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REVIEW ARTICLE

A Critical Review of *Karvira* (*Nerium indicum* Mill)

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ABSTRACT

Ecological, geographical and climatic diversities of India have enriched her with a large diversity of medicinal plants, which is well reflected in its rich heritage of traditional medicinal system, the *Ayurveda*. The medicinal properties and clinical uses of thousands of plants have been described in *Ayurvedic* classics, the core ones being *Brihattrayi and Nighantus*. One such plant mentioned in *Ayurveda* is *Karvira, i.e. Nerium indicum.* Since long, it is being used by *Ayurvedic* physicians in various diseases, especially the skin diseases. Scientific studies now also support its use in a variety of conditions as wound infections, inflammation, cancer, diabetes and CNS depression. Various active constituents as glycosides are responsible for its therapeutic effects. The objective of this review to provide ancient and latest scientific knowledge regarding *Karvira*, so as to aid further researches in this direction.

Key words: *Brihattrayi, Karvira, Krimi, Nerium indicum, Nighantus*

INTRODUCTION

About 80% of the world's population relies solely or largely on traditional remedies for their healthcare needs. With rising esteem of *Ayurveda* and herbal medicine, use of medicinal plants is expected to rise globally. Today about 70,000 to 80,000 plant species are used for medicinal or aromatic purposes globally. [1] India is perhaps the richest nation with regard to herbal medicinal wealth (about 15000-20000 plants have good medicinal value), [1] and hence is also known as the "Emporium of medicinal plants". The use of medicinal plants in India dates back to the time of *Rigveda* since 5000 BC, known as the *Vedic* period. *Acharya Charaka*, the renowned physician of *Ayurveda*, defined *Ayurveda* as the science which relates with *Ayu* (life) and imparts knowledge about the drugs along with their properties and action.[2] Hence the *Ayurvedic* literatures contain profuse descriptions regarding the therapeutic usage of thousands of plants, one such plant being *Karvira* i.e. *Nerium indicum.*

Botanical description

Nerium indicum is an evergreen shrub or small tree in the Dogbane family Apocynaceae. It has synonyms like *Nerium oleander* and *Nerium odorum*. It is also known as oleander from its superficial resemblance to the unrelated plant *Olive olea*. The white and red flowered variety both are equated with *Nerium indicum.* It is commonly found as an ornamental shrub in the gardens throughout India. It is cultivated all over the world, especially in south-west Asia. *N. indicum* is exclusively native to India, Bangladesh, Nepal, Myanmar and China. It is about 5metertall, large glabrous erect shrub with milky juice. It has linear- lanceolate, dark green shiny and thickened leaves. Flowers are fragrant, red, white and rose-colored. Whole plant of *N. indicum*, especially roots are highly toxic. Generally, the parts used for medication are roots and leaves. The chief resources of the traditional *Ayurvedic* knowledge of medicinal plants, the *Samhitas* and *Nighantus* also described the two main varieties of *Karvira*, the white and red ones, which have been botanically identified as *Nerium indicum*. In *Raj Nighantu* a total of four kinds of *Karvira* are described, viz. white, red, and yellow and black. Botanically, the yellow variety is *Thevetia peruviana* (Pers.) while the black variety is still not known.

Medicinal uses of *Karvira*

Nerium indicum is used as a traditional medicine in many parts of the world, especially in India and China. Its most common use is in the ailments of skin.

A. In Ayurveda

Karvira has been frequently described in *Brihattrayi*, *Nighantus* and other classical *Ayurvedic* texts. *Charka* has prescribed the leaves of white flowered variety externally in chronic and obstinate skin

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diseases of serious nature including leprosy. *Bhavaprakasha* has described *Karvira* as a *visha* (poison) and indicated it in treatment of *Vrana* (infected wounds), *Kustha* (skin diseases including leprosy), *Krimi* (microbes and parasites), *Kandu* (itching), etc. [3]

B. Ethno medicinal uses

N. indicum is also very popular for its ethno medicinal uses, such as in cardiac disease, asthma, corns, cancer, epilepsy, wound healing and inflammation. A green dye which originated from its flower is used in the treatment of skin diseases and wound healing and it also possess anti-inflammatory property. This plant is used in Trinidad and Tobago for reproductive problems. Hot water extract of the leaves and seeds are used for upper respiratory tract and gastrointestinal infections in Kenya. In Calabria, southern Italy, the plant is used for the treatment of malaria in local folklore medicinal systems. The juice prepared from the stem bark of *N. indicum* is used to cure ear pain in the traditional therapeutic systems in the Kancheepuram district of Tamil Nadu, India. It is also used as anti-diabetic in Morocco. In Iloilo, Philippines, the plant is used as an ethno-medicine to treat fever, headache and dermatological problems. In the Errachidia province of Morocco, *N. indicum* is used in the treatment of hypertension and diabetes. [4]

C. Uses supported by modern science

In the past few decades, extensive research on the pharmaceutical properties of *N. indicum* has proved its medicinal properties such as antibacterial, antifungal, antiviral, cardio-stimulatory, cardio-tonic, anti-epilepsy anti-malarial etc.[5] Active constituents mainly responsible for its pharmacological properties are polysaccharides, terpenoids, alkaloids, glycosides, saponins, and tannin. Leaves contain two principal glycosides neriin and oleandrin, having properties similar to digitalin. Phytochemical analysis of its various extracts is shown in [Table 1].

Table 1: Phytochemical analysis of plant extracts in different solvents [6]

Tests	Benzene	Chloroform	Ethanol	Aqueous
Terpenoids	+	+	+	
Cardiac glycosides	+	+	+	+
Alkaloids	+	+	+	+
Flavanoids	-	-	-	
Saponins	+	+	+	
Tannins	+	+	+	+
Phenolic compounds	-	-	-	
Phlobatanin	-	-	-	
Carbohydrates	+	+	+	+

MATERIALS AND METHODS

The aim of study is to put together the *Ayurvedic* and modern knowledge of *Karvira*, so as to facilitate further research in today's scientific era. In the present day scenario of medical practice, uncertainty in the effectiveness of *Ayurvedic* medicines is an important area of concern, but many a times the cause of therapeutic failure is the lack of proper knowledge about the drugs or plants. This review is also an attempt to address such issues regarding *Karvira* and serves to give the classical facts about *Karvira* in reference of modern pharmacological research. For this purpose, detailed and critical study of the available literatures have been done from following sources:

1. Brihattrayi: Charaka Samhita, Sushruta Samhita, Ashtanga Sangraha
2. Nighantus: Dhanvantari Nighantu, Madanpala Nighantu, Kaideva Nighantu, Bhavaprakasha Nighantu and Raj Nighantu.
3. Different research papers from Google search

DISCUSSION

Use of *Nerium indicum* is known since the *Vedic* period, somewhere as a toxic plant and somewhere as a medicine. It is delineated in *Sam Vidhana Brahamana* and recommended for brushing the teeth. [7] Its therapeutic uses described in various classical texts are as follows:

Brihattrayi

Charaka and ***Sushruta*** both have classified *Karvira* under the group *Tikta varga* (the bitters) and *Moola visha* (poisonous roots). *Charaka* has frequently indicated it in *Kustha roga* (skin diseases). He mentioned *Karvira* as one of the *Kusthaghna dravya*,i.e. alleviates different types of skin disorders. For the treatment of *Kustha*, he recommended the use of *Karvira* intake orally as well as locally. [8] Many formulations of *Karvira* for external use are described in *Aragvadhiya adhyaya* chapter of *Charaka Samhita.*[9]

Sushruta indicated *Karvira* in the treatment of *Ashmari* (stones), *Updamsh* (gonorrohea), *Bhagandara* (fistula) and different types of skin disorders. [10] He has suggested application of *Karvira* paste for treating alopecia, and root powder mixed with water for venereal disease.[11] *Sushruta* quoted "*Karvira soma*" also in *Chikitsa sthana, Svabhavapratishedhniyam rasayanam* as one of the 24 varieties of *soma* which is used as *Rasayana.* [12] *Karvira* is one of the eight *moolavisha's* mentioned in classics. [13] Similarly, ***Vagbhata*** also indicated it in the treatment of skin diseases as *Kikkis* (Striae gravidarum) [14] and *Indralupta* (hair loss). [15] Fine paste of *Dugdhika* (*Euphorbia thymifolia*) and *Karavira* made with milk is applied to scalp to cure *Palitya* (whitening of hair). [16]

Nighantus

Nighantus are those *Ayurvedic* texts, which give detail accounts of the medicinal plants and are thus the classical pharmacopoeia of medicinal herbs used in *Ayurveda*. ***Dhanwantri Nighantu*** has clearly stated *Karvira* to be poisonous and has recommended its external use only. It is *Chakchushya* (beneficial for eyes) and useful in *Kandu, Kushta, Charmaroga* (skin disorders) etc. [17] It has been indicated in the treatment of eye disease, wounds and itching by ***Kaideva Nighantu*** [18]. *Kaideva* also indicated only external application of *Karvira*. [18] ***Bhavaprakasha Nighantu*** has said that the application its paste alleviates the venereal diseases (*Upadamsa*).[19] He also states that *Karvira* has *Vranashodhana* and

Vranaropana (antiseptic) activities, acts against *Krimi* (microbes) and is very useful in the treatment of *Kushtha*. He also classified it under the *Upavishas*.[20] *Raj Nighantu* described twenty two synonyms of *Karvira*. *Ashva-maraka* and *Haya-maraka* (so toxic that it can even kill a horse) are the common synonyms and indicate that it is a poisonous drug. [21]

Other classical texts

Chakrapani, the renounced physician of 11th century indicated application of medicated oil with *Karvira* on *Pama* (eczema).[22] *Vrinda Madhava* also described an oil preparation of the root of *Karvira* and *Vatsanabha* (Aconite) with *Gomutra* (cow urine) for the treatment of different types of skin diseases as *Charmadala* (xerodermia pigmentosa), *Sidhma* (pityriasis versicolor), *Pama* (bullae), *Krimi* (microbes), *Kitibha* (psoriasis). [23] The powder of leaves has been indicated as a snuff for treating epilepsy. [24]

API (Ayurvedic Pharmacopoeia of India)

According to API, *Karvira* exhibits the properties *laghu* (light), *ruksha* (dry) *and tiksna* (sharp) *guna*; *katu* (pungent), *tikta* (bitter), *kashaya* (astringent) *rasa* (taste); *katu vipaka* (after digestion develops pungent taste); and *ushnavirya* (hot potency). It is indicated in *Hrdroga* (cardiac disease), *Jvara* (fever), *Krimiroga* (disease due to microbes and parasites), *Kandu* (itching), *Kushtha* (skin diseases), *Netraroga* (eye diseases), *Vrana* (*wounds*), *Tamakashvasa* (asthma), etc.

Table 2: Therapeutic actions & Uses of *Karvira* as per different *Ayurvedic* Texts

Therapeutic action & uses	CS	SS	AH	DN	KN	MN	BP	RN	API
Kandu (Itching)	+		+	+	+	+	+	+	+
Kushtghana (anti-leprosy)	+	+	+	+		+	+	+	+
Charma roga (anti-skin disease)		+				+		+	+
*Netra roga (*Eye diseases)				+	+	+	+		+
Vrana (Wounds)		+			+	+	+	+	+
Jawaraghna (Antipyretic)				+					
Hridya (Beneficial for heart)									+
Krimighna (anti-helminthic, anti-microbial)					+		+		+
Vishajanya vikara (diseases due to toxicity)					+	+		+	
Updansha (Veneral diseases)		+						+	
Indralupta (Alopecia)			+						

(CS= Charaka Samhita, SS= Sushruta Samhita, AH= Ashtanga Hridaya, DN= Dhanvantari Nighantu, KN= Kaiydeva Nighantu, MN= Madanpala Nighantu, BP= Bhavprakasha Nighantu, RN= Raj Nighantu, API= Ayurvedic Pharmacopoeia of India)

Other medical sciences

In **Homoeopathy**, tincture of *Nerium oleander* leaves is used in diseases of nervous system, hemiplegia and paralytic conditions, but under strict medical supervision. [25]

Phyto-chemicals and modern researches

Today, many modern researchers have also explored the therapeutic potential of *Karvira* i.e. *N.indicum*. [26],[27],[28] It has been found that *N.indicum* contains many important phyto-chemicals such as:

- In the root bark: Plumericin, alpha-amyrin, beta-sitosterol, kaempferol,cardioactive glycosides named odorosides A-H.
- In the leaves: Cardiac glycosides kaneroside, neriumoside, digitoxigenin, alpha –L-olendroside -5α-adynerin and other glycosides.Gentiobiosyl – oleandrin, odoroside A and oleandrin were the main glycosides identified.

Neriene has potent cardiotonic activity similar to digitaline. It is also found effective against skin diseases,wound infections, cancer, diabetes, inflammation and CNS depression.[26]

Numerous studies have elucidated the inhibitory activity of *Nerium indicum* against different microbes such as fungi, virus and bacteria, and the antimicrobial activity of *Nerium indicum* leaves have been ascertained.[27] In vitro a**ntimicrobial activity** of *Nerium oleander* root bark and leaf extracts against the bacteria as *Bacillus pumilus*, *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Aspergillus niger* has been demonstrated. The chloroform, ethanol and methanol extracts of *Nerium oleander* showed high activity. [28] Studies have shown its anti-fungal activity too, such as 50% of ethanol fraction of its leaves against *Aspergillus niger* and *Candida albicans*,[29] the ethanolic flower extracts of this plant against different fungal pathogens,[30] 50% of the ethanol fraction of its leaves against *Aspergillus niger* and *Candida albicans*,[31] etc.

N. indicum is also known for its action on heart. The cardio-stimulatory effect of crude ethanolic extract of *N. oleander* leaves has been demonstrated on pig cardiac model. Three parameters namely, force of myocardial contraction, heart-beat rate and flow of cardiac blood were measured under the influence of this extract. The results displayed that under the influence of 100 mg/ml extract, the heart beat rate was increased from 28 beats/min to 41 beats/min, blood flow volume increased from 0.4 ml/min to 1.9 ml/min and the amplitude of myocardial contraction increased from 22-49 mm. In above experiment, the results of crude ethanolic extract of *N. oleander* leaves was seen to be much higher than that of the positive control acetylcholine and adrenaline. [32]

Table 3: A comparison of pharmacological activities /therapeutic actions of *Nerium indicum* mentioned in modern research and *Ayurvedic* texts

Modern	References	Ayurvedic	References
Cardio stimulator	Adome *et al*.[25]	*Hridya*	API [30]
Antimicrobial activity	Hussain *et al*. [26]	*Krimighna*	Bhavaprakasha nighantu [31]
Antifungal activity	Hadizadeh *et al* [27]		
Wound infections		*Vrana*	Bhavaprakasha nighantu[32]
Anti-cancer activity	Newman RA *et al* [28]		
Skin disease		*Kushthaghna/ Charma roga*	Dhanvantari nighantu[33]
Anti-malarial activity	Sharma P *et al* [29]		

CONCLUSION

Man's acquaintance with the medicinal properties of plants is of antiquity. *Ayurveda* is the oldest medical science known to mankind, and *N. indicum* is one such plant which is being used since long in *Ayurveda*, as well as in ethnomedicinal practices all over the world. This review elucidates the fact that *Nerium indicum* is a popular remedy for various diseases among different ethnic groups. *Ayurvedic* and traditional practitioners have been using it in the treatment of many diseases such as dermatitis, eczema, psoriasis, herpes, sores, abscesses, warts, corns, skin cancer, ringworm, scabies, epilepsy, asthma, malaria, heart disease etc. A critical study of the classical *Ayurvedic* texts shows that *N. indicum* is undoubtedly an important *Kushthaghna dravya* (anti-leprotic substance), and hence its most common use is in different types of skin disorders including leprosy. Today, its antifungal and antibacterial activity in reference of skin disease and its other spectrum of medicinal usage have mostly been proved by many researches. The facts described in classics regarding *N. indicum*, are thus now clinically being proven and re-established on modern parameters too, which again shows that the knowledge of our ancestors about herbal medicine was very vast and accurate. All above facts have been carefully covered in this study and hence is hoped that this review will facilitate further exploration of the medicinal and pharmacological properties of *N. indicum*.

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