REVIEW

A Pharmacological Review: *Leptadenia reticulata* (Wight & Arn.); Jivanti: the Real Life Giving Plant

Jayesh M. Dhalani, Pankaj B. Nariya

Department of Chemistry, RK University, Rajkot, India

Correspondence:

Pankaj Nariya, Department of Chemistry, School of Science, RK University, Bhavnagar Highway, Kasturbadham, Tramba, Rajkot, India

E-mail: pankaj.nariya@gmail.com

Tel: +919898081779

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The present review reveals a comprehensive description of various pharmacological studies carried out on *Leptadenia reticulata*, a source of several active compounds, i.e. *Leptadenia reticulata* plant belonging to family *Asclepiadaceae*, it is also known as 'Jivanti', used for the treatment of various ailments in human civilization as well as used in folk medicine as a remedy in various reported herbal formulations. The plant has been found to exhibit diverse pharmacological activities like antibacterial activity, anticancer activity, lactogenic effect, antioxidant activity, anti-implantation activity, anti-asthmatic activity, modulating effect, activity of silver nano particles, hepatoprotective activity, antifungal activity, antidiabetic activity and anti-inflammatory activity. Traditionally, the plant promotes fitness and vigor, the tone of voice, cures eye diseases, fever, and night blindness, cough, maintain pregnancy and gangrene. In this review, we give the recent scientific update on this plant with therapeutic potential and discuss the methods of carrying out studies. The present review draws the attention of researchers towards the potential therapeutic activity of *Leptadenia reticulata* for their active constitute.

INTRODUCTION

Leptadenia reticulata (Robert Wight & George Arnott Walker Arnott), one of the important medicinal plants, is known for their activity of leaves, roots, and tender stalks. *L. reticulata* belongs to family *Asclepiadaceae*. Other names of plant are Jivanti, Swarn Jivanti or Dori.¹ *L. reticulata* dispersed in hot and subtropical parts of Madagascar, Mauritius, Peninsula, Philippines, Sri Lanka, Asia and Africa, Burma. In India, it originates from Sikkim, Nilgiris, South India, Himalayan ranges, Gujarat, Konkan, Punjab, Khasia hills, Deccan and Karnataka. As *Atharva Veda* suggests, it is of Indian origin.¹ *L. reticulata* is a climber/liana having a stem with cork-like, extremely cracked bark with several branches. Seed germination takes place starting June to September, after one or two showers of rain fall in grassland conditions. Flowering takes place all over the year. The time for fruit formation only during December to February. Maturation of fresh fruit/seeds continues up to mid-May and dispersion of seeds takes place during June to July.¹

In literature survey, Jivanti has measured a stimulant and tonic. *Atharva Veda*, *Kanda* eight, and *Sukta* two show its therapeutic use dates back to about 4500 to 1600 BC. The *Atharva Veda* mentioned its uses as a life and provide strength, propagator of milk and useful in many other ailments. *Charaka* described it is significant Rasayana medicine, capable of maintaining youthful vigor and strength. *Vagbhata* included it in the ten drugs that constitute the jivaniya gana or the vitalizing group. It promotes fitness and vigor, improves the tone of voice, cures eye diseases, fever, night-blindness, cough and alleviates.² Its curative characteristics make it a significant element in the preparation of 'Chyawanprash'.¹ Mentioned it as a prolapsed of the uterus, eye tonic, stimulant, galactagogue, controlling habitual abortion, maintain pregnancy and astringent.³ The bhils of southern Rajasthan take its leaves, paste, and roots orally with water to cure gangrene. It is a stimulant and tonic.⁴

Preliminary phytochemical study of *L. reticulata* different parts shows the presence of carbohydrates,

steroids, terpenoid, glycoside, coumarins, flavonoids, tannin, phenolic compound and alkaloids.^{5,6} Also some phytoconstitute are reported from *L. reticulata* are ferulic acid, β -sitosterol, diosmetin, stigmasterol, rutin, β -amyrin, α -amyrin, simiarenol, hentriacontanol, reticulatin, deniculatin, leptaculatin.⁷⁻¹⁰

Many products are currently available in the market which contains Jivanti due to its therapeutic activity like Himalaya galactin, Safe herbs by Vasu healthcare, Jivanti powder/capsules by evaidyaji, Jivanti flow granules by Adhyani Herbal Pvt. Ltd., Leptaden by Alarsin Pharmaceuticals. Since, review on *L. reticulata* was not available on one platform during extensive literature search it was thought worthwhile to undertake a detailed review study. In this review massive effort was made to compile the details of pharmacology activity of *L. reticulata*.

PHARMACOLOGICAL ACTIVITY

ANTIBACTERIAL ACTIVITY

Kalidass et al. observed that chloroform, alcohol and petroleum extracts show the potential antibacterial activity with ten different strains of microorganisms. The reference antibiotic *chloramphenicol* showed the highest antimicrobial activity against all tested microorganism (**Table 1**). *E. coli* and *Staphylococcus* were most sensitive to the chloroform extract, and *E. coli*, *Proteus bulgaris*, *Bacillus cereus* and *Klebsiella pneumoniae* were fairly sensitive to the petroleum ether extract. Alcohol extracts clearly imperative antibacterial activity against *Pseudomonas aeruginosa*, *B. cereus*, *S. epidermidus* and *P. vulgaris*.¹¹

ANTI-FUNGAL ACTIVITY:

In this experiment, 50% ethanolic extract of *L. reticulata* aerial part was subjected in vivo to the antifungal activity in rat animal model. The open wound infected with *Aspergillus flavus* was treated with *L. reticulata* extract for eight days. This treated wound showed visible healing sign at day 9, the swab made from the healing wound region showed the absence of the fungal hyphae by Grams staining as well as by Lacto Phenol Cotton Blue staining method. In the infected but untreated group, the wound progressed, and the animal was in distress and could account for 40% mortality within 8 days. The swab made from the wound region of the survived rats showed the presence of *A. flavus* hyphae. The roots and leaves of *L. reticulata* tested useful in various skin diseases, inflammation of the skin and wounds.^{12,13} In this study, a significant wound healing property was observed on topical application of the alcoholic extract of *L. reticulata* to the rats which was infected with *A. flavus* similar trend was also noted.^{13,14} Mishra et al. also reported the *in vitro* antifungal activity of different extracts of *L. reticulata* aerial parts for against *Trichoderma koningii*, *Candida tropicalis*, *Aspergillus ruannti*, *Candida albicans*, *Trichodermataviride* and *Aspergillus flavus*. From the study methanolic extract exhibited excellent antifungal activity against all the chosen strains. MIC was performed using broth dilution method, and at concentrations of 2 mg/ml, 5 mg/ml and 10 mg/ml in DMSO. The zone of inhibition was studied through agar disc diffusion method. In antifungal studies, cotrimazole (25 μ g/ml) was used for reference control. The result of

Table 1. Antimicrobial activities of *Leptadenia reticulata*

Strains	Chloroform Extract	Alcohol Extract	Petroleum Ether Extract
<i>Serratia marcescens</i>	00.000	00.000	08.000
<i>Klebsiella pnemoniae</i>	21.000	00.000	22.000
<i>Pseudomonas aeruginosa</i>	00.000	12.000	00.000
<i>Escherichia coli</i>	22.000	00.000	20.000
<i>Salmonella typhi</i>	00.000	00.000	00.000
<i>Staphylococcus aureus</i>	20.000	00.000	17.000
<i>Bacillus cereus</i>	11.000	10.000	14.000
<i>Staphylococcus epidermidus</i>	00.000	08.000	00.000
<i>Streptococcus pyogenes</i>	00.000	00.000	00.000
<i>Proteus vulgaris</i>	17.000	06.000	21.000

MIC study revealed the antifungal activity of the extract against the tested strains of microorganisms involving concentration ranges of 150 and 300 µg/ml. Zone of inhibition study bare that the extracts have antifungal activity in a concentration-dependent manner against the chosen organisms and comparable with the standard drug.¹⁵

In the whole study, petroleum ether extract found inactive against all tested strains. Acetone and chloroform extract showed moderate antifungal activity against *A. ruantii* and *A. flavus*. The aqueous extract is powerful against *Candida* species. Methanolic extract imparts remarkable antifungal activity against all test strains. The result of this experiment indicates the potential value of *L. reticulata* in the treatment of diverse pathogenic diseases.¹⁵

ANTICANCER ACTIVITY AGAINST DALTON'S ASCITIC LYMPHOMA (DAL)

For evaluation of anticancer activity, an assay was performed according to the DAL method. According to the method, mice were divided into three groups i.e. G1 (Control), G2 (*L. reticulata* leaf ethanol extract treated-LELR), G3 (Fluorouracil treated group).^{16,17} The DAL cells were procured from Amala Cancer Institute, Thrissur, Kerala and injected intraperitoneally (10^6 cells/mice) to all groups of animals. On the 2nd day, the animals of G2 were treated with 200 mg/kg of LELR while G3 with 5-fluorouracil (20 mg/kg) and the treatment was continued for next ten days. G1 was not allocated any treatment after inoculation with DAL cells. The mice were observed for the next 10 days for the development of ascetic tumor. After 10 days, observed parameters like a decrease in tumor weight of the mice, packed cell volume, cancer cell number, and an increase in life span (Table 2).¹⁶ The above study shows that decrease in the cancer cell number observed in the LELR treated group G2 indicates that the test drug is having a clearly inhibitory effect on the tumor cell proliferation.¹⁶ These results help to rationalize the ethno-pharmacological claims regarding presence of anticancer properties in *L. reticulata*.

LACTOGENIC EFFECT:

Formulations of *L. reticulata* with different plants are available in the market which gives lactogenic effect. GALACTIN VET Bolus of The Himalaya Drug company and polynutrient formulation of *L. reticulata*, *A. racemosus*, *W. somnifera*, *A. donax*, *C. pareira*, *F. vulgare*, *E. alba* and *S. nigrum* was

given to Holstein and Jersey cross bred cows. (5 bori/daily for 10 days) The results are shown in Table 3.¹⁸ The results revealed the potential of the lactogenic effect of the plant.

ANTIOXIDANT ACTIVITY OF LEPTADENIA RETICULATA LEAVES DPPH SCAVENGING ASSAY

Sujatha et al. observed that the *L. reticulata* methanolic leaf extract show high potential of free radical scavenging activity (IC_{50} : 18.56 ± 0.29 µg/mL) against L-ascorbic acid (6.40 ± 0.21 µg/mL), and butylated hydroxyl toluene (BHT) (IC_{50} : 10.00 ± 0.29 µg/mL). Results indicating that extract gives marked radical scavenging activity with standard data.¹⁹

ANTI-IMPLANTATION ACTIVITY

In this experiment, proven fertile females Wistar rats, weighing between 200 and 250 g were selected and left overnight with males of proven fertility in the ratio of 3:1. On day one pregnancy was confirmed by the presence of spermatozoa in the vaginal smear. Twelve pregnant rats were selected for anti-implantation activity. Six rats received vehicle while the other six received *L. reticulata* (300 mg/kg) orally suspended in tween80 from day 1 to 7 of the pregnancy. On the 10th day of gestation, laparotomy was performed under ether anesthesia, and the uterine horns were inspected for some implants. Anti-implantation activity was determined.^{20,21} Colony-bred immature female rats (25-30 days old) were divided into four groups (six in each group) and treated (Tables 4, 5).

In this study, the whole plants were tested for its anti-implantation and estrogenic properties. One dose of *L. reticulata* possesses a significant estrogenic activity shown by its uterotrophic effects in immature female rats and by its ability to increase the weight to genital organs in ovariectomized rats. Both activities were confirmed by the potentiating of the effect of ethynyl estradiol. *L. reticulata* also possesses a very strong anti-implantation activity which may be due to its estrogenic activity (Table 6).²⁰

ANTI-ASTHMATIC ACTIVITY:

Anti-asthmatic activity experiment was done on a Guinea pig, and rat.^{22,23} Results of the experiment was histamine (10 µg/ml) produced dose-dependent contraction of guinea pig ileum. Pretreatment with hydro alcoholic extract of *L. reticulata* (0.8 mg/ml) significantly inhibited ($p < 0.01$) the contractile effect of histamine.²⁴

Table 2. Effect of LELR on DAL induced mice

Groups	Cancer cell Number	Packed cell volume (PCV) (%)	Increase in tumour weight (g)	Number of days survived	Increase in life span (ILS) (%)
G1	1.82±0.18	51.35±0.46	10.86±0.48	20±0.2	--
G2	0.94±0.10*	37.80±0.58**	5.64±0.54**	25±1.2*	26.6%
G3	0.82±0.36*	28.56±0.18**	3.86±0.40**	28±3.2*	40%

All values are presented as mean±SEM of six animals. One-way ANOVA followed by Newman-Keul's multiple comparison tests *p<0.05, **p<0.001 compared to G1. G1- Control (DAL induced, non-treated), G2 – 200 mg/kg of LELR treated group, G3 – 20 mg/kg of 5-flourouracil treated group.

Table 3. Average milk yield (in liters), fat (%), SNF (%) before, during and after treatment

Parameters	Before treatment (7 days)	During treatment (10 days)	After treatment (15 days)
Average milk yield	7.56±0.60	8.25±0.64	8.26±0.67
CLR Reading	27	27.5	28
Fat %	4.20	4.25	4.25
SNF %	8.5	8.6	8.6

GALACTIN VET Bolus improved milk yield, fat%, SNF% and CLR reading in dairy cows and no adverse effect found during the study period and the result was found as given in Table 3.

Table 4. Anti-implantation activity of LRA in female rats when fed orally from days 1 to 7 of pregnancy

Treatment (day 1 – day 7)	No. of pregnancies/ no. of treated	No. of implantation (mean ± S.E)	Average litters delivered
Vehicle (0.5 ml / rat p.o.)	6/6	8.5±8.2	8.5
LRA (300 mg/kg p.o.)	6/6	0	0

Table 5. Effect of LRA on uterine weight of immature female rats in the presence and the absence of estrogens

Treatment (dose, mg/kg body weight)	Uterine weight mg/100g	Vaginal cornification
Vehicle (0.5 ml/rat p.o.)	33.64±0.98	Vagina not open (0 to +)
LRA (300 mg/kg p.o.)	78.62±6.37*	Open (+++)
EED (0.1 µg/rat i.m.) + LRA (300 mg/kg p.o.)	129.97±9.13*	Open (+ to ++)
EED (0.1 µg/rat i.m.)	120.60±6.02*	Open (+++)

*p < 0.001 when compared with control, + nucleated epithelial cells; ++ nucleated and cornified cells, +++ cornified cell. EED - ethynyl estradiol, *p < 0.001, when compared with control

Table 6. Effect of LRA on the weight of uterus, cervix, and vagina of ovariectomized rats

Treatment (dose, mg/kg body weight)	Weight in mg/100g (mean $\pm$ SEM)		
	Uterus	Cervix	Vagina
Control (tween-80, 1%)	69.081 $\pm$ 0.069	29.42 $\pm$ 0.128	36.42 $\pm$ 0.108
Ethanol extract (300 mg/kg p.o)	107.236 $\pm$ 0.423 ^a	37.27 $\pm$ 0.157	42.78 $\pm$ 0.102 ^a
Ethynyl estradiol (0.1 μ g/kg i.m)	158.366 $\pm$ 0.322 ^a	47.29 $\pm$ 0.149	50.48 $\pm$ 0.062 ^a
Ethynyl estradiol (0.1 μ g/kg i. m) and Ethanol extract (300 mg/kg p.o)	261.41 $\pm$ 0.3040 ^b	77.34 $\pm$ 0.26	80.27 $\pm$ 0.212 ^b

^a=p<0.001 vs. control group, ^b=p<0.001 vs. EED group.

MODULATING EFFECT OF *LEPTADENIA RETICULATA* (RETZ) WIGHT & ARN.

Modulating effect of *L. reticulata* (Retz.) proved by Girishkumar et al. with chromate (VI)-induced immunosuppressant, and oxidative stress on mouse splenic lymphocytes and bone marrow derived macrophages. MTT assay (lymphocytes macrophages), trypan blue dye exclusion test and levels of lipid peroxides on mouse splenic lymphocytes were done. The outcome of this experiment specifies that the cells treated with chromate (VI) decreased cell viability, showed marked suppression of cell proliferation, and increased levels of lipid peroxides. It was found statistically significant (P<0.001) as compared to controls and also observed that all the (Padavashesha kashaya, Tarpana kashaya, and Aqueous extract) three various forms of the extract of *L. reticulata* were able to defend with chromate (VI)-induced immune toxicity on splenic lymphocytes with respect to cell proliferation and cytotoxicity.²⁵

BIO-ACTIVITIES OF SILVER NANO PARTICLES SYNTHESIZED FROM *LEPTADENIA RETICULATA* LEAF EXTRACT

Kumara reported that silver nano particles of *L. reticulata* leaf extract give biological activities against different pathogenic microorganisms. Synthesized of silver nano particles (AgNPs) from *L. reticulata* leaves methanolic extract were tested for antimicrobial activity by using agar well diffusion method against *Bacillus subtilis*, *Micrococcus luteus*, *Escherichia coli*, and *Klebsiella pneumonia*. It shows potential antibacterial activities. The zone of inhibition against *E. coli* (20.0 $\pm$ 0.4 mm) and *B. subtilis* (24.3 $\pm$ 1.3 mm) was recorded at 150 μ g/

ml concentration of AgNPs. Minimum zone of inhibition was observed against *M. luteus* (8.7 $\pm$ 1.4 mm) at 25 μ g/ml concentration of AgNPs. If the concentration of AgNPs increased, then the zone of inhibition increased. AgNPs are more efficient with Gram-positive bacterial strains compared to Gram-negative bacteria strains.²⁶ Antibacterial activity of silver nano particles (116.28 mg/L) against *E. coli* CCM 3954 shows result regarding zone of inhibition (9 $\pm$ 1.0 mm).²⁷ Difference between both result (with plant and without plant) indicating the potential of plant extract effort.

HEPATOPROTECTIVE ACTIVITY OF *LEPTADENIA RETICULATA* STEMS AGAINST CARBON TETRACHLORIDE

In carbon tetrachloride (CCl₄)-induced hepato toxicity in rats was evaluated by Amit Kumar et al. In this experiment, aqueous and ethanolic extracts of plant were used. In this experiment, considerably reduced symptoms of liver injury and liver damage by restoration of the architecture of liver as indicated by lower levels of serum bilirubin and protein as compared to normal and silymarin treated group. After a diagnosis of liver sections, it is proved that extracts of *L. reticulata* prevented damage induced by CCl₄ and showing the absence of necrosis, fatty infiltration, and presence of normal hepatic cords.²⁸

ANTIDIABETIC ACTIVITY

Venkatesan et al. reported that *L. reticulata* plant gives antidiabetic against in streptozotocin-induced diabetic rats. Ethanol extract of *L. reticulata* gives significant effect against diabetic rats. For that petroleum ether, ethyl acetate and ethanol extract (200 mg/kg) was given to diabetic rats. Metformin

(50 mg/kg) was taken as a standard drug. Ethanolic extract shows $P < 0.05$ value. So, it does prove that *L. reticulata* plant has good potential of antidiabetic activity.²⁹

ANTI-INFLAMMATORY ACTIVITY:

Mohanty et al. performed the anti-inflammatory activity of water, methanol and ethyl acetate extract of *L. reticulata*. Diclofenac sodium (50 mg/kg) was taken as reference drug. For that group I taken as a control, group II to IV receives (400 mg/kg) methanol, ethyl acetate, and water extract respectively, group V to VII (600 mg/kg) methanol, ethyl acetate and water extract. Group VIII was treated by diclofenac sodium. The experiment was carried out using λ -carrageenan, and formalin-induced paw edema test. The result shows that all extracts are having significant ($p < 0.05$) anti-inflammatory activity in rats but a substantial increase in the percentage of inhibition of edema was found in ethyl acetate.³⁰

CONCLUSION

L. reticulata, the versatile medicinal plant and a tremendous source of various types of above mentioned pharmacological activities, and already it is referred to in the Ayurveda system of medicine. So, it is real Jivanti for human health. Some research has been carried out during the past few decades to explore the therapeutic activity of different parts of *L. reticulata* but some of them phytochemical study of this plant still lacks which draw the attention of researchers towards potential therapeutic activity of this medicine plant for their active constitute. The global situation is now changing towards the use of nontoxic plant products. So, time has come to make proper use of traditional knowledge of *L. reticulata* through a modern way of drug discovery. Hence, extensive research exploration is required to find active constitute from this plant for exploiting their therapeutic utility.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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Фармакологический обзор: *Leptadenia reticulata* (Wight & Arn.); Дживанти: Настоящее животворящее растение

Джайеш М. Дхалани, Панкаж Б. Нария

Кафедра химии, Университет РК, Раджкот, Индия

Адрес для корреспонденции:

Панкаж Б. Нария, Кафедра химии, Университет РК, Кастурбадхам, магистраль Бхавнагар, Трамба, Раджкот, Индия
E-mail: pankajnariya@yahoo.co.in
Тел: +919898081779

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Настоящий обзор рассматривает подробные описания различных фармакологических исследований, проведённых на *Leptadenia reticulata*, которое является источником нескольких активных составов. Растение *Leptadenia reticulata* подсемейства *Asclepiadaceae*, известное как дживанти, используется при лечении различных заболеваний, а также в роли лекарства в различных растительных препаратах. Установлено, что растение отличается широким спектром фармакологических активностей, среди которых антибактериальная, противоопухолевая, лактогенное действие, антиоксидантная активность, антиимплантационная активность, антиастматическая активность, обладает эффектом модуляции, активностью наночастиц серебра, гепатопротекторной активностью, противогрибковой активностью, антидиабетической активностью и противовоспалительной активностью. Как правило растение способствует укреплению общего состояния здоровья и жизнедеятельности, тона голоса, лечению глазных заболеваний, ночной (куриной) слепоты, кашля, гангрены и повышению иммунитета при беременности. В настоящем обзоре представлены новые научные открытия в области исследования этого растения с терапевтическим потенциалом и рассмотрены методы проведённых исследований. Данный обзор направлен на привлечение внимания учёных к потенциальному терапевтическому эффекту *Leptadenia reticulata* и его активных составов.