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Artemisia pallens Wall. ex. DC: A comprehensive review

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ABSTRACT

Davana (*Artemisia pallens* Wall. ex DC) is a well-known and precious essential oil-bearing plant under the family Compositae (Asteraceae). It is an erectly grown herbaceous plant exclusively cultivated as a short-term crop in south India during winter. It is distributed in the northern hemisphere in subtropical Africa, South Africa, West America, and South America; however, it is indigenous to southern India. The yearly productivity of davana oil typically falls between 8 to 10 tones. Davana oil is mainly used to flavor pastries, cakes, tobacco, and some beverages. It consists of diverse phyto-molecules and is an important and unique commodity in the fragrance, flavor, and liquor industries. It has excellent biological potential and contains volatile and nonvolatile constituents such as terpenoids, flavonoids, and alkaloids, which have high pharmacological values. Several investigations have focused on validating the importance of chemical constituents and the biological efficacy of essential oils and various extracts in multiple industries. The review focuses on the complete agronomic practices, botany, breeding, biotechnology, and chemistry of davana essential oil (DEO), *viz*, volatile and nonvolatile constituents, phytomedicinal and pharmacological properties, which may help researchers achieve their future goals for approaching its industrial or commercial viability as a natural product ingredient.

Implication for health policy/practice/research/medical education:
This review article provides comprehensive information on davana in all aspects of production technology, essential oil, chemistry, and application in the flavor, fragrance, and pharmaceutical industries. The provided information, other than food industry, might be used for new drug development.

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Introduction

The genus *Artemisia* is renowned for its aromatic and pharmaceutical properties, having broad applications in various industries. The plants of this genus are mostly distributed in the northern hemisphere, subtropical Africa, South Africa, West America, and South America. This genus is recognized by 475 species in the world (1), of which 47 species and 19 varieties are distributed in India (2). Among the 47 species, 4 of ones are endemic to India (3). *Artemisia pallens*, a domesticated species, is highly valued for its sensitivity and economic significance as an aromatic crop. It is exclusively cultivated for its essential oil and ornamental purposes. *A. pallens,* locally known as davana (Kannada)/davanam (Tamil), is indigenous to southern India and was introduced into Myanmar (1). It is a 45-60 cm tall, erect-branched annual herb with greyish whitish tomentum (4). The inflorescence head or capitulum is axillary, peduncled to sessile, and heterogeneous, consisting of yellow-colored glabrous florets. Its cultivation is widespread in southern Karnataka and also found in states such as Kerala, Maharashtra, and Tamil Nadu (5). The natural habitat of davana is unknown. Though it is said to be native to southern India, it might have been brought from the Himalayan region. It can be evident from the distribution of all other Indian *Artemisia* species reported from the Himalayan region excluding

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A. nilagirica (C.B. Clarke) Pamp. and *A. indica* Willd. Presently it is only under cultivation and the duration of davana brought to cultivation is immemorial. Davana is one of the winter-loving crops. The crop cycle is completed within four months and this crop is more convenient for small land farmers. The aromatic oils derived from various species of *Artemisia* have been prized for their flavor-enhancing properties and contributions to medicine (6,7). These essential oils, renowned for their diverse aromatic profiles and therapeutic potentials, have been integral to the culinary and pharmaceutical realms, enriching flavors and aiding in various medicinal applications.

Davana essential oil (DEO) has a calming and emotional balancing effect that helps alleviate anxiety. When applied to the skin, it emits a unique scent on each individual, making it a prized ingredient in high-end perfumery for creating distinctive fragrances. In traditional Indian medicine, Davana has been used to treat diabetes mellitus and is known for its immunomodulatory, anthelmintic, antipyretic, and wound-healing properties. Additionally, it serves as a mood enhancer and aphrodisiac, as well as an effective antiseptic and disinfectant (8). Davana oil can also be used as a natural insect repellent and is believed to reduce the risk of chronic diseases, heart failure, and cancer (9). Within the realm of Iranian traditional medicine, specific *Artemisia* species have long been valued for their multifaceted medicinal advantages. Notably, indigenous communities have turned to the aerial components of *Artemisia* species for their antiviral qualities and ability to alleviate spasms (10,11).

Several investigations have explored the chemical composition of essential oils extracted from diverse species within the *Artemisia* genus, conducted in various geographical regions worldwide (12). In a recent breakthrough, the optimization of *Agrobacterium tumefaciens*-mediated genetic transformation has opened up new possibilities for *A. pallens*. This advancement hints at the potential efficacy of genetic engineering techniques for enhancing the production of artemisinin and its derivatives from *A. pallens* (13).

Artemisia pallens stands out due to its extensive use in traditional medicine for treating various ailments, including inflammation, digestive disorders, and infections. Recent studies have begun to uncover its potential pharmacological activities, such as antioxidant, anti-inflammatory, and antimicrobial effects. Despite the promising findings, research on *A. pallens* is fragmented, with studies often focusing on isolated compounds or specific activities without providing a holistic view of its medicinal potential. Furthermore, there is a lack of comprehensive reviews that synthesize existing data and highlight areas requiring further investigation. This review aims to consolidate the existing knowledge on *A. pallens*, providing a detailed account of its production technology, essential oil chemistry, pharmacological activities, and therapeutic potential. This review not only addressed as a valuable resource for researchers and healthcare professionals but also identify key areas for future research, ultimately aiding in the development of new therapeutic agents.

Review methodology

Articles about davana were selected for review based on specific keywords, publication in high-impact journals, and recently published davana manuscripts, ensuring that they contain the required information for comprehensive analysis. Davana related articles were screened and all the data were analysed and made the review in acceptable order of information. To conduct a comprehensive literature review on davana, various online reference databases including Scopus (https://scopus.com), PubMed (https://pubmed.com), Mendeley (https://mendeley.com, and Web of Science (https://webofknowledge.com) were accessed. However, most of the databases did not have free access thereby Google Scholar (https://scholar.google.com/) was the most comprehensive resource available for free also accessed to retrieve even the most esoteric information. The search encompassed multiple key terms related to various aspects of davana, such as its cultivation, genetics, breeding, biotechnology, pests and diseases, irrigation, harvesting, oil extraction techniques, chemical composition, pharmacological value, traditional benefits, and medicinal values. Only reports published in English were considered for inclusion in this review. All the databases were screened manually using DOI number to avoid confusion while writing. Additionally, references cited in the retrieved articles were further examined to ensure a thorough compilation of relevant information.

Botany

The genus *Artemisia* is a subtropical and temperate genus that comes under the family Asteraceae (Compositae). One notable species is *A. annua* used as a source of antimalarial drug, artemisinin. Another economically important species *A. pallens* is an aromatic crop and a source of davana oil extensively used in the perfumery industries. *A. pallens* is a herb, up to 60 cm high, arachnose-tomentose, strongly pleasant odorous. Stem erect and cylindric (Figure 1A). The leaves are alternate, uni-pinnatifid, or bi-pinnatifid, measuring 1.5-3 × 0.5-1.2 cm, and are decurrent at the base with arachnose-tomentose surface on both sides. The leaf segments are linear-oblong, 2-6 × 1-2 mm, with entire margins and obtuse apices. The petiole is plot, 2-10 mm long, and narrowly winged. The heads are found in axillary, solitary, or appearing as terminal panicles due to the reduction of upper leaves, second in racemes, and sub-globose, measuring 3 – 5 × 4 – 7 mm. They are heterogamous with the outer 1–2 rows of florets being female, and the inner florets being bisexual. The florets are 5-lobed and yellow, either sessile or subsessile, with five stamens bearing free epipetalous filaments and a bifid style. The involucre bracts

Figure 1. (A) *Artemisia pallens* plant, (B) Head inflorescence of davana at blooming stage.

are 2 – 3-seriate, with oblong to elliptic-linear structures, entire margins, obtuse apices, and arachnose-tomentose surfaces. They are herbaceous, with the outer involucre bracts being oblong, measuring 5–6 × 1.5–2 mm, and the inner involucre bracts being obovate, 3–5 × 1.5 – 2 mm, and convex. The outer florets are 2.5 × 0.5 – 1 mm, female, and fertile, while the inner disc florets are 3.5 × 1 mm, hermaphrodite, and fertile. The corolla is tubular, 2–3 × 0.5 – 1 mm, yellow, and glabrous, with 5-lobed structures. The corolla tube is cylindric and 2.5 mm in length, with lobes that are ovate-deltoid, approximately 5 × 4 mm, with entire margins and acute apices. The stamens number five and are epipetalous, with filaments measuring 5 mm in length, and anthers that are oblong, approximately 6 × 0.3 mm, and awned at the apex with the awn being about 4 mm in length. The ovary is obovoid, 1 × 0.4 mm, and glabrous, with a style that is 2 mm long and 2-lobed, with the style lobes being recurved and truncate at the apex. The achene is obovoid, 1.5 × 0.5 mm, and glabrous, with no pappus present.

Genetics, breeding, and biotechnology

Genetics

Mitotic chromosomal investigations revealed that *Artemisia pallens* Wall is a diploid (2n = 16) with a symmetrical chromosomal karyotype (14,15). Pollen mother cells (PMCs) were studied meiotically; it was discovered that lagging and uneven distribution of univalent and chromosomal anomalies may account for part of the pollen sterility in this species (16). M_1 plants produced from seeds treated with gamma rays at varied dosages showed a variety of mitotic and meiotic abnormalities. Mitotic inhibition and mitotic index increased and decreased dose-dependently in response to gamma rays (17). Genetic diversity was analyzed by Farooqui et al (18) in five accessions taken from davana growing locations for ten metric variables. Only two characteristics, plant height, and oil content, showed significant genotypic variation. Although oil content heritability was 91% in the broad sense, the range (0.09% to 11%) was precise for any propagating effort to be successful.

Breeding

Long before the publishing of research on flower physiology and the paucity of genetic variety in davana, a breeding effort for enhancing davana herb output began in 1986 and 1987. Because davana is not a self-pollinating species that has not been exposed to any manmade selection, the programme was founded on the notion that there should be enough genetic variety in the species to allow for genetic improvement through selection (19). Mutation breeding was established to create genetic diversity to solve the issue of insufficient genetic variability for genetic development (20).

Reproductive biology

For pollination, fertility, and seed set, a breeding programme requires reproductive biology and the best planting season. The capitulum of the davana comprises a heterogamous head featuring bisexual disc florets at the center and a limited number of pistillate ray florets along the periphery, with a maximum of 43.65 florets per head (Figure 1B). It took 19 days for the flower head to attain full bloom after observable commencement. During the 80-90 days after transplantation into the main field, the number of capitula per plant varied between 293 and 816. Each capitulum had an average diameter of 3.15 mm, and the combined weight of 10 capitula was 0.231 g (4). Anthesis took place between 7:30 AM and 12:30 PM, peaking around 10:30 AM, while another dehiscence occurred within the same time frame, with a peak at 9:30 AM. The maximum for both events was observed at 7 AM on the day following anthesis. Pollen grains are spherical and 19.76 µ in diameter, with a fertility rate of 34.55%. In 10% of Kwack's medium, pollen germination reached a maximum of 20%. The November crop had the highest seed set percentage. Under the conditions of open pollination, bagging, and isolation, there was no variability in the percentage of seed set (21).

Selection

By employing 3 rotations of simple mass selection with broad plant spacing and utilizing the honeycomb pattern (22), the herb production of davana could potentially be enhanced by approximately 38% compared to the unselected population. The oil content and the davanone constituent of the oil were not affected by herb yield selection (19). A new variety named PKM-1(Acc. No. AP. 7) was improved through the mass selection of the local type (Chinnamanur) by the Tamil Nadu Agricultural University (TNAU) in Tamil Nadu state, India. This crop cycle is 145 to 150 days and the herbage yield is 17.45 t/ha while it can be cultivated in June-July/November-December (23).

Mutation induction

Because davana develops little flowers, recombination breeding is difficult to achieve variety. As a result, mutation breeding is preferred for creating variety in davana (24). Using mutagenic agents such as chemical (EMS) and radiation (gamma rays), several studies sought to create genetic diversity. Farooqi et al (20) studied the sensitivity of davana to gamma rays with irradiation dosages such as 1 Kr to 10 Kr and 10 Kr to 100 Kr at intervals of 1 Kr and 10 Kr, respectively. For several growth characteristics, such as germination (50-70 Kr), root growth (40 Kr), shoot growth (more than 100 Kr), and seedling growth (more than 100 Kr), the lethal dosage (LD_{50}) was 70 Kr. Seeds were irradiated with gamma rays at 15, 20, 25, 30, 35, 40, and 50 kR and seeded in triplicate experiments (25). Irradiation decreased the germination of the seeds, the height of plant, the survival of seedlings, and the fertility of pollen in M_1 plants, according to tests. However, the superior qualitative mutants were identified among segregating M2 plants, which were grown as single plant progenies. The induced mutants of davana treated with 0.05% EMS, exhibited notable morphological diversity (24). This included variations, such as early and late flowering types, bushy types with high yields, taller plants producing more capitula, and genotypes with high oil yield and rich in davanone.

Biotechnology

Two features of aromatic plant biotechnology are immediately applicable. (i) Tissue culture under aseptic conditions, which allows for year-round availability and quick multiplication regardless of the exterior environment; it is especially important for prime and uncommon plants. (ii) Large-scale cultivation and cold storage of cells allow for the preservation of their biosynthetic capabilities, facilitating the production of crucial secondary metabolites, flavors, medicines, and various pharmaceutical products (26). Micropropagation has a higher multiplication rate than traditional techniques of propagation; however, the field performance of tissue-grown plants relies on factors such as the original material, composition of the growth medium, use of growth regulators, specific cultivars, and prevailing environmental conditions. Growers may now use certain well-developed in vitro procedures to assist them satisfy the demands on spice and pharmacological sectors. Determination of somatic clones of plants obtained from micro propagation can help aromatic plants propagate economically viable in vitro (27). Recent advancements in engineering the terpenoid pathway highlight the potential of aromatic plants to serve as significant sources for generating chemical and medicinal feed stocks from renewable sources (28).

Tissue culture

Micro propagation through direct induction of numerous shoots, as well as callus differentiation, is useful strategies for propagating davana plants quickly (29). *A. pallens* was cultured in vitro using different types of explants on MS medium (Murashige and Skoog medium) supplemented with various concentrations and combinations of growth regulators. The development of seedling explants to multiple shoots cultured in MS liquid medium with a variety of growth hormones such as BA + IAA and NAA, as well as rooting in regenerated shoots using NAA (0.1 ppm), KN (1.0 ppm) + NAA (0.1 ppm) + IAA (0. l ppm), or IAA (0. l ppm). Media containing BA + 2,4-D led to the formation of disorganized callus. BA + IAA medium promoted the development of semi-organized tissues interspersed with shoot buds, while BA + NAA + IAA medium stimulated the growth of multiple shoot cultures (30).

Shoot tip explants treated with 2 mg/L 2,4-D displayed the strongest callogenic response (31). The highest shoot proliferation and length occurred on the MS medium with 3 mg/L kinetin, while the MS medium containing 3 mg/L IBA resulted in the greatest root formation and length. Shariff and Chandra (29) achieved ample root proliferation with numerous lateral roots using MS medium supplemented with 0.5 mg/L IBA. Alok et al (13) reported an average of 36 shoots per explant when culturing attached cotyledons on MS medium supplemented with 2 mg/L BAP and 0.1 mg/L NAA over 45 days. Optimal rooting was achieved when transferring shoots to half-strength MS medium supplemented with either 1 mg/L IBA or 1 mg/L NAA.

Recently, a hairy root culture (HRC)-based method for in vitro production has emerged as a promising biotechnology strategy. Hairy root development is caused by *Agrobacterium rhizogenes*-induced disease in plants, which is identified by rapid growth, growth in a medium devoid of hormones, and genetic integrity. These roots will produce secondary metabolites in the same way as complete plants do, and they are also susceptible to up scaling in the bioreactor. HRCs are being used as one of the preferred tissue culture techniques for large yields of important secondary metabolites with medicinal and commercial use (32). Suspension cultures of plant cells represent a renewable and valuable source of biological material that can serve various purposes, including the potential secondary metabolites production (33). Leaf explants treated with 2 mg/L kinetin exhibited the highest callogenic response. Analysis of the callus extracts from methanol, dichloromethane, and petroleum ether revealed the presence of notable secondary metabolites, including phenols, alkaloids, tannins, steroids, terpenoids, and glycosides (34).

Genetic engineering

The establishment and refinement of protocols for plant regeneration and genetic transformation in *A. pallens* will be beneficial for manipulating the metabolic pathway to

enhance the production of valuable compounds (13,35). The greatest transformation efficiency was observed when stem explants were co-cultured with *Agrobacterium rhizogenes* and cultivated on half-strength MS medium. Jogam et al (36) cloned 3 putative reference genes, namely ADP-ribosylation factor (Arf), ubiquitin (Ubi) and β-actin (Act) as well as a functional gene involved in the carotenoid biosynthesis pathway, phytoene desaturase (Pds), in order to compare the expression of the transgenic and *A. pallens* genes.

Agro-technology

Soil and climate

Davana cultivation thrives in a range of soil types, spanning from sandy loam to medium black. However, when aiming for high essential oil production, soil quality and seasonal factors become pivotal considerations. Conversely, for non-essential oil purposes like bouquets and garlands, these factors are less critical (37). Optimal oil output is achieved in rich red loamy soils, necessitating adequate watering (38). Consequently, davana is predominantly cultivated in South India, particularly in Karnataka and Tamil Nadu (23). Winter cultivation yields the highest oil content, favored by gentle rains and mild temperatures devoid of frost. Conversely, high temperatures and heavy rains during flowering jeopardize plant development and diminish oil production. Davana is typically grown as a short-term crop from November to February/March, and as a ratoon crop from April to May (39).

Varieties

Commonly, local varieties are being cultivated. However, a new variety, PKM-1, was developed and released by TNAU in Tamil Nadu. It produces 16.78 t/ha herbage and 20.32 kg/ha oil yield with medium duration. The foliage displays a prominent silvery-green hue, featuring abundant branching from the plant's base and emitting a highly fragrant aroma. The initial harvest can be conducted just 40 days after transplanting. Moreover, it exhibits tolerance in the field against aphids and damping off (23).

Nursery

Davana cultivation begins with nursery preparation using freshly harvested seeds. Approximately 1.5 kg of viable seeds per hectare is necessary. The seeds are dampened, bundled, and stored in a cloth or gunny bag for 2-3 days, with periodic moistening. Before sowing, the seeds are treated with Captan or Thiram at a rate of 3 g/kg. Additionally, treating seeds with GA3 (50 ppm) for 20 minutes enhances germination, seedling length, and vigor index (40). Conversely, enhancing seeds with petroleum ether resulted in improved seed quality parameters such as 1000 seed weight, germination, and vigor index (41). Typically, nursery beds that are 2 meters long and 1 meter broad are ideal. The beds should have a cold-free surface. The finely prepared FYM is then mixed in at a rate of 10 kg per bed. It is preferable to sow seeds (1 g/m^2) in October; pre-germinated seeds are put in nursery beds and watered daily. Dried seeds were blended with sand in a 1:10 ratio and evenly distributed across the bed while sowing. After that, a thin layer of sand was evenly spread over the seeds, and the beds were manually watered twice a day. An application of 10 kg/ha of Heptachlor to the soil approximately 10 days before planting has proven effective in deterring ants. Seed germination happens in around 4-5 days, and within 6 to 8 weeks after sowing, the seedlings are ready to transplant. To promote seedling development, a 0.2% urea solution was prepared freshly and applied as foliar spray onto the seedlings 4 weeks after planting (42).

Transplanting

Timing is crucial for achieving optimal seed output and quality in davana cultivation. It is recommended to transplant on the 15th of November for superior germination percentage, seedling height, dry matter output, and vigor index (40). Before transplanting, the field should be well-prepared and finely tilled, potentially converting it into beds as needed. Irrigation of the beds should be done the day before transplantation. Transplantation involves spacing 2 to 3 seedlings at 6-inch row intervals and 3-inch plant intervals. Following transplantation, seedlings receive a thorough hand watering. Seedlings transplanted at 35 days old exhibit improved growth metrics including survival percentage, plant length, number of branches per plant, number of flower heads per plant, seed yield per plant, seed weight per 1000 seeds, subsequent seed germination, and vigor index (43).

Intercultural operation and fertilizers applications

Manual weeding is employed to maintain the field free of weeds during the initial stages of crop establishment and growth, as well as following the first harvest. The crop receives light irrigation daily for approximately 10 days after transplanting, followed by irrigation twice a week thereafter (44). The impact of irrigation intermediate durations and plant spacing geometry on the productivity and economics of both primary and ratoon crops of davana revealed that closer spacing of 15 cm × 10 cm and watering at 15 mm CPE resulted in higher yields of fresh herbage and essential oil. the similar trend was seen. It is also achieved in davana as the ratoon crop yielded greater gross, net returns, and B: C ratios to follow the same protocol (45). Defoliated seedlings boosted seed yield per plot, herbage yield per plot, germination, and vigour index in ratoon crops, according to studies (40).

In commercial davana cultivation, effective nutrient management practices are essential to maximize yield and profitability, with Integrated Nutrient Management (INM) practices emerging as a promising solution (46). Nitrogen application improves biomass production, essential

oil output, and nitrogen, phosphorus, and potassium absorption substantially. With a broadcast of 80 kg N/ha, the output of essential oil increases dramatically. Applying 80 kg N/ha, the nitrogen usage efficiency, apparent nitrogen recovery, and physiological efficiency were highest and dropped as the nitrogen level increased. The maximum merits including the height of the plant, number of branches, shoot fresh and dry weight, output of dry matters, fresh yield of herbage, and yield of essential oil in davana were obtained when N was applied at 93.75 kg per ha (47). A 75% RDF + *Azospirillum* 2 kg ha^{-1} application boosting vegetative development was responsible for the much greater maximum fresh herbage yield per plant (46); it also reduced the nitrogen and phosphorus by 25% than recommended level as well as improvised davana growth and yield. Hence, applying 75% of the recommended NPK dose along with *Azospirillum* at 2 kg/ha proved to be economically viable for davana cultivation (48).

Growth regulators are one of the many management strategies that affect the essential oil content of aromatic crops. Gibberellins, kinetins, and brassinolides are highly efficient growth regulators for boosting the quality of aromatic crops. Aromatic crop herbage and essential oil output can be increased by using suitable growth hormones at the proper intensity and at the optimal time of crop's growth (49). The davana crop's herbage and oil output are influenced by a foliar spray of GA_3 at 200 ppm (50).

Plant protection

Davana typically avoids major insect pest attacks, post-harvest, leaf-eating caterpillars, termites, and aphids may pose a threat. However, root-knot nematodes, particularly *Meloidogyne incognita* and *M. javanica*, have been observed to cause a significant 50% reduction in essential oil yield. As the nematode inoculum levels increase, shoot length, root height, stem and root fresh or dry weight, and oil output all decline (51). To combat root-knot nematodes and promote plant growth, farmers may utilize neem oil seed cakes, which also serve as a fertilizer (52).

Damping-off, a major disease in davana caused by the fungus *Rhizoctonia* spp. is responsible for this sickness. The disease is often severe during the nursery stage, particularly in high humidity and overcast weather conditions, resulting in significant seedling mortality. Regulating irrigation can help reduce the incidence of the disease. It can be managed by treating seeds with Emisan 0.2% or Ridona MZ 0.1% before planting (53).

Harvest

The crop is typically harvested when a significant number of flower buds begin to bloom usually around the end of February or the March first week. Typically, a crop will be cut above 4 inches from the ground with herbage during harvest. In different phases of plant growth, the quantities of essential oil and makeup of davana vary. The essential oil concentration of flower heads is observed to be greater during complete emergence than at anthesis and seed set initiation (54). The primary constituents of the essential oil were davanone, (E)-ethyl cinnamate, and bicycle germacrene during all four developmental phases (vegetative, early flowering, full blooming, and seed set) (55). In a good seed production operation, seed maturity is the most significant element affecting seed quality overcome by collect davana seeds reaching physiological maturity the 35th day after anthesis (56).

Distillation

Davana herbage is dried under shade for 2-3 days before undergoing steam distillation to extract the oil. The quality and quantity of the oil are influenced by the crop's approximate maturity and adequate shadow drying of the herbage. An average yield of 0.2% from 2 days of dried material for roughly may be deemed well in large-scale distillation (44). To achieve high-quality oil, the dried material is steam-distilled while, hydro-distilled for essential oil quantification in laboratory conditions, especially for a tiny sample. In hydro-distillation, glass flask filled with plant material and water is added until about three-quarters of the material are submerged, subsequently, the mixture is heated. Water vapors and vaporized oil travel into the condenser during boiling, where they are condensed and collected in a graded receive. The oil content of the substance may be calculated based on the amount of oil recovered.

In commercial settings, steam distillation stands as the favored technique. The distillation setup includes (i) a steam-generating boiler; (ii) a distillation still to hold the material and allow steam passage; (iii) a condenser for converting vaporized oil into liquid; and (iv) a receiver to gather the oil (Figure 2). Both the boiler and distillation still are typically fabricated from steel.

A steel conduit links the boiler to the distillation apparatus, facilitating the transport of steam. Positioned at the bottom of the still, the plant material rests upon a perforated grid (plate). Connected to the distillation

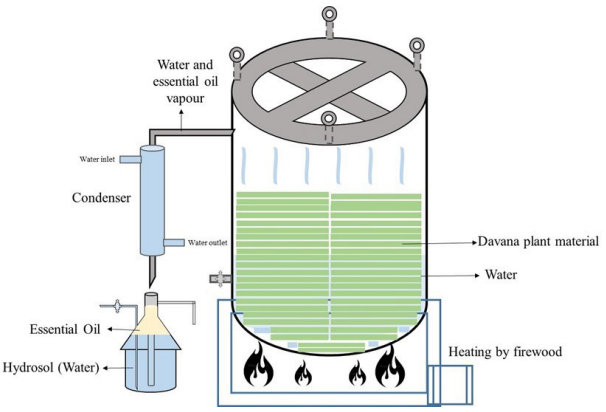


Figure 2. Block diagram of field distillation unit used for *Artemisia pallens* essential oil distillation.

apparatus is a pipe leading to the condenser. This condenser comprises numerous metallic pipes enveloped within a casing. Equipped with both inlet and outlet ports, the condenser utilizes water flowing between the pipes to condense steam and essential oil vapors into liquid form. These condensed substances are subsequently collected in the steel receiver. Due to its lighter and insoluble nature, the oil floats atop the water surface. The air-dried herbage is chopped into smaller pieces and loaded into the still for distillation. During filling, the material should be tightly packed to prevent steam channels from forming, which can lead to reduced yields during distillation. The distillation process typically takes 5-6 hours to complete. The bottom layer, which contains minute amounts of water and oil, should be clarified after the top, transparent layer of oil has been decanted. This mixture is treated with a saturated solution of sodium chloride to separate the oil, resulting in distinct layers of water and oil. The lower water layer is drained using a separating funnel, and the upper oil layer is collected (57).

Yield and oil content

Fresh herbage yields roughly 12 tons/ha from the main crop as well as the ratoon crop, yielding about 8-10 kg of davana oil after shade drying and distillation. The essential oil quality and quantity are impacted by the crop's approximate maturity and adequate shadow drying of the herbage. A yield of 0.2% from material dried for approximately 2 days may be considered satisfactory for large-scale distillation. When extracting oil from the entire plant, the flower heads contribute the majority of the oil in the range of 0.53%. The leaf and stem contribute very little (0.14%) to the overall percentage of oil content than whole plant (0.29%) (57).

Davana essential oil

A large number of chemical constituents are found in *A. pallens* broadly classified into DEO with its components and the non-volatile components of the plant.

Physical properties of essential oil

DEO is brownish-yellow oil with a fragrant persistent fruity odour. Flavour Extracts Manufacturers Association (FEMA) no. 2359 and CAS 80160303 have been assigned for DEO and it is considered as a GRAS substance (58). As per the Bureau of Indian Standards, the quality parameters like optical rotation, refractive index, and specific gravity for DEO fall in the range of +34˚ - +41˚, 1.4775-1.4995 and 0.9160-0.9560, respectively. It has also been suggested that a good quality DEO should have at least 40% davanone (60). While Coleman (61), have mentioned an optical rotation range of +35˚ to +5˚. The qualitative aspects of DEO, as reported by various authors, have been summarized in Table 1. An acid value of 2.0-3.0 and ester value of 30-40, has been reported for DEO (60,62).

Essential oil composition

DEO is extracted from the flowering aerial parts of the plant. The harvested biomass is generally hydro- or steam-distilled to extract the DEO, having sweet, fruity, and balsamic smell (66,67). DEO is characterized by davanone isomers, davana ether isomers, and other furan derivatives. DEO has been the area of interest for several researchers for the characterization and isolation of the volatile constituents of the oil (54,66-77). Davanone, an odorless sesquiterpene ketone, is the primary chemical constituent of davana oil and is present in the range of 30 to 65% depending upon the climatic condition and the growth stage of the plant (70). Perfumery and flavor industries demand davanone rich oil (more than 50%); however, its abundance may enhance the overall aroma of the oil. It would be because of its fixative property (54,76). The constituents accountable for the scent of the oil include davana ether (70), 2-(3-methylbut-2-enyl)-3-methyl-2,5-dihydrofuran, 2-(3-methylbut-2-enyl)-5-(5-cinnamoyloxy-2-oxo-1,5-dimethylhex-3-enyl)-3-methyl-2,5-dihydrofuran (75), and hydroxy dihydrorosefuran (71). Simpa and Van Der Wal (68) isolated davanone from DEO and verified it by chemical and spectroscopic techniques. Later on, another sesquiterpene ketone, named artemone, was also isolated (69). Thomas and Pitton (70) isolated stereoisomers of 2, 6, 10-trimethy1-2:5, 7:10-diepoxy-dodeca-3,5,11-triene from DEO. Later on, Thomas and Ozainne (73) isolated and synthesized nordavanone. By the end of the twentieth century, over thirty terpenoids had been identified in davana oil (54,74,76,77). The EO of davana was grown in Bangalore using gas-liquid chromatography and reported 32 constituents, out of which 19 compounds were unidentified (74). Catalan et al (76) reported 3, 4 epoxy derivatives of isodavanone (sesquiterpene ketone) and cirsimaritin from the aerial parts of davana. The volatile constituents of davana EO have been analysed using GC/GC-MS and reported 53 compounds, out of which 34 were identified. Among these, eight constituents were reported for the first time (77). 11-Hydroxy-8-oxo-

Table 1. Physical properties of *Artemisia pallens* essential oil

Optical rotation	+34° – +41˚	+35.5° – +60˚	+51.72˚	+ 37.24° – + 54.73°	+35˚	+40° – +60˚
Refractive index	1.4775–1.4995	1.4750–1.4900	1.4885	1.4858–1.4950	1.488	1.4780–1.4900
Specific gravity	0.9160–0.9560	0.9750–0.9885	0.967	0.9581–0.9695	0.9605	0.9200–0.9800
References	59	61	62	63	64	65

Parameters are presented as per Bureau of Indian Standards (BIS).

9,10-dehydro-10, 11-dihydronerolidol was isolated, which might play a crucial part in the biogenesis of Furano-sesquiterpenes. The essential oil content and chemical constituents were isolated at three plant growth stages (blooming stage, anthesis, and seed set initiation) and 26 compounds were reported (46). The highest content of essential oil was found at the complete flower heads emergence stage, followed by anthesis and seed set initiation stages (55). The major constituent of davana oil, davanone, and linalool decreased whereas farnesol, bicyclogermacrene, davana ether, 2-hydroxyisodavanone, *trans*-ethyl cinnamate, *trans*- and *cis*-methyl cinnamate increased from the emergence of flower heads stage to the seed set initiation stage. For the first time, the presence of *trans*- and *cis*-ethyl cinnamates, geranyl acetate, and *trans*- and *cis*-methyl cinnamates was identified in davana oil. Coleman et al (60) reported the DEO, acquired from Grasse, France, using SPME/GC-MS (headspace analysis) and identified 64 compounds. The volatile components of DEO and identified 32 compounds out of which *cis*-davanone (45.8%), bicyclogermacrene (9.6%), linalool (2.5%), caryophyllene oxide (2.2%) and phytol (2.1%) were the major constituents (61). Later on, Jakab et al (78) studied the thermo-oxidative decomposition of davana oil obtained from Reinbeck, Germany, and identified 75 constituents out of which davanone (29.5%), bicyclogermacrene (11.68%), (*trans*)-ethyl cinnamate (6.34%), and davana ether isomer (5.41%) were the major constituents. Recently, Singh et al (62) investigated DEO and identified ninety-nine compounds. Major components were *cis*-davanone (53.0%), bicyclogermacrene (6.9%), *trans*-ethyl cinnamate (4.9%), davana ether isomer (3.4%), spathulenol (2.8%), *cis*-hydroxy davanone (2.4%), *trans*-davanone (2.1%), artedouglasia oxide A (2.0%), and *epi*-*α*-cadinol (2.0%). Bicyclogermacrene, *trans*-ethyl cinnamate, and spathulenol were isolated for the first time along with two previously isolated compounds, *cis*-davanone and *cis*-hydroxydavanone. Although this herb is endemic to Southern states in India, cultivation of *Artemisia pallens* was also tried in Kashmir valley. A group of researchers identified 26 essential oil components from DEO obtained from the davana of Kashmir valley. The oil is constituted of davanone (72.59%), (E)-ethyl cinnamate (8.40%), β-eudesmol (3.20%), davanol isomer 2º (2.86%), (E)-methyl cinnamate (2.41%), davanol isomer 1º (2.05%), bicyclogermacrene (1.66%), geranyl acetate (1.38%), and linalool (1.08%) as the primary constituents (79). With 72% davanone content, this oil could be very competitive in the market. But no further reports were found on DEO from Kashmir valley.

Qualitative and quantitative assessment of major components

Simpa et al (68) were the first to isolate and report the structure of davanone. They went for fractional distillation of davana oil (50 g) using a vigorous column, which yielded a high boiling fraction amounting to about 12 g. This fraction had about 73% pure davanone in it, which was further purified using column chromatography, resulting in an 85% pure fraction. Finally, preparative gas chromatography was used to get a 98% pure davanone sample. The authors reported the following organoleptic properties for the compound (davanone): specific rotation [α]D21= +77.7º, refractive index nD20= 1.4722 (68). The structure was further established by degradative analysis by Thomas et al (72). Naturally occurring davanone is to be the *cis*/threo isomer and has been assigned through spectroscopic and degradative analysis (Figure 3).

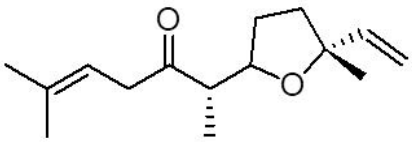


Figure 3. cis/threo-Davanone [6S,7S,10R-2,6,10-oxydododeca-2,11-dien-5-one] structure.

Odorous components

Initially, davanone, the major constituent of DEO, was believed to be the compound responsible for the oil's sweet fruity odor. However, on rigorous purification, it was odourless, which prompted researchers to look for the odorous principle. In column chromatography, the odour imparting principle was eluted just before the davanone fraction (Table 2). On gas chromatography using a carbowax column, the compounds showed a retention time just prior to that of davanone and were found to be a mixture of three isomers having practically identical NMR and mass spectra (70). These were the isomers of davana ether and reported to be the ones responsible for the fragrance. The same group of researchers also reported davanafurans as an additional component imparting the fruity odour of the oil (82). Later on, Chandra et al (75) reported two new odorous furanoid components, namely, 2-(3-methylbut-2-enyl)-3-methyl-2,5-dihydrofuran and 2-(3-methylbut-2-enyl)-5-(5-cinnamoyloxy-2-oxo-1,5-dimethylhex-3-enyl)-3-methyl-2,5-dihydrofuran. Misra et al (77) identified yet another fragrant compound from DEO called hydroxydihydrorosefuran.

Considerations on previous identifications

It is usually difficult to identify essential oil components from oils, which are rich in sesquiterpenoids. The reason could be one or more of the following: (i) the column might be overloaded with sample, due to inappropriate injection volume, resulting in co-elution and peak overlapping; (ii) poor chromatographic resolution might lead to mis-interpretation; (iii) structurally similar sesquiterpenes show similar mass spectra, leading to mis-identification; (iv) databases like Wiley's and NIST are not exclusive for essential oil components, resulting in generation of hits,

which are not even volatile; (v) certain complex essential oils like patchouli, vetiver, and davana, readily consist of co-eluting components, which render the mass spectra too overcrowded and difficult to interpret; (vi) identifying essential oil components from alcoholic and hydro-alcoholic extracts, leading to the identification of more number of non-volatile compounds as the components of essential oils.

Certain essential oils like orange, lemon, and bergamot oils are known to have nitrogen-containing compounds like indole, methyl anthranilate, pyrazine, and pyridine. Also, pyrazine and pyridine compounds are reported in black pepper and vetiver oils (83). But these nitrogen-containing compounds are present in trace amount and mostly consist of low molecular weight (~200 amu), similar to that of sesquiterpenes. So, compounds like 1-monooleoylglycerol trimethylsilyl ether (MW 501), and methyl- 6, 9, 12, 15-docosatetrinoate (MW 346.5) are unlikely to be components of DEO. The roots of davana yield an essential oil rich in terpenes, with the root-specific enzyme ApTPS1 producing germacrene, a significant component of root volatiles (84). Further, compounds like 2-aminononadecane, N-methyl-1-octadecamine, epinephrine (a non-volatile human-derived hormone), and 2-amino-5-[(2-carboxy)-vinyl]-imidazole are not derived from any essential oil component pathway of DEO and thus, present a sort of ambiguity to their identifications (80). Compounds like acetaldehyde, acetone, ethanol, and acetic acid (60) are possible in SPME analysis, when there is a short exposure time. Hence, these compounds are not included in the Table 2.

Table 2. Compounds reported in *Artemisia pallens* essential oil

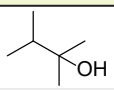
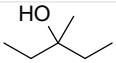
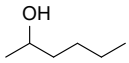
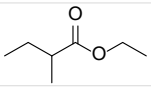
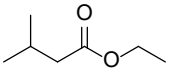
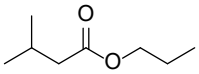
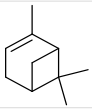
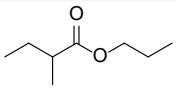
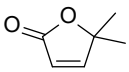
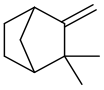
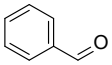
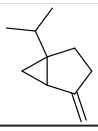
S. No.	Structure	RI	Name	MW[a]	References
1		725*	2,3-Dimethyl-2-butanol	102	(62)
2		745*	3-Methyl-3-pentanol	102	(62)
3		795*	1-Methylcyclopentanol	100	(62)
4		796	2-Hexanol	102	(62)
5		848*	Ethyl-2-methylbutyrate	130	(62)
6		849	Ethyl isovalerate	130	(62)
7		930*	Propyl isovalerate	144	(62)
8		932	α-Pinene	136	(60,62)
9		944*	Propyl-2-methylbutyrate	144	(60,62)
10		945*	5,5-Dimethyl-25H-furanone	112	(62)
11		946	Camphene	136	(62,74,77)
12		952	Benzaldehyde	106	(60,62)
13		969	Sabinene	136	(60,62,77,82)

Table 2. Continued

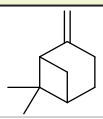
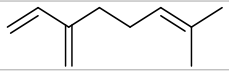
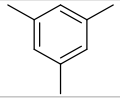
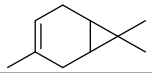
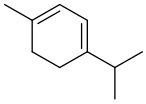
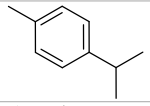
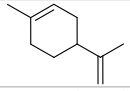
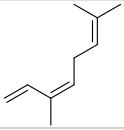
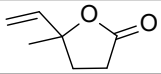
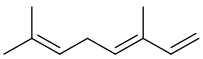
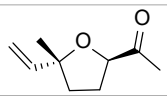
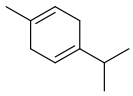
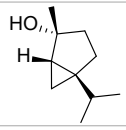
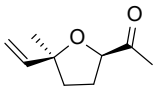
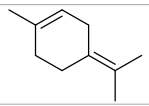
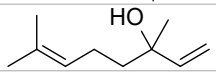
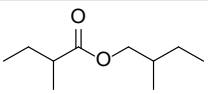
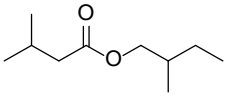
S. No.	Structure	RI	Name	MW[a]	References
14		974	β-Pinene	136	(60,62)
15		988	Myrcene	136	(54,62)
16		994	Mesitylene	120	(62)
17		1008	3-Carene	136	(80)
18		1014	α-Terpinene	136	(62)
19		1020	*p*-Cymene	134	(54,60,62,74,77,80)
20		1024	Limonene	136	(62,80)
21		1032	*cis*-β-Ocimene	136	(62)
22		1034	Lavender lactone	126	(62,80)
23		1044	*trans*-β-Ocimene	136	(60,62,80)
24		1046	*cis*-Arbusculone	154	(62)
25		1054	γ-Terpinene	136	(54,60,62,74)
26		1065	*cis*-Sabinene hydrate	154	(60,62)
27		1066	*trans*-Arbusculone	154	(62)
28		1086	Terpinolene	136	(62,80)
29		1095	Linalool	154	(54,60,62,74,77,80,81)
30		1100*	2-Methylbutyl-2-methylbutyrate	172	(60,62)
31		1103	2-Methylbutylisovalerate	172	(62)

Table 2. Continued

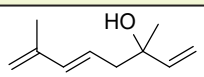
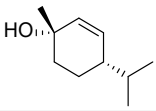
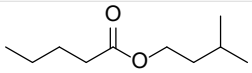
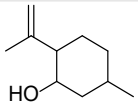
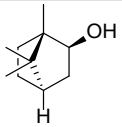
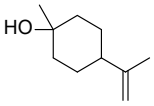
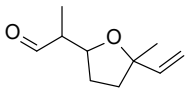
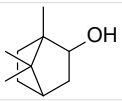
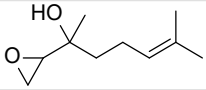
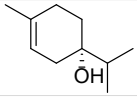
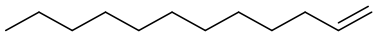
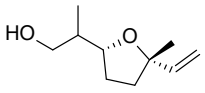
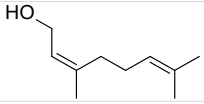
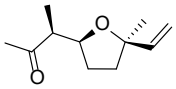
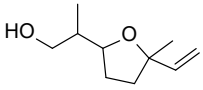
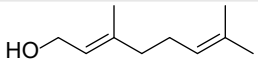
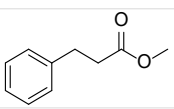
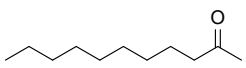
S. No.	Structure	RI	Name	MW[a]	References
32		1114*	Hotrienol	152	(80)
33		1118	*cis-p*-Menth-2-en-1-ol	154	(62)
34		1134*	Isoamyl valerate	172	(80)
35		1145	Isopulegol	154	(80)
36		1155	Isoborneol	154	(74)
37		1156	*Z*-β-Terpineol	154	(80)
38		1159*	Lilac aldehyde C	168	(80)
39		1165	Borneol	154	(74,77)
40		1173	Linalool oxide	170	(77)
41		1174	Terpinen-4-ol	154	(54,60,62,80)
42		1187	1-Dodecene	168	(62)
43		1219*	Lilac alcohol D	170	(80)
44		1227	Nerol	154	(77)
45		1228	*nor*-Davanone	182	(54,60,62)
46		1235*	Lilac alcohol A	170	(80)
47		1249	Geraniol	154	(54,61,62,74,77)
48		1278	Methylhydrocinnamate	164	(60,62)
49		1293	2-Undecanone	170	(62)

Table 2. Continued

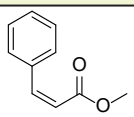
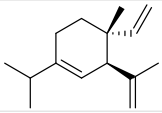
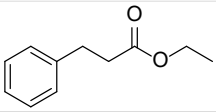
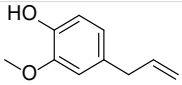
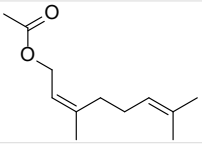
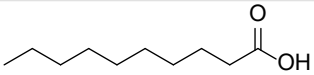
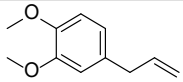
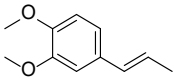
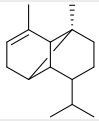
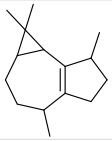
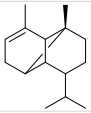
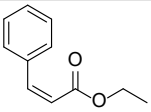
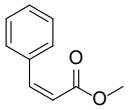
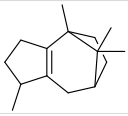
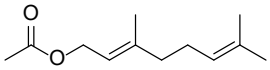
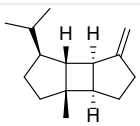
S. No.	Structure	RI	Name	MW[a]	References
50		1299	*cis*-Methylcinnamate	162	(54,61,62)
51		1335	δ-Elemene	204	(62)
52		1348	Ethyl hydrocinnamate	178	(60,62)
53		1356	Eugenol	164	(74)
54		1359	Neryl acetate	196	(80)
55		1364	Decanoic acid	172	(62)
56		1368*	Methyl eugenol	178	(74)
57		1369*	Methyl isoeugenol	178	(74)
58		1373	α-Ylangene	204	(80)
59		1374	Isoledene	204	(60,62)
60		1374	α-Copaene	204	(60,62)
61		1376	*cis*-Ethylcinnamate	176	(54,61,62,80)
62		1376	*trans*-Methylcinnamate	162	(54,61,62,80)
63		1379	β-Patchoulene	204	(62)
64		1379	Geranyl acetate	196	(54,60-62)
65		1387	β-Bourbonene	204	(62)

Table 2. Continued

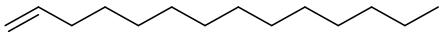
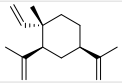
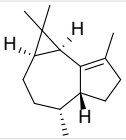
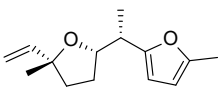
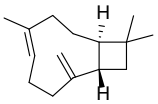
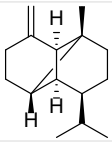
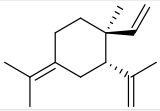
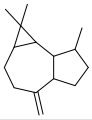
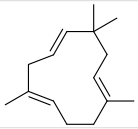
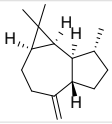
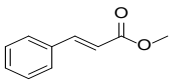
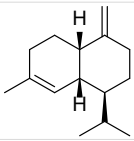
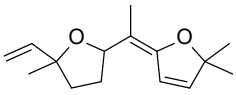
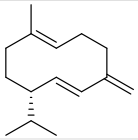
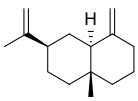
S. No.	Structure	RI	Name	MW[a]	References
66		1388	1-Tetradecene	196	(62)
67		1389	β-Elemene	204	(61,62,68,80)
68		1409	α-Gurjunene	204	(60,62)
69		1414	*cis*-Threo-davanafuran	220	(54,62)
70		1417	β-Caryophyllene	204	(60,62,80)
71		1430	β-Copaene	204	(62)
72		1432	γ-Elemene	204	(62,72)
73		1439	Aromadendrene	204	(60-62)
74		1452	α-Humulene	204	(62)
75		1458	Allo-aromadendrene	204	(60-62)
76		1465	*trans*-Ethylcinnamate	176	(54,61,62)
77		1478	γ-Muurolene	204	(62)
78		1483*	Davana ether	234	(54,60-62,77)
79		1484	Germacrene D	204	(62)
80		1489	β-Selinene	204	(60,62)

Table 2. Continued

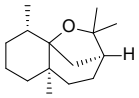
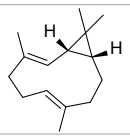
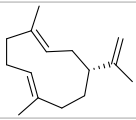
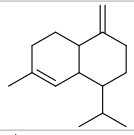
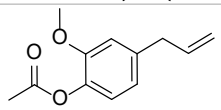
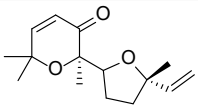
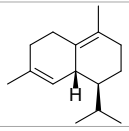
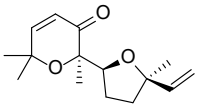
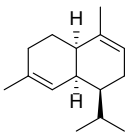
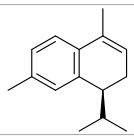
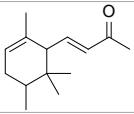
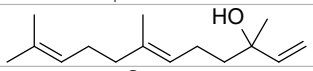
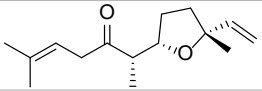
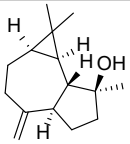
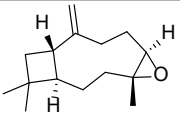
S. No.	Structure	RI	Name	MW[a]	References
81		1495*	Dihydroagarofuran	222	(77)
82		1500*	Bicyclogermacrene	204	(54,60-62)
83		1508	Germacrene A	204	(62)
84		1513	γ-Cadinene	204	(54,61,62,74)
85		1521*	Acetoeugenol	206	(74)
86		1522	Artedouglasia oxide C	250	(62)
87		1522	δ-Cadinene	204	(54,61,62)
88		1534	Artedouglasia oxide A	250	(62)
89		1537	α-Cadinene/α-Amorphene	204	(60,62)
90		1544	α-Calacorene	200	(62)
91		1546*	α-Irone	206	(80)
92		1561	*E*-Nerolidol	222	(54)
93		1571*	Davanone D	236	(60,62)
94		1577	Spathulenol	220	(61,62,80)
95		1582	Caryophyllene oxide	220	(61,62)

Table 2. Continued

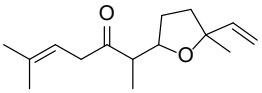
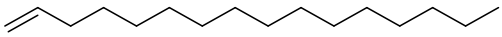
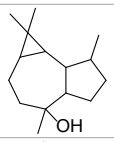
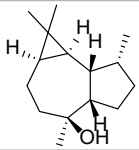
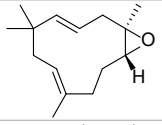
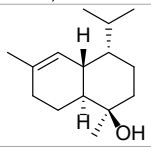
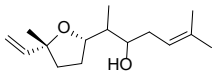
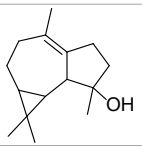
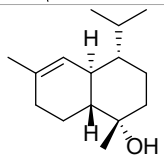
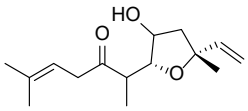
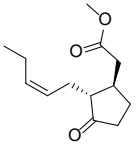
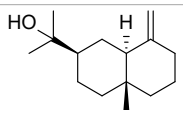
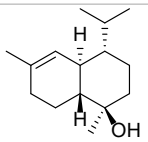
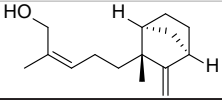
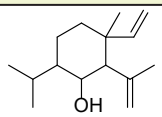
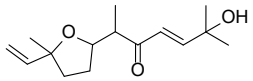
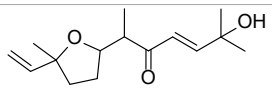
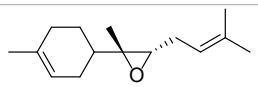
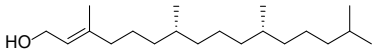
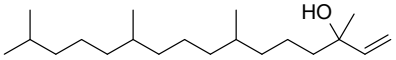
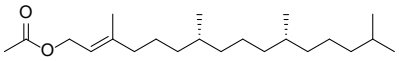
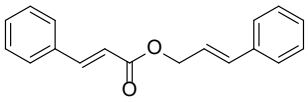
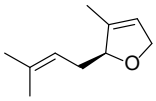
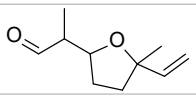
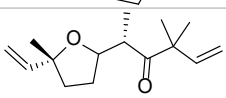
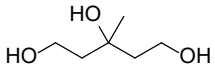
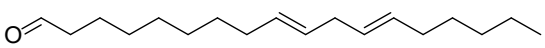
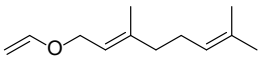
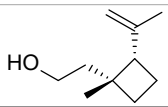
S. No.	Structure	RI	Name	MW[a]	References
96		1587	*cis*-Davanone	236	(54,60-62,77)
97		1588	1-Hexadecene	224	(62)
98		1590	Globulol	222	(61,80)
99		1592	Viridiflorol	222	(60-62)
100		1608	Humulene epoxide	220	(62)
101		1615*	τ-Cadinol	222	(54)
102		1615	Davanol (Isomer I)	238	(54,61,62,77)
103		1620*	Isospathulenol	220	(62)
104		1638	Epi-α-Cadinol	222	(62)
105		1644*	2-Hydroxyisodavanone	252	(54)
106		1648	*cis*-Methyl jasmonate	224	(62)
107		1649	β-Eudesmol	222	(54,62,80)
108		1652	α-Cadinol	222	(62,80)
109		1678	β-Santalol	220	(54)

Table 2. Continued

S. No.	Structure	RI	Name	MW[a]	References
110		1687*	6-epi-Shyobunol	222	(80)
111		1718*	*cis*-Hydroxydavanone	252	(62,77)
112		1722	Farnesol	222	(54,62,74,77)
113		1814*	*Z*-Bisabolene epoxide	220	(80)
114		1942	Phytol	296	(61)
115		1946	Isophytol	295	(61)
116		2218	Phytyl acetate	339	(61)
117		2447*	Cinnamyl cinnamate	264	(77)
118		NR	α-Dihydrorosefuran	152	(77)
119		NR	Lilac aldehyde	168	(77)
120		NR	Artemone	236	(54,77)
121		NR	3-Methyl-1,3,5-pentantriol	134	(80)
122		NR	9,10-Octadecadienal	264	(80)
123		NR	Geranyl vinyl ether	180	(80)
124		NR	Grandisol	154	(80)

RI: Retention indexes from R. P. Adams book; *Retention index from Pubchem; [a]Molecular weight from Pubchem; NR: Not reported.

Non-volatile chemical constituents

Rojatkara et al (85) isolated 4, 5β-epoxy-10α-hydroxy-1-en-3-one-trans-germacran-6α, 12-olide from the aerial parts of davana, and the structure was confirmed by NMR spectroscopy. Pujar et al (86) isolated 4, 5β-epoxy-10β-hydroxy-1-en-3-one-trans-germacran-6α, 12-olide from the aerial parts of davana, and structure confirmation was done by NMR spectroscopy. Elango et al (87) have done activity-guided isolation of arbutin (4-hydroxyphenyl-β-D-glucopyranoside) from the aqueous-methanolic extract of the plant. Ruikar et al (88) studied the acetone extract of the plant by GC-MS and isolated alpha-santonin through fractionation of the extract. Ruikar et al (89) isolated pallensin and 4-epipallensin for the first time, along with the known santonin and 4-epivalgarin, from the acetone-extracted aerial part of the plant. Recently, Honmore et al (90) isolated two spiro compounds from the acetone extract of davana roots (Table 3).

Biological activities

Artemisia pallens exhibits a range of biological and pharmacological potential (Table 4) attributed to its

Table 3. Major chemical constituents of *Artemisia pallens* investigated from different places

Country	Major components	Reference
	Volatile constituents	
India	*cis*-Davanone (38.0%), Nerol (10.0%), Geraniol (5.0%) and *trans*-Davanone (5.0%)	(77)
India	Davanone (67.1-22.9%), Bicyclogermacrene (13.0-2.0%), *(trans)*-Ethyl-cinnamate (9.4-3.1%) and Davana ether (8.4-0.5%)	(54)
India	Davanone (55.1%) and Bicyclogermacrene (7.6%)	(55)
India	*cis*-Davanone (53.0%) and Bicyclogermacrene (6.9%)	(62)
Virginia	Bicyclogermacrene (17.60%) and *cis*-Davanone (13.63%)	(60)
Austria	*cis*-Davanone (45.8%) and Bicyclogermacrene (9.6%)	(61)
Hungary	Davanone (29.5%), Bicyclogermacrene (11.6%), *trans*-Ethyl cinnamate (6.34%) and Davana ether isomer (5.41%)	(78)
	Non-volatile constituents	
India	Germacranolide (4, 5β-epoxy- 10α -hydroxy- 1-en-3-one-*trans*-germacran-6 α,12-olide) and (4, 5 β-epoxy- 10 β -hydroxy-1-en-3-one-*trans*-germacran-6 α,12-olide)	(85)
India	Eudesmanolides (pallensin and 4-epipallensin)	(86)
India	Glycoside (Arbutin)	(87,91)
India	Sesquiterpene lactone (alpha-santonin)	(88)
India	Alkaloids, Steroids, Flavonoids, Reducing sugars, Tannins, Saponins, Anthraquinone, Saponins and Phenols	(92-95)
India	Spiroethers	(90)

Table 4. Biological activities of *Artemisia pallens*

Traditional uses and biological properties	Method	Reference
Treatment of diabetes mellitus, antipyretic, anthelmintic, tonic properties, cold, antibacterial, antifungal, wound healing, measles, cough, depression, and high blood pressure	Folklore usage by *Nilgiri tribals*	(94,96)
Analgesic and Anti-inflammatory activities	Tail flick method in rats, inhibition of paw edema in rats	(62,93)
Antimicrobial activity	*In vitro* using microbes	(5,61,87,90,97-99)
Alleviation of acetaminophen-induced toxicity	*In vivo* using Wistar rats	(100)
Anti-asthmatic activity	*In vivo* using sprague-dawley rats	(101)
Free radical scavenging & hepatoprotective activity	*In vivo* using sprague-dawley rats	(95)
Anticorrosive activity	Weight loss and polarization techniques	(87,91,102)
Antioxidant activity	DPPH assay	(92,94)
Anticancer activity	*In vitro* cell invasion and wound healing assays	(103)
Antidiabetic activity	Oral administration in male wistar rats	(104)
Antihelmintic activity	*In vivo* using *Helminthes* worms	(105)
Arthropod deterrents activity	*In vitro* K & D module assay	(106)
Antihypertensive activity	*In vivo* using albino Wistar rats	(107)

diverse phyto-molecules. Traditionally, davana oil is used to treat measles, colds, cough, diabetes, depression, and hypertension. Several research has demonstrated its anti-inflammatory, analgesic, antimicrobial, hepatoprotective, and anti-asthmatic properties among others.

Anti-inflammatory and analgesic property: Methanolic extract of davana showed potent anti-inflammatory activity on carrageenin-induced paw edema in rats, which might be due to saponins and flavonoids. It also had significant analgesic properties (93). Davana oil and *cis*-davanone exhibited significant pro-inflammatory cytokines inhibitory potential in a dose-dependent manner in HaCat cell lines (62).

Antimicrobial activity: Ruikar et al (5) evaluated n-hexane, chloroform, and methanol extracts of dried plant material for their antimicrobial activity against yeast and six bacterial strains. However, only methanolic extract exhibited antimicrobial activity. Davana aqueous-methanolic extract has shown significant antibacterial activity against *Shigella flexneri* and *Pseudomonas aeruginosa* at 100 mg/mL of concentration. The principal constituent of the extract, 4-hydroxyphenyl-β-D-glucopyranoside (arbutin), showed similar antibacterial activity at 17 mg/mL of concentration (87). The antimicrobial properties of acetone and ethanol extracts were compared to 0.2% chlorhexidine, which ethanol

extract had more potential against microbial disease in the oral cavity (97). Davanone, a significant constituent of davana oil, possesses antibacterial and antifungal activities (98,99). DEO has shown antimicrobial behaviour against *Salmonella enterica* subsp. enteric, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and the yeast *Candida albicans*. The Davana fraction showed activity against yeast and all the seven tested bacteria except *Proteus vulgaris* and *P. aeruginosa* (61). Recently, investigation of acetone extract of davana root and its isolates against *E. coli, P. aeruginosa, B. subtills,* and *S. aureus* showed that the highest activity of the compounds was against *S. aureus* with MIC value of 12.78 µM as compared to the other strains (90).

Anti-asthmatic property: The aerial plant part extraction by methanol of davana alleviated acetaminophen-induced toxicity (100). The methanol extract of davana had potent anti-asthmatic activity through various mechanisms including the inhibition of oxido-nitrosative stress, IgE, TGF-β, TNF-α, and interleukins, as well as an increase in Nrf-2 levels in rats with ovalbumin-induced airway hyperresponsiveness (101). Moreover, Vengala (107) evaluated the methanolic extract of davana for antihypertensive activity in diabetic albino Wistar rats and found significant results.

Hepatoprotective and antioxidant activities: Ashok et al (95) investigated hepatoprotective, and the free radical scavenging activity of davana phenolic rich fraction on RIF+INH induced oxidative stress in rats and found it active. The total phenolic and total flavonoid contents were (312.60 ± 1.24) µg and (322.20 ± 1.39) in 1000 µg of davana extract. DPPH, hydroxyl radical, nitric oxide, and superoxide radical assay models were used to evaluate hepatoprotective and free radical scavenging activities. The presence of phenolic group can be responsible for the observed hepatoprotective and the free radical scavenging activities. The methanolic extract of davana showed good antioxidant activity because of phenols and flavonoids occurrence (102).

Anticorrosive property: Davana aqueous-methanolic extract and arbutin have shown significant anticorrosive efficacy (94%) facing mild steel in 1M HCl at 200 mg/L portion (87). A combination of arbutin and methanolic extract of davana acted as supreme anti-corrosive agents (103).

Anti-cancer activity: Davanone, isolated from davana oil, could be a potent agent to treat acute myeloid leukemia as it induced cytotoxicity in AML cell line NCI-H526 without provoking much harm or toxicity to normal AML-193 cells (99).

Anti-diabetic activity: The methanolic extract from the aerial parts of davana has able to lower blood glucose levels in glucose-fed hyperglycemic and alloxan-induced diabetic rats. The extract showed antidiabetic activity in glucose-fed rats at 100 mg/kg. In contrast, the extract led to moderate hypoglycaemic activity in fasted normal rats at a wider dose (1000 mg/kg) (104).

Anthelmintic and arthropod deterrent activity: DEO has strong anthelmintic activity against earthworms *(Pheretima posthuma),* tapeworms *(Taenia solium),* and roundworms *(Ascaris lumbricoides)* (105). DEO, synthetic davanone, and hydroxy precursors have been found to be arthropod deterrents against disease vectors (106).
Overall, the multifaceted biological activities of *A. pallens* make it a valuable plant with potential therapeutic applications across various domains.

Conclusion

Artemisia pallens is a rich source of potent volatile and non-volatile phyto-molecules. Various studies have proved that davana extract and the essential oil extracted from davana have enormous potential for various health issues. However, studies about comprehensive metabolic profiling, bioactivity-guided isolation of bioactive compounds, and their mechanism of action are still to be addressed for their therapeutic efficacy, optimum biological properties, and health-promoting benefits. Phyto-molecules from the plant can be used to synthesize various novel compounds with significant biological activities. Developing methods for isolating bioactive molecules can uncover their potential in treating cancer, inflammation, diabetes, hypertension, and other health conditions. Promising pharmacological leads may be taken up for further clinical evaluations. Studies to validate the traditional claims of the davana are still to be explored.

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Conflict of interests

The authors declare that there is no conflict of interest.

Ethical considerations

The authors have completely observed ethical issues

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