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Review Article

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HYAMAARA- A REVIEW FROM CLASSICS

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ABSTRACT

Karvira or Hyamaar is a plant commonly seen all over India in gardens and in wild, poisoning of the plant is rare but cant be diagnosed easily. In current article we have focused on the plant through the review from all aspects starting from Vedas till modern available texts.

KEYWORDS: Karveera, Karvir, Nerium, Thivetia, Indian Olander.

INTRODUCTION

As a part of civilization human discern the knowledge of plants surrounding him. Many such uses are documented in the history of cultural civilization. We can study about such plants from cave paintings, literature available, *Vedas*, texts written by *Sages*, *Saints*, commentator on Health, Psychology, Literature, Mythology, etc.

i. Vedic Kaala

Vedas are known most ancient texts available in our culture; these are the base of our civilization. Four *Vedas-Riga*, *Yajur*, *Atharva* and *Saam* are the main.

- *Karvira* is mentioned in *Rugveda* under *Hridya Vanaspati*.
- Maitrayani and Kathak-Samhita described it by Srekaparna.

स्रेकपर्णाऽष्ठीवन्ता।मॆत्र४/१३/४: काठक१६/२१

- In Samavidhana Bramhana Karvira is demarcated for tooth brush use (Sa. 2/4/1)
- Flowers of *Karvira* are described in *Mahabhashya*.

ii. PuranaKala

In kautilya Arthashastra Karvira is used in formulation termed as Madanayoga.

In Mruchhakatik 102 – garland of Karvira flowers were given to wear to those persons who

were sentenced to death.

In Mahabharata Kanchan Shaila was termed as Karviraban (MahabharataAranyakparva 115).

iii. Samhita Kaala

Karvira is mentioned by all the *Acharyas* of *Brihatryai*. In the review of *Brihatryai* some references of *Shweta Karvira* had been found- Cha. Chi. 7/104, 105 & As. Hr. Chi. 19/61. This gives clue of two verities of *Karvira* Viz, *Rakta* (RED) and *Shweta* (WHITE). The roots of plant of *Karvira* are mentioned as toxic or poisonous by *Charaka* (Cha. Chi. 23/11). *Acharya Charaka* stated *Karvira* in *Snaana* and *Paana* (Bathing and internal administration).

Acharya Sushruta mentioned 'Karvira Soma' (Su. Chi 29/5, 13, 20, 26) as variety of Soma. Also karvirar shaar mentioned for treatment of Ashmari.

iv. SangrahaKaala

Sangraha kaala considered as the fruitful period of Ayurvedic Medicine; where many Lexicon works were created, Ashtang Sangraha and Hridya was popular work, also Rasa Aushadhi was introduced in the treatment.

Vagbhatta used *Karvira* in the treatment of *Garbhini Kandu* and *Kikwis* (As. Hr. Sha. 1/61), *Karviradi Agad* for the treatment of *Sarpavish* (As. Hr. U. 36/70).

Rasa Vagbhatta classified Karvira among the Upavisha.

v. MadhyamKaala

Karvira MoolaLepa (Sha. Sa. U. 11/105) and Karviradi Tailam mentioned by Sharangdhar. Vishatailam, Vajraka Tailam, Mahatrunaka Tailam, Karvirayadi Tailam and Shweta Karvirayadi Tailam was introduced by Chakradatta for the treatment of Kushtha; Chirbilvadi Lepa for the treatment of Vranashotha in his work where Karvira was used among the ingredients.

Bhavprakash and Dhanvantari Nighantu had mentioned the external use of Karvira.

vi. Modern period

Many researchers have been conducted on *Karvira* for evaluation of its chemical, Physical, Toxicological and Pharmacological properties. Glycosides present in Karvira- Tevetin A, B and other chemicals their pharmacodynamics and pharmacokinetics were evaluated by different scholars, selected are mentiones in the previous work done chapter here.

a. Vernacular Names

Names used for Karvira in different languages (Acco Raja Nighantu).

Table no 2: Vernacular Names of Karvira.

Sr.No	Language	Names
1	Sanskrita	Karvira
2	Hindi	Safed Kaner, Lal Kaner
3	Marathi	Kaner, Karvir, Kalhher, Patari, Kanartamvadi
4	English	Oleander
5	Bengali	Shweta Karvira, Lal Karvira
6	Kannada	Vakana Linge, Kangna Linge
7	Tamil	Kanel Chettu
8	Arabic	Sumul, Himara dakhali
9	Pharasi	Kharajahar
10	Latin	Nerium oleander

From 'INDIAN MEDICINAL PLANTS' - Peet Karvira

Table no 3: Vernacular Names of Karvira.

Sr.No	Language	Names of Karvira
1	Bombay	Chinakarab, Kokilphul, Kolkaphul
2	Deccan	Pila Kaner, Pilephul ka Kaner
3	Burma	Hpayoungban, Molamiyaipan
4	Gold Coast	Exile oil plant, Milk Bush
5	Gujarat	Pila Kaner, Pilokaner
6	Madras	Manjalalari
7	Malaya	Guinnyeh, Maloaie, Mallaye
8	Malayalam	Panchaarali, Arali
9	Mundari	Marangakanaili, Kaili
10	Telugu	Ganneru (Pachchaganneru)
11	West Indies	Jaca, Ahouai, Abia de matto

From 'Materia Medica of India And Their Theraputics'-

Table no 4: Vernacular Names of Karvira.

Sr. No	Language	Names of Karvira
1	Arab	Sumul-himar
2	Bengali	Karabi
3	Kannada	Kanagila
4	Chinese	Kiah chuh-au
5	Tamil	Kasturi patte
6	Latin	Nerium odorum or Nerium oleander

Arabic meaning of 'Sumul-himar' and 'Pharasi Kharajahar' is 'Gardhabha Visha', and Arabic 'Samulmar' is 'Sarpa visha'- Vanoushadi Nidarshika.

b. Botanical Names

Thevetia nerifolia Juss. Ex Steud. Termed for Peet Karvira; some other botanical names are defined for Peet Karvira are-

- Cerebera thevetia L.
- Cascabela thevetia (L.) Lippold
- Thevetia peruviana (Pers.) K. Schum

c. Classification of Karvira

Table no 5: Classification of Karvira.

Sr. No	Text	Varga / Gana	
1	Charaka	Kushtaghna, Tikta Skanda, Moola Visha	
1	Samhita	Varga, Tikta Varga	
2	Sushruta	Lakshadi Gana, Shiro Virechana Varga,	
	Samhita	Moola Viha Varga, Tikta Varga	
3	Vagbhatta	Lakshadi Gana	
4	Bh.N	Guduchyadi Varga, Vishopvisha Varga	
5	D.N	Karviradi Chaturda Varga, Upvisha gana in	
3		Mishrakadi gana, Saptamovarga	
6	R.N	Karviradi Varga	
7	K.N	Avshishta ansha of Aushadhi Varga	
8	Sha.N	Guduchyadi Varga	
9	Sho.N	Karviradi Varga, Paniyadi Varga	
10	M.N	Haritkyadi Varga	
11	N.A	Kutajadi Varga	

d. Rasa Panchakam

Table no 6: Rasapanchak of Karvira.

Sr.No	Nighantu	Rasa	Guna	Virya	Vipaka	prabhava
1	K.N	Katu, Tikta	Laghu	Ushna	katu	-
2	Bh.N	Tikta, Kashaya, Katu	-	Ushna	Katu	-
3	R.N	Katu	Tikshna	-	-	-
4	Sha.N	Katu, Tikta, Kshaya	Tikshna, Laghu	Ushna	-	-
5	M.N	-	Laghu	Ushna	-	-
6	D.N	Katu, Tikta	-	Ushna	-	-
7	N.A	Katu, Tikta	-	ushna	Katu	-

e. Karma

In all Karma of Karvira are-

- 1. Kaphashamak
- 2. Vatashamak
- 3. Vranashodhan
- 4. Vranaropan

- 5. Chakshushya
- 6. Kushtaghna
- 7. Kandughna
- 8. Grahi
- 9. Mootral
- 10. Arshahra
- 11. Pramehaghna
- 12. krimighna

f. Indications

- 1. Kushta
- 2. Kandu
- 3. Kotha
- 4. Visphota
- 5. Padma
- 6. Visarpa
- 7. Krimi
- 8. Arsha
- 9. Paalitya
- 10. Netrakopa
- 11. Indralupta
- 12. Dushtavrana
- 13. Prameha
- 14. Jwara
- 15. Shirashool
- 16. Bhagandar
- 17. Shosha
- 18. Ashmari
- 19. Gandamala
- 20. Updamsha

g. Part Used

Table no 7: Karvira Part Use.

Sr.No	Author	Part Used	Other description
1	Charaka samhita	Moola, Moolatwak	Panchanga in Kushtha
2	Sushruta Samhita	Moola, Moolatwak	Panchanga in Kushtha, leaves in Arsha
3	Nighantu Adarsha	Moolatwak, Patra, Pushpa	-
4	Raj Nighantu	Moolatwak, Patra	-

h. Dosage (Aoushadhi Matra)

Shudha Karvira Moola Churna- 30 to 150 mg

Tincture- 10 to 14 drops

i. Shodhana

General Shodhana^[4]

All the *Upavisha* are processed in cow's milk for their *Visha Shodhana*.

Vishesh Shodhana^[5]

*Karvira*is purified by *Swedana* process in *Dolayantra* for 3hr, by using *Godugdha* (Cow milk). After 3 hr pieces of *Karvira* are dried in shadow.

j. Vishishta yoga

Table no. 8: Formulations of Karvira.

Sr.No	Yoga	Reference
1	Karviradya taila	Bhaishajya Ratnavali
2	Karviradi tailam	Vaidya Chintamani
3	Karvaviradya Tailam	Vaidya Chintamani
4	Vajratailam	Vaidya Chintamani
5	Karviradi Lepam	Astang Hridyam
6	Shweta Karviradi Lepam	Astang Hridyam
7	Yekanga Shophhara Lepam	Ash. Hr. Chi. 17/25
8	Palita Rogahara Lepam	Ash. Hr. U. 24/35
9	Garidamalaku Chandadi Tailam	Ash. Hr. U.
10	Jyotishmati Tailam	Ash. Hr. U. 28/34
11	Mustadi Churnam	Ash. Hr. Chi. 19/67
12	Sleshmavisarpahara Lepam	Charaka chi.21/87
13	Vishahar anjana	Charaka chi.23/69
14	Visha Tailam	Vaidya Chintamani
15	Pallavadya Tailam	Materia Medica Nadkarni
16	Shweta Karviradya Tailam	Charaka- Chakradatta
17	Karvira moola Lepa	Sharangdhar Samhita
18	Charmaroganashaka Tailam	Vanoushadhi Chandrodya

19	Vaatnashak Tailam	Vanoushadhi Chandrodya	
20	Kasisadi Tailam	API	

Modern Review

a. Botanical Classification

Thevetia neriifolia Juss

Table no. 9: Botanical Classifications.

Level	Classification	Description
Kingdom	Plantae	Plants
Subkingdom	Tracheobionta	Vascular plants
Superdivision	Spermatophyte	Seed plants
Division	Magnoliophyta	Flowering plants
Class	Magnoliophyta- Dicotyledons	-
Subclass	Asteridae	-
Order	Gentianales	-
Family	Apocynaceae	Dogbane family
Genus	Thevetia Adans.	Thevetia
Species	Thevetia neriifolia Juss. ex Steud	Lucky Nut

b. Geographical Description

Habitat

It is grown as ornamental plant in gardens. It is the native of Central and South America which is now grown throughout the tropical and subtropical areas around the world.

Botanical Description

Karvira has many verities according to the color of flowers as Red, Yellow, White, Pink, etc. its leaves are long and thick. Fruits of red and white verities are long 4 to 6 inch in length and seeds are many. The fruit of yellow verity is round light green colored (unripe), black (ripened) and has 2 seeds of woody color. It is poisonous (Bhavaprakash).

It is large evergreen glabrous shrub with milky juice inside.

LEAVES- occur in 3 whorls, shortly stalked, coriaceous, 6-20*1-2 cm, linear, lanceolate, acuminate, tapering into short petiole, dark green and shining above, midrib stout, nerves numerous spreading horizontally.

FLOWERS- red, rose colored or white, fragrant, in terminal cymes.

CALYX- Lobes lanceolate.

COROLLA- 2.3 to 3 cm in diameter, fragrant, lobes rounded.

FILAMENTS- Hairy, appendages of anthers twice as long as the cells, Anthers joined

together adnate to stigma. Cells long spurred at base.

FRUIT- it is of follicles, cylindrical 15-17.8 cm long, rigid, straight, apressed, longitudinally striate, (yellowish green to light brown in *Nerium oleander*).

Seeds- They are numerous, small, tipped with coma of light brown hairs.

COTYLEDON- Flat

Hand book of Medicinal Plants and The Wealth of India

Macroscopic

ROOT: - The root system is highly branched; roots are grayish in color with long irregular streaks.

STEAM: - Steam is branched, grayish or grayish green in color with similar types of streaks on the bark surface.

BARK: - Silvery gray white soft.

LEAVES: - The leaves are exstipulate, petiolate (petiole short), whorled and each whorl having normally 3 layers, liner, lanceolate, entire, acuminate, thick and coriaceous, venation is unicostate, reticulate with midrib being stout and being arising in very large number running almost running parallel to each other, leaves are dark green in red flowered variety and light green in white variety. They are of 17 cm in length and 1-3 cm in width.

Pharmacology

The fixed oil of *Thevetia nerifolia* is inert if it is pure. Bark is bitter and powerfully cathartic, antipyretic in small doses, 2 gm of powdered bark is being equal to an ordinary dose of Cinchona, but its use is attended with considerable danger. In longer doses 30 to 60 ml of the tincture it is emetic and in still longer doses it is acrid poison. A watery solution of drug is readily absorbed from the tissues and does not set up any marked local irritation. (Nadkarni's Materia Medica).

All the parts of plants are poisonous root and the root bark are powerful diuretic and cardio tonic like Strophanthus and Digitalin. An infusion is given in cardiac systole as well as in dropsy.

Oleandrin is hypodermically injected, causes the heart's beat to fall from 75 - 80 to 10 - 12, if continued for sometime the heart ceases to beat and with it the respiration also. (Materia Medica of India and their Therapeutics).

Milky juice of plat is highly poisonous and Kernel is a powerful acro-narcotic poison. Oil

from seeds is emetic and purgative. In Gold Coast, seeds are chewed as purgative. In Guianna, the seeds are used as purgative in Rheumatism and dropsy. It is also considered a good alexiteric and is prescribed with run. (Indian Medicinal Plants).

It is antihelmintic, antipyretic and antiseptic, also posses' cardiotonic properties. (Handbook of Medicinal Plants).

Chemical Constituent

A sample of kernels of Thevetia neriifolia, on extraction with petroleum ether gave 57% of pale yellow oil with following characteristics- Sp.gr 0.903; n⁴⁰ 1.4599; acid. Val 4.3; Sap. Val194.1; iod. Val 76; and unsapon. Matter 1.4%%. The fatty acid composition of the oil was as fallows; palmitic 17.1, stearic 11.8; arachidic 0.4; oleic 64.3; and linoleic 6.3%. Presence of two unknown nature abonian (m.p. 185⁰ decomp.) and kokilphin (m.p. 189⁰) reported in the seeds. The solvent extracted oil is free from cardiac glycosides and appears to be suitable for soap making and edible purposes which is used for burning purposes. (The Wealth of India).

Toxins of Thevetia neriifolia

Table no. 10: Glycosides of Karvira.

Sr.No	Toxin	Chemical formula	Mol.Wt	CAS number
1	Thevatin A	$C_{42}H_{64}O_{19}$	872.93	37933-66-7
2	Thevetin B	$C_{42}H_{66}O_{18}$	858.95	11005-70-2
3	Peruvoside	$C_{42}H_{44}O_9$	548.65	1182-87-8

Glycosides of Thevetia neriifolia

Thevetin is the major component of seeds. It is the mixture of 2 triosides- Cereberoside (Thevetin B) and Thevetin A. small amount of another trioside 2'-O-acety Cereberoside is also present with Thevetin. Pure Thevetin A and Cereberoside in the ratio of 1:2 were obtained by partial chromatography and countercurrent techniques. (The Wealth of India).

Monosides separated from seeds were Neriifolin, Cerebrin 2'-O-acetylneriifolin, peruvoside, theveneriin (Ruvoside), and Peruvosidic acid (perusitin). These glycosides do not appear to occur as such in the seeds and are presumably formed as a result of enzymic hydrolysis of the triosides.

On partial hydrolysis, thevetin A yields the monoside Peruvoside from which Theveneriin (ruvoside) can be prepared by reduction; peruvoside and theveneriine are related to each

other as aldehyde and alcohol. A mixture of cereberin and 4'-O-acetylneriifolin obtain by careful acetylation of neriifolin. Oxidation of peruvoside with CrO₃ give peruvosidic acid.

Peruvoside

It is the most important and a large amount of work has been done on its pharmacology, toxicology and clinical aspects with its indication among most useful cardiac glycoside. Preliminary work of cardiotonic effect of peruvoside showed that it exerts quick and powerful positive inotropic effect in experimental animals. Using the heart-lung preparation of dog it was found that in failing heart peruvoside is almost as quick-acting and potent as the standard drug Ouabain. In therapeutic dose peruvoside produce fall in right atrial pressure and a rise in cardiac output; similar results were obtain on pig's heart-lung preparation.

In experimental heart failure in anesthetize cats and dogs, a strong positive inotropic action observed with peruvoside when administered intravenously; the pulse rate restored to the normal, the ventricular function improved with no pathological ECG changes.

Comparison between Ouabain and Proscillaridin showed that peruvoside was much more potent than proscillaridin in its inotropic effect. Whereas the inotropic effect and therapeutic dosage-range of peruvoside were similar to Ouabain, peruvoside differ from the latter in its lower toxicity and normalizing effect on pulse rate (The Wealth of India).

The acute and sub-acute toxicity study indicate that peruvoside has a high therapeutic index and the electrocardiographic changes produced by it closely resemble those seen with other cardiac glycoside. Acute toxicity studies showed that the order of sensitivity to peruvoside in different animals was in descending order: dogs, cats, pigeons, and guinea pigs. The usual mode of death with a toxic dose was ventricular fibrillation resulting in cardiac arrest (The wealth of India).

All the reports of clinical trial with peruvoside indicate that the drug has quick action when administered intravenously, dependable absorption and action when administered orally, and low, acute and cumulative toxicity. The drug can be used in patient with liver and kidney disease. Among the cardiac glycosides currently used most commonly are digoxin for oral administration and ouabain (G- strophanthin) by intravenous route. Peruvoside has been proved more advantageous than both these drugs, it is useful in treating acute and chronic cardiac insufficiency. (The Wealth of India).

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Bhiogade et al.

Thevetin and other Glycoside

The vetin is the first isolated pure glycoside of Thevetia. It is reported as having Digitalis like

effect. It is one eight potent and identical as Ouabain; with lethal dose for cat being 0.85 mg

per kilogram. It shows clinical efficacy in treatment of cardiac decompensation and in

tachycardia of thyroidism; the effective dose is close to toxic dose. (The Wealth of India)

Kernels contain 3 to 4 % of Thevetin. Thevetin A reported less potent than Thevetin; potency

of neriifolin is moderate whereas Cereberin is weaker and Cereberoside is weakest of

glycoside in cariotonic activity. A minor component Theveneriin is quick acting low toxic

glycoside by parental route; its absorption in GIT is poor and erratic. (The Wealth of India).

The principle cardio tonic substance present in the leaves of Nerium indicum is Oleandrin

which is also the active principle of leaves of N. oleander. Neriodin, Oleanolic acids are also

present. The action of neriodin is similar to Oleandrin; it is twice as active as Digitoxin.

Processes have been patented for the extraction of cardio-active principles from leaves. (The

Wealth of India).

c. Toxicity of Nerium odorum

Neriodorin has picrotoxic effect of muscular twitching and titanic spasm more powerful than

strychnine. Karbin acts like digitalis on heart and that of strychnine on spinal cord.

Active Principles: Neriodorin, Neriodorein, Karbin

Fatal Period: 24 Hours

Fatal Dose: ½ ounce of plant root

d. Sign and Symptoms

i. Vomiting

ii. Pain in abdomen

iii. Frothy salivation

iv. Restlessness

v. Slow and weak pulse

vi. Hampered respiration

vii. Difficulty in Swallowing

viii. Lock jaw

ix. Muscular twitching

Titanic spasm effecting one side more than other Χ.

- xi. Exhaustion
- xii. Drowsiness
- xiii. Coma
- xiv. Death due to heart failure

e. Treatment

- i. Washing of stomach
- ii. Symptomatic treatment
- iii. Administration of an anesthetic usually necessary
- iv. Morphine injection is beneficial

f. Post mortem appearances

This is not specific hemorrhagic patches seen on heart. *Nerium odorum* resist heat can be determined from burn evidences of victims.

g. Medico legal aspects

Villagers especially girls used its root decoction for suicide. Root is used for local and internal for abortion. Accidental poisoning is due to its application in venereal diseases and other growth conditions. Homicide is rare. It is used for cattle poisoning.

h. Toxicity of Thevetia neriifolia

Active Principle: Thevetin, Thevitoxin, Cereberin, Thevetin A, Thevetin B, and Peruvoside.

Fatal Dose: 8-10 seeds Fatal Period: 24 hours

For children's: Kernel of one fruit may be fatal

For Adults: Kernel of 10 fruit may be fatal

Sign and Symptoms (Bisht 1965)

- i. Vomiting- projectile vomiting proceeded by intense nausea; with bile stain vomitus.
- ii. Restlessness- it is directly proportional to degree of toxicity.
- iii. Abdominal Cramps- it occurs often.
- iv. Diarrhea: it is uncommon
- v. CNS Manifestation: They are not common but secondary due to cardiovascular manifestation.

- vi. Cardiovascular Manifestation- it is most important in all cases with exception in ECG changes- -
- Bradycardia- this is directly proportional to degree of toxicity.
- b. Arrhythmia- common feature seen more often with increased degree of toxicity.
- c. Hypotension-important feature of toxicity; it rises with increased dosages.
- d. Tachycardia- seen only in cases with vomiting and shock.
- e. Shock- seen in moderate to severe degree of toxicity.
- Delayed reactions- toxicity controlled by treatment seen upto 72 hr.
- vii. ECG shows verity of changes includes-
- 'P' wave changes absent or grossly distorted 'P' wave.
- b. Prolong P-R interval.
- c. Depressed ST segment.
- d. Irregular rhythm, non respiratory sinus arrhythmia.
- e. I degree heart block, sinus arrest with nodal escape; Wenchbach's phenomenon- bidirectional S.A-A.V. heart block; complete heart block with strokes-Adams syndrome.
- f. Supraventricular tachycardia, ventricular tachycardia or atrial flutter.
- g. Atrial fibrillation seen in terminal stages.
- viii. Hyponatremia dominant hyperpotassemia, hyperchloremia, normal serum calcium and dominant acidosis.
- ix. Death due to peripheral vascular failure, arrhythmias and gastro-intestinal disturbances leading to fatal acidosis.
- x. Significant changes occur in post- mortem with gross organ congestion, heart is dilated inflammation of splanchnic vessels.

h. Diagnosis

It depends on clinical manifestations and personal history. Immunoassay gives the presence of cardioglycoside in the blood. Serum potassium should be monitored. ECG, electrolyte, and renal function test should be appraised. Vomitus and gastric aspirate may present with remnant of seeds.

Management

General principles

Hospeetlize patient with cardiac monitoring; treatment according to the degree of poisoning.

Immediate gastric decontamination.

- Electrolyte and arrhythmia correction
- ECG for cardiac monitoring.
- Check serum potassium level.

Life supportive procedures

- Adequate airway and ventilation
- Adequate IV and oral fluids
- Electrical pacing or atropine for bradycardia
- Lidnocane for ventricular arrhythmias
- Phenytoin to control dysarrhythmias to maximum dose of 1000mg.
- Insulin, glucose, NaHCO₃ and ion-exchange resins to control hyper kalemia
- Calcium chloride is contraindicated (Goldfrank, 1986)
- Decontamination d done in conscious cases by induced emesis and gastric lavage; afterwards oral charcoal should be given for adsorbing plant toxins.
- Patient intoxicated with Nerium oleander by Digoxin-specific Fab antidote.(Shamik 1988)

Post Mortem Changes

Congestion of organs, engorgement of veins, sub-endocardial ecchymosis, signs of gastrointestinal irritation both side of heart full with blood.

Medico legal Aspect

Villagers especially girls used its root decoction for suicide. Root is used for local and internal for abortion. Accidental poisoning is due to its application in venereal diseases and other growth conditions. Homicide is rare. It is used for cattle poisoning.

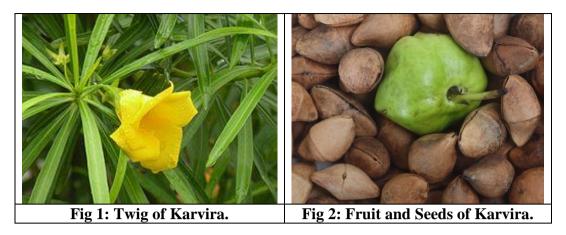




Fig. 3: Ripe fruit of Karvira.

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