this plant from sixteenth century onwards; however not abundantly utilized in drugs, chiefly utilized to poison dogs, cats, crows, etc and they took a further 200 years to discover the therapeutic value of nux-vomica. In consequence of its poisonous nature, nux vomica was very reluctantly introduced into the European pharmacopoeias. Indeed, it was recognized in America (1830) before it was official in England, although long before this date it was a dispensatory drug. In 1799, however, it was official in the Pharmacopeia Borussica, and in two other Continental European pharmacopeias. It was prescribed as a stimulant of the digestive system and a nervine tonic. However, the ancient texts of Ayurveda quoted that the Visha (poison) converts into Amrita (nectar) after utilize legitimate. Ayurvedic physicians successfully employed this drug in a series of illnesses after proper shodhana (purificatory measures) through a few particular media. Shodhana procedures not only represent a process of purificatory measures, but also in addition to a process of detoxification and the ultimate objective of Shodhana is to enhance the biological efficacy of the drug.

The seeds mainly used as an aphrodisiac, appetizer, anti periodic, digestive, purgative, and stimulant. They are conjointly utilized in anemia, asthma, bronchitis, intermittent & malarial fever and in weakness of extremities. Indian nuxvomica seeds contain 2.6 to 3% of total alkaloids approximately, of which 1.25 to 2.5% is
strychnine and brucine is regarding 1.5 to 1.7%. The seeds additionally contain chlorogenic acid, a glycoside (loganin), and 3% of fixed oil\(^{12}\).

**Derivation of botanical name:**

*Strychnos*, said to be from Greek word 'strychnon' but no origin is apparent. Usually translated as 'nightshade' after Pliny.

‘Nux-vomica’ does not, as many people believe, mean ‘no vomiting’ or ‘stops vomiting’. ‘Nux’ is Latin for ‘nut’ and ‘vomica’ means ‘lump’ or ‘abcess’. In the context of this plant, then, ‘nux-vomica’ means ‘the seed looks like a nut and has a lump on it’\(^1\).

**Selected vernacular names\(^6\):**

- English- Strychnine tree, Snake-wood, Nux-vomica, Poison nut, Quaker button.
- Hindi- Kuchla, Bailewa, Chibhige, Chilbinge, Kajra.
- Bengali-Kuchila, Thalkesur.
- Odiya- Kachila, Kora, Kosila, Kuchla.
- Gujarati: Kuchln.
- Kannada- Hentmushti, Ittangi, Itti, Kanjir’a, Mushti, Kasaragadde, Kasaraka, Ittinji.
- Malayalam- Kanjirrant, Kariram, Kanniram.
- Punjabi- Kagophale, Kajra, Kuchila.
- Tamil- Yetti, Yetti-maram, Kagodi, Kanjirai, Ettik-kottai, Kancirai.
- Telgu-Mushti, Musidi, Indupu.
- Arabic- Izar’agi, Khanek-ul-kella.
- Persi- Fulusmahi, Laraki.
- Singhali- Goda-kadura-atta, Kanchura.

**Classical names:**

*Kupeelu, Vishatinduka, Karsakara, Kakatinduka, Kakapiluka, Kulaka etc.*

**Occurrence & Distribution:**

The plant is growing in Ceylon, East Bengal, Burma, Thailand, Laos, Cambodia, and S. Vietnam. The seeds of Nux-vomica collected from different parts of India and mainly exported from Mumbai, Chennai, Cochin, Cocanada and Kolkata\(^9\). This tree is
found throughout the tropical India including Uttar Pradesh, Bihar, Orissa and West Bengal, ascending up to an altitude of 1350 m and most typical within the forests along the western coast, sometimes also cultivated in gardens.

The tree is found growing in the region, where the absolute maximum shade temperature varies from 35°C to 45°C and minimum from 4°C to 18°C, and where rainfall ranges from 75 to 375 cm. or more. This tree is a shade-bearer, growing under a moderate canopy even in semi-evergreen forests. It produces root-suckers and is free from damage by browsing, as animals avoid it.

The identification of *Strychnos nux-vomica* Linn can be confirmed after comparing the following characters described in various texts.

**A.] Taxonomical Classification according to Bentham & Hooker:**

- Kingdom: Plantae
- Division: Spermatophyta
- Sub division: Angiosperms
- Class: Dicotyledon
- Sub class: Gamapetalae
- Series: Bicarpellatae
- Order: Gentianales
- Family: Loganiaceae
- Genus: *Strychnos*
- Species: *S. nuxvomica* L.

**B.] Characters of the Taxonomic positions:**

1. Division: *Spermatophyta* - seed plants
2. Sub-division: *Angiosperms* - seeds are enclosed in the fruit.
3. Class: *Dicotyledon* - having two cotyledons in the seed.
4. Sub-class: *Gamopetalous* - having a corolla composed of partially or wholly fused petals forming a corolla shaped like a tube or funnel.
5. Order: *Gentianales* - an order of dicotyledonous plants having gamopetalous flowers. E.g., Gentianaceae; Apocynaceae; Asclepiadaceae; *Loganiaceae*; Oleaceae; Salvadoraceae etc.
The family includes 13 genera with more than 400 species of woody vines, shrubs, or trees native primarily to tropical areas of the world. Members of the family bear leaf-like appendages at the base of the leafstalks and have terminal flower clusters. The ring of petals on each flower has four or five overlapping lobes. Fruits vary from capsules to fleshy drupes.89

Earlier treatments of the family have included up to 29 genera. Phylogenetic studies have demonstrated that this broadly defined Loganiaceae was a polyphyletic assemblage, and numerous genera have been removed from Loganiaceae to other families (sometimes in other orders), e.g., Gentianaceae, Gelsemiaceae, Plocospermataceae, Tetrachondraceae, Buddlejaceae and Gesneriaceae. Some classification schemes, notably Takhtajan's, break the remaining Loganiaceae even further, into as many as four families; Strychnaceae, Antoniaceae, Spigeliaceae and Loganiaceae. Recent DNA studies of the Gentianales have found strong support for the Loganiaceae (as defined here) as a clade containing 13 genera.90

**Present Genera in the Loganiaceae family:**
- *Antonia* Pohl
- *Bonyunia* R. H. Schomb. ex Progel
- *Gardneria* Wall.
- *Labordia* Gaudich.
- *Logania* R.Br.
- *Mitrasacme* Labill.
- *Mitreola* L.
- *Neuburgia* Blume
- *Norrisia* Gardner
- *Spigelia* L.
- *Strychnos* L.
- *Usteria* Willd.

**Excluded genera:**
- *Androya* H.Perrier -> Scrophulariaceae
- *Anthocleista* Afzel. ex R.Br. -> Gentianaceae
- **Buddleja** L. -> Scrophulariaceae  
- **Desfontainia** Ruiz & Pav. -> Columelliaceae  
- **Emorya** Torr. -> Scrophulariaceae  
- **Fagraea** Thunb. -> Gentianaceae  
- **Gelsemium** Juss. -> Gelsemiaceae  
- **Gomphostigma** Turcz. -> Scrophulariaceae  
- **Mostuea** Didr. -> Gelsemiaceae  
- **Nuxia** Comm. ex Lam. -> Stilbaceae  
- **Peltanthera** Benth. -> Gesneriaceae  
- **Plocosperma** Benth. -> Plocospermataceae  
- **Polypremum** L. -> Tetrachondraceae  
- **Potalia** Aubl. -> Gentianaceae  
- **Retzia** Thunb. -> Stilbaceae

**Characters of Loganiaceae family:**

Plants belong to this family are trees or shrubs often climbing or herbs.

- Leaves- opposite, entire, generally connected by interpetiolar stipules or a raised, transverse line,
- Inflorescence - cymose,
- Flowers- regular, hermaphrodite,
- Calyx- inferior, 4-5-toothed
- Corolla- gamopetalous, 4-5-lobed; lobes imbricate or valvate
- Stamens- 4-5, inserted on the corolla-tube and alternate with its lobes
- Ovary- free usually 2-celled; ovules 1 or more in each cell; style simple; stigma often 2-lobed.
- Fruit- a capsule or berry, 1-many-seeded; albumen copious; cotyledons broad or narrow; radicle usually inferior, very nearly allied to the *Rubiaceae* from which it differs by the free ovary. The genera usually included in the Loganiaceae are not closely related to each other.

7. **Genus: Strychnos** - *Strychnos* is a genus of flowering plants, belonging to family Loganiaceae (sometimes Strychnaceae). The genus includes about 190 species of trees and lianas, distributed around the world's tropics.
- The Strychnine tree, *Strychnos nux-vomica*, native to tropical Asia, is the source of the poison strychnine.

- *Strychnos ignatia* ("St. Ignatius bean") is a closely related Asian shrub/tree.

- *Strychnos toxifera* is one of the two plant sources of the poison curare.

- Another notable species are *Strychnos spinosa* (Lam.), commonly known as the Natal orange and *Strychnos pungens*, from Southern Africa; which are drought-tolerant and produce edible fruits.

- The ripe seeds of *Strychnos potatorum*, known as *Nirmali*, can be ground and used as a coagulant to purify water; or they may be rubbed against the inside walls of the earthenware water containers.

### Specific genus characters:

- Trees or scandent shrubs with short, watch-spring, axillary tendrils,
- Leaves - opposite, entire, usually 3-5-nerved; stipules O
- Flowers - white, pentamerous, small, in terminal or axillary cymes
- Calyx- small, 4-5 toothed
- Corolla –funnel shaped or tubular; lobes 4-5, valvate
- Stamens- 4-5, inserted in the throat of the corolla
- Ovary- 2-celled throughout or 1-celled in the upper portion;
- Ovules -several in each cell on fleshy placentas; style filiform; stigma capitates;
- Fruit- a globose berry with one -several large seeds immersed in pulp.
- Seeds- more or less compressed; embryo small, eccentric, in cartilaginous albumen cotyledons foliaceous.

#### Scandent shrubs with circinate tendrils

Berry 1-2-seeded, 0.5-0.6 inch in diameter ... 1. *S. colubrina.*
Berry many-seeded, 1-1.5 inch in diameter ... 2. *S. dalzellii.*

#### Trees

Fruit black, 1-seeded, 0.5 inch in diameter ... 3. *S. potatorum.*
Fruit orange, many-seeded, 2-4 inch in diameter 4. *S. nux-vomica.*
8. **Species:** *S. nux-vomica* Linn.

   **External morphological characters:**
   - A medium sized deciduous tree, 15-30 meter in height and up to 70 cm in diameter with fairly straight and cylindrical lobe having dark gray or yellowish gray bark and minute tubercles.
   - Leaves: broadly elliptic, 7.5-15×4.5-7.5 cm, 5-nerved, glabrous, shining.
   - Flowers: greenish white in terminal cymes.
   - Fruits: globose, orange red when ripe containing many discoids, compressed coin like seeds in fleshy pulp.
   - Seeds: concave on one side and convex on the other covered with fine gray silky hairs radiating from the centre.
   - Flowers appeared during March-April and fruits ripen during the winter.

**Parts Used:**

   Seeds, leaves, bark, wood and root.

**Collection:**

   The fruit is a berry about the size of a small orange. When ripe it has a hard orange yellow epicarp and a white, pulpy interior in which 1-5 seeds are embedded. The seeds are washed free from pulp and dried in the sun on mats. Seeds are then graded according to size, any piece of seed, which are light in weight and float on the surface of water, are rejected.

**Adulterants:**

1) Dried ripe seeds of *Strychnos potatorum*. These seeds are smaller in size and thicker than Nux-vomica. They are bitter in taste and have emetic property. In India they are used for clearing turbid water and are known as clearing nuts. The seeds contain diaboline an indole alkaloid and other alkaloids. Strychnine is however, absent.

2) Dried ripe seeds of *Strychnos nux blanda*. They are brighter and have yellowish-buff colour. They do not contain any alkaloid and are free from bitter taste.

**Allied Drug:**

- **Ignatius Beans:** Ignatius beans are dried ripe seeds of: *Strychnos ignatii* Bergius.
  
  Family: Loganiaceae.

  Geographical Source: Native of South Philippine Islands.
Seeds are about 1.5 cm long, dark grey and ovoid. Trichomes are not lignified and easily rubbed off so in commercial drug trichomes are absent.

Chemical Constituents: 2.5 to 3% alkaloids of which strychnine is 45 to 60%.

Uses: Similar to Nux-vomica and for the manufacture of strychnine and brucine.

Propagation and cultivation

- Climate and soil: The plant can grow well in dry or humid tropical areas of the country. It grows over laterite, sandy, and alluvial soils. It produces root suckers and is free from damage by browsing, as animals avoid it.

- Propagation material: Seeds are the best material for propagation of Kupeelu plant. The collected seeds are dried in the sun after removing the pulp. Preferably, fresh seeds should be used. The plant can also be propagated through cuttings.

- Nursery technique:
  1. Raising propagules: A nursery of the plant is raised in December or January in climatic conditions of South India. Seeds are sown in polybags of size 25 cm x 20 cm, filled with soil, sand, and FYM (farmyard manure) mixture. Seeds are directly sown in the polybags after appropriate pretreatment. The polybags are watered regularly so as to keep them moist. The seeds germinate in about 20–30 days. Sometimes the germination may continue up to 45 days. The seedling growth is very slow but roots grow very fast. For vegetative propagation, semi-hardwood cuttings can be prepared in early summer and kept under moist conditions after treating with commercially available rooting hormones. Rooting percentage is quite low, often less than 25%.
  2. Propagule rate and pretreatment: About 1 kg seeds are required to raise 1 hectare of plantation. Seeds have low germination rate and fresh seeds of Strychnos nux-vomica lose viability yearly. Germination can be increased by treating the seeds with hot water (50 °C) for 6–12 hours prior to sowing.

- Planting in the field
  1. Land preparation and fertilizer application: The land is ploughed with disc harrow and tillers to achieve a fine tilth and make it weed-free and arable. Pits of size 45 cm x 45 cm x 45 cm are dug at a spacing of 5 m x 5 m and refilled with mixture of soil and manure in 1:1 ratio. Appropriate quantities of sand may be
added if the soil is heavy. About 10 kg of well-rotten FYM is applied in each pit at the time of its refilling.

2. Transplanting and optimum spacing In South India, the seedlings are transplanted with the onset of South-west monsoon in May or early June. An optimum spacing of 5 m × 5 m is recommended, which gives a stand of 400 trees per hectare.

3. Intercropping system The plant can be grown as a pure crop or herbaceous crops can be grown with it as intercrops after the first year.

4. Interculture and maintenance practices About 10 kg of well-rotten FYM is mixed in the soil during refilling of pits before planting. An additional 10 kg manure may again be applied to the soil around the plants during October–November at the time of weeding. A total of 20 kg FYM/plant/year in subsequent years results in best growth of plants. This is to be applied in two split doses in June–July and September October. Supplementary doses of inorganic fertilizers (NPK [nitrogen, phosphorus, and potassium]) do not lead to any significant additional growth in the young plantations. The area around the basin of the plant should be kept weed-free by frequent weeding. The interspaces can be kept weed-free by hand weeding or spraying of herbicides like 0.8% paraquat or 0.4% glyphosate.

5. Irrigation practices The crop needs no irrigation during the rainy season and in dry weather; saplings may be irrigated on alternate days, especially in the early years of growth. For matured trees, irrigation by ring method around tree base at a distance of 30 cm during summer months is beneficial.

6. Disease and pest control No significant pest or disease is observed on the crop.

- Harvest management
  1. Crop maturity and harvesting The tree has a long span of life, that is, 50–60 years. It takes about 15–20 years for the tree to initiate flowering. The seeds are collected December onwards when they mature. Fruits can be harvested periodically for many years.
  2. Post-harvest management Mature fruits are manually collected and seeds from them are extracted, washed, dried in shade, and stored for trade.
  3. Chemical constituents Strychnine and brucine are two most important and toxic alkaloids present chiefly in the seeds. Varying percentages of these two alkaloids
are also present in the other parts of the tree like root bark, root-wood, stem-bark, stem-wood, and in leaves.

4. **Yield and cost of cultivation** Considering a crop stand of 400 plants per hectare and average produce range of 50–75 kg of dry seeds per tree per year, a yield of 12–20 tonnes/hectare is estimated from a 20-yearold plantation annually. The estimated cost of raising 1 hectare plantation in the first year is Rs 100 000 only, while an amount of approximately Rs 6500 per hectare is incurred per year in subsequent years.

- **Market trend – 2006/07**
  Market demand: Above 100 MT per year

**Morphology of seeds**\(^{18}\):
- **Size**: 10 to 30 mm in diameter; 4 to 6 mm thick.
- **Shape**: Disc shaped, flat, some concavo–convex, few seeds irregularly bent, margins rounded or acute.
- **Surface**: Grey to greenish-grey covered with numerous, closely appressed silky hairs, radiating from the centre, hairs impart a Characteristic sheen. Hilum is present in the centre of the flat surface of the seed. From the hilum, a ridge which is not raphe connects the position of the micropyle at the circumference.
- **Endosperm**: It is present below the testa and is grey and horny. Below the endosperm in the centre is a narrow slit like cavity.
- **Embryo**: It is seen at the micropylar end with a cylindrical radicle and two cordate cotyledons.
- **Odor**: None
- **Taste**: Very bitter.

**Chemical constituents of Strychnos nuxvomica Linn.**:

The principal constituents of Nux-vomica are the two alkaloids, strychnine and brucine, in addition to which they contain a small percentage of a glucoside, loganin, which is much more abundant in the pulp, and an acid that has been termed igasuric acid, but is probably identical with caffeotannic acid. Strychnine \((C_{21}H_{22}O_2N_2; m.p. 286\text{ to }288^0\text{C})\) and brucine \((C_{23}H_{26}O_4N_2; m.p. 178^0\text{C})\) are the most important and strongly toxic alkaloids present in this, besides other minor alkaloidal constituents. These alkaloids occur not only in the seed but also in the roots, bark,
leaves, fruit-pulp, and the hard fruit-shells. The alkaloid content of the seeds ranges from 1.8 to 5.3 per cent. No quaternary bases are found in the seeds. Minor alkaloids present are vomicine (C_{22}H_{24}N_{2}O_{4}; m.p. 278-80^\circ), α-colubrine (C_{22}H_{24}O_{3}N_{2}; m.p. 184^\circ), β-colubrine (C_{22}H_{24}O_{3}N_{2}; m.p. 222^\circ), pseudostrychnine (C_{21}H_{22}O_{3}N_{2}; m.p. 266-68^\circ) and N-methyl sec.-pseudobrucine(C_{24}H_{28}O_{5}N_{2}). The glycoside loganin is also present. Pseudostrychnine is said to be nontoxic^{20}.

Strychnine, C_{21}H_{22}O_{2}N_{2}, crystallises in colourless, odourless prisms melting at 265^\circ, and having an intensely bitter taste, though very slightly soluble in water (1 in 7000). The hydrochloride crystallises in needles which are soluble in water, but less soluble in water acidified with hydrochloric acid.

Brucine, C_{23}H_{26}O_{4}N_{2}, is also crystalline and more soluble in water than strychnine (1 in 320); melting-point 178^\circ; is probably dimethoxystrychnine. Caffeotannic acid (chlorogenic acid) is also found in the leaves and seeds of Caffea arabica, Linne, and in other plants; exposed to the air in the presence of ammonia it turns green (viridic acid)^{19}.

**The chemical constituents present in different parts are as follows:**

Strychnine, Brucine, and vomicine (all parts); icajine and novacine (N-methyl-pseudobrucine) in all aerial parts; pseudobrucine, pseudostrychnine (also in stem-bark), (+)-mavacurine (first quarternary alkaloid encountered in Strychnos species; also in root), strychnine and isostrychnine (fruits, seeds, root-bark); the alkaloids of fruits and seeds are common; the components other than those above isolated from different parts are as follows: alpha and beta colubrines, N-methyl-sec-pseudo-β-colubrine, isobrucine, N-oxides of brucine, isobrucine, isostrychnine and pseudostrychnine; methoxy strychnine, 4-hydroxy strychnine, 2-hydroxy-3-methoxystrychnine: diaboline; cantheyine; loganin (also in seeds), deoxyloganin, loganic acid, ketologanin, secologanin, salidroside and its xylose derivative, cuchiloside (fruits); 3-methoxy icajine, kaempferol, quercetin and its 3-O’-methylether; p-hydroxy- and 2-hydroxy-4-methoxy-benzoic acids; sinapic, syringic and vanillic acids (leaves); 4-hydroxy-3-methoxy-strychnine, normacusine B, protostrychnine (root-bark); 15-hydroxystrychnine also isolated from the plant^{21}.

Nux-vomica seeds, in addition to the various alkaloids, contain 4.2 per cent of an oleic-rich fat with the following constants: acid val., 9.1; iodine
val., 71.9; sap. val., 330.4; and unsapon. matter, 11.5%. The composition of the fatty acids is as follows: myristic, 0.9; palmitic, 12.6; stearic, 6.6; arachidic, 7.0; behenic, 1.7; oleic, 62.0; and linoleic, 9.2%. The unsaponifiable matter contains a-amyrin and cycloartenol (mp. 99°C). The fat is externally used in rheumatism, and could also be tried in soap-making. The seeds yield a dye.

Seasonal variations of strychnine and brucine in different vegetative parts of *Strychnos nux-vomica* were determined by HPLC. Root bark and stem bark are rich in these two alkaloids. Root wood, stem wood, and twigs are poor sources of strychnine and brucine. In the stem bark, stem wood, and leaves, the alkaloids gradually decrease in amount up to December (winter). In the root bark, there is a tendency towards a gradual increase in these alkaloids up to December. In a previous study twenty-two identified alkaloids have been isolated from the root bark and leaves of a Sri Lankan *Strychnos* species supplied as *S. nux-vomica*.

**Histo-chemical Test**:

1. **Strychine Test**: To a thick section of endosperm add ammonium vanadate and sulphuric acid. Middle portion of endosperm is stained purple because of strychnine.
2. Strychnine also gives violet color with potassium dichromate and conc. Sulphuric acid.
3. **Brucine Test**: To a thick-section add concentrated nitric acid. Outer part of endosperm is stained yellow to orange because of brucine.
4. **Hemicellulose Test**: To a thick section add iodine and sulphuric acid. The cell walls are stained blue.
5. **Organoleptic Test**: Put a little drug at the tip of the tongue. It tastes bitter.
6. **Biological Test**: 2 µg (2/1000 mg.) of strychnine if injected into a tail of a two-week old mouse will cause palpitation of the tail.

**Pharmacological properties of Kupeelu**:

*Kupeelu* has been attributed different pharmacological properties. Its seeds possess Tikta, Katu and Kashaya *Rasa*; Laghu, Ruksha, Teekshna *Guna*; Ushna *Virya* and *Katu Vipaka*.

According to some author, its unripe fruits are *Sheeta Virya* and the ripe fruits having *Guru & Vishada Guna* with *Madhura Vipaka*.
Various synonyms and *rasa panchaka* of *Kupeelu* as mentioned in different *Nighantus* are presented below:

**Table 2.6: Synonyms & Rasa panchaka of Kupeelu**

<table>
<thead>
<tr>
<th>Name of the Nighantu</th>
<th>Name of the drug</th>
<th>Synonyms</th>
<th>Rasa</th>
<th>Guna</th>
<th>Veerya</th>
<th>Vipaka</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodhala N. (12th A.D)</td>
<td>Vishatindu</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Abhidhana Ratnamala (Sudrasta N. (12-13th A.D)</td>
<td>Kakatinduka</td>
<td><em>Kupeelu</em> Kakapeelu Kakenduka</td>
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<td></td>
</tr>
<tr>
<td>Kaiadeva N. (15th A.D)</td>
<td>Kakatinduka</td>
<td>Markatatinduka Kakenduka <em>Kupeelu</em> Kakapilu Suhulatinduka Tinduki Bisphurjani Bikarani</td>
<td>Tikta</td>
<td>Laghu</td>
<td>Sheetala</td>
<td>Katu</td>
<td>Ousadhi varga Amradiphala varga</td>
</tr>
<tr>
<td>Bhavaprakash N. (16th A.D)</td>
<td><em>Kupeelu</em></td>
<td>Kulaka Kakatinduka Kakapiluka Kakendu Vishatindu Markatatinduka</td>
<td>Tikta</td>
<td>Laghu</td>
<td>Sheetala</td>
<td>Katu</td>
<td>Amradiphala varga</td>
</tr>
<tr>
<td>Raj N. (16th A.D)</td>
<td>Tinduka</td>
<td>Kakapilu Kakanda Kakatinduka Kasphurja Kakendu Kakaha Kakavijaka</td>
<td>Kasaya Amla Ripen fruit-Madhura</td>
<td>Guru</td>
<td>Amradi varga</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Priya N. (19th A.D)</td>
<td>Karsakara</td>
<td></td>
<td>Katu Tikta</td>
<td>Sara</td>
<td>Ushna</td>
<td>Shatapuspadi varga/197</td>
<td></td>
</tr>
<tr>
<td>Saraswati N. (19th A.D)</td>
<td>Vishamusti</td>
<td>Swetamusti Keshamusti Karkoti Vishahva</td>
<td>Tikta</td>
<td>Laghu</td>
<td>Sheetala</td>
<td>Katu</td>
<td>---</td>
</tr>
<tr>
<td>Shankar N. (19th A.D)</td>
<td><em>Kupeelu</em></td>
<td>Unripe fruit-Laghu Unripe fruit-Sheeta Ripe fruit-Guru</td>
<td>Ripe fruit-Madhura</td>
<td>---</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nighantu Adarsha(19th A.D)</td>
<td>Vishatinduka</td>
<td>Nagavallidala</td>
<td>Katu Tikta</td>
<td>Vishatindukadi varga,</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Therapeutic uses of different parts of the plant:

After going through a thorough review of different Ayurvedic as well as modern text books it has been revealed that different parts of this plant is having a wide spectrum of activities in a number of diseases. Some of the reported therapeutic uses of the different parts of Kupeelu are mentioned below:

- **Fruit:** The unripe fruits aggravate vata, causes constipation while the ripe fruits alleviate all three doshas, used in urinary disorders and diseases due to impure blood. For the treatment of paralytic affection of paws and foot, its ripe fruit pulp is also used.

- **Seeds:** Ayurvedic literatures highlighted the pharmacological actions of Kupeelu seeds such as Shothahara, Putihara, Vedanasthapana, Uttejaka, Nadibalya, Deepana, Pachana, Grahi, Shoolaprashamana, Hridayottejaka, Kaphaghna, Kasahara, Vajikarana, Balva,, Kushtaghna, Kandughna, Swedapanayana etc. Shodhita Kupeelu seeds are specially recommended during senility as Rasayana since it’s seeds are considered to be potent drug in countering old age problems on account of growing age in old persons facing degeneration and natural decay of cells and tissues (dhatuksaya) in senility (vardhakya). Seeds are used as a tonic, antidiarrhoeal, antidysenteric, antispasmodic, emetic, febrifuge, stimulant and tonic. Generally used in cholera, diabetes, emotional disorders, hysteria, epilepsy, intermittent fevers, gout, rheumatism, hydrophobia, impotence, insomnia, paralytic and neuralgic affections, prolapsed rectum, antidote to alcoholism etc. Seeds are also beneficial in general exhaustion, opium poisoning, retention or nocturnal incontinence of urine, spermatorrhoea, given in combination with carminatives and antacids in dyspepsia and vomiting. Nux-vomica seeds produce a sort of intoxication, for which they are habitually taken by some natives as an aphrodisiac by cutting down into small pieces and chewed with a packet of betel leaf. The seeds also yield oil, and a dye; the dye gives a brown color to cotton fabrics. Oil, obtained by heating the fresh seeds, is used externally in rheumatism. The seeds are furthermore used in the distillation of country spirits to make them more potent.

- **Leaves:** The leaves when applied as poultice, promote healthy action in sloughing wounds or ulcers, more especially in those cases when maggots have formed. It arrests any further
formation of them, and those in the deeper parts perish immediately when the poultice is applied¹¹.

- **Bark**: Juice of the stem bark is given in cholera and acute dysentery¹⁴.
- **Wood**: The juice of the fresh wood is reported to be a popular remedy for dysentery, fever, cholera and dyspepsia¹⁵.
- **Root**: Root bark is bitter and useful in cholera, intermittent fevers⁶. In Ceylon, the roots are ground with water and applied externally for the management of snake bite. In Cambodia, the seed is used as an emetic. Internally, an infusion of the bark is given in epilepsy; externally, the bark is used in the treatment of ulcers, atonic and leprotics³¹. Powder of *Shodhita Kupeelu* seeds are used generally in a dose of 60-250 mg in different diseased conditions⁶. Few of its specific indications are given below in combination with other drugs,

- **Jwār (Fever)**: Purified *Kupeelu* seeds with equal quantity of *maricha* (fruit of *Piper nigrum*) powder is rubbed with decoction of *indrayava* (seed of *Holarrhena antidysenterica*) and made into pills. It removes constipation and fever due to vitiation of *vāta*³².
- **Agnimandya (Loss of digestive power)**: *Kupeelu, navasadara* (*NH₄Cl*) and *hingu* (Asafoetida) are rubbed with sour (lemon juice) and made into pills of the size of bengal gram. It alleviates loss of digestive power and other disorders caused by the same³³.
- **Visucika (Cholera)**: *Kupeelu, hiugu and navasadara* each is fried on fire and all mixed together. It is rubbed with water and made into pills that control *visucika*³⁴.

**Important compound formulations**

- **Ayurveda**: Classical pharmacopoeias of Ayurveda prescribe certain compound formulations containing *Kupeelu* as an ingredient for the management of different disease conditions. Some of the frequently practiced compound formulations are as follows;
Table 2.7: Kupeelu as an ingredient of certain compound formulations along with its therapeutic indication

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Name of the drug</th>
<th>Rogadhikara</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Agnitundi vati</td>
<td>Agnimandyadi rogadhikara</td>
</tr>
<tr>
<td>2.</td>
<td>Shulaharana yoga</td>
<td>Shula rogadhikara</td>
</tr>
<tr>
<td>3.</td>
<td>Kupeelubeejadi kwatha</td>
<td>Lasikamehadhikara</td>
</tr>
<tr>
<td>4.</td>
<td>Krimimudgara rasa</td>
<td>Krimi rogadhikara</td>
</tr>
<tr>
<td>5.</td>
<td>Krimighatini gutika</td>
<td>Krimi rogadhikara</td>
</tr>
<tr>
<td>6.</td>
<td>Kitmarda rasa</td>
<td>Krimi rogadhikara</td>
</tr>
<tr>
<td>7.</td>
<td>Maha vishagarbha tailam</td>
<td>Vatavyadhyadikara</td>
</tr>
<tr>
<td>8.</td>
<td>Vishatindukadi tailam</td>
<td>Vataraktadhikara</td>
</tr>
<tr>
<td>9.</td>
<td>Vishatindukadi lepa</td>
<td>Upadamsaroga chikitsa prakaranam</td>
</tr>
<tr>
<td>10.</td>
<td>Navajivana rasa</td>
<td>Used as Rasayana</td>
</tr>
<tr>
<td>11.</td>
<td>Ekangaveer rasa</td>
<td>Vatavyadhyadikara</td>
</tr>
<tr>
<td>12.</td>
<td>Khanjanikari rasa</td>
<td>Khanjanika chiktsa prakaranam</td>
</tr>
</tbody>
</table>

❖ Unani:

Certain compound formulations containing Kupeelu are also well practiced in Unani System of Medicine. Among them, few important formulations are reported here,-

❖ **Hab khas** - This formulation used as (i) Nervine tonic, (ii) Aphrodisiac (iii) Cerebral and cardiac tonic, (iv) Stomachic (v) Agent for enhancing blood circulation (vi) Appetizing (vii) Tonic for old persons. Young persons are advised to use this medicine during the winters only.

❖ **Roghan kuchla** - This medicated oil used externally as Anti-rheumatic and antiarthritic preparation.

❖ **Majun izaraqi** - This formulation used as (i) Nervine tonic (ii) Useful in facial paralysis and paralysis. (iii) Antirheumatic. (iv) Stomachic (v) especially useful as a prophylactic for old persons, in cold weather.

❖ **Uses in Homeopathic medicine:**

Nux-vomica is one of the most frequently used homeopathic remedies, especially for acute conditions. Homeopaths prescribe this medicine for hangovers, back
pain, digestive problems, headaches, allergies, colds, flu, emotional stress, constipation, menstrual problems, and hemorrhoids.

The remedy is primarily indicated in ailments that are caused by abuse of narcotic drugs, alcohol, coffee, or tobacco, overindulgence in rich food and drink, and mental strain brought about by too much work. Nux-vomica patients are typically thin and workaholics who wear themselves down by working late, eating heavily, neglecting exercise, and overindulging in mood-altering foods such as coffee or alcohol. They are hurried and have an overactive mind, even at night, which is why they often suffer from insomnia. Their digestive systems are weakened by the rich, spicy, stimulating food and drink they crave and consume. As such, they suffer from diarrhea, constipation, hemorrhoids, digestive problems, and an overall weakened vitality. Nux-vomica patients catch colds easily and are hypersensitive to light, touch, noise, smells, and the effect of medicines. They are also sensitive to the cold and dislike cold weather immensely. Patients may be tidy and fastidious.

Children who require Nux-vomica are mischievous, stubborn, sensitive, and easily offended. They like to get their own way and become difficult if they do not. Mentally, Nux-vomica patients are irritable, impatient, jealous, suspicious, malicious, never satisfied or content, anxious, argumentative, critical, stubborn, and rude. They have a violent temper and are often suicidal. They also have a difficult time concentrating and their memory often fails them.

**Specific Indications**

- The headaches indicative of Nux-vomica are concentrated in the forehead (over the eyes) or back of the head. The pains are sharp, bursting pains and the scalp may feel sore and bruised. Constipation and other gastric symptoms are often present. This headache is typical of a hangover headache. It may be caused by alcohol, cold wind, damp weather, insomnia, mental strain, or overeating. The headache is aggravated by eating, cold air, moving the eyes, or shaking the head. Stillness and quiet relieves the headache, as does pressure, rising in the morning, or lying in bed at night.

- The Nux-vomica cold occurs as a result of exposure to cold, dry wind or from indigestion. Colds generally settle in the nose, throat, chest, and ears. Colds are accompanied by a hoarse voice, headache, sore throat, sneezing, chills, a tickling
cough, fever, and bone pains. The voice sounds nasal from the stuffy nose, which is plugged in open air and at night. The nose emits a watery discharge during the day and in a warm room. The patient has a desire for cold water and the eyes are watery. Colds are better from fresh air and worse upon rising in the morning and after eating. The earache that accompanies the cold is made worse by swallowing. The ear is itchy and painful.

- Flus and hay fever both exhibit the Nux-vomica cold symptoms. The flu may be accompanied by an aching, sore sensation. The hay fever may last throughout the year.

- Digestive complaints are brought about by overindulging in rich, spicy foods, alcohol, tobacco, or coffee. Disturbances include diarrhea, constipation, and abdominal pains and may be accompanied by nausea, vomiting, and indigestion. The patient feels bloated and full. The abdomen is painful and cramped and the patient may be doubled over. He may strain to urinate, defecate, or vomit.

Recent Research in Homeopathy:
Because Nux-vomica is prescribed so frequently in homeopathic treatment, it has figured in several different areas of research into homeopathic remedies:

- **Gastritis**: Studies were done as early as 1966 comparing patients who received Nux-vomica 4X for gastritis compared with a group that received a placebo. While one study showed that twice as many patients responded to the homeopathic remedy as responded to the placebo, other studies found no difference in the rate of response.

- **Alcoholism**: A study published in 2001 reported that Nux-vomica reduced alcohol intake in rats that had been conditioned to crave alcohol. The rise in the number of animal studies using Nux-vomica, however, has led to some debate among homeopaths regarding the morality of experimentation on animals.

- **Abnormal psychology**: The compilation of the Constitutional Type Questionnaire, or CTQ, as a homeopathic psychological research instrument has led to studies comparing its findings to those of mainstream psychological measures. One group of researchers reported that subjects who fit the Nux-vomica profile on the CTQ scored high in neurotic traits as well as high in chemical intolerance.
Preparations\textsuperscript{49}: 

The seeds of the tree are ground until powdered then mixed with milk sugar. This solution is then diluted and succussed to create the final preparation. Nux-vomica is available at health food and drug stores in various potencies in the form of tinctures, tablets, and pellets.

Pharmacology\textsuperscript{50}:

- **Effects on Central nervous system:**
  
  Nux-vomica is known to have its effect on ganglionic cells of the motor tract of the spinal cord. As per some of the workers, it is also having mild action on the sensory tract and increases nerve conduction. Strychnine, brucine and Nux-vomica are having similar actions on central nervous system. Strychnine is potent and is having quick action than brucine and brucine is potent than Nux-vomica. Therapeutic doses of strychnine or Nux-vomica do not have any action on temperature. Strychnine has its convulsing action due to interference with the postsynaptic inhibition that is mediated by glycine. Glycine is an inhibitory transmitter to motor neurons and inter neurons in the spinal cord. Strychnine acts as selective competitive antagonist to block the inhibitory effects of glycine at the glycine receptor.

- **Effects on respiratory system:**
  
  Strychnine when used in maximum dosage is known to increase the respiratory rate. It is also known to increase the capacity of lungs. It is used as respiratory stimulus, which acts through the centric center of respiration.

- **Effects on cardiovascular system:**
  
  Strychnine increases the force, volume and the rate of pulse. It is also known to increase the arterial pressure. In toxic doses, tachycardia may develop and blood pressure rises.

- **Effects on gastrointestinal system:**
  
  Nux-vomica is largely used in disorder of gastro intestinal system. It is also used in hepatic disorders. It is used in atony and relaxation of stomach and bowels. Nux-vomica is known to reduce spasmodic conditions of bowels and is used successfully in habitual constipation. In children it is used in intestinal
colic, chronic non-specific diarrhoea and simple atonic in digestion. In one of the studies, Nux-vomica is said to be useful in severe gastritis.

- **Miscellaneous actions:**
  Nux-vomica is used as an aphrodisiac medicine as it is largely used in erectile dysfunction. In small doses, it acts as a central nervous system stimulant and increases potency and libido. Nux-vomica is used in urinal incontinence in children and aged in the paralyzed sphincter.

**Pharmacokinetics:**

Nux-vomica is rapidly absorbed from gastrointestinal tract while strychnine is absorbed from G.I tract, nasal passage or parenterally injection site. Strychnine is found in plasma RBC, bile, liver and tissue of G.I tract. The half-life of strychnine is 10 hrs.

**Metabolism:**

Strychnine is mainly metabolized in liver. It is metabolized by enzyme of hepatic microsomes. Strychnine is excreted from urine without any change. 10-20 % of strychnine is eliminated through urine in first 24hrs. The excretion is inversely proportional to the dose ingested. Strychnine is totally excreted within 48 to 72 hrs.

**Toxicity:**

In toxic dose, strychnine produces restlessness and suffocation. There after tremors are developed all over the body. Convulsions are developed and all the muscles are affected at the same time. Poisthotonous i.e. the body resting on head and healing takes place. The patient is very much excited and very small stimulus can aggravate the symptoms. In the period of convulsions patient is completely conscious and depressed. Convulsions occur intermittently. The frequency and intensity of the convulsions depends upon the sensory stimulus. If the patient is not treated properly patient may die due to respiratory arrest within 2-4 hrs. If the patient after the fatal dose survives for more than 12 hours, the prognosis is said to be good.
Some important experimental & clinical research works on Nux-vomica:

Following studie were carried out on nux-vomiva seeds to evaluate its activity clinically and also in different experimental models.

1. **Analgesic and anti-inflammatory activity of brucine and brucine N-oxide**

To understand the purpose of the traditional processing method of the seeds of *Strychnos nux-vomica* L. (Loganiaceae) as well as analgesic and anti-inflammatory activities of brucine and brucine N-oxide extracted from this medicinal plant, various pain and inflammatory models were employed in this study to investigate their pharmacological profiles. Both brucine and brucine N-oxide revealed significant protective effects against thermic and chemical stimuli in hot-plate test and writhing test. The results suggest that central and peripheral mechanism are involved in the pain modulation and anti-inflammation effects of brucine and brucine N-oxide, biochemical mechanisms of brucine and brucine N-oxide are different even though they are similar in chemical structure.

2. **The apoptotic effect of Brucine on human hepatoma cells**

In an attempt to dissect the mechanism of *Strychnos nux-vomica*, a commonly used Chinese folk medicine in the therapy of liver cancer, the cytotoxic effects of four alkaloids in *Strychnos nux-vomica*, brucine, brucine N-oxide, strychnine, and isostrychnine, on human hepatoma cells (HepG2) were screened by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrasolium bromide (MTT) assay. Brucine, among the four alkaloids, exhibited the strongest toxic effect, the mechanism of which was found to cause HepG2 cell apoptosis, since brucine caused HepG2 cell shrinkage, the formation of apoptotic bodies, DNA fragmentation, cell cycle arrest, as well as phosphatidylserine externalization, all of which are typical characteristics of apoptotic programmed cell death.

3. **Antioxidant properties of the purified Strychnos Nux-vomica L. seeds**

This report investigates the antioxidant properties of the purified *Strychnos nux-vomica* L. seed extract for protection against non-enzymatic formation of lipid peroxides and on reduced glutathione (GSH) levels in rat liver homogenate. Results were compared with the natural antioxidant vitamin E. For the first time
it could be reported that this drug protects against cumene hydroperoxide (CHP) induced lipid peroxidation in a dose dependent manner. It also inhibits the process of the lipid peroxidation, once induced. The drug significantly maintains the hepatic content of glutathione in a dose and time dependent manner, even in the presence of the above toxin (CHP). Thus it appears that S. nux-vomica is a potent antioxidant and the mechanism of action could be through the scavenging of free radicals.

4. **Anti-oxidative & Anti-inflammatory properties a polyherbal formulation containing *Strychnos nux-vomica* Linn.**

BHUX is a polyherbal formulation consisting of water-soluble fractions of five medicinal plants (*Commiphora mukul, Terminalia arjuna, Boswellia serrata, Semecarpus anacardium and Strychnos nux-vomica*). The present study was undertaken to evaluate its antioxidant and antiinflammatory effects. These studies suggest that BHUX is acting mainly at three levels, i.e., as a potent natural antioxidant, by reduction of key inflammatory mediators of arachidonic acid cascade and by preventing 15-LOX-mediated LDL oxidations, to prevent atherosclerosis.

5. **The anti-tumor effects of seeds of *Strychnos nux-vomica***

To screen the anti-tumor effects of the four alkaloids: brucine, strychnine, brucine N-oxide and isostrychnine from the seed of Strychnos nux-vomica, MTT assay was used to examine the growth inhibitory effects of these alkaloids on human hepatoma cell line (HepG2). Brucine, strychnine and isostrychnine revealed significant inhibitory effects against HepG2 cell proliferation, whereas brucine N-oxide didn't have such an effect. In addition, brucine caused HepG2 cell shrinkage, membrane blebbing, apoptotic body formation, all of which are typical characteristics of apoptotic programmed cell death.

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cell shrinkage, membrane blebbing, apoptotic body formation, all of which are typical characteristics of apoptotic programmed cell death. Therefore, this paper indicates that the major alkaloids present in the seed of *Strychnos nux-vomica* are effective against HepG2 cells proliferation, among which brucine proceed HepG2 cells death via apoptosis, probably through the participation of caspase-3 and cycloxygenase-2.

6. **Treatment of Reiter's disease with Nux-vomica**
   It was reported that the case of a 35 year-old man suffering from Reiter's disease did not respond to Lycopodium or Nux-vomica in medium dilutions, but did respond to Nux-vomica in very high potency.

7. **Effects of strychnine on nicotinic responses**
   In this study, evidence is provided that strychnine, a competitive antagonist at glycine-gated Cl⁻ channels, is also a potent competitive antagonist at native α-7-containing, α-bungarotoxin-sensitive nicotinic acetylcholine receptor (nAChRs). To address the effects of strychnine on two types of nicotinic responses, the whole-cell mode of the patch-clamp technique was applied to rat hippocampal neurons in culture.

8. **Cytoprotective action of strychnine in renal proximal tubule**
   Glycine-induced cytoprotection of renal proximal tubules exposed to chemical- or hypoxic/anoxic-induced cell death is shared by a few amino acid agonists of the neuronal strychnine-sensitive glycine receptor. The goal of this study was to determine if antagonists of the strychnine-sensitive glycine receptor attenuated the cytoprotective effects of glycine. Strychnine did not antagonize the cytoprotective effects of glycine in proximal tubules exposed to antimycin A. In contrast, strychnine was cytoprotective, was equipotent as glycine (EC₅₀=0.4 mM), and the combination of strychnine and glycine was additive. Likewise, bicuculline and norharmane were cytoprotective but 20–50% less potent than glycine. These results suggest that glycine and strychnine act at a common site to produce proximal tubule cytoprotection, but this site does not share the same potency and agonist/antagonist properties as the neuronal strychnine-sensitive glycine receptor.
9. The mechanism of cytoprotective action of strychnine and glycine

Previous studies have demonstrated that strychnine mimics the cytoprotective effects of glycine and that strychnine binds specifically to renal proximal tubules (RPT) at cytoprotective concentrations. The goal of this study was to determine a mechanism by which strychnine and glycine are cytoprotective. Antimycin A (0.1 μM) caused chloride influx subsequent to mitochondrial inhibition and prior to the release of lactate dehydrogenase (LDH) activity (a marker of cell death/lysis). The addition of strychnine or glycine prevented the chloride influx and LDH release. The chloride channel inhibitors ethacrynic acid, furosemide, anthracene-9-carboxylic acid, DIDS, and SITS decreased LDH release in RPT exposed to antimycin A with a rank order of potency of DIDS > ethacrynic acid=furosemide=anthracene-9-carboxylic acid > SITS. These data, in conjunction with the preceding paper, indicate a critical role for chloride influx in cell death/lysis; support the existence of a novel strychnine binding site on the plasma membrane of RPT that is coupled to a chloride channel; and suggest that glycine and strychnine are cytoprotective through their inhibition of chloride influx.

10. Renal cytoprotective action of Strychnine and Glycine in the late phase of necrotic cell injury

The aims of this study were to determine whether the cytoprotective properties of strychnine applied to various types of nephrotoxicants and to examine the temporal aspects of the cytoprotection of glycine and strychnine. Tubular release of LDH activity was used as a marker of cell death. Glycine (2 mM) or strychnine (1 mM) added 5 min prior to the toxicant decreased LDH release in rabbit RPT suspensions exposed to 25 μM tetrafluoroethyl-L-cysteine (TFEC), 10 μM HgCl₂, 0.5 mM t-butyl hydroperoxide (TBHP), or 0.2 mM bromohydroquinone (BHQ) for 4 hr, or 2 mM sodium cyanide (NaCN) for 2 hr. The results demonstrate that strychnine and glycine protect RPT from a variety of diverse nephrotoxicants, strychnine and glycine do not need to be present at the time of toxic insult, strychnine and glycine cytoprotection is reversible, and strychnine and glycine act in the late phase of necrotic cell injury.

11. Antidiarrhoeal activity of Strychnos nux-vomica root bark

Shodhana of Kupeelu

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A study was undertaken to evaluate the effect of aqueous and methanolic plant extracts of *Acorus calamus* rhizome, *Pongamia glabra* leaves, *Aegle marmelos* unripe fruit and *Strychnos nux-vomica* root bark for their antidiarrhoeal potential against castor-oil induced diarrhoea in mice. The methanolic plant extracts were more effective than aqueous plant extracts against castor-oil induced diarrhoea. The methanolic plant extracts significantly reduced induction time of diarrhoea and total weight of the faeces. The result obtained establishes the efficacy of these plant extracts as antidiarrhoeal agents.

12. Antisnake venom activity of ethanolic seed extract of *Strychnos nux-vomica* Linn.\(^ {62}\)

The whole seed extract of *S. Nux-vomica* (in low doses) effectively neutralized *Daboia russelii* venom induced lethal, haemorrhage, defibrinogenating, PLA2 enzyme activity and *Naja kaouthia* venom induced lethal, cardiotoxic, neurotoxic, PLA2 enzyme activity. The seed extract potentiated polyvalent snake venom antiserum action in experimental animals. An active compound (SNVNF) was isolated and purified by thin layer chromatography and silica gel column chromatography, which effectively antagonised *D. russelii* venom induced lethal, haemorrhagic, defibrinogenating, oedema, PLA2 enzyme activity and *N. kaouthia* induced lethal, cardiotoxic, neurotoxic, PLA, enzyme activity. Polyvalent snake venom antiserum action was significantly potentiated by the active compound. Spectral studies revealed it to be a small, straight chain compound containing methyl and amide radicals. Detailed structure elucidation of the compound (SNVNF) is warranted before its clinical trials as a snake venom antagonist.

**Signs and symptoms of nux-vomica poisoning.**\(^ {63-64}\)

- If the seeds are swallowed uncrushed, the seeds of Nux-vomica have no poisonous action as they are not dissolved (Pulverized) in gastrointestinal tract and are passed in the faeces as a whole.
- When the crushed seeds are given the symptoms are delayed for an hour or more.
- If the alkaloid is given the symptoms occur very rapidly.
During convulsions the face is cyanosed and has anxious looks, eyes staring, eyeballs prominent and pupils are dilated.

The duration of convulsions varies from half to two minutes.

Striking feature of strychnos poisoning is that patient remains conscious till the end and mind clear.

Reflex excitability is so great that even the slightest sensory stimulus induces symmetrical extensor thrusts and sustained tonic convulsions later.

Vomiting is usually absent and if sets in, it remains till death.

Prognosis is assessed basing on the duration and frequency of convulsions.

In fatal cases, death occurs from asphyxia or any subsequent attack or from medullary paralysis.

In cases ending in recovery, the convulsions become shorter, milder and the period of intermission is much longer.

Post-mortem appearances:

They are not characteristic.

Rigor Mortis appears early but is not necessarily prolonged.

Haemorrhges are sometimes found under the peritoneal coat of the stomach.

The lungs, liver, kidneys, brain and spinal cord are congested.

Differential diagnosis:

Dhanustabha (Tetanus)

Apasmara (Epilepsy)

Yoshapasmara (Hysteria)

Many of the strychnine poisoning resembles the clinical features of tetanus and hence strychnine poisoning has to be diagnosed from tetanus. The following are the some of the distinguishing points between strychnine poisoning and tetanus.

Table 2.8: Differential diagnosis between Strychnine poisoning & Tetanus:

<table>
<thead>
<tr>
<th>Strychnine Poisoning</th>
<th>Tetanus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Circumstantial evidence</td>
<td>1. History of injury</td>
</tr>
<tr>
<td>2. Sudden onset</td>
<td>2. Gradual onset</td>
</tr>
<tr>
<td>3. All the muscles are affected at a time</td>
<td>3. Only group of muscles are affected at a time</td>
</tr>
</tbody>
</table>
4. Trismus is the late feature
   4. Usually begins with trismus

5. Muscular relaxation during the interval of convulsions
   5. Sustained rigidity even in between the convulsions

6. Death results in few hours (4-6)
   6. Death results within few hours and may be delayed for several days

7. Recovery chances are great
   7. Recovery chances are less

8. Chemical analysis reveal the poison
   8. Chemical analysis reveals nothing

9. Rapid progress
   9. Slow progress

**Medico Legal Importance:**
- In India, it is used as an aphrodisiac
- Seeds are used for killing cattle and as arrow poison
- Accidental death is more common due to an over dose of strychnos containing medicinal preparation.
- Suicide is rare because of painful death
- It is one of the most deadly poisons
- Sometimes used for homicide in the form of alkaloid (Rare in India)

**Post Mortem Findings:**
- Rapid and persistent rigor mortism
- Livid patches may appear on the body
- Body temperature shows slightly raised levels for a while after death instead of usual fall (Post mortem caloricity)
- Mucus membrane of stomach and duodenum shows patches of ecchymosis or congestion
- Liver and kidney are usually congested
- Heart is empty and contracted
- Lungs are congested
- Brain and upper part of the spinal cord are congested
- As strychnine resist putrefaction, it can be detected by chemical analysis long after death.
- Signs of Asphyxia
- Apart from the routine viscera, heart and spinal cord are to be preserved.
Management:

- The First step is the effective control of convulsions.
- The patient should be kept in a dark room, free from noise and disturbance.
- Stomachs wash with warm water and dilute solution of potassium permanganate.
- Acidifying the urine will increase excretion of strychnine.
- Treat the symptoms on general lines.
- Convulsions may be controlled with diazepam IV slowly.

Contraindication:

Nux-vomica is contraindicated in pregnancy and breast-feeding. It is contraindicated in contact dermatitis\(^6^5\).

Drug interactions:

No drug interactions are reported for Nux-vomica\(^6^5\).

Dosage:

The therapeutic dose of Nux-vomica is 60 mg - 250 mg\(^8^6\). The smallest dose which is known to produce death in humans is 30 grains i.e. equal to one seed of Nux-vomica. The minimal oral dose of strychnine in adult is 30 - 120 mg\(^6^5\). The lethal dose in children is 15 mg. If strychnine is given parenterally, the lethal dose is again lowered\(^6^5\).

Table 2.9: Strychnine toxicity (LD\(_{50}\) values)\(^6^6\)

<table>
<thead>
<tr>
<th>Animal</th>
<th>mg/kg body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rabbit</td>
<td>0.6</td>
</tr>
<tr>
<td>Dog</td>
<td>1</td>
</tr>
<tr>
<td>Rat</td>
<td>5</td>
</tr>
<tr>
<td>Pigeon</td>
<td>21</td>
</tr>
<tr>
<td>Possum</td>
<td>30</td>
</tr>
<tr>
<td>Human</td>
<td>1-30</td>
</tr>
</tbody>
</table>

Note: LD\(_{50}\) values represent the lethal dose for 50% of a population.

Purificatory procedures of Nux-vomica through different media:

The seeds of *Strychnos nux-vomica* are popularly used in therapeutics dates from ancient time. Being extremely toxic, the raw seeds are forbidden and must be processed before clinical use. In Ayurvedic & Unani system of medicine various processes of detoxification of Nux-vomica have been described using some specific medias either alone or in combination with other medias.
1. Dipping in *Gomutra* (cow urine)
2. Boiling in *Godugdha* (cow milk)
3. Dipping in *Gomutra* followed by boiling in *Go dugdha*
4. Frying in *Goghrita* (cow ghee)
5. Dipping in *Gomutra* then boiling in *Godugdha* followed by frying in *Goghrita*
6. Keeping in *Gomaya* (cow dung)
7. Dipping in *Kanji* (sour gruel)
8. Frying in *Eranda taila* (castor oil)
9. Dipping in *Adraka swarasa* (ginger juice)
10. Boiling in *Multani mitti* (soil of Multan)

Some previous research works on processed seeds of Nux-vomica:

1. Analysis of strychnine from detoxified *Strychnos nux-vomica* [corrected] seeds using liquid chromatography-electrospray mass spectrometry

*Strychno nux-vomica* seeds were detoxified using traditional methods described in the literature (Chung and Shin, 1989). The *Strychno nux-vomica* seeds (10 g) were roasted with sea sands (10 g) until the seeds became dark yellow. Then, these seeds were boiled in water for 10 min and then dried. The dried materials were parched with sesame oil turning the seeds to a pale yellow color.

This study resulted in finding the content of strychnine in detoxified seeds to be one tenth of unprocessed *Strychnos nux-vomica* [corrected] seeds.

2. Ayurvedic processed seeds of *nux-vomica*: Neuropharmacological and chemical evaluation

The effect of detoxification on *Strychnos nux-vomica* seeds by traditional processing with aloe and ginger juices, by frying in cow ghee, and by boiling in cow milk was investigated. The seeds processed in milk (D) showed the lowest strychnine content in the cotyledons, exhibited marked inhibition of PTZ induced convulsions and maximal potentiation of hypnosis, and were the safest (LD₅₀).

3. Changes in alkaloid composition of the seeds of *Strychnos nux-vomica* on traditional drug-processing

In the course of this study on the drug-processing of the seeds of *Strychnos nux-vomica* L. (Loganiaceae), the alkaloid composition of the heat-treated seeds of S. nux-vomica was compared to that of the untreated seeds. On heat treatment, the contents of the major alkaloids such as strychnine and brucine declined.
significantly with increases in the amounts of isostrychnine, isobrucine, strychnine N-oxide and brucine N-oxide.

4. **Antinociceptive effects of crude alkaloids from the processed and unprocessed seeds of *Strychnos nux-vomica* in mice**

In the course of this study the antinociceptive effects of the crude alkaloid fractions (CAF) of Nux-vomica (the dried seeds of *Strychnos nux-vomica* L.) and the influences of various processing methods upon their antinociception in three analgesic tests in mice were examined. In the tail-pressure test, the CAF (0.01--1 micrograms/kg, i.p.) of Nux-vomica that was unprocessed or treated with sand-, licorice-, oil- or vinegar and sand-processing showed clear antinociception. The CAF (1 microgram/kg, i.p.) of vinegar-processed Nux-vomica showed antinociception, without effects at lower doses of 0.01 and 0.1 microgram/kg and those treated with urine- or urine and sand-processing were without effects at doses of 0.01--1 microgram/kg. Morphine (2 mg/kg, s.c.) showed short-lasting antinociception, without effects at a dose of 1 microgram/kg. In the hot-plate test, the CAF (100 microgram/kg, i.p.) of Nux-vomica having undergone sand-processing produced a significant antinociception, without effects at lower doses of 0.01 and 1 microgram/kg. The CAF (0.01--100 microgram/kg, i.p.) of Nux-vomica that was unprocessed or treated with oil- or vinegar and sand-processing and morphine (1 and 100 micrograms/kg, s.c.) were without effects. In the acetic acid-induced writhing test, the CAF (1 microgram/kg, i.p.) of Nux-vomica that was treated with sand-processing significantly inhibited the writhing behavior, while those of Nux-vomica that was unprocessed or treated with oil- or vinegar and sand-processing and morphine were without effects at a dose of 1 microgram/kg. The present results demonstrate the antinociceptive effects of the CAF of Nux-vomica and suggest that sand-processing is good for the analgesic potency of Nux-vomica. It is also suggested that the CAF of Nux-vomica has distinct antinociceptive potency, even after treatment with licorice-, oil-, vinegar and sand-processing.

5. **Cytotoxicities of alkaloids from processed and unprocessed seeds of *Strychnos nux-vomica***

The cytotoxicities of 6 crude Strychnos alkaloid fractions from the seeds of *Strychnos nux-vomica* unprocessed or processed with various traditional
processing methods were examined. The processing method with sand bath exhibited a wide safety margin compared with other traditional processing methods or no processing. The isomers of Strychnos alkaloids and their N-oxides showed much lower cytotoxicities among these alkaloids. Isobrucine N-oxide showed the lowest cytotoxicity. The contents of isomers and N-oxides of Strychnos alkaloids were the highest in the sand processing. It was concluded that processing of Nux-vomica plays a critical role in its toxicity.

6. **Role of milk in Shodhana (detoxification) with special reference to Nux-vomica**

This study showed presence of strychnine and brucine in milk after *Shodhana* of Nux-vomica.
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