Chapter 161

Essential oils in androgenetic alopecia management: An integrative review

https://doi.org/10.56238/devopinterscie-161

Elenise Penha Viveiros
Federal University of Piauí, Brazil
E-mail: elenisepenha@gmail.com

André Luis Menezes Carvalho
Federal University of Piauí, Brazil
E-mail: aluismenezes@ufpi.edu.br

Talissa Brenda de Castro Lopes
Federal University of Piauí, Brazil
E-mail: talissa.brenda@gmail.com

Igor Frederico da Silveira Ramos
Federal University of Piauí, Brazil
E-mail: igorfrederico10@gmail.com

Paula Natanielle Nunes Alves
Federal University of Piauí, Brazil
E-mail: paulannalves@hotmail.com

ABSTRACT
The present study aims to present which essential oils (OEs) have published scientific studies on their action on hair growth and potential use in the management of androgenetic alopecia (AGA). The searches were conducted between May and June 2021, in the electronic databases PubMed, Science Direct, and VHL, using the descriptors "androgenetic alopecia", "alopecia", "hair loss", "hair growth", "essential oil", "volatile oil" and "aromatherapy". In vitro and in vivo clinical studies were found with the OEs of the following species: Artemisia argyi, Angelica sinensis, Cananga odorata, Cedrus atlantica, Chamaecyparis obtusa, Laurus nobilis, Mentha piperita, Myrtus communis, Platycladus orientalis, Pimenta racemosa, Pogostemon patchouli , Rosmarinus officinalis, Salvia officinalis, Salvia sclarea, Thymus satureioides and Zizyphus jujube, alone or together with other vegetable oils and compounds. Research has shown that EOs stimulate hair growth by increasing microcirculation in the follicles, reducing scalp inflammation, or increasing the expression of growth factors. After reviewing the literature, it was concluded that there are several promising botanical ingredients for the treatment of alopecias, but there are still few solid and well-conducted clinical trials concerning AGA. Therefore, more studies need to be conducted for an effective evaluation of natural and complementary treatment options that better serve patients.

Keywords: Hair growth, Hair loss, Aromatherapy, Natural treatment.

1 INTRODUCTION

Hair loss disorders comprise an extensive group of dysfunctions of varying etiology called alopecias, which often occur in the general population (Hosking et al., 2018). Even if they are aesthetic conditions, without threat to life, the implications on social interactions and the well-being of patients are undeniable (Lee et al. 2010).

Alopecias can be classified as cicatricial or non-cicatricial. Cicatricial alopecias occur when inflammation of the scalp leads to the destruction of pilosebaceous structures and subsequent replacement with fibrous scar tissue (Jaller et al., 2019). In these cases, hair loss is irreversible, since humans are usually born with approximately 5 million follicles and no follicular addition occurs after birth (Brotzu et al., 2018).

In non-cicatricial alopecias, on the other hand, there is no trigger for the destruction of hair follicles. Androgenetic alopecia (AAG) falls into this category, being the most common subtype of chronic hair loss (Mingsan et al., 2020). It is characterized by a progressive reduction in capillary density in the scalp, due to the miniaturization of thick and long terminal wires for vellus hairs (short hairs, usually body), and prolongation of the stationary (telogen) phase of the hair growth cycle (Marks & Senna, 2019).

AGA affects more than 50% of men and almost 50% of women by the age of 50. It can also affect children and adolescents (Griggs et al. 2019), although rarely. Its occurrence increases with age and can produce psychological impacts on individuals as thinning, shortening and hair loss progressively advance (Sasaki, 2018).

In general, hair loss in cisgender men by AGA is mainly attributed to the action of androgen hormones on follicular receptors and polymorphic genetic predisposition already existing without the presence of both factors, dysfunction will not occur (Marks & Senna, 2019). The two aspects, allied or there are no other agents, provoke the degrowth of metabolic functions in the hair follicles and hair bulbs, compromising the physiological functions of the scalp as a whole. Impairment in local circulation may also occur in some cases due to tension in the scalp (Damodaran & Gupta, 2011).

Conventional treatments consist mainly of oral systemic antiandrogens and topical medications to improve local microcirculation. In addition to pharmacological options, there is hair transplantation. The latter, however, has problems, such as surgical risk and continuous fall after the operation (Mingsan, 2020). The pharmacological treatments with the best level of evidence in terms of safety and efficacy for AGA are oral finasteride and topical minoxidil. In women, topical minoxidil solution is considered as the most effective and safe treatment (Varothai & Bergfeld, 2014). Minoxidil, a derivative of pyrimidine, is a widely available drug on the market. However, its use is limited and temporary due to its unpredictable efficacy and significant side effects (Zhang et al., 2016), such as facial hypertrichosis in 3 to 5% of women and contact dermatitis in 6.5% of patients. This variable efficacy makes it difficult to predict treatment success on an individual basis (Trüeb, 2002). In addition to conventional allopathic agents, there are numerous cosmeceuticals, herbal medicines, nutritional supplements and various agents that claim to have an action against AGA with pilot studies in vitro, animal and human models (Premanand et al., 2020).

Over the years, many topical herbal formulations have been developed and marketed around the world to prevent hair loss or promote hair growth. There are several advantages to using natural drugs for AAG, including the possibility of better patient compliance, fewer side or adverse effects, easy availability, and low cost. In addition, molecules of natural origin may have more than one biochemical mode of action for the treatment of hair loss (Herman & Herman, 2016).

Among the substances derived from plants, essential oils (OEs) stand out. They are a complex mixture of molecules of low molecular weight and lipophilic nature, characteristics that allow them to cross membranes, change their composition and increase the fluidity of cell membranes (Sharifi-rad et al., 2017).

These properties make bioactive OEs with promising topical functions, especially for the scalp, as well as providing unique and pleasant aromas (Sharmeen et al., 2021).

The empirical use of OEs for the treatment of hair and scalp dysfunctions is already a reality in hair therapy clinics. However, publications of well-conducted trials investigating the effects of volatile oils on alopecias are still scarce (Katzer et al., 2019). Given the above, the objective of the review is to present the essential oils with effect on hair growth with emphasis, specifically, on the management of androgenetic alopecia.

2 METHODOLOGY

The integrative literature review was guided by the following research question: "Which essential oils aid in hair growth and can be used in AAG?". The research question was elaborated through the PICO strategy (patient, intervention, comparison/control and *outcomes*/results), where: P = patients with AGA; I = use of essential oils; C = comparison with conventional methods of treatment; O = hair growth (Souza et al., 2010). Between May and June 2021, scientific articles on the effect of essential oils on hair growth were surveyed, and carried out in any country, without the restriction of publication date.

The following steps were applied to this review model: 1) identification of the theme and elaboration of the research question; 2) establishment of criteria for inclusion and exclusion of studies during the literature search; 3) definition of the information to be extracted from the selected studies; 4) critical evaluation of the studies included in the integrative review; 5) discussion of results; and 6) assembly of the review/synthesis of knowledge.

2.1 INCLUSION AND EXCLUSION CRITERIA FOR STUDIES

Observational studies with in vivo, in *vitro*, *and in silico* activity analyses and clinical trials evaluating the capacity to stimulate hair growth of essential oils with AGA were included. No reviews or meta-analyses were included. Articles on other types of alopecia other than androgenetic, such as alopecia areata, cicatricial alopecias, or alopecias induced by the use of chemotherapeutic agents, were excluded. Nor did studies conducted using plant extracts enter the review.

2.2 SEARCH, SELECTION, AND SUMMARIZATION OF STUDIES

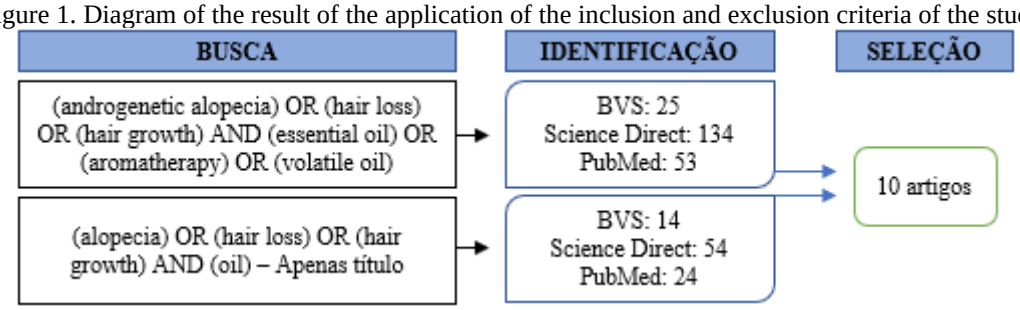
The databases used were PubMed, Science Direct and the National Health Library (VHL). To search for scientific productions, the following descriptors were defined in English: "*androgenetic alopecia*", "*alopecia*", "*hair loss*", "*hair growth*", "*essential oil*", "*volatile oil*", "*aromatherapy*" used with the Boolean operators OR and AND. We used the following search terms in PubMed that were adapted to the search strategy of the other data: "(*androgenetic alopecia*) OR (hair *growth*) OR (*hair loss*) AND (*aromatherapy*) OR (*essential* oil) OR (*volatile oil*)".

The identification of the adequacy of the studies in response to the guiding question of the research took place initially through the reading of the titles and abstracts of the studies. Finally, the selected studies were evaluated in full to select which scientific productions corresponded to the theme of interest and would be included in the review. The results were summarized and organized in the form of tables composing a synthesis of the information taken from the articles. No software or platform was used to verify the data and articles.

3 RESULTS

After searching and applying the inclusion and exclusion criteria, ten studies remained that met the requirements of this analysis. Thus, the final sample of this work was composed of ten scientific articles published between 2003 and 2020. The diagram with the steps and quantities of articles is represented in Figure 1.

Figure 1. Diagram of the result of the application of the inclusion and exclusion criteria of the study.



Source: Authors (2021).

Of the total number of selected articles, eight refer to experiments in mice or cells. The synthesis of how these studies were conducted is shown in Table 1.

Table 1. Summary of the conduct of experiments in mice or cells included in the review.

AUTHOR/YEAR	OE SPECIES	MODEL	INTERVENTION	CONTROL GROUP
Lee et al. 2010	*Chamaecyparis obtusa* (leaves)	C57BL/6 M mice.	1% OE in 40% ethanol applied topically and daily, for 30 days	CN: Alcohol 40%
		HaCaT human keratinocytes	0.3 x 10^6 HaCaT cells sown in 96-well plates and treated for 24h	CN: DMSO
Yoon et al., 2010	*Zizyphus jujube* (seeds)	BALB/c Mice F.	0.1%, 1% and 10% of EO applied topically, 1x/day, for 21 days	NC: untreated
Park et al., 2013	*C. obtusa*	C57BL/6 F mice.	3% OE in jojoba oil applied topically 6 days a week for 4 weeks	CP: MXD 3% CN: Sun. salina
Oh et al., 2014	*Mentha piperita* (leaves)	Mice C57BL/6 males	3% OE in jojoba oil applied topically 6 days a week for 4 weeks	CP: MXD 3% CN: Sun. salina

Lee et al., 2016	Lavender	C57BL/6 F mice.	OE at 3% or 5% in jojoba oil applied topically 6 days a week for 4 weeks	CP: MXD 3% CN: Sun. salina
Zhang et al., 2016	*Platycladus orientalis* (cedrol isolated)	C57BL/6 mice	10, 20 and 30 mg/ml of OE in alcohol 85% applied topically 1x/day for 21 days	CP: MXD 2% CN: Alcohol 85%
Zhang et al., 2019	*P. orientalis* (dried leaves are *Cacumen Platycladi*)	C57BL/6 F mice.	0.1 and 0.2 g/kg of LE applied topically, 1x/day, for 28 days	CP: MXD 2% CN: Et. 60%
		Dermal papilla cells	5×10^3 cells treated with LE at concentrations of 4, 20 and 100 µg/ml, for 48 h.	CP: MXD CN: not cited
Mingsan et al., 2020	*Artemisia argyi Angelica sinensis* (in AQH oil)	Kunming Mice M.	Previously testosterone-induced alopecia (0.1% in Et. 50%). Groups treated with 0.02 ml of LE, 1 or 2x a day, for 21 days	CP: MXD 0,02 ml CN: sterile water

Legend: CN – negative control. CP – positive control. DMSO – dimethylsulfoxide. Et – ethanol. F. – female. M. – male. MXD – Minoxidil. OE – essential oil. Sun. – solution. Source: Authors (2021).

All experimental studies conducted in mice analyzed the state of the hair follicles using histological sections of the animals' skin. In addition to histopathology, other evaluations were performed by the authors and are shown in Table 2.

Table 2. Summary of the analyses performed in the experiments in mice or cells included in the review.

AUTOR/ YEAR/OE	METHODS OF ANALYSIS	EFFECT OF THE OE	PROPOSED MECHANISM
Lee et al. 2010 *C. obtuse*	- Analysis of growth factor expression in keratinocytes - GC/MS for characterization of OE subfractions	- In vivo: hair growth with a faster onset - In vitro: detection of growth factors VEGF and KGF related to hair growth	EO increases the production of cell growth factors involved in the regulation of morphogenesis and hair growth
Yoon et al., 2010 *Z. jujube*	- Measurement of length, weight, and thickness of hair	0.1%, 1% and 10% of oil produced a greater effect on hair growth and thickness compared to the other groups.	No mechanism of action of the compound was elucidated or commented on in the article
Park et al., 2013 *C. obtusa*	- Enzymatic analysis of AF and cytokine expression - Immunohistochemistry	- Increased AF activity - Expression of IGF-1 and VEGF	EO stimulates VEGF, which promotes the production of protease related to matrix lysis required in revascularization and increases vascular permeability
Oh et al., 2014 *M. piperita*	- Detection of alkaline phosphatase activity in dermal skin (AF) - Analysis of IGF-1 gene expression	- Accelerated hair growth - Increase in dermal thickness, number and depth of hair follicles in histological analysis. - Increased AF and γ-GT activity - Remarkably increased IGF-1 mRNA expression with OE, even better than with MXD	EO increases AF activity in the dermal papilla, which improves local circulation, and induces increased IGF-1, a potent mitogen

Lee et al., 2016 Lavender	- Photo analysis - Quantification of mast cells	- Increased number, lengthening and depth of follicles - Increased dermal thickness and reduced amount of mast cells in the follicles	OE maintains the anagen phase and delays the transition to the catagen phase
Zhang et al., 2016 *P. orientalis*	- Photo rating - Measurements of length and weight of grown hair	Significant promotion of capillary, dose-dependent growth, particularly for females	No mechanism of action of the compound was elucidated or commented on in the article
Zhang et al., 2019 *P. orientalis*	- Photo rating - Analysis of OE by GC-MS	-In vivo: accelerated hair growth -In vitro: increased cell proliferation, dose-dependent effect	OE may delay the onset of follicular telogen phase in certain areas of the skin
Mingsan et al., 2020	- Hormonal dosage	Promotion of hair growth similar to the MXD group	EO improves microcirculation and regulates hormonal imbalance

Legend: cDNA – complementary DNA. FA – alkaline phosphatase. GC/MS – gas chromatography coupled to mass spectrometry. IGF-1 – insulin-like growth factor type 1. KGF – keratinocytes growth factor. mRNA – messenger RNA. MXD – Minoxidil. OE – essential oil. PCR – polymerase chain reaction. RT-PCR – Reverse transcription polymerase chain reaction. VEGF – vascular endothelial growth factor. γ-GT – gamma glutamyltransferase. Source: Authors (2021).

Few clinical studies were found in the procedure of searching for articles for review. Since the objective was to search for articles regarding AGA, the articles found on alopecia areata and central cicatricial alopecia were left out of the selection. The articles resulting from clinical studies included in this study are summarized in tables 3 and 4.

Table 3. Summary of the conduct of the clinical studies included in the review.

AUTOR/ YEAR	OE SPECIES	GROUP	INTERVENTION	CONTROL GROUP
Bureau et al., 2003	*Cananga odorata* + *Atlantic cedrus* + *Laurus nobilis* + *Myrtus communis* + Salvia officinalis + *Salvia sclarea* + *Pimenta racemosa* + *Pogostemon patchouli* + *Rosmarinus officinalis* + *Thymus satureioides*	Male and female volunteers diagnosed with AGA	Lotion with mixture of OE's followed by low-intensity electromagnetic pulses (12.5 V/m at 1 cm and 10 MHz, via helmet for 30 min) administered regularly for 26 weeks	CN: placebo (*neopentyl glycol dictanoate* + calamus essence)
Pahini et al., 2015	*Rosmarinus officinalis*	Volunteers diagnosed with AGA	Randomly assigned patients treated with rosemary oil for 6 months.	CP: MXD 2%

Legend: AAG – androgenetic alopecia. CN – negative control. CP – positive control. MXD – Minoxidil. OE – essential oil. Source: Authors (2021).

Clinical studies fall short in some respects. Pahini et al. (2015) do not describe negative control in their trial with the use of rosemary oil, comparing only with minoxidil. Bureau et al. (2003) is the only model among all the review to use a placebo as a negative control. However, the authors evaluate a mixture of eleven volatile oils to test the hypothesis, as well as adding an additional therapy, the low-intensity

electromagnetic pulse, without positive control. This large number of variables hinders the analysis and the proposition of a mechanism of action (Table 4).

Table 4. Summary of the analyses performed in the clinical studies included in the review.

AUTHORS / YEAR	METHODS OF ANALYSIS	EFFECT	OE MECHANISM
Bureau et al., 2003	- Evaluation of capillary quality and quantity - Self-assessment scale - Histological analysis - Immunohistochemistry	Significant increase in density, amount of anagen hair. Good acceptability of patients	No mechanism of action of the compound elucidated or commented on in the article
Pahini et al., 2015	Photomicrograph of the scalp	Significant hair growth in both groups	Increased capillary microperfusion

Legend: MXD – Minoxidil. OE – essential oil. Source: Authors (2021).

4 DISCUSSION

EOs are volatile products produced by the secondary metabolism of plants, composed primarily of terpenes, terpenoids, and aromatic and aliphatic constituents (abelan et al., 2021). The present study represents an attempt to associate the results observed in the works that address the use of LEs for hair growth with the management of patients with AGA through an integrative review. All articles were based on experiments that analyzed the ability to stimulate hair growth of an isolated essential oil, in mixture with other OE's or having some isolated component.

In general, the experiments developed by the researchers have similar methods: EO applied topically for cell stimulation and proliferation in hair follicles, when in vivo analysis, or to incite the production of factors linked to hair growth. From this common skeleton that variations arise in relation not only to the type of LE used, but also in the variables analyzed.

The studies show inconstancies in the presence of the control groups. Of the selected articles, not all of them used positive and negative controls at the same time (tables 1 and 3), which is expected from a scientific experiment. This choice compromises an adequate and comparative analysis of an observed effect. The control of the vehicle used is also important to be examined and does not appear in all experiments. As described in table 1, Lee et al. (2010) and Yoon et al. (2010) did not use positive control to compare their results, compromising the study. The standard positive control used in growth research through topical mechanisms is minoxidil, a drug that is part of the classic treatment for AGA.

4.1 CAPILLARY CYCLE AND GROWTH FACTORS

Human hair spends a few years in its life cycle, while the murine hair cycle lasts only about 3 weeks, so the time of the hair cycle in humans and mice is different. On the other hand, the structures of the hair cycles of humans and mice are similar (Zhang et al., 2016), which enables preclinical research. For this reason, C57BL/6 mouse models were widely used in the evaluation of hair growth (Table 1). In addition,

these animals are preferable because of their trunk pigmentation, which is produced only during the anagen phase of the cycle (Zhang et al., 2019). When shaving the mice, all the hair follicles are synchronized in the telogen stage, highlighting the pink coloration of the skin (Oh et al., 2014). However, the methodologies used specimens whose hair has been cut and not fallen. Therefore, they do not reliably represent the mechanism of alopecia, which highlights the importance of well-structured clinical studies.

Hair growth is a complex and cyclically controlled process, characterized by phases of regeneration (anagen), regression (catagen), rest (telogen), and fall or exogenous phase (Zhang et al., 2016). The process is cyclical and continuous. Hair length is due to the time that the hair follicle remained in the anagen phase (Abelan et al., 2021). This phase is the longest, with an average duration of 3 years, ranging from 1 to 6 years, depending on the location of the hair on the body. The longer this phase, the longer the hair will be. After the period of proliferation, the follicle goes to the phase of involution through the apoptosis of follicular keratinocytes, which culminates in the resting stage with organ inactivity. The telogen stage persists for 2 to 3 months in the scalp strands and precedes the final phase of natural hair loss (Qi & Garza, 2014).

In healthy conditions, the anagen phase is more prevalent. From 90% to 95% of all hair, strands are at this stage at any given time. However, in alopecias this phase is gradually shortened, leading to the miniaturization of the wires and reduction of capillary density (Rossi et al., 2016). Because of the length of the hair cycle, treatment for AGA can only have results visualized months after the beginning.

Zhang et al. (2019) performed tests on dermal papilla cells (table 1) for analysis of the EO of *P. orientalis.* It is also possible to observe in the first table that Lee et al. (2010) used keratinocytes and mice when evaluating the EO of *C. obtusa.* The dermal papilla is the grouping of mesenchymal cells at the base of the follicle, which plays an essential role in hair growth. Keratinocytes are responsible for the proliferative phase and are also one of the main targets of the toxic effect of environmental or xenobiotic agents. As the rate of blood flow around the hair bulbs rises during the growth stage, it can result in a good bioavailability of many drugs in these sites (Orafidiya et al., 2004), having beneficial consequences or not, depending on the pharmacological effect of the substance.

For hair growth to follow normally, there are maintenance factors of the anagen step, they are insulin-like growth factor 1 (IGF-1), basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF). In addition to these, the increased expression of cytokines that promote apoptosis, such as transforming growth factor-beta 1 (TGFβ 1), interleukin-1 alpha (IL-1α) and tumor necrosis factor-alpha (TNFα), which are important for physiological continuity of hair development (Trüeb, 2002).

Park et al. (2013) and Oh et al. (2014), to analyze the action of the OEs of *C. obtusa* and *M. piperita* about hair growth (table 1), investigated the activity or presence of growth factors in skin tissues, compared with the positive control group of minoxidil. This drug promotes the expression of VEGF in cultured cells of the dermal papilla. Thus, VEGF can contribute to the extension of the anagen phase in AGA (Lee et al. 2010). The OEs showed positive growth effects, such as accelerated onset and stimulation of growth factors.

4.2 ANDROGENETIC ALOPECIA: CAUSES AND CONVENTIONAL TREATMENTS

Progressive hair loss can happen at various stages of life. The new paradigm of AAG is that genetic inheritance and androgens (represented by the metabolite dihydrotestosterone - DHT) are the primary contributors to a secondary dysfunction: microinflammation, which reinforces the process of progressive follicular miniaturization. In addition to inflammation, microbial over colonization of the infundibulum of the pilosebaceous unit is also a protagonist in alopecia (Sadgrove, 2018). In summary, it is known that there are several factors associated with AGA such as mental and psychological influences, infections, heredity, medications, nutritional status, and changes in autoimmune, endocrine, and hormonal functions (Mingsan et al., 2020).

The complex microbiological system of the skin plays a key role in homeostasis. Changes in the physiological microbiota of the scalp, whether of bacterial or fungal origin, have been found in patients with alopecia areata and AAG, leading to the belief that these changes in the microbiome may be related to micro inflammatory processes or changes in the hair follicle cycle in patients with alopecia (Barquero-orias et al., 2021).

There are limitations in the treatments of AAG due to the lack of therapies that induce and maintain the remission of the disease. Recent drug treatments for alopecia do not treat the specific cellular mechanisms of this dysfunction, being more attenuating than curative. There is an unmet demand for therapies that provide satisfactory long-term results (HOSKING, 2018).

There are two chemical agents approved by the United States Federal Drug Administration (FDA) to treat baldness, finasteride and minoxidil for male and female AAG. In Brazil, the National Health Surveillance Agency (ANVISA) approved minoxidil, finasteride and a topical lotion containing 0.025% of 17α-estradiol. Despite the low number of drugs approved by regulators for the treatment of AAG, physicians have the freedom to prescribe off-label medications (Katzer et al., 2019).

Minoxidil was introduced in the early 1970s as a drug for hypertension. However, its side effect of hypertrichosis turned it into a topical formulation for the treatment of AAG (Messenger & Rundegren, 2004). Systemic finasteride has also demonstrated major side effects, including sexual dysfunction, mood disorders, and post-finasteride syndrome with related depression (HOSKING, 2018). Estrogens are also used in women with AGA, prescribed in the form of oral contraception or hormone replacement therapy. Women with this condition should also avoid androgens and their precursors, since they can aggravate hair loss (Trüeb, 2002).

4.3 NATURAL TREATMENTS

The use of plants and herbs has been a reality in cosmetics for years and tends to increase more and more in the market. The products are directed towards sustainability to follow the profile of customers who are increasingly aware and informed about the ingredients and production chains. Thus, consumers have increasing demands for more natural and ethically correct products (Fonseca-Santos et al., 2015). Because

of this, in the search for innovative and effective ingredients, research has increasingly turned to investigating ethnobotanical resources in order to find herbal preparations that can be used for the health, beauty and care of the body as a whole (Hughes et al., 2019).

Aromatherapy has been used for thousands of years and has been adopted as an alternative medicine for many medical conditions. OE therapy presents evidence of efficacy for labor pain, reduced blood pressure in hypertension, stress in healthy adults, anxiety in perioperative patients, and improved sleep quality in various populations (Freeman et al., 2019). Clinical aromatherapy as a complementary therapy is rapidly growing worldwide. Therapeutics may be beneficial in the hospital or outpatient setting for the control of symptoms such as nausea, general well-being, anxiety, depression, stress and insomnia, being beneficial for preoperative anxiety, oncology, palliative care, hospice and end of life (Farrar & Farrar, 2020).

Natural treatments are not necessarily alternatives to conventional ones. Complementarity leads to promising results and has the possibility of better responses in patients. Especially in the case of AGA, due to its multifactorial etiology, it is possible to combine treatments targeting more than one target of origin of hair loss. Studies investigating combination therapies for AGA have reported greater efficacy than monotherapy. Combining therapies may be an effective, safe, and promising option for the treatment of alopecia (Zhou et al., 2020).

The side effects are related both to the active principles of conventional therapies and to the vehicles used. An example of this is Minoxidil, which is often handled in a hydroalcoholic vehicle, which can cause dryness of the wires and scalp. This effect does not occur if oily vehicles are used, such as those used by Aromatherapy for the application of OEs, fixed vegetable oils.

Vegetable oils can add benefits to treatments. There are even studies investigating its action against hair loss. Cho et al. (2014) verified positive results in relation to pumpkin seed oil for hair growth, with no adverse effects observed. In general, fixed oils have emollient properties and good compatibility with the corneal extract, in addition to other characteristics particular to each plant type, according to the species and/or part of the plant from which the extraction was made. As summarized in table 1, Park et al. (2013), Oh et al. (2014), and Lee et al. (2016) in their analyses of the OE of *Chamaecyparis obtusa*, peppermint and lavender, respectively, chose as a vehicle the vegetable oil of jojoba, one of the preferred carrier oils of Aromatherapy.

Jojoba oil is made up of almost 98% pure waxes, sterols and vitamins with few triglyceride esters, so it is widely known as liquid wax rather than oil or fat. It is an emollient agent and conditioning agent of high thermal and oxidative stability, widely used in general and cosmetic industry. One of the most outstanding features is the structural similarity of jojoba oil to skin sebum, leading to a smoothing effect on dry skin and inhibition of excess flaking of epidermal cells (Gad et al., 2021).

There are promising plant-based actives for the treatment of AGA. Some phytoestrogens have a chemical structure similar to human estrogen and proven ability to bind to estrogen receptors in humans.

In view of this, there is the possibility of stimulating hair growth through phytohormones (Herman & Herman, 2016). However, better developed clinical trials are needed to achieve a high level of scientific evidence and verify the real efficacy and safety of plant products that have accompanied humanity since antiquity (Sharifi-Rad et al., 2017).

4.4 ESSENTIAL OILS AND ANDROGENETIC ALOPECIA

According to the sixth edition of the Brazilian Pharmacopoeia, essential oils are those obtained from plant species, by physical processes, which evaporate without leaving residue at room temperature. They are made up of complex combinations of substances with low molecular weight, which determine their taste and odor. They may be isolated or mixed with each other, deterpened, rectified or concentrated. They can also be termed as volatile oils (Anvisa, 2019).

Essential oils have increased in popularity in recent years due to the fast-growing market for aromatherapy (Esposito et al. 2014). In addition to the improvement in the quality of life, they are widely used in the cosmetic industry as fragrances, capable of transmitting a number of unique and pleasant aromas, and bioactives with anti-aging, antimicrobial, sunscreen and whitening properties. This breadth of advantages makes OEs valuable and highly valued ingredients in the cosmetic and herbal industry (Sharmeen et al., 2021).

Of the OEs employed in the experiments only Park et al. (2013), Oh et al. (2014) and Lee et al. (2016) made reference to the brand of commercially acquired oil (table 1). The origin of the plant specimen, as well as the extraction method used influence the composition of the volatile oil obtained. The oils marketed are the closest to the practice and there is still a certain uniformity of composition, since the industrial batches are usually standardized. However, the chemotype and geotype of EO may be of fundamental importance for its greater or lesser efficacy against an intended result (Wolffenbüttel, 2019).

In addition to uses in various traditional healing systems around the world (Sharifi-Rad et al., 2017), volatile oils have excellent potential for developing technological formulations. The active compounds of herbal products, when applied topically, must be able to penetrate the epidermal barrier and reach the specific sites of the hair follicles to affect hair growth through different biological pathways (Herman & Herman 2016). Taking into account the properties and biocompatibility of certain OEs, their association with nanotechnologies is promising. Saporito et al. (2017) produced lipid nanoparticles with rosemary and eucalyptus LEs with positive results. The nanoparticles were based on natural lipids to potentiate the healing process of skin wounds.

It is important to emphasize the attention that should be paid to the doses used and the frequencies of application, preferably evaluating each patient according to their characteristics such as gender, age and clinical picture. In children, for example, the risk of systemic absorption sufficient to cause hemodynamic effects and other side effects is theoretically higher due to lower body weight and increased scalp area relative to body weight (Griggs et al., 2019).

Among the various OEs mentioned in the ten articles included in this review, only six had experiments dedicated to the oil in its individual form. Of these, it is plausible to highlight the volatile oils that can be obtained on the market by the popular names rosemary, hinoki cypress, peppermint, lavender and apple tuia.

4.4.1 Rosmarinus officinalis (rosemary)

Rosemary is an aromatic herb widely used worldwide. Native to the Mediterranean region, Rosmarinus officinalis has been popularly used to treat headaches, poor circulation, as a mild analgesic and anti-inflammatory (Labib et al., 2019).

Pahini et al. (2015) (tables 3 and 4) found that rosemary EO has similar effects to minoxidil in patients with AGA. And the extract of the leaves had also already been tested, with positive effects for hair growth (Murata et al. 2013). Borges et al. (2019) draws attention to the fact that sometimes high doses are required for the EO to exert pharmacological effects and this fact can be circumvented with the use of nanoemulsions to increase bioavailability.

Despite the benefits, rosemary oil should not be used during pregnancy due to its abortifacient potential. It should be used with caution in individuals with primary hypertension and diabetes, and use by epileptics is not recommended due to considerable camphor content (from 6.4% to 30%) (Abelan et al., 2021).

4.4.2 Chamaecyparis obtusa (hinoki cypress)

A conifer evergreen tree native to Japan, *Chamaecyparis obtusa* can grow up to 30–40 m tall and 50–150 cm wide (Kim & Lee, 2020). It is used for civil construction and furniture due to its advantage in structural properties and natural odor. In addition, it has been used commercially in soaps, toothpaste and cosmetics as a functional additive. Its OE popularly known as Hinoki gold oil and contains several types of terpenes that have been shown to exert antioxidant and anti-inflammatory effects, including sabinene, limonene, bornyl acetate, borneol, α-terpineol and elemol, while fruit essential oils contain myrcene, γ-terpinene, p-cymene, borneol, α-terpineol and β-caryophyllene (An et al., 2013).

Lee et al. (2010) and Park et al. (2013) analyzed the hair growth-related effects of *C. obtusa* EO (tables 1 and 2). The authors observed that the EO promoted hair growth through the increase of enzymes, cytokines and growth factors closely related to the development of hair follicles and that cause an increase in the circulation that provides the nutrients necessary for hair growth.

4.4.3 Mentha piperita (peppermint)

The experiments of Oh et al., (2014) were performed with EO of M. *piperita* (Tables 1 and 2) acquired commercially, resulting in the effective stimulation of hair growth. The analyses found that, at a concentration of 3%, peppermint EO facilitates hair growth, promoting the conservation of dermal papilla

vascularization, which may contribute to the induction of the initial anagen (growth) stage. The authors suggest that OE can be used as a preventive medicine for hair loss in humans.

Peppermint oil has a fresh, strong menthol odor and a pungent flavor followed by a cooling sensation. It is an OE widely used in Aromatherapy, bath preparations, dental products and topical preparations with anti-itching and relief for inflammation or skin irritation (Herro & Jacob, 2010). Menthol is the main constituent of peppermint oil, which is a cyclic alcohol widely used as a component of food and cosmetics (Oh et al., 2014).

4.4.4 Lavandula officinalis (lavender)

The OE of *Lavandula officinalis*, synonym *L. angustifolia* is traditionally used as an antiseptic, relaxing, carminative and sedative agent in aromatherapy. Its anti-inflammatory and analgesic properties can relieve pain and soothe irritated skin, and antimicrobial properties can help with some skin treatments (Abelan et al., 2021).

The marked effect of lavender EO on promoting hair growth in murine was observed by Lee et al. (2016) (tables 1 and 2). There was a significant increase in the number and depth of hair follicles, and skin thickness. In addition, they noticed cellular changes in the skin treated with LE, through the more pronounced presence of mast cells, cells closely linked to the murine capillary cycle.

Lee et al. (2016) do not communicate which species of lavender was the oil used in the research. They characterize the components of commercially acquired EO. However, this information is important, since different cultivars exhibit diverse patterns of antibacterial activity and a variety of antioxidant properties (Insawang et al. 2019).

Interestingly, the most significant studies of OE in humans have focused attention on the healthy potential of lavender EO, whose chemical composition has been pointed out to be responsible for many of the observed biological effects (Sharifi-Rad et al., 2017). The main components of lavender EO reported were linalyl acetate (43.1%) and linalool (32.7%). It also contains numerous monoterpenes (cineole, borneol, geraniol) and also organic acids, coumarins, mineral salts and tannins, responsible for the pharmacological activity of lavender (Abelan et al., 2021).

4.4.5 Platycladus orientalis (apple tuia)

Platycladus orientalis is a commonly planted ornamental conifer, whose leaves are important for Traditional Chinese Medicine and, like *C. obtusa*, belongs to the *Cupressaceae* family (Fei et al., 2019). The leaves have a wide spectrum of pharmacological activities, such as anti-inflammatory, antioxidant, antimicrobial, disinfectant, diuretic, hair growth promoter, neuroprotective and antifibrotic activities (Shan et al., 2014).

This cypress is traditionally used to potentiate hair growth, being added to shampoos or water and widely adopted by people suffering from hair loss (Zhang et al., 2016). The plant extract has inhibitory capacities of 5α-reductase thus having interesting effects on AAG (Park et al. 2003).

When comparing the EO activity of P. orientalis leaves with their ethyl acetate fractions, butanol fraction, and minoxidil fractions, Zhang et al. (2019) (tables 1 and 2) noticed that the group treated with EO showed faster-onset hair growth with a more noticeable effect on hair follicle length.

Zhang et al. (2016) (table 1 and 2) isolated the major component of OE from *P. orientalis* and found that the compound promotes hair growth in mice, of high efficacy in females. This element is cedrol, sesquiterpineol with several properties, among them the ability to increase blood flow around the hair follicles and improve the transport of nutrients and oxygen to the hair follicle cells (Deng et al. 2021).

4.5 CLINICAL MANAGEMENT OF AGA

Because several factors play a role in the pathophysiology of AGA, the management of this clinical condition can be very complex (Jaller et al., 2019). Individuals affected and concerned about their clinical condition often seek treatment advice from primary care physicians, dermatologists, or plastic surgeons. Professionals should be well-informed to recommend to their patients safe and effective therapies aimed at avoiding "miraculous" cures (Sasaki, 2018). Because of this, it is of paramount importance that the patient is followed up with trichologists and hair therapists specialized and able to develop the appropriate counseling and management of hair loss.

An important diagnostic tool with easy handling in various capillary conditions is trichoscopy. Useful for determining the course of the disease, it consists of dermoscopy of hair and scalp. This noninvasive method also allows to evaluate clinical prognoses and treatment efficiency (Kasprzak et al., 2019). The differentiation of AGA from other forms of alopecia is essential and can be achieved through a complete clinical and histopathological evaluation: tricoscopic evaluation. Treatment should be started as early as possible in an attempt to halt the progress of dysfunction and preserve the remaining hair follicles.

Although mechanisms related to androgens and genetic predisposition are likely to contribute to the etiology of AGA in cisgender women, the disorder remains complex and without having its mechanisms fully and completely unraveled (Marks & Senna, 2019). However, female AAG, or female pattern hair loss, can be improved by antimicrobial or anti-inflammatory therapies that are used as adjuvants for androgen-dependent treatments, whether synthetic or natural (Sadgrove, 2018). Finasteride is not indicated for women of childbearing age, since 5α-reductase inhibitors can cause malformation of the external genitalia of male fetuses (Trüeb, 2002). Patients often choose alternative therapies to this specific class of drugs.

Special cases of AGA such as in children and transgender patients require redoubled attention as there is no specific treatment approved. In childhood cases, there are case reports even in children aged 6 to 8 years and genetic predisposition is considered a major factor (Siah et al., 2016). Some therapeutic agents used in adults with AGA have also been used successfully in younger adults (Griggs et al., 2019).

In more delicate cases, more natural topical treatments look promising because of the lower likelihood of side and adverse effects. The hormones used for trans patients' reaffirmation are often the factors that trigger AGA (Marks & Senna, 2019). In these cases, the choice of alternative therapies, moreover, would exclude the possibility of drug interactions that classical therapies could provide. OE therapies would be beneficial in these cases.

Finally, it is necessary to be aware that OEs also present risks and must be chosen and manipulated by qualified professionals. In addition, care is needed regarding the safety of use. Oils can induce allergies in predisposed patients, just as some species can be caustic, or produce skin irritation if used pure on the skin (Posadzki et al., 2012).

5 CONCLUSION

OEs represent a promising treatment for patients with AGA and other alopecias. They can play an adjuvant function, potentiating the effect of hair growth, or even be an alternative therapy option to conventional drugs, in cases with indication for such dynamics. Like, for example, when significant adverse effects occur or allergy to prescribed allopathic substances. Still, proper dosage and scheduling are essential for effective treatment, as well as choosing the appropriate EO according to each patient's need.

The volatile oils investigated by the scientific articles used in this review showed positive results in relation to the hair growth of the experimental models developed, especially the OEs of rosemary (*Rosmarinus* officinalis), hinoki cypress (*Chamaecyparis obtusa*), peppermint (*Mentha piperita*), lavender (*Lavandula officinalis*) and apple tuia (*Platycladus orientalis)*) that can be found commercially. Even though OEs are surrounded by benefits, thorough and systematic research on the safety and efficacy of the use of OEs in hair growth is still scarce. For an adequate use of volatile oils in the management of AGA, it is essential to expand research and clinical trials, as well as standardization and establishment of treatment protocols that offer safety and efficacy to patients.

REFERENCES

Abelan, U. S., de Oliveira, A. C., Cacoci, É., Martins, T., Giacon, V. M., Velasco, M., & Lima, C. (2021). Potential use of essential oils in cosmetic and dermatological hair products: A review. *Journal of cosmetic dermatology*, 10.1111/jocd.14286. Advance online publication.

An, B. S., Kang, J. H., Yang, H., Jung, E. M., Kang, H. S., Choi, I. G., Park, M. J., & Jeung, E. B. (2013). Anti-inflammatory effects of essential oils from Chamaecyparis obtusa via the cyclooxygenase-2 pathway in rats. *Molecular medicine reports*, 8(1), 255-259.

Anvisa. (2019). Agência Nacional de Vigilância Sanitária. *Farmacopeia Brasileira*, 6 (1).

Barquero-Orias, D., Moreno-Arrones O. M. & Vañó-Galván S. (2021). Alopecia and the Microbiome: A Future Therapeutic Target? *Actas Dermosifiliogr*. 112(6), 495-502.

Borges, R. S., Ortiz, B., Pereira, A., Keita, H., & Carvalho, J. (2019). Rosmarinus officinalis essential oil: A review of its phytochemistry, anti-inflammatory activity, and mechanisms of action involved. *Journal of ethnopharmacology*, 229, 29-45.

Brotzu, G., Fadda, A. M., Manca, M. L., Manca, T., Marongiu, F., Campisi, M. & Consolaro, F. (2018). A liposome-based formulation containing equol, dihomo-γ-linolenic acid (DGLA), and propionyl-L-carnitine to prevent and treat hair loss: a prospective investigation. *Dermatologic Therapy*, e12778.

Bureau, J. P., Ginouves, P., Guilbaud, J. & Roux, M. E. (2003). Essential oils and low-intensity electromagnetic pulses in the treatment of androgen-dependent alopecia. *Advances in therapy*, 20(4), 220-229.

Cho, Y. H., Lee, S. Y., Jeong, D. W., Choi, E. J., Kim, Y. J., Lee, J. G., et al. (2014). Effect of Pumpkin Seed Oil on Hair Growth in Men with Androgenetic Alopecia: A Randomized, Double-Blind, Placebo-Controlled Trial. *Evidence-Based Complementary and Alternative Medicine*, 2014, 1-7.

Damodaran, R. G. & Gupta, R. (2011). Hair Loss and the Applied Techniques for Identification of Novel Hair Growth Promoters for Hair Re-Growth. *Pharmacognosy Journal*, 3(22), 1-5.

Deng, Y., Huang, F., Wang, J., Zhang, Y., Zhang, Y., Su, G., & Zhao, Y. (2021). Hair Growth Promoting Activity of Cedrol Nanoemulsion in C57BL/6 Mice and Its Bioavailability. *Molecules (Basel, Switzerland)*, 26(6), 1795.

Esposito, E. R., Bystrek, M. V., & Klein, J. S. (2014). An elective course in aromatherapy science. *American journal of pharmaceutical education*, 78(4), 79.

Farrar, A. J., & Farrar, F. C. (2020). Clinical Aromatherapy. *The Nursing clinics of North America*, 55(4), 489-504.

Fonseca-Santos, B., Corrêa, M. A. & Chorilli, M. (2015). Sustainability, natural and organic cosmetics: consumer, products, efficacy, toxicological and regulatory considerations. *Brazilian Journal Of Pharmaceutical Sciences*, 51(1), 17-26.

Freeman, M., Ayers, C., Peterson, C., & Kansagara, D. (2019). Aromatherapy and Essential Oils: A Map of the Evidence. *Department of Veterans Affairs* (US).

Gad, H. A., Roberts, A., Hamzi, S. H., Gad, H. A., Touiss, I., Altyar, A. E., Kensara, O. A. & Ashour, M. L. (2021). Jojoba Oil: An Updated Comprehensive Review on Chemistry, Pharmaceutical Uses, and Toxicity. *Polymers*, 13(11), 1711.

Griggs, J., Burroway, B. & Tosti, A. (2019). Pediatric Androgenetic Alopecia: a Review. *Journal of the American Academy of Dermatology*, S0190-9622(19)32565-4. Advance online publication.

Herman, A. & Herman, A. P. (2016). Mechanism of action of herbs and their active constituents used in hair loss treatment. *Fitoterapia*, 114, 18-25.

Herro, E., & Jacob, S. E. (2010). Mentha piperita (peppermint*). Dermatitis : contact, atopic, occupational, drug*, 21(6), 327-329.

Hosking, A.-M., Juhasz, M. & Atanaskova Mesinkovska, N. (2018). Complementary and Alternative Treatments for Alopecia: A Comprehensive Review. *Skin Appendage Disorders*, 1-18.

Hughes, K., Ho, R., Butaud, J.-F., Filaire, E., Ranouille, E., Berthon, J.-Y. & Raharivelomanana, P. (2019). A selection of eleven plants used as traditional Polynesian cosmetics and their development potential as anti-ageing ingredients, hair growth promoters and whitening products. *Journal of Ethnopharmacology*, 245 (112159).

Insawang, S., Pripdeevech, P., Tanapichatsakul, C., Khruengsai, S., Monggoot, S., Nakham, T., Artrod, A., D'Souza, P. E., & Panuwet, P. (2019). Essential Oil Compositions and Antibacterial and Antioxidant Activities of Five Lavandula stoechas Cultivars Grown in Thailand. *Chemistry & biodiversity*, 16(10), e1900371.

Jaller, J. A., MacQuhae, F. & Nichols, A. J. (2019). Clinical Trials and Hair Loss. *Alopecia*, p. 267-284.

Kasprzak, M., Sicińska, J. & Tostic, A. (2019). Follicular Map: A Novel Approach to Quantitative Trichoscopy. *Skin Appendage Disord*, 5(4), 216-220.

Katzer, T., Leite Junior, A., Beck, R. & da Silva, C. (2019). Physiopathology and current treatments of androgenetic alopecia: Going beyond androgens and anti-androgens. *Dermatologic therapy*, 32(5), e13059.

Kim, S. C., & Lee, J. W. (2020). The complete chloroplast genome of Chamaecyparis obtusa (Cupressaceae). *Mitochondrial DNA. Part B, Resources*, 5(3), 3278–3279.

Labib, R. M., Ayoub, I. M., Michel, H. E., Mehanny, M., Kamil, V., Hany, M., Magdy, M., Moataz, A., Maged, B., & Mohamed, A. (2019). Appraisal on the wound healing potential of Melaleuca alternifolia and Rosmarinus officinalis L. essential oil-loaded chitosan topical preparations. *PloS one*, 14(9), e0219561.

Lee, G.-S., Hong, E.-J., Gwak, K.-S., Park, M.-J., Choi, K.-C., Choi, I.-G., Jang, J.-W. & Jeung, E.-B. (2010). The essential oils of Chamaecyparis obtusa promote hair growth through the induction of vascular endothelial growth factor gene. *Fitoterapia*, 81(1), 17-24.

Lee, B. H., Lee, J. S., & Kim, Y. C. (2016). Hair Growth-Promoting Effects of Lavender Oil in C57BL/6 Mice. *Toxicological research*, 32(2), 103–108.

Marks, D. H. & Senna, M. M. (2019). Androgenetic Alopecia in Gender Minority Patients. *Dermatologic Clinics*, 38(2), 239-247.

Messenger, A. G., & Rundegren, J. (2004). Minoxidil: mechanisms of action on hair growth. *The British journal of dermatology*, 150(2), 186-194.

Mingsan, M. Mengfan, P., Dandan, L. & Zhengwang, Z. (2020). Effects of AiQingHua oil on microcirculation disturbance and alopecia mice model. *Journal of King Saud University - Science*, 32(6), 2669-2674.

Murata, K., Noguchi, K., Kondo, M., Onishi, M., Watanabe, N., Okamura, K., & Matsuda, H. (2013). Promotion of hair growth by Rosmarinus officinalis leaf extract. *Phytotherapy research: PTR*, 27(2), 212-217.

Oh, J. Y., Park, M. A. & Kim, Y. C. (2014). Peppermint Oil Promotes Hair Growth without Toxic Signs. *Toxicological Research*, 30(4), 297-304.

Orafidiya, L., Agbani, E., Adelusola, K., Iwalewa, E., Adebanji, O., Adediran, E., & Agbani, N. (2004). A study on the effect of the leaf essential oil of Linn. on cyclophosphamide-induced hair loss. *International Journal of Aromatherapy*, 14(3), 119-128.

Panahi, Y., Taghizadeh, M., Marzony, E. T., & Sahebkar, A. (2015). Rosemary oil vs minoxidil 2% for the treatment of androgenetic alopecia: a randomized comparative trial. *Skinmed*, 13(1), 15-21.

Park, Y. O., Kim, S. E., & Kim, Y. C. (2013). Action Mechanism of Chamaecyparis obtusa Oil on Hair Growth. *Toxicological research*, 29(4), 241-247.

Park, W. S., Lee, C. H., Lee, B. G., & Chang, I. S. (2003). The extract of Thujae occidentalis semen inhibited 5alpha-reductase and androchronogenetic alopecia of B6CBAF1/j hybrid mouse. *Journal of dermatological science*, 31(2), 91-98.

Posadzki, P., Alotaibi, A., & Ernst, E. (2012). Adverse effects of aromatherapy: a systematic review of case reports and case series. *The International journal of risk & safety in medicine*, 24(3), 147–161.

Premanand, A., Ancy, V. B., Jeevanandam, J., Rajkumari, B. R. & Danquah, M. K. (2020). Phytochemicals as emerging therapeutic agents for alopecia treatment. *Phytochemicals as Lead Compounds for New Drug Discovery*, 221-238.

Qi, J., & Garza, L. A. (2014). An overview of alopecias. *Cold Spring Harbor perspectives in medicine*, 4(3), a013615.

Rossi, A., Anzalone, A., Fortuna, M. C., Caro, G., Garelli, V., Pranteda, G., & Carlesimo, M. (2016). Multi-therapies in androgenetic alopecia: review and clinical experiences. *Dermatologic therapy*, 29(6), 424-432.

Sadgrove, N. (2018). The new paradigm for androgenetic alopecia and plant-based folk remedies: 5α-reductase inhibition, reversal of secondary microinflammation and improving insulin resistance. *Journal of Ethnopharmacology*, 227(5), 206-236.

Saporito, F., Sandri, G., Bonferoni, M. C., Rossi, S., Boselli, C., Icaro Cornaglia, A., Mannucci, B., Grisoli, P., Vigani, B., & Ferrari, F. (2017). Essential oil-loaded lipid nanoparticles for wound healing. *International journal of nanomedicine*, 13, 175-186.

Sasaki, G. H. (2018). Hair Biology and Androgenetic Alopecia. *Advances in Cosmetic Surgery*, 1(1),185-192.

Shan, M. Q., Shang, J., & Ding, A. W. (2014). Platycladus orientalis leaves: a systemic review on botany, phytochemistry and pharmacology. *The American journal of Chinese medicine*, 42(3), 523-542.

Sharmeen, J. B., Mahomoodally, F. M., Zengin, G. & Maggi, F. (2021). Essential Oils as Natural Sources of Fragrance Compounds for Cosmetics and Cosmeceuticals. *Molecules*, 26(3), 666.

Sharifi-Rad, J., Sureda, A., Tenore, G., Daglia, M., Sharifi-Rad, M., Valussi, M., Tundis, R., et al. (2017). Biological Activities of Essential Oils: From Plant Chemoecology to Traditional Healing Systems. *Molecules*, 22(1), 70.

Siah, T. W., Muir-Green, L. & Shapiro, J. (2016). Female Pattern Hair Loss: A Retrospective Study in a Tertiary Referral Center. *International journal of trichology*, 8(2), 57-61.

Souza, M. T. de, Silva, M. D. & Carvalho, R. de. (2010). Integrative review: what is it? How to do it? *Einstein (São Paulo)*, 8(1), 102-106.

Trüeb R. M. (2002). Molecular mechanisms of androgenetic alopecia. *Experimental gerontology*, 37(8-9), 981-990.

Varothai, S., & Bergfeld, W. F. (2014). Androgenetic Alopecia: An Evidence-Based Treatment Update. *American Journal of Clinical Dermatology*, 15(3), 217-230.

Wolffenbüttel, A. N. (2019). *Base da química dos óleos essenciais e aromaterapia*. Laszlo.

Yoon, J. I., Al-Reza, S. M., & Kang, S. C. (2010). Hair growth promoting effect of Zizyphus jujuba essential oil. *Food and Chemical Toxicology*, 48(5), 1350-1354.

Zhang, Y., Han, L., Chen, S.-S., Guan, J., Qu, F.-Z., & Zhao, Y.-Q. (2016). Hair growth promoting activity of cedrol isolated from the leaves of *Platycladus orientalis*. *Biomedicine & Pharmacotherapy*, 83(1), 641-647.

Zhang, Y., Chen, S.S., Qu, F.Z., Su, G.Y. & Zhao, Y.Q. (2019). In vivo and in vitro evaluation of hair growth potential of Cacumen Platycladi, and GC-MS analysis of the active constituents of volatile oil. *Journal of Ethnopharmacol*. 238(1), 0378-8741.

Zhou, Y., Chen, C., Qu, Q., Zhang, C., Wang, J., Fan, Z., Miao, Y., & Hu, Z. (2020). The effectiveness of combination therapies for androgenetic alopecia: A systematic review and meta-analysis. *Dermatologic therapy*, 33(4), e13741