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Review Article

CRITICAL ANALYSIS OF *SNUHI* - *EUPHORBIA NERIIFOLIA* (*UPAVISHA*- POISONOUS PLANT) AND ITS APPLICATION AS A THERAPEUTIC AID

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ABSTRACT

Traditional system of medicines has vast applications of poisonous plants; hence the knowledge about poisonous plant and its therapeutic effects becomes very essential to develop a new drug for the new diseases like Covid 19 and other diseases. Many research studies have showed that the poisonous medicinal plants are endowed with properties like Antidiabetic, Anticancer, Antibacterial, Antifungal, and Cytogenetic effect. This study focused on one such drug called *Snuhi* - Euphorbia Neriifolia, a *Upavisha* or a poisonous plant to evaluate its therapeutic effects, which would be helpful for the mankind after the proper *Shodhana* (purification), by conducting experimental studies, toxicity studies and thereby applied in various diseases for its therapeutic benefits and to relieve the sufferings of the patients.

INTRODUCTION

The emergence of more effective and consistent pharmaceutical agents began in the 1920s that led by analgesics such as aspirin, morphine, insulin and anti-infective agents including sulphonamides and penicillin. [1] Recently, the herb that had been used in China for over 2000 years named Qinghao was extracted for the antimalarial drug artemether. [2]

New therapies have a rich history of development that evolves quickly with societal trends and has an exciting future. An exponential increase in complex interactions between medical practitioners, pharmaceutical companies, governments and patients has been observed in the last century. [3]

Pharmaceutical industry has developed to a larger extent, so that more effective medicines are emerged improving the quality of life of those suffering from many diseases, such as corticosteroids that controlled inflammatory diseases, antihistamines for allergies, xanthines for asthma patients and effective medications for psychological illnesses. [4]

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In India since ancient times, several medicinal plants have been used to cure specific ailments. Mainly the indigenous systems of medicine, namely Ayurveda, Siddha, and Unani, have been in existence for several centuries. Some drugs of Ayurveda have already reached the market place approaching the modern diseases. [5]

According to the World Health Organization (WHO), 80% of the developing countries rely on traditional medicines, mostly plant drugs, for their primary health care needs. Even the modern pharmacopoeia consists of synthetic analogues built on prototype compounds isolated from plants and contains at least 25% drugs derived from plants. [6]

Many research studies have showed that the poisonous medicinal plants are endowed with properties like Antidiabetic, Anticancer, Antibacterial, Antifungal, and Cytogenetic effect.[6] Paracelsus; Father of Toxicology states that everything is poisonous, only the dose distinguishes them (Paracelsus 1493-1541). Likewise when a poisonous plant is used in lower concentration, it becomes a potential drug in treating diseases like diabetes, Cancer etc. [7] Ayurveda is a life science with an objective of long and healthy lifespan that focuses on both the treatment and prevention of the diseases. Ayurveda works with the principle of balancing the physical, psychological, emotional and

spiritual health using various medicines and treatment approaches involving herbs, minerals and metals. [8]

A vast description is available regarding the concept of *Mahavisha* and *Upavisha dravyas* that include various poisonous plants, like *Bhanga* (*Cannabis Sativa* linn) *Ahiphena* (*Papaver somnifera* linn), *Vatsnabha* (*Aconitus ferox*), *Kupilu* (*Strichnos nuxcomica* linn), *Dhatura* (*Dhatura metel* linn), and minerals like *Parada* (mercury) and Arsenic etc. *Shodhana* (purification) of *Vishadravya* is an important step and the procedure in the *Agada tantra* which makes the toxic drug useful for the therapeutic use. [9] In this study an effort has been made to study in detail one such drug called *Snuhi- Euphorbia Neriifolia*, a *Upavisha* or a poisonous plant and evaluate its therapeutic effects, where the new drugs or the new treatment and the approaches are very much required in the present era due to the emergence of new diseases with unknown sources.

Study of *Visha* and *Upavisha* in detail and application of the drugs both of plant and animal origin after the *Shodhana* is the main aim of the *Agada tantra* branch of Ayurvedic science. *Snuhi* is one among the *Upavishas*, a poisonous plant which is classified under various categories by different Acharyas based on their therapeutic properties. Acharya Charaka has included *Snuhi* under the *Tikshna Virechana dravyas*, whereas Acharya Sushruta included it in the *Shyamadi gana* and *Adhobhagahara dravya*. Acharya Vagbhata has dealt *Snuhi* in *Mushakadi gana* and in *Guduchyadi varga* of all the *Nighantus*. [10]

In Charaka samhitha, we find *Snuhi* in detail explained under the *Virechana Dravyas* in *Adhyaya* of *Kalpasthana*. It has two varieties as *Alpakantaka* and *Bahukantaka* with its twenty *Virechana* formulations. Among the two, *Bahukantaka snuhi* is considered as the best or *Sreshta* because of its drastic purgative action. *Ksheera* or Latex of *Snuhi* is one of the main ingredients in preparation of the *Ksharasutra* and has proved to be one of the best treatment options for *Bhagandara* (Fistula in ano). [11]

Rasatarangini also speaks *Snuhi* as one of the *Upavisha*. [12] *Snuhi* which is botanically identified as *Euphorbia Neriifolia* Linn., belongs to Euphorbiaceae family. [13] It is distributed in North West Himalaya, Peru, Burma, West Peninsula and is a large glabrous fleshy erect shrub or small tree reaching 20 ft or more. [14] Etymological derivation of drug *Snuhi* reflects it secretes milky white latex which is used as drastic purgative. [15] It is a well-known plant available throughout India with various vernacular names like Hiju (Assam), Mansasij, Hildaona (Bengali), Yale kalli (Kannad) and Ilaikalli in Tamil. [16]

Various researchers have conducted many number of studies on *Snuhi* and found to possess number of chemical constituents such as 12-Deoxy-4β-hydroxyphorbol-13-dodecanoate-20-acetate, euphol, euphorbol hexacosanoate, n-hexacosanol and 24-methylenecycloartenol isolated from bark; cycloartenol, 24-methylenecycloartenol, ingenol triacetate, euphorbol, 12-deoxy euphorbol-13,20-diacetate, delphinidin-3,5-diglucoside and tulipanin-3,5-diglucoside from its roots. [17] *Snuhi* is utilized with almost all of its parts and about 462 formulations involving *Snuhi* as the ingredient are described in Ayurvedic science and as a treatment for 62 different diseases. [18] In *Sudha kalpa Adhyaya* of *Kalpasthana*, Acharya Charaka has enumerated its twenty *Virechana* formulations. [19]

Apart from its traditional benefits in *Kustha*, *Udara*, *Shotha*, *Pandu*, *Gulma*, *Dushivisha* and *Visha chikitsa*, many in vitro and in vivo experimentations, *Snuhi* (*Euphorbia neriifolia* Linn.) extracts and isolates have been reported for its analgesic, anesthetic, anti-anxiety, anti-convulsant, anti-psychotic, anti-arthritis, anti-diabetic, anti- inflammatory, anti-diarrheal, anti-microbial, antioxidant, anti-ulcer, diuretic, hemolytic, immunomodulatory, pesticidal effect, radioprotective, wound healing property, cytotoxic and anti-carcinogenic.[20]

Description of *Snuhi- Euphorbia Neriifolia*

Snuhi (*Euphorbia neriifolia* Linn.) is commonly known as Indian Spurge tree. It is regarded as one of the *Upavisha* or the toxic plant characterized by presence of latex which exudes on breaking. It is available and found throughout the Deccan Peninsula of India. [21]

Botanical Name: *Euphorbia Neriifolia* Linn.

Family: Euphorbiaceae

Common Names: Sanskrit - *Vajri*, *Snuhi*, *Sudha*, *Samantadugdha*, *Snuk*, *Sehunda*, Hindi - *Sehunda*, *Thohar*, Marathi - *Nivdunga*, English - Common Milk Hedge.

Description: It is a Xerophytic, succulent, large, much branched shrub, erect, prickly, which grows up to 2-6 meters.

Properties

Ayurveda - *Sthavara Upavisha*, Modern Toxicology - Organic irritant poison

Gana: *Charaka - Virechana*, *Shatashodhanavruksha Sushruta - Adhobhagahara*,

***Rasa Panchaka*:**

Guna- *Laghu*, *Tikshna*, *Guru*
Rasa - *Katu*,
Veerya - *Ushna*
Vipaka - *Katu*

Doshaghnata - *Kaphavataghna*

Karma - *Vishaghna Bahya- Lekhana*, *Vedanasthapan Abhyantar-Raktashodhak*, *Shothahara*, *Twakdoshahara*, *Tikshnavirechak*, *Kaphanissarak Rogaghnata- Gulma*, *Udararoga*, *Yakrutplihavruddhi*, *Shotha*, *Kushtha*, *Vatarakta*, *Upadanhsa*, *Kasa*, *Shwas*, *Pratishyay*, *Dushivisha*, *Visha Prayojyanga- Moola*, *Kanda*, *Patra*, *Kshira*.

Active Principle: Euphol, Nerifoliol. [22]

Fatal Dose: Root Powder: 0.5-1g, Stem Juice: 5-10ml, Milky Latex: 125-50mg. [22]

Fatal Period: 12hrs. [22]

Cultivation and Propagation: *Euphorbia Nerifolia* is suited for any well drained soil in full sun and needs no maintenance; therefore it is an easy species to grow. Normally used as ornamental and for good landscaping smaller gardens, Euphorbias are more commonly sold as crests that tend to stay leafier and long. [10]

Actions and Uses

Snuhi plant is laxative, alexipharmic, appetizing, carminative, and useful in abdominal diseases, bronchitis, tumors and ulcers. Apart from its major part the latex, the other parts of *Snuhi* are also useful in Glandular swellings and its leaves are useful in tumors, abdominal swelling and inflammation.

Classification

Table 1: Classification of *Snuhi*

S.No	*Samhitha*	Classification
1.	Modern	Irritant organic vegetative poison [22]
2.	Ayurvedic	*Sthavara Upavisha varga.* [22]
3.	*Charaka-Samhita*	*Shodhanarthaprayukta Vruksha*[23] *Tikshanavirechana dravya* [23]
4.	*Sushruta-Samhita*	*Shyamadi gana* [24] *Adhobhagahara dravya* [25]
5.	*Ashtang-Hrudaya*	*Virechanakaraka dravya* [26] *Mushakadi gana* [26]
6.	*Dhanvantari-Nighantu*	*Guduchyadi varga* [27]
7.	*Shodhala-Nighantu*	*Guduchyadi varga* [28]
8.	*Madanpala-Nighantu*	*Abhayadi varga* [29]
9.	*Kaiyadeva-Nighantu*	*Aushadhi varga* [30]
10.	*Raja –Nighantu*	*Shalmalyadi varga* [31]
11.	*Bhavaprakasha-Nighantu*	*Guduchyadi varga*[32]
12.	*Shaligrama-Nighantu*	*Guduchyadi varga* [33]
13.	*Priya Nighantu*	*Shatapushpadi varga* [34]
14.	*Nighantu Adarsha*	*Aamalkyadi varga* [35]
15.	*Yogaratnakara*	*Upavisha* [36]
16.	*Rasaratnasamucchaya*	*Dughada-varga* [37]

Table 2: Chemical Constituents [38,39]

Parts of the plant	Chemical Constituents
Powdered plant, stem and leaves	Several triterpenoids like Glut-5-en-3$-ol, Glut 5(10)-en1-one, taraxerol and $-amyrin
Latex	Triterpene – nerifoliene, euphol, neriifoliol, neriifolene, euphorbon, resin, gum, caoutchouc, malate of calcium, euphol, monohydroxy triterpene, neriifoliol, taraxerol, beta- amyrion, glut-5-(10)-en-1-one, neriifolione, cycloartenol
Leaf	Friedelan-3, D: B- friedolan-5-(10)-en-1-one, taraxerol
Bark	Euphol, Euphorbol, hexacosanoate, n- hexacosanol, 12- deoxy 4-β- hydroxyphorbol-13-dodecanoate-20-acetate, pelargonin – 3, 5- diglucoside, 24-methylene cycloartenol, tulipanin-3, 5- diglucoside
Stem	Euphol, friedelan-3, D: B friedoolan-5(10)-en-1-one, glut-5(10)-en-1-one, taraxerol
Root	Alnus-5(10)-ene-1-one, anthocyanins, euphol, pururate dikinase, terpenes, 24-methylene cycloartenol, tulipanin-3, 5- diglucoside
Ethanolic extract of fresh root	Antiquorin

Chemical Composition

Euphol, Nerifoliol, taraxerol, neriifolione, flavonoids. [22]

Shodhana* of *Snuhi-Ksheera

According to Yogaratnakara, *Snuhi-Ksheera* is a purified one and as a result it doesn't require further purification. But *Rasa-tarangini* describes *Shodhana* that needs to be done by adding two *Palas* of *Chinchapatra* rasa to 2 *Pala Snuhi ksheera* and mixed well. This whole solution is dried in sun till it gets into the powder form and this dried powder of *Snuhi-Ksheera* is ready after purification and can be used in preparations. [40,41]

Therapeutic benefits

Various studies have shown that the drug *Snuhi* comprises multiple pharmacological properties such as Immuno-modulatory, Anti-Bacterial activity, Hepatoprotective activity, wound healing, Antiinflammatory, Analgesic, Antioxidant, Diuretic and Antipsychotic activity etc. [42-47]

Immuno-modulatory Activity

In the study of Kalpesh Gaur et al, oral administration of 70% v/v hydro-alcoholic extract of dried leaves of *Euphorbia neriifolia* at a dose of 400mg/kg/day of body weight in the healthy albino rats showed the Immuno-modulatory activity. This immnomodulatory activity was done by testing the survival rate of rats against abdominal sepsis caused by E. coli. The humoral immune responses were determined by haemaglutination antibody titre method and cellular immune responses were determined by footpad swelling method. Hematological parameters and phygocytic index was determined by carbon clearance method. The hydro-alcoholic extract of *E. neriifolia* possessing significant protection against E.coli induced abdominal sepsis, significant increase in total leucocyte count, differential leucocyte count and phygocytic index were determined. These results indicate that the hydro-alcoholic extract of dried leaves of *E. neriifolia* possess the immunomodulatory activity. [42,43]

Wound healing Activity

In one of the study, wound healing activity of aqueous extract of *E. neriifolia* was evaluated by producing a cutaneous surgical wound and treating it with the tropical application of 0.5% and 1% sterile aqueous solution of the aqueous extract of the latex of *E. neriifolia.* This study showed facilitated healing process evidenced by increase in tensile strength, epithelization, DNA content and angiogenesis which indicates the wound healing property of *E. neriifolia.* [44]

Anti-Bacterial activity

In the study of Kumar Swami et al, phytochemical and anti-microbial studies of leaf extract of E. neriifolia were evaluated. It involved the phytochemical analysis of leaf extracts of medicinal plant E. neriifolia and their antibacterial activities against bacterial isolates Staphylococcus aureus, Klebsllia pneumonia, E. coli, Proteus vulgaris, Pseudomonas fluroscens were investigated. The analysis revealed the presence of flavenoids, saponin, tannins, phlobatannins, cadenoids, phenol and terpenoids. The water and ethyl acetate extract exhibited very less activity and maximum activity was observed in choloroform extract against K. pneumonia (5mm). This research study supports the local use of the leaf of plant E. neriifolia for bacterial infections and wound healing property. [45]

Hepatoprotective activity

Hepatoprotective activity of saponin fraction isolated from leaf of *E. neriifolia* on CCl4 induced hepatotoxicity of rats was studied by *Papiya Bigoniya*. CCl4 (5mg/kg) is a hepatotoxic agent which induces per oxidative degeneration of membrane lipids causing hypo perfusion of membrane. It was observed that the hepatic glutathione and SOD decreased whereas SGPT, SGOT, ALP increased in blood. This hepato-protection activity was compared with silymerin a well-known standards hepatoprotectants and they found that *E. Neriifolia* exhibits good Hepatoprotective properties. [46]

Anti-inflammatory and Analgesic activity [45]

With Eddy's hot plate method and tail-flick method, the Hydro-alcoholic extract was evaluated for analgesic action in albino rats and showed significant reduction in the carrageenan induced paw oedema in rats. The analgesic activity was evidenced in albino rats by increase in reaction time by Eddy's hot plate method and tail-flick method. The study also assessed the anti-inflammatory activity of latex of petroleum ether fraction of *E. nerifolia* by *Papaya Bigonia*. [42,47]

Anti-Cancer activity

The anti-carcinogenic effect of E. neriifolia leaves and isolated flavanoid was studied by Veena Sharma and Pracheta against N-Nitrosodietyleamine induced renal carcinogenesis in mice. Experimental mice were pretreated with 150-400mg/kg body weight of EN, 0.5% and 1% mg/kg body weight of butylated hydrolanisole (BHA) as a standard anti-oxidant and 50mg/kg body weight of ENF for 21 days prior to the administration of a single dose of 50mg/kg body weight of DENA.

Levels of renal markers (urea and creatinine) xenobiotic metabolic enzymes (cyt p450 and cyt 65), lipid peroxidation (LPo), antioxidants (SOD, CAT, GST and GSH) and other biochemical parameters – AST, ALT, ALP, TP,TC were measured to determine renal carcinogenesis caused by DENA. Pre-treatment with EN and ENF counteracted DENA induced oxidative stress and exerted its protective effect by restoring the levels of antioxidants, biochemical parameters, renal markers and xenobiotic enzymes in renal tissues. The study showed anti-carcinogenic potential of the hydroethanolic extract of *E. neriifolia* and ENF against DENA induced renal carcinogenesis of mice. [48]

Diuretic activity

Wister albino rats of both sexes were investigated for diuretic activity of *E. neriifolia*. They were deprived of food and water for 16 hours and received the priming dose of normal saline 25ml/kg orally, immediately after administration of vehicle, different doses of extract of *E. neriifolia* and standard frusemide (5mg/kg). The urine was collected in measuring cylinder upto 5h after drug administration. Flame photometer was measured by the concentration of Na+ and K+ in urine. *E. neriifolia* extract considerably increased the urine volume and proved to be an effective hypernatraemic and hypercholaemic diuretic. [42, 49]

Antipsychotic activity

In the study of Bigoniya P, Rana AC, psychopharmacological profile of the hydroalcoholic extracts of E*. neriifolia* leaves in mice and rats were studied. Mice and rats were devoid of catalepsic effect thereby suggesting specific dopaminergic receptor modulating activity. The extract 400mg/kg potentiated pentobarbitone induced hypnosis. The study observed that the leaf extract significantly reduces apomorphine induced stereotypyin mice at all doses (100, 200, 400mg/kg body weight). It showed protection against maximal electroshock induced convulsions at 400mg/kg. It had antipsychotic action at 400mg/kg by increasing the percentage of time spent in open arm in elevated plus maze. It increases transfer latency at 200-400mg/kg and also in combination with scopolamine. Results of the study showed that *E. neriifolia* leaf extract possess antipsychotic, anti anxiety, anti-convulsant activity properties. [42, 50]

Antioxidant activity

The antioxidant activity and in vitro free radical scavenging of ethanolic extract of E*. neriifolia* was evaluated by various antioxidant assays such as TAC, FRAP, FTC, TBA and non-specific activity. Phytochemical screening and the total phenolics, flavonols and proanthrocinidin content were also studied and all the anti oxidant activities were compared with standard antioxidants. A positive correlation between the antioxidant activities and physiochemical assays was observed and the highest scavenging activity of extract was noted at concentration of 1mg/ml. Result obtained indicate antioxidant property of ethanolic extract of *E. neriifolia*. [42, 51, 52]

Anti-diabetic and anti-hyperlipidemic activity

In a study, high fat streptozotocin (HFD-STZ) induced type-2 diabetic rats were used to examine the effect of repeated oral administration of ethanolic extract of E. neriifolia at dose of 200 and 400mg/kg on fasting glucose levels and lipid metabolism in streptozotocin induced type-2 diabetic rats. Decrease in fasting blood glucose, triglyceride, cholesterol, LDL levels in HFD-STZ induced type-2 diabetic rats, and significant increase in HDL levels were observed after 21 days of oral administration of 400mg/kg of E. neriifolia etanolic extract. Repeated oral administration of ethanolic extract of E. neriifolia exhibits anti-diabetic potential along with potent lipid lowering effect. [53]

DISCUSSION

As we all know poison can be converted into excellent medicine if processed and administered properly but the same can work in an opposite way if handled improperly and might lead to dangerous effects. Ayurveda emphasizes the use of *Visha* and *Upavishas* in various formulations after the proper *Shodhana* (purification) as well as used as single drugs in the healthcare. [9]

Once the poisonous plants are transformed into potential drugs after proper purification its therapeutic efficacy increases and becomes safe. Such poisonous plants are widely used in the Ayurvedic system of medicine for therapeutic purpose after proper processing called as '*Shodhana*' [54] Unfortunately, those poisonous plants have the potential to produce notorious toxic effects, even death also, if those are not processed properly or if are taken in a large dose.

One of the recommendations of the World Health Organization (WHO) guidelines for conducting toxicity study is to observe the recovery of the experimental animals from toxicity after a certain interval of toxicity study. [55]

One such toxic plant and a most beneficial therapeutic herb which is highly beneficial for the mankind is *Snuhi* that is described in vast w.s.r Ayurvedic science. There are about 45,000 medicinal plant species in India. Therapeutic use of medicinal plant is as old as humankind. *Samhitas*, Vedas and holy books has mentioned effective therapeutic use of

various medicinal plants. *Snuhi* is an important medicinal plant included in *Upavisha* by *Rasatarangini*.

Ayurvedic science attributes *Vednahar*, *Kapha-Vatahar*, *Dahashamak, Vishaghna, Dirghroghar, Kushthaghna, Vranaropan, Dushtavranahar, Plihaghana, Shothahar, Shofahar, Panduhar, Udarhar, Pramehahar, Medohar, Unmadhar, Ashthilikahara* etc properties to *Snuhi* whereas modern research studies lists the properties as Immunomodulatory activity, Wound healing activity, Anti-Bacterial, Hepato-protective activity, Anti-inflammatory and analgesic activity, Anti oxidant activity, Diuretic activity, Anti Diabetic activity, Anti Hyperlipidemic activity, Anti-psychotic, Anti Carcinogenic.

Nowadays researches are mainly focused to develop new methods for cancer etc dreadful diseases and their treatment predominantly using different plant species. Likewise, *Snuhi* (*Euphorbia neriifolia* Linn.) has been studied for various ethnomedicinal properties including anticancer, anti diabetic etc.

Traditional system of medicines has vast applications of these plants; hence the knowledge about poisonous plant and its therapeutic effects becomes very essential to develop a new drug for the new diseases like Covid 19. This study focuses on one such unique drug called *Snuhi* that is more poisonous as a drug and after purification, a very useful medicinal plant. This study might provide a novice idea for the researchers either in formulating an effective medicine for the successful management of the diseases or to use as an effective ingredient in any of the formulation. These plants, though poisonous with poisonous parts like leaves, roots and stem. They have proved to be very effective in many disorders with their chemical constituents and constitute the heart of the Ayurvedic and Herbal medicine.

CONCLUSION

Once the poisonous plants are transformed into potential drugs after proper purification its therapeutic efficacy increases and becomes safe. Such poisonous plants are widely used in the Ayurvedic system of medicine for therapeutic purpose after proper *Shodhana* or the purification under the name *Vishas* and *Upavishas* in the *Agada tantra* branch of Ayurveda. This study focused on one such drug called *Snuhi - Euphorbia Neriifolia*, a *Upavisha* or a poisonous plant to evaluate its therapeutic effects, properties etc which can be helpful for the researchers for the application of the drug in the present era due to the emergence of new diseases with unknown sources.

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