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A Review on Natural Remedies for Androgenic Alopecia in Women



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ABSTRACT

Alopecia is an imbalance between hair loss and regrowth. Androgenic alopecia is an extremely common pattern of female hair loss. Multiple factors contribute to hair loss such as hormones, nutrient mediators, genetic factors, and androgenic factors especially Dihydrotestosterone (DHT). DHT plays a very vital role in androgenic alopecia. Various diseases or hormonal disorders will cause hormonal changes in women. The most common causes of the high level of testosterone in women are hirsutism, polycystic ovary syndrome, and congenital adrenal hyperplasia. An excess amount of testosterone in the body is then converted into DHT by the action of the enzyme called type II 5-alpha reductase. Women with androgenic alopecia do not have higher level of circulating androgen as DHT binds to androgen receptors which gradually lead to the transformation of 'normal hair follicles' to 'miniaturize hair follicles'. Treatment with 5-alpha reductase inhibitors has increased response rate and degree of hair regrowth. The treatment of androgenic alopecia is limited but Caffeine, Pumpkin seed oil, and Saw Palmetto contains phytosterols and multiple phytoconstituents acting as DHT and blocks the enzyme 5-alpha reductase. Diagnosis in women is done by looking at their history, physical examination of hair, history of hair thinning, reduced hair density etc. Women with androgenic alopecia were found to have increased serum concentration of DHT. Since naturally obtain drugs have lesser side-effect, it can be treatment of choice. Additionally, it has low cost and it is easily available.

INTRODUCTION:

Alopecia is a clinical term for hair loss. The hair follicle from which hair develops is impacted by endogenous and exogenous factors ^[1]. Hair loss can be caused because of various reasons, for example hereditary inclination, natural trigger, introduction to synthetic substance, medicines, nutritional deficiency, tremendous stress or illness and so on^[2]. Alopecia can be partitioned into two non-scarring and scarring structures ^[1]. Non-scarring alopecia, dissimilar to scarring alopecia, prompts hair loss without obliterating hair follicles. The most widely recognized kinds of non-scarring hair loss are male and female androgenic alopecia ^[3]. In women, androgenic alopecia happening over the vast majority of the scalp, appear as diffuse hair loss. In men pattern of hair loss usually begins with a receding hairline which progressively thin the top of the head ^[4]. Androgenic alopecia (AGA) is a profoundly common and chronic problem that is described by propelling scaling down of the hair follicle ^[3, 4]. AGA's most noteworthy predominance is seen in Caucasians and age between 30 furthermore, 70 years ^[1, 3, 4]. The earliest sign of AGA can be seen after puberty ^[3]. AGA is commonly due to the abundance production of testosterone in the body, the most well-known reason for the significant level of testosterone in women's body are hirsutism, polycystic hyperplasia, and congenital adrenal hyperplasia; testosterone then converted into Dihydrotestosterone (DHT)^[1,3,5]. DHT play very important role in AGA by the activity of iso-enzyme called type II 5- alpha-reductase ^[1]. Women with AGA do not have significant level of flowing androgen as DHT binds to androgen receptors which continuously lead to change of 'typical hair follicle' to 'miniaturize hair follicle'^[1,3]. Early analysis and treatment are desirable to prevent continuous hair loss ^[2, 4, 6]. AGA needs long term treatment, and therefore natural source can give valuable treatment along with less side-effect, when compared with the conventional marketed drug ^[2]. Nutritional supplements, DHT blockers, and 5- alpha reductase inhibitors improved scalp blood flow are the nature's fortune and discovered various herbs with demonstrated records for treatment of alopecia ^[6]. Since natural drugs there are numerous favorable circumstances of utilizing them like patient compliance, easily availability, ease, and more than one method of activity for the treatment of alopecia ^[2, 6].

Pathophysiology:

Robert S. English Junior has described a hypothesis that explains the possible mechanism of how Androgenic alopecia progresses in women. It usually begins with a widening of the

hairline at the scalp as shown in figure 1. The first consensus that was believed is that a hormone called dihydrotestosterone (DHT) is primarily responsible for the hair loss which is formed by the reduction of testosterone by the action of the enzyme called as type II 5- α reductase enzyme with subsequent accumulation of the DHT in the hair base follicles and hair miniaturization and ultimately hair loss. Further investigation found out even physiological factors and structural features play role in female alopecia. Some inflammatory substances like prostaglandins and even reactive oxygen species play an important role in androgenic alopecia where these substances increase the inflammation and cause damage to the hair follicles thus halting hair growth. It was discovered that as the androgenic alopecia continues fibrosis of the tissue occurs as a result of the damage caused by inflammation and it becomes inactive. The sebaceous glands also have unusually high activity in such hair follicles affected by androgenic alopecia. Other factors were reduced vascularity leading to low oxygen levels along with skull shape and scalp tension above the galea aponeurotica which is a dense fibrous network below the affected hair follicles^[7]. G. Fabbrocini *et al* in her review has discussed that also genetic factors such as specific genes that allow normal levels of androgens that circulate to attack the hair follicles thus beginning the apoptosis process. Several environmental factors which are yet unknown also work for hand by hand with these genetic factors thus increasing the chances and likelihood of having androgenic alopecia^[3]. It has been found out that female pattern hair loss in women shows parallel increase with age with women who are older than in young women. Differences have also been found out between various ethnic races such as white women in United Kingdom showing more susceptibility than in East Asian women such as Korea and China. These racial differences may be attributed to molecular action which differs due to genes and several biochemistry factors that regulate hair growth backed up by the fact that hirsutism is less common in East Asian Population^[8]. Tatiele Katzer *et al* has elaborated on possible environmental factors that lead to androgenic alopecia such as UV radiation, chemical irritants, pollutants and certain microbes along with lifestyle habits such as smoking. Cigarette contains tobacco which has the potential of releasing free radicals. These free radicals increase the incidence of DHT entering in the hair follicles along with pro-inflammatory cytokines. A study showed that monozytic twins though sharing the same exact genes can still show differences in developing androgenic alopecia due to differences in their life style which includes longer sleep, Diabetes mellitus, Poly cystic ovarian syndrome etc⁹. Silke Redler *et al* in her review has described that when the WNT signaling pathway is activated by a compound called as

methyl vanillate then it leads to increased hair growth thus pointing to an important role of this signaling pathway in development of androgenic alopecia^[10].



Figure No. 1: Stages of progression of alopecia androgenetica

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https://commons.wikimedia.org/wiki/File:Ludwid_scale_for_female_pattern_baldness.png. Copyright by, Keministi, 2018
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Diagnosis:

Diagnosis of alopecia androgenetica is possible by many ways but firstly clinical assessment of the scalp is important. If in case alopecia androgenetica cannot be confirmed then it is feasible to examine the hair roots. Other Methods such as trichoscopy, contrast-enhanced phototrichogram (CE-PTG), a daily assessment of the hair loss, wash test, hair pull test, reflective confocal laser scanning microscopy *in vivo* (R-CSLM) and Trichogramma unit area measurement can also be used¹. The Hair pull test is a diagnostic assessment which is noninvasive in nature and also used clinically. It has a pre-requirement that the patient should not use any shampoo on their hair for at least a day before the test is being carried out. The test is performed by holding a bunch of 50 to 60 hairs with the thumb, middle finger and index finger followed by tugging them slowly in the direction of the fingers following the hair shaft. This test is done in the left and right parietal regions as well as frontal and occipital regions of the scalp. If at least 6 hairs detached then the test is considered as conclusive. As a contrast to a Hair pull test a Trichogram is a semi-invasive test where a needle holder is used to tug about 20 to 30 hairs and the sampled hair is examined below the light of a microscope. Under the microscope after observation calculation is done for anagen to telogen ratio^[5].

Sometimes histopathological assessment is needed where two biopsy punches about 4mm in size are taken from the middle of the baldness area from lateral to the midline where the anagen bulb is present. The samples from the biopsy are then carefully explored to study various parameters such as the number of hair follicles, diameter, and morphology. The patient's age, baldness in family, thyroid problems, chemotherapeutic drugs treatment etc. also need to be considered ^[5]. Dermoscopy is a new method that has been introduced to diagnose various types of alopecia and can be performed by either dry method or wet method in which liquid paraffin was applied on top of the scalp ^[11]. The data was analyzed in excel sheet and the calculations were carried out. The results showed presence of honeycomb pigmentation as well as peripilar pigmentation and also showed pilosebaceous single hair unit in female patient ^[11].

Herbal remedies for androgenic alopecia:

Treatment for androgenic alopecia suggests for a long-term therapy. There are certain medications available in the market for hair loss out of which only two conventional drugs are approved by FDA i.e Minoxidil and Finasteride. Topical treatment for Minoxidil is available in two concentrations a 2% approved for Female Pattern Hair Loss (FPHL) and a 5% approved for Male Pattern Hair Loss (MPHL). Oral administration for Finasteride is available at 1mg. Many side effects have been reported for the long-term treatment of these conventional medications along with certain disadvantages. Finasteride causes dizziness, headache, impotency, breast enlargement tenderness, increase in body hair growth and hypersensitivity reactions ^[12,13,14]. Contact dermatitis, facial hypertrichosis and short-term hair loss are the most common adverse effects of minoxidil. Rare adverse effects are seen because of the constituents used as vehicles such as propylene glycol causing skin irritation along with true allergic reactions. Pregnant women excretes a very low level of minoxidil into breast milk and hence administration of minoxidil is restricted^[15]. Finasteride is not FDA approved in case of females and not advised for pregnant and lactating women due to its feminization in male fetus ^[16]. These side effects can be avoided by using an alternate herbal treatment.

Table No. 1: List of Herbs Used in Treatment of Androgenetic Alopecia

Biological Name	Family	Common name	Part used	Chemical constituent	Action	Reference
<i>Serenoa repens</i>	Arecaceae	Saw palmetto	Berries	phytosterols (β -sitosterol), fatty acids, β -carotene, and polysaccharides	Inhibits 5α reductase enzyme Blocks Dihydrotestosterone Nucleic uptake	2,17,18
<i>Cucurbita pepo</i>	Cucurbitaceae	Pumpkin seed oil	seeds	unsaturated fats, sterols or phytoestrogens and tocopherols	Aromatherapy	2,19-21
<i>Rosemarinus officinalis</i>	Labiatae	Rosemary oil	fresh leaves and blooming buds	rosmarinic acid caffeic acid, chlorogenic acid, carnosic acid, rosmanol, carnosol, ursolic acid, glycolic acid, and rosmarinic acid.	Aromatherapy	2,11,21,22
<i>Capsicum annum</i>	Solanaceae	Capsicum	Fruits	Carotenoids	antioxidant and anti-inflammatory	23-29
<i>Camellia sinensis</i>	Theaceae	Coffee	seeds	xanthine alkaloids	Decrease in TGF- β 2 expression	30-35
<i>Glycyrrhiza glabra</i>	Fabaceae	Liquorice	leaves, roots and seeds	campesterol, glycyrrhizin, cholesterol, palmitic acid, linoleic acid, linoleic acid, oleic acid, β -sitosterol, stigmasterol, trigonellin, brassicasterol	Blocked activity of Testosterone	36-38

Saw palmetto (SP):

Saw palmetto (SP) (*Serenoa repens*) is an extract from the berries of the saw palmetto palm tree (American pre-dominant tree) belonging to the *Arecaceae* family, containing phytosterols (β -sitosterol), fatty acids, β -carotene, and polysaccharides; SP is a competitive, non-selective inhibitor of two types of 5α -reductase [2]. SP blocks nuclear uptake of Dihydrotestosterone (DHT) in target cells and diminishes DHT binding to androgen receptors by approximately half [2,17]. Also, the concentration increases 3α -hydroxy steroid dehydrogenase movement expanding the transformation of DHT to its more fragile metabolite and androstanediol [17]. The mechanism of action of saw palmetto is similar to Finasteride, a marketed conventional drug that is, inhibition of 5α -reductase [18]. Some other uses of saw palmetto are as follows: expectorant, asthma, chest congestion, thyroid disorders, polycystic ovary syndrome, benign prostatic hyperplasia (BPH), increase metabolism and so on [17].

Pumpkin seed oil (PSO):

Pumpkin seed (*Cucurbita pepo*) is an individual from the squash family *Cucurbitaceae*, native to North America [2]. Two most common pumpkin species are *Cucurbita pepo* and *Cucurbita maxima* [19]. The chemical constituents likewise differ species to species however it was discovered that the yield of unsaturated fats, sterols or phytoestrogens and tocopherols remained the significant three components of pumpkin seeds [20]. Phytosterols known to inhibit 5α -reductase which is present in pumpkin seed oil; prevent the conversion of testosterone to active Dihydrotestosterone (DHT) [2]. For treatment AGA, presence of lipids adds a synergistic effect [21]. Pumpkin seed oil (PSO) has additionally been accounted to be successful treatment for indicative benign prostatic hyperplasia (BPH) [21]. Studies showed successful treatment for AGA, as PSO marks the supplement's on hair growth [2]. Some other uses of pumpkin seed are as antioxidant, anticancer, anti-diabetic, anti-inflammation, anti-hyperlipidemia, anti-cardiovascular, hypertension, antibacterial and so on [19,20]. (fig. 2) [19]

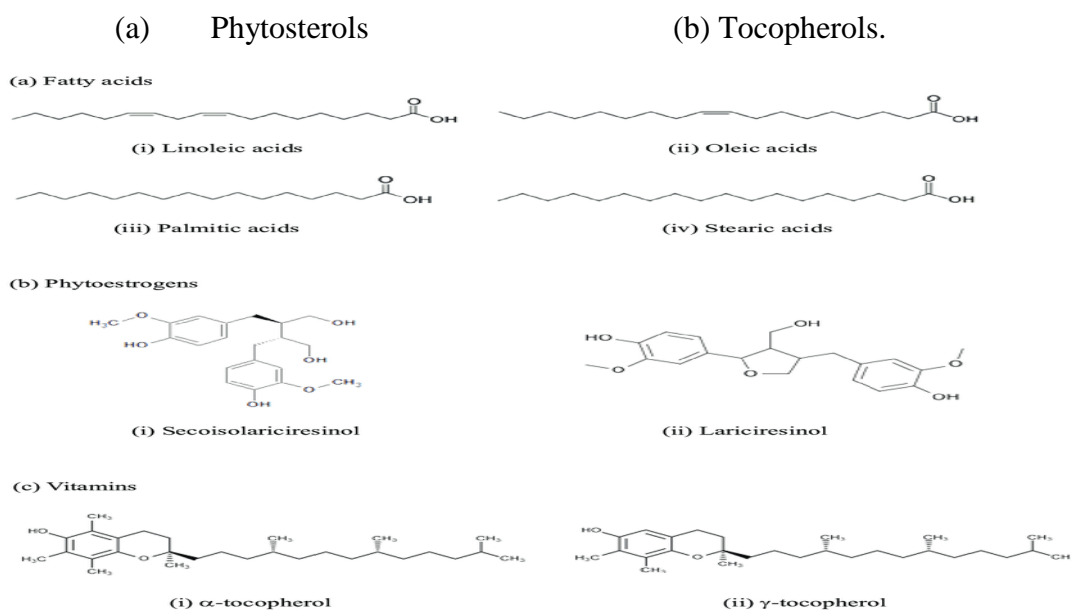


Figure No. 2: Structures of major compounds isolated from pumpkin seeds

- Adapted from Beni Lestayri and Edy Meiyanto. A Review: The Emerging Nutraceutical Potential of Pumpkin Seeds. 2018, Indonesian Journal of Cancer Chemoprevention 9(2):92
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Rosemary oil:

Rosemary (*Rosemarinus officinalis*) belongs to family *Labiatae* which is an aromatic evergreen herbs [2, 11]. Its fresh leaves and blooming buds contain rosmarinic acid, caffeic acid, chlorogenic acid, carnosic acid, rosmanol, carnosol and diverse diterpenes and numerous other cancer preventive agents, ursolic acid, glycolic acid, and rosmarinic [21]. Constituents of rosemary are 1-2% volatile oil, 0.8-6% of esters and 8-20% of alcohols [11]. Herbal oil therapy of rosemary topically enhances hair follicles and it is demonstrated as safest approach to a different type of alopecia, it also enhances micro capillary perfusion [2, 11]. Rosemary oil gave off a non-prescriptive alternative for AGA [2]. It was seen that when contrasted with Minoxidil, rosemary results did not show a noteworthy contrast from outcome acquired of minoxidil, as it is conventional marketed medicine for alopecia [19, 22]. Some other uses of Rosemary are antioxidant, antibacterial, antifungal, and anti-inflammatory properties [2, 22]. (Fig. 3) [22].

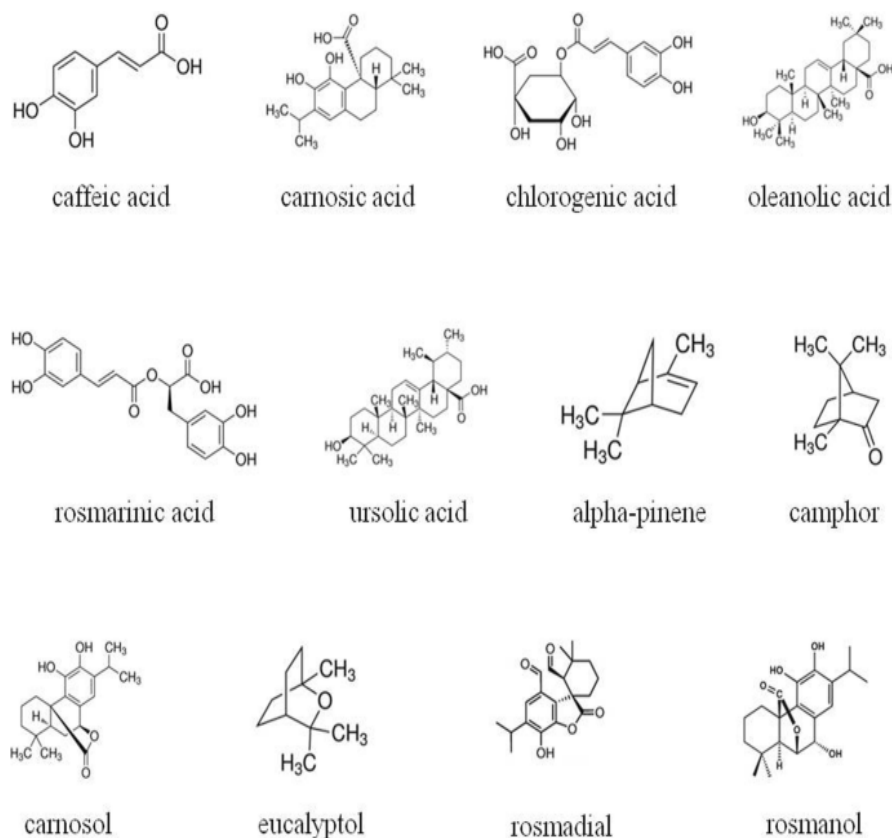


Figure No. 3: Structures of major compounds present in Rosemary

- Adapted from De Oliveira JR, Camargo SE, De Oliveira LD. *Rosmarinus officinalis* L. (rosemary) as therapeutic and prophylactic agent. *Journal of biomedical science*. 2019; 26:5.
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Capsicum:

Capsicum annum is a tamed genus of the plant race *Capsicum* belonging to the family of Solanaceae. The coloring matter that is accountable for the color of peppers is from a group of compounds called carotenoids which have in built antioxidant and anti-inflammatory attributes due to their power to destroy radical oxygen species (ROS) and reactive nitrogen species (RNS)^[23-26]. The chief compounds that show biological activity are capsaicin and isoflavone whereas the plant possesses other constituents which are namely capsanthin, capsorubin etc. (fig. 4). In a research study supervised by Harada N *et al* it was noted that the joint administration of these two molecules might show an increment in hormone known as insulin-like growth factor-I (IGF-I) production in hair follicles thereby increasing hair

growth^[27]. Moreover, Heinzelmann T *et al* when injected intradermal injection of capsaicin in mice led to beginning of anagen phase^[28]. Parisi OI *et al* conducted an experiment in which they prepared a new anti-baldness agent based on Interconnected Polymers Technology (IPSTiC) which contained extract of *Capsicum annum*. The developed product was evaluated on both safety as well as biological activity aspects. The product passed all the safety tests such as photo stability, freeze-thaw test as well as thermal stability under test conditions. The destroying property of Nitric Oxide radicals and inhibition action on 5 α -reductase enzyme were conducted separately. Both the tests were performed in triplicate and the obtained data was shown as mean values^[29].

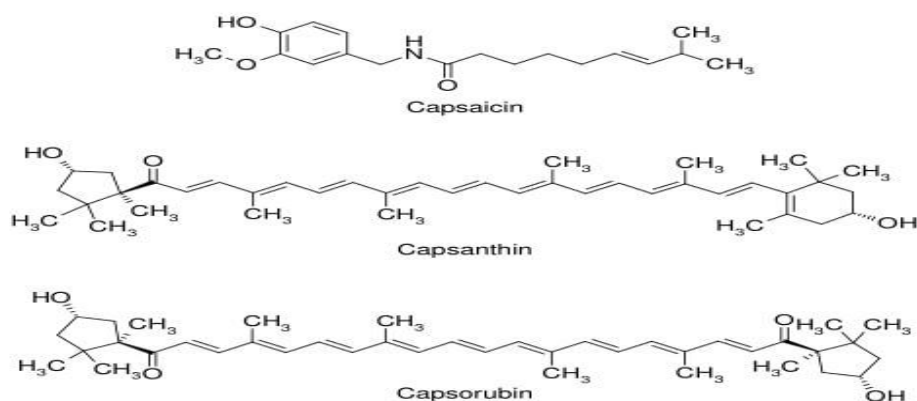


Figure No. 4: Structures of major compounds present in capsicum

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Caffeine:

Caffeine is a commonly consumed central nervous system (CNS) stimulant in the world^[30]. It is isolated from *Camellia sinensis* belonging to the family theaceae. This plant secondary metabolite is held by the group of xanthine alkaloids (fig. 5). It has been discovered in beyond 60 different plant species conversely and it can be made synthetically in lab by chemical reactions^[31]. Bussoletti C *et al* evaluated a shampoo containing caffeine in women having telogen effluvium and the results indicated an improvement in the quality of life^[32]. Fischer TW used a shampoo containing caffeine in a group of female volunteers and after a period of about six months, the hair loss was significantly reduced along with improvement in hair strength^[33].

Camacho-Martinez FM *et al* and Harries M *et al* conducted an experiment in which they checked the effect of caffeine exposure on TGF β -2 gene expression and it was observed that the gene expression was reduced by a considerable amount [34, 35].

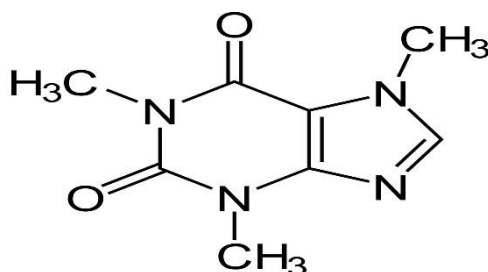


Figure No. 5: Chemical structure of caffeine

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https://commons.wikimedia.org/wiki/File:Koffein_-_Caffeine.svg, Copyright by NEUROtiker, 2007

Liquorice:

Glycyrrhiza glabra is a leguminous plant of the Fabaceae descent that is also called Indian liquorice and is also known by other names such as jequirity, crab eye, and olho de Pombo, etc. This plant grows extensively in dry weathers of tropical and subtropical zones for example India, Sri Lanka, Nigeria and the West Indies. The leaves, roots and seeds of *G. glabra* are used for medicinal intentions, an exercise that mostly dates back to the distant past. The chemical constituent Glycyrrhizin (fig. 6) is responsible for providing sweetness to the plant which is found in the root. The seeds carry compounds such as campesterol, glycyrrhizin, cholesterol, palmitic acid, linoleic acid, oleic acid, β -sitosterol, stigmasterol, trigonellin, brassicasterol^[36]. Upadhyay S *et al* experimented to analyze the effect of petroleum ether and ethanol fraction of Liquorice seeds on Androgenic Alopecia. They used a mixture of finasteride, the extract of liquorice in ether and petroleum extract along with testosterone and prepared them in 95% ethanol and heated gently in a round bottom flask. The experiment was conducted on male albino rats which were separated into 4 groups. The testosterone solution was given intravenously first on all 4 groups of rats and later the extracts of seeds and finasteride were applied topically. The injection of testosterone caused miniaturization of the hair follicles and the hair follicles were halted in the telogen

phase however when the extract was administered it blocked the effects of testosterone and halted alopecia. Also, the comparison was done between the extract and Finasteride and the number of hair (Density) was greater in the former^[37,38].

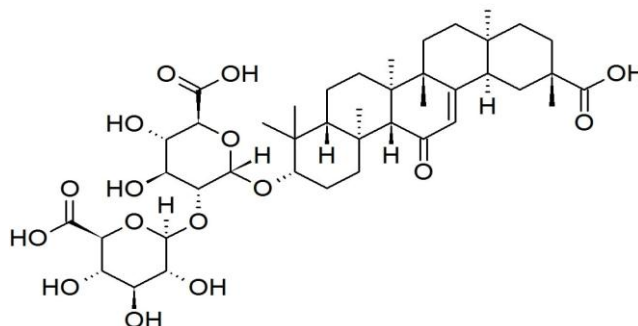


Figure No. 6: Chemical structure of Glycyrrhizin

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Saw Palmetto:

In a Placebo batch of Double-blind Randomized Controlled Trial (RCT), 26 patients were given 200mg *Serenoa repens* + 50mg β -sitosterol for 21 weeks from which 60% of patients showed improved results compared to the baseline and only 11% for control^[39]. Whereas, in RCT of Finasteride 1mg, 100 patients were given *S.repens* 320mg daily for 24 months which showed a greater amount of hair growth in Finasteride group i.e 68% of patients showed improvement and on the other hand only 38% of patients were treated with an increase in hair growth^[40].

A cohort study on 50 patients was tested with topical concentrated Saw palmetto serum of 3.3ml for 4 weeks and lotion of 2ml for 24 weeks showed increase in average and terminal hair count at 12 and 24 weeks^[41].

A nonclinical trial was tested on female rat liver microsomes which were used as source of protein and testosterone marked as substrate, it determined the components such as lauric acid and oleic acid against 5 α -reductase for their *in-vitro* potency^[42]. The activity of 5 α -reductase was drastically inhibited by 76% with 10 μ g/ml of Saw Palmetto^[43].

Determination of Hair loss induced by DHT through Animal studies on Mouse Model.

This study involved 24 pathogenic free mice ranging from age of 6 to 8 weeks with weight of 18 to 22g. DHT of 0.5ml was injected for 5 weeks into the neck region of each mouse. Then the mouse model was divided into DHT group (n=8), DHT+Finasteride group (n=8, by administering 0.01% of Fin solution intragastrically for 5 weeks everyday) and DHT+LSESr group (n=8, by administering intragastrically with 50% LSESr solution for 5 weeks every day). Meanwhile, Blank groups were assigned to 8 mice with no drug^[44]. Hair Growth of DHT-Induced HairLoss Mouse Model was improved by LSESr (Liposterolic extracts of *Serenoa repens*) Treatment. The results indicated that LSESr treatment after the injection of DHT the results showed that LSESr treatment turned the color of skin from pink to gray for 1st week; at the 3rd week the hair growth begins upto the 5th week. The hair growth in LSESr leads to hair regeneration. LSESr treatment was better in comparison with DHT-induced mouse model with no LSEr group and Fin treatment conditions were also achieved. Also, in DHT group the weight of hair was decreased significantly as that of the Blank group^[44].

Pumpkin seed oil:

A placebo batch with Double-blind RCT study was done on 76 patients, Pumpkin seed oil (400mg daily) showed 40% mean an increase in hair count in comparison with 10% placebo after 24 weeks with satisfaction and improvement in patients^[21]. A placebo-controlled, randomized, double-blind trial was conducted to analyze the tolerability and activity of Pumpkin seed oil with minimal to average AGA. Analysis at baseline and at 12 and 24 weeks were identified by phototrichography method for hair counts and hair diameters. Results in an intervention and control group showed a statistical difference in hair count at the 24th week. However, the hair diameter was similar for both the groups at the 24th week. In PSO treated patients, there was a significant mean increase of 30% and 40% in hair counts from baseline at 12 and 24 weeks whereas in Placebo-treated patients only a 5% and 10% increase in hair count was observed^[21]. Animal studies of six mice were undertaken by removing dorsal hair in an area of 2x2.5cm. Control group and Testosterone(5%) + PSO(10%) group were formed in which application of drug(100ul) was done for 6 days/week for 3 weeks. After 38 weeks, results of testosterone + PSO hair growth was lower than the control group but PSO have the property to prevent testosterone activity to a significant effective level^[45].

Rosemary oil:

In a RCT study of 2% Minoxidil as control treatment on 100 patients, Rosemary oil lotion (3.7mg/ml) showed that rosemary oil was non inferior to minoxidil and there was significant increase in hair count at 6 months in both groups ^[46]. During a pharmacokinetic study in rat, on topical application of ointment on the limb it was measured that its bioavailability was 60% and peak time was 4.5hrs. It was noted that alcohol enhances the absorption of rosemarinic acid when applied topically ^[47].

An animal study on six mice with testosterone-induced alopecia were administered topically with hydroalcoholic extract of Rosemary oil: rosemary (2mg/day/animal) and after the 16th day of treatment it resulted in a significant increase of hair growth compared to the one in control. To identify the Evaluation studies for efficiency of 5 α -reductase, in vitro test of hydro alcoholic extract was performed and the results showed that the binding of dihydrotestosterone (DHT) to its receptor was strongly inhibited ^[48].

Capsicum:

In a cohort study on 14 patients, Capsaicin cream (0.075%) showed 50% hair growth after 3 weeks and regrowth of hair by the 21st day ^[49]. An IPSTiC (Interconnected Polymers Technology) Hair Patch test was conducted to determine inhibition of 5 α -reductase activity. The activity of 5- 5 α -reductase is conversion of testosterone into dihydrotestosterone(DHT) an active compound. Inhibition of this enzyme is done by homogenate obtained from LNCaP cells as source of an enzyme. The results from the inhibition were equal to 68.3 \pm 0.7% for Hair Patch test ^[29].

A combination therapy of two bioactive components i.e isoflavone and capsaicin contributes to hair growth by increasing insulin-like growth factor (IGF-I) production in hair follicle when the release of calcitonin peptide from the sensory neuron is increased. In mice, the anagen phase is induced by administering capsaicin injection intradermally. In the telogen phase of the hair growth cycle when capsaicin injection was administered intradermally, it showed hair growth on the back skin of mice along with mast cell degeneration ^[50].

Caffeine:

A caffeine-containing shampoo (10 mg/mL caffeine) was evaluated in females ($n = 30$) by making use of the hair pull test to check hair loss to examine the quality of life ^[32]. After a

study period of about 6 months daily implementing on the head with exposure time of 2 mins, a reduction in hair loss was observed in more than 50% of the participants. Also, a satisfactory cosmetic efficacy was observed which included a refinement in the strength of the hair, a reduction in the extent of hair falling out and a diminished progression of the balding checked by the investigator's questionnaire.

In females with AGA, a randomized double-blind parallel trial was undertaken ($n = 140$) which juxtaposed the power of a caffeine-containing shampoo to a control shampoo with the absence of caffeine^[33]. The last shampoo application was done not before 48 h prior to application of the test products. Hair loss was checked on the basis of the outcomes of a hair pull test in addition to subject and investigator questionnaires. The experimental effects showed profitable results related to the introduction of caffeine in the shampoo: Lesser hairs were tugged out after 6 months in the hair pull test, hair loss intensity was reduced and there was a tendency to surge in hair strength when compared to the control shampoo checked by the investigator's questionnaire. No adverse events were observed for the caffeine-containing shampoo for the control shampoo, showing that the inclusion of caffeine in the product does not compromise its safety. In a more detailed study, hair follicles were sampled by micro dissection by performing biopsies from healthy women undergoing facelift surgery which were subsequently cultivated in the lab and exposed to caffeine at 10 or 50 $\mu\text{g/mL}$ ^[35,36].

Liquorice:

Animal study for the treatment of Androgenic alopecia

A study involving 24 rats were divided into 4 groups with 6 rats in each group. All these rats were intramuscularly induced with a 0.1mL dose of testosterone. Topical application of 0.4mL finasteride, petroleum ether, and ethanolic extract of seed were given on rats of group 2,3,4 for 21 days on the dorsal surface of skin. Results of the quantitative study after 21 days showed that due to testosterone dose in group 1, visible hair loss from the cranial region and hair thinning of dorsal region were observed. In group 2, alopecia wasn't observed due to simultaneous treatment of finasteride along with testosterone. Even in group 3, alopecia wasn't observed as testosterone effect was combatted by petroleum ether extract of seed. In group 4 also alopecia wasn't developed as the testosterone effect was antagonized by ethanolic extract of seed. Hence, both the seed extracts block the conversion of testosterone into dihydrotestosterone^[38]. These seed extracts also have the presence of flavonoids, phenolics, glycosides which combats the effect of testosterone. In other studies, concentrated

2% of hydro-alcoholic extract was compared with 2% standard Minoxidil which showed that hydro-alcoholic extract showed better activity in hair growth than that of Minoxidil^[51].

CONCLUSION:

Androgenic alopecia is a most common type of alopecia prevalent in women. The major cause is due to hormonal changes caused by an excess amount of testosterone which gets converted to DHT by a catalyst i.e 5 α -reductase. To inhibit this enzyme FDA approved two drugs i.e Minoxidil and Finasteride which when given orally prevent the conversion of testosterone to DHT by inhibiting the enzyme. While administering these drugs, it showed certain side effects like skin irritation, rashes, scalp dryness, impotency, breast enlargement, etc. An alternative to these conventional medications was established by introducing herbal remedies that were easily available and were of low cost. Saw palmetto (*S. repens*), Pumpkin seeds (*C. pepo*), Rosemary oil (*R. officinalis*), Capsicum (*C. annum*), Coffee (*C. sinesis*), Liquorice (*G. glabra*) were held under animal studies for their efficacy regarding their hair growth cycle, hair follicles, hair thinning and hair regrowth properties. We conclude that many herbal extracts have phytoconstituents that can treat alopecia either by blocking DHT and 5-alpha reductase activity or by covering all the nutritional requirements for the scalp. In comparison with conventional therapy, herbal drugs have higher potency with least side effects and have more future advancements when applied topically. Future aspects of herbal drugs can be used in combination for better effectiveness and safety.

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CONFLICT OF INTERESTS

The authors have declared no conflicts of interest.

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