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A Systemic Review on Hirsutism: Recent Perspectives

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ABSTRACT

Hirsutism in females is a prevalent clinical issue. "Hirsutism" is characterized by excessive terminal hair development in females, such as the face, abdomen, chest, and back, in the androgen-dependent regions of the body, usually growing in a typical male allocation pattern due to endocrine. The treatment of hirsutism depends on its cause. One of its main causes may be due to the enzyme 5-α-reductase, which converts testosterone to more effective 5-α-dihydrotestosterone androgen. It can be treated by medications (synthetic as well as by natural products), hair removal products or equipments. Synthetic products can be harmful and may cause some side effects like acne, rashes, itching, sometimes it may cause in the male fetus feminization. Procedures like laser and intense plused light may also cause pain, discomfort, secondary infection, and others. Moreover, the procedures are expensive. Hirsutism market is growing globally in terms of production and revenue generation. This indicates the need of better introduction of cost effective solutions in the market. This review describes about hirsutism, its etiology along with diagnosis and treatment. Synthetic drugs as well as natural plant products that can be used for the treatment of hirsutism, their mechanism of action, side effects and their use are discussed. Additionally, other methods to address hirsutism are mentioned.

INTRODUCTION

Products for treating hirsutism are being produced globally. This market is growing worldwide. Many medications and cosmetic procedures are available in the market. North America is considered to hold the largest hirsutism treatment market in the world. The increasing market growth rate suggests a growing demand. Hirsutism can be seen in women of all age groups but is more likely to occur among women with increasing age, especially after the menopause. The presence of a male-like pattern of terminal, coarse hair in females is termed as Hirsutism and it impacts 5-10% of women [1]. The term 'hirsutism' originates from Latin, which means excessive hair development or hairiness, particularly in females and children, with an adult male like distribution pattern; on the other hand, 'hypertrichosis' is a Greek term usually referring to localized and generalized excess hair [2, 3].

Except on the lips, hand palms, and feet soles, human skin has hair follicles everywhere. All these follicles, at some moment during life, generate and contain hair, vellus, or terminal. The nature of the hair and the amount of hair-occupied follicles are quite variable at any given time. This results in some fundamental complaints such as too much of hair which is hirsutism or too little hair which is baldness, or both. Excess or deficient hair complaints are subjective and heavily affected by the prevailing "hairiness" norms of society and culture. The notion of ordinary hair patterns is always confused with the present "ideal hair pattern". For instance, the present "ideal" female in the United States essentially has no terminal hair except for eyelids, eyebrows, scalp, and pubis. This norm places most ordinary females in the category of hirsute [4]. The frequency of hirsutism in women with childbearing age is 5-10% and one of the Indian studies mentions that this frequency is affected by the genetic factors and by the racial factors. Northern fair-skinned Europeans and people of Southern Asia have the minimum volume of terminal hairs. Whereas the women of Southern Europe and dark skin Mediterranean women have the maximum volume of terminal hairs. The North Indian Sindhi and Punjabi communities tend to have the greatest amount of excess hair as compared to women in other states.

Hirsutism can occur owing to variables that are androgenic (secondary hirsutism), non-androgenic and idiopathic hirsutism (reason of occurrence is completely not known). Androgenic variables affect over 80% of patients, 70-80% of whom include women with polycystic ovary syndrome (PCOS) [5].

PATHOGENESIS

Most of our body portions other than lips, palms and feet soles are covered with hair. It is essential to learn about the distinct hair types to recognize the distinction between 'hirsutism' and 'hypertrichosis'. Two distinct hair types, terminal and vellus hairs are present [6]. Terminal hairs are stiffer and longer (around 0.5 cm) with smaller and blunter tips, that penetrate into the dermis. Terminal hairs are more pigmented than vellus hairs. Growth and thyroid hormones, based on body region and androgens, stimulate the growth of terminal hairs. Vellus hairs, generally unpigmented, are brief, fine and short hairs [7]. They do not comprise the compact keratinocyte core. Vellus hair growth is stimulated by growth hormones and thyroid hormones. Clinically, terminal and vellus hairs can be distinguished based on their length and pigmentation.

Hirsutism differs from hypertrichosis in such a way that hair development in hypertrichosis is widespread unisexual and is independent of androgen. Hypertrichosis can occur due to the use of some drugs, metabolic or non-androgenic disorders and hereditary factors; but not due to excessive androgen. It may be caused by drugs like cyclosporine, glucocorticoid, penicillamine, corticotrophin, methyldopa, mercury poisoning, citalopram, valproic acid, phenytoin, and heavy metals [8]. If it is caused due to medication then it can be treated easily within a week or two by discontinuing the medication. It can also occur in patients having diseases like juvenile dermatomyositis, tuberculosis, malnutrition, hyperthyroidism etc [9].

Symptoms of hirsutism

Symptoms depend upon its causes, but it may also include the following:

- Excessive development of male-like terminal body hair in body regions such as face, abdomen, back, buttocks and internal thighs.
- Sudden change in hair color, growth rate, distribution or thickness.
- Male pattern baldness.
- Other skin conditions like seborrhea or acne.
- Development of warts in between the skin folds.
- Observation of masculine characteristics such as increased muscle mass or deepened voice.

Causes

During puberty, the ovary of a girl starts to evolve by generating a mixture of male and female sex hormones that leads to the development of secondary features in armpits and pubic areas of female-like hair growth. A too high percentage of sex hormones (androgen) leads to hirsutism when the ratio of male and female hormones is imbalanced.

The following factors can cause hirsutism:

- **Polycystic ovary syndrome (PCOS)**: Sex hormone imbalance is the most prevalent cause of hirsutism. This leads to irregular periods, infertility, obesity, and sometimes numerous cysts.
- **Cushing's syndrome**: This happens when the body is subjected to the cortisol hormone at elevated concentrations. It may grow from too much cortisol produced by the adrenal glands. It may also happen over a lengthy period of time owing to taking medicines such as prednisone.
- **Congenital adrenal hyperplasia**: The abnormal development of steroid hormones, such as cortisol and adrenal, characterizes this disorder.
- **Tumors**: Hirsutism may also lead from a tumor that secretes androgen in ovaries or adrenal glands.
- **Medications**: Medications like danazol, fluoxetine which are used to treat women in case of endometriosis; corticosteroids and depression respectively, can also cause hirsutism.
- **Enzymes 5-α-reductase:** Androgen affects terminal hair development. The dermal papilla includes androgen receptors and 5-α-reductase enzymes (type 1 and type-2). These two enzymes convert testosterone to 5-α-dihydrotestosterone, which has higher androgenic affects. Hirsutism is prevalent in hyperandrogenic women, however normal androgen concentration in patients may also influence [10].

HIRSUTISM DIAGNOSIS

Visual scoring of hirsutism

The hirsutism scale ranges from low to elevated. For the evaluation of hair development in the female, distinct techniques are used to evaluate the spectrum of hirsutism. In 1961, a scoring scheme was proposed to assess this by Ferriman and Gallwey. Nine body-dependent

regions such as upper lip, chin, chest, arm, upper abdomen, lower abdomen, upper back, lower back and thigh were included in this method [11].

This scoring scheme evaluates each of the 9 body components for the nature of hair with scores varying from zero (no terminal hair growth visible) to four (excessive hair growth). It is feasible to achieve a maximum score of 36, but the minimum score of more than or equal to 8 also suggests hirsutism, as originally described by Ferriman [12]. This scoring system also has limitations in case of women who have removed their hairs cosmetically [13]. Fig. No. (i) shows the modified system for Ferriman Gallwey scoring.

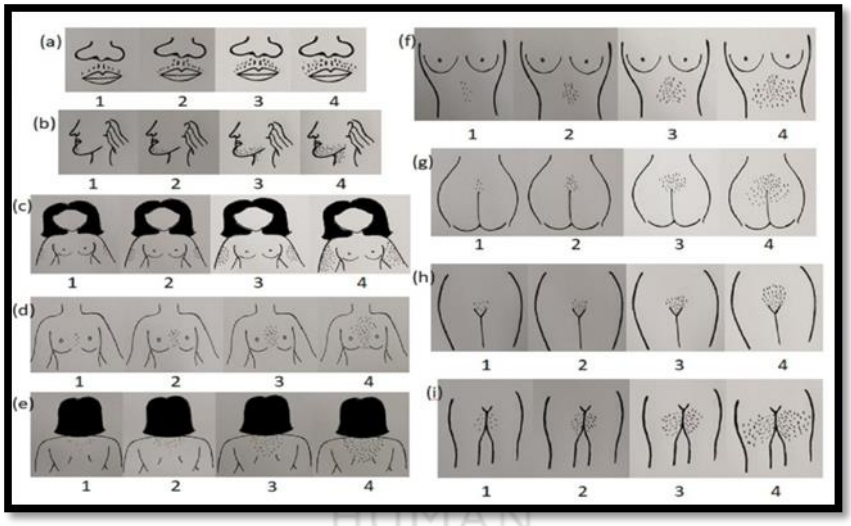

Fig. No. (i)- Sketch of modified system for Ferriman Gallwey scoring

[Nine regions of the body (a. upper lips, b. chin, c. arm, d. chest, e. upper back, f. upper abdomen, g. lower back, h. lower abdomen, i. thigh)]

Medical background

Medical history must cover menstruation history (as irregularity in menstruation can also cause hirsutism), beginning and advancement of hairiness, weight gain, continuous or any prior health problem and the treatment and family hyperandrogenism history. An enhanced evidence of women's internal aggregation with polycystic ovary syndrome, hyperandrogenism changes in metabolism [14]. In an adult woman a menstrual cycle length over 35 days then it can be a sign of oligomenorrhea. Moreover, it is 12-15.3% prevalent to occur in different studies around the world [15]. Oligomenorrhea is one of the most prevalent gynecological issues among reproductive-age females, it is the shift in menstrual cycle regularity that involves lengthy menstrual cycles [16].

Clinical inspection

Clinical inspection may include hairiness evaluation and evaluation of other variables of hyperandrogenism such as acne, hair loss, seborrhea, and acanthosis nigricans. Height, weight and blood pressure are to be recorded [17]. Transabdominal ultrasound can be used for young girls, even if this method is less precise in tiny follicles calculation [18]. Magnetic resonance and computed tomography of the pelvis could be done if there is any doubt in adrenal origin [19].

Cushing's disease or thyroid disorder can also cause hirsutism hence it is important to rule them out.

Testing in laboratory

In females with mild hirsutism, laboratory testing of s-testosterone is contentious, as some specialists suggest against testing. Whereas it is suggested that at least one serum androgen concentration be determined before beginning therapy. Free concentrations of testosterone are more susceptible to androgen excess than total testosterone measurement. In females with polycystic ovary syndrome and obesity, sex hormone-binding globulin is often reduced. Patients with polycystic ovary syndrome have frequently improved free serum testosterone with enhanced luteinizing hormone (LH) and lower follicle-stimulated hormone (FSH) (LH:FSH= 1:2 or 1:3). In order to rule out acromegaly, somatomedin C and prolactin are taken. Dehydroepiandrosterone are used to exclude the adrenal source [20].

TREATMENT

To treat hirsutism there are various methods like topical medications and cosmetic procedures. Most of the patients coming for hirsutism prefer cosmetic remedies to overcome it. The cosmetic procedure includes shaving, plucking, waxing and others. These are temporary procedures as the hair grows again.

Synthetic medications

The treatment for hirsutism is still under development. A proper method for the treatment of hirsutism is not available because the exact effect of androgen on hair follicle over a different part of the body is fully not known. The primary objective of the treatment is to continuously

remove the hair or correct the hormonal imbalance, either prevent or slow the development of excessive hair and enhance the patient's appealing appearance and life [21].

Spironolactone

Spironolactone (50-200 mg daily intake) is an antagonist of aldosterone and antiandrogen. It demonstrates the androgen receptor's dose-dependent competitive inhibition as well as 5-α-reductase activity inhibition [22]. Spironolactone is an efficient treatment in doses varying from 50/200mg per day for androgen dependent hirsutism. The regular dosage of 2 X 50 mg or 3 X 75 mg with or without an oral contraceptive pill combination is used cyclically [23]. Together with oral contraceptives, spironolactone is more efficient than just oral contraceptives. [24].

This drug was usually tolerated with fewer side effects based on a few clinical trials. Few women developed frequent menstruation while using spironolactone alone. Spironolactone can increase the quantity of potassium by blocking the impact of aldosterone on kidney. If a female has kidney insufficiency, spironolactone should not be provided. However, blood pressure and potassium concentration must be checked in every 4 weeks during the first few months of the therapy.

Finasteride

Finasteride works as an enzyme inhibitor which is adviced as an androgen which competitively inhibits 5α reductase. This results in inhibition of transformation of testosterone to dihydrotestosterone. In women suffering from hirsutism, finasteride is used as a dose of 1mg to 5mg per day [22]. It requires a longer duration of treatment. Women who are potential to bear child should not take this medication as because there are chances of the male fetus feminization.

Metformin

Metformin is an agent that sensitizes insulin. Metformin decreases the production of androgen and increases sex hormone-binding globulin concentrations, thus reducing the amounts of free and biologically active androgen circulating that can theoretically improve hirsutism. Evidence is missing in the use of insulin-sensitizing agents for clinically important enhancement in hirsutism [25]. Usually, the dose size given is 500mg 3 times per day. Side

effects of using metformin can be liver, lung, kidney relate diseases and heart failure history. Because of so many side effects, metformin is prescribed less for hirsutism.

Flutamide

Flutamide is a non-steroidal agent that operates on the site of the androgen receptor by inhibiting or reducing androgen synthesis. During clinical practice, flutamide is given as a dose of 62.5 mg to 500 mg. Some of finasteride's potential side effects include liver failure and hepatic toxicity [26].

Eflornithine

Eflornithine is a decarboxylase inhibitor of ornithine which is irreversible, an enzyme catalyzing the rate-limiting step needed for follicular polyamine synthesis, which is necessary for hair growth. It does not take hair off but decreases development. Its systemic circulation is very low [27, 28]. Only the experimental overuse of this has shown skin irritation. Side effect includes itchiness and dryness of skin [28, 29].

A couple of years ago, a 4-month open-label study was conducted which discovered that 11.5% of eflornithine applied twice daily over the upper lip region efficiently reduced hair growth rate, density and length [30]. A randomized checked bilateral vehicle research of eflornithine cream coupled with laser therapy versus laser therapy alone for female facial hirsutism discovered a statistically important better impact in eflornithine plus laser hair removal compared to laser alone [31]. It may also be used as a supplement for hirsutism pharmacotherapy.

Bicalutamide

Bicalutamide is a type of non-steroidal anti-androgen agent. It is also used to treat prostate cancer but it's of the concentration can be given to patients suffering from hirsutism due to polycystic ovary syndrome. For prostate cancer, the concentration is 50 mg/day but for hirsutism, it is 25 mg/day [32]. Hepatotoxic results are seen for dose 50 mg/day.

The drugs listed above are reported under research studies. Among the marketed prpducts only eflornithine creams are indicated for the treatment of hirsutism. The list of the marketed eflornithine formulations are shown in Table no. 1.

Table No. 1- List of some eflornithine marketed formulations [33].

Dose size (w/w)	Brand name	Manufacturer	Dosage form	Route of administration
13.9%	Vaniqa	SkinMedica Pharmaceuticals, Inc.	Cream	Topical
13.9%	Elyn Cream	Ajanta Pharma Ltd.	Cream	Topical
13.9%	Eflora Cream	Sun Pharmaceutical Industries Ltd.	Cream	Topical
13.9%	Hinder Cream	Eris Lifesciences Ltd.	Cream	Topical

HERBAL MEDICATIONS

There is an increasing demand for naturally derived products. Consequently, the presence of anti-androgenic activities in plants, foodstuffs, herbs gives a good alternative for the synthetic products and there is very less adverse effect for these alternatives [34].

Green tea (Camellia sinensis)

Green tea supports the cardiovascular system along with that, it reduces the chances of type 2 diabetes and cancer. As because green tea consists of epigallocatechins [35] that reduces or inhibits 5-α-reductase which helps to inhibit the testosterone conversion to dihydrotestosterone [36]. As known, this mechanism can control the androgen-dependent condition but yet no randomized study has been performed on this.

Reishi (Ganoderma lucidum)

In a study held in 2005, is has shown that out of 19 edibles and medicinal mushroom's methanol extracts *Ganoderma lucidum* has shown the strongest 5-α-reductase inhibitory effect [37]. *Ganoderma lucidum*'s ethanolic extract is discovered to be most potent, followed by the extract of petroleum ether and then aqueous extract [38]. These studies discovered that reishi efficiently reduced the 5-α-reductase level preventing testosterone from being converted to dihydrotestosterone.

Soymilk (Glycine max)

It has shown that the extract of soymilk which was prepared from soybeans, reduces hair thickness and length, also reduces hair growth and hair follicle dimension in the rat as well as in human [39]. Soymilk which is a kind of soyfood contains soy isoflavones [40]. It is being

demonstrated that the administration of soy isoflavones in women with PCOS has beneficial effects on markers of insulin resistance. No side effects are reported after the application of soy isoflavones in women suffering from polycystic ovary syndrome [41]. We also know that polycystic ovary syndrome is a condition in which hirsutism may occur.

Saw palmetto (Serenoa repens)

Saw palmetto is an American dwarf palm plant. Permixon is a compound which can be extracted from its fruit. It extracts also has phytoestrols which is believed to have an effective effect on benign prostate hyperplasia [42, 43]. It is also effective in androgenic alopecia [44] and polycystic ovary syndrome. It is clinically proven that it has effects in lowering the level of 5-α-reductase [45]. It is also found that saw palmetto is safer and more effective than finasteride.

Licorice (Glycyrrhiza glabra)

Glycyrrhiza glabra Linn or licorice belongs to the kingdom Plantae. In Chinese pharmacy, it is considered as a first class drug and when consumed for a long time it provides rejuvenating property. Along with many more useful constituents, licorice roots consist of steroid glycyrrhizin and glycyrrhitic acid which has weak anti-androgenic activity [46]. Licorice impacts the endocrine system because it also includes isoflavones or phytoestrogens that can mimic the effects of estrogen. It is used in eastern and western countries for treating many diseased conditions. When women were administered with licorice continuously, the level of testosterone dropped whereas the discontinuation of it leads to an increase in testosterone level [47].

Spearmint (Mentha spicata [Labiatae])

Spearmint is taken as tea that is highly efficient in humans and is helpful in many illnesses. It has characteristics that reduce testosterone in it. Women usually use it to treat hirsutism in Middle Eastern regions. It has anti-androgenic characteristics that assist lower the blood amount of free testosterone, leaving the total testosterone and dehydroepiandrosterone unaffected. In a clinical study, a substantial reduce in free testosterone with a rise in luteinizing hormone, follicle-stimulating hormone (FSH) and estradiol was discovered after consumption of spearmint tea by women with hirsutism [48]. There was no important decline in the total amount of testosterone or dehydroepiandrosterone. Another research showed that

for 30 days, twice daily drinking of spearmint tea in patients with hirsutism induced by polycystic ovary syndrome considerably lowered the amount of androgen and gonadotropins. But in the scale of Ferriman Gallwey, there was no objective shift [49]. Using spearmint tea sustainably results in further reduction of hirsutism.

Papain (Carica papaya)

Papain is a natural source, it can also be used as a harmless therapy for hirsutism, which is cheap and readily accessible. In a study, papain cream has shown better depilatory activity than papain gel. Papain is a substance which is proteolytic. It hydrolyses polypeptide, which may eliminate keratin by enzyme [50].

Lavender (Lavandula angustifolia)

It is discovered that lavender oil is effective against many bacterial species. These includes some of those resistant to antibiotics like methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant Enterococcus (VRE) [51]. Lavender oil possesses both estrogenic and anti-androgenic properties [52]. Lavender oil is mainly used for its sedative, spasmolitic, wound healing, skin purifying, circulation-stimulating features [53]. In a study, it was found that lavender oil was efficient in decreasing idiopathic hirsutism when applied locally over the skin. So it can be an effective treatment for hirsutism [54].

Tea tree oil (Melaleuca alternifolia)

Tea tree oil can be used in dermatological diseases like acne and mycosis, and also in vaginal and mouth infections [55]. Tea tree oil belongs to *Malaleuca* species. A study which was carried out on human cell line indicated that tea tree oil has estrogenic and antiandrogenic activities [56]. In another study, it was found that tea tree oil can be an effective therapy for hirsutism [54].

The list of plant-derived anti-androgen with their effects are shown in table no. 2.

Table No. 2- List of some plant-derived anti-androgen with their effects.

Sl. No.	Name of the plant	Scientific name	Clinical/Biological effect
1.	Green tea	*Camellia sinensis*	Inhibits 5-α-reductase impact thus reducing testosterone conversion to dihydrotestosterone[35,36].
2.	Reishi	*Ganoderma lucidum*	Inhibits the imact of 5α reductase, thus reducing testosterone to dihydrotestosterone conversion[37,78].
3.	Soymilk	*Glycine max*	Soy isoflavones affecting the insulin resistance[39, 40, 41].
4.	Saw palmetto	*Serenoa repens*	Lowers the level of 5α reductase[42, 43, 44, 45].
5.	Licorice	*Glycyrrhiza glabra*	Reduces the testosterone level[46, 47].
6.	Spearmint	*Mentha spicata*	Increases level of FSH, LH, and estradiol. Also decreases free testosterone. This was reported to reduce the level of hirsutism[48, 49].
7.	Papain	*Carica papaya*	Elimination of keratin by the proteolytic substance (papain) by hydrolyses polypeptides[50].
8.	Lavender	*Lavandula angustifolia*	Anti-androgenic activity[51, 52, 53, 54]
9.	Tea tree oil	*Malaleuca alternifolia*	Anti- androgenic activity[54, 55, 56]

OTHER COSMETOLOGY PROCEDURES

Reduction of hair and removal of hair are two of the world's most prevalent cosmetic procedures conducted by the dermatologists. It is a secure and efficient procedure. This can be done by Laser (Light Amplification by Stimulated Emission of Radiation)/IPL (Intense Pulsed Light system)/LHE (Light, Heat and Energy device)-based equipment can be used for unwanted hair removal. This should be marked as "Laser and light based methods for long-term hair reduction". Instead of permanent hair removal, the phrase "long term hair reduction" should be used because the worldwide laser and light based technology experience is barely some couple of decades old. It includes device that utilizes light and heat, either individually or both, and that utilizes the fundamentals of selective photothermolysis principle [57].

Laser techniques

With the introduction of fresh devices each year, lasers are developing rapidly. The removal of hair by laser is an easy operation that requires some minor installations. It can be done in the clinic/ minor surgery room/ day care theater of the dermatologist. For the treating physicians, operating table/ cosmetic chair, proper lighting, and comfortable seating are essential. Proper cooling system, as recommended by the manufacturer, must be accessible for each individual machine. It is preferred to use a metal free surfaced cosmetic chair (which may accidentally reflect laser/light beams) and washable material. Eflornithine can be used together with laser in combination therapy. It can be started immediately after the laser treatment and there seems to be some additional benefits of this combination [58]. By targeting melanin in the hair shaft, follicular epithelium, and hair matrix, the mechanism of action of these systems is to emit light with wavelengths ranging from 600nm-1200nm, which is selectively absorbed by melanin [59]. There are various laser system accessible:

- Ruby laser- 694 nm
- Alexandrite laser- 755 nm
- Diode laser- 800 nm
- Neodymium - yttrium-aluminium-garnet (Nd:YAG) laser- 1064 nm [58, 60]

IPL (Intense pulsed light system)

Intense pulsed light system without heat can be used within the range of 550-1200 nm [58]. IPL is similar to treatment with laser. However, laser focuses on the skin only one wavelength of light, whereas IPL, releases light of many distinct wavelength, like a flash of photo. IPL's light is more dispersed and less focused that a laser. IPL penetrates the second layer of skin (dermis) without damaging the top layer (epidermis), thus causing less skin damage. IPL can be used anywhere over the body, but it may not work on uneven areas as well. For individuals who wants to get thick, elevated keloid scars or who have darker skin tones, it is not recommended. It is also less effective on light-colored hair than on darker hair [61]. In a research study, clinical comparison of four hair removal lasers and light sources was done. The selected sources were- (i) an intense pulsed light with a red filter; (ii) an intense pulsed light with a yellow filter; (iii) an 810 nm diode laser; and (iv) a 755 nm alexandrite laser. From that study, it was concluded that while hair removal with frequently

used technologies is, as anticipated, extremely efficient, therapy with light-based machines can cause less pain while showing laser-like efficacy [62].

Potential side effects [63, 64]

- There may be pain and discomfort; mild oral analgesic can be prescribed.
- Antibiotic/ steroid creams and mild emollients are used to treat vesiculation and local crusting.
- Secondary infection is uncommon. If occurs, antibiotic cream and antibiotics can be used to treat it.
- Hyperpigmentation can happen rarely and is treated with a sunblock and/ or a mild steroid cream such as hydrocortisone and/ or cream of hydroquinone. This is usually temporary and needs to be examined by the patient.
- Localized hypertrichosis or compensatory hypertrichosis in other areas is uncommon, but can happen and trigger patient anxiety. They may also require laser treatment.

Patents on topical products for hirsutism

The list of some patents on topical products for hirsutism are shown in Table no. 3.

Table No. 3- List of some patents on topical products for hirsutism.

Sl. No.	Title; Year	Outcome
1.	Topical hirsutism treatment; 2017	A topical composition comprising with capryloyl glycine for the treatment of hirsutism[65].
2.	Azasteroid compound for treating alopecia, hirsutism and seborrhea; 2014	Compounds with general formula (I) are novel compositions that are effective in the treating baldness, female hirsutism or seborrhea, or function to prevent prostate cancer from metastasizing to the bone, in which R<1> and R<2> are hydrogen, hydroxyl or lower alkoxy[66].
3.	Reducing hair growth, hair follicle and hair shaft size and hair pigmentation; 2011	Uses natural and/or synthesized serine proteases inhibitory agents or botanical extracts comprising serine protease inhibitory activity, with or without the addition of one or more isoflavones, and their capacity to influence changes in mammalian hair development, hair follicle and hair shaft size and hair pigmentation[67].
4.	Botulinum toxin for the treatment of reduction of hair growth; 2010	Preparation of a cosmetic method using botulinum toxin for preventing hair growth[68].
5.	Composition and methods for inhibiting 5-alpha reductase; 2005	Compositions for controlling androgen activity in target organs and cells through the modulation of 5-alpha reductase activity for the treatment of diseases related to androgen hyperactivity including hirsutism[69].
6.	Topical preparation for treatment acne and hirsutism; 2003	Topical preparation of a treatment for acne and hirsutism comprising of saw palmetto berry extracts. To enhance the penetration through the hair follicles it was combined with two classes of low irritability penetrating agent[70].
7.	Reduction of hair growth; 2001	Mammalian hair development is decreased by applying over the skin that raises the concentrations of cellular ceramide[71].
8.	A composition for the treatment of androgenic alopecia and hirsutism; 1998	A cosmetic or pharmaceutical composition for preventing and/or treating androgenic alopecia and/or hirsutism comprising of lipophilic fruit extract of *Serenoa repens* plants[72].
9.	Topical composition for inhibiting hair growth; 1997	A topical composition for inhibiting mammalian hair growth, comprising a water-soluble, hair-growth-inhibiting agent dispersed in an oil-in-water emulsion in the form of lotion or cream[73].
10.	Methods for the treatment of hirsutism; 1979	Method of preparation and uses of certain 4′-substituted and to 3′,4′-disubstituted anilides as antiandrogens. For the treatment of androgen dependent disease states[74].

WORLD BUSINESS IN THE TREATMENT OF HIRSUTISM

Globally, there are several products for hair removal that can be gender specific or based on the body area. Most of these products, however, are mainly cosmetic products and are only used for momentary removal of hair. They include epilators, lasers, hair removal creams/ lotions, IPLs, medications and sprays. These products may provide temporary hair removal, limit hair development at hormonal level or slow hair development at hair follicle level. The market segment of home hair removal is growing quickly. Several new products have entered the worldwide market, like home-based equipment such as IPL devices for hair removal. Key market players include Ajanta Pharma, Allergan PLC, Alpaya Dermaceuticals, Jubilant Cadista, Sciton Inc., Nisim Inc., Wet and Dry Personal Care, Bausch Health Companies Inc. (Solta Medical Inc.), Cynosure Inc., Lumenis Inc., AbbVie Inc., Bayer AG, Bristol-Myers Squibb Company, Pfizer Inc., Alma Lasers Ltd, Sun Pharmaceutical Industries Ltd. and others [75]. The global hirsutism market revenue share (%) for 2018 is shown in Fig. No. (ii).

Fig. No. (ii)- Global Hirsutism Market 2018: Revenue share (%) (Source of information: Mordor Intelligence)

In the forecast period by 2023, the global market for treatment of hirsutism is expected to grow by~ 13.6% at the Compound Annual Growth Rate and is estimated to achieve 5295 million USD. Global market based on hirsutism may be segmented based on etiology (idiopathic hirsutism, secondary hirsutism and others), diagnostics (imaging tests – CT scan, Ultrasound; blood tests - DHEA-sulfate test, testosterone level test; physical examinations-inspection, palpation, percussion, auscultation, etc.) treatments (medications, procedures).

Medication may be classified into anti-androgen products, oral contraceptives, topical creams. Laser therapy, Electrolysis and other mechanical methods are among the procedures used to treat hirsutism. Treatment for hirsutism and the associated business is segmented into clinics and hospitals, medical research centers, educational institutions, etc based on end-users.

Global scenario can be divided into geographical zones- America, Europe, Asia-Pacific, Middle East and African regions. America holds the largest hirsutism market share followed by Europe. Among them North America and United Kingdom holds the largest market respectively. In the Asia-Pacific region, a growing development is seen in cosmetic procedures to remove excessive body hair, where Japan is leading. The Middle East and Africa contribute less market share and the growth rate is slower than other regions[75, 76]. The growth for these regions are driven by factors such as technological advancement and increased demand for treatments. The list of predicted market growth based on regions (2019-2024) are shown in Table No. 4.

Table No. 4:- Predicted Hirsutism Market Growth based on regions (2019-2024) [77].

Growth rate	Countries
High	Germany, United Kingdom, France, Spain, Italy, China, Rest of Europe, Japan, India, Australia, South Korea, Rest of Asia Pacific.
Medium	Canada, United States, Mexico, Brazil, Rest of South America, Argentina
Low	GCC (Gulf Cooperation Council), South Africa, Rest of Middle East and Africa

CONCLUSION

Women's hirsutism implies masculine pattern hair appearance in androgen-dependent fields. Identifying this condition is very crucial because it impacts a woman's perception of her feminity considerably. Hirsutism is mainly a symptom of excess androgen which unknowingly women getting rid of by using cosmetic methods [78]. Also, it becomes important to make women aware of this as nowadays women are preferring to use cosmetic methods over medications. Synthetic medications as well as the procedures have lots of side effects. Moreover, the procedures are costlier which is not affordable for everyone. Since herbal formulations can be useful in many ways with lesser side effects hence, more research in the field of natural remedies must be done to get permanent relief from it. Herbal formulations can be a better alternative.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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