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Review on therapeutic approach of anti-acne treatment by *Azadirachta indica* and *Ocimum gratissimum*

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Abstract

Millions of people worldwide suffer with acne vulgaris, a common skin ailment marked by the development of comedones, papules, pustules, and in more severe cases, nodules and cysts. There has been a boom in research into alternative remedies, especially herbal pharmaceuticals, due to growing resistance to traditional therapy and side effects associated with long-term use. Two well-known herbs with strong anti-acne effects are *Ocimum gratissimum* (scent leaf/ African basil) and *Azadirachta indica* (neem). The purpose of this review is to assess *Azadirachta indica* and Ocimum gratissimum's medicinal potential for acne vulgaris. We examine the phytochemistry of these herbs, emphasizing their potent components, which include thymol, eugenol, azadirachtin, nimbidin, and nimbin. These compounds have antibacterial, anti-inflammatory, and antioxidant qualities that make them useful in the treatment of acne. Finally, clinical studies examining the safety and effectiveness of topical formulations derived from *Azadirachta indica* and *Ocimum gratissimum* are reviewed, emphasizing their potential as monotherapies or adjuncts to conventional treatments. In summary, *Azadirachta indica* and *Ocimum gratissimum* represent promising candidates for the development of novel, effective, and safe herbal therapies for acne vulgaris, offering a natural alternative for people seeking sustainable and holistic approaches to skincare.

Keywords: *Azadirachta indica* (Neem); *Ocimum gratissimum* (African Basil); Acne Therapy; Anti-Inflammatory; Antiseptic; Antioxidants

1. Introduction

The growing fields of psychodermatology and neurodermatology have long recognized the comorbidity of long-term skin diseases with mental health issues. The condition known as acne vulgaris is a prevalent skin ailment that is frequently associated with psychological consequences such as anxiety and despair. One of the most prevalent chronic inflammatory disorders of the pilosebaceous follicles, acne is caused by a variety of factors and includes immunological hypersensitivity, hormone imbalance, altered follicular keratinization, and bacterial (*Propionibacterium-acnes*) colonization. It is also triggered by androgen. Acne has long-term consequences that can be significant, including the development of cutaneous and psychological scars that endure a lifetime, even while it lacks the urgency of a life-threatening condition and does not compromise general fitness. It undermines one's self-esteem and causes emotional discomfort due to perceived disfigurement, which lowers one's self-esteem and causes physical, social, and psychological pain. Out of all the herbal medicines available, *Azadirachta indica* (neem) and *Ocimum gratissimum* (scent leaf) have drawn a lot of interest due to their ability to treat acne vulgaris. Both *Ocimum gratissimum* and *Azadirachta indica* have a long history in traditional medicine and are well-known for their wide range of pharmacological characteristics, which include antioxidant, antibacterial, and anti-inflammatory effects. Numerous studies have been conducted to examine the potential therapeutic benefits of bioactive chemicals found in these herbs, such as nimbidin,

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nimbin, azadirachtin (found in *Azadirachta indica*), eugenol, and thymol (found in *Ocimum gratissimum*), on a range of skin diseases, including acne vulgaris [1].

2. *Ocimum gratissimum*

For human health, medicinal plants are extremely important. For this reason, according to estimates from the World Health Organization, 80% of people in poor nations receive their primary medical treatment from traditional practitioners. Consequently, medicinal plantshave been crucial in meeting people's sociocultural and therapeutic needs. In addition to being utilized as food and spices, several of these plants are also exploited as natural resources for the discovery and creation of novel medications. Numerous ethnobotanical surveys conducted in Africa and other parts of the world revealed that *Ocimum gratissimum*,a well-known plant, is frequently used to treat a variety of illnesses [2]. The plant is used in religious rites and traditional medicine in India to treat skin diseases, diarrhoea, and stomach-aches. *Ocimum gratissimum*, popularly known as clove basil, wild basil, holy basil, orAfrican basil, is a treasured medicinal herb that has been utilized for millennia. It is a memberof the Lamiaceae family, and it is referenced in the ancient Ayurvedic classic the Charaka Samhita. By its powerful flavour and pungent scent, it is considered to be a form of "elixir of life" and is said to improve life [3]. It is a cough elixir, and the leaves, when chewed after meals,have digestive properties. *Ocimum* leaves are also used as a preservative and to limit bacterial growth.

2.1. Taxonomical Classification

Botanical characterization of *Ocimum gratissimum L* [4]

Figure 1 Plant of *Ocimum gratissimum*

- Kingdom – Plantae
- Division-Magnoliophyta
- Class - Magnoliopsida
- Order - Lamiales
- Family - Lamiaceae
- Genus - Ocimum
- Species - O. gratissimum
- Subfamily - Nepetoideae
- Tribe - Ocimeae
- Botanical name - *Ocimum gratissimum* L

2.2. Morphological Classification

Organoleptic properties of *Ocimum gratissimum [4]*:

Figure 2 Morphological outlook of *Ocimum gratissimum*

- Odour- Strong Aromatic
- Taste- Pungent
- Lamina length- 12.4 cm
- Shape of Lamina- Ovate-lanceolate
- Lamina Margin- Serrate
- Plant Height- 102.6 cm
- Stem Colour- Dark brown
- Flower Colour- Cream
- Seed Shape- Globose
- Seed Colour- Brown

2.3. Distribution

Ocimum gratissimum plant native to Africa Madagascar, Southern Asia, and the Bismarck Archipelago and naturalised in Polynesia, Hawaii, Mexico, Panama, West Indies, Brazil, and Bolivia. Some of the species are found in Nigeria and also in Tropical and Sub tropical regions. The fragrant herb *Ocimum gratissimum* has been widely distributed throughout tropical and subtropical areas of the globe. Since it has escaped cultivation, it has spread to disturbed natural vegetation, savannas, coastal thickets, and riparian regions, where it grows as a weed in waste areas, pastures, and roadsides. Small and abundant, the seeds of this species are readily dispersed by wind, animals, people, and other factors. They can also contaminate soil and garden detritus. Once established, *Ocimum gratissimum* can spread andcreate dense, monospecific thickets that suppress local biodiversity and outcompete native plants [5].

2.4. Pharmacological properties of Ocimum gratissimum

2.4.1. Antioxidant Property

Ocimum gratissimum's anti-oxidant qualities have been linked to its medicinal advantages. Studies have demonstrated the presence of antioxidant vitamins including ascorbic acid and alpha-tocopherol in its leaf extracts. Studies have demonstrated the protective effects of flavonoids and phenols against cellular damage caused by oxidative stress. By scavenging or quenching free radicals, chelating metal ions, or inhibiting enzyme systems that produce free radicals, flavonoids and phenols have anti-inflammatory and anti-oxidative properties [6]. The aqueous extract of *Ocimum gratissimum* contains alkaloids, terpenoids, glycosides, and saponins, which may further enhance its anti-oxidative and anti-inflammatory properties. *Ocimum gratissimum* and eugenol essential oils were investigated for their antioxidant properties using test models for 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,20-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS). The significant IC50 values of 23.66 and 23.91 for the DPPH and ABTS models, respectively, indicate that *Ocimum gratissimum* essential oils may have antioxidant qualities. Pure eugenol lacks the antioxidant potential of *Ocimum gratissimum* oils. According to the analytical findings, *Ocimum gratissimum* might be able to scavenge free radicals [7].

2.4.2. Anti-Inflammatory Property

There have been studies of the plant's anti-inflammatory benefits. At dosages of 50, 100, and 200 mg/kg body weight, *Ocimum gratissimum* extract was able to minimize inflammation in rats that had been induced with carrageenan [8]. By substantially decreasing carrageenan- induced paw oedema in rats, the extract at 100 mg/kg body weight implies that

it may be usedtherapeutically to treat inflammations [9]. At dosages of 100–800 mg/kg, *Ocimum gratissimum* was found to have anti-inflammatory effects on rats with colitis induced by dextran sodium sulphate (DSS), where repair was clearly visible. It was discovered that the extract helped male AJ mice with eosinophilic airway inflammation caused on by Blomia tropicalis. Utilizing a mouse model, methanolic extract dosages of 25, 50, and 100 mg/kg of the plant were found to be effective in alleviating respiratory allergy.

2.4.3. Anti-Bacterial Property

Ocimum gratissimum leaves have an array of bioactive compounds, notably flavonoids,phenols, alkaloids, and essential oils, that promote the plant's therapeutic qualities. *Ocimum gratissimum* is a beneficial natural medicine against a variety of bacterial diseases due to its antibacterial features. *Ocimum gratissimum* leaves have antibacterial properties against a range of bacterial species. The studies have shown that the plant is effective against prevalent infections like Salmonella species, Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus, as well as Gram-positive and Gram-negative bacteria [10]. It is speculated that *Ocimum gratissimum* works against bacteria through a variety of routes. One of the main ways is the bioactive chemicals found in the leaves altering the membranes of bacterium cells. Cell death may result from this disturbance, which can also cause cellular contents to spill out. To further enhance its antibacterial properties, *Ocimum gratissimum* comprises some chemicals that have been proven to hinder the development of bacterial enzymes and proteins necessary for their survival and replication. *Ocimum gratissimum* leaves' antibacterial properties have important ramifications for both conventional and alternative medicine. Various preparations, including decoctions, infusions, and poultices produced from the leaves, are used in traditional medicine to treat wounds, bacterial infections, and other conditions. The potential of *Ocimum gratissimum* as a source of novel antibacterial chemicals or as a supplemental therapy to current antibiotics is gaining attention in modern medicine [11].

2.4.4. Anti-Fungal Property

The essential oil that's acquired by steam-distilling the aerial sections of *Ocimum gratissimum* has antifungal properties. The findings demonstrated that all of the fungi examined, including the phytopathogens, Botryosphaeria rhodina, Rhizoctonia sp., and two strains of Alternaria sp., were inhibited in their growth by the essential oil. Colletotrichum species insulated from rotten tomatoes were estimated against ethanolic, hot water, and cold water extracts of *Ocimum gratissimum*. The hot water extract had the largest zone of inhibition, followed by the ethanolic extract and the cold-water extract. antifungal properties against Trichophyton rubrum, Microsporum canis, M. gypseum, and T. mentagrophytes.Research on Trichophyton rubrum, the most current dermatophytes in Brazil, revealed that *Ocimum gratissimum's* extract and its essential oil exhibited potent antifungal properties, with the hexane extract showing the highest efficacy [11].

2.5. Phytochemical Screening

2.5.1. Plant Material Preparation and Extraction

After thoroughly cleaning, leaf samples were left to dry for two weeks at room temperature. Then, with the help of an automated pulverizer, they were ground into a fine powder. The powdered sample's measured amounts were extracted sequentially in 99% ethanol, ethyl acetate, and aqueous for 72 hours, with intermittent stirring. The cheesecloth was used tofilter the extracts, and Whatman No. 42 (125mm) filter paper was used to re-filter the filtrate. Using a freeze-dryer, the recovered filtrates were lyophilized and then preserved in an airtight container for additional examination [12].

2.5.2. *Qualitative Analysis of Phytochemistry*

Preliminary phytochemical analysis was conducted to identify the bioactive components of flavonoids, alkaloids, saponins, tannins, steroids, phenols, and glycosides that were present inthe crude aqueous, ethanol, and ethyl acetate extracts [12]. The froth and emulsion tests were used to find saponins, while Mayer's, Wagner's, and hydrochloric acid were used to identify alkaloids. 10% NaOH was used to detect the presence of flavonoids, and the Salkowski test was employed to detect the presence of steroids. The ferric chloride reagent was used to identify tannins and phenols, while Legal's test was used to identify glycosides. The table.no.01 represents the data of active components in extracts of *Ocissimum gratissimum* in different solvents [12].

Table 1 Active components present in extracts of *Ocimum gratissimum* [12]

Phytochemical	Water		Ethanol		Ethyl acetate	
	O. gratissimum	*N. laevis*	*O. gratissimum*	*N. laevis*	*O. gratissimum*	*N. laevis*
Saponins	–	–	–	+	+	–
Alkaloids	+	+	+	+	+	+
Tannins	+	+	+	+	+	+
Flavonoids	+	+	–	–	–	–
Glycosides	+	+	+	+	–	–
Phenol	+	+	+	+	+	+
Steroids	–	–	–	–	–	–

3. *Azadirachta indica*

For centuries, individuals have been mindful of *Azadirachta indica*, also known by its traditional name, Neem, as a source of active components. *Azadirachta indica* is regarded as aversatile medicinal tree. Neem is a magnificent natural source of raw materials for cosmetics that may be produced on a large scale because of its low toxicity and vast spread. This tree is similar to mahogany in biology, and because the seeds and leaves contain more secondary metabolites that are easier to extract, they can be used for a variety of purposes in agriculture,medicine, and cosmetics. It is therefore possible to link one or more phytochemicals—such asflavonoids, for example—to their positive benefits. Generally speaking, the combination of its ingredients produces a more potent result [13]. The phytocomponent concentration can change according to the harvesting method, storage conditions, moisture level, light, temperature, and pH fluctuations. Antiseptic, anti-inflammatory, and chemopreventive properties have been reported in recent research [14]. Additionally, several pharmacological characteristics were reported, including anti-leishmaniasis, microbicidal, nematicidal, antipyretic, antifertility, hypoglycemic, cardioprotective, antiulcer, neuroprotective, antioxidant, hepatoprotective, antidiabetic, and hypolipidemic qualities [15].

3.1. Taxonomical Classification

Botanical characterisation of *Azadirachta indica* [16]

Figure 3 Plant of *Azadirachta indica*

- Scientific name: Azadirachta
- Kingdom: Plantae
- Division: Magnoliophyta
- Order: Sapindales
- Family: Meliaceae

- Species: A. indica
- Subfamily: Melioideae
- Rank: Genus
- Genus: Azadirachta

3.2. Morphological Classification

Organoleptic properties of *Azadirachta indica* [17]

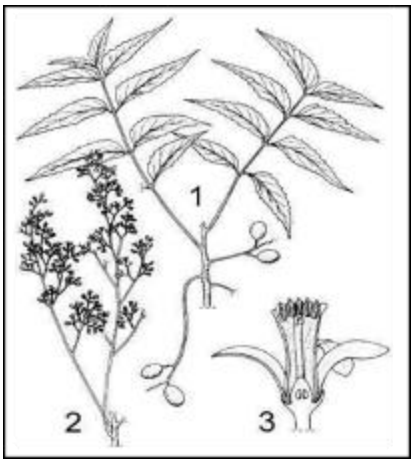

Figure 4 Morphological outlook of *Azadirachta indica*

- Odour: strong, pungent, and somewhat bitter
- Taste: Bitter
- Lamina Length: 6-10 cm
- Shape of Lamina: Lanceolate – ovate-oblong
- Lamina Margin: serrated or toothed
- Plant Height: 15-20 meters
- Stem colour: Grayish to dark brown Flower Colour: White to pale yellow Seed Shape: Oval or ellipsoidal

3.3. Distribution

Neem is native to dry areas of the subcontinent, Myanmar and China. Neem is one of themost widespread trees in tropical and subtropical areas. Neem was naturally distributed in Thailand Malaysia and Indonesia. Neem naturally occurs in Acacia forests, dry deciduous andthorn forests. In its exotic range, it has become invasive in several habitats including agricultural land and dry forest [18]. From sea level up to an altitude of 1500 m neem can be found. It also can be found in places where average annual rainfall ranges from 400 to 1200 mm and where the average annual maximum temperature may be as high as 40 degrees Celsius. Adult trees tolerate some frost but seedlings are sensitive to it. In a wide range of soils, from acidic to alkaline PH neem can grow but it does better in poor soils, sandy, stony, shallow, marginal sloping places, or on rocky crevices. Neem is a full sunlight species thatcan survive in extreme PH conditions, from 3 to 9. It can extract nutrients from highlyleached sandy soil. Neem withstands up to 2500 mm of rainfall in well-drained soils. It has some tolerance of salinity and has been used in sugarcane plantations with a significant soil salinity [18].

3.4. Pharmacological properties of Azadirachta indica

3.4.1. Antioxidant property

One of the main mediators responsible for the development of many diseases is the free radical or reactive oxygen species. On the other hand, one of the crucial stages in illness prevention is the neutralisation of free radical activity. Antioxidants also help to activate an antioxidative enzyme that helps to reduce the damage caused by reactive oxygen species and free radicals. Free radicals are stabilised and deactivated by antioxidants, oftentimes before they assault targets in biological cells. There have been reports of antioxidant action in medicinal herbs. Because they are a rich source of antioxidants, plants—fruits, seeds, oil, leaves, bark, and roots—play a significant role in preventing disease. The antioxidant activityof *Azadirachta indica* leaf and bark extracts has been investigated; the results of this study

showed that all of the tested neem leaf and bark extracts/fractions cultivated in the highlands exhibit notable antioxidant qualities. Another significant study was conducted to evaluate the antioxidant activity of extracts from the leaves, fruits, flowers, and stem bark of the Siamese neem tree. The findings indicate that the extracts from the leaves, flowers, and stem bark have a strong potential for antioxidant activity [19].

3.4.2. Anti-inflammatory property

Various studies have demonstrated the neem plants' ability to reduce inflammation. Nimbidin from neem trees was used orally in an experiment based on rat models to evaluate its anti- inflammatory response. It was established that phagocytosis was inhibited and that, in response to inflammatory stimuli, macrophage migration to their peritoneal cavities was severely inhibited [19]. Furthermore, nimbidin also prevented phagocytosis in vitro when rat peritoneal macrophages were exposed to it, and phorbol myristate acetate induced a respiratory burst in these cells. After being exposed in vitro to lipopolysaccharide-stimulated macrophages, nimbidin reduced the synthesis of prostaglandin E2 and nitric oxide. Evaluations have also been conducted on the anti-inflammatory properties of neem fruit skin and its particular component, azadiradione. The results have concluded that the animals treated with 100 mg/kg dose of this fruit skin extract and azadiradione exhibited significant anti-inflammatory activities [19].

3.4.3. Anti-Microbial property

Since several studies have suggested that neem extracts may help control certain pathogenic bacteria from food and other spoiling organisms, neem extracts are rich in antibacterial components. Zones of inhibition have been seen in NLEs, providing additional evidence of their antibacterial qualities. Notably, the extract exhibited far larger zones of inhibition than 3% sodium hypochlorite. To assess the minimum fungicidal and minimum inhibitory concentrations (MIC) of leaf and seed extracts against different dermatophytes, anotherinvestigation was conducted. As a consequence, the MIC of seed extracts was found to be 31 µg/mL for every dermatophyte that was examined. Moreover, it was shown that a concentration of 15 µg/mL of seed extract was adequate to alter the growth pattern of the organisms under investigation [20]. Anopheles stephensi was subjected to an evaluation of the effects of neem limonoids, including azadirachtin, salannin, deacetylgedunin, gedunin, 17 hydroxyazadiradione, and deacetylnimbin. At all concentrations, azadirachtin, salannin, and deacetylgedunin had substantial bioactivity, while the remaining neem limonoids demonstrated lower levels of activity. Furthermore, at 1 ppm concentration, azadirachtin generated about 100% larval death, making it the most powerful in all studies. Neem bark extract's antiviral activities showed that, at concentrations of 50–100 µg/ml, the bark extract significantly inhibited HSV 1 entry into cells. Neem seed extract looks to be a promising anticandidal agent, according to the study's evaluation of the extracts' antifungal effectivenesson Candida spp.

3.4.4. Anti-angiogenic property

The plant *Azadirachta indica* may possess antiangiogenic qualities. Neem leaf glycoprotein (NLGP) is a potent immunomodulator that has been shown to control CD8 + T cells, NKT, and effector NK cells to modulate both systemic and local immunity. In models of melanoma and carcinoma-bearing mice, it has been demonstrated that NLGP downregulates CD31, VEGF, and VEGFR2 and restores normal vascular tone. An investigation has been carriedout on human umbilical vein endothelial cells (HUVECs) using the ethanolic extract of neem leaves (EENL). EENL has been shown to significantly lower HUVEC-mediated angiogenesis in both in vitro and in vivo settings [21]. Nimolone, nimbolide, 6-diacetyl nimbinene, and 2, 3- dehydrosalannol are among the compounds of EENL that considerably reduce HUVECmotility, invasion, proliferation, and angiogenic response. Neem seeds, leaves, flowers, and fruits contain bioactive components that exhibit considerable suppression of angiogenesis, redox potentiality, and malignant cell growth, suggesting that they may have anti-cancer properties. In this case, cancer protection may be partially attributed to suppression of the NF-κB pathway [21]. The neem leaf ethanolic fraction (EFNL) inhibits the development of breast cancer. Vascular endothelial growth factor A (VEGF-A) is down-regulated in rats treated with EFNL, according to an in vivo investigation. Neem leaves are used in the green manufacture of silver nanoparticles, which demonstrate a decrease in neovascularization. When such nanoparticles are applied to developing chicken embryonated eggs, they significantly reduce the number of viable blood arteries at the chorioallantoic membrane, which causes the embryo to die [21].

3.5. Phytochemical Screening

3.5.1. Plant Material Preparation and Extraction

Extracting active compounds from *Azadirachta indica*, or neem, involves several steps. After collecting and cleaning the plant material, it's dried and ground into a fine powder. The ground material is then extracted using a suitable solvent, such as ethanol, methanol, orwater, through methods like Soxhlet extraction, maceration, ultrasonic

extraction, or supercritical fluid extraction. Parameters such as temperature and time are adjusted during theextraction process, followed by filtration to remove solid residues. The extract is then concentrated and optionally purified before characterization and storage. It's important to adhere to safety protocols and consult relevant literature or experts for specific extraction protocols [22].

3.5.2. Qualitative Analysis of Phytochemistry

Qualitative analysis of the phytochemistry of *Azadirachta indica*, commonly known as neem, involves identifying and characterizing the presence of various bioactive compounds present in the plant. This typically includes compounds such as limonoids, azadirachtin, nimbin, flavonoids, and other terpenoids. Techniques such as thin-layer chromatography (TLC), gas chromatography-mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), and nuclear magnetic resonance spectroscopy (NMR) are commonly employed for this purpose. By comparing the retention times, spectral data, and other characteristic properties of the compounds with standard references or databases, researchers can identify and qualitatively analyze the phytochemical composition of neem extracts. This analysis provides valuable insights into the potential pharmacological and therapeutic properties of neem and aids in further research and development efforts. The table.no.02 represents the data of active components in extracts of *Azadirachta indica* in different solvents [22].

Table 2 Active components present in extracts of *Azadirachta indica [22]*

Test ➡ / Extract ⬇	**Saponin**	**Tannins**	**Phenol**	**Glycoside**	**Terpenoid**	**Carbohydrate**	**Flavonoids**	**Alkaloids**
Benzene	+	-	-	-	-	-	+	+
Ethanol	-	+	+	+	+	+	+	-
Toluene	+	-	-	+	+	-	+	+
Butyl alcohol	+	+	+	+	+	+	+	-
Ethyl acetate	+	+	-	+	+	+	+	+
Acetone	+	+	+	+	+	+	-	-

4. Conclusion

In conclusion, the exploration of *Azadirachta indica* and *Ocimum gratissimum* as herbal remedies for anti-acne treatment has illuminated a promising avenue within the field of dermatology. The rich phytochemical profiles of these botanicals, comprising compounds such as nimbin, neem oil, eugenol, and ursolic acid, demonstrate multifaceted therapeutic effects that target various aspects of acne pathogenesis. The reviewed literature underscores the anti-inflammatory, antimicrobial, and antioxidant properties exhibited by *Azadirachta indica* and *Ocimum gratissimum,* presenting a compelling case for their integration into acne management strategies.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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