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Exploring Traditional uses, phytochemistry, pharmacology and future prospectives of Santalum album

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ABSTRACT

One of the rarest and most precious natural smell sources, Indian *sandalwood*, or Santalum album L. (Santalaceae), has substantial industrial and medicinal use. For the past 250 years. S album is a popular option all over the world since it is cultivated in India and its fragrant oil is well-known for both its medicinal qualities and sweetness.Many ancient medicinal systems have employed sandalwood and the essential oil derived from sandal heartwood to cure and prevent a wide range of ailments, including Ayurveda, Unani, and Siddha medicine.Due to its abundance of phytochemicals, especially sesquiterpenes, *Sandalwood* has a wide range of medicinal and medical uses. A comprehensive bibliographic analysis was conducted by examining internationally known books, index- and non-indexed journals, and widely used scientific databases [Pub Med, Sci-Hub,SciFinder, Scopus, ACS, and Web of Science]. Numerous pharmacological properties, from antibacterial to anticancer, have been shown in contemporary pharmacological investigations. *Sandalwood* oil and its components have not shown any appreciable toxicity; however, more Study on the chemical components and how they exhibit specific biological activities is required to fully comprehend the phytochemical composition and the intricate pharmacological impact of this plant. The poor productivity of this endangered plant and its rising commercial exploitation have sparked concerns about how to conserve it and increase its output using contemporary equipment and methods. The review covers the traditional use, phytochemistry, pharmacology, distillation, and biological activities of *Sandalwood* to reveal its value for industry and medicine as well as any Study gaps that need to be filled.

Keywords: *Santalum album, Pharmacology, Phytochemistry, Biological activity, Traditional uses.*

1. INTRODUCTION

Indian sandalwood, also known as Chandana in Sanskrit, is without a doubt one of the most valuable gifts from ancient India to the globe.*Sandalwood* was an essential component of Indian mythology, ceremonies, and culture long before the Chinese and Europeans realized its worth [1]. The heartwood of the tree is revered, and the paste that is created by grinding it is essential to Hindu ceremonies and rituals and is also a natural component of prayer and meditation. Indian sandalwood oil [SWO] has been extensively utilized in Ayurvedic and traditional Chinese medicine [2].

The key ingredient in sandalwood album oil, alpha santalol, has been used to cure several ailments, such as colds, viral infections, and stomach problems.Presumptive coolants include *Sandalwood* paste and oil. The wood paste is applied as an ointment to reduce heat and improve appearance [3]. It has also been said that the aroma of the essential oil calms the mind and improves.The medicinal and scientific benefits of Indian Sandalwood are currently being rediscovered from the standpoint of modern medicine. Sandalwood has been found to offer a wide range of beneficial pharmacological properties, including anti-inflammatory, anti-oxidant, anti-microbial, and antiproliferative effects [4].Alpha santalol, the primary component of SWO, has been shown to have chemopreventive qualities and might not be toxic to normal cells. The two main processes via which alpha santalol damages cancer cells are the induction of cell cycle arrest and the death of cells. To support the results, more Study is needed to ascertain the effects of SWO generally and alpha santalol in particular on both healthy and malignant tissue. Alpha santalol may show promise as an anticancer medication in the future for the treatment of malignancies such as skin, breast, prostate, and oral cancer. if additional Study validates its selective ability against cancer cells [5].

It has also been demonstrated that SWO and alpha santalol, its active ingredient, inhibit UV and chemical-induced skin cancer. Furthermore, it has been discovered that alpha santalol reduces inflammation via changing the interaction of several chemokines and cytokines. In addition to cytokines, alpha and beta santalol have been shown to inhibit the lipopolysaccharide-mediated arachidonic acid pathway, which lowers PGE2 and thromboxane B2. Perhaps as a result of PDE inhibition, its anti-inflammatory qualities have sparked attention in the treatment of several inflammatory skin conditions, including psoriasis and atopic dermatitis [6].

Alpha santalol and SWO both have anti-inflammatory effect that may make them useful in topical anti-inflammatory product applications. The antihyperlipidemic and antihyperglycemic effects of SWO, a blend of beta and alpha santalol, have been demonstrated by alpha santalol [7].Numerous studies have examined its neuroleptic effects and linked beta and alpha santalol to them. According to a Study on animals, they may elevate the levels of amine metabolites in the brain, such as homovanillic acid, 3, 45dihydroxyphenylacetic acid, and/or 4 hydroxyindoleacetic acid. This may indicate a comparable, albeit slightly different, effect to that of an inhibitor of tyrosinase, an essential enzyme involved in the synthesis of melanin [8].SWO has been discovered to have activity against viruses such as herpes, viral warts, molluscum contagiosum, influenza, and yeasts, as well as bacteria such as Staphylococcus aureus, fungal dermatophytes, and yeasts, though its exact antimicrobial properties are yet unknown. Ten individuals were instructed to apply a drop of topical SWO twice a day to the wart area and gently rub the area afterward [9]. The experiment was open-label, and the subjects were requested to repeat the application every two to three weeks for a total of twelve weeks. Eight out of ten [80%] of the treated warts had completely resolved by the end of the Study, with the remaining two showing substantial improvement [25–90%].None of the participants reported experiencing pain, discomfort, erythema, itching, skin peeling or scarring, irritation, or any negative side effects [10].

2. ORIGIN AND DISTRIBUTION

Native to the tropical area encompassing eastern Indonesia, the Indian peninsula, and northern Australia is S.album. The Indonesian islands of Timor and Sumba as well as the drier tropical parts of India are the primary distribution areas. It originated in the southern Indian highlands, primarily in the districts of Karnataka, Tamil Nadu, Maharashtra, and Andhra Pradesh that border them. The species is mostly found in scrub and dry deciduous woodlands in these locations [11]. The vegetation is a classic thicket of monsoon vines growing on pristine sand. It has been observed on the dunes near the mangroves and the coast, just above the typical high tide line. It grows above the beach on low lateritic cliffs as well. Actually, the tree is an obligatory hemiparasite plant that feeds on a variety of hosts, including Lantana acuminata, Pongamia glabra, and Cassia siamea. These days, it can be found planted in Sri Lanka,the Philippines, China, India, Indonesia, Malaysia, and Northern Australian [12].

Distillation of Sandalwood oil

In India, the process known as water distillation has been used to extract *Sandalwood* oil since ancient times. The raw material is heated over an open flame after being submerged in water in a copper vessel. Through a bamboo or copper conduit that is constantly replenished with cold water, the vapors from the still's body are directed toward receivers. In these regions, the species is mostly found in arid deciduous and scrub woodlands. Sandalwood billets, roots, and a sizable quantity of chips make up the raw material in a contemporary operation.which are a combination of sapwood and heartwood [13].The roots provide the largest proportion of oil, while the chips yield the lowest. Good billets and roots frequently produce 4.5 to 6.25 percent on average. Initially, the wood is put into a chipping machine, which consists of a fast-revolving disc with six radially mounted knives on it. After that, the wood is crushed by these blades into a coarse powder [14]. The latter is then fed into disintegrators after that.which further break down the wood into a finer texture. In certain industries, the wood is chopped into small sticks or chips by hand using hatchets and adzes instead of using a chipper [15]. Disintegrators are then fed these. To create a powder that will not "pack in" too tightly in the stills but instead form a uniform porous body of material that allows steam to pass easily over the entire mass of powder to be distilled, the powder that comes out of the disintegrator is carefully sieved and remixed. The stills, which are often constructed of copper and very seldom of iron, have goosenecks to transfer the steam and oil vapor to tubular condensers clad with tin [16]. Although the stills' shapes and sizes vary, the typical setup consists of a still that can store between 3/4 and 1 ton of powdered wood, with the latter usually resting on a false bottom with holes in it.

Typically, the "burden" in the still has some room on top of it. The still's height is almost 25% more than its circumference. Typically, 20 to 40 pounds of low-pressure steam is used for distillation [17]. Because it produces a marginally greater oil output and saves a little amount of time, high-pressure steam distillation has been suggested for the extraction of *Sandalwood* oil. Usually, distillation takes 48 to 72 hours. Every factory has a different distillation end point based on its financial situation [18].When the oil yield is no longer economically viable, the latter is terminated. Crude *Sandalwood* oil floats on the surface of the distillate as it gathers in the receivers. Typically, shallow ladles are used to skim this off, and the oil and water layers are then further separated in a separating funnel. When a little scum with suspended woody matter rises to the top, the crude oil is transferred to a different vessel and left there for a while. Next, the oil is meticulously purified [19].

Physicochemical Properties

The volatile oil derived from the roots and heartwood of Santalum album L. has an aroma that is characteristic of East Indian sandalwood; it is heavy, sweet, and lingering. It is rather sticky and yellowish. Table 1 shows the qualities of East Indian *Sandalwood* oil as reported by Gildemeister and Hoffmann [20].

Table 1. Physicochemical Properties of *sandalwood.*

Specific Gravity at 15°	0.973 to 0.985
Optical Rotation	-16° 0' to -21° 0' in exceptional cases lower rotations have been observed
Refractive Index at 20°	1.504 to 1.509
Acid Number	0.5 to 8.0 (see below)
Ester Number	3.0 to 17.0
Ester Number after Acetylation	Not less than 196
Total Alcohol Content, Calculated as:	
Santalol	Not less than 90% (see below)
Solubility at 20°	Soluble in 3 to 5 vol. and more of 70% alcohol; in 5 to 6 vol. and more of 69% alcohol; in 6 to 7 vol. and more of 68% alcohol.

Traditional Uses

The main reasons S. album is farmed are for its aromatic oil and lumber. The lumber is robust and long-lasting, weighing 870 kg/cubic meter. Its heartwood, which has a tight texture, is utilized for carving and ornamentation. Though it has been used as fuel, most people believe the wood is too valuable for this application [21]. The heartwood of *Sandalwood* yields a light yellow to yellow viscous liquid that has notes of sweetness, animalic overtones, persistence, spice, warmth, woodiness, and nuttiness. It is widely used in the pharmaceutical, cosmetic, aromatherapy, and perfumery industries. Because they work well as fixatives, they are highly prized in the toiletry and perfumery sectors, particularly for some delicate scents that are incredibly uncommon and delicate [22].*Sandalwood* oil is a necessary component of any heavy or oriental kind of perfume mix. Because of its natural propensity to absorb the majority of the ethereal notes of other entire herbs or flowers and improve their perfumery status and stability, sandal oil is typically used as the basis in Indian attars [23]. The oil is used to flavor a variety of food items, including puddings, candies, pan masala, baked goods, frozen dairy desserts, gelatine, and alcoholic and non-alcoholic beverages. *Sandalwood* oil has been approved for use as a food additive by the US Food and Drug Administration, the Joint FAO/WHO Expert Committee, and the Flavour and Extract Manufacturers Association Council of Europe [24].Its seeds contain fatty oil that can be used to make paint, and its fruits are tasty. Heartwood powder is crushed into a paste and applied as a cosmetic, used to produce incense sticks, and burned as scents in homes and temples. The bark has considerable potential in the tanning industry and contains 12–14% tannin [25]. Animals that graze on S. album leaves find it tasty. Leaves enrich soil because they generate good green manure. In terms of medicine, *Sandalwood* is considered a diuretic, expectorant, stimulant, astringent, sedative, cooling, and disinfectant in the genitourinary and bronchial systems. The plant's wood, root, bark, and leaves were utilized by indigenous doctors to treat liver diseases like jaundice [26].

In addition to being a blood cleanser and tonic for the heart, stomach, and liver, it is also particularly helpful in treating gastric irritation, jaundice, dysentery, tension, and bewilderment. *Sandalwood* is used in the Ayurvedic system to cure a variety of different conditions, including bleeding diarrhea, intrinsic hemorrhage, hemorrhaging piles, vomiting, poisoning, hiccups, the first stage of the pox, urticaria, eye infections, and inflammation of the umbilicus [27]. In addition to being a blood cleanser and tonic for the heart, stomach, and liver, it is also particularly helpful in treating gastric irritation, jaundice, dysentery, tension, and bewilderment. *Sandalwood* is used in theAyurvedic system to cure a variety of different conditions, including bleeding diarrhea, intrinsic hemorrhage, hemorrhaging piles, vomiting, poisoning, hiccups, the first stage of the pox, urticaria, eye infections, and inflammation of the umbilicus [28].

Pharmacology

Sandalwood and its oil have shown a wide spectrum of pharmacological actions in addition to its importance in perfumes and cosmetics. S. album has been the subject of in-depth Study to support its traditional medicinal claims and uncover new biological efficacies. Table 2 highlights the range of biological effects that have been documented from several pharmacological investigations on *Sandalwood* and its oil, from antibacterial to anticancer. This is a summary of the pharmacological actions of *Sandalwood* and its oil that have been documented [29].

Table 2 Pharmacological activity of *sandalwood*

Pharmacological activity	Description	Reference
Antioxidant	Sandalwood extracts exhibit antioxidant properties, helping to combat oxidative stress in the body	[29]
Anti-inflammatory	The oil has been shown to reduce inflammation, which can aid in treating various inflammatory conditions	
Antibacterial	Sandalwood oil demonstrates antibacterial effects against various pathogens, contributing to its use in skincare	[37,39]
Antifungal	Effective against fungal infections, making it useful in treating conditions like athlete's foot	[41]
Antiviral	Exhibits antiviral activity against viruses such as Herpes simplex types 1 and 2	[43,44]
Anticancer	Research indicates potential anticancer properties, with studies showing inhibition of cancer cell proliferation	[50,52]
Neuroleptic	Sandalwood oil has sedative effects, helping to alleviate anxiety, insomnia, and nervous tension.	[58]
Antihyperglycemic	Demonstrated effectiveness in managing blood sugar levels, beneficial for diabetes management.	[60]
Antihyperlipidemic	Helps in managing lipid levels, potentially protecting against cardiovascular diseases	[59]
Cardioprotective	Shown to protect cardiac tissue from damage in various animal models, indicating potential heart health benefits.	[61]
Sedative	Produces a calming effect, aiding in relaxation and reducing stress.	[65]
Expectorant	Used traditionally in Ayurveda for respiratory issues, helping to clear mucus from the airways.	[49]
Diuretic	Promotes urine production, which can aid in detoxification and fluid balance.	[66]

Hepatoprotective activity

The hydro-alcoholic extract of S. album leaves showed significant hepatoprotective activity against CCl_4 and paracetamol-induced hepatotoxicity by significantly increasing the levels of glutathione, superoxide dismutase, catalase, and protein and reducing the activities of serum marker enzymes, bilirubin, and lipid peroxidation in a dose-dependent manner. This was further corroborated by histological analyses and a drop in the liver's overall weight [30].

CNS Effects

It is discovered that Santalum album L. has memory-enhancing potential. According to sedative effect studies, inhaling East Indian *Sandalwood* oil reduced mice's motility by 40–77% when compared to a 0% control group. *Sandalwood* oil and aqueous extract have already been shown to have sedative properties [31]. *Sandalwood* oil relieves heated, tense, and irritated emotional states that lead to headaches, insomnia, and tense muscles. It's supposed to have a relaxing effect on anxiety. Santalols are a bioactive component that have been demonstrated to have depressive effects on the central nervous system (CNS); hence, they may be useful for those who have trouble sleeping [32].

Four synthetic *Sandalwood* chemicals and oil were shown to precisely stimulate olfactory receptor neurons in a first-of-its-kind investigation. Additionally, it was demonstrated that heartwood solvent extracts have neuroleptic properties in mice. When administered intragastrically and intracerebroventricularly, alpha- and α-santalols markedly elevated the levels of homovanillic acid, 3, 4-dihydroxyphenylacetic acid, and/or 5-hydroxyindoleacetic acid in the brains of mice [33]. It has been demonstrated that alpha-santalol is a potent antagonist of serotonine 5 HT2A and dopamine D2 receptor binding. Furthermore, alpha-santalol's antipsychotic impact was identical to that of chlorpromazine.Significant physiological changes, including sedative and calming effects, were elicited by alpha-santalol, while transdermal absorption of *Sandalwood* oil led to physiological deactivation but behavioral activation [34].The main ingredient of the oil, alpha-santol, has recently been shown in TLC254 bioautographic assays to be a potent inhibitor of tyrosinase and cholinesterase in vitro. As a result, the essential oil has a lot of potential for use in both skin care and Alzheimer's disease treatment [35].

Anti-ulcer Activity

Oral S. album stem hydroalcoholic extract-treated rats successfully avoid stomach ulcers brought on by chemical (local irritant and drug-NSAID) and physical (stress) methods. This indicates that the rats are relatively protected against gastric ulcers [36].

3. ANTIBACTERIAL ACTIVITY

While many other investigations concentrated on Australian *Sandalwood* oil, a number of studies have examined the antibacterial qualities of East Indian *Sandalwood* oil . *Sandalwood* oil and its synthetic counterparts had the highest antibacterial activity against axilla bacteria in a comparative investigation using 26 essential oils [37].Sandalwood oil is a powerful antibacterial agent that works against methicillin-resistant Staphylococcus aureus and antimycotic-resistant Candida species. The crude extract of sandalwood oil and its components, α- and β-santalol, has antibacterial qualities against Helicobacter pylori, a Gram-negative bacterium that is strongly linked to the development of gastric, duodenal, and stomach ulcers. Furthermore, santalol has anti-influenza qualities against the H3N2 virus, while sandalwood oil has action against the Type 1 Herpes simplex virus [38]. In another study, the maximum inhibitory effects of sandalwood oil against Bacillus mycoides and Escherichia coli were demonstrated. It has been demonstrated that the methanol extract of S. album is very active against Candida albicans and effective against Salmonella typhi, Bacillus subtilis, Staphylococcus aureus, and Pseudomonas aeruginosa. In tests against Trichophyton rubrum, Trichophyton mentagrophytes, and Microsporum canis, sandalwood oil has shown anti-dermatophytic qualities. [39]. Furthermore, it was shown that the components of sandalwood oil, -and -santalol, were active against both Staphylococcus aureus and S. typhimurium, but epi--santalene was inactive against S. typhimurium. Trans-11-octa-decen-9-ynoic acid, one of the seed's primary constituents, has been demonstrated to inhibit gram-positive bacteria and several harmful fungi. Higher and/or medium concentrations of santalols were reported to have higher antibacterial action against yeast, bacteria at low concentrations, and both gram-positive and gram-negative bacteria[40].Additionally, it was demonstrated that young tree shoots were bactericidal against 13 different bacterial species.

Antifungal Activity: It has been observed that *Sandalwood* oil exhibits anti-fungal properties against Trichophyton mentagrophytes, T. rubrum, and Microsporum canis. Against the human pathogenic fungal strains Microsporum canis, Trichophyton mentagrophytes, and T, *Sandalwood* oil was found to be effective [41].

Antiviral Activity: Studies on biology have also demonstrated *Sandalwood*'s antiviral properties. It has been demonstrated that *Sandalwood* oil can be used to prevent and treat skin blemishes, warts, and other virally-induced skin tumors [42]. Ayurvedic and Chinese medicine are examples of traditional medical systems that also highlight the antiviral properties of *Sandalwood* oil. *Sandalwood* oil showed dose-dependent antiviral efficacy against Herpes simplex viruses [HSV]-1 & 2 by inhibiting viral replication in an in vitro investigation [43]. Additionally, it was thought that *Sandalwood* oil modified the amounts of acid-soluble sulfhydryl, gluthatione, and S-transferase in the liver, which helped protect the cells. *Sandalwood* oil inhibited the herpes simplex virus type 2 [HSV-2] on RC-37 cells in vitro. It's interesting to note that *Sandalwood* oil only inhibited the virus's ability to interface with host cells non-specifically before the virus was able to adsorb into the cells [44].

The constituents found in sandalwood oil, specifically - and β-santalols, their blends, and their derivatives, have been linked to the management of human warts, specifically those brought on by DNA pox virus, which results in Molluscum contagiosum, and HPV. These ingredients have also been suggested as a treatment for RNA viruses such as HIV, as well as a cure for psoriasis, seborrheaic dermatitis, allergic or eczematous skin rashes, acne lesions on the face and body, and the elimination of pustular acne lesions caused by bacterial infections such as streptococcal and staphylococcal acne [41,43,44]Furthermore, products derived from *Sandalwood* oil and sotalol made claims about their ability to heal herpes and cold sores.The Indian *Sandalwood* tree's single cell and somatic embryo suspension cultures have recently been shown to be a viable and renewable source of shikimic acid, which is needed to synthesize Tamiflu, the only neuraminidase inhibitor medication against the influenza A virus that is available for commercial use [45].Antioxidant effectiveness Investigations into phytochemistry and pharmacology demonstrated the existence of antioxidant properties, supporting their traditional medicinal uses. Nitric oxide [NO] levels were studied in vitro for possible regulatory effects of S. album and other Indian medicinal plants using sodium nitroprusside as a NO donor. Most plant extracts demonstrated significant dose-dependent direct scavenging action on NO. Its ability to scavenge nitrous oxide and act as an antioxidant has been found. Santalum album can prevent oxidative stress-induced cell damage and lipid peroxidation in cardiac tissue. It can also prevent DOX-induced production of inflammation and apoptosis in cardiac tissue [46].It has recently been demonstrated that S. album's cyanidin-3-glucoside, an anthocyanin pigment, has antioxidant and nutritional value. Furthermore, employing nine in vitro antioxidant tests, a comparison investigation revealed that callus cells produced in vitro exhibited similar antioxidant properties when exposed to *Sandalwood* oil [47]. Sandalwood oil increased the amounts of glutathione S-transferase [GST] and acid-soluble sulfhydryl [SH] in the liver of mature male Swiss albino mice.Increased levels of acid-soluble SH and GST activity suggested that *Sandalwood* oil may have a chemopreventive effect on carcinogenesis by inhibiting certain processes. Similar to this, methanolic *Sandalwood* extracts showed promise to treat dementia and memory loss linked to Alzheimer's disease by inhibiting aacetylcholinesteraseand scavenging super oxide and DPPH free radicals in albino mice [48]. An in vivo Study has recently shown the anti-hyperglycemic and antioxidant properties of *Sandalwood* oil and its main ingredient, α-santalol, in diabetic male Swiss albino mouse models generated by oxidative stress mediated by D-galactose and alloxan.

Hemolytic activity: Haemolytic activity is an indicator of a compound's overall cytotoxicity towards normal, healthy cells. According to a Study, the plant's leaf extract generated the RBC lysis. However, parenteral injection is the sole way in which this hemolytic activity occurs. According to the Study, the plant's leaves contained saponins that have hemolytic properties against blood [49].

Anticancer activity: Research on animal models and skin cancer cell lines has shown the molecular mechanisms and chemopreventive effects of santalol on the development of skin cancer. It's also been shown that oil can cause cancer cells to undergo apoptosis and cell cycle arrest'

[50]. Oil has been shown to have anticancer properties in in vitro models of melanoma, non-melanoma, breast, and prostate cancer, as well as in chemically-induced skin carcinogenesis in CD1 and SENCAR mice and ultraviolet-B-induced skin carcinogenesis in SKH-1 mice. In both mouse strains, α-santalol, a constituent of sandalwood oil, delayed the development of papillomas. [51]. Alphasantalol has been found to induce apoptosis in human epidermal carcinoma A431 cells by activating caspase, which leads to a loss of mitochondrial potential and cytochrome release, at concentrations between 25 and 75 μM. In a similar study, topical application of α-santalol was shown to have chemopreventive benefits in female hairless mice strain SKH-1, as demonstrated by lower tumor incidence, multiplicity, and ornithine decarboxylase activity[50,52]. Moreover, it was shown that α-santalol suppressed lipid peroxidation in skin and liver microsomes in vitro, reduced tumor multiplication, and delayed the formation of skin tumors. By acting as an antioxidant, these activities could have stopped UVB-induced skin tumors from developing [53].In a UV B-induced skin cancer growth model in SKH-1 mice, alpha-sotalol was found to drastically upregulate levels of apoptosis-related proteins, caspases 3 and 8, as well as the tumour suppressor protein p53, through an extrinsic mechanism. When α-santalol activated caspase-3, human prostate cancer cells underwent apoptotic induction. Chips made from the heartwood of sandalwood were utilised to investigate the potential of two aromatic glycosides, six neolignans, and three novel sesquiterpenoids to promote tumour growth [54]. The chips' ability to activate Raji cells' early Epstein-Barr virus antigen (EBV-EA) in vitro was examined. Furthermore, in in vivo studies, it demonstrated a strong suppressive impact on EBV-EA activation and a strong inhibitory effect on two-stage carcinogenesis on mouse skin [55].

Moreover, α-santalol derivatives demonstrated tumor-selective cytotoxicity in HL-60 human promyelocytic leukaemia cells and TIG-3 normal human diploid fibroblasts.Two lignans obtained from the heartwood samples were shown to be cytotoxic to human promyelocytic leukaemia cells (HL60) and human lung adenocarcinoma cells (A549) when exposed to apoptosis-induced tumour cells [56]. The efficacy of α Santalol, the active ingredient in sandalwood essential oil, as a shield against skin cancer has been studied in mice models of skin carcinogenesis.antipyretic characteristics Sandalwood oil dramatically decreased the amount of heat produced by yeast-induced pyrexia in albino rats when it was given at a dose of 200 mg/kg. anti-inflammatory qualities Santalols have demonstrated a potent anti-inflammatory impact in a number of experimental animals [57]. Santalum album had significant anti-inflammatory and antiulcer effects as evidenced by its ability to control paw oedema brought on by carrageenan, granuloma brought on by cotton pellets, and ulcers brought on by pylorus ligation. These findings could validate the traditional medical system's successful usage of this plant to treat inflammatory diseases like ulcers. Mice exposed to methanolic extracts of heartwood demonstrated both in vitro antioxidant activity and in vivo anti-inflammatory and analgesic effects [58].

Antihyperglycemic and antihyperlipidemic effect

Research conducted on the effects of long-term oral administration of Sandalwood's petroleum ether fraction on hyperglycemia and hyperlipidaemia in streptozotocin-induced diabetic rats revealed a decrease in blood glucose levels. Additionally, the group using metformin had lower blood glucose levels compared to the diabetic control group's higher levels [59]. Furthermore, in treated diabetic rats, levels of triglycerides [TG], low density lipoprotein [LDL], and total cholesterol [TC] were reduced, but levels of cardioprotective HDL were elevated. There was a notable decrease in the atherogenic index, which suggested that S. album may have antihyperglycemic and antihyperlipidemic properties [60].

Cardioprotective activity

It has been demonstrated that the aqueous extract of sandalwood significantly reduces lipid peroxidation on doxorubicin-induced cardiotoxicity in rat models and significantly protects against ISO-induced myocardial infarction in albino Wistar rats, both of which are dose-dependent [61].

Physiological effects

Numerous physiological activities and sensory stimulation are reported to be impacted by *Sandalwood* oil and its main component, α-santalol. While the oil was found to increase systolic blood pressure, skin conductance level, and pulse rate, α-santalol was found to increase mood and attention ratings more than the oil [62]. It has been observed that inhaling *Sandalwood* oil improves hearing [63]. It was recently demonstrated that the myocardial contractility and heart rate of an isolated and failing frog heart were significantly elevated by sandalwood tea. Furthermore, it demonstrated effective anti-fatigue characteristics in contracting the isolated rabbit aortic strips' smooth muscle. Despite occasional reports of discomfort or sensitisation reactions in humans, sandalwood oil did not exhibit any phototoxic effects [64].

Metabolic effects

It has been demonstrated that exposing nursing mouse pups to sandalwood oil trans-mammary changes the neonatal hepatic xenobiotic metabolising enzymes. Moreover, it is reported that the components of sandalwood oil and their transit through milk changed the way the liver metabolised xenobiotics, causing the liver's glutathione-S-transferase, glutathione reductase, and glutathione peroxidase activities to increase [65]. Hepatic cytochrome B5 and acid-soluble sulfhydryl concentrations increased along with a reduction in hepatic cytochrome P 450.

Genotoxicity effects: After Study, *Sandalwood* oil's potential to damage DNA in Bacillus subtilis was determined to be non-genotoxic.Equally, the suppression of B. subtilis induced by *Sandalwood* oil demonstrated its non-genotoxic nature [66].

Genitourinary system effects

Due to its astringent qualities and effect on the mucous membranes of the genitourinary tract, *Sandalwood* oil has been used for years to treat genitourinary tract infections like cystitis and gonorrhea. It also helps reduce the risk of infections like herpes virus by removing mucous congestion and restoring mucous membranes [67]. Due to its historical use, *Sandalwood* oil is now a popular choice in current cosmeceutical applications for anti-aging skin care, toning effects, and scar prevention.

Insecticidal activities

Sandalwood oil is used as an acaricide because it repels Varroa jacobsoni from honey bee colonies. There have also been reports of a slight activity against the mushroom fly, Lycoriella mali.It was also discovered that termites could not penetrate the oil [68].Santalol is effective against Tetranychus urticae spider mites due to its acaricidal and oviposition-deterring properties.

Dietary aspects

With a daily consumption of 0.0074 mg/kg, *Sandalwood* oil is regarded as safe as a flavoring ingredient. It has been used orally as a dietary supplement for a long time with no negative effects ever observed. *Sandalwood* oil was demonstrated to have an antagonistic effect on intestinal spasms brought on by acetylcholine, histamine, and barium chloride by inhibiting hyperactive small intestine movement in mice [69]. Additionally, it was recently proven that in streptozotocin-induced diabetic rats, leaf extracts from the *Sandalwood* tree have antihyperglycemic and antihyperlipidemic properties [70].

Aromatherapy Sandalwood

Oil is prized for its own sweet, warm, rich perfume of balsamic vinegar and is calming, soothing, cooling, and sensuous. It works wonders when used with lotions, creams, bath oils, aftershaves, and massage and facial oils. It works well with practically any oil by supplying or strengthening the base note and giving its fixative ability [71]. It combines particularly well with floral or other oils that are dominated by their top or middle notes. It works well with formulae that are both feminine and masculine. All skin types can use it, although chapped, dry, sensitive, or irritated skin can benefit most from it. It helps calm a nervous mind and encourages sound sleep [72]. In times of emotional d can be utilized for respiratory tract infections and chronic bronchitis involving a persistent dry cough [73]. Modern aromatherapy uses *Sandalwood* oil to treat a variety of ailments. *Sandalwood* is frequently utilized in skin care products because of its emollient qualities [74]. Because of the oil's calming properties, it can be used to hot, tense emotional states that result in headaches, sleeplessness, and tightness in the nerves. When its calming, demulcent properties are needed, itdue to its astringent properties, *Sandalwood* aids in clearing mucous congestion. *Sandalwood* oil reduces the chance of infection and aids in mucous membrane restoration. It has been used for gonorrhea and cystitis-two types of genitourinary tract infections—for many years. *Sandalwood* oil is mostly used for dry skin issues brought on by moisture loss and skin inflammation [75]. It is calming, cooling, and hydrating when applied topically [76]. It can be applied to treat acne and greasy skin as well as ease psoriasis and eczema. Topical application [such as massage, compress, bath, sitz bath, douche, ointment, skin care, etc.] and inhalation [such as direct inhalation, diffuser, oil, vaporizer, and steam inhalation] are the two main ways of administering medication [77].

4. PHYTOCHEMISTRY

The chemical composition of *Sandalwood*, the most expensive wood and essential oil source, has been thoroughly studied. It takes 30 years for *Sandalwood* to accumulate oil in the heartwood when it grows naturally [78]. Any essential oil's yield and composition are greatly impacted by the age of the tree, the color of the heartwood, the maturity of the organs, the specific tree, its location inside the tree, environmental cues, and genetic variables of the plant [79]. The heartwood's steam distillate is traditionally sold as a marketable *Sandalwood* essential oil, following a long-standing custom. A well-established tree's essential oil yield can vary from 2.5 to 6%, contingent upon the tree's age, heartwood color, individual tree under examination, placement within the tree, and growing environment.Furthermore, the oil extracted from both young and adult sandal trees has distinct compositions, and the oil content and composition from heartwood samples taken at different stages of the tree's growth also differ [80].

The chemical components of *Sandalwood* oil, including its isolation, synthesis, and quantitative measurement, have been the subject of many studies. Shankaranarayana and colleagues conducted extensive Study on the phytochemical and associated features of *Sandalwood*, such as the chromatographic separation of alpha and beta santalenes, the column chromatographic separation of α- and ε-santalols. Some of the simple techniques for extracting sandal oil with a higher yield include benzene extract rectification, the formation of sodium santal-bate-dimethyl sulphate inclusion complex, estimation of oil in depot-based sandalwood, the potential for fragrant product development from less odorous sandalwood oil, estimation of content and composition of oil from central and transition zones of sandal disc, use of sandalwood extractives, recovery of essential oil from hydrolyzed exhausted sandalwood powder [HESP], and isolation of santalols from sandalwood oil [81].. Commercial Sandalwood oil mostly consists of sesquiterpene alcohols such as α- and β-santalols [$C_{15}H_{24}O$], bergamotols, and numerous of their stereoisomers. Consisting of sesquiterpene hydrocarbons such as α-and β-santalenes [$C_{15}H_{24}$], bergamotenes, α-, β-, and γ-curcumenes, β-bisabolene, and phenylpropanoids, among others, are among the minor constituents. In general, α-santalols outnumber β-santalols.Verghese and colleagues determined that the primary components of essential oils are sesquiterpene alcohols, cis- and cis-[illegible]-santalol, α-transbergamotol, and epi-cis--santalol [82]. Minor constituents include hydrocarbon santene [C_9H_{14}], trans-santalol and cis-lanceol, -santalene, β-santalene, -bergamotene, epi-β-santalene, -curcumene, β-curcumene, γ-curcumene, -bisabolene, -bisabolol, and heterocyclics [83].

Additional elements present in sandalwood oil comprise alcohol, santenol [$C_9H_{16}O$] and teresantalol [$C_{10}H_{16}O$]; aldehydes, isovaleraldehyde and nor-tricycloekasantalal [$C_{11}H_{16}O$]; ketones, l-santenone [$C_9H_{14}O$] and santalone [$C_{11}H_{16}O$]; and acids, teresantalic acid [$C_{10}H_{14}O$], which is partially free and partially esterified, along with α- and β-santalic acids [$C_{15}H_{22}O_2$] [84]. A study was done on the genetic diversity across Sandal populations from various provenances in India as well as the correlation between girth and heartwood/oil yield. While the constituents of Australian and Indian *Sandalwood* oils are similar, their amounts vary, resulting in two completely different but related oils. Sesquiterpenes are the main components of Australian *Sandalwood* oil. These include E, E-farnesol, and α-bisabolol, as well as the key sesquiterpene alcohols, α-santalol and -santalol [85].

It is important to note that the concentration of secondary metabolites is determined by extrinsic factors like extraction techniques and by genetic, environmental, and intrinsic properties of the plant material. Additionally, it was reported that a tree that is 10 years old has somewhat higher levels of santyl acetate and santalene than a tree that is 30 years old [86]. The quantity and content of essential oil were also investigated from the roots of the East Indian *Sandalwood* tree. Solvent extraction of *Sandalwood* yielded a 10.3% oil recovery rate from the roots [87]. 53 components totaling 99.9% of the oil were found by GC and GC/MS analysis [88]. These included 5 sesquiterpenoid isomers [4.4%], 9 sesquiterpenes [7.8%], 30 sesquiterpenols [78.5%], and terpenoid acid [0.4%] [89].With 19.6% and 16.0% of the total, respectively, α- and α-santol were the main components of the essential oils. The amount of α-santalol was lower than the 41–55% suggested range, although it was still rather near to the 18% standard. Bisabolenol A, B, C, D, and their isomers made up a substantial portion of the oil overall, or 25.0%.[82] In a different investigation, GC-MS analysis revealed 32 active phytocompounds in total that were found in the stem extracts of the Santalum album[83]. In a follow-up investigation, 35 volatile metabolites were found in the heartwood of a 15-year-old tree using GC-MS analysis [90]. Seven α-santolderivatives, including [9R,10E]-9-hydroxy-α-santalal, [10R,11R]-10,11-dihydroxy-α-santalol, [9E]-11,13-dihydroxy-α-santalol, and [10E]-12-hydroxy-αsantalic acid, were isolated using bioassay-guided fractionation of the heartwood of Santalum album. Through spectroscopic investigation, their structures were identified. A method for profiling metabolites such as n-alkanes, sesquiterpene, sesquiterpenoids, fatty acids, alcohols, and hydrocarbons of *Sandalwood* oil was developed: HPTLC-based assessment of sesquiterpenoids from *Sandalwood* oil [91].The functional characterization of new sesquiterpene syntheses from Indian *Sandalwood* was investigated by Srivastava and colleagues[86]. The Study examined the feasibility of accurately differentiating the woods based on factors such as anatomical structure, hot water extract color, oil chemical composition [primarily santol concentration], and DNA fingerprinting.We looked into the relationship between the structure and action of smelly chemicals found in *Sandalwood*. Additionally, the association between the odor and structure of [Z]-α-santol, the primary component of *Sandalwood* essential oil with a distinct woody scent, and its variations was examined, with a particular emphasis on the connection between the compounds' odour and side chain structure [92].

According to the Study, the comparable Z-isomer odors were found to be similar to those of the equivalent saturated compounds, but they were distinct from the corresponding E-isomer odors, which were fresh, fatty, or odorless [93]. These findings suggested that the smell of α-santalol is significantly influenced by the side chain's relative arrangement to the santalane frame. The woody odor of α-santalol and its investigated derivatives is eliminated by the E-configuration in the side chain, but not by the Z-configuration or saturation of the carbon side chain. Studies on the sandal tree's seed and seed oil, as well as the removal of unsaponifiables from the oil, partial hydrogenation of the seed, the fatty acid content of the seed coat, and compositional changes in the seed oil during storage, were also documented [94].There have been reports of betulinic acid isolation from the coat of sandal seeds and its decrease of botulin. The use of dried *Sandalwood* seeds and bark was investigated.From S. album leaves, a variety of flavonoid components were extracted and described, including vicenin-2, vitexin, isovitexin, orientin, isoorientin, chrysin-8-C-β-D-glucopyranoside, chrysin-6-C-β-Dglucopyranoside, and isorhamnetin. Ranade compiled information on the analysis, artificial alternatives, and industrial, and medicinal applications of *Sandalwood* oil. Makoto also gave a summary of studies on the artificial and natural scents of *Sandalwood*.It was stated that *Sandalwood* scent compounds were synthesized from camphoric aldehyde [95].

Z- santalal is produced by oxidizing santalol with MnO_2 in hexane and isomerizing it with 0.5–2% glacial acetic acid to produce E-- santalal. This approach of creating a perfume with a similar flavor was patented. An analysis of the safety of oil in food products was conducted. An analysis was conducted to compare the chemical composition of several kinds of fragrant *Sandalwood*, such as S. album, S. spicatum, and S. austrocaledonicum [96]. Setzer described the use of several essential oils, including *Sandalwood* oil, in aromatherapy.Gleason talked about the prospects and uses of Indian *Sandalwood* oil as a base ingredient for high-end fragrances.Techniques for adulteration identification and detection were created [96,97].

5. FUTURE PROSPECTIVE

Many chemical elements of *Sandalwood* and its oil that are biologically active have been identified and isolated thanks to phytochemical Study. However, there is a chance to discover new chemical entities. Study on the pharmacological properties of *Sandalwood* and its components has not only confirmed the efficacy of ancient medical methods but also revealed various new therapeutic potentials. Chinese medicine has employed S. album oil to treat alcoholic hepatitis, depression, polio, schizophrenia, coronary heart disease, blood sugar regulation without hypoglycemia danger, and the creation of several cosmetic items [98].*Sandalwood* components have been shown in recent pharmacological and clinical investigations to have antioxidant, anti-allergic, anti-β-hexosaminidase release, cancer cell growth inhibitory, and mammalian DNA polymerase-inhibitory properties. The majority of biological activities have been linked to the components of sesquiterpenoids, such as santalols and the α- and ε-santalenes. Cloning and characterization of several genes and encoded enzymes involved in the production of santalene are now feasible [99].This achievement has focused on the potential for improved comprehension of the phytochemical variety and biosynthetic pathways of bioactive santalols through genetic approaches. Additionally, the way to obtain a diversity of *Sandalwood* sesquiterpenoids in desired proportions for the flavor and scent business was paved using microbial metabolic engineering techniques.Biotechnological methods could help increase the production of *Sandalwood* resources and bioactive components in response to rising worldwide demand. Additionally, to aid with industrial high-throughput screening for drug development, bioinformatics techniques and tools have been created for the prediction and detection of natural products from genomic sequences [100].Addressing the complex Study and analytical needs has been made easier by recently developed better analytical instruments and techniques, such as spectroscopic approaches for quality control and precision chromatography systems [such as MDGC, GC-MS]. Additionally, it has recently been highlighted that Ayurvedic knowledge, traditional documented usage, tribal non-documented use, and a comprehensive literature search should be done in order to maximise efforts in drug development from plant sources and identification of viable candidate plants. Researchers are putting a lot of effort into creating novel, potent plant-based pharmaceuticals, nutraceuticals, and cosmeceuticals by looking for hints in the vast body of traditional and ethnobotanical knowledge. Research activities include the rigorous scientific confirmation of conventional herbal compositions with compelling data, in addition to the isolation and characterisation of novel molecular entities [101]. This is due to the growing interest in plant-derived products worldwide due to the negative side effects of their synthetic counterparts. There are still many traditional medicinal uses for *Sandalwood* and its essential oil that have not been proven by science. This presents a chance for chemo-biological and clinical Study. The amount of *Sandalwood* available worldwide is declining, while demand is rising [102].The

Sandalwood tree is classified as vulnerable on the International Union for Conservation of Nature's [IUCN] Red List of Threatened Species because of the dangers it confronts from the mycoplasmal spike disease, illicit poaching, and overexploitation to meet rising worldwide demand.Therefore, in vitro micropropagation through callusing, somatic embryogenesis, regeneration protocols, and somatic embryo development with increased accumulation of elements of *Sandalwood* oil may offer enormous opportunities for biotechnological methods of species conservation [103].

6. CONCLUSION

One of the most well-known and frequently utilized plants in perfumes and cosmetics is santalum album. In addition to its usage in perfumes and cosmetics, *Sandalwood* contains a variety of pharmacological properties, making it a valuable medicinal plant. Although *Sandalwood* has been the subject of much Study over the past 20 years, there is still more room to be explored to fully realize the plant's potential benefits for humankind. The structure, synthesis, and pharmacological efficacy of intriguing chemical compounds, particularly the sesquiterpenoids of *Sandalwood*, have been the subject of Study for over a century by scientists worldwide.Recent efforts to validate the traditional medicinal applications of essential oils and their constituents through contemporary experimental methods have sparked a renewed interest in pharmacological and mechanistic studies. *Sandalwood* and its oil have been shown in numerous investigations to possess a wide range of pharmacological properties, from antibacterial to anticancer. It also exhibits notable activity in a number of skin conditions. *Sandalwood* has not been extensively studied in toxicology. A summary of all recorded activity pertaining to this plant is required. This overview compiles many reported uses of *Sandalwood* oil and the plant itself.

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