International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

An Overview of Herbal Ingredients with Anti-dandruff Activity in Shampoo Formulations

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DOI: https://doi.org/10.55248/gengpi.2023.4125

A B S T R A C T

Dandruff is a common scalp disorder affecting almost 50% of the human population caused by M. globosa and M. furfur which are two naturally occurring skin fungus. This review discusses in detail the anatomy, pathophysiology, causes and symptoms, and treatment methods available for Dandruff. It also highlights the herbal ingredients with anti-dandruff activity that are used in novel shampoo formulations as a treatment strategy. This review discusses various bioactivities through which these compounds treat dandruff such as anti-inflammatory, antifungal, as well as their mechanism of action. Due to its amphibious status, dandruff is the most commercially exploited skin and scalp disorder/disease by personal care enterprises because there is less medical intervention for treatment.

Keywords: Hair; Scalp; Organic Shampoos; Anti-inflammatory; Anti-fungal

1. Introduction

Hair has long been a source of fascination and obsession, from the biblical story of Samson and Delilah and the fairy tale of Rapunzel to the eponymous 1960s rock musical and the latest coiffures. Too little or too much hair can both cause psychological and social distress. Each hair follicle is connected to a sebaceous (oil) gland, which opens to the skin via the follicle. [1] Hair has been a prominent theme in mythology and has been celebrated in the fine arts. Both art forms have depicted the fortunes and misfortunes of those with fine heads of thick hair, as well as those among the great who have lost it. Hair type is an important factor in the study of physiognomy. According to Della Porta, the brains are moist, and where there is a lot of humor and warmth, there is a lot of hair, with the idea of convenience in mind because "the hair protects the head from cold and heat." [2] The most common hair concerns in the Philippines are (1) hair fall, (2) dandruff, and (3) having great-smelling hair despite the hot weather. [3] One author categorizes dandruff into three stages. Mild, medium, and severe Mild dandruff is perfectly normal. Dandruff affects 50% of the global population, with 8 out of 10 Filipinos suffering from it. [4]

Many people and researchers believe that dandruff is a lighter manifestation of seborrheic dermatitis. This is characterized by tenuously connected white to gray flakes that occur on the scalp, either diffusely or in patches. It also causes the scalp to itch and feel dry, although there is no visible inflammation. Beyond the scalp area, dandruff flakes may be seen on the eyelashes, brows, corners of the eyes and nose, or any other area of the skin with hair. [5] Dandruff scale is a collection of corneocytes which have managed to retain a high level of cohesion with each other and thus become disconnected from the stratum corneum's surface. A pilosebaceous follicle is at its center and the size and abundance of the dimensions vary from one location of the scalp to another. Dandruff is commonly composed of parakeratotic cells and their amount is proportional to the severity of clinical signs that may be impacted by seborrhea. Throughout this way, pityriasis simplex, also recognized as 'sicca,' denotes the appearance of fine squames, typically of small size, which give the process an asteatotic and farinaceous appearance. The dandruff in steatoid pityriasis, also known as 'oleosa,' is seborrhoeic, thick, and adhesive, and the scale is often greater. [6]

This review includes information that was gathered about the use of natural and herbal plants in anti-dandruff shampoo. In addition, this review includes the physico-chemical properties, botanical sources, bioactivity, and toxicological data of herbal compounds as ingredients in shampoo formulations. Moreover, it is possible that some compounds with anti-dandruff activity that may not be included in this review hence, the researchers will primarily focus on the compounds included in this review.

1.1 Methods

The article review uses peer-reviewed publications and studies that have been recovered from various journals databases like PubMed, Google Scholar, ResearchGate, and Elsevier. The search started in June 28, 2022 which has a direct focus on the following, (1) hair anatomy and physiology, (2) the pathophysiology and treatment of dandruff, (3) herbal ingredients with anti-dandruff activity, (4) the physciochemical properties, botanical sources, bioactivity, and toxicological data of herbal ingredients with anti-dandruff activity, and (5) the advantages and disadvantages of novel shampoo formulations containing these herbal ingredients.

2. Hair Anatomy and Physiology

Hair is characteristic of mammals, where it performs a variety of functions. Physical protection, thermal insulation, camouflage, sweat and sebum dispersion, sensory and tactile functions, and social interactions are all examples. [7] From a macrostructural perspective, hair varies in length, diameter, color, and cross-sectional shape between ethnic groups and individuals. [8]

2.1. Parts of the Hair

Dermal papilla and the matrix is present in the hair. The Dermal papilla regulates the hair cycle and hair growth and contains androgen receptors that are sensitive to the presence of DHT while the matrix surrounds the dermal papillae and contains all of the active cells required for hair growth and development of the various parts of the hair, particularly the outer root sheath, inner root sheath, and hair shaft. [9] Hair has two distinct structures: the follicle in the skin and the visible hair shaft on the body surface. (fig. 1.) [10]

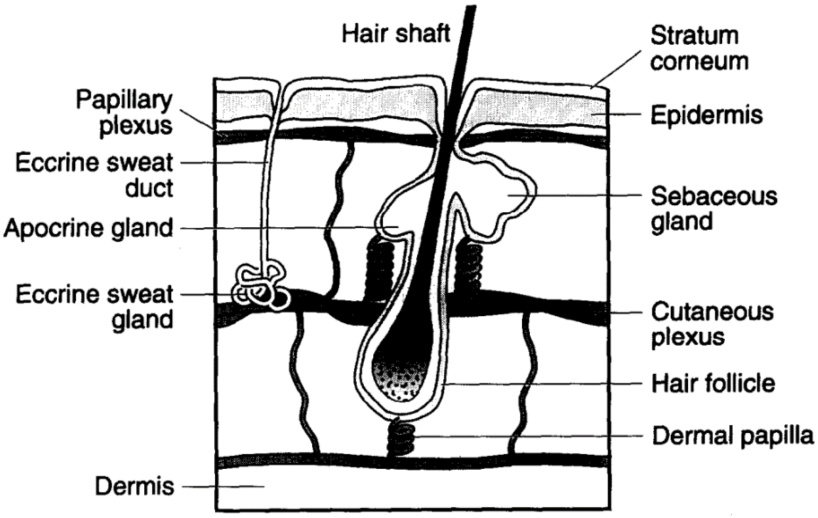

Fig.1. Diagram of the hair shaft and the hair follicle from Anatomy and physiology, 1993. [2]

2.1.1. The Hair Shaft

Individual hair shafts in men can range in diameter from 15 to 120 pm, depending on the type of hair and where the follicle is located on the body. Keratin is a sulfur-rich protein family found in hair. Keratin forms long fibers in the hair shaft that become very tightly bound together. As a result, the structure is extremely tough and stable. [10] The hair shaft has three layers: the medulla, cortex, and cuticle. The medulla is an unorganized and unstructured area located in the innermost region of the hair shaft that is not always present. [9] It is the central axis of some hairs and is surrounded by the cortex. It contains a column of large vacuolated and keratinized cells. [11] In contrast to the medulla, the cortex is highly structured and organized. The cortex is the peripheral part and is made up of approximately 50–60% macrofibrils, which consist of rods of microfibrils embedded in a matrix and represents the majority of the hair fiber composition and plays an important role in the physical and mechanical properties of hair. [8] The cortex comprises the bulk of the hair shaft and contains melanin; situated between the medulla (in larger hairs) and cuticle. [11] It is made of keratin and is responsible for the strength and durability of hair, as well as its water uptake. The cortex contains melanin as well and determines hair color based on the number, distribution, and type of melanin granules present. Comprises the bulk of the hair shaft and contains melanin; situated between the medulla (in larger hairs) and cuticle. [9] Human hair's cuticle is made up of a single layer of elongated, overlapping individual cells. Each cuticle cell is about 0.5 to 1.0 pm thick and about 45 km long.The cuticle is the outer protective layer of the hair that connects to the internal root sheath. [10] It is a complex structure with a single lipid molecular layer that aids in water repellency. [9] The cuticle protects the hair shaft and may be completely lost at the ends of long hairs. The cuticle's integrity and properties have a significant impact on the appearance of the hair. [11]

2.1.2. The Hair Follicle

Hair follicles are embedded in the skin's epidermal epithelium, about 3-4 mm below the skin's surface. [10] The mature (anagen) hair follicle is divided into two parts: a 'permanent' upper part that does not cycle visibly and a lower part that is constantly remodeled during each hair cycle. The infundibulum, which is the opening of the hair canal to the skin surface, and the isthmus make up the upper part of the hair follicle. The lower, cycling portion represents the anagen bulb, (figure 2) the actual hair shaft factory. [7]

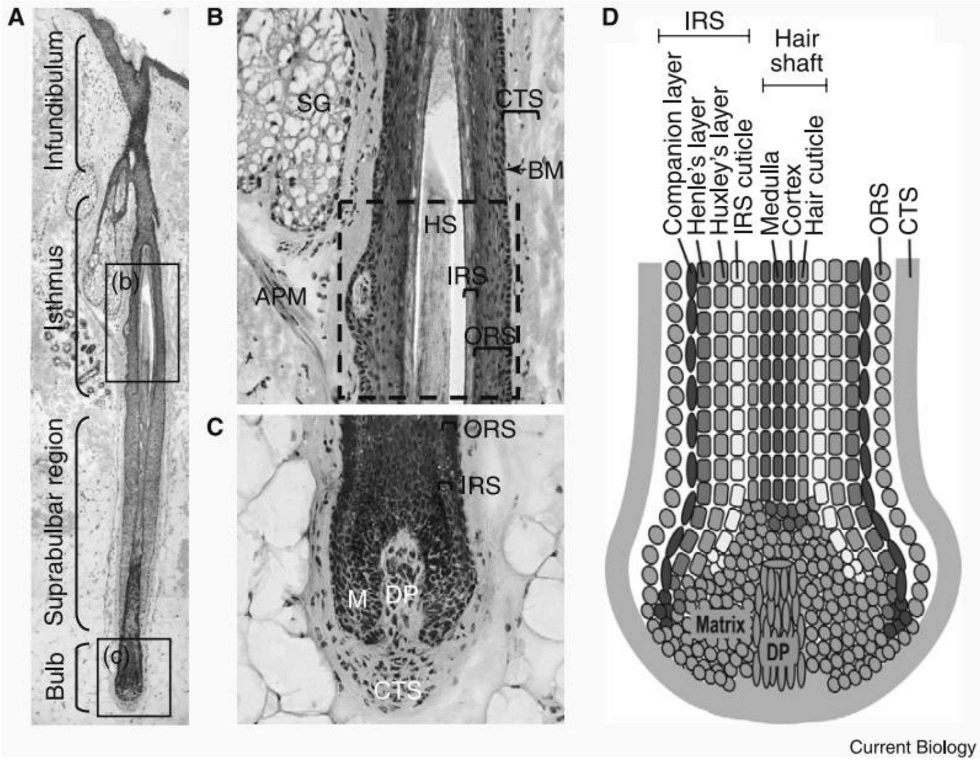

Fig. 2. Histomorphology of the hair follicle from The Hair Follicle as a Dynamic Miniorgan, 2009 [7]

The follicle is the essential growth structure of hair. The follicle consists of the outer root sheath (ORS), the inner root sheath (IRS), and the hair bulb. The outer root sheath (ORS), which contains keratinocytes, has been identified as a reservoir of multipotent stem cells, namely keratinocyte and melanocyte stem cells. The ORS forms a distinct bulge area between the arrector pili muscle insertion and the sebaceous gland duct. On the other hand,there are three layers in the inner root sheath: Henle's layer, Huxley's layer, and cuticle layer. The IRS cuticle layer connects to the hair shaft's cuticle, securing the hair shaft to the follicle. IRS cells produce keratins and trichohyalin, which act as an intracellular cement, giving the IRS strength to support and shape the growing hair shaft while also guiding its upward movement [8] The hair bulb is the portion of the follicle which actively produces the hair. The hair bulb encloses the follicular dermal papilla which is thought to be one of the most important factors in instructing the hair follicle to grow and form a specific sized and pigmented hair shaft. [8] The hair follicle can be divided into three distinct zones. The innermost zone, in and around the bulb, is where hair cells are biologically synthesized. The next section, directly above the bulb, is the keratinization zone (keratogenous zone), where the hair hardens and solidifies. The final zone is the permanent hair zone. The hair shaft is made up of dehydrated, cornified cells that have formed into fibrils and are joined together by an intercellular binding material. [10]

Moreover, hair follicles are intimately linked to two glands: the sebaceous and apocrine glands. (fig 1) [10] The hair follicle and the sebaceous gland are anatomically and functionally fused in most parts of the body to form what is known as a pilosebaceous unit. Except for the palms, soles, and dorsum of the foot, sebaceous glands are present on the entire body's surface. They are located just beneath the skin's surface, and their ducts lead directly into the tunnel of the hair follicle. Apocrine and sebaceous gland ducts empty into the follicle. Eccrine sweat gland ducts, on the other hand, are located near the follicles but do not empty into them. In humans, apocrine glands are localized in the axilla, the external auditory meatus, the eyelids, and the perineal region. Apocrine glands are different from the type of sweat glands than are found on the scalp in that they secrete by the separation of cytoplasm from the secreting cells. Also, apocrine glands discharge directly into the hair follicle rather than onto the surface of the skin. [10] Some, but not all, hair follicles are surrounded at the level of the sebaceous gland by a collar of nerves known as the hair end organ, which is divided into an outer circular layer and an inner longitudinal layer. [8]

2.2. Hair Growth

Along with sweat glands, sebaceous glands, and nails, hair is a protective bodily part that is regarded as an accessory structure of the epidermis. Protection, sensory abilities, thermoregulation, and sexual appeal are all influenced by hair. The dermal papillae (DP), which include fibroblasts and are found at the deepest end of the follicle, the matrix cells, as well as the terminally developed and dead keratinocytes form the complex organ called as hair. It is believed that fibroblasts are crucial for the maintenance of hair growth as well as the induction of new hair follicles. Therefore, a complex set of paracrine interactions mediated by DPC are necessary for the regulation of hair follicle renewal. Additionally, it has been shown that DPC-derived substances have an impact on the cells around them, which in turn stimulate hair growth. Anagen (growth phase), catagen (regression phase), and telogen (resting phase) are the three phases that make up the cyclical process of hair growth. These cyclic alterations cause the epithelial and dermal hair follicle components to rapidly restructure.

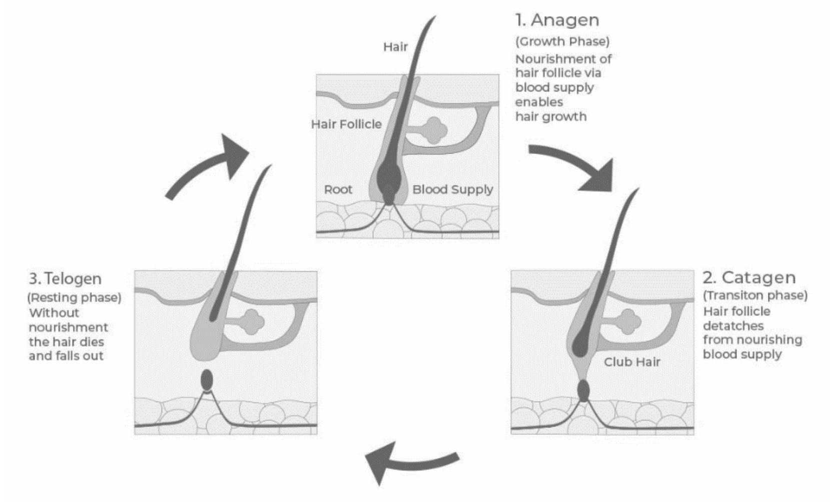

Fig. 3: Natural Hair Growth Cycle [12]

Also known as the 'Growth Phase' or 'Active Phase', the Anagen Phase is when the cells in the root of your hair are most rapidly dividing so more new hair is formed. Following the Anagen Phase, your hair cycle enters a short transitional phase known as the Catagen Phase, which signals the end of active hair growth and cuts individual hairs off from the blood supply and from the cells that produce new hair. Approximately 3% of all hairs are in this stage at any time. The third stage of a person's natural hair growth cycle is the Telogen Phase, a resting period when strands remain in their follicles but are not actively growing. An estimate of 10-15% of your hairs are in the Telogen Phase at any given moment.

2.3. Problems Related to Human Hair

2.3.1. Hair Loss

Hair often experiences a predictable growth cycle. The hair develops throughout the anagen period, which can span two to six years or more and then rh rests for roughly three months during the telogen period. The hair falls out and is replaced by new hair at the conclusion of the telogen period. Every day, the average person sheds roughly 100 hairs. Hair loss is a distressing ailment that can be brought on by numerous physiological, medicinal, or dietary issues. For instance, male pattern baldness, also known as androgenetic alopecia, is becoming acknowledged as a physically and psychologically significant medical condition that frequently demands expert care from general practitioners. [13] Hair loss can also result from some hair care habits, such as wearing tight weaves or ponytails or frequently bleaching or perming the hair. Some people pluck their hair out compulsively and trichotillomania is the name of this psychological illness. [14]

2.3.2. Dandruff

The optical sense of distinct flake formations on an abnormality if it appears on the scalp, in the hair, or on garments is a common ailment known as dandruff. It does not appear to be inflamed compared to seborrheic dermatitis, it just affects the scalp. The high temporal link between sebaceous gland activity and dandruff suggests that sebum plays a factor in it. The incidence is higher during infancy, lower from infancy to puberty, higher throughout adolescent and young adulthood, and lower later in life according to this correlation. Additionally, dandruff develops exclusively on skin where there is a lot of sebum [15].

2.3.3. Weathering

Weathering is the gradual deterioration of the hair's cuticle and cortex from the root to the tip as a result of normal daily wear and tear. Despite the fact that every hair experiences some degree of aging. When hair is repeatedly mistreated, it invariably experiences more severe weathering. Weathering characteristics include deteriorated cuticles, transverse fissures resembling the trichorrhexis nodosa nodes and longitudinal fissures known as split ends. Bleaching is one of the specific causes of weathering. Existing melanin in the cortex is oxidized by it. Longer bleaching sessions are needed for darker hair. Brown hair is easier to bleach than red hair. Some of the disulfide bonds in the keratin are broken by the oxidation reaction, which can harm the cuticle, increasing its permeability. [16]

3. Dandruff

More than half of the world's population suffers from the prevalent, chronic scalp illness known as dandruff (pityriasis capitis, also known as pityriasis simplex capillitii) [17]. The prevalent scalp conditions known as dandruff and seborrheic dermatitis (D/SD) are thought to be the same core ailment with only slight variations in severity. A susceptibility for the illness is mostly independent of heredity [18]. Dandruff only affects the scalp and is characterized by itchy, flaky skin that is not visibly inflamed. SD causes flaking, scaling, irritation, and pruritus in the face, upper chest, and retro-auricular region in addition to the scalp. It can also have noticeable erythema. In SD and dandruff, flakes can be oily or dry and range in color from white to yellow [19].

3.1. Pathophysiology

3.1.1. Dandruff composition

A corneocyte cluster that has maintained a high level of cohesiveness with one another and separates as such from the stratum corneum's surface is what causes dandruff. Scale size and abundance vary from one location to another and across time. Dandruff frequently contains parakeratotic cells as part of it. Their quantities are correlated with how severe the clinical signs are, which seborrhea may also affect. This is frequently more common among those with oily skin. The cause is a yeast called *Malassezia globosa*, which feeds on scalp oils. Some people's bodies view this oil breakdown as an irritant, so the scalp responds by speeding up skin cell renewal, which results in dandruff [20].

3.1.2. Microbial etiology

Dandruff may be brought on by a number of etiopathologic routes with intricate processes. It was commonly believed that the lipophilic yeast of the genus *Malassezia* contributed to dandruff [20][21]. *Malassezia* concentrations rise by 1.5 to 2 times the typical amount during dandruff. Whether yeast has a part in any quantitative microbiological evaluation of any type is up for discussion [20]. But there have been reports of increased dandruff incidence, a compromised barrier effect, and intracellular lipid levels in the stratum corneum of the scalp [21]. *Malassezia* populations decline in response to the use of antifungal products, while bacterial populations are seldom impacted. The excellent therapeutic response of dandruff to different steroids is another intriguing part of the microbiological origin of dandruff. The immunological flare-up is known to be inhibited by steroids, and the microorganism will take advantage of the immune suppression opportunity. However, a question about the microbiological origin of dandruff is raised by the positive therapeutic response and lengthy remission time with steroid therapy. Seven different varieties of *Malassezia* (M. M. globosa M. Resticta evasive, M. M. Sloofiae M. Sympodialis M., furfur, and pachydermatis, which have been linked to the development of dandruff [20].

3.1.3. Non-microbial etiology

It is commonly known that dandruff has non-microbial causes. Desquamation of the scalp is a recognized side effect of prolonged exposure to sunshine [22]. Dandruff can also be partially brought on by minor scalp irritation brought on by excessive washing, frequent combing, the use of specific cosmetic products, dust, and grime. However, the aforementioned hypotheses are not sufficiently supported by experimental data [23].

3.2. Causes and Symptoms

In areas with a high concentration of sebaceous glands, including the scalp, the retro-auricular location, the face (nasolabial folds, top lip, eyelids, and eyebrows), and thus the upper torso, SD frequently manifests and including erythematous plaques with greasy-looking, yellowish scales of varying extremes [19]. One indication or characteristic of dandruff or seborrheic dermatitis that has just recently been identified is that the poor scalp skin physiology caused by dandruff or seborrheic dermatitis might negatively affect several aspects of the hair fibers on the scalp (paralleling similar observations for scalp psoriasis) [23]. Localized inflammation in the subject's dandruff-prone scalp infests the adjacent normal tissue, increasing the expression of these genes. Another argument is that individuals with dandruff exhibit, for some unspecified reason, an increased epidermal immune response compared to those without, as is well-established in psoriasis and atopic dermatitis, and that dandruff may be the outcome of this priming [24.

3.3. Treatment

The goal of treating SD and dandruff is to eliminate illness symptoms, particularly pruritus, and to establish remission over the lengthy period with medication. External antifungal and anti-inflammatory medications are the most often used therapy since the primary underlying pathogenic processes involve *Malassezia* growth and local skin irritation and inflammation [19]. Those keratinolytic medications are another option for treating dandruff. The pathophysiology of dandruff includes keratinocyte hyperproliferation, which leads to keratinization being out of balance. The corneocytes group and appear as thick flakes of skin. In essence, keratolytic substances like sulfur and salicylic acid break the bonds that hold the corneocytes together and let those dandruff to rid away [20.

4. Botanical Ingredients with Anti-dandruff Activity

4.1. Linalool

4.1.1. Physico-chemical Properties

Linalool (3,7-dimethyl-1,6-octadiene-3-ol), also referred to as linalyl alcohol, is an acyclic monoterpene tertiary alcohol with a chemical formula of $C_{10}H_{18}O$, constitutes one of the main floral aromas of nature. This compound has a molar mass of 154.25 g/mol, a boiling point of 198 ℃, and a flash point of 75 ℃[25]. Linalool was found to be a volatile component of essential oils of various aromantic species. Most of which were used in traditional medicine systems in order to relieve the symptoms and even cure several acute and chronic ailments. The pharmacological action of these species was due to the content of alcohols such as linalool and its corresponding ester, linalyl acetate, which are reported to have antimicrobial activity against fungi and bacteria [26].

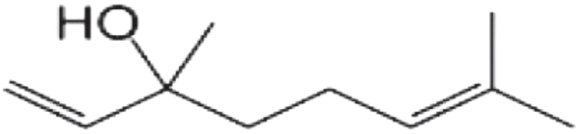

Fig. 5. The Chemical Structure of Linalool

The two enantiomers of Linalool are synthesized in plants: (3S) - (+) -linalool (coriandrol) and (3R) - (–) - linalool (licareol). In terms of its structure and chiral properties, the S-form is nine times stronger than that of the R -form. Due to this, it is found in 60 to 90% of cosmetic products, as an important fragrant ingredient that is widely used in formulations such as shampoos and body lotions [27].

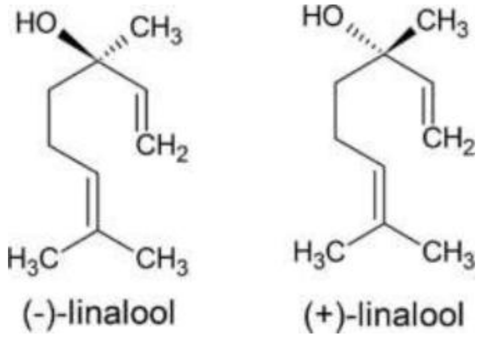

Fig. 6. The Enantiomers of Linalool

4.1.2. Linalool in Nature

Table 1. Main Sources of essential oils from plants containing Linalool [28]

Essential oil	Botanical Source	Linalol content (%), characteristic enantiomer
Rosewood, rosewood	*Aniba rosaeodora* Ducke wood, Lauraceae	about 100;*(R) - (-)*
Ho leaf	*Cinnamomum camphora* Nees & Eberm var. linaloolifera, Lauraceae	66-95; (*R*) - (-)
Ho (China) = Shiu (Japan, Taiwan)	Wood of *Cinnamomum camphora* Nees & Eberm var. linaloolifera, Lauraceae	90; *R* - (-)
Orthodon oil	Aerial parts of *Orthodon linalooliferum* Fujita, Lamiaceae	82; *S* - (+)
Coriander	Fruits of *Coriandrum sativum* L., Apiaceae	45-85; *S* - (+)
Lavender	The flowering peaks of *Lavandula officinalis* Chaix sin. L. angustifolia Mill., Lamiaceae	25-38;(*R*) - (-)
Lavender spike	The flowering tops of *Lavandula latifolia* (DC) Vill., Lamiaceae	19-48;(*R*) - (-)
Linaloe (Mexican lavender, or Indian lavender)	Wood of *Bursera delpechiana* Poiss e.g. Angl, Bursera spp., Burseraceae	30;(*R*) - (-)
Bushy lippia	Leaves of *Lippia alba* (Mill.) NEBr. ex Britton and P. Wilson, Verbenaceae	65; *S* - (+)
Winged thorn ash	*Zanthoxylum alatum* Roxb., Rutaceae seeds	71; ND
Sweet basil	*Ocimum basilicum* L., Lamiaceae leaves	26-50; (*R*) - (-)
Sacred basil (tulsi)	*Ocimum sanctum* L., Lamiaceae leaves	26; *S* - (+)
Ash basil	*Ocimum canum* Sims leaves, Lamiaceae	25; *S* - (+)
Ylang ylang	Flowers of *Cananga odorata* (Lam.) Crochet f. & Thomson forma genuina, Annonaceae	15-24;(*R*) - (-)
Neroli	*Citrus aurantium* L. flower, Rutaceae, bitter orange	28-40;(*R*)- (-)
Sweet orange	Flowers of *Citrus sinensis* Osbeck, Rutaceae	15-32; *S* - (+)
Sweet marjoram	Aerial parts of *Origanum majorana* L., Lamiaceae	30-40; *S* - (+)
Petitgrain oils with bitter orange	Leaves and twigs of *Citrus aurantium* L., Rutaceae	>27; *S* - (+)
Clary sage	Aerial parts of *Salvia sclarea* L., Lamiaceae	10-21; racemate
Laurel	Leaves of *Laurus nobilis* L., Lamiaceae	16;(*R*) - (-)

Essential oils containing linalool are found in approximately 200 monocotyledonous and dicotyledonous plant families that are widely present in boreal and tropical regions; namely, Lamiaceae, Lauraceae, and Rutaceae. The main source of (R) - (–)-linalool is Rosewood oil, while the main source of (S) - (+) -linalool is coriander oil. In addition, the enantiomer that is most common in nature is (R) - (–)-linalool [29].

4.1.3. Bioactivity of Linalool

4.1.3.1. Antibacterial and Antifungal Activity

In a study based on the antifungal activity of *Ocimum sanctum*, linalool was found to be the most cytotoxic lead molecule even in low concentrations against *Candida* (at 50 µg/mL killed 53.2%), which was found to be the most effective molecule, then followed by methyl eugenol and eugenol. The cessation of cell growth is correlated with the inhibition of enzyme activity wherein H+ efflux is an instantaneous process that occurs in response to H+ ATPase action. The H+ ATPase pump in the plasma membrane controls intercellular pH, maintains ion balance, and provides the electrochemical proton gradient required for food intake [30]. Linalool was found to be more effective against Gram-positive bacteria than Gram-negative bacteria at a concentration of 0.1% (v/v), wherein its antibacterial property has been related to functional membrane destabilization and increased susceptibility of bacterial strains to conventional antimicrobial drugs [31]. *Malassezia furfur*, a fungus and a known cause of dandruff, has been found to be inhibited by *O. sanctum* by its antifungal properties [32]. However, there is no sufficient data to understand and provide a profound explanation of its activity against dandruff hence.

4.1.3.2. Anti-inflammatory Activity

In vitro, R-(-)-linalool inhibits the production caused by the liposaccharides of the cytokines TNF-α and IL-6 this activity was found to be dose-dependent [33]. It has been shown in various *in vitro* and *in vivo* that R-(-)-linalool acts by inhibiting the production of inflammatory cytokines through antagonizing the NMDA effects and reducing the release of NO which impedes the NK-κB and MAPK pathways [34]. In addition, the results of a study suggest that linalool is seen as a therapeutic candidate for the treatment of inflammatory diseases [35]. Linalool and linalyl acetate play a huge role in the anti-inflammatory effect shown by essential oils which suggest that plant species containing monoterpene compounds are considered to be anti-inflammatory agents [27]. To date, there are no current studies supporting the activity of linalool against dandruff-induced inflammation.

4.1.3.3. Improved percutaneous penetration of drugs

Linalool and other terpenes and terpenoids have the ability to enhance the cell wall permeability of drugs through mucus membranes and skin hence, it can be utilized as an absorption promoter in topical formulations [36]. Hydrogel formulations of linalool have been found to have higher and better absorption in the stratum corneum than oily solutions or emulsions [37].

4.1.3.4. Toxicological Data

A panel of experts studied the toxicity and dermo-toxicity of linalool in cosmetic preparations and achieved a non-toxic dose [38]. The use of linalool as an ingredient, according to the OECD report (CAS Number 78-70-6 2002), suggested that the compound has an LD_{50} following a cutaneous administration of 2000 mg/kg of body weight [39]. In *in vitro* tests, linalool presented no mutagenicity, genotoxicity, or carcinogenicity under the current conditions of use. Human dermatological research reveals that linalool and linalyl esters are not phototoxic and natural linalool rarely causes allergic contact dermatitis [40].

Linalool is non-toxic, recent in vitro and in vivo scientific research has shown that it possesses a wide spectrum of bioactive qualities that may be used in pharmaceutical and cosmetic applications. The usage of essential oils and their natural derivatives, such as linalool, as well as all scientific validation work on their functional benefits and safety, have demonstrated true efficacy as an adjuvant and in different medicinal applications. Aside from these benefits, it is important to note and regulate their usage to minimize the hazards of incorrect overuse. It is also important to remember that accidental cases of misuse, which according to data in the scientific literature remain limited and rare, should not lead to an extreme and exaggerated consideration of a risk whose danger is primarily related to misuse and a lack of recommendations for these uses whose beneficial effects are confirmed. The use of linalool, for its positive effects, must be directed by a suggested method, led by the user's warning, so that users make appropriate utilization of it.

4.2. Carvacrol

4.2.1. Physico-chemical Properties

Carvacrol (2-methyl-5-(1-methylethyl)-phenol) (Fig. 1). Carvacrol can be produced through a variety of methods, including sulfonation of para-cymene followed by alkali fusion, chlorination of alpha-pinene with tert-butyl hypochlorite, or aromatization of carvone in the presence of sulfuric acid using an efficient solid acid catalyst. [41] Its molecular formula is C10H14O. Carvacrol is a colorless or yellowish thick liquid and has a thymol odor. Carvacrol has a boiling point of 237.7 °C, while 1.0°C for the melting point. The flash point of Carvacrol is at 100°C and has a solubility of 0.01M which makes it slightly soluble in water, soluble in ethanol, ether, alkali, and very soluble in acetone. [42]

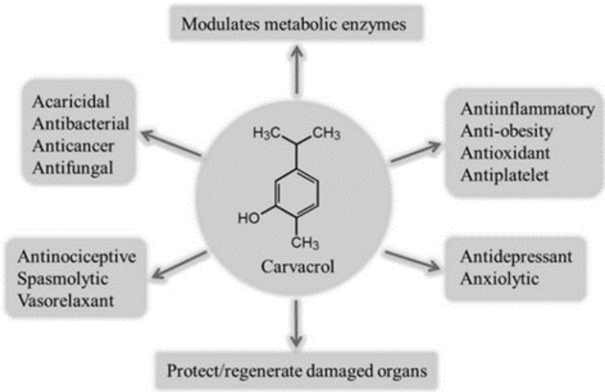

Fig. 7. The structure of Carvacrol and its biological properties [42]

4.2.2. Carvacrol in nature

Carvacrol is found in , found in many aromatic plants including Origanumdictammus (dittany of Crete), Origanum vulgare (Greek oregano, wild marjoram), Origanummajorana (marjoram), Thymbracapitata (Spanish origanum) Saturejahortensis (summer savory), Thymus vulgaris and Thymus zygis (thyme), Thymus serpyllum (white thyme), and Saturejamontana (winter savory). [41] In the species Origanumminutiflorum and Origanumonites the carvacrol composes 92% of the essential oil [42]

4.2.3. Bioactivity of Carvacrol

4.2.3.1. Antibacterial and Antifungal Activity

Carvacrol's antibacterial action, which is stronger against Gram-positive bacteria than Gram-negative bacteria, is primarily based on bacterial membrane damage; it causes dissolution of the proton motive force and subsequent reduction in ATP synthesis, which leads to reduction in other energy-dependent cell processes such as enzyme and toxin synthesis. Carvacrol, in particular, has been extensively tested in food as an antimicrobial agent to control Gram-positive and Gram-negative pathogens such as Bacillus cereus, Enterococcus faecalis, Listeria monocytogenes, Staphylococcus aureus, Escherichia coli, Pseudomonas fluorescens, Salmonella typhimurium, Vibrio cholerae, and V. vulnificus. [43] The hydrophobicity of essential oils and their phytochemicals (for example, monoterpenes) allows them to interact with the fungal cell membrane and interfere with its integrity. They can partition into the lipids of fungal membranes, making them more permeable and damaging their integrity, resulting in mycelial death. One study claims that some evidence suggests that carvacrol works by interacting with the cell membrane and making it permeable. Carvacrol has the ability to disintegrate the outer membrane of Gram-negative bacteria, releasing lipopolysaccharides (LPS) and increasing the cytoplasmic membrane's permeability to ATP. [44] A study about the antifungal activity against *Candida albicans* and *Malasseziafurfur* shows that carvacrol has strong activity against C. albicans. However, not efficient enough for M. furfur. [45]

4.2.3.2. Anti-inflammatory Activity

Previous studies show that carvacrol has an anti-inflammatory property. Specifically, one study states that Carvacrol's anti-inflammatory properties are dependent on its ability to reduce the production of inflammatory mediators such as IL-1b and prostanoids, possibly by inducing IL-10 release. [46] Another study about the effects of Carvacrol in osteoarthritis shows that Carvacrol inhibited the production of nitric oxide (NO) and prostaglandin E2 (PGE2), as well as the expression of inducible NO synthase (iNOS) and cyclooxygenase (COX-2). Furthermore, Carvacrol inhibited the protein expression levels of matrix metalloproteinase (MMP)3 and MMP-13 in IL-1-stimulated human OA chondrocytes as well as the activation of the nuclear factor (NF)B signaling pathway in IL-1-stimulated human chondrocytes. As a result, carvacrol may have therapeutic potential in the treatment of OA. [47] However, the need to conduct more studies regarding the anti-inflammatory activity of Carvacrol relating to dandruff is still as relevant as ever.

4.2.3.3. Improved percutaneous penetration of drugs

Carvacrol has been shown to have analgesic and anti-inflammatory activity by inhibiting cyclooxygenase, but it may cause gastrointestinal toxicity due to its non-selective inhibition. One study sought to create a transdermal microemulsion from Origanum vulgare essential oil in order to deliver carvacrol into and through the skin, thereby alleviating gastrointestinal issues. Microemulsion could be used to achieve transdermal carvacrol delivery because it delivered more carvacrol through the skin layer and significantly retained carvacrol in the skin layer. Calvacrol's anti-inflammatory activity was also significantly enhanced by microemulsion. vulgaris essential oil. [48]

4.2.3.4. Toxicological Data

The toxicology of carvacrol is poorly understood. It has The median lethal dose of carvacrol administered orally to rats is 810 mg/kg body weight (Hagan et al., 1967), whereas the median lethal dose of carvacrol administered intravenously or intraperitoneally to mice is 80.00 and 73.30 mg/kg body weight, respectively. Mice given 33.3 mg/kg carvacrol (intraperitoneal) had no adverse effects, and mice given 50 mg/kg had nonspecific effects and slight ataxia, but mice given higher doses (110-233.3 mg/kg carvacrol) had ataxia, decreased spontaneous motor activity, and somnolence prior to death. [41]

4.3. Terpinen-4-ol

4.3.1. Physico-chemical Properties

Terpinen-4-ol, which has the chemical formula C10H18O with a molecular weight of 154.25, is an isomer of terpineol. Terpinen-4-ol is a colorless to pale yellow liquid with a pine odor and has a distinctive, pleasant scent. It is obtained as an extract from the leaves, branches, and bark of Melaleuca alternifolia Cheel, and it is a key component of tea tree oil. Terpinen-4-ol is volatile and soluble in ether, acetone, and other solvents with a moderate polarity. Over 200 derivatives of plants, herbs, and flowers possess it. It's being used to make artificial geranium and pepper oils as well as herbaceous and lavender notes in fragrance. Furthermore, it is employed as a topical antibacterial and experimental drug.[49].

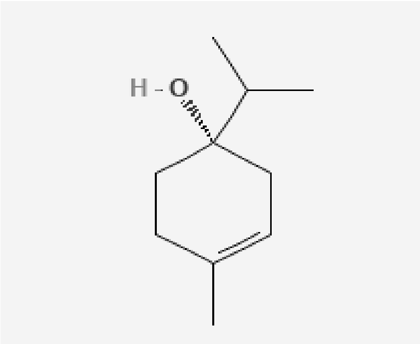

Fig. 8. Chemical Structure of Terpinen-4-ol

4.3.2. Terpinen-4-ol in Nature

Terpinen-4-ol originates naturally in a range of plant essential oils, is harmless for the environment, has a pleasant scent, and has a number of biological functions which are listed on the table below:

Table 2. Main Sources of essential oils from plants containing Terpinen-4-lol

Familia	Genus	Species	Part	Content of terpinen-4-ol in its essential oil (mg/g)
Cupressaceae	Sabina	S.vulgaris A	Fruit	223.0
	Juniperus	J.indica Bertol	Leaf	37.0-130.0
Annonaceae	Xylopia	X.aethiopica	Fruit	129.0
Labiatae	Origanum	O.majorana	All parts	323.0
		O.ramonense Danin	leaf	168.0
		O.sbusp.viride	All parts	168.2
	Nepeta	N.asterotrichus	All parts	228.0
	Stachys	S.gluinosa	All parts	131.0
	Ocimum	O.americanum	All parts	176.0
	Elsholtzia	E.fruiticosa	All parts	126.0

Terpinen-4-ol exhibits a number of biological activities, including attracting, repelling, fumigant lethality, growth inhibition of insects, and antimicrobial activity. These biological properties open up a wide variety of possibilities for the creation and use of terpinen-4-ol in pesticides.

4.3.3. Bioactivity of Terpinen-4-ol

4.3.3.1. Antibacterial and Antifungal Activity

One of the main bioactive constituents of tea tree oil is terpinen-4-ol which is a chemical that is composed of more than 100 distinct compounds and is prevalent in many aromatic plants.[50]. Terpinen-4-ol is an effective antibacterial substance with antifungal properties. Terpinen-4-ol may induce anticancer effects by selectively inducing necrotic cell death and cell-cycle disruption in melanoma cell lines or by inducing caspase-dependent apoptosis in human melanoma cells, according to a series of recent investigations. [51]. Terpinen-4-ol, the most prevalent monoterpene found in tea tree oil, and one of the monoterpenes that comprise 80–90% of the composition of tea tree oil. [52] Terpinen-4-ol was investigated for its antibacterial activity against microbes like Staphylococcus aureus, including its Minimal Inhibitory and Minimal Bactericidal Concentrations (MIC and MBC) and a review of aureus biofilms was done. Furthermore, a molecular docking analysis and an in silico investigation of its pharmacokinetic parameters were carried out. The MIC and MBC of terpinen-4-ol were 0.25% (v/v) and 0.5% (v/v), respectively, which is a bactericidal action. The in silico report revealed sufficient absorption and dispersion of the molecule in vivo, and terpinen-4-ol has good antibiofilm action. It draws attention to the positive potential of terpinen-4-ol as an antibacterial agent and lends encouragement to forthcoming pharmacological research on this compound with an eye towards its own therapeutic use. [53] Lastly, tea tree oil rich in terpinen-4-ol has been developed for the treatment of candidiasis due to its powerful antifungal characteristics. Terpinen-4-ol has an antibacterial action in addition to promoting the synthesis of anti-inflammatory cytokines and suppressing the production of pro-inflammatory cytokines, which aids in tissue regeneration. [49]

4.3.3.2. Anti-inflammatory Activity

Terpinen-4-ol has remarkable anticancer impact on a variety of cancer cell types both in vitro and in vivo. A substantial portion of the essential oil extracted from various aromatic plants contains terpinen-4-ol. It works as an antioxidant and anti-inflammatory. [55] Thorough research is still being done on the role of terpinen-4-ol as an anticancer agent, notably in the skin, and the underlying signal transduction pathways of various forms of cell death. It has been demonstrated that terpinen-4-ol induces apoptosis rather than necrosis as its mode of action. Terpinen-4-ol and various anticancer medications have been demonstrated to have a synergistic growth-inhibitory effect by reducing the lifespan of various cancer cells. Since a variety of skin malignancies can be treated with reduced medication doses, such combinations might be predicted to be more successful and less hazardous. [56] Terpinen-4-ol is the most pharmaceutical active component in upcoming formulations to treat a number of ocular and dermal diseases caused by demodicosis that may be affiliated with or without concurrent bacterial or fungal infections. Terpinen-4-ol also has anti-inflammatory properties by suppressing superoxide production and pro-inflammatory cytokines.

4.3.3.3. Improved percutaneous penetration of drugs

When it comes to safe and acceptable permeation enhancers to encourage the percutaneous absorption of a variety of medications from topical formulation into the lower skin layers, essential oils and their components may be preferred over the synthetic chemicals that have been utilized conventionally. With minimal cytotoxicity, terpinen-4-ol significantly promotes the permeation of both hydrophilic and lipophilic medications. Terpinen-4-ol enhanced permeability between 3.9 and 5 times and was a successful enhancer for the percutaneous penetration of medications like hydrocortisone. [57]

4.3.3.4. Toxicological Data

Both intrinsic and extrinsic mechanisms can be used by terpinen-4-ol to induce apoptosis in human leukemic MOLT-4 cells. Superoxide synthesis by monocytes is inhibited, but not by neutrophils, demonstrating the possibility of type-specific regulation of cell types during inflammation by these substances. Through an inherent mechanism that involves the loss of mitochondrial transmembrane potential (MTP) and increased secretion into the cytoplasm, induced-MOLT-4 cell death is regulated. Terpinen-4-ol apparently triggered apoptosis via an extrinsic mechanism by stimulating caspase-8, which led to the cleavage of cytosolic Bid. In particular, tea tree oil's water-soluble components, such as terpinen-4-ol, can inhibit activated human monocytes from generating pro-inflammatory mediators. [58]

4.4. Eugenol

4.4.1. Physico-chemical Properties

Eugenol (2-methoxy-4-prop-2-enylphenol), originally derived from guaiacol, eugenol is a phenylpropanoid containing an allyl chain substituted para to the hydroxy group. With antibacterial, analgesic, and antioxidant qualities, it is a key ingredient in clove essential oil. It has long been used to treat pulpitis and toothaches in dentistry. It functions as an allergen, a human blood serum metabolite, a sensitizer, a volatile oil component, a flavoring agent, an antibacterial agent, an antineoplastic agent, an apoptosis inducer, an anesthetic, analgesic, a voltage-gated sodium channel blocker, an NF-kappaB inhibitor, and an anti-inflammatory agent. It is a phenol, a monomethoxybenzene, and a phenylpropanoid. It originates from guaiacol [59].

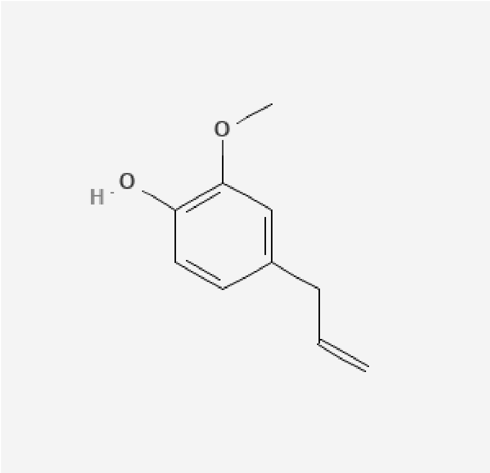

Fig. 9. Chemical Structure of Eugenol [x59]

When combined with Iron(III) chloride, eugenol easily goes through a double displacement reaction. It goes as follows: C10H12O2 + FeCl3 C10H9O2Fe + 3HCl. Bromine forms 1, 3, and Dibromobutyl benzene interact with eugenol and oxygen. The following is the chemical reaction. C10H12O2 + Br2 → C10H12Br2 + O2. The physical characteristics of eugenol include: A clove-like aroma, appearance of a pale yellow oily liquid, complexity of 145, vapour pressure of about 4 torr, hydrogen bond donor 1, and miscibility with alcohol, ether, chloroform, and oils [60].

4.4.2. Eugenol in Nature

The class of natural compounds known as phenylpropanoids includes eugenol, a volatile, bioactive, naturally occurring phenolic monoterpenoid. It is typically present in several different aromatic herbal plants, such as clove, tulsi, cinnamon, nutmeg, and pepper, but is mostly isolated from clove plant (Eugenia caryophyllata). Eugenol has a wide range of uses in many industries, including the pharmaceutical, food, taste, cosmetic, and agricultural ones. For example, the pharmacological characteristics of eugenol are widely known. analgesic, anti-inflammatory, anti-cancer, anti-microbial, and anti-cancer. As a local anesthetic and disinfectant, eugenol and its many derivatives are utilized in medicine. Despite having many uses, eugenol can have a number of negative side effects, especially if taken in excess of the prescribed dosage. Convulsions, nausea, lightheadedness, and a fast heartbeat are possible side effects [61].

4.4.3. Bioactivity of Eugenol

4.4.3.1. Antibacterial and Antifungal Activity

The hydroxyphenyl propene eugenol is found naturally in the essential oils of various plants from the Lamiaceae, Lauraceae, Myrtaceae, and Myristicaceae families. It is one among the primary components of clove (Syzygiumaromaticum (L.) Merr). & L.M. Perry, Myrtaceae) oil and is frequently used as a flavoring ingredient in both foods and cosmetics. Eugenol is said to have positive impacts on human health, which is in line with a vast body of recent scientific research. Antioxidant and anti-inflammatory properties are primarily linked to these benefits. Eugenol has also demonstrated remarkable antibacterial action in trials, being effective against fungi and a variety of gram-negative and gram-positive bacteria [62]. The free OH group in the structure of eugenol has been linked to its possible antibacterial effects against a variety of species, including Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli. Eugenol is a hydrophobic molecule that can easily pierce the lipopolysaccharide cell membrane and enter the cytoplasm. It is thought that this property of eugenol causes it to work against Gram-negative bacteria by disrupting the cytoplasmic membrane. Once within the cell, it has the potential to modify the cell's structure and cause intracellular components to seep out. Aspergillus niger, Candida albicans, Penicillumglabrum, Penicillumitalicum, Fusaria oxysporum, Saccharomyces cerevisiae, Trichophyton mentagrophytes, Lenzitesbetulina, Laetiporussulphurous, and Trichophyton rubrum are just a few of the fungal strains that have been shown to be resistant to eugenol in Eugenol is believed to disrupt the function of cell membranes in fungi, suppress virulence factors, and impede the production of fungal biofilms [63].

4.4.3.2. Anti-inflammatory Activity

Eugenol is a well-liked anesthetic and pain reliever used in dental procedures. In numerous studies, including one using a rat model, it has been discovered to inhibit voltage-gated sodium channels (VGSC) in the primary supply neurons of the teeth. According to available data, eugenol can prevent the Raf/MEK/ERK1/2/p47-phosphorylation pathway from being used by neutrophils to produce superoxide anions. It is also known to be an inhibitor of pro-inflammatory mediators, such as IL-1 and IL-6, tumor necrosis factor alpha (TNF-), prostaglandin E2 (PGE2), expression of inducible oxide nitrate synthase (iNOS) and cyclooxygenase-2 (COX-2), nuclear factor kappa B (NF-B), leukotriene C4 and 5-lipoxygenase (5-LOX Its anti-inflammatory capabilities include stopping neutrophil/macrophage chemotaxis and obstructing the production of inflammatory neurotransmitters like prostaglandins and leukotrienes. Eugenol dimers have also demonstrated chemopreventive properties by obstructing macrophage cytokine expression [63]. A number of stimuli, including N-formyl-methionyl-leucyl-phenylalanine (fMLP), leukotriene B4 (LTB4), and carrageenan, have been used to study the anti-inflammatory effects of eugenol on leukocyte migration. After a complex chain of events involving endothelium-leukocyte contacts and subsequent extravasation to the inflamed region, polymorphonuclear (PMN) cells are recruited to the inflammatory site [64].

4.4.3.3. Improved percutaneous penetration of drugs

Mutalik and colleagues have used mouse skin to evaluate penetration enhancers in vitro, including eugenol. In their research, eugenol was also discovered to boost glibenclamide and glipizide solubility and skin retention. Zhao and colleagues investigated the impact of eugenol on the percutaneous absorption of a medication via pig skin. The research revealed that, in comparison to the control group, eugenol was able to significantly increase the permeability coefficient of tamoxifen. The study also discovered that eugenol's apparent capacity to improve permeability is due to lipid extraction and enhanced tamoxifen partitioning to the stratum corneum [65]. Eugenol can be produced synthetically or organically from clove or other oils. The percutaneous transfer of medicines with systemic effects in mammals is now known to be enhanced by eugenol, according to new research. This invention therefore provides a topical composition for the transdermal delivery of physiologically active agents to mammals that includes an effective amount of a systemically active, water soluble or solubilizable drug, an amount of eugenol that facilitates percutaneous transfer, and a pharmaceutically acceptable vehicle that includes at least one pharmaceutically acceptable solvent or solubilizer for said eugenol. According to this innovation, the amount of drug that must be administered transdermally in order to create a therapeutic dose is known as the effective amount of drug. The exact dose will depend on a number of variables, including the desired physiological effect, the frequency of administration, the drug's metabolism in the body and on the skin, its half-life, the amount of eugenol included in the composition, and maybe other percutaneous transfer enhancers. As previously mentioned, the composition contains eugenol in amounts that promote percutaneous transfusion. For the majority of medications, this percentage typically varies from 4 to 16 percent by weight of the composition [66].

4.4.3.4. Toxicological Data

The Federal Food, Drug, and Cosmetics Administration has classified eugenol as a generally recognized as safe drug. However, in-depth toxicity studies should be carried out to confirm that eugenol is safe for the general public's health. While eugenol is a structurally simple molecule, it is extensively used for a variety of purposes in a variety of industries, including pharmaceuticals, food and cosmetics, dentistry, agriculture, and others. In addition, some minor changes to eugenol's molecular structure may result in different molecular properties that may have different biological activities. Numerous investigations have revealed interactions between eugenol and other antibacterial substances that make it possible to employ eugenol as a suitable food additive. Antimicrobial tests show that eugenol is also capable of rupturing bacterial membranes, which may boost the penetration of some antibiotics [67].

4.5. Tannic Acid

4.5.1. Physico-chemical Properties

The chemical formula for the commercial tannic acid is sometimes can be given as $C_{76}H_{52}O_{46}$, which corresponds to a decagalloyl glucose, in reality, but it is a mixture of polygalloylquinic acid or polygalloyl glucose esters with galloyl molecules varying from 2 to 12 depending on the plant source [68].Tannic acid is a form of polyphenol that is sometimes referred to as gallotannic acid or acidumtannicum. Tannic acid is a weak acid since it includes several phenolic groups. Quercus infectoria, tara pods, Sicilian sumac leaves, and gallnuts from Rhussemialata are all sources of this acid in nature. Species of tannins are found across the plant kingdom. They frequently occur in both angiosperms and gymnosperms [69].

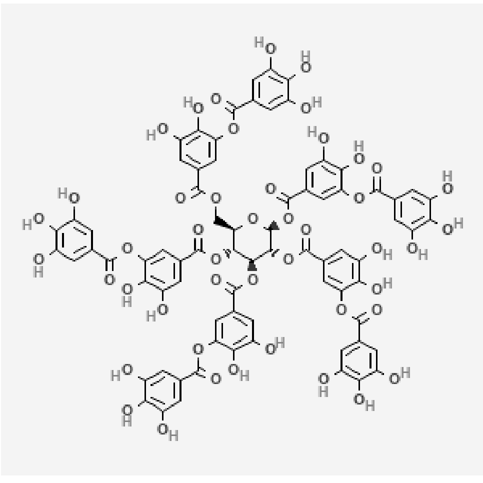

Fig. 10. Chemical Structure of Tannic Acid

Numerous plants contain tannins, which are polyphenolic compounds with carbohydrate backbones. The particular tannin known as tannic acid has a glucose core surrounded by 10 galloyl (3,4,5-trihydroxyphenyl) units. However, the molecules of commercial tannic acid have 2–12 galloyl moieties. Tannic acid doesn't have any carboxyl groups, but since there are so many phenolic hydroxyls, it has a low acidity. It is also very water soluble thanks to the hydroxyls. It is classified as a nonhazardous chemical by all regulatory bodies [69].

4.5.2. Tannic Acid in Nature

Species of tannins are found across the plant kingdom. They frequently occur in both angiosperms and gymnosperms. In 180 groups of dicotyledons and 44 families of monocotyledons (Cronquist), Mole examined the distribution of tannins. Tannin-free species have been found in the majority of dicot families (which are tested by their ability to precipitate proteins). Actinidiaceae, Aceraceae, Bixaceae, Anacardiaceae, Myricaceae for dicot, and Grossulariaceae, Najadaceae, and Typhaceae for monocot are the most well-known families whose members all have tannin in the species studied. Seventy-three percent of the species tested (N = 22) belong to the Fagaceae family of oaks. Only 39 percent of the Mimosaceae species evaluated (N = 28) for acacias had tannin, compared to 6 percent for Solanaceae and 4 percent for Asteraceae. The majority of the plentiful polyphenols are thought to be condensed tannins, which are nearly present in all plant families and make up up to 50% of the dry weight of the leaf. A few families, such as Cucurbitaceae, Boraginaceae, and Papaveraceae, do not contain any species that are rich in tannin. As opposed to the gallic kind found in temperate woods, the tannins found in tropical woods have a tendency to be cathartic in nature [70].

4.5.3. Bioactivity of Tannic Acid

4.5.3.1. Antibacterial and Antifungal Activity

One of the biggest problems with antibacterial testing is antibiotic resistance. It causes a greater death rate, longer hospital stays, and higher medical expenses. Infections such as pneumonia, TB, blood poisoning, gonorrhea, and foodborne illnesses are on the rise, and their treatment with antibiotics is getting increasingly challenging and occasionally impossible. Tannic acid has generated a lot of interest due to the wide range of chemical and biological characteristics it possesses. The quest for efficient antimicrobial drugs that disclose more direct bactericidal pathways has been affected by the multidrug-resistant bacteria's fast expansion [71]. On both Gram-positive and Gram-negative bacteria, tannic acid has been shown to have antibacterial action. The observed TA action against Gram-negative bacteria has been of particular importance since they have posed a significant barrier to current treatment. The usefulness of tannins against bacteria hasn't been studied much in preclinical or clinical settings, though [72].

4.5.3.2. Anti-inflammatory Activity

In those who are healthy, inflammation results from an injury that triggers the body's defensive reaction. The body's effort to neutralize, eliminate, or block off the toxic chemical results in inflammation. Dilation of the capillaries, increased blood flow, and exudation of plasma fluids into the region of damage cause physiologic changes such as swelling, redness, and discomfort. Tannins may influence the inflammatory response by scavenging free radicals activities. The relationship between inflammation and free radical reactions is well supported by the available research. A feedback cycle is started when superoxide, hydroxyl radicals, and other oxidizing species are produced; these radical byproducts of inflammatory processes function as triggers for more inflammation [73].

4.5.3.3. Improved percutaneous penetration of drugs

Tannins are naturally occurring plant phenol derivatives of different molecular weights produced by plants as metabolic byproducts. The most common and basic hydrolyzable tannin, tannic acid (TA, penta-m-digalloyl glucose), possesses astringent, antioxidant, antibacterial, antiviral, and anti-inflammatory effects. The hydroxyl groups of glucose are esterified with five digallic acids, and the glucose moiety serves as the structural core of TA. Although tannin extracts have been used to speed up wound healing for a long time, their precise mechanism of action is still not well understood. It is thought that tannins help speed up the healing of wounds by scavenging free radicals and reactive oxygen species (ROS), encouraging wound contraction, and enhancing capillary vessel growth and fibroblast proliferation [74].

4.5.3.4. Toxicological Data

Coffee and tea naturally contain tannins, and almost all plants and trees have some kind of tannin in their leaves, twigs, bark, wood, or fruit. The Food and Drug Administration (FDA) has designated tannic acid as generally recognized as safe (GRAS) for use as a direct food additive (with restrictions) in several food and beverage items. When given orally to rabbits, tannin was absorbed by the digestive system, processed, and eliminated within 24 hours. According to animal studies, it is non-mutagenic and non-carcinogenic and has minimal acute, subchronic, and chronic oral toxicities. The possibility of tannin reaching either surface (drinking water) or ground water or bioaccumulating in the environment will be constrained by its environmental destiny. Tannin is anticipated to biodegrade in the environment, with initial degradation projected to take place within days and final aerobic degradation likely to take place within weeks. Sand-based soils have the potential for migration to groundwater drinking water sources, but migration in other soils will be constrained by the rate of primary degradation and the strong sorption to soils and sediment, making it likely that drinking water exposures to worry-inducing substances will be in the low to moderate range [75].

5. Advantages and Disadvantages

Herbal cosmetics are frequently created to moisturize dry skin, have an anti-aging effect, reduce wrinkles, brighten skin, remove dark spots, control oil production, have an anti-dandruff effect, protect skin, care for hair, and have an anti-oxidative antipollution effect [76]. Using plants and herbal remedies with anti-dandruff characteristics is the best way to cure dandruff. Studies examining the essential oils' antifungal effects have also been published. A study examines the anti-fungal effectiveness of several plant extracts against *Malasseziafurfur* and there are many organic plant extracts with anti-dandruff qualities. Such plant extracts can have their antifungal qualities evaluated, and they can be utilized successfully in place of chemical agents in a variety of anti-dandruff formulations. Plant extracts are recognized for their conditioning qualities, which are helpful for preserving the general health of the scalp and hair, in addition to their antifungal capabilities [77]. Herbal ingredients have higher MIC (Minimum Inhibitory Concentration) when compared to synthetic ingredients such as Zinc pyrithione, Ketoconazole, Selenium sulfide, Salicylic acid, etc., a reason for synthetic preparations being more preferred than organic formulations in prescriptions. This means that plant-based ingredients require a higher amount of concentration in order to inhibit the growth of *Malassezia*. Apart from that, herbal shampoos yielded low ZOI (Zone of Inhibition) in diameter. Previous studies show that herbal-containing shampoos for dandruff were found to be effective. However, they have a less anti-dandruff effect than commercial synthetic shampoos [78,79]. Thus, while anti-dandruff shampoos from botanical sources may be more sustainable and ethical, its efficacy is still questionable due to results of high MIC and low ZOI in several studies and tests.

6. Conclusion

Hair is an important aspect of how people perceive their own appearance, which has effects on self-esteem and self-confidence. Dandruff, a relatively common scalp condition with a high incidence in the population, is caused by a combination of host factors and *Malassezia furfur*. The majority of commercially available anti-dandruff shampoos contain antifungal drugs that appear to diminish the occurrence of the condition. Globally, anti-dandruff shampoos are known for their therapeutic use as there is a wide range of formulations available in the market. Shampoos based on herbal ingredients are commonly sold for their organic nature, and there is little regard for their action against the said skin disease as they have not been successful in avoiding its recurrence as the cause of dandruff varies according to individual susceptibility, so does the treatment strategy. Some shampoos based on organic and herbal ingredients are popular remedies for dandruff, but these show limited efficacy and duration of action. Due to this, dandruff has become one of the most commercially exploited diseases due to irresponsible marketing of the anti-dandruff effects of several natural ingredients. With that said, there is also a great lack of related information, tests, and studies regarding these compounds such that their efficacy and biological activity are not well understood. Hence, there is a need to deeply study these plant compounds so that significant data will be the basis in formulating more refined anti-dandruff shampoos in the future. Manufacturers may consider other novel delivery systems that are being extensively researched in pharmaceutical formulations and may be effective in the treatment of dandruff. Novel formulations containing established anti-dandruff compounds with prolonged contact time at the site of action are needed and can thus be beneficial in anti-dandruff therapies.

Acknowledgements

The researchers would like to thank our clinical instructor, Sir Joseph Mari Querequincia, for guiding and giving his advice that aided in the completion of this journal. They would like to acknowledge their internship coordinator, Ma'am Jacqueline Padilla, RPh, MSPharm and the Dean of Allied Health Sciences, Fatima May R. Tesoro, RPh, MSPharm, for the opportunity to be able to create and publish the journal.

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