



A Review on Bioactive Compounds and Medicinal Uses of an Endangered Medicinal Plant *Leptadenia Reticulata*

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ABSTRACT

For achieving the supreme ends consisting of righteousness, wealth, artistic values and spiritual freedom, health is considered as a prerequisite. The important components of the concept of positive health are preventive and curative aspects of disease. Medicinal plants occupied an important position in the socio-cultural, spiritual and medicinal arena of rural people of India. One such medicinal plant is *Leptadenia reticulata* also known as Jivanti/ dodi, is a twining shrub of Asclepiadaceae family endangered in nature. It is used as a tonic to vitalize, nourish and rejuvenate the body and increases longevity, memory enhancement, immunomodulation and adoption. In formulation of drugs, a number of phytochemical constituents of jivanti are incorporated. Research works are going on to explore the wide area of applications of *Leptadenia reticulata*. This review article delineates the potency of *Leptadenia reticulata*.

Keywords: *Leptadenia reticulata* (Retz), Stigmasterol, Galactagogue, Lactogenic, Rasayanic herb.

INTRODUCTION

The basic healthcare needs of more than 80% of world's population depend primarily on herbal medicine as estimated by the World Health Organization¹. Ayurveda, Yoga, Unani, Siddha, Homeopathy and Naturopathy constitute a major share of herbal drugs of all the officially recognised systems of health in India as shown in figure 1. Herbal drugs or dietary supplements have no separate category of as per the Indian Drugs Act in present time². These non-allopathic systems of medicine are still used by more than 70% of India's population. In India plant derived medication system has a very long, safe and continuous usage in Ayurveda, Yoga, Unani, Siddha, Homeopathy and Naturopathy. The existence and use of herbal drugs run side-by-side with Allopathy and are not in 'the domain of obscurity'³.

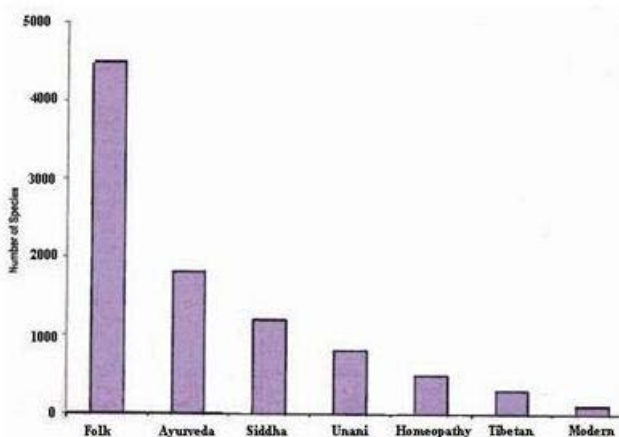


Figure 1: Plants being used by various systems of medicine (Report of the Task Force on Conservation & Sustainable use of Medicinal Plants, India, 2000)

Scientific research discovered fairly large number of plants that are found to be useful as drugs. Whereas some of the plants used in traditional medicine and it can be concluded that this is a good approach for discovering other useful drugs from plants⁴.

Leptadenia reticulata (Jivanti) is distributed in tropical and sub-tropical parts of Asia and Africa. In India, it is found in Gujarat, sub-Himalayan tracts from Punjab to Sikkim and Khasi hills and throughout peninsular India, ascending up to an altitude of 900 metres. Jivanti is jeevana tonic that boosts energy level of the body as per according to ayurveda. It is beneficial for the patient for the persons who suffer from weak debility or a lack of energy. It also increases longevity, memory enhancement, immunomodulation and adoption⁵. Lactogenic, anabolic and galactagogue effect was also observed in it⁶⁻⁸. It is also found to be effective in diseases, wounds and inflammation related to skin, fever, cough (with phlegm), dehydration, tuberculosis, colitis, chicken pox, dysentery, respiratory disorders, eye diseases and night blindness. Further it can also be applied in treating various body ailments like bleeding disorders, burning sensation of the body. The extracts of roots and leaves of the plant are found to be possessing antibacterial and antifungal activities. It also promotes gametogenic and androgenic functions of the testes of animal.

Plant is of great value in 'tridoshas' (Vatta, Pitta and Kapha) and is also effective in general debility, involuntary seminal discharge, as a stimulant and snake bite^{9, 10}, abortifacient, restorative, antifibrifuge, prostitutes, wound healer and in mouth ulcer¹¹.

PHYTOCHEMICAL CONSTITUENTS

L. reticulata (Retz.) Wight. & Arn is one of the ingredient in more than 23 pharmaceutical products are available in the market. It is in great demand in market both at local as well as the international level. The major phytochemical compound is stigmasterol. It also contains β -sitosterol α -amyrin, β -amyrin, ferulic acid, luteolin, diosmetin, rutin, stigmasterol, hentriacontanol, a triterpene alcoholsimiarenol and apigenin as shown in figure 2.¹²⁻¹⁴

Phytochemical constituents isolated from aerial parts are pregnane glycosides (reticulatin, deniculatin, leptaculatin), which on hydrolysis give calogenin tocopherols. Other are acetyl alcohol, lupanol 3-O diglucoside, leptidine 1, saponins, flavonoid, luteolin, diosmetin and tannin. Two resins and also a bitter neutral principle, albuminous and colourinsing matter, Ca-oxalate, glucose, carbohydrate and tartaric acid were isolated from leaves¹⁴.

Reticulin, Deniculatin and Leptaculatin are three novel pregnane glycosides isolated from *Leptadenia reticulata* (fam. Asclepiadaceae) and their structure were elucidated with modern physico-chemical methods and chemical transformations. Reticulin, Deniculatin and Leptaculatin were defined as calogenin-3-O- β -cymaropyranosyl-(1 \rightarrow 4)-O-3-O-methyl- α -D-galactopyranosyl-(1 \rightarrow 4)-O- β -D-digitoxopyranosyl-(1 \rightarrow 4)-O- β -D-cymaropyranoside, calogenin-3-O-3-O-methyl- α -D-galactopyranosyl-(1 \rightarrow 4)-O- β -D-digitoxopyranoside and calogenin-3-O- β -D-glucopyranosyl-(1 \rightarrow 4)-O- β -D-glucopyranosyl-(1 \rightarrow 4)-O- β -D-cymaropyranoside, respectively¹⁵.

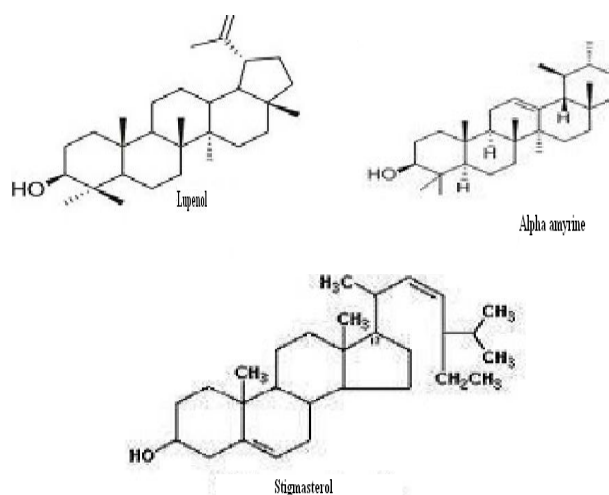


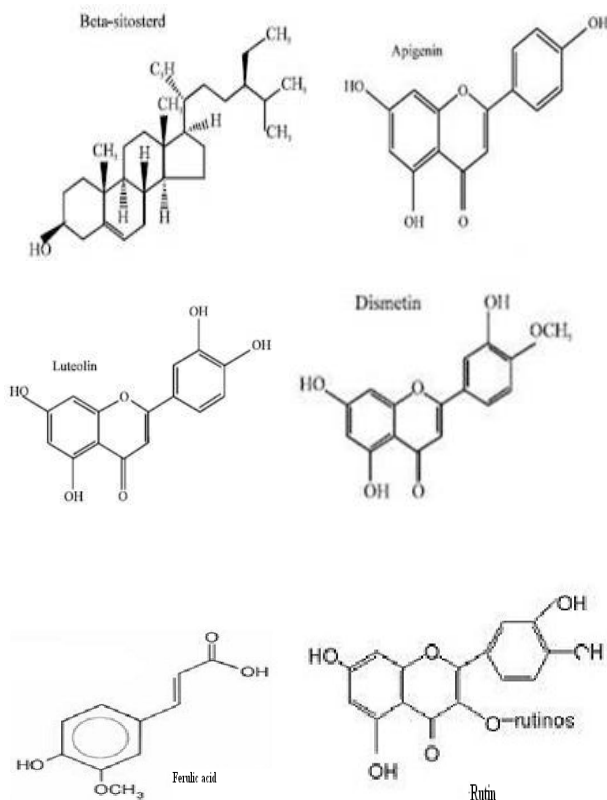
Figure 2: Structures of phytochemical constituents present in *Leptadenia reticulata*

6-7% moisture, 17.5% total nitrogen, different flavonoids, moisture (6-7%); total ash (5.5 to 6.5%); insoluble ash (0.1%), calcium 0.6%), sodium and potassium calculated as chlorides (2.16 to 2.24%), reducing sugars aldohexos, ketohexoses and pentoses, other constituents like proteins, gums, a steam volatile unidentified ferric (Fe^{+++}) greening substance and a substance which holds reducing sugars molecules in glycosidal linkage are found in the preliminary phytoconstituent studies of aerial part of *L. reticulata*. The total phenolic and flavanoid content of the plant were measured using methanolic and acetone extracts and was found to be 2.77 % w/w in methanol extract & 1.33 % w/w in acetone extract eq Gallic acid. Total flavanoid content was found to be 3.21% w/w eq. to quercetin in methanol extract¹⁶.

BOTANICAL DESCRIPTION

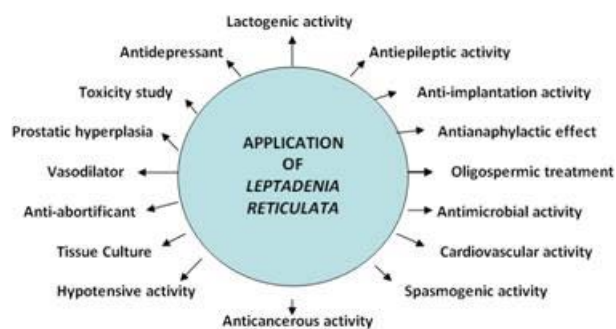
| | |
|-------------------|-----------------|
| Kingdom | Plantae |
| Class | Angiospermae |
| Cladus | Eudicots |
| Order | Gentianales |
| Family | Asclepiadiaceae |
| Subfamilia | Asclepiadoideae |
| Subtribe | Leptadeniinae |
| Genus | Leptadenia |

Leptadenia reticulata Wight and Am. is a much branched twining shrub of Asclepiadaceae family. Flowers are greenish yellow, in many flowered cymes (in lateral or subaxillary cymes), the follicles are sub woody and turgid. Flowering occurs in May and June, while fruiting begins in October and continues up to November. Its flowers and tender leaves are used as vegetable¹⁷ and to make bread¹⁸. Stem is cylindrical with bent at places whereas surface is rough, longitudinally ridged, wrinkled and furrowed, transversely cracked and with vertically elongated lenticels at places. It is 5 to 10 cm long, 0.5 to 2.5 cm in diameter. Externally whitish brown, internally



pale brown and bark is yellowish brown, corky, deeply cracked. The shape of leaves varies from ovate to cordate, 4 to 7.5 cm long, 2 to 5 cm and petiole 1 to 3 cm long, glabrous above and pubescent below. The roots are externally rough, white or buff colored with longitudinal ridges and furrows and in transverse section the wide cork, lignified stone cell layers and medullary rays can be seen and its size varies from 3 to 10 cm in length and 1.5 to 5 cm in diameter¹⁹⁻²². The tubers contain fructosan of the insulin type and are used as vegetable²³.

APPLICATIONS



Antiepileptic activity

Epilepsy is one of the most serious and prevalent brain disorders. The conventional antiepileptic drugs produce a number of side effects and drug interactions which impairs the health of the patient even more than the disorder itself. The methanolic extract of *L. reticulata* was found to be significant against maximum electro shock and Pentylene tetrazol²⁴.

Hepatoprotective potential

The potential of the ethanolic extract of *L. reticulata* as the antiulcer drug at dose levels of 100 mg/kg and 200 mg/kg produced a significant decrease in the ulcer index²⁵. The hepatoprotective action of ethanolic extract of *L. reticulata* showed significant reduction in the elevated serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP) levels. Also marked reduction in fatty degeneration and centrilobular necrosis in animals were observed in histopathological studies and efficacy of extract was almost comparable to that of standard drug²⁶.

Hypotensive action

An aqueous extract of *L. reticulata* showed potent and prolonged hypotensive action in anaesthetised dogs, the initial hypotension followed by a complete recovery and a secondary progressive hypotension. It did not possess parasympathomimetic or adrenolytic actions but blocked pressor response to nicotine.

Anti-implantation activity

A strong anti-implantation (inhibition 100%) and uterotrophic activity was observed with no antiestrogenic activity at the dose level of 300 mg/kg. could be detected when ethanolic extract of the whole plant of *Leptadenia*

reticulata has been given to albino rats to explore its anti-implantation and hormonal activities²⁷.

Lactogenic activity

L. reticulata is also used as supplement in drugs to improve the lactations in women. Stigmasterol is an active constituent of Jivanti. Stigmasterol showed lactogenic properties as assessed on protein and glycogen contents of mammary glands, photomicrographic and secretory rating of lactating mammary glands. It produced a significant galactopoietic response without any changes in the composition of milk or blood.

Antimicrobial activity

The antimicrobial activity of methanol and acetone extracts of *Leptadenia reticulata* was tested against five Gram-positive bacteria. The investigated the methanol extracts showed strong bactericidal activity while acetone extract of *L. reticulata*, did not show any activity against the five Gram-positive bacteria²⁸. In another study the ethanolic extract of *L. reticulata* found to possess antifungal activity against *Aspergillus flavus* and also the mean WBC count was significantly increased in the treated group whereas eosinophyll count showed a reverse trend²⁹.

The extraction of the stem and leaf were obtained using 4 solvents viz., hexane, chloroform, ethyl acetate and methanol, which was then used for column chromatography. Three compounds were isolated. From the hexane extract of the leaves α -myrillin acetate, a triterpenoid was isolated whereas the hexane extract of stem yielded triterpenoid, lupeol. The chloroform extract of the leaf gives phenolic acid and gallic acid. Antibacterial activity was shown by lupeol and gallic acid against *Streptococcus pyogenes* and lupeol also inhibited the growth of *Proteus mirabilis* to certain extent. Extracts and isolated compounds have shown better results as antifungal agent than antibacterial. Further vitamins such as carotene, thiamine, riboflavin, ascorbic acid and minerals such as calcium and iron were also obtained from leaves and stem of *L. reticulata*. The amount vitamins and minerals were comparatively in higher than other green leaf and stem vegetables³⁰.

Cardiovascular activity

Another study explored large number of medicinal plants that are used in Ayurveda, depending on the Doshas affecting the Hrd Rog (cardiac disorder), or to reduce obesity (Medorog) or inflammation (Shoth) are described. *Leptadenia reticulata* is one of the plants used for curing heart disease and also act as hypotensive. These plants are used for the management of CVS disorders as per the specific etiology of the patient according to Ayurvedic principles³¹.

Anti-abortion

Clinically trials using leptaden found to be effective in treatment of threatened and recurrent abortion. Herbal drug Leptaden consists of Jeevanti (*Leptadenia reticulata*)

150 mg and Kamboji (*Breynia patens*) 150 mg. During the trial period leptaden were given to all the patients having known history of abortion. 2 tablets t.d.s. and Progesterone (depot) 125 mg. I.M. was given once a week till 22nd week of pregnancy without any other hormone treatment. Leptaden with Progesterone found to be effective against abortion problem and seem to have brought down the incidence of recurrent abortion. It is safe to use throughout pregnancy³².

Oligospermic treatment

Another study evaluated the Speman tablets in the cases of oligospermia. *Leptadenia reticulata* is one of the compositions with 32 mg in each Speman tablate (of The Himalaya Drug Co.). The tablet was given 2 t.i.d. orally for 3 months to the oligospermia patients. Spemen remarkably improved the total count and the motility of the sperms. Speman is cost effective and very beneficial with no side effects in ameliorating oligospermia³³.

Prostatic hyperplasia

Leptadenia reticulata is one of the ingredient in Speman, an Ayurvedic preparation where whole plant without roots is used. 16 mg kg⁻¹ Qty. per tab. is used for the treatment of Benign Prostatic Hyperplasia. The patients of benign prostatic hyperplasia were given tablet of Speman (325 mg) (as informed by the manufacturer, The Himalaya Drug Co., Bombay). The drug found to be effective and bring about symptomatic relief by improving dynamics of micturation which is disturbed in BEP³⁴.

Antianaphylactic activity

The antianaphylactic effect of DLH-3041 (polyherbal formulation) was studied on the rat mesenteric mast cells. DLH-3041 (Himalaya Drug Company, Bangalore) contain *Leptadenia reticulata* (stem) as one of the content of herbal formulation. DLH-3041 showed beneficial effect on degranulation actively and passively sensitized mesenteric mast cells³⁵.

Anticancerous activity

One research evaluates the effect of ethanolic extract of *Leptadenia reticulata* leaves (LELR) against Dalton's Ascitic Lymphoma (DAL). The ethanolic extract of leaves (200 mg kg⁻¹, i.p.) causes a significant increase in the life span and a decrease in the cancer cell number and tumour weight. The extract also normalized the hematological parameters. The LELR treated group shows decrease in the cancer cell number and indicates that the test drug is having significant inhibitory effect on the tumor cell proliferation³⁶.

Vasodilation

In another study aqueous extract of stem of *Leptadenia reticulata* in dogs shows transient negative inotropic, chronotropic and prolonged hypotensive effect³⁷.

Antidepressant

Leptadenia reticulata is one of the important constituent in formulation of drug named as Malkanguni which is an antidepressant drug. Usual dose of the drug was 10 to 15 min per day. The drug is found to be effective with no side effect against for depression. It also showed marked improvement in hysteria³⁸.

Toxicity study

Study on *Leptadenia reticulata* aqueous extract was also performed to access its toxic effect. It was observed that they can tolerate dose safely up to 3.125 g kg⁻¹ when aqueous extract and leptaden was given orally for three alternate days and three consecutive days to rats. High dose increases mortality³⁹.

Tissue culture

Leptadenia reticulata is endangered specie therefore for its propagation and sustainable utilization there is need to apply non-conventional method. This problem can be solved by culturing tissue and cell of plant under *in vitro* condition. This technique of plant tissue culture helps to bring out improvement in terms of plant quality and productivity.

Micropropagation method was applied to the nodal shoot segments which were transferred on MS medium along with 0.6 µM indole-3-acetic acid (IAA) and 9 µM N6-henzyladenine (BA) at 26±2°C. After 25-30 days three to four shoots differentiated from each node and further shoots were transferred on fresh medium with BA and IAA. Then plantlets were transferred to sterile soilrite with half strength MS macrosalts. After hardening and acclimatization plants were then transferred to the field⁴⁰.

In another attempt regeneration of plant was done through indirect somatic embryogenesis where leaf, internode, node and shoot-tip were used as explants and callus was derived from them. Murashige and Skoog (MS) medium supplemented with 8.87 µM benzyladenine (BA) and 2.46 µM indole-3-butyric acid (IBA). Good results were obtained with shoot-tip and node explant derived calli induced somatic embryos. Further embryos are converted to plantlet at higher rate when half-strength MS solid medium with 1.44 µM GA₃ and BA (0.22 or 0.44 µM)⁴¹.

Further research was carried out for conservation, propagation and sustainable utilization of jivanti using biotechnological approaches. In this experiment nodal shoot segments each with 2-3 nodes was surface sterilized with 0.1% Bavistin for 30 min and then with 0.1% tetracycline solution, followed by 0.1% HgCl₂ for 4-5 minutes. These explants were then inoculated on MS medium containing additives (283.50 µM ascorbic acid + 119.0 µM citric acid) with Benzylaminopurine (BAP, 2.22-44.40 µM), Kinetin (4.65-23.20 µM) Adenine sulphate (AS, 27.10-135.50 µM)⁴².

Another study involves the development of simple and efficient method for *in vitro* regeneration of *Leptadenia*

reticulata. Different cytokinins of different concentration on various media have been investigated for multiple shoot induction using nodes, internodes, meristem as explants. MS media supplemented with 0.25mg/l BA and 0.25mg/l Kn has shown the best response for multiplication. Good amount of callus obtained on B5 media. Among old and young axillary nodes, old axillary node showed positive response and developed healthy multiple shoots and satisfactory results were not obtained in internodes. The *in vitro* grown shoots rooted maximum on full strength MS media containing 2mg/l IBA followed by 200 mg/l activated charcoal. Success rate was 93% in the field⁴³

CONCLUSION

The plant is the one of the ingredient of many formulations which has been used to recover from physiological, bacterial diseases or even form cancer. Only few researchers worked on the different extracts of the plant on few of the diseases occurring in human being. Still many pharmacological activities of the plant remain to be explored. Its antioxidant immunomodulatory and anticancerous activities could be correlated with its components like flavonoids, glycosides etc. Phytosterol and Pentacyclic triterenoidal content like β -sitosterol and β -amyrine is responsible for anti inflammatory and vasodilator properties. Plant tissue culture as a technology is alternate method for its propagation and has been increasingly exploited to achieve success. Therefore further research is needed to explore its components and for *in vitro* regeneration method, so maximum utilization of plant can be done for human welfare.

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