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Insights into the pharmacotherapeutic Potentials of a well-known Indian medicinal plant *Artemisia pallens*

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Abstract
Natural herbal medicines are in great demand in the developed countries for primary health care because of their safety, efficacy and minimal side effects. Since ancient era plants and their extracts have been analyzed and reported for their bioactive components which contribute to various significant therapeutic properties. *Artemisia pallens* Wall, a medicinally important plant, belongs to family Asteraceae. The phytochemical studies of the plant parts showed the presence of alkaloid, phenols, phenylpropanoids, glycosides, flavonoids, saponin, triterpene, steroids, fatty acids, fatty esters hydrocarbons, and miscellaneous compounds which could be used in traditional medicines to cure various health issues. *A. pallens* has been used in Ayurveda for the treatment of measles, cough, cold, depression, diabetes and high blood pressure. The plant contains essential oil called Davana contributes to the various therapeutic properties like anti-microbial, anthelmintic, antipyretic, anti-spasmodic, wound healing activity, stimulant, etc. It is the most important aromatic plants used commercially in perfumery and cosmetic industries and India is the major exporters of Davana oil to the rest of the world. The current review deals with the study of existing therapeutic importance of *A. palllens* with diverse future potential perspectives.

Keywords: *Artemisia pallens*, Davana, phytochemicals, therapeutics, natural, traditional

Introduction
Mother Nature has been a great source of medicinal agents from the ancient era and the number of drugs has been isolated from various natural sources. These medicines are described traditionally in our ancient text like in Vedas. These medicines or herbal remedies play a vital role in treating various ailments as it contains natural bioactive compounds which are responsible for its various therapeutic activities. Over 50% of all modern clinical drugs are of natural product origin and natural products play an important role in drug development programs in the pharmaceutical industries [1].

India is one of the richest sources of medicinal and aromatic plants. India has abundant natural flora and fauna which is the wealth of the nation. India has the diversity of agro-climatic conditions and different ecosystems from temperate in Himalaya to tropical in South India, Dry in Central India to humid and wet in Assam and Kerala. This diversity provides favorable conditions for the growth of different medicinal and aromatic plants. Herbal drugs are simple, effective, and offer a broad spectrum of activity and because of these advantages, the demand for plant-based medicines is increasing worldwide [2].

The use of plants as a source of medicine has been inherited and is an important component of the health care system in India and abroad even in the present era. These are not only used for primary healthcare in rural areas in developing countries but also in developed countries as well where modern medicines are predominantly available [3].

The genus *Artemisia* of family *Asteraceae* (*Compositae)* is one of the largest and most complicated and difficult taxa to understand. The generic name 'Artemisia' is derived from 'Artemis', which refers to Diana, a Greek Goddess. There are about 500 species of *Artemisia* reported in the world and out of which about 45 species, are found in India. However, there are only a few *Artemisia* species, which have been collected and their essential oil has been assayed and out of these some are the cultivated ones like; *A. pallens* and *A. annua*, the essential oils are well known and marketed and have a good demand [4]. Aromatic plants are the natural source of perfumes and fragrance widely exploited by essential oil industries across the world. India stands 3rd in essential oil production in the world, the first being France while Britain takes the 2nd place.

A. pallens Walls ex D.C. (Davana) (Asteraceae) is an aromatic medicinal herb native in the southern part of India, especially in the states of Karnataka, Tamil Nadu, Andhra Pradesh, and Maharashtra. In the regional languages of the south, it is known by several names as "davanam" in Tamil, "davanamu" in Telugu and "davana" in Kannada. Its leaves and flowers are highly valued in the making of floral decorations and oils. A number of researchers have reported the chemical composition of oil obtained from *A. pallens* plant [5]. Leaves are very small, bluish-green with yellow flowers and inconspicuous. It is utilized in traditional Ayurvedic medicinal formulations. The oil of *A. pallens* is used as a flavoring agent for cakes, pastries, tobacco, and in some costly beverages. Reported pharmacological properties of the plant are anthelmintic, tonic, antipyretic, anti-diabetic, anti-fungal, anti-bacterial, anti-microbial, anti-oxidant, analgesic, stimulant, immunomodulator, and anti-inflammatory activity [6,7].

Davana is an important high valued annual aromatic herb of India and commercially cultivated in south India as a short duration crop from November to March. India has a monopoly in the production and export trade of davana oil.

Davana is traditionally used in religious ceremonies and in making garlands, bouquets, floral decorations, and floral chaplets, lends an element of freshness and a rich sumptuousness of fragrance to religious occasions [8,9].

Plant Profile

- **Family:** *Asteraceae*
- **Indian Name:** Davanam (Sanskrit), Marikolundu (Tamil), Davana (Hindi, Kannada)
- **Species and Varieties:** *A. pallens Wall*
- **Distribution:** All the parts of India

Davana is an aromatic, erect herb, about 60 cm tall, with much-divided leaves and small yellow flowers. The stem and leaves are covered with grayish-white tomentum. The leaves are alternate, petiolate, and lobed. The inflorescence is capitulated with flowers that are peduncle to sessile, axillary or forming lax racemes, simple, heterogamous having bisexual disc florets in the centre and a few pistillate ray florets on the periphery [10].

The outer florets are glabrous except for a few cottony hairs, tubular, generally 3-lobed. The stigma is generally 2-lobed and rarely 3-lobed. The inner florets are glabrous except for a few cottony hairs, tubular, 5-lobed, and bisexual: the stamens are 5 in number with free, epipetalous filaments and a dithecous inflorescence: it has syngenecious anthers which are connective, prolonged, tapering style and bifid [11].

Cultivation

It is being commercially cultivated in Karnataka, Maharashtra, Kerala, Tamil Nadu, and Andhra Pradesh in an area of about 1000 hectares for its fragrant leaves and flowers. It grows from seeds and cuttings and reaches maturity in four months. The plant is woody in the lower part of the stem, but with yearly branches. Davana is mostly cultivated in the red soil regions in South India. It comes up very well in rich loamy soils. Davana is an annual herb, requiring about four months reaching maturity, at which it attains a height of about around one and a half feet. The season is very important when the crop is grown for the production of oil. The crop is allowed to grow until it flowers, which take about 4 months from sowing. It is grown as short term crop from November to February/March and as a rotation crop extending up to April/May. The crop does not withstand heavy rains. The total yield of the main crop and the ration crop is about 14 tons per hectare, which on shade drying and distillation yields about 10 kg of Davana oil. In large scale distillation, an average yield of 3.2% from a material dried for about 2 days may be considered satisfactory. The oil content in davana is maximum in the flower head and is much less in the leaf and stem [12,13].

Phytochemical Screening

The various solvent extracts of the aerial parts of *A. pallens* were subjected to preliminary phytochemical screening using the standard screening methods [14,15].

Alkaloids

1 ml of 1% HCl was added to 3 ml of the extract in a test tube. The mixture was then heated for 20 minutes, cooled, and filtered. About 2 drops of Mayer's reagent was added to 1 ml of the extract. A creamy precipitate was an indication of the presence of alkaloids.

Tannins

1ml of freshly prepared 10% $Pb(CH_3COO)_2$ was added to 1ml of the extract. The presence of white precipitate showed the absence of tannins.

Phenolic compounds

2 drops of 5% $FeCl_3$ to the extract in a test tube. The presence of greenish precipitate indicated the presence of phenolic.

Glycosides

10 ml of 50% H_2SO_4 was added to 1 ml of the extract and the mixture heated in boiling water for about 15 minutes. 10 ml of Fehling's solution was then added and the mixture boiled. A brick-red precipitate was confirmed for the presence of glycosides.

Flavonoids

1 ml of 10% NaOH was added to 3 ml of the extract. There was yellow coloration which is indicative of the presence of flavonoids.

Steroids

Salkowski test: 5 drops of concentrated H_2SO_4 was added to 1 ml of the extract in a test tube. Red coloration was observed which is indicative of the presence of steroids.

Saponin

- **Frothing test/Foam Test:** 2 ml of the extract was vigorously shaken in the test tube for 2 minutes. Frothing was observed.
- **Emulsion Test:** 5 drops of olive oil was added to 3 ml of the extract in the test tube and vigorously shaken. The presence of stable emulsion formed indicates the presence of saponin.

Traditional Uses

The leaves and flowers yield an essential oil known as oil of Davana. Several species yield essential oil and some are used as fodder, some of them are a source of the valuable anthelmintic drug santonin. Davana blossoms are offered to Shiva, the God of Transformation, by the faithful, and decorate his altar throughout the day. Davana has been widely used in Iraqi and Indian medicine for the treatment of diabetes mellitus. Oral administration of an aqueous/methanolic extract from the aerial parts of the plants was observed to reduce diabetes in glucose-fed hyperglycemic and alloxan-treated rabbits and rats [16,17,18,19].

- Davana oil is used in making perfumery and fragrances.
- Davana oil is soothing to rough, dry, chapped skin, skin infections, and cuts.
- *A. pallens* is a preferred food for the larvae of a number of butterfly species.
- Davana leaves and stalks are used in making bouquets, garlands, fresh or dry flower arrangements.
- Davana oil is emotionally balancing and calming, aids in calming down anxiety.
- When applied on the skin, Davana is said to smell differently on different persons. This peculiar property is highly valued in high-class perfumery to create fragrances with truly individual notes.
- Davana has been traditionally used in Indian folk medicine for the treatment of diabetes mellitus.
- It has immunomodulating, anthelmintic, anti-pyretic, and wound healing activity.

- It is used as an aphrodisiac and mood elevator.
- It is a remarkable anti-septic and disinfectant.
- This oil also has mild insect repellant properties.
- It is used to reduce the risk of chronic diseases, cardiovascular disorders, and cancer.

Phytochemical Constituents

The chemical constituents of *A. pallens* are saponin alkaloids, sterol glycosides, davanone, isodavanone, linalool, dehydro-α-linalol, terpinen-4-ol, davanafurans, artemone, eudesmanolide, pallensin, epipallensin, santonin, germacranolide, artesin (sesquiterpene ketones), stereoisomers hydrocarbons, ester, oxygenated compounds, tannins, mucilage, and phenols (Figure 1). It was concluded that all extracts contain more important chemical constituents for various pharmacological activities [15,16].

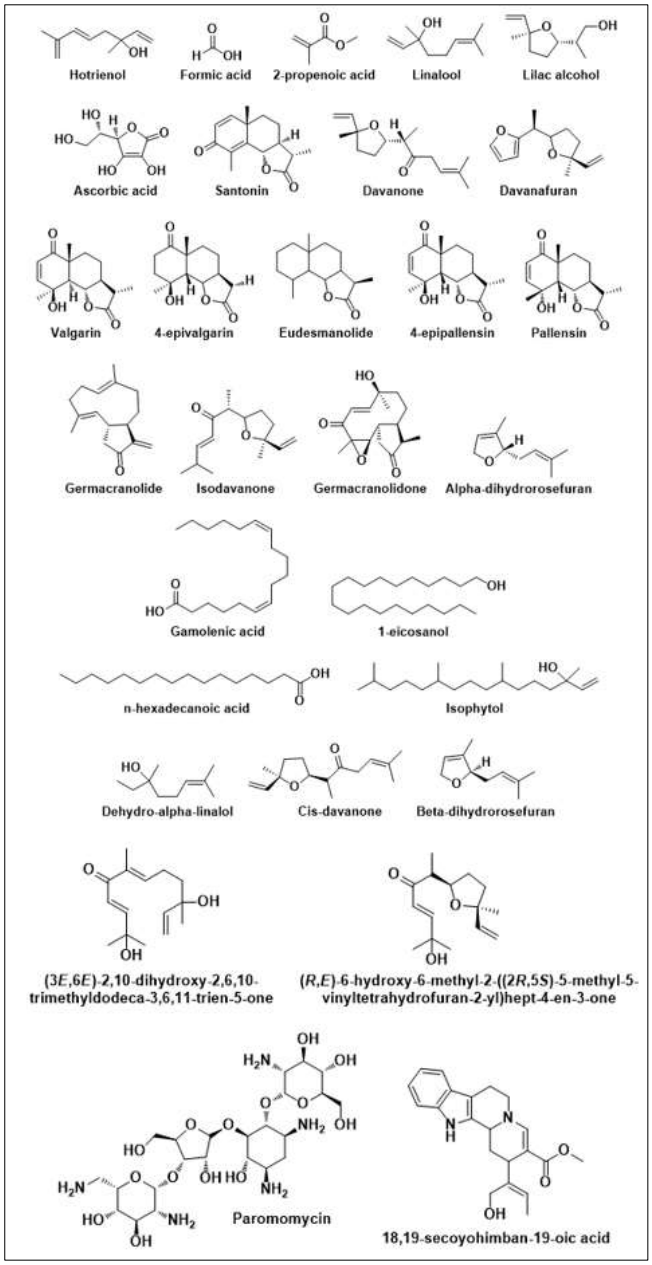

Fig 1: Major phytoconstituents present in *A. pallens*.

Pharmacotherapeutic potentials

Analgesic and Anti-inflammatory activity

A. pallens was studied for anti-inflammatory action by carrageenin-induced rat paw edema. The analgesic activity was tested by tail-flick method and hot plate method in albino rats and mice. The methanolic extract of *A. pallens* in doses of 100 mg/ml, 200 mg/ml, and 500 mg/ml showed 68.85%, 74.53%, and 81.13% inhibition of paw edema respectively at the end of 3 hrs. In the hot plate and tail flick model, the methanolic extract of *A. pallens* in the above doses increased the pain threshold significantly also administration of *A. pallens* showed dose-dependent action in all experimental animal models. The plant had saponins, flavonoids, sesquiterpenoids, oils, phenols, and tannins. The results of the present study suggest that *A. pallens* has potent analgesic and anti-inflammatory activities [17].

Anti-oxidant

Anti-oxidants are molecules that can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. The dietary antioxidants include selenium, vitamin A and the related carotenoids, vitamin C, vitamin E, various phytochemicals such as lycopene, lutein, and quercetin. They are believed to play a role in preventing the development of such chronic diseases such as cancer, heart disease, stroke, Alzheimer's disease, rheumatoid arthritis, and cataract. *A. pallens* is a valuable medicinal plant. The essential oils from *Artemisia* are of botanical and pharmaceutical interest. Its root, stem, bark, leaves, fruits, seeds, and seed oil are applied in traditional medicines to cure various health complaints. The anti-oxidant potential of various extracts is determined using spectrophotometric methods. The results of DPPH and Nitric Oxide assay confirm that extracts obtained from roots of *A. pallens* possess significant anti-oxidant properties [18].

Anti-microbial activity

The essential oils are one of the secondary metabolites of plants and consist of different chemical components such as terpenoids, phenols, alcohols, aldehydes, ketones, etc. Most probably terpenoids present in these are responsible for inhibiting the growth of organisms. In order to search for antimicrobial activity of secondary metabolites, screening of aerial parts of *A. pallens* was carried out. Air shade-dried powdered plant material was extracted using solvents of increasing polarity from non-polar (n-hexane), semi-polar (chloroform) to polar (methanol). Extracts were analyzed for their antibacterial capacity against six bacterial strains and yeast strain. The antibacterial activity was determined by using the disc diffusion method. *Bacillus cereus* was found to be a more susceptible strain. Only the methanolic extract of *A. pallens* showed the activity. Therefore, this was selected for further investigation to determine its therapeutic potential. The anti-bacterial activity of methanolic extract of *A. pallens* is found to be more active whereas non-polar and semi-polar extract does not show any activity against the test organisms [19]. Two different extracts of *A. pallens* is evaluated for its antimicrobial properties (zone of inhibition) in triplicate and their mean value has been calculated. The gold standard, 0.2% chlorhexidine has been tested for its antimicrobial property in triplicate and means value will be calculated. Acetone extract and ethanol extract show 0.5 mm and 2 mm zone of inhibition (ZOI), respectively. Ethanol extract represents maximum zone of inhibition compared to acetone extract. Acetone extract shows average ZOI (1 mm) which is comparable to the gold standard. Ethanol extract had a

significant inhibitory effect on the growth of microorganisms [20].

Anthelmintic activity

The essential oil of *A. pallens* exhibited excellent anthelmintic activity against the earthworms, roundworms, and tapeworms at all the three concentrations. The activity of the essential oil has been found to be better than that of piperazine phosphate against these worms. The time required for paralysis and death of roundworms and tapeworms in the case of essential oil was two to three times less than the standard piperazine phosphate, under same concentrations. Against the earthworms the activity of the essential oil is 85% more than that of piperazine phosphate at the concentration of 0.1%. The control Tween 80 and normal saline did not show any activity against the worms. The observed definite anthelmintic activity of the essential oil against these worms not only confirms the reported use of *A. pallens* as an anthelmintic in the Indian system of medicine [21].

Anti-cancer activity

Saponins are plant glycosides with favorable antitumorigenic properties as inhibit tumor cell growth by cell cycle arrest and apoptosis with IC_{50} value of up to 10 µg/ml. A reduction in the expression of the anti-apoptotic protein Bcl-2 together with caspase activation was observed. The member of newly isolated and described saponin is increasing constantly and many further saponins will be identified due to improved methods of purification and detection. Saponins possess impressive anticancer effects and might help to develop improved anticancer regimens. The combined application of saponins with other antitumor drugs offers an interesting development in cancer treatment since in other studies reports additive or even synergistic effects between saponins and other drugs have been observed. These combinations will lead to essentially improved possibilities for the treatment of cancer. Most important is the saponin mediated potentiation of tumor growth inhibition and the possibility to overcome drug resistance [22].

Anti-diabetic activity

The anti-diabetic activity of *A. pallens* might be due to the presence of many natural compounds that might play a role in controlling diabetes. Oral administration of the methanol extract of the aerial parts of *A. pallens* Wall which has been used in Indian folk medicine for the treatment of diabetes Mellitus leads to significant blood glucose-lowering effect in glucose fed hyperglycemic and alloxan-induced diabetic rats. This effect of the extract was found to be dose-dependent. In fasted normal rats, the extract caused a moderate hypoglycemic effect at a higher dose whereas the water extract was found to be inactive. The methanolic extract of *A. pallens* seems to be the best choice for preparing anti-diabetic medicines because of its anti-diabetic properties [23].

Larvicidal activity

Mosquitoes and other parasites and insects can transmit major diseases and ultimately cause millions of deaths every year. Also to our concern, these are getting resistant to synthetic market drugs over time. Hence, there is a need for alternative forms of drugs like herbal or Ayurvedic to avoid such kind of concerns. *A. nilagirica* as already has been discussed to contain many essential oils and other chemical compounds, based on this factor a study was conducted to examine the larvicidal activity of the plant. In this study, the plant extract was proved significant against the action of *Aedesal bopictus* [24].

Conclusion

This present interesting review comprehensively highlighted the overall basics, plant profile (Genus, Species, Family, Distribution, and Varieties), cultivation aspects, traditional uses, prominent pharmacotherapeutic potentials (anti-cancer, anti-diabetic, anti-inflammatory, anti-oxidant, anti-microbial, larvicidal, anthelmintic, and analgesic), phytochemical screenings, and major phytochemical constituents present in various parts (root, stem, leaf, seed, and fruit) of *A. pallens*. This information will be quite useful for the enthusiastic modern-day researchers of numerous streams (pharmacognosy, chemistry, botany, natural products, medicine, etc.) in developing diverse imperative formulations for treating several key ailments. This study will also open new avenues for therapy of both human and veterinary perspectives.

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