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Therapeutic and skincare products used in hirsutism and hypertrichosis

Abstract

Introduction. Hirsutism is a disorder manifested by excessive hair growth in the telogen phase in androgen-dependent areas: on the face, lower back, thighs and breasts in women with hormonal disorders. Hypertrichosis is excessive hair covering the entire skin surface or limited to certain areas of the skin, independent of androgens. It may occur in both men and women and is not limited to androgen-dependent areas. Hormonal disorders are not observed in hypertrichosis. It may be genetically determined or caused by medications taken by the patient: minoxidil or cyclosporine A. Hypertrichosis most often occurs on the arms and lower legs.

Aim. The aim of the study was to identify the therapeutic and skincare products used in hirsutism and hypertrichosis available on the Polish market.

Material and methods. In 2022 and 2023, therapeutic and skincare products used in hirsutism and hypertrichosis available in 10 randomly selected pharmacies and 10 drugstores in the Lubelskie Voivodeship in Poland were analyzed.

Results. Together 53 therapeutic and skincare products used in hirsutism and hypertrichosis were found. The therapeutic products were available with doctor's prescription only (Rp.), while the skincare products were available without prescription, like cosmetics. In the analyzed preparations for hirsutism, the most frequently used active substances are dienogest and cyproterone acetate.

Conclusion. The most commonly used form of drugs in hirsutism are tablets, and in hypertrichosis – foams that facilitate the removal of unwanted hair. The new promising formulas for treatment of hirsutism and hypertrichosis contain eflornithine, acyclovir, licorice and vitamin D.

Keywords: hirsutism, hypertrichosis, skincare products, therapeutic products.

DOI: 10.12923/2083-4829/2024-0013

INTRODUCTION

Hirsutism is a disorder manifested by excessive hair growth in the telogen phase in androgen-dependent areas, i.e. on the face, lower back, thighs and breasts in women [1]. Its name comes from the Latin word *hirsutus* meaning “hairy” [2]. It occurs in approximately 35% of women with mild symptoms. Hirsutism is one of the symptoms of masculinization in hyperandrogenism [3]. It is quite a troublesome disorder for women, also affecting many aspects of everyday life and quite often causing great shame, and even depressive disorders. Hirsutism is a multidisciplinary problem, therefore the diagnosis and treatment require the cooperation of many doctors, specialists in dermatology, gynecology and endocrinology [4].

Hirsutism in women is a consequence of hyperandrogenism [5]. Androgens are hormones that stimulate the growth of male reproductive organs, and in women they are responsible for increasing libido and are precursors of estrogens. Hyperandrogenism can cause many troublesome symptoms related to the hypothalamic-pituitary-ovarian system and systemic symptoms. It may arise as a result of many factors: too much androgen production in the ovaries and adrenal glands, increased sensitivity of receptors to androgens, too high activity of the 5-alpha-reductase enzyme.

Currently, the mechanism causing excessive sensitivity of the skin to androgens is not fully understood, however, it is suspected that the activity of 5-alpha-reductase has a significant impact [6].

There are three periods in a woman's life when hair growth increases: pregnancy, puberty and the postmenopausal period. This is a natural phenomenon effected by physiological changes caused by steroids and other hormones secreted by the anterior pituitary gland. In the case of puberty, we observe an increase in the concentration of adrenal androgens, and only later an increase in estrogens. As for pregnancy, the reasons have not been fully explained. Higher levels of total testosterone are observed during pregnancy, but the bound fraction remains unchanged. However, in the postmenopausal period, the ovaries produce not estrogens, but androgens [7].

The degree of hair growth will be influenced by factors such as: genetic – they may determine the amount of hair per cm²; ethnic – will determine the location of hair; fetal – they determine the number of hair buds, hormonal – they influence the thickness and even the speed of hair growth. The final effect will depend on the activity of enzymes converting dehydroepiandrosterone (DHEA), on the capacity of sex hormone binding globulin (SHBG) and on the activity of 5-alpha-reductase [8]. Factors increasing the risk of hirsutism also include obesity [9].

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Excess of androgens can be caused by ovarian, adrenal and genetic causes, as well as by medications. In the case of ovarian causes of hyperandrogenism, we can distinguish polycystic ovary syndrome, hyperketosis syndrome and androgen-producing ovarian tumors [10].

Polycystic ovary syndrome (PCOS) is one of the most common endocrine diseases affecting women of reproductive age. According to the Rotterdam criteria, as many as 18% of women suffer from it. It is characterized by ovulatory cycle disorders and hyperandrogenism. Additionally, PCOS may result in insulin resistance, dyslipidemia, type 2 diabetes, androgenetic alopecia and even cardiovascular diseases. Hirsutism and acne occurring in the course of PCOS may be the result of increased testosterone levels in the blood of affected women [11]. It has been found that up to 40-50% of affected women experience inhibition of sex hormone binding protein (SHBG) secretion, resulting in an increase in free testosterone levels. However, 9-43% of women with PCOS suffer from hyperprolactinemia, but this symptom is not included in the definition of polycystic ovary syndrome. Moreover, in the course of PCOS, ovarian ultrasound imaging shows the presence of cysts numbering more than 5-11 and having a diameter of 5-8 mm [12]. PCOS treatment should be tailored to the patient and directed at her symptoms.

It was found that it is possible to effectively reduce the concentration of androgens of ovarian origin by administering gonadoliberein agonists, despite the fact that the concentration of LH is not increased. However, administration of a combined oral contraceptive pill does not cause a decrease in androgen concentration [13,14].

Androgen-producing ovarian tumors are very rare. They usually develop between the ages of 20 and 40 and the risk of malignancy is low. Ovarian tumors secreting androgens should be suspected in women who have observed rapidly developing virulization or when the level of total testosterone in the blood is above 200 ng/dl [15].

In the case of adrenal causes of hyperandrogenism, we distinguish: congenital adrenal hyperplasia, Cushing's syndrome and androgen-producing adrenal tumors. Symptoms of congenital adrenal hyperplasia may include hirsutism or virulization occurring after puberty. This disease is often confused with PCOS due to the occurrence of scanty periods and anovulation. An enzymatic deficiency in the cortisol metabolism pathway is observed in a large number of sick women. There is also an increased level of androgens of adrenal origin, such as dehydroepiandrosterone (DHEA), on the other hand, androstenedione and testosterone concentrations are usually normal. According to many sources, metabolic disorders occurring in congenital adrenal hyperplasia may occur in 5-20% of women suffering from hirsutism [16].

Androgen-producing adrenal adenomas or carcinomas are a rare cause of hyperandrogenism. They cause a significant increase in adrenal androgens, with the DHEAS concentration most often being higher than 8 µg/ml. These tumors only rarely produce testosterone [14].

Cushing's syndrome is a set of various clinical symptoms associated with elevated levels of glucocorticosteroids (GKS) in the blood [17]. The symptoms include central obesity, thinning of the skin, fat above the collarbones and neck, osteoporosis, hypertension and diabetes. There are two types of pathological hair growth in Cushing's syndrome. The first one is characterized by increased growth of thin hair on the face, which

is caused by excess GKS. An increase in the production of adrenal-type androgens may lead to true androgenic hirsutism with the growth of thick hair. Treatment involves surgical removal of the tumor that produces adrenocorticotrophic hormone (ACTH) or cortisol [17].

Hirsutism may also be caused by various drugs, such as diazoxide, glucocorticoids, cyclosporine, phenytoin, danazol [18], as well as by ACTH, anabolic steroids, progestogens derived from 19-nortestosterone or over the counter (OTC) preparations containing androgens. Discontinuing a given group of drugs may reduce or even eliminate the symptoms of hirsutism.

Hirsutism is manifested by excessive hair in areas of the body where there is no hair in normal conditions: the upper lip, chin, chest, back, abdomen and even the inner side of the thighs or in the upper part of the pubic triangle. In the case of hirsutism, we can also observe the occurrence of seborrhea, acne, menstrual disorders and even androgenetic alopecia [19].

It was found that as many as 36.9% of women over 45 years of age suffering from hirsutism report excessive hair on the cheeks, and as many as 27.9% report the occurrence of unwanted hair on the upper lip. Moreover, it was observed that hair loss on the temples occurred with an excessive amount of hair on the cheeks, while hair loss in the frontal area occurred with increased hair growth over the upper lip [20]. The amount of facial hair usually increases with the age of the affected woman. Moreover, in people with excessive hair growth and coccygeal pits, the occurrence of hair around the anus is observed [21]. A change of pubic hair in women to the male type of hair is also observed [22]. Attention should be paid to skin changes such as acanthosis nigricans – these are brown and thickened areas of skin around the armpits or neck coexisting with hirsutism [23]. Symptoms of virulization are also occasionally observed in patients with excessive hair growth, such as clitoral hypertrophy, deepening of the voice timbre or increased muscle mass. Women suffering from hirsutism and PCOS are at increased risk of hypertension, hyperlipidemia, type 2 diabetes and coronary heart disease. Insulinemia is found in over 50% of women with PCOS. If hyperprolactinemia is detected, galactorrhea and even infertility may occur. If a woman also suffers from Cushing's syndrome, symptoms such as abdominal obesity, thinning of the skin, and increased fat tissue in the neck area may occur [16].

Hair occurring in hirsutism is most often rough, thick and highly pigmented [24]. However not every more visible hair will mean that the patient suffers from hirsutism. The more colored hair will simply be more visible and may only give the impression of excess hair. Moreover, it is necessary to distinguish hirsutism from hypertrichosis. Hypertrichosis is excessive hair covering the entire skin surface or limited to certain areas of the skin, but is independent of excess androgens. It may occur in both men and women and is not limited to androgen-dependent areas. Moreover, hormonal disorders are not observed in hypertrichosis. It may be genetically determined or caused by medications taken by the patient, e.g. minoxidil or cyclosporine A. Hypertrichosis most often occurs on the arms and lower legs [25,26].

In order to undertake appropriate and effective therapy, a thorough and detailed family history must first be collected [16,27]. Information about the menstrual cycle should be collected and the presence of other related symptoms should be assessed using specific tests [24]. Hypertrichosis can be detected very often in the family history of women suffering

from hirsutism [16,27]. This is especially important in the case of PCOS or non-classical congenital adrenal hyperplasia (NC-CAH) if the family history of hirsutism is confirmed. It was found that if the mothers or sisters of the surveyed women suffered from PCOS, they were more likely to develop hirsutism (20-40%) compared to the rest of the population. Both women and men have a congenital skin sensitivity to androgens, and the presence of excessive hair growth in fathers and/or hirsutism in mothers may indicate the occurrence of hirsutism in daughters [28].

If a patient is suspected of having hirsutism, appropriate tests should be performed. First, it should be determined whether hirsutism occurs simultaneously with hyperandrogenism, and only at the next stage should the causes be determined [16]. The tests are performed in the morning, when the patient is in the follicular phase of the menstrual cycle, or after a gestagen test, when amenorrhea occurs or is infrequent [24]. First, diagnostic tests should determine the total testosterone concentration in the patient's serum in accordance with the guidelines of the American Endocrine Society of 2018 [29] and the concentration of DHEAS and 17-OH-progesterone (17-OHP). The further steps will depend on the results of the above-mentioned tests [24]. If we suspect the presence of Cushing's syndrome, the patient should be referred to an endocrinology clinic for accurate and specialized diagnosis. However, if the patient was treated at a dermatology clinic and was diagnosed with hyperandrogenism, the level of free testosterone, SHBG, thyroid-stimulating hormone (TSH) and glucose may be additionally tested, if justified [24]. If the patient is suspected of having PCOS, the concentration of luteinizing hormone (LH), FSH, SHBG, total testosterone should be determined and the LH/FSH ratio should be calculated, as well as the free androgen index (FAI) coefficient. Additionally, an ultrasound examination should be performed and the presence of metabolic disorders should be determined. Free Androgen Index is calculated as the quotient of total testosterone concentration in blood and SHBG $\times 100\%$. The correct value of the FAI coefficient should be lower than 5%. To determine the occurrence of metabolic disorders, a glucose tolerance test should be performed, the serum level of triglycerides should be assessed together with high density lipoproteins (HDL), low density lipoproteins (LDL), homeostatic model assessment (HOMA) coefficient. Oral glucose tolerance test (OGTT) must be done too. To exclude the presence of an adrenal or ovarian tumor, ultrasound, computer tomography or magnetic resonance imaging should be performed. However, if adrenal hyperplasia is suspected, an adrenocorticotropin (ACTH) test should be performed. If Cushing's syndrome is suspected, serum cortisol concentration should be measured and the amount of cortisol excreted in a daily urine collection [24] should be determined. In addition, trichoscopy may be helpful to confirm the presence of androgenetic alopecia in a suspected patient. In this test, the condition of the scalp is checked and the occipital area is compared with the frontal parietal area [30].

The Ferriman and Gallway scale is used to assess the severity of hirsutism. In the modified scheme, scores are established for 9 different areas and the points are counted. This method is particularly useful for recording the progress of therapy. It visually assesses the intensity of hair in 9 androgen-dependent regions: upper lip, chin, breasts, upper back, buttocks, middle part of the abdomen, lower abdomen, as well as on the arms and thighs. Hair intensity is assessed on a scale of 0-4 points.

Three forms of hirsutism were differentiated on the basis of this scale: mild with a score of 8-15; moderate for 16-25 points and severe for scores above 25 points [31].

Cebeci et al. conducted research on a group of 227 women suffering from hirsutism aged 18-45. The study determined the distribution and density of hair in 9 body regions. They determined that the chin, thighs, upper lip and lower abdomen were the areas whose scores were most important for the final result in the Turkish population. Taking into account the fact that the study group consisted only of people suffering from hirsutism and that less hair growth was observed in the upper abdomen, lower and upper back and upper arms, it can be concluded that these four mentioned body areas can be omitted in assessment using the Ferriman and Gallway scale in patients from Turkey. However, performing a hair examination on these body parts is not easy in conservative societies [32].

Idiopathic hirsutism is a type of hirsutism in which no major changes in testosterone and DHEAS concentrations are observed [33], and the women menstruate normally. It was found that in a large group of patients there were only mild androgenic disorders, in particular an increase in the action of androgens on the skin and hair follicles, which in turn resulted in increased sensitivity of the skin to androgens. Idiopathic hirsutism is a major psychological problem. As many women age, mild hirsutism may occur on the face and body. Even though it does not become dynamic, it is a serious problem for these women and is difficult to accept. Moreover, ethnic factors have a great influence here, because exactly the same hair for a Mexican woman will be natural and for a Swedish woman it will indicate the possibility of hirsutism [7].

Hirsutism is a chronic disorder and quite often recurs after discontinuation of treatment. Most often, drugs are used to reduce the effect of androgens on hair follicles or mechanical hair removal is used. First, the cause of hirsutism must be determined. If it is ovarian or adrenal tumors, surgical treatment is used. However, if the cause is different, we use anti-androgen drugs, even if idiopathic hirsutism is diagnosed. Unfortunately, the first effects of treatment can usually be observed only after a few months, which may discourage patients from taking medications [16]. The drugs most often prescribed to patients include cyproterone acetate with ethinyl estradiol or pure cyproterone acetate. Preparations containing spironolactone are also used quite often. In Europe, only one drug is registered for the local treatment of hirsutism. It is eflornithine in the form of cream. This medicine is almost unavailable in pharmacies, but it can be purchased on various websites, making it available to patients to a limited extent. However, women quite often prefer to use cosmetic treatments and mechanical methods of removing unwanted hair, which bring immediate results. Hair can be bleached or removed by depilation. Depilation methods, e.g. shaving with a razor, plucking hair with wax, are much cheaper than epilation treatments [34]. Although mechanical hair removal treatments provide only a short-term improvement effect, they bring the desired, beneficial and quick cosmetic effect. If the patient has minimal hirsutism, bleaching and epilating unwanted hair may be sufficient. Preparations containing hydrogen peroxide are most often used for whitening, but using it for too long may lead to irritation. When it comes to shaving, this is a safer method and will not cause hirsutism to worsen. However, on the other hand, it can cause inflammation of hair follicles. Epilation treatment involves removing the hair bulb, which extends

the hair regrowth time. This treatment can be performed using waxing, sugaring, electrolysis, electrocoagulation, blend method, laser method, ultrasound, threading and also using electric epilators [35].

AIM

The aim of the study was to identify the new therapeutic and skincare products used in hirsutism and hypertrichosis available on the Polish market considered representative for Central Europe inhabited by quite homogenous Caucasian population.

MATERIAL AND METHODS

In 2022 and 2023, therapeutic and skincare products used in hirsutism and hypertrichosis available in 10 randomly selected pharmacies and 10 drugstores in the Lubelskie Voivodeship in Poland were analyzed.

RESULTS AND DISCUSSION

Together 53 therapeutic and skincare products used in hirsutism and hypertrichosis were found and listed in the table (Table 1). The therapeutic products were available with doctor's prescription only (Rp.), while the -skincare products were available without prescription, like cosmetics.

Analyzing the preparations for hirsutism available on the Polish market, over 50 products were found. Of these, 29 were in the prescription drugs category and 24 in the skincare product category. This means that as many as 54.72% of the found preparations had the Rp marking. However, the search did not find any dietary supplements or OTC drugs used in hirsutism.

Among the collected preparations for hirsutism, most were in the form of tablets – as many as 39.62% of all preparations collected. The next quite frequently used forms are foams – 16.98% and creams – 9.43%. The fewest preparations were in the form of capsules, mousses, pastes or sticks – only 1.89% each.

There were 29 preparations containing active substances. The most common active substance in the analyzed preparations is dienogest. It is found in 20.69% of preparations containing the active substance and in 11.32% of all the analyzed preparations. Another quite common active substance is cyproterone acetate, found in 17.24% of preparations containing one of the listed active substances and in 9.34% of all the combined preparations. However, leuprorelin, clomiphene citrate, eflornithine and urofollitropin occurred least frequently in the analyzed preparations – each in 3.54% of preparations containing the active substance among those listed and in 1.89% of all preparations.

Unwanted hair growth can be devastating for the patient, so he or she seeks various treatment methods. The simplest and most popular method is depilation, which removes hair from the skin using chemicals. However, this is only a temporary effect. Additionally, depilation may cause skin allergies, skin burns and even lead to increased hair growth [36]. Bleaching products are often ineffective on dark hair and may irritate the skin. Electrolysis is a very effective treatment, but it is expensive and time-consuming – currently it has been largely replaced by laser techniques [37].

In this analysis of preparations, almost half of the collected products were used for hair removal. This shows how popular

these products are. However, due to the fact that the effect is only temporary, such treatments must be repeated often, which is burdensome for patients. Therefore, discovering new, safe methods of treating hirsutism is of great importance, due to the expensive electrolysis and photoepilation treatments, as well as the serious side effects of oral therapies [36].

The drugs most often prescribed to patients suffering from hirsutism are contraceptives. These preparations inhibit circulating LH and FSH, thereby reducing the production of androgens by the ovaries [37,38]. Recommended contraceptives most often contain cyproterone acetate, drospirenone or dienogest. These are anti-androgen substances. They should not be used in women suffering from migraine headaches, systemic lupus erythematosus or embolism. Although they are the most frequently used agents, especially at the beginning of treatment, they have many side effects, such as: decreased libido, breast pain, nausea, weight gain or depression. Fuchs et al. conducted a study comparing the effect of various anti-androgen contraceptives on hirsutism. They concluded that cyproterone acetate and drospirenone will be the best for patients suffering from both PCOS and hirsutism. The selection of the appropriate drug should depend on the patient's symptoms because each agent has a different effect on different hairy areas of the body [39]. Additionally, a review of studies examining the combination of metformin with the oral contraceptive pill (OCP) was conducted. It was found that the combination of metformin and OCP is more effective in the treatment of hirsutism in adult women with PCOS than metformin and OCP alone [40].

Other frequently used androgen receptor antagonists are: cyproterone acetate, flutamide, spironolactone and finasteride [38]. Mūderris et al. conducted a study on the effectiveness of the lowest dose of flutamide at the dose of 62.5 mg/day. They showed that flutamide at the lowest dose is as effective as 250 mg/day. Moreover, they confirmed that a dose of 65 mg of flutamide would reduce the hair growth score according to the Ferriman-Gallway scale both after 6 and 12 months, without the need for additional hair removal. When using doses of 250 mg or 65.5 mg, no serious side effects were observed. Additionally, it was confirmed that flutamide does not affect the hormonal balance [41]. Castelo-Branco et al. tested the safety and tolerability of flutamide in long-term therapy. They conducted a study on 83 patients with hirsutism for 84 months. Patients received a dose of 250 mg/day, and sexually active people additionally took contraceptive pills. They confirmed the effectiveness of flutamide in the treatment of hirsutism, but also observed a multiple relationship between the occurrence of side effects and non-compliance with therapeutic recommendations. Patients most often reported abdominal pain, flatulence, diarrhea, dry skin and headaches [42].

According to a review by van Zuuren, flutamide was found to be more effective than placebo by both physicians and patients when compared with all the other antiandrogen drugs [43].

Cyproterone acetate (CPA) is a substance with progestogen and anti-androgen properties. It inhibits the release of LH and also blocks the binding of androgens to their receptors. CPA reduces the diameter and density of hair in patients with idiopathic hirsutism. It is used alone or in combination with estrogens in Europe, but not in the United States. Franco Lumachi conducted a study in which he administered cyproterone acetate to patients in the form of contraceptive pills.

TABLE 1. Therapeutic and skincare products used in hirsutism and hypertrichosis available on Polish market.

No.	Name	Formulation	Category: therapeutic (T), skincare (S)	Ingredients	Manufacturer
1	Alexya hair growth blocker	Cream-gel	S	Aqua, Glycerin, Carthamus Tinctorium oil, Butylene Glycol, Phenoxyethanol/caprylyl glycol, Sorbitan Caprylate, Panthenol, Acrylates/C10-C30 Alkyl Acrylate Crosspolymer, Dihydromyricetin, Tocopheryl acetate, Sodium Hydroxide, BHA, Spironolactone, rice starch,	Alexya
2	SPIRONOL 25 mg	tablets	T	Lactose monohydrate, sodium lauryl sulfate, talc	GEDEON RICHTER POLSKA
3	Verospiron, 50 mg	capsules	T	Spironolactone, sodium lauryl sulfate, magnesium stearate, corn starch, lactose monohydrate, quinoline yellow, Titanium dioxide, gelatin	GEDEON RICHTER POLSKA
4	Finospir 25 mg	tablets	T	Spironolactone, lactose monohydrate Corn starch, povidone, po lisorbate 80, peppermint oil, Anhydrous colloidal silica, magnesium stearate, Flutamide, magnesium theearate, colloidal anhydrous silica,	Orion corporation/ Orion OYJ,
5	Apo-Flutam 250 mg	tablets	T	lactose monohydrate, Cellulose microcrystalline, Croscarmellose sodium	Aurovitas Pharma Polska Sp.z o.o.
6	Flutamid EGIS	tablets	T	Flutamide, potato starch, lactose monohydrate, Microcrystalline cellulose, Polyvinylpyrrolidone, sodium lauryl sulfate, magnesium stearate, colloidal anhydrous silica	EGIS
7	Vaniqa (11,5%)	cream	T	Eflornithine, cetostearyl alcohol, macrogol cetostearyl ether, dimethicone, glyceryl stearate, macrogol stearate, methyl p-hydroxybenzoate paraffin oil, phenoxyethanol, propyl parahydroxybenzoate (E216), purified water and stearyl alcohol	Almirall
8	Eligard 7,5mg	powder and solvent for preparing solution for injection	T	Leuprorelin acetate, poly(DL-lactate-co-glycolic acid) (50:50) N-methylpyrrolidone	Recordati Polska
9	Leuprostin, 5 mg	Subcutaneous implant	T	Leuprorelin, polylactic acid	SANDOZ
10	Librexa	Subcutaneous implant	T	Leuprorelin acetate, DL copolymer of lactide and glycolide (1:1) DL-lactide polymer	Lek-AM
11	Clostilbegyt 50mg	tablet	T	clomiphene citrate, gelatin, magnesium stearate, stearic acid, talc, potato starch, lactose monohydrate Menotropin, lactose monohydrate, polysorbate 20, sodium hydroxide, hydrochloric acid, sodium chloride, water for injection, hydrochloric acid 10%	EGIS
12	Menopur 75j.m	powder and solvent for solution for injection	T	Menotropin, lactose monohydrate, 0.9% sodium chloride solution	FERRING GmbH
13	Mensinorm 75 j.j.	powder and solvent for solution for injection	T	Urofollitropin, lactose monohydrate, water for injection, sodium chloride	Imed/IBSA
14	Fostimon, 75 j.m	powder and solvent for solution for injection	T	Dexamethasone, lactose monohydrate, pregelatinized starch, corn anhydrous colloidal silica, magnesium stearate	IBSA FARMACEUTICI ITALIA S.R.L
15	Dexamethasone Krka 0,5mg	tabletsi	T	Dexamethasone, lactose monohydrate, potato starch, Gelatine, magnesium stearate	Krka
16	Pabi-Dexamethason 1mg	tablets	T	Dexamethasone, lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate	Adamed
17	Demezón 1 mg	tabletsi	T		Sun-Farm

cont. TABLE 1. Therapeutic and skincare products used in hirsutism and hypertrichosis available on Polish market.

No.	Name	Formulation	Category: therapeutic (T), skincare (S)	Ingredients	Manufacturer
18	Androcur 50mg	tabletski	T	cyproterone acetate, lactose monohydrate, corn starch, povidone K 25, colloidal anhydrous silica,	BAYER PHARMA AG
19	Diane-35	Tablets	T	magnesium stearate cyproterone acetate,	BAYER PHARMA AG
20	Syndi-35	Tablets	T	ethinylestradiol	SYMPHAR
21	OC-35	Tablets	T	cyproterone acetate ethinylestradiol	POLFARMEX
22	Cyprodiol	Tablets	T	cyproterone acetate ethinylestradiol	SUN FARM
23	Bonadea	Tablets	T	Dienogest, etinyloestradiol	Zentiva
24	Jeanine	Tablets	T	Dienogest, etinyloestradiol	BAYER PHARMA AG
25	Face & Body shaving cream	shaving cream	S	Aqua, Triethanolamine, stearic acid, palmatic acid, isobutane, PEG-40 hydrigenated castor oil, propylene glycol, PEG-7 glyceryl cocoate, pro- pane, panthenol, butane, bisabolol, tocopheryl acetate, citric acid.	Saffee
26	L'ORÉAL PARIS MEN EXPERT Hydra Sensitive	shaving cream	S	Aqua, Stearic Acid, Triethanolamine, Palmitic Acid, Glycerin, Isobutane, Polysorbate 20, Cocamide Mea, Sodium Chloride, Trideceth-9 PG- Amodimethicone, Trideceth-12, Dimethiconol Stearate, Propane, Aloe Barbadensis Leaf Juice, Parfum, Myristic Acid, Butane, Cetyl Hydroxy- ethyl Cellulose, Lauryl Betaine.	L'Oréal Polska Sp. z o.o.
27	GILLETTE Series Conditioning shaving cream	shaving cream	S	Aqua, Triethanolamine, Palmitic Acid, Stearic Acid, Isobutane, Lau- reth-23, Isopropyl Isostearate, Dimethicone, Sodium Lauryl Sulfate, Pro- pane, Parfum, Sodium Benzoate, Hydroxyethylcellulose, Stearyl Alcohol, Lauryl Alcohol, Dimethiconol, Chondrus Crispus Powder, Dimethicone PEG/PPG-20/23 Benzoate, DMDM Hydantoin, Myristyl Alcohol, Benzyl Salicylate, Coceth-7, PPG-1-PEG-9 Lauryl Glycol Ether, Limonene, BHT, Theobroma Cacao Seed Butter, PEG-40 Hydrogenated Castor Oil, Cetyl Alcohol, Iodopropynyl Butylcarbamate.	Procter and Gamble DS Polska Sp. z o.o.
28	NIVEA MEN shaving cream	shaving cream	S	Aqua, Isobutane, Laureth-23, Triethanolamine, Palmitic Acid, Stearic Acid, Glycerin, Cannabis Sativa Seed Oil, Helianthus Annuus Seed Oil, Tocopheryl Acetate, Propylene Glycol, Sorbitol, Coco-Caprylate/Capr- ate, Hydroxypropyl Methylcellulose, PEG-7M, Myristic Acid, Arachidic Acid, Oleic Acid, Potassium Hydroxide, Butane, Propane, Silica, BHT, Piroctone Olamine, Parfum	NIVEA Polska Sp. z o.o. Grupa Beiers- dorf
29	BOND Inspired by Whisky shaving cream	shaving cream	S	Aqua, Triethanolamine, Palmitic Acid Butane, PEG-12 Dimethicone, Glycerin, Propane, Stearic Acid, Laureth-23, PEG-75 Lanolin, PEG-7 Glyceryl Cocoate, Isobutane, Parfum, Allantoin, Ca.eine, Xanthan Gum, Quercus Petraea Bark Extract, Sodium Benzoate, Potassium Sorbate, Benzyl Salicylate	Pharma CF Sp. z o.o
30	ISANA MEN shaving cream	shaving cream	S	Aqua, Glycerin, Triethanolamine, Stearic Acid, Palmitic Acid, Butane, Laureth-23, Propane, Aloe Barbadensis Leaf Juice, Sodium Laureth Sulfate, Parfum, Phenoxyethanol	Rossmann SDP Sp. z o.o.,
31	TOLPA dermo men face & hair gel-foam 2in1	shaving cream	S	Aqua, Disodium Cocoamphodiacetate, Cocamidopropyl Betaine, Lauryl Glucoside, Sodium Chloride, Lactic Acid, Parfum, Cannabis Sativa Seed Oil, Panthenol, Urea, Glycerin, Aesculus Hippocastanum Seed Extract, Peat Extract, Sodium Lactate, Glycol Distearate, Coco-Glucoside, Glyceryl Stearate, Glyceryl Oleate, Alcohol Denat., Salicylic Acid, Citric Acid, Benzoic Acid, Methylpropanediol, Sorbic Acid, Benzyl Alcohol, Caprylyl Glycol	Torf Corporation Sp. z o.o.,
32	NIVEA MEN Sensitive	shaving cream	S	Aqua, Palmitic Acid, Stearic Acid, Cocos Nucifera Oil, Potassium Hydroxide, Glycerin, Olea Europaea Fruit Oil, Dimethicone, Maris Sal, Chamomilla Recutita Flower Extract, Hamamelis Virginiana Bark/Leaf Extract, Caprylic/Capric Triglyceride, Maltodextrin, Cetearyl Alcohol, Myristic Acid, Arachidic Acid, Oleic Acid, Sodium Hydroxide, Parfum	NIVEA Polska Sp. z o.o. Grupa Beiers- dorf,
33	LIDER Classic shaving cream	shaving cream	S	Aqua, Stearic Acid, Potassium Hydroxide, Cocos Nucifera Oil, Sorbitol, Sodium Hydroxide, Parfum, Cellulose Gum, Sodium Metasilicate, Amyl Cin- namal, Benzyl Salicylate, Citronellol, Limonene, Linalool, CI 19140, CI 42090 Sodium palmate, Sodium palm kernelate, Aqua (Water), Glycerin, Sodium cocoate, Glycine soja (Soybean) oil, Limonene, Parfum (Fragrance)*, Camelina sativa seed oil, Caprylic/capric triglyceride, Sodium chloride, Tet- rasodium glutamate diacetate, Glucomannan, Linalool, Coconut fatty acid, Aloe barbadensis leaf extract, Camellia sinensis (Green tea) leaf extract	Miraculum S.A.
34	BULLDOG Original	Shaving soap	S	Aqua, Glycerin, Sodium Cocoyl Isethionate, Coco-Glucoside, Sorbitol, Diso- dium Lauryl Sulfosuccinate, Niacinamide, Sodium Chloride, Butyrosper- mum Parkii Butter, Persea Gratissima Oil, Betula Alba Juice, Persea Gratis- sima Fruit Extract, Olea Europaea Fruit Oil, Ascorbyl Palmitate, Tocopheryl Acetate, Citric Acid, Dehydroacetic Acid, Parfum, Phytosterols, Propanediol, Sorbitan Oleate, Sodium Benzoate, Potassium Sorbate, Benzyl Alcohol	Bulldog Skincare For Men
35	FLUFF sooth- ing shaving mousse, avocado and niacinamide	Mousse	S	Aqua, Glycerin, Sodium Cocoyl Isethionate, Coco-Glucoside, Sorbitol, Diso- dium Lauryl Sulfosuccinate, Niacinamide, Sodium Chloride, Butyrosper- mum Parkii Butter, Persea Gratissima Oil, Betula Alba Juice, Persea Gratis- sima Fruit Extract, Olea Europaea Fruit Oil, Ascorbyl Palmitate, Tocopheryl Acetate, Citric Acid, Dehydroacetic Acid, Parfum, Phytosterols, Propanediol, Sorbitan Oleate, Sodium Benzoate, Potassium Sorbate, Benzyl Alcohol	Nacomi Group Sp. z o.o

cont. TABLE 1. Therapeutic and skincare products used in hirsutism and hypertrichosis available on Polish market.

No.	Name	Formulation	Category: therapeutic (T), skincare (S)	Ingredients	Manufacturer
36	GILLETTE VENUS Satin Care Dry Skin shaving cream	shaving cream	S	Aqua, Glycerin, Palmitic Acid, Triethanolamine, Isopentane, Glyceryl Oleate, Stearic Acid, Isobutane, Sorbitol, Parfum, Hydroxyethylcellulose, PEG-90M, PEG-23M, Myristic Acid, Linalool, BHT, Benzyl Salicylate, Lauric Acid, Limonene, Butyrospermum Parkii Butter Extract, Silica, CI 42090	Procter and Gamble DS Polska Sp. z o.o
37	JOANNA shaving gel for women with honey melon extract	shaving gel	S	Aqua, Palmitic Acid, Triethanolamine, Oleth-20, Isopentane, Parfum, Sorbitol, Propylene Glycol, Paraffinum Liquidum, Hydrogenated Polyisobutene, Isobutane, Phenoxyethanol, Glycerin, Hydroxyethylcellulose, BHT, Ethylhexylglycerin, PEG-14M, Cucumis Melo Juice, Butane, Propane, Citric Acid, Sodium Benzoate, Potassium Sorbate, CI 42090, CI 47005, Hexyl Cinnamal, Coumarin, Linalool	Laboratorium Kosmetyczne Joanna Sp. j. B. Górka, R. Korczak Mościcka
38	V shaving gel without water ENUS	shaving gel	S	Aqua, Glycerin, PEG-12 Dimethicone, Betainę, Phenoxyethanol, Parfum, Acrylates/C10-30 Alkyl Acrylate Crosspolymer, PEG-40 Hydrogenated Castor Oil, Butylene Glycol, Theobroma Cacao Shell Extract, Aingiber Oficinale Root Extract, Elettaria Cardamomum Seed Extract, Piper Nigrum Seed Extract, Panthenol, Ethylhexylglycerin, Sodium Hydroxide, CI 42090	PharmaCF Sp. z o. o.
39	NIVEA MEN Sensitive cool- ing shaving foam for men	Shaving cream	S	Aqua, TEA-Stearate, Isobutane, Laureth-23, Glycerin, Chamomilla Recutita Flower Extract, Fucus Vesiculosus Extract, Maltodextrin, Caprylic/Capric Triglyceride, Coco-Caprylate/Caprate, Hydroxypropyl Methylcellulose, PEG-7M, Potassium Stearate, Butane, Propane, Piroctone Olamine, Linalool, Parfum, CI 42053	NIVEA Polska Sp. z o.o. Grupa Beiers- dorf,
40	VENUS Pro-Sensitive soothing shaving foam with aloe and D-panthenol	Shaving cream	S	Aqua, Triethanolamine, Palmitic Acid, Butane, Glycerin, Propane, Stearic Acid, Laureth-23, PEG-75 Lanolin, PEG-7 Glyceryl Cocoate, Isobutane, Parfum, Aloe Barbadensis Leaf Juice, Panthenol, Boswellia Serrata Gum, Xanthan Gum, Dipropylene Glycol, Sodium Benzoate, Potassium Sorbate	PharmaCF Sp. z o.o
41	BIELENDA Vanity Soft Expert shaving soap with aloe leaf juice	soap	S	Aqua (Water), Stearic Acid, Ethylhexyl Stearate, Glycerin, Cocamidopropyl Betaine, Glyceryl Stearate, Cocos Nucifera (Coconut) Oil, Aloe Barbadensis Leaf Juice Powder, Panthenol, Allantoin, Sodium Hyaluronate, Sodium Chloride, Potassium Hydroxide, Xanthan Gum, Disodium EDTA, Phenoxyethanol, Ethylhexylglycerin, Parfum (Fragrance), CI 19140, CI 42090	Bielenda Kosmetyki Naturalne Sp. z o.o
42	BIELENDA Vanity sugar creamy paste for depilation of armpits, bikini and legs	sugar creamy paste	S	Aqua (Water), Petrolatum, Cetearyl Alcohol, Thioglycolic Acid, Calcium Hydroxide, Cetareth-18, Glyceryl Stearate SE, Potassium Hydroxide, Glycerin, Sucrose, Mel Extract, Beeswax, Kaolin, Tocopheryl Acetate, Propylene Glycol, Disodium EDTA, Parfum (Fragrance), CI 19140.	Bielenda Kosmetyki Naturalne, Sp. z o.o
43	VENUS cream depilation stick	stick	S	Aqua (Water), Potassium Thioglycolate, Cetearyl Alcohol, Paraffinum Liquidum, Potassium Hydroxide, Steareth-21, Cetareth-20, Stearic Acid, Calcium Hydroxide, Palmitic Acid, Persea Gratissima Oil, Aloe Barbadensis Leaf Juice, Panthenol, Hydroxyethylcellulose, Parfum, Sodium Benzoate, Potassium Sorbate, Disodium EDTA, Linalool, Benzyl Alcohol, Benzyl Benzoate	PharmacCF Sp. z o.o.
44	VEET Minima depilatory strips	depilatory strips	S	Hydrogenated Styrene/Methyl Styrene/Indene Copolymer, Paraffinum Liquidum, Silica, Polyethylene, Pentaerythrityl Tetra-Di-t-Butyl Hydroxyhydrocinnamate. Chusteczki ingredients: Ingredients: Paraffinum Liquidum, Hexyldecyl Stearate, Parfum, Tocopheryl Acetate, Limonene.	Reckitt Benckiser (Poland) S.A
45	JOANNA Sen- sual facial de- pilation patches, gel formula	facial depilation patches	S	Hydrogenated Polydicyclopentadiene, Paraffinum Liquidum, Cera Microcristallina, Citrus Grandis Fruit Extract, Bambusa Arundinacea Stern Extract, Helianthus Annuus Seed Oil, Tocopheryl Acetate, PEG-8 Dioleate, Parfum, CI 77891, CI 42090, CI 47000	Laboratorium Kosme- tyczne Joanna Sp. j. B. Górka, R. Korczak, Mościcka
46	ISANA wax strips for body depilation	strips for body depilation	S	Triethylene Glycol Rosinate, Glyceryl Rosinate, Hydrogenated Microrystalline Wax, Aloe Barbadensis Leaf Juice, Vitis Vinifera Seed Oil, Ricinus Communis Seed Oil, Caprylic/ Capric Triglyceride, Parfum, CI 77891, CI 75470	Rossmann SPD Sp. Z.o.o.
47	JOLEN HAIR BLEACH HAIR LIGHT- ENER FOR FACE, BODY AND EYE- BROWS	cream	S	Cream Contains: Water, Hydrogen Peroxide, Glyceryl Stearate, Isopropyl Myristate, Stearyl Stearate, Propylene Glycol, Stearic Acid, Stearamidopropyl Dimethylamine, Phosphoric Acid, Accelerator Contains: Ammonium Bicarbonate	Jolen
48	Atywia Daily	tablets	T	Etynylestradiol + Dienogest	EXELTIS POLAND SP.Z O.O
49	Aidee	tablets	T	Etynylestradiol + Dienogest	Symphar Sp.z o.o.
50	Dionelle	tablets	T	Etynylestradiol + Dienogest	DR. KADE Pharmazeutische Fabrik GmbH.
51	Dorin	tablets	T	etynyloestradiol dienogest	SUN FARM
52	Vibin mini	tablets	T	etynyloestradiol drospirenon	POLPHARMA S.A.
53	Yasminelle	tablets	T	etynyloestradiol drospirenon	BAYER SCHERING PHARMA AG

He showed that different doses of CPA reduced hair growth scores. Moreover, it was shown that the administration of CPA in combination with estrogen was more effective than the administration of finasteride in the treatment of hirsutism, resulting in a 60% and 40% reduction in the Ferriman-Gallwey scale score, respectively. However, when taking OCP with cyproterone acetate, the risk of thromboembolism is higher than in women taking levonorgestrel [44].

Spironolactone is a competitive aldosterone antagonist and has been primarily used as a diuretic and blood pressure lowering drug. However, it has also anti-androgenic effects because it competes with testosterone and DHT for binding to the receptor. Spironolactone at a dose of 100 mg/day was more effective compared to placebo. Its effectiveness has also been confirmed as monotherapy and in combination with OCP. However, monotherapy has been found to be less effective than combination therapy [45]. Spironolactone is often used in women for whom OCP alone is ineffective. Additionally, combining spironolactone with OCP may reduce the occurrence of irregular uterine bleeding that may occur with spironolactone monotherapy. Erenus et al. showed that cyproterone acetate in combination with spironolactone was as effective as the combination of cyproterone acetate with estrogens. Moreover, a greater reduction in the Ferriman-Gallwey score was achieved with spironolactone (42.4%) than with finasteride (15.5%) after 9 months of therapy. However, after 6 months of therapy, the result was similar – 33.1% for finasteride and 29.6% for spironolactone [44]. Spironolactone may adversely affect the lipid profile. It causes an increase in LDL and a decrease in HDL. Nakhjavani conducted a study in which he examined the effect of spironolactone on the blood lipid profile. He stated that a dose of 100 mg of spironolactone may have an adverse effect on the lipids of women with hirsutism and caution should be exercised in women with metabolic disorders, e.g. dyslipidemia [46].

Finasteride is a type 2 5-alpha reductase inhibitor. It thus inhibits the conversion of testosterone to dihydrotestosterone (DHT), a stimulant of scalp hair loss and increased body hair growth [47]. Finasteride reduced the severity of hirsutism on the Ferriman-Gallwey scale by 26-60% in patients treated for 6-12 months [44]. Sahin et al. conducted an observer-blind study comparing the effects of cyproterone acetate and estrogen or cyproterone acetate and estrogen in combination with finasteride (5 mg). The cyproterone acetate and estrogen. It was found that after 12 months, the combination of cyproterone acetate and estrogen and finasteride resulted in a greater reduction in hirsutism score than cyproterone acetate and estrogen. This combination therapy reduced the level of androgens of both glandular and peripheral origin and inhibited the enzyme 5-alpha-reductase [48]. A study was also conducted, in which women with hirsutism received topical finasteride cream (0.5%) on half of their faces and a placebo on the other half. It was found that in the place where finasteride cream was applied, the thickness and number of hairs were lower than in the case of placebo. The effect of finasteride 0.5% cream on diode laser therapy was tested. Finasteride in combination with laser therapy has been found to be beneficial in the healing process. Combination therapy can delay hair regrowth between laser treatments and shorten the duration of laser therapy [49]. Additionally, a study was conducted to evaluate the effect of finasteride at a dose of 2.5 mg/day and 5 mg/day. During 10 months of therapy, intermittent use of 2.5 mg of

finasteride appears to have the same effect as continuous administration of the same dose, but with fewer side effects. Side effects, such as dry skin, decreased libido or gastrointestinal disorders, were stronger at a dose of 5 mg/day than at a dose of 2.5 mg/day. However, it cannot be clearly stated whether finasteride is equally effective when administered regularly, intermittent or in lower doses because the study was not very long and the number of participants was small [47].

Eflornithine was once used as an anticancer drug and to treat African sleeping sickness. However, it has been noticed that patients lose hair during therapy. As a result of this discovery, research was conducted to obtain a form suitable for local use. Since 2000, eflornithine has been recognized by the Food and Drug Administration as a topical treatment for hirsutism. Eflornithine is an ornithine decarboxylase inhibitor, which inhibits the synthesis of ingredients necessary for hair growth. It is used in the form of 11.5% Vaniqa cream. Unfortunately, discontinuation of the preparation most often results in the return of unwanted hair, but with less hair density. The drug's effectiveness was tested on 596 patients. They received eflornithine or placebo twice a day for 24 weeks. In the group taking the active substance, hair thickness decreased by 26%, and in the placebo group by 5%. Moreover, it has been shown that the use of eflornithine during laser therapy will improve the effectiveness of laser therapy. However, eflornithine is still a little known substance in Poland and its high price may be a factor that severely limits its use [50]. Moreover, Vaniqa is difficult to find on the market, it is the easiest to find it on various websites, not necessarily pharmacies. This creates an additional risk of uncertain source of the preparation.

Acyclovir is a promising substance in the treatment of hirsutism. It is an antiviral drug used mainly in the treatment of herpes. Samei et al. conducted a study on female mice. A cream with or without acyclovir was applied to the shaved skin. An increase in hair growth time was observed in mice receiving acyclovir cream without any noticeable side effects such as redness or swelling. Acyclovir caused a reduction in the number of hair follicles and their diameter compared to the control group. This creates the possibility of using acyclovir as an additional agent in the treatment of hirsutism in the future [36].

Licorice also has potential use in the treatment of hirsutism. Various studies have shown that licorice inhibits androgen synthesis. It blocks the activity of 17-hydroxysteroid dehydrogenase and 17,20-lyase and affects the activity of 5-alpha- and 5-beta-aromatase. These are enzymes involved in the synthesis and metabolism of androgens. It was found that glycyrrhizic acid present in herbal products reduces testosterone levels and regulates ovulation. Taking into account the results obtained, licorice was proposed for the treatment of PCOS and hirsutism. However, Faghihi et al. conducted a study in which they found that adding licorice to laser hair removal therapy could improve its effectiveness in people with hirsutism [51].

Vitamin D may also have a significant impact on both hirsutism and PCOS. It has been found that women with PCOS are more likely to have vitamin D deficiencies. Calcium and vitamin D can directly reduce circulating androgens in the blood. Researchers showed that supplementation of vitamin D with calcium for 8 weeks resulted in a reduction in free testosterone and DHEAS compared to placebo. In addition, vitamin D influences the balance between androgens and estrogens [52]. Ostadmohammadi et al. conducted a study in which patients

randomly received 50,000 IU of vitamin D every 2 weeks and a probiotic every day or a placebo for 12 weeks. They found that combined administration of vitamin D with a probiotic for 12 weeks in women with PCOS improved their mental health, total testosterone and hirsutism. Hyperandrogenism is observed in the course of PCOS, which may cause hirsutism. It was found that probiotics can improve androgen levels by increasing insulin sensitivity and modulating intestinal microflora. Vitamin D, by influencing the activity of enzymes of the steroidogenic pathway, may reduce the concentration of total testosterone [53].

CONCLUSIONS

1. In the analyzed preparations for hirsutism, the most frequently used active substances are dienogest and cyproterone acetate.
2. The most commonly used form of drugs in hirsutism are tablets, and in hypertrichosis – foams that facilitate the removal of unwanted hair.
3. The new promising formulas for treatment of hirsutism and hypertrichosis contain eflornithine, acyclovir, licorice and vitamin D.

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