



Medicinal plants used in Mexico for the treatment of alopecia

Juan Carlos Vázquez Martínez¹, Marcial García Pineda², David Segura Cobos³, Elizabeth Alejandrina Guzmán Hernández^{4*}

^{1,2} Jardín Botánico, Carrera de Biología, Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México, Tlalnepantla, Estado de México, México

^{3,4} Carrera de Médico Cirujano, Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México, Tlalnepantla, Estado de México, México

Abstract

Dihydrotestosterone (DHT), an androgenic hormone, is a sex steroid produced in the gonads. The target sites of DHT and testosterone are similar. Excess of DHT causes miniaturization of hair reducing the anagen phase and increasing the telogen phase leading to hair loss. Normally up to ten percent of testosterone in the body irreversibly gets converted into DHT by the action of enzyme 5-alpha-reductase. Inadequate blood flow to the scalp can also be another reason for hair loss encountered due to lower oxygen and nutrients reaching it. Androgenetic alopecia (AGA) occurs due to hormonal imbalance affects both sexes; in males, it leads to major hair loss. Conventional drugs such as minoxidil and finasteride are widely used for the treatment; however, several drawbacks such as allergic contact dermatitis, burning, ejaculation disorder, and decreased libido are reported. This review presents a general description of studies plants used in Mexico for the treatment of alopecia.

Keywords: Hair loss, androgenetic alopecia, herbal treatments

Introduction

Hair is a filamentous biomaterial that grows from follicles found in the dermis. Found exclusively in mammals, hair is one of the defining characteristics of the mammalian class. The word "hair" often refers to two distinct structures: 1) the part beneath the skin, called the hair follicle or when pulled from the skin, called the bulb. This organ is located in the dermis and maintains stem cells, which facilitate regrowth of hair after fall or wound and 2) the shaft, which is the hard filamentous part that extends above the skin surface [1].

Hair growth is the cumulative, physical consequence of coordinated process of cellular proliferation and differentiation within a hair follicle. The stem cells, which commit to the fate of a hair follicle, enter a period of massive proliferation that results in the formation of mature hair follicle. Hair follicles are primarily composed of epithelial and dermal components. Hair follicles are hair shaft-producing mini-organs and exhibit regular cycles of regeneration, known as the hair cycle [2]. The hair follicle, undergoes successive cyclic periods of growth, involving an active growing phase (anagen) during which the previous hair is shed, a small transitional regressive phase (catagen) and a dormant resting phase (telogen) [3], which allows the follicle to produce different types of hair in response to hormonal changes. Each strand of hair on the human body is at its own stage of development.

Once the cycle is complete, it restarts and a new strand of hair begins to form. The growth or anagen phase of human scalp hair lasts 2-7 years during which the hair follicle actively produces precursor cells that differentiate into

different types of hair cells. Catagen which lasts for several weeks, is the stage during which production of precursor cells ceases and the hair bulb rapidly involutes the final phase is called telogen phase which is the resting phase of the hair cycle which lasts for an average of 3 month [4].

Ten to fifteen percent of the hair follicles on one's head are in this phase of growth at any given time.

Three months later, these hairs begin to fall. The anagen phase begins again once the telogen phase is complete. The preceding hair strand is pushed up and out by the new, growing strand. Most common interest in hair is focused on hair growth, hair types and hair care, but hair is also an important biomaterial primarily composed of protein, notably keratin [5].

Hair loss is a disorder in which the hair falls out from skin areas where they are usually present, such as the scalp and the body. This loss interferes with the many useful biologic functions of the hair, including sun protection (mainly to the scalp) and dispersal of sweat gland products. As hair cover to the scalp has psychological importance in our society [6].

It can be divided into 2 groups: scarring and non-scarring alopecia:

Scarring alopecia: This type of alopecia is the most drastic in terms of the damage that the follicle receives for which it is usually irreversible, as this damage creates a total malformation or rupture of the follicular structure. It occurs when there was a blow or deep cut over the area of the follicles causing a scarring on them which creates fibrosis in the tissue that causes the complete death of the follicle, there is no treatment that helps repair dead follicles, without

However, a hair implant from an undamaged donor area can be used [7].

Non-scarring alopecia: it is the result of a dysfunction of the hair follicle, the follicle remains alive, so recovery is possible, so in this classification there are several types, among which are: alopecia areata or the different "Efluvios", which are temporary hair loss [8], and Androgenetic Alopecia.

In androgenetic alopecia (AGA) shortening of the anagen phase and continuous miniaturization of sensitive hair follicles takes place that result into conversion of thin terminal hairs into fine vellus hairs. The 5 α -reductase type-2 enzyme plays a central role by intra-follicular conversion of testosterone to dihydrotestosterone [9]. Some degree of follicular miniaturization and consequential hair loss is universal and is considered a physiological secondary sexual characteristic.

Currently, treatments cleared by the US Food and Drug Administration (FDA) for AGA includes medications (topical minoxidil and oral finasteride) and a medical device (low level laser therapy).

Topical minoxidil, at 5%, has been shown to increase the hair count by 12% on average at 12 months [10]. Irritation from propylene glycol, its vehicle, is common and a different preparation in a propylene glycol-free foam vehicle can be substitute to reduce the potential of irritation. Oral finasteride, a 5 α -reductase inhibitor, is another FDA-approved medication for the treatment of male pattern baldness. At 1 mg/day, the increase in hair count at 12 months was 22% on average [11]. Direct comparison between oral finasteride and topical minoxidil at 12 months show the superiority of the former, with an increase in hair count of 29% versus 15% of the latter. According to a very large prospective study, the effect of finasteride on sexual functioning is minimal [12], for most men and should not impact on the decision to prescribe or take finasteride, 9 although in a small subset of patients altered sexual functions such as erectile dysfunction and diminished libido have been reported [13]. A low-level laser therapy comb is another FDA-approved treatment for AGA. It emits beams at a wavelength of 655 nm. In a multicentre 6-month trial, this device has been shown to increase hair count by 16% on average [14] many other products to treat male pattern baldness are available, but the level of evidence is not as strong as it is for the aforementioned therapy [15]. The treatment of AGA is costly, requires a lifelong commitment and may have side-effects. Thus, topical, over-the counter, non-pharmacological cosmetic haircare products that are effective for male pattern baldness could be more acceptable and provide alternatives for men suffering from hair loss.

Due to the side effects produced by these drugs, other treatment alternatives that improve AGA have been sought, in their different stages, such as the use of cosmeceuticals [16].

There are various plants, extracts used in different part of world for care of the hair and have hair growth promoting activity, and numbers of herbal products acclaimed with hair growth promoting activity. All over the world, many polyherbal mixtures are employed as hair tonic, hair growth promoter, hair conditioner, hair cleansing agent, anti-dandruff agents, as well as for the treatment of alopecia and lice infection [17].

2. Methods

Ethnobotanical documentation of plants Mexican used for hair loss, strengthening the scalp and stimulating hair growth was made, of which finasteride and minoxidil treatments were omitted.

Study exploration was conducted using online databases — PubMed and Science Direct using keywords Androgenetic, Alopecia, Hair Loss, *Aloe vera*, *Allium cepa*, *Allium sativum*, *Arnica montana*, *Baccharis glutinosa*, *Coconut nucifera*, *Cucurbita pepo*, *Cuscuta reflexa*, *Grape sed*, *Junglans regia*, *Persea Americana*, *Rosmarinus officinalis*, *Sida rhombifolia*, *Urtic dioica* and *Verbena carolina*.

3. Results

Table 1: Shows the list of plants that have been mentioned as being used in the treatment of alopecia:

Scientific name	Family	Botanical name
<i>Aloe vera</i>	Asphodelaceae	Sabila
<i>Allium cepa</i>	Amaryllidaceae	Onion
<i>Allium sativum</i>	Amaryllidaceae	Garlic
<i>Arnica montana</i>	Compositae	Arnica
<i>Baccharis glutinosa</i>	Asteraceae	Batamote
<i>Coconut nucifera</i>	Arecaceae	Coconut
<i>Cucurbita pepo</i>	Cucurbitaceae	Pumpkin
<i>Cuscuta reflexa</i>	Convolvulaceae	Zacapale
<i>Grape sed</i>	Vitaceae	Grape
<i>Juglans regia</i>	Juglandaceae	Walnut
<i>Persea americana</i>	Lauraceae	Avocado
<i>Rosmarinus officinalis</i>	Lamiaceae	Rosemary
<i>Sida rhombifolia</i>	Malvaceae	Brush
<i>Urtic dioica</i>	Urticaceae	Nettle
<i>Verbena carolina</i>	Verbenaceae	Verbena

Sida rhombifolia. Grows in tropical and warm regions and is distributed throughout the tropics and is known for its wide range of medicinal uses [18]. The dialect name of *S. rhombifolia* is "Gorjejit" in Amharic and "Aratha" in Jimma [19] and different names are given in different localities of English speakers, such as Queensland *hemp*, *sida hemp*, *Cuba jute*, *arrow leaf sida*, and *broom jute sida*, and in French speakers, Chanvre du Queensland and herbedure [20]. Has considerable reputation for its medicinal value in traditional medicine. The plant is much used for poulticing ulcers, boils, swellings, broken bones, cuts, herpes, and styles and for a skin application in chicken pox. The roots and stems are useful in fever, heart disease, piles, and all kinds of inflammation. Stem is also employed as demulcent and emollient [21]. *S. rhombifolia* possesses pharmacological properties such as antimalarial properties, antibacterial, antiviral activities, and hepatoprotective, anti-inflammatory, and analgesic properties, and phytochemical analysis of the aerial parts of it showed the presence of coumarins: scopoletin (1) and escoporone (2); a ferulic acid derivative, ethoxyferulate (3); two flavonoids: kaempferol (4) and kaempferol-3-O- β -D-glycosyl-6"- α -D-rhamnose (5); and three indoquinoline alkaloids: quindolinone (6), 11-methoxy-quindoline (7) and quindoline (8). The quindolinone (6) and the salt of cryptolepine (9) induced vasorelaxation.

Baccharis glutinosa. In traditional medicine antifungal activity has been observed on phytopathogenic fungi [22-25]. The compounds responsible for this property have not been reported yet, although flavonoids and other phenolic compounds, diterpenoids and volatile constituents are reported as the major phytoconstituents of other *Baccharis* species, [28] and some of them have been identified as antifungal agents [26-27]. A flavone, an acetylenic lactone, a prenylated coumarin, and a 3-methyl ether flavone were identified as the antifungal compounds present in from *B. pedunculata* leaves [28]. Also, the prenylated coumarin, oxoaurapten isolated from *B. darwinii* was highly active against dermatophytes [29]. Similarly, other compounds such as sakurasosaponin and jacquinoic acid, extracted from *Jacquinia* species (*J. flammea* and *J. pungens*, respectively), showed antifungal or repellent activity [30].

Rosmarinus officinalis. The essential oil improves microcirculation surrounding the hair follicle [31]. Bioactive compounds of *R. officinalis* are phenolic acids, mainly caffeic and rosmarinic acid, and monoterpenoids like 1,8-cineole [17]. A clinical study from 2015 compared the efficacy of rosemary essential oil to minoxidil 2 % solution for the treatment of androgenetic alopecia. Patients used either minoxidil 2 % solution (n = 50) or rosemary essential oil (n = 50). Significant increase in hair count was reported for both treatments without significant difference between the study groups. Scalp irritation was more frequent in minoxidil 2 % solution group [31].

Fresh leaves and flowering buds contain rosmarinic acid, caffeic acid, chlorogenic acid, carnosic acid, rosmanol, carnosol, and different diterpenes and many other natural antioxidants, ursolic acid, glycolic acid, and rosmarinic. The rosemary oil contains esters (2%-6%) largely as borneol, cineoles, and several terpenes, chiefly α -pinene, camphene, 1%-2% volatile oil containing 0.8%-6% of esters and 8%-20% of alcohols [32]. Caffeic acid, 1, 8-cineole, and rosmarinic acid are potential therapeutic agents obtained in rosemary oil by steam distillation [32]. It was observed that when compared to Minoxidil, Rosemary results did not show a significant difference from the results obtained of Minoxidil. Rosemary acts by improving blood circulation and improving vascularity helping the regeneration of follicles similar effect that is provided by Minoxidil [33].

Verbena carolina. This plant is popularly known as 'verbena', 'ajenjo grande', 'hierba de San José', 'nardo de campo', 'Santa María', 'poleo negro' and 'wahichuri' (Tarahumara language). Most of the plant, except for the roots, is used as a decoction in folk medicine with applications against diarrhea, vomit and dysentery, or as a purgative. Furthermore, the decoction of the aerial parts of *V. carolina* is used to dissolve bladder stones, as a diuretic and to treat wounds, dandruff, allergies and dermatitis [34]. This plant is one of the constituents of a skin care preparation which shows melanogenesis suppression [35]. *V. carolina* shows antifungal and antioxidant activity, the major phyto-constituents are verbenaline, hastatoside, verbascoside and hispidulin 7O β GH.

Persea americana Mill. Is a popular tropical fruit that is cultivated in tropical and Mediterranean climates. The fruits are high in fatty acids, fiber, potassium, vitamin B3, and bioactive compounds such as vitamin E, carotenoids, and

sterols [36-37]. Avocado has broad functional benefits, including anti-cancer, anti-inflammatory, anti-oxidant, and anti-microbial activity [38]. Specifically, avocado oil is rich in monounsaturated fatty acids, which are good for human health, and is considered a functional food [39-40]. Many beneficial effects of avocado oil have been reported; however, little is known about the potential efficacy of avocado oil on SNHL. Sensorineural hearing loss

Therefore, we aimed to investigate the efficacy of avocado oil on SNHL in vitro and in vivo and elucidate its mode of action. For the present study, we used enhanced functional avocado oil extract (DKB122). DKB122 led to recovery of otic hair cells in zebrafish after neomycin-induced otic cell damage. Also, DKB122 improved auditory sensory transmission function in a mouse model of noise induced-hearing loss and protected sensory hair cells in the cochlea. In addition, RNA sequencing was performed to elucidate the mechanism involved. KEGG pathway enrichment analysis of differentially expressed genes showed that DKB122 protected House Ear Institute-Organ of Corti 1 (HEI-OC1) cells against neomycin-related alterations in gene expression due to oxidative stress, cytokine production and protein synthesis [41].

Cucurbita pepo. The fruits and seeds of some of its cultivars are often used for food. The oil is a typical product of pumpkin seeds, which is rich in nutrients such as fatty acids, beta-carotene, lutein, gamma and beta-tocopherols, squalene, and phytosterols [42]. Some reports of the activity of pumpkin oil in the treatment of symptomatic benign prostatic hyperplasia [43] have been published. Their activity is likely associated with phytosterols that inhibit 5 α -reductase and have anti-androgenic action as has been displayed in rats. The exact mechanism is still unclear, though a large number of studies in animals indicate potential inhibition of 5 α -reductase [43-45]. In 2014, Cho et al. [46] published the first randomized, double-blind controlled study examining the effectiveness and tolerability of pumpkin oil in male patients with mild to moderate forms of androgenic alopecia. The experimental group was given a dietary supplement with 400 mg of pumpkin oil daily for 24 weeks, while the control group was given a placebo. Changes were evaluated by four outcomes: assessment of standardized clinical photographs, patient self-assessment scores, scalp hair thickness, and scalp hair counts. Mean hair count increases of 40% were observed in the experimental group, whereas increases of 10% were observed in placebo-treated men. The study showed that the oil had a positive anabolic effect on hair growth, likely through the mechanism of inhibiting 5 α -reductase. However, the levels of DHT or prostate specific antigen have not been measured to confirm the mechanism of action of pumpkin oil. Despite the fact that men with baldness on the front of the scalp were included in the study, the results of the oil's action were not published in these patients [46].

Urtica dioica. Is the most widely studied ones symptomatic benign prostate hyperplasia (BPH) is the best researched indication of this plant which is mainly due to its 5 α -R inhibition activity [47-49]. Inhibition of 5 α -R precludes the conversion of testosterone to dihydrotestosterone (DHT) high levels of which are associated with BPH [50]. The same pathogenesis is also valid for AGA. Although *U. dioica* leaves have traditionally been used for hair loss [50]. In a study

performed with a combination of herbal extracts including *U. dioica*, the combination was found to increase the proliferation of human dermal papilla cells significantly at concentrations ranging from 1.5% to 4.5% [51]. *U. dioica* contains β sitosterol which stimulates angiogenesis by increasing vascular endothelial growth factor (VEGF) synthesis and supports new hair growth [52].

Aloe vera. Contains polysaccharide, amino acid, steroid, anthraquinone, various vitamins and minerals [53]. *A. vera* usually used as hair promoter, burn wound healing, anti-inflammatory, diuretic, emolien, antipyretic, antibacterial, and laxative [54]. Malic acid and other ingredients of *A. vera* can promote cell proliferation in the hair follicle and improve the hair growth. Celery herb contains flavonoid (apigenin and apiin), phenol, saponin, coumarin, and steroid. Celery herb is traditionally used as diuretic, anti-rheumatic, antihypertension, anti-diabetic, and hair promoter [55]. According to Huh et al. [56], apigenin, a flavonoid from celery, has an important role in hair elongation. Studies conducted by (Pamudji et al., 2015) showed that the administration of clear water in oil microemulsion increased hair growth dramatically started at day 7 (220%) and day 14 (275%) and slowed-down at day 21 (163%) with similar profile shown by oil in water (74.5, 65.8, 31.7%, respectively). On the contrary, the hair growth promotion of oil in water microemulsion delayed to day 14 but maintained till day 21 (143.7, 214.5, 171.9 at day 7, 14, and 21, respectively).

Cuscuta reflexa Roxb. Known as “amarvela” or “akashbel” in vernacular, is a parasite, with slender long yellow stems. It is distributed in tropical and temperate regions and common throughout India. It grows on different host plants, mostly thorny herbs [57].

Traditionally, it is used as a purgative in the treatment of protracted fever, diaphoretic, and demulcent [58-59]. Methanolic extract is reported to show antisteroidogenic properties [60]. In our earlier studies, we have shown that the petroleum ether extract of this herb exhibited hair growth promotion on denuded skin surface of albino rats [61-62], Pandit et al., (2008), showed that the petroleum ether extract of *C. reflexa* inhibiting the enzyme 5α -reductase, so it can stimulate hair growth in androgenic alopecia.

Grape seed. Having presence of anthocyanins, flavan-3-ols (catechins), vitamin E (α -tocopherol), petiole, linoleic acid, flavonoids (resveratrol, quercetin and catechin, and polyphenols (flavonoids, phenolic acids, phenolic alcohols, stilbenes, and lignans), procyanidins (B4 and B6), and trimer gallate, unsaturated fatty acids, and phytosterols in which catechins, epicatechins, trans-resveratrol, and procyanidin B1 are the most active and potential ones [63-65]. It was found that proanthocyanidins found in grape seed oil and extract showed an activity in the proliferation of hair follicle cells isolated from mice by about 230% relative to controls (100%) also possessed remarkable hair-cycle-converting activity from the telogen phase to the anagen phase in C3H mice in vivo test systems [63-66].

Allium cepa. Sulphurous. Organosulfur compounds, polyphenols, anthocyanins, flavonoids, gallic and ferulic acids, quercetin and its glycosides, from onion juice act as irritants, antioxidant (ROS scavenging) [67], antiinflammatory (\downarrow COX-2 expression, \downarrow 25 phosphatase) [68], thereby causing

mild dermatitis which might provoke hair growth. A study where *A. cepa* juice was used as a treatment for alopecia has shown significantly more hair re-growth after six months of the treatment (86.9 %) [69].

Allium sativum. Its components include allin, cycloalliin, S-allyl-L-cysteine, S-methyl-L-cysteine, S-ethylcysteine, S-1-propionyl-L-cysteine, S-allylmercapto-L-cysteine, fructosyl-arginine, and beta-chlorogenin. It also consists of L-arginine, L-cysteine, and L-methionine [70]. Antioxidant effects S-allylcysteine (SAC) and S-allylmercaptocysteine (SAMC) are the major organosulfur compounds in aged garlic extract which prevent oxidant damage. AGE exerts antioxidant action by scavenging reactive oxygen species (ROS), enhancing the cellular antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase and increasing glutathione in the cells. AGE protects DNA against free radicals and defends against UV-induced damage. It also protects against some forms of UV-induced immunosuppression [71-72].

Cutaneous microcirculation: A randomized placebo-controlled double-blinded study show that 5 h after the administration of garlic powder a significant increase in capillary skin perfusion occurs by 55% in the healthy volunteers. The increased erythrocyte velocity results from vasodilation of precapillary arterioles which increases diameter of erythrocyte column by an average of 8.6% [69].

Juglans regia. Constituents: Fatty acids, linoleic acid (50.58 - 66.60%) are the predominant fatty acid followed by oleic acid (14.88 - 28.71%) and linolenic acid (9.16 -16.42%). The other fatty acids were found in trace contents. The macronutrient contents of walnut are 100 g-1 for K (911.0 - 684.3), P (434.7 - 356.2), Ca (756.7 - 388.2), Mg (444.0 - 330.8) and Na (48.9 - 26.1) while micronutrient contents of walnut are Fe (6.6 - 4.3), Cu (2.8 - 1.8), Mn (5.7 - 2.7) and Zn (4.3 - 2.7). The potassium contents were found to be higher than those of the other minerals in all kernels of the walnuts. The fruit contains essential minerals which are helpful in the growth of healthy hair. Iron increases blood circulation and oxygen supply as stated earlier. Zinc helps to secrete the scalp with much needed oil and avoid dandruff that may cause hair loss. In case of Copper, study shows that these tripeptide complexes may actually be able to regrow hair, even in patients with total hair loss due to alopecia. Healthy tissue concentrations of copper lies between 1.7 and 3.5 milligrams [73].

Arnica montana: One hundred and fifty therapeutically active substances are present in *A. montana* plant, i.e. sesquiterpene lactones, i.e. helenalin, 11a,13-dihydrohelenalin and their short-chain carbonic acid esters (0.3–1% of dry weight in the flower heads, 0.1–0.5% in leaves), flavonoids (0.6–1.7%) by micellar electrokinetic capillary chromatography in the form of flavonoid glycosides, flavonoid glucuronides and flavonoid aglycones; essential oils, composed thoroughly of fatty acids, thymol derivatives, monoterpenes and sesquiterpene. Other constituents of *A. montana* are carotenoids; diterpenes; arnidol (a triterpene); pyrrolizidine alkaloids (tussilagine and isotussilagine); polyacetylenes; coumarins (umbelliferone and scopoletin); phenolic acids (chlorogenic acid, caffeic acid and cynarin, 1.0–2.2%)[26]; lignans; dicaffeoyl quinic derivatives (1,3- 3,5 and 4,5 dicaffeoyl quinic acids); and oligosaccharides. It contains sesquiterpene lactones being metacryl, isobutyryl, tygloyl, methacryloyl, isovaleryl

helenalin derivatives, apigenin, luteolin, hispidulin, quercetin and kaempferol glycosides [74]. The plant extracts have been reported to possess antibacterial, antitumor, antioxidant, anti-inflammatory, antifungal and immunomodulatory activity [74]. Flowers extract is used in hair oil as tonic material. It stimulates the hair follicles [75].

Coconut oil. Gopala Krishna, et al., in 2010 [76] had described the chemistry of coconut oil it is made up medium-chain triglycerides (derived from coconut oil or palm kernel oil), Medium-chain triglyceride oils are made predominantly of caprylic fatty acids. Research on medium-chain triglyceride oils has been focused on these synthesized esters of C:8 and C:10 fatty acids. Both are classified as medium-chain fatty acids. The main fatty acid in coconut oil is lauric acid. Coconut oil has long life and it has antiviral and antibacterial activity. The coconut oil is used in baking industries, pharmaceuticals and as cosmetics as hair oil. They also reported that the coconut oil easily absorbed in the body and have function similar to breast milk fat of human and therefore it is also used in infant food. In a scientific study by Nema *et al.*, in 2009 [77] states that, they tested each drug for their hair growth activity in a concentration range for 1-10% separately in herbal hair oil containing amla, hibiscus, brahmi and methi. The formulation containing 7.5% of each drug used for the study and showed excellent hair growth activity with standard (2% minoxidil ethanolic solution) by an enlargement of follicular size and prolongation of the anagen phase. The conclusion of this study was that the herbal hair oil has stimulating activity for hair growth.

3. Conclusion

Androgenetic alopecia is a type of most prevalent alopecia and of major concern. It occurs majorly due to excess of testosterone getting converted into DHT via enzyme 5-alpha-reductase in the body and also can be due to inadequate blood flow in the scalp. Minoxidil and finasteride are FDA approved drugs where minoxidil increases the blood flow and vascularity in the scalp when topically applied and finasteride inhibits the enzyme 5-alpha-reductase preventing the conversion of testosterone to DHT when given orally. Side effects accompanied with these FDA approved drugs include scalp dryness, impotence, skin irritation, decreased libido, rashes, erectile dysfunction, testicular pain, burning, ejaculation disorders, redness, breast enlargement or tenderness, erythema, and headache.

To overcome these side effects, herbal therapy can be a potential treatment. *Aloe vera*, *Allium cepa*, *Allium sativum*, *Arnica montana*, *Baccharis glutinosa*, *Coconut nucifera*, *Cucurbita pepo*, *Cuscuta reflexa*, *Grape sed*, *Junglans regia*, *Persera americana*, *Rosmarinus officinalis*, *Sida rhombifolia*, *Urtic dioica* and *Verbena carolina*, using in combinations of two or more together can open new perspective in the cosmetic field which can be safe, effective, and useful.

5. References

- Pastel S, Sharma V, Chauhan NS, Thakur M, Dixit VK. Hair Growth: Focus on Herbal Therapeutic Agent. *Curr Drug Discov Technol.* 2015; 12(1):21-42.
- Buffoli B, Rinaldi F, Labanca M. The human hair: from anatomy to physiology. *Int J Dermatol.* 2014; 53:331-341.
- Phillips TG, Slomiany WP, Allison R. Hair Loss: Common Causes and Treatment. *Am Fam Physician.* 2017; 96(6):371-378.
- Suchonwanit P, McMichael AJ. Alopecia in Association with Malignancy: A Review. *Am J Clin Dermatol.* 2018; 19(6):853-865.
- Lolli F, Pallotti F, Rossi A, Fortuna M. Androgenetic alopecia: a review. *Endocrine.* 2017; 57(1):9-17.
- Dhariwala MY, Ravikumar P. An overview of herbal alternatives in androgenetic alopecia. *J Cosmet Dermatol.* 2019; 18(4):966-975.
- Lourith N, Kanlayavattanukul M. Hair loss and herbs for treatment. *J Cosmet Dermatol.* 2013; 12(3):210-22.
- Semwal D, Kotiyal R, Chauhan A. Alopecia and the herbal drugs: an overview of the current status. *Advances in Biomedicine and Pharmacy,* 2015; 2 (6): 246-254.
- Shen YL, Li XQ, Pan RR, Yue W, Zhang LJ, Zhang H. Medicinal Plants for the Treatment of Hair Loss and the Suggested Mechanisms. *Curr Pharm Des.* 2018; 24(26):3090-3100.
- Usmania BA, Kataria MK. Minoxidil emulgel for androgenic alopecia: a literature review including patents. *Int J Pharm Drug Anal.* 2017; 5:49-58.
- Haber RS, Gupta AK, Epstein E, Carviel JL, Foley KA. Finasteride for androgenetic alopecia is not associated with sexual dysfunction: a survey-based, single-centre, controlled study. *J Eur Acad Dermatol Venereol.* 2019; 33(7):1393-1397.
- Traish, A.M. Negative impact of testosterone deficiency and 5 α -reductase inhibitors therapy on metabolic and sexual function in men. *Adv. Exp. Med. Biol.* 2017, 1043, 473-526.
- Rossi A, Mari E, Scarnò M. Comparative effectiveness of finasteride vs *Serenoa repens* in male androgenetic alopecia: a two-year study. *Int J Immunopathol Pharmacol.* 2012; 25:1167-1173.
- Padois K, Cantieni C, Bertholle V, Bardel C, Pirot F, Falson F. Solid lipid nanoparticles suspension versus commercial solutions for dermal delivery of minoxidil. *Int J Pharm.* 2011; 416:300-304.
- Ateeq Ahmad SS. A new topical formulation of minoxidil and finasteride improves hair growth in men with androgenetic alopecia. *J Clin Exp Dermatol Res.* 2015; 06:6-11.
- Zgonc Škulj A, Poljšak N, Kočevar Glavač N, Kreft S. Herbal preparations for the treatment of hair loss. *Arch Dermatol Res.* 2019; 115-125.
- Dhariwala MY, Ravikumar P. An overview of herbal alternatives in androgenetic alopecia. *J Cosmet Dermatol.* 2019; 18(4):966-975.
- Woldeyes S, Legesse A, inebeb T. Evaluation of Antibacterial Activities of Compounds Isolated From *Sida rhombifolia* Linn. (Malvaceae) *Natural Products Chemistry & Research.* 2012; 1(1):1-8.
- Kothai S., Thirunalasundari T. Antimicrobial activity of chewing sticks of Jimma Ethiopia against *Streptococcus pyogenes*. *Journal of Phytology.* 2011; 3(8):34-37.
- Verdcourt B. The variation of *Sida rhombifolia* L. (Malvaceae) in East Africa. *Kew Bulletin.* 2004;

- 59(2):233–239.
21. Desalegn A, Andualem B. Synergistic antibacterial effect of *Sida rhombifolia* leaf extracts and *Apis mellifera* honey against standard and drug resistant clinical isolated pathogenic bacteria. *World Applied Sciences Journal*. 2014; 32(8):16001610.
 22. Tequida Meneses M, Cortez-Rocha MO, Rosas-Burgos EC, Lopez-Sandoval S, Corrales-Maldonado C. Effect of alcoholic extracts of wild plants on the inhibition of growth of *Aspergillus flavus*, *Aspergillus niger*, *Penicillium chrysogenum*, *Penicillium expansum*, *Fusarium moniliforme* and *Fusarium poae* moulds. *Rev. Iberoam. Micol*. 2002; (19): 84–88.
 23. Suarez Jiménez GM, Cortez Rocha MO, Rosas Burgos EC, Burgos Hernández A, Plascencia Jatomea M, Cinco Moroyoqui FJ. Antifungal activity of plant methanolic extracts against *Fusarium verticillioides* (Sacc.) Nirenb, and fumonisin B1 production. *Rev. Mex. Fitopatol*. 2007; 25(2):134–142.
 24. Rosas Burgos EC, Cortez Rocha MO, Cinco Moroyoqui FJ, Robles Zepeda RE, López Cervantes J, Sanchez-Machado DI, *et al.* Antifungal activity in vitro of *Baccharis glutinosa* and *Ambrosia confertiflora* extracts on *Aspergillus flavus*, *Aspergillus parasiticus* and *Fusarium verticillioides*. *World J. Microbiol. Biotechnol*. 2009; 25(12): 2257–2261.
 25. Valenzuela Cota DF, Buitimea Cantua GV, Rosas Burgos EC, Cinco Moroyoqui FJ, Yepiz Gomez MS, Cortez-Rocha MO, *et al.* The antifungal effect of *Jacquinia macrocarpa* plant on the growth of *Aspergillus flavus*, *Aspergillus parasiticus* and *Fusarium verticillioides*. *Revista Mexicana de Micología*. 2014; 39: 1–1.
 26. Feresin GE, Tapia A, Jiménez A, Ravelo AG, Zacchino S, Sortino M, *et al.* Constituents of the Argentinian medicinal plant *Baccharis grisebachii* and their antimicrobial activity. *J Ethnopharmacol*. 2003; 89(1): 73–80.
 27. Johann S, Pizzolatti MG, Donnici CL, de Resende MA. Antifungal properties of plants used in Brazilian traditional medicine against clinical relevant fungal pathogens. *Braz. J. Microbiol*. 2007; 38(4): 632–637.
 28. Abad MJ, Bermejo P. *Baccharis* (Compositae): a review update. *Arkivoc* 2007; vii: 76–96.
 29. Kurdelas RR, Lima B, Tapia A, Feresin GE, González-Sierra M, Rodríguez MV, *et al.* Antifungal activity of extracts and prenylated coumarins isolated from *Baccharis darwinii* Hook & Arn. (Asteraceae). *Molecules*. 2010; 15:4898–4907.
 30. García Sosa K, Sánchez Medina A, Álvarez SL, Zacchino S, Veitch NC, Sima-Polanco P, *et al.* Antifungal activity of sakurasaponin from the root extract of *Jacquinia flammea*. *Nat Prod Res*. 2011; 25(12): 1185–1189.
 31. Panahi Y M, Taghizadeh E, Marzony T and Sahebkar A. Rosemary oil vs minoxidil 2% for the treatment of androgenetic alopecia: a randomized comparative trial. *Skinmed*. 2015; 13:15–21.
 32. Al Sereiti MR, Abu Amer KM, Sen P. Pharmacology of rosemary (*Rosmarinus officinalis* Linn.) and its therapeutic potentials. *Indian J Exp Biol*. 1999; 37:124-130.
 33. Panahi Y, Taghizadeh M, Marzony E. Rosemary oil vs minoxidil 2% for the treatment of androgenetic alopecia: a randomized comparative trial. *Skinmed*. 2015; 13(1):15-21.
 34. Márquez AC, Lara F, Esquivel B, Mata R. Plantas Medicinales de México II. Composición, Usos Y Actividad Biológica. UNAM; México City, México: 1999. p. 165.
 35. Lara Issasi G, Salgado C, Pedraza Chaverri J, Medina Campos ON, Morales A, Águila MA, *et al.* Antimicrobial, Antioxidant Activities, and HPLC Determination of the Major Components of *Verbena carolina* (Verbenaceae). *Molecules*. 2019; 22; 24(10).
 36. Dreher M.L., Davenport A.J. Hass avocado composition and potential health effects. *Crit. Rev. Food Sci. Nutr*. 2013; 53:738–750.
 37. Krumreich FD, Borges CD, Mendonça CRB, Jansen-Alves C, Zambiasi RC. Bioactive compounds and quality parameters of avocado oil obtained by different processes. *Food Chem*. 2018; 257:376–381.
 38. Daiuto ÉR, Vieites RL, Tremocoldi MA, Vileigas DF. Physico chemical stability of avocado product (*Persea americana* Mill.) stored under low temperature. *Alimentos e Nutrição*. 2010; 21:99–107.
 39. Martinez Padilla LP, Franke L, Xu XQ, Juliano P. Improved extraction of avocado oil by application of sono-physical processes. *Ultrason. Sonochem*. 2018; 40:720–726.
 40. Ortiz Avila O, Esquivel Martinez M, Olmos Orizaba BE, Saavedra Molina A, Rodríguez Orozco AR, Cortés Rojo C. Avocado oil improves mitochondrial function and decreases oxidative stress in brain of diabetic rats. *J. Diabetes Res*. 2015; 2015:485759.
 41. Nam YH, Rodríguez I, Jeong SY, Pham TNM, Nuankaew W, Kim YH, *et al.* Avocado Oil Extract Modulates Auditory Hair Cell Function through the Regulation of Amino Acid Biosynthesis Genes. *Nutrients*. 2019; 8:11(1).
 42. Zambo I (1988). Analytical standardization of peponen. In: *Medifora*. pp 89, 96.
 43. Hong H, Kim C-S, Maeng S. Effects of pumpkin seed oil and saw palmetto oil in Korean men with symptomatic benign prostatic hyperplasia. *Nutr Res Pract*. 2009; 3:323–327.
 44. Gossell-Williams M, Davis A, O'Connor N. Inhibition of testosterone-induced hyperplasia of the prostate of Sprague Dawley rats by pumpkin seed oil. *J Med Food*. 2006; 9:284–286.
 45. Carbin B-E, Larsson B, Lindahl O. Treatment of Benign prostatic hyperplasia with phytosterols. *Br J Urol*. 1990; 66:639–64.
 46. Cho YH, Lee SY, Jeong DW. Effect of pumpkin seed oil on hair growth in men with androgenetic alopecia: a randomized, double-blind, placebo-controlled trial. *Evidence Based Complement Altern Med*. 2014; 2014:7.
 47. Nahata A, Dixit VK. Ameliorative effects of stinging nettle (*Urtica dioica*) on testosterone induced prostatic hyperplasia in rats. *Andrologia*. 2012; 44(S1):396–409.

48. Lichius JJ, Lenz C, Lindemann P, Müller HH, Aumüller G, Konrad L. Antiproliferative effect of a polysaccharide fraction of a 20% methanolic extract of stinging nettle roots upon epithelial cells of the human prostate (LNCaP) Pharmazie. 1999; 54(10):768–71.
49. Nahata A, Dixit VK. Evaluation of 5 α -reductase inhibitory activity of certain herbs useful as androgens. Andrologia. 2014; 46(6):592–601.
50. Monograph. Altern Med Rev. 2007;12(3):280–4. *Urtica dioica*; *Urtica urens* (nettle)
51. Rastegar H, Ashtiani HA, Aghaei M, Barikbin B, Ehsani A. Herbal extracts induce dermal papilla cell proliferation of human hair follicles. Ann Dermatol. 2015; 27(6):667–75.
52. Saeidnia S, Manayi A, Gohari AR, Abdollahi M. The story of beta-sitosterol-a review. European J Med Plants. 2014; 4(5):590–609.
53. Boudreau MD, Beland FA. An evaluation of the biological and toxicological properties of *Aloe barbadensis* (Miller) *Aloe vera*. J Environ Sci Health. 2006; 24(1):103-54.
54. Aburjai T, Natsheh FM. Plants used in cosmetics. Phytother Res. 2003; 17(9):987-1000
55. Syamsuhidayat SS. Inventaris Tanaman Obat Indonesia. Vol. I. Jakarta, Balitbang: Kesehatan, Depkes RI; 1991. p. 62, 476. 5. Huh S, Lee J, Jung E, Kim SC, Kang JI, Lee J, et al. A cell-based system for screening hair growth-promoting agents. Arch Dermatol Res. 2009; 301(5):381-5.
56. Huh S, Lee J, Jung E, Kim SC, Kang JI, Lee J, et al. A cell-based system for screening hair growth-promoting agents. Arch Dermatol Res. 2009; 301(5):381-5.
57. Dorr I. Sieve elements in haustoria of parasitic angiosperms. In: HD Behneck, RD Sjolund, eds. Sieve Elements Comparative Structure, Induction and Development. Berlin, Germany: Springer Verlag. 1990; 240– 56.
58. Chopra RN, Nayer SL, Chopra IC. Glossary of Indian Medicinal Plants. New Delhi, India: CSIR; 1992: 85.
59. Kirtikar KR, Basu BD. Indian Medicinal Plants, Vol. III. Delhi, India: Periodical Experts Book Agency.1984; 1740.
60. Gupta M, Mazumder UK, Pal DK, Bhattacharya S. Onset of puberty and ovarian steroidogenesis following administration of methanolic extract of *Cuscuta reflexa* Roxb. stem and *Corchorus olitorius* Linn. Seed in mice. J Ethnopharmacol. 2003; 89: 55– 9.
61. Roy RK, Thakur M, Dixit VK. Effect of *Cuscuta reflexa* Roxb on hair growth activity of albino rats. Indian Drugs. 2006; 43(12): 951– 6.
62. Roy RK, Thakur M, Dixit VK. Development and evaluation of polyherbal formulation for hair growth-promoting activity. J Cosmet Dermatol. 2007; 6: 108– 12.
63. Garavaglia J, Markoski M, Oliveira A and Marcadenti A. Grape seed oil compounds: biological and chemical actions for health. Nutr Metab Insights.2016; 9:59-64.
64. Patel S, Sharma V, Chauhan NS, Thakur M, Dixit VK. Hair growth: focus on herbal therapeutic agent. Curr Drug Discov Technol. 2015; 12:21-42.
65. Masoudi M, Saiedi M. Anti-cancer activity of grape seed. Pharm Lett. 2017; 9:143-154.
66. Takahashi T, Kamiya T, Yokoo Y. Proanthocyanidins from grape seeds promote proliferation of mouse hair follicle cells in vitro and convert hair cycle in vivo. Acta Derm Venereol. 1998; 78:428-432.
67. Cheng A, Chen X, Jin Q, Wang W, Shi J, & Liu Y. Comparison of phenolic content and antioxidant capacity of red and yellow onions. Czech Journal of Food Science. 2013; 31(5), 501–508.
68. Ying TH, Yang SF, Tsai SJ, Hsieh SC, Huang YC, Bau DT. et al. Fisetin induces apoptosis in human cervical cancer HeLa cells through ERK1/2-mediated activation of caspase-8-/caspase-3-dependent pathway. Archives of Toxicology. 2012; 86(2), 263–273.
69. Jung EM, Jung F, Mrowietz C, Kiesewetter H, Pindur G, Wenzel E. Influence of garlic powder on cutaneous microcirculation. A randomized placebo-controlled double-blind cross-over study in apparently healthy subjects. Arzneimittelforschung. 1991; 41:626–30.
70. Allison GL, Lowe GM, Rahman K. Aged garlic extract and its constituents inhibit platelet aggregation through multiple mechanisms. J Nutr. 2006; 136:782S–788S.
71. Borek C. Antioxidant health effects of aged garlic extract. J Nutr. 2001; 131:1010S–5S.
72. Imai J, Ide N, Nagae S, Moriguchi T, Matsuura H, Itakura Y. Antioxidant and radical scavenging effects of aged garlic extract and its constituents. Planta Med. 1994; 60:417–20.
73. Muradoglu F, Oguz HI, Yildiz k and Yilmaz H: Some chemical composition of walnut (*Juglans regia* L.) selections from Eastern Turkey. African Journal of Agricultural Research. 2010; 5(17): 2379-2385.
74. Kriplani P, Guarve K & Baghael. *Arnica montana* L. A plant of healing: review. Journal of Pharmacy and Pharmacology. 2017; 69(8), 925–945.
75. Kapoor VP. Herbal cosmetics for skin and hair care. Indian Journal of Natural Products and Resources (IJNPR) [Formerly Natural Product Radiance (NPR)]. 2005; 4(4): 306- 314.
76. Gopala Krishna, Gaurav Raj, Ajit Singh Bhatnagar, Prasanth Kumar and Preeti Chandrashekar. “Coconut Oil: Chemistry, Production and Its Applications- A Review. Indian coconut journal (India). 2010; 73 (3): 15-27.
77. Nema Rajesh Kumar, Pooja S, Banerjee, Megha Sharma. Preparation, evaluation and hair growth stimulating activity of herbal hair oil. J of Chemical and Pharmaceutical Research. 2009; 1(1): 261-267.