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Phytochemistry, pharmacology and traditional uses of *Leptadenia pyrotechnica*- An important medicinal plant

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ABSTRACT

Traditional Systems of medicines always played important role in the global health. In the traditional health medicinal plants providing a new areas of drug research. The demand for plant based medicines, food supplement, health products, pharmaceuticals and cosmetics are increasing in both developing and developed countries due to the growing recognition that the natural products are non toxic, have less side effects and easily available. *Leptadenia pyrotechnica* (Forsk.) commonly known as Kheep belonging to family Asclepiadaceae. *Leptadenia pyrotechnica* leafless much branched shrub. All parts of *Leptadenia pyrotechnica* are used in traditional medicines. The present article gives an account of updated information on its phytochemistry pharmacological properties. Ethnomedical uses say to possess significant antioxidant, anti-inflammatory, antibacterial, anthelmentic, antilipoxygenase, cytotoxic, antitumour, hypolipidemic and anti atherosclerotic activity. The present review contains wide number of isolated chemical constituents and various ethnomedical and traditional uses of *Leptadenia pyrotechnica*. It include information about historical background, conceptual basis, different disciplines studied in the systems, research and development aspects, drug manufacturing aspects and impact of globalization.

1. Introduction

Ayurveda is one of the world's oldest system of medicine. The sciences of life (Ayurveda) mainly emphasize on the balance of the body and mind which provides happiness, health and help to prevent illness.[1] Elimination of impurities and increase the resistant power of body is the main aim of Ayurveda.[2] The World Health Organization revealed that more than 80% of the world's population relies on traditional herbal medicine for their primary healthcare.[3] Herbal and natural products have enormous popularity as self-medication products.[4] Herbal medicines are the oldest remedies known to mankind. Herbs had been used by all cultures throughout history but India has one of the oldest, richest and most diverse cultural living traditions associated with the use of medicinal plants.[5] Medicinal plants are an important therapeutic aid for various ailments. In India, from ancient times, different parts of medicinal plants have been used to cure specific ailments.[6] *Leptadenia pyrotechnica* (Forsk.) belonging to family Asclepiadaceae, commonly known Khimp. It is an erect, ascending, leafless shrub up to 0.5 meter to 2.6 meter high with green stem and yellowish green alternating much branched with a valuable desert plant. It is commonly used in traditional system of medicine.[7]

1.2 Taxonomical Classification

Kingdom	-	Plantae
Subkingdom	-	Viridaeplantae
Phylum	-	Magnoliophyta
Subphylum	-	Spermatophytina
Class	-	Magnoliopsida
Subclass	-	Lamiidae
Order	-	Gentianales
Family	-	Asclepiadaceae
Genus	-	*Leptadenia*
Specific	-	*Pyrotechnica*

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1.3 Synonyms

India	-	Khip, Kheep, Khimp
Sudan	-	Kalumbo, Saabe, Kalimbo
Pakistan	-	Kip, Khip, Kheep

1.4 Species of *Leptadenia* [7]

Leptadenia arborea	-	*Leptadenia hastate*
Leptadenia abyssinica	-	*Leptadenia spartum*
Leptadenia delilei	-	*Leptadenia heterophylla*
Leptadenia ephedriformis	-	*Leptadenia jacquemontiana*
Leptadenia forskalli	-	*Leptadenia lancifolia*
Leptadenia gracilis	-	*Leptadenia madagascariensis*
Leptadenia pallid	-	*Leptadenia pyrotechnica*
Leptadenia reticulate	-	*Leptadenia spartium*

1.5 Geographical distribution

Leptadenia pyrotechnica occurs throughout the state of Rajasthan and found in dry habitats particularly in desert zones. In India it is commonly found in Punjab, Banswara, Palod, Dungarpur, Kota and Western Uttar Pradesh.[8]

1.6 Morphology

Leptadenia pyrotechnica is an erect, ascending, shrub up to 0.5 meter to 2.6 meter high with green stem and pale green alternating bushy branches with watery sap. Leaf is rarely found and are deciduous when present are 2.6-6.5 X 0.2-0.3 cm, sessile, narrowly linear to linear lanceolate, caduceus. Flowers are in cluster lateral umbellate cymes, greenish yellow. Corolla lobes valvate, outer corona is of 5 scales, stamina corona of raised undulate fleshy ring. Each flower is bisexual pentamerous actinomorphic, sepals joined as base only, corolla sympetalous. Follicles 7.0-14.0X0.5-0.8 cm, terete, lanceolate, tapering to selender beak, glabrous. Seeds are 5-7 mm long, ovate lanceolate, glabrous, hairy with tufted hairs 2.6-3.7 cm long. Flowering and fruiting occurs from August to January.[9]

1.7 Traditional uses

Leptadenia pyrotechnica and its parts are traditionally used for different purposes. The fiber of *Leptadenia pyrotechnica* is used as antihistaminic and expectorant.Whole plant is used for the treatment of wound in Yemen folks and proved to have antibacterial activity against *Staphylococcus aureus & Bacillus subtilis.* Fresh juice of the plant is used for abortion. Plant sap is applied to eczema and other skin disease and is also given in diabetes. The latex or the leaf paste is applied over the thorn injury for thorn removal. Whole plant infusion is mixed with buttermilk and given for uterine prolapsed and stomach disorders in sariska region of Rajasthan. It is used to cure constipation and is considered good for health in Bikaner region of Rajasthan. In the sudanodeccanian region of central Sahara it is traditionally used in fever, cough, kidney disorders, stones, urinary disease.[10-18]

2.Phytochemistry

Mohammad et al. (2011) studied the aqueous ethanolic extract of aerial part of *Leptadenia pyrotechnica* and found that the crude extract contained five polyphenolic compounds (gallic acid, vanillic acid, caffeic acid, epicatechin and quercetin-3-β-D-glucoside) in which epicatechin, quercetin-3-β-D-glucoside and vanillic acid were highest in concentration.[19]

Amal et al. (2009) studied the antitumour activity of L. pyrotechnica and isolated the six flavanoids namely kaempferol-3-O-α-L-rhamnopyranosyl(1’’’→6’’)-O-β-D glucopyranoside, kaempferol 4’-methyl ether 3-O-β-D-rutinoside (kaempferide 3-O-β-D-rutinoside), kaempferol-3-O-β-D-glucopyranosyl (1’’’→6’’)-O-β-D-glucopyranoside, kaempferol-3-O-β-D-glucopyranoside, texasin 3-O-glucoside & quercetin 3-O-galactoside and concluded that the antitumour activity of L. pyrotechnica seemed mainly due to the flavanoids present in it.[20]

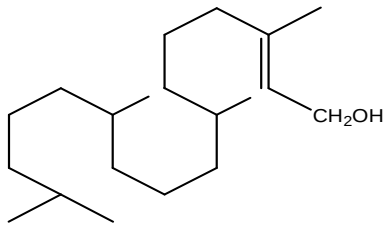
Moustafa et al. (2009) reported the isolation of twenty four alkaloids from the aerial parts of the *Leptadenia pyrotechnica*. Almost all of the alkaloids belonged to pyridine, pyrrole, pyrazine & indole types which were characterized by using GC-MS Analysis.[21]

Moustafa et. al. (2009) reported three cardiac glycosides from *Leptadenia pyrotechnica* which were characterized as 14,19-dihydroxycard-20(22)-enolide-3-o-[β-d-glucopyranosyl-β-d-digitoxoside],14,19-dihydroxycard-20(22)-enolide-3-o-[β-d-glucopyranosyl-β-d-ucopyranoside] and 14 ,19-dihydroxycard-20(22)-enolide-3-o-β-d-digitoxoside. The isolation & characterization of these compounds were carried out by RLCCC, HPLC, FAB, ESI, MASS & N.M.R.[22]

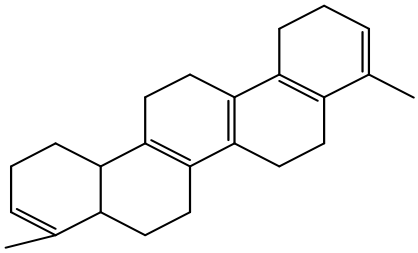
Moustafa et al. (2009) reported six Flavonoids from aerial parts of *Leptadenia pyrotechnica*. which were characterized as kaempferol-3-o-α-1-rhamnopyranosyl(1’’’→6’’)-o-β-d-glucopyranoside, kaempferol-3-o-β-d-rhamnopyranosyl(1’’’→6’’)-o-β-d-glucopyranoside, texasin-7-o-β-d-glucopyranoside, kaempferol-3-o-β-d-glucopyranoside, kaempferol and kaempferide-3-o-αrhamnopyranosyl(1’’’→6’’)-o-β-d-glucopyranoside. The isolation & characterization of these compounds were carried out by LPLC, PC, HPLC, MASS, N.M.R, U.V. etc. [23]

Sherwani et al. (2009) reported the isolated 12, 13-epoxy octadec-cis-9-enoic acid (vernolic acid) (32%) from the seeds of *Leptadenia pyrotechnica* which was identified and characterized by using standard gunstone’s method of direct acetolysis. The fatty acid was also isolated by using chromatographic methods and structure elucidation was carried out by spectral techniques.[24]

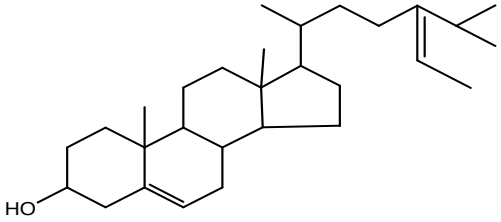
Moustafa et al. (2007) reported various lipid constituents from the aerial parts of the *Leptadenia pyrotechnica*. The compounds were characterized as three terpenes i.e Phytol, Squalene and taraxerol; five sterols as cholesterol,campasterol, stigmasterol, β-sitosterol and Fucosterol; fifteen fatty acids, eleven n-alkanol,series of n-alkane, one n-alkene named as 3-tetradecene and first time eighteen aromatic hydrocarbons were isolated i.e. 5-phenyl-undecanes and 6-phenyl-tridecane were the major constituents. The structures of these compounds were established by GC, GC-FID, GC-MS and Spectroscopic techniques.[25]



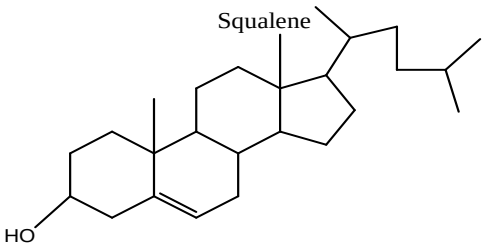
Phytol

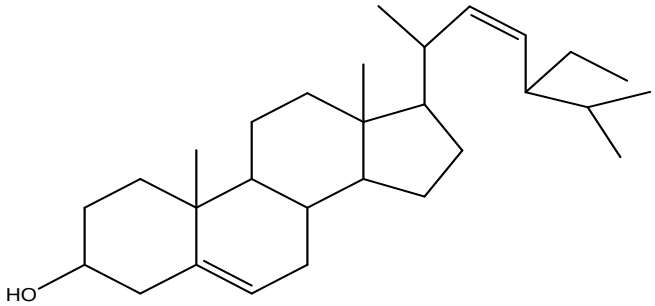


Squalene



Fucosterol





Stigmasterol

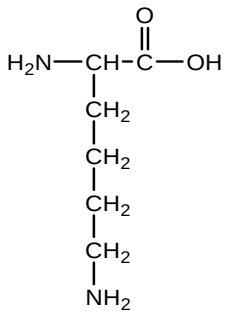
Cioffi et al. (2006) reported eighteen-new pregnane glycosides from the whole plants of the *Leptadenia pyrotechnica* with sarcostin,11-hydroxy sarcostin and deacetylmetaplexigenin as the aglycon moieties and acetyl,benzoyl,cinnamoyl,p-coumaroyl and nicotinoyl ester moieties linked at C-12 and/orC-20 of the aglycon and hexapyranose, 6-deoxy-3-o-methylhexapyranose and 2,6-dideoxy-3-o-methyhexapyranose sugars linked at C-3 of their aglycons.[26]

Afifi et al. (2002) reported sterols, triterpenes and five flavonoid compounds from the *Leptadenia pyrotechnica*. The sterols and triterpenes were β-amyrin, β-sitosterol, lupeol and betulin and five flavonoids were quercetin, kaempferol-3-o-β-D-glucoside, isorhamnetin-3-o-rutinoside, quercetin-3'-o-β-D-glucoside & rutin. The isolation and identification of these compounds were achieved through different chromatographic and spectroscopic methods.[27]

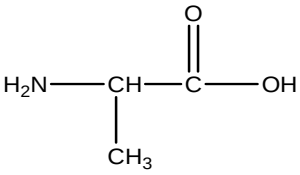
Ali et al. (2001) reported a new glycerol-oleanolic acid conjugate named pyrotechnoic acid from the ethanolic extract of *Leptadenia pyrotechnica* and the structure was established with the aid of 1D and 2D N.M.R. Spectroscopy.[28]

Manavalan et al. (1980) reported the isolation of the two triterpenoid from the dried aerial parts of *Leptadenia pyrotechnica*. i.e. taraxerol, fernenol, β-sitosterol. Such terpenoids were reported for the first time from this genus.[29]

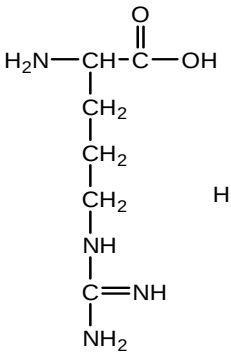
Dhawan et al. (1976) reported free pools of amino acids and sugars from the *Leptadenia pyrotechnica*. The compounds were characterized as l-lysine-alanine, l-arginine, l-threonine, l-methionine and l-isoleucine. Two dipeptides were also characterized as dl-alanyl-l-alanine and glycyl-l-alanine and the sugar & isolated from the stems of the *Leptadenia pyrotechnica* were raffinose, sucrose, glucose, and fructose.[30]



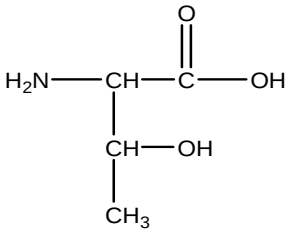
Lysine



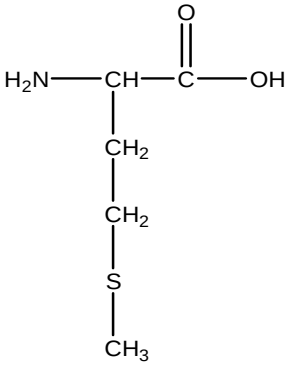
Alanine



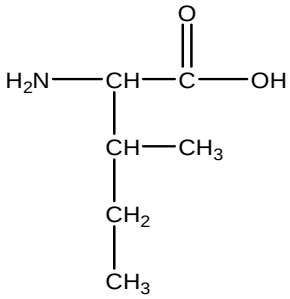
Arginine



Threonin

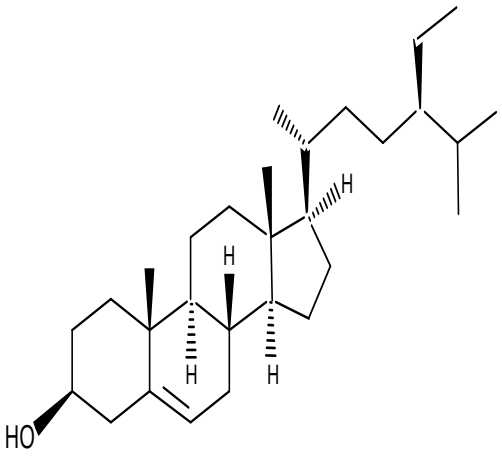


Methionine

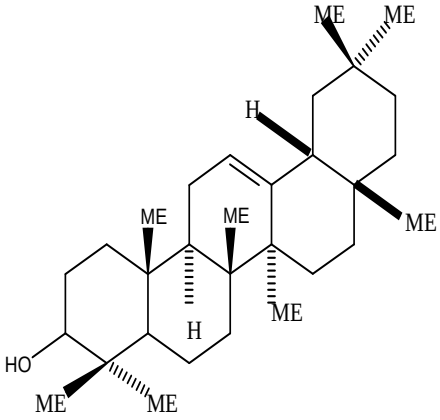


Isoleucine

Rastogi et al. (2008) Mentioned the presence of cetyl alcohol, β-sitosterol, n-triacontane, β-amyrin acetate & Lupanol-3-O-diglucoside. However, the uncharacterized compound namely leptidine glucoside was isolated. i.e. whole plant of *Leptadenia pyrotechnica*.[31]



β-Sitosterol



β-amyrin

3.Pharmacology

Saleh *et al*. (2012) showed antioxidant and anti-inflammatory activities of ethanolic extracts of *Leptadenia pyrotechnica*, Haloxylon salicornicum and Ochradenus baccatus. The ethanol extracts of *L. pyrotechnica* (400 mg/kg), H. salicornicum (200 and 400 mg/kg) and O. baccatus (400 mg/kg) produced significant reduction of carrageenan induced paw edema. It was noticed that oral pretreatment with the same extracts and doses for 5 days before induction of colitis, protected against diarrhea, colonic ulceration and MPO activity elevation. Results showed valuable effect of *L. pyrotechnica*, H. salicornicum and O. baccatus extracts against acetic acid-induced ulcerative colitis possibly by their antioxidant and anti-inflammatory properties.[32]

Mehmooda *et al.* (2012) showed antibacterial activity of *Leptadenia pyrotechnica* roots and fruit extracts against Staphylococcus epidermidis and S. aureus by using agar-well diffusion assay. S. aureus was found highly susceptible and inhibited by all solvent extracts. These plant parts effectively inhibited the growth of both the pathogens; however, root extracts showed a little more supremacy in this respect. Methanolic extract of both parts generated the best results by inhibiting growth of both pathogens.[33]

kumar *et al.* (2011) evaluated the methanolic extract of whole plant *Leptadenia pyrotechnica* for Anthelmentic activity against Pheretima posthuma. They concluded that it took less time to cause paralysis and death of Pheretima posthuma as compared to the standard drug. Consequently *Leptadenia pyrotechnica* possessed dose dependant anthelmintic activity (50 and 100 mg/kg).[34]

Mohammad et al. (2011) studied the antioxidant, anti-lipoxygenase and cytotoxic activity of the aqueous ethanolic extract of aerial part of *Leptadenia pyrotechnica* and found that the crude extract contained five polyphenolic compounds (gallic acid, vanillic acid, caffeic acid, epicatechin and quercetin-3-β-D-glucoside) in which epicatechin, quercetin-3-β-D-glucoside and vanillic acid were highest in concentration. They also proved that there was a linear correlation between the total phenolic content and the reducing antioxidant capacity of plant extract and that the ethyl acetate fraction exhibited relatively better antioxidant properties. The ethyl acetate fraction and crude ethanolic extract possessed significantly higher LOX inhibitory activity (IC50 = 2.75µg/ml). The higher cytotoxicity of *Leptadenia pyrotechnica* was due to the antioxidant property and also occurred non-phenolic compounds with stronger activity.[35]

Khasawneh *et al*. (2011) investigated antioxidant, anti-lipoxygenase and cytotoxic activity of ethyl acetate, n-butanol and water partitioning fractions of aerial parts of the *Leptadenia pyrotechnica* by using FRAP, ABTS, DPPH and β-carotene bleaching assay for antioxidant activity & MCF-7 Human breast cancer cell line or cytotoxic activity which showed good antioxidant, anti-lipoxygenase and cytotoxic potentials.[36]

Amal *et al*. (2009) studied the antitumour activity of L. pyrotechnica and isolated the six flavanoids namely kaempferol-3-O-α-L-rhamnopyranosyl(1’’’→6’’)-O-β-D glucopyranoside, kaempferol 4’-methyl ether 3-O-β-D-rutinoside (kaempferide 3-O-β-D-rutinoside), kaempferol-3-O-β-D-glucopyranosyl (1’’’→6’’)-O-β-D-glucopyranoside, kaempferol-3-O-β-D-glucopyranoside, texasin 3-O-glucoside & quercetin 3-O-galactoside and concluded that the antitumour activity of L. pyrotechnica seemed mainly due to the flavanoids present in it.[37]

Jain *et al.* (2007) studied the hypolipidemic & anti-atherosclerotic efficacy of methanolic extract of the aerial part of L. pyrotechnica in cholesterol fed rabbits. The administration of L. pyrotechnica (250 mg/kg body weight per day orally) extract significantly ($p<0.001$) prevented the rise in serum total cholesterol, LDL-cholesterol, VLDL-cholesterol, triglycerides and atherogenic index. Hepatic and aortic total cholesterol, triglycerides and lipid peroxidation were also lowered significantly in the extract treated rabbits. The Plant extracts also significantly prevented the atheromatic changes and plaque formation in the aorta and favoured increased fecal cholesterol output. Thus, the results indicated hypolipidemic and antiatherosclerotic effects of methanolic extract of L. pyrotechnica.[38]

Mahida *et al*. (2007) investigated antibacterial activity of methanolic extract of the aerial part of the *Leptadenia pyrotechnica* which were tested against Staphylococcus epidermidis, Staphylococcus aureus, Salmonella typhi and Salmonella paratyphi-A and showed minimum inhibition in the petri dishes.[39]

AlFatimi *et al*. (2007) investigated antioxidant, antimicrobial and cytotoxic activities from the Dichloromethane, methanol and aqueous extracts of the whole plant of the *Leptadenia pyrotechnica* by using DPPH method, antimicrobial activities were tested invitro by agar diffusion method against Staphylococcus aureus, Bacillus Subtilis, Escherichia coli, Pseudomonas aeruginosa and Micrococcus flavus at 10, 50 % conc. of *Leptadenia pyrotechnica* which showed very weak effects and cytotoxic activities using FL- cells, a human amniotic epithelial cell lines which showed strong effects.[40]

Katewa *et al*. (2006), reported *Leptadenia pyrotechnica*, known as Khimp in Shekhawati region of Rajasthan, had been employed for the treatment of skin diseases and diabetes.[41]

Cioffi *et al.* (2006) investigated anti- proliferative activity of the whole plant of the *Leptadenia pyrotechnica*.[42]

Sharma *et al*. (2003) investigated *in vivo* and *in vitro* antimicrobial activity of the stem extracts of the *Leptadenia*

pyrotechnica against the fusarium oxysporum at 10, 50 & 100% conc. and showed minimum inhibition.[43]

4. Conclusion

Medicinal plants are the local heritage with the global importance. World is endowed with a rich wealth of medicinal plants. Medicinal plants also play an important role in the lives of rural people, particularly in remote parts of developing countries with few health facilities. Presently there is an increasing interest worldwide in herbal medicines accompanied by increased laboratory investigation into the pharmacological properties of the bioactive ingredients and their ability to treat various diseases. Numerous drugs have entered the international through exploration of ethnopharmacology and traditional medicine. Although scientific studies have been carried out on a large number of Indian botanicals, a considerably smaller number of marketable drugs or phytochemical entities have entered the evidence based therapeutics. Efforts are therefore needed to establish and validate evidence regarding safety and practices of Ayurvedic medicines. The outcome of these studies will further expand the existing therapeutic potential of *Leptadenia pyrotechnica* and provide a convincing support to its future clinical use in modern medicine.

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