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Balancing Hormones and Skin Health: A Focus on Oral Contraceptives in Dermatology

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Abstract

Oral contraceptives (OCs) have gained significant importance in dermatology, particularly in the treatment of androgen-related skin conditions such as acne, hirsutism, and androgenetic alopecia. By regulating hormonal imbalances, OCs help reduce excess androgen levels that contribute to these dermatologic issues. The combination of ethinyl estradiol and various progestins, especially those with anti-androgenic properties like drospirenone and cyproterone acetate, has been proven effective in managing skin conditions by reducing sebum production, minimizing acne lesions, and controlling excessive hair growth. These benefits make OCs a popular choice for women with conditions like polycystic ovary syndrome (PCOS), where androgen excess is a central factor. Despite their efficacy, the use of OCs in dermatology must be carefully tailored to each patient, considering factors such as individual risk profiles and potential adverse effects. Side effects like venous thromboembolism, mood changes, and breakthrough bleeding can affect patient adherence and treatment outcomes. However, with ongoing advancements in OC formulations and personalized medicine, future therapies are expected to offer improved safety profiles and greater efficacy. As research continues, the role of OCs in dermatology will likely expand, providing more targeted and accessible treatment options for androgen-driven skin conditions, enhancing both clinical outcomes and patient satisfaction.

Keywords: Oral contraceptives, Dermatology, Adverse effects, Challenges

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Introduction

OCs, commonly known as birth control pills, are one of the most widely used methods of contraception globally [1]. First introduced in the 1960s, these pills revolutionized reproductive healthcare by giving women greater control over family planning and fertility [2]. The two primary types of OCs are combined OCs (COCs), which contain both estrogen and progestin, and progestin-only pills (POPs) [3]. COCs work by suppressing ovulation, thickening cervical mucus to block sperm, and altering the uterine lining to prevent implantation. POPs, commonly known as the "mini pill," are often recommended for women who cannot tolerate estrogen, such as those who are breastfeeding or have certain health conditions [3].

The benefits of OCs extend beyond preventing pregnancy. For instance, COCs are frequently prescribed to regulate menstrual cycles, alleviate symptoms of PCOS, and reduce the severity of premenstrual syndrome [4]. Moreover, studies have shown that long-term use of COCs can reduce the risk of ovarian and endometrial cancers by up to 50% [5]. However, OCs are not without risks. They can slightly increase the likelihood of developing blood clots, particularly in smokers and women over the age of 35 [6]. POPs have fewer associated risks but may cause irregular bleeding in some users. Despite these considerations, OCs remain a highly effective and convenient option for many women, with typical use resulting in a failure rate of around 7%, compared to nearly 20% for condoms [7].

Recent advances have led to more innovative formulations of OCs, with lower hormone doses to minimize side effects. For example, ultra-low-dose pills like Yaz and Loestrin are designed to reduce mood swings, nausea, and bloating often associated with traditional options [8]. Additionally, there is increasing attention on improving accessibility, such as over-the-counter availability and cost reduction initiatives. In low-income settings, expanding access to OCs has been shown to significantly reduce unintended pregnancies, contributing to better health outcomes and socioeconomic opportunities for women. The development and ongoing refinement of OCs underscore their pivotal role in advancing women's health and empowerment worldwide [9].

OCs and Dermatology

OCs, commonly referred to as birth control pills, have long been used as a reliable method of contraception, but they also play a significant role in dermatology [10]. These medications, especially COCs containing both estrogen and progestin, have been shown

to effectively address a variety of skin conditions, particularly those influenced by hormonal fluctuations [11]. Their use in dermatology is primarily focused on conditions like acne, hirsutism (excessive hair growth), and even certain aspects of aging skin (Table 1) [12, 13]. By regulating hormones that affect sebum production and skin inflammation, OCs offer a therapeutic option for women struggling with persistent skin issues [13].

Hormonal imbalances are a key contributor to skin problems like acne, which often arise due to overactive sebaceous glands driven by androgens such as testosterone [14]. By suppressing ovarian androgen production and increasing levels of sex hormone-binding globulin (SHBG), OCs can reduce circulating free testosterone levels [15]. This hormonal modulation decreases sebum production and inflammation, making OCs particularly effective for women with moderate to severe acne, including cases resistant to topical treatments [16]. Thus, OCs provide both contraceptive benefits and solutions for dermatological challenges, making them a multifaceted treatment option.

One of the most well-documented uses of OCs in dermatology is in the treatment of acne vulgaris, particularly in women with hormonally driven acne that worsens during the menstrual cycle [17]. Studies have demonstrated that certain COCs, such as those containing ethinyl estradiol with drospirenone (e.g., Yaz) or norgestimate (e.g., Ortho Tri Cyclen), can reduce inflammatory and non-inflammatory acne lesions by 40% to 70% after six months of use [18, 19]. These results are attributed to the reduction in sebum production, which is driven by the suppression of androgen activity. In contrast, POPs or contraceptives with androgenic progestins may not provide the same dermatological benefits, emphasizing the importance of selecting the right formulation for acne treatment [20].

In addition to acne, OCs can be used to manage hirsutism, a condition characterized by excessive hair growth in areas such as the face, chest, or back, typically due to elevated androgen levels [21]. OCs reduce the production of androgens and increase SHBG, which binds free androgens in the bloodstream [22]. This process lowers androgenic stimulation of hair follicles. A 2019 meta-analysis found that OCs improved hirsutism in women with PCOS by approximately 30% - 40% when used consistently over 6 to 12 months [23].

Literature also suggest that OCs may have secondary benefits for reducing seborrhea (excessive oily skin) and mitigating conditions like hormonal melasma [24]. Hormonal melasma is a form of hyperpigmentation often linked to estrogen and progesterone fluctuations. While melasma management with OCs is less consistent and may require adjunctive therapies, some studies have observed improvement in cases where hormonal regulation is achieved [25]. This makes OCs a versatile option for addressing multiple dermatological concerns, particularly those stemming from endocrine abnormalities [26].

OCs are a game-changer in dermatology, offering women a treatment option that goes beyond skin-deep benefits. For many women, managing chronic acne or other hormone-related skin issues can significantly improve self-esteem and quality of life [27]. By providing effective solutions for conditions like acne and hirsutism, OCs enable women to feel more confident in their skin. Additionally, their dual-purpose nature-providing both contraception and dermatological benefits-enhances convenience and cost-effectiveness for patients [28].

The future of OCs in dermatology is bright, with ongoing innovations focused on minimizing side effects while maximizing skin-related benefits. Ultra-low-dose formulations and new combinations of hormones are being developed to provide effective treatments with reduced risks of adverse effects like weight gain, mood swings, or nausea [29]. Furthermore, increased awareness among dermatologists and patients about the multifaceted benefits of OCs ensures that more women can access treatments tailored to their needs. As a cornerstone of hormone-based dermatological care, OCs continue to empower women by offering healthier skin and improved well-being.

Choice of OCs Based on Dermatology Needs

The selection of OCs in dermatology is highly individualized and depends on the specific skin condition being treated, the patient's hormonal profile, underlying health risks, and tolerance for potential adverse effects [30]. Conditions such as acne, hirsutism, androgenetic alopecia, and seborrhea are closely tied to androgen activity, making anti-androgenic or low-androgenic OCs the most suitable options (Table 2) [31]. The dermatologic benefits of OCs stem from their ability to modulate hormonal imbalances, suppress androgen levels, and regulate sebaceous gland activity [32]. However, careful consideration of the patient's overall health and lifestyle is crucial to selecting the right formulation.

For patients with acne, especially moderate to severe forms, COCs containing ethinyl estradiol and anti-androgenic progestins like drospirenone or cyproterone acetate are often preferred [19]. These progestins block androgen receptors and reduce sebaceous

Table 1: Need for OCs in dermatology.

Dermatological condition	Need for OCs	Role of OCs	Benefits
Acne	Acne is often exacerbated by excess androgens, leading to increased sebum production and clogged pores	OCs containing anti-androgenic progestins (e.g., drospirenone, cyproterone acetate) reduce androgen levels, thus controlling sebum production and acne lesions	Reduces inflammatory and non-inflammatory acne lesions. Improves skin texture and reduces acne severity
Hirsutism	Excessive hair growth in women in androgen-sensitive areas like the face, chest, and back due to elevated androgen levels	Anti-androgenic progestins in OCs block androgen receptors, reducing hair growth in unwanted areas	Slows down excessive hair growth, improves the appearance of facial and body hair
Androgenetic alopecia	Hair thinning and loss caused by androgens leading to miniaturization of hair follicles	OCs help lower free testosterone levels, which prevents hair follicle miniaturization and reduces hair loss	Slows hair loss and may stimulate hair regrowth, particularly in women with androgenic alopecia
PCOS	PCOS often results in hormonal imbalances, including elevated testosterone, causing acne, hirsutism, and hair thinning	OCs regulate hormonal levels, suppress ovulation, and reduce androgen production, addressing the underlying causes of acne and hirsutism	Helps manage multiple symptoms of PCOS, including acne, hirsutism, and irregular menstrual cycles
Seborrhea (Oily skin)	Overproduction of sebum caused by elevated androgen levels can contribute to oily skin and acne	OCs containing anti-androgenic agents regulate sebum production and reduce skin oiliness	Reduces excessive oiliness and helps improve skin appearance, particularly in those prone to acne

Table 2: Choice of OCs based on specific dermatology need.

Dermatological condition	Preferred OC	Progestin(s) used	Mechanism of action
Acne	Yaz, Yasmin, Diane-35, Ortho Tri Cyclen	Drospirenone, Cyproterone acetate, Norgestimate	Anti-androgenic progestins reduce sebum production and acne lesions
Hirsutism	Yaz, Yasmin, Diane-35, Ortho Tri Cyclen	Drospirenone, Cyproterone acetate, Norgestimate	Anti-androgenic progestins block androgen receptors and reduce hair growth
Androgenetic alopecia	Yaz, Yasmin, Diane-35, Ortho Tri Cyclen	Drospirenone, Cyproterone acetate, Norgestimate	Reduces free testosterone and DHT, preventing hair follicle miniaturization
PCOS	Diane-35, Yaz, Yasmin, Ortho Tri Cyclen	Drospirenone, Cyproterone acetate, Norgestimate	Regulates hormonal imbalance, reduces androgens, and restores menstrual cycles
Seborrhea (Oily skin)	Yaz, Yasmin, Ortho Tri Cyclen	Drospirenone, Norgestimate	Anti-androgenic effects decrease sebum production and skin oiliness
Mild acne (Less severe)	Mircette, Alesse	Desogestrel, Levonorgestrel	Low-androgenic progestins reduce androgen activity and sebum production

Table 3: Commercially available OCs.

Name	Dosage	Prescription indications	Common side effects
Yaz	3 mg drospirenone + 0.02 mg ethinyl estradiol	Acne, hirsutism, seborrhea, PCOS	Headaches, nausea, mood changes, weight gain, breast tenderness, increased potassium levels
Yasmin	3 mg drospirenone + 0.03 mg ethinyl estradiol	Acne, hirsutism, seborrhea, PCOS	Nausea, breast tenderness, headache, mood changes, elevated potassium levels
Diane-35	2 mg cyproterone acetate + 0.035 mg ethinyl estradiol	Acne, hirsutism, androgenic alopecia, PCOS.	Nausea, weight gain, mood changes, headaches, breakthrough bleeding, risk of blood clots (VTE)
Ortho Tri Cyclen	0.18 to 0.25 mg norgestimate + 0.035 mg ethinyl estradiol.	Acne, hirsutism	Headaches, nausea, mood swings, breakthrough bleeding, weight gain, increased risk of blood clots
Mircette	0.15 mg desogestrel + 0.02 mg ethinyl estradiol	Mild acne	Nausea, headaches, mood changes, breast tenderness, breakthrough bleeding
Alesse	0.1 mg levonorgestrel + 0.02 mg ethinyl estradiol	Mild acne	Nausea, weight gain, headaches, mood changes, breakthrough bleeding
Seasonale	0.15 mg levonorgestrel + 0.03 mg ethinyl estradiol	Acne, endometriosis, menstrual regulation	Nausea, headaches, breakthrough bleeding, breast tenderness, mood changes
Loestrin Fe 1/20	1 mg norethindrone acetate + 20 mcg ethinyl estradiol	Acne, menstrual regulation	Nausea, weight gain, headaches, mood changes, breakthrough bleeding
NuvaRing	0.12 mg etonogestrel + 0.015 mg ethinyl estradiol	Acne, menstrual regulation	Vaginal irritation, headaches, nausea, breast tenderness, increased risk of blood clots

gland stimulation, which helps in controlling both inflammatory and non-inflammatory acne lesions [33]. Studies have shown significant improvement in acne severity with these formulations within 3 to 6 months of use. For example, COCs like Yaz (drospirenone + ethinyl estradiol) and Diane-35 (cyproterone acetate + ethinyl estradiol) are specifically designed to counteract androgen excess, making them excellent choices for women who experience acne associated with PCOS or other androgen-driven conditions [34, 35].

In cases of hirsutism, where excessive terminal hair growth occurs in androgen-sensitive areas like the face or chest, progestins with potent anti-androgenic effects are ideal [36]. OCs like Diane-35 are commonly prescribed for this purpose, particularly in patients with PCOS, as they reduce free testosterone levels and slow the rate of hair growth [37]. For mild hirsutism, lower-dose anti-androgenic OCs such as those containing drospirenone (e.g., Yasmin) may also be effective [37]. Patients with androgenetic alopecia, characterized by hair thinning, benefit from the same formulations, as they counteract the androgen-mediated miniaturization of hair follicles [38].

For women with sensitive skin or milder forms of acne, low-androgenic progestins such as norgestimate (found in Ortho Tri Cyclen) or desogestrel (found in Mircette) may be sufficient [39]. These third-generation progestins provide a balance between effective androgen suppression and minimal side effects, such as mood changes or weight gain. However, women with oily skin or seborrhea may require stronger anti-androgenic options to reduce sebum production effectively. Conversely, second-generation progestins like levonorgestrel are generally avoided in dermatology due to their mild androgenic properties, which can worsen acne or oily skin in some individuals [40].

The choice of OC must also account for the patient's risk profile. Women with a higher risk of VTE, stroke, or cardiovascular disease may need alternative treatments, as certain progestins, such as drospirenone and cyproterone acetate, carry an increased risk of VTE compared to older formulations [41]. Similarly, lifestyle factors such as smoking or a history of migraines with aura further influence the selection process. Physicians must weigh the dermatologic benefits of each OC against its potential systemic risks, tailoring the choice to the patient's unique health needs.

In summary, the choice of OC in dermatology is driven by the nature and severity of the skin condition, the patient's hormonal and health profile, and their individual tolerance for potential side effects. Anti-androgenic OCs are typically preferred for androgen-driven conditions, while low-androgenic formulations may suffice for milder cases. By carefully balancing therapeutic efficacy and patient safety, dermatologists can optimize treatment outcomes and improve the quality of life for their patients.

Commercially Available OCs

OCs have proven to be valuable tools in managing dermatologic conditions influenced by androgens, such as acne, hirsutism, and androgenetic alopecia. Several formulations, each with unique properties, are used in dermatology (Table 3). These primarily include

COCs that contain ethinyl estradiol (a synthetic estrogen) combined with different progestins [42, 43]. The purpose, role, mechanism of action, properties, and adverse effects of commonly used OCs in dermatology are discussed below.

Ethinyl Estradiol + Drospirenone (e.g., Yaz, Yasmin)

This combination is widely used for treating moderate to severe acne and hirsutism. Drospirenone, a synthetic progestin, has anti-androgenic and anti-mineralocorticoid properties, making it effective in dermatology [44]. Drospirenone counteracts androgens by directly blocking androgen receptors in sebaceous glands, reducing sebum production and inflammatory acne lesions [45]. Estrogen (ethinyl estradiol) complements this action by increasing SHBG, which binds free testosterone, thereby lowering circulating androgen levels [46]. Properties are (i) Anti-Androgenic: Drospirenone is derived from spironolactone and reduces the effects of androgens on the skin, (ii) Anti-Mineralocorticoid: It has a mild diuretic effect, which reduces bloating and water retention, and (iii) Skin Benefits: Effective in reducing acne severity and androgen-dependent hair growth in hirsutism [45, 46].

While generally well-tolerated, drospirenone-containing OCs have a slightly higher risk of VTE compared to other progestins (10 cases per 10,000 women-years). Other side effects include nausea, breast tenderness, and mild potassium elevation in some individuals [47].

Ethinyl Estradiol + Norgestimate (e.g., Ortho Tri Cyclen)

Ortho Tri Cyclen is United States Food and Drug Administration approved for treating moderate acne in women seeking contraception [48]. Norgestimate is a third-generation progestin with low androgenic activity, making it particularly effective for dermatologic purposes. Norgestimate reduces sebaceous gland stimulation by minimizing androgen activity [49]. Ethinyl estradiol enhances this effect by increasing SHBG levels, reducing free testosterone and dihydrotestosterone [50]. Properties are (i) Low androgenic activity: Norgestimate minimizes androgen-mediated skin effects like sebum production and hair growth and (ii) Efficacy in acne: Studies have shown significant reductions in both inflammatory and non-inflammatory acne lesions within 3 to 6 months of use [49, 50].

Common side effects include headache, mood changes, and breakthrough bleeding. Although the risk of VTE is lower compared to drospirenone-containing pills, it is still present, particularly in smokers and women over 35 [50].

Ethinyl Estradiol + Cyproterone Acetate (e.g., Diane-35)

Diane-35 is particularly effective for severe acne, hirsutism, and androgen-dependent alopecia. It is often prescribed in women with PCOS, where androgen excess is a primary contributor to symptoms [51]. Cyproterone acetate, a potent anti-androgenic progestin, blocks androgen receptors and reduces androgen synthesis by inhibiting gonadotropin secretion [52]. It works synergistically with ethinyl estradiol to reduce sebaceous gland activity and excessive hair growth [52]. Properties are (i) Strong anti-androgen: Cyproterone acetate is one of the most effective progestins for managing androgen excess and (ii) Use in PCOS: Particularly beneficial in PCOS patients experiencing acne, hirsutism, and irregular cycles [52].

Side effects include weight gain, mood disturbances, and decreased libido. Additionally, this combination has been associated with an elevated risk of VTE (16 to 20 cases per 10,000 women-years), making it unsuitable for women with clotting disorders or significant cardiovascular risk factors [51, 52].

Ethinyl Estradiol + Levonorgestrel (e.g., Alesse)

While not specifically marketed for dermatologic conditions, Alesse can be used for acne treatment due to its ability to suppress ovarian androgens. However, its androgenic activity may limit its effectiveness compared to other formulations [53]. Levonorgestrel suppresses ovulation and reduces ovarian androgen production [54], while ethinyl estradiol increases SHBG levels to lower circulating androgens [46]. Properties are (i) Moderate androgenic activity: Levonorgestrel has mild androgenic effects compared to newer progestins, which may reduce its efficacy in treating acne and (ii) Contraceptive reliability: Alesse remains a popular contraceptive due to its long history of use and affordability [53].

Its androgenic properties may cause side effects such as acne flare-ups or worsening of seborrhea in some women. Additionally, VTE risk is present, though lower than with drospirenone or cyproterone acetate [53].

Ethinyl Estradiol + Desogestrel (e.g., Mircette)

Desogestrel is another third-generation progestin that has very low androgenic activity, making it effective for acne management [55]. Mircette is often prescribed for women who need contraception and desire a mild improvement in skin health [56]. Desogestrel reduces sebaceous gland stimulation by binding to androgen receptors with low affinity [55]. Ethinyl estradiol enhances androgen reduction by increasing SHBG levels [46]. Properties are (i) Low androgenic activity: Desogestrel provides a favorable balance for treating mild to moderate acne without exacerbating androgen-related symptoms and (ii) Efficacy: Studies have shown a reduction in acne lesions in women using desogestrel-based COCs within three months [55, 56].

As with other COCs, risks include breakthrough bleeding, nausea, and VTE. The risk of VTE with desogestrel is comparable to drospirenone-containing OCs [55, 56].

In summary, although the adverse effects vary slightly depending on the progestin used, common minor adverse effects include nausea, breast tenderness, mood changes, and breakthrough bleeding [57]. Major adverse effects, such as VTE, ischemic stroke, and myocardial infarction (MI), are rare but can be severe, particularly in smokers or women with underlying risk factors [58]. Additionally, certain progestins (e.g., levonorgestrel) may exacerbate androgenic symptoms in some women, while others (e.g., drospirenone and cyproterone acetate) are associated with higher VTE risks [59]. Each commercially available OC has unique properties that make it suitable for different dermatologic conditions. Anti-androgenic progestins like drospirenone and cyproterone acetate are ideal for severe acne and hirsutism, while low-androgenic formulations like norgestimate and desogestrel are effective for moderate acne. Levonorgestrel-based pills are less favored in dermatology due to their androgenic effects [60]. The choice of OC depends on the patient's specific dermatologic needs, risk factors, and tolerance for potential side effects.

General Adverse Effects of OCs

OCs, while widely used and generally safe, are associated with both minor and major adverse effects. These effects depend on the type of OCs (COCs or POPs), the hormonal composition, and individual patient factors such as age, smoking status, and pre-existing health conditions [57, 58]. Below is a detailed exploration of minor and major adverse effects, supported by statistical insights and examples.

Minor adverse effects

Minor adverse effects of OCs are common, particularly in the first few months of use, as the body adjusts to hormonal changes. These effects are usually mild and transient, but they can impact quality of life and adherence to the medication.

Nausea

Likely due to estrogen's effect on the gastrointestinal system. Approximately 10% to 30% of new OC users experience nausea. Symptoms typically resolve after 2 to 3 months of consistent use or can be alleviated by taking the pill with food or at bedtime [61].

Breast tenderness

Estrogen-induced fluid retention and stimulation of breast tissue. Reported in 20 - 25% users, especially with higher estrogen doses (>30 mcg ethinyl estradiol). Women taking OCs like Ortho Tri Cyclen may report sensitivity or discomfort in the breasts during the initial cycles [62].

Spotting/breakthrough bleeding

Irregular shedding of the endometrial lining due to hormonal fluctuations, particularly in low-dose estrogen pills or during the first 3 - 6 months of use. Occurs in 10 - 20% of users, higher in POPs due to their lack of estrogen. Continuous-use OCs like Seasonique, designed to reduce menstrual frequency, may cause spotting during extended cycles [63].

Headaches

Hormonal changes, particularly fluctuations in estrogen levels. Up to 10% of users report mild headaches. Symptoms may worsen for women with a history of migraines. Switching to lower-dose estrogen pills (e.g., 20 mcg formulations like Alesse) can often alleviate symptoms [64].

Mood changes and depression

Hormonal impact on serotonin regulation in the brain. A study found a 23% increased risk of antidepressant use in OC users, particularly adolescents. OCs containing drospirenone (e.g., Yaz), which have anti-androgenic properties, may stabilize mood in some women but worsen it in others [65].

Weight changes

Fluid retention from estrogen or changes in appetite regulation. Progestins with androgenic activity may promote weight gain by increasing muscle mass or fat distribution. Most studies indicate negligible weight changes, with <5% of users reporting noticeable effects [66].

Libido changes

Reduced free testosterone levels due to increased SHBG. Varies widely; some users report a decrease, while others experience improvement in libido due to reduced anxiety about pregnancy or hormonal regulation of mood [67].

Gastrointestinal upset

Hormonal effects on the gastrointestinal tract, such as delayed gastric emptying or increased sensitivity. Affects 5 to 10% of new users [68].

Major adverse effects

Major adverse effects of OCs, while rare, are clinically significant and require careful evaluation of patient history and risk factors. These effects are most strongly associated with the estrogen component and the type of progestin used.

Venous thromboembolism

VTE, which includes deep vein thrombosis and pulmonary embolism, is one of the most serious adverse effects of OCs [69]. The estrogen component in COCs is the main contributor, as it increases the production of clotting factors such as Factor VII, Factor VIII, and fibrinogen while reducing anticoagulants like protein S [70]. This shift toward a hypercoagulable state raises the risk of blood clots. The overall risk of VTE in COC users is estimated to be 3 - 9 cases per 10,000 women-years compared to 1 - 5 cases in non-users [71]. Risk increases with higher estrogen doses and certain progestins like drospirenone or desogestrel, which are associated with 2 - 3 times greater VTE risk compared to levonorgestrel-containing pills [72]. Additional factors such as smoking, obesity, prolonged immobility, or a genetic predisposition (e.g., Factor V Leiden mutation) amplify this risk [71]. Although the risk of VTE is substantially lower than during pregnancy (10 - 20 cases per 10,000 women-years), it remains a significant concern for COC users [73].

Cardiovascular events (stroke and MI)

Stroke and MI are other major adverse effects linked to COCs [74]. Estrogen promotes arterial thrombus formation through mechanisms such as increased platelet aggregation and arterial vasospasm, while progestins may adversely affect lipid metabolism and arterial health [75]. The risk of ischemic stroke is approximately 1.6 times higher than COC users compared to non-users. However, this risk is much higher in women with predisposing factors, such as hypertension, smoking, or migraines with aura. For example, women with migraines and aura who use COCs have a twofold increased risk of stroke compared to non-users. MI, while rare in younger, healthy women, is a significant concern in older users, especially smokers or those with diabetes or hyperlipidemia [76]. Among women over 35 years of age who smoke, the risk of MI is up to 10 times higher with COC use compared to non-users [76].

Hypertension

OCs are known to cause mild to moderate elevations in blood pressure in some users [77]. Estrogen in COCs increases the activity of the renin-angiotensin-aldosterone system, leading to sodium and water retention, which raises blood pressure [78]. While most cases involve mild increases, about 1 - 5% of users may develop clinically significant hypertension, particularly in those with a pre-existing predisposition to elevated blood pressure [79]. This effect is dose-dependent, with higher estrogen doses (>50 mcg) historically associated with greater risk. Modern low-dose COCs (20 - 30 mcg of ethinyl estradiol) have reduced this risk, but regular monitoring of blood pressure is recommended, especially in women with a family history of hypertension or cardiovascular disease [80, 81].

Breast cancer risk

The relationship between OCs and breast cancer is complex and controversial [82]. Current or recent COC use has been associated with a slight increase in breast cancer risk, likely due to the mitogenic effects of estrogen and progestins on breast tissue [83]. A 2017 study published

in The New England Journal of Medicine found that COC users have a 20% higher relative risk of developing breast cancer compared to non-users. However, the absolute risk remains low, with approximately 13 additional cases per 100,000 women-years of use [84]. The risk appears to decline after discontinuation, normalizing within 10 years. Women with a strong family history of breast cancer or known genetic mutations (e.g., BRCA1/BRCA2) may be more susceptible and should weigh the risks and benefits carefully with their healthcare provider [85].

Hepatic effects (liver tumors and gallbladder disease)

COCs can have adverse effects on the liver, particularly with long-term use. Estrogen increases the risk of benign hepatic adenoma s, which are rare but potentially dangerous if they rupture and cause internal bleeding [86]. The risk of these tumors is estimated to be 1 to 3 per 100,000 users, but it increases with higher doses of estrogen and prolonged use (more than five years). Additionally, COCs can exacerbate gallbladder disease by increasing cholesterol saturation in bile, leading to gallstone formation [87]. Women with a history of gallbladder disease or biliary tract disorders are at higher risk, and COC use may aggravate symptoms or necessitate gallbladder removal [88].

Impact on lipid metabolism

The progestin component of COCs can influence lipid profiles. Older progestins with androgenic activity (e.g., levonorgestrel) may increase LDL 'bad cholesterol' and lower HDL 'good cholesterol', thereby raising cardiovascular risk [89]. Newer progestins like drospirenone and desogestrel have a more favorable effect on lipid metabolism, but the net impact varies depending on the individual's baseline lipid profile and other risk factors [90].

In summary, while OCs are generally safe and effective, their adverse effects range from mild, transient symptoms (e.g., nausea, spotting, mood changes) to rare but serious conditions (e.g., VTE, stroke, cancer). Patient-specific factors, such as age, smoking status, and medical history, must be considered to minimize risks. Advances in OC formulations, such as lower estrogen doses and anti-androgenic progestins, have helped reduce the incidence of adverse effects while maintaining efficacy.

Challenges in the Use of OCs in Dermatology

While OCs have proven to be effective in treating a range of dermatological conditions, their use is not without challenges (Table 4). One significant issue is the risk of adverse effects, particularly the major ones such as VTE, stroke, and cardiovascular complications. These risks, although rare, are heightened in specific populations, such as women who smoke, are obese, or are over the age of 35. This necessitates careful patient screening and monitoring, which can be time-consuming and requires medical expertise. Additionally, minor side effects such as mood changes, weight gain, and irregular bleeding can reduce patient adherence, potentially compromising therapeutic outcomes [91, 92].

Another challenge lies in the variation in individual responses to OCs [93]. The effectiveness of a particular formulation in treating acne, hirsutism, or other androgen-driven conditions can differ widely among individuals due to variations in hormonal sensitivity, genetic predisposition, and underlying health conditions like PCOS. This makes the process of selecting the "right" OC often a trial-and-error approach, which can frustrate both patients and physicians. Moreover, many patients discontinue OCs due to misconceptions about their safety or concerns about long-term effects, such as fears of infertility or cancer, even though evidence has shown that OCs can reduce the risk of ovarian and endometrial cancers [93].

A further challenge is access and affordability [94]. While OCs are widely available in many parts of the world, cost can still be a barrier for some patients, especially when newer formulations like those containing drospirenone or cyproterone acetate are prescribed. In addition, certain cultural or religious beliefs may limit the use of OCs, regardless of their dermatological benefits. The stigma around using contraceptives solely for non-contraceptive purposes, such as treating acne or hirsutism, also continues to hinder acceptance in some communities [94].

Future Outlook for OCs in Dermatology

The future of OCs in dermatology is promising, with ongoing advancements in hormone formulation and delivery mechanisms aimed at reducing side effects and improving patient outcomes (Table 5). Fourth-generation progestins such as drospirenone and dienogest are paving the way for safer and more targeted therapies, offering potent anti-androgenic effects with lower androgenic activity and improved tolerability. Future formulations may continue to refine the hormonal composition to minimize risks like VTE while enhancing dermatologic benefits [95, 96].

Innovations in non-hormonal options may also expand treatment possibilities. For instance, research into selective androgen receptor modulators and other targeted therapies could complement or even replace OCs in the management of androgen-driven skin conditions. These therapies would reduce reliance on systemic hormones, potentially lowering the risk of side effects while still offering effective treatment for conditions like acne, hirsutism, and alopecia.

Additionally, the field of precision medicine holds great potential for improving OC use in dermatology. Advances in genetic testing and

Table 4: Challenges in the use of OCs in dermatology.

Challenge	Description	Impact on dermatological treatment
Adverse effects	OCs can cause side effects like nausea, weight gain, mood changes, headaches, breakthrough bleeding, and an increased risk of blood clots	Side effects can reduce patient adherence to treatment and lead to discontinuation, affecting treatment efficacy
Increased risk of VTE	Some progestins, particularly drospirenone and cyproterone acetate, are associated with a higher risk of VTE, especially in women with other risk factors like smoking	For patients with a history of VTE or other risk factors, using OCs could lead to serious complications, limiting options
Individual variability in response	Different patients may respond differently to OCs due to variations in hormonal sensitivity, genetic factors, and skin type	Personalized treatment may require trial and error, which can be frustrating for both patients and clinicians
Non-adherence	OCs require consistent daily use, and missed doses can reduce their effectiveness, especially in managing dermatological conditions like acne or hirsutism	Non-adherence can lead to suboptimal results, particularly for conditions that take longer to improve, like acne or alopecia
Access and affordability	OCs can be expensive, particularly newer formulations, and may not be covered by insurance in some regions or for certain indications	Cost barriers can limit access to effective treatment, especially in underserved populations or countries with limited access

Table 5: Future outlook for OCs in dermatology.

Aspect	Description	Future outlook
Hormonal formulation advancements	Development of new progestins with lower androgenic effects and fewer side effects, such as lower risks of VTE and cardiovascular issues	Safer and more effective formulations with improved safety profiles, targeting specific hormonal imbalances without causing adverse effects
Non-hormonal alternatives	Research into non-hormonal treatments such as selective androgen receptor modulators and other targeted therapies	Non-hormonal options may become viable alternatives, offering effective treatment for dermatologic conditions with fewer side effects
Personalized medicine	Advances in genetic testing, hormone profiling, and individual response tracking to tailor OC prescriptions for specific patients	Personalized treatment plans based on genetic and hormonal profiles, improving efficacy and reducing trial-and-error prescribing
Improved patient adherence	Innovations in OC delivery methods, including long-acting or extended-release formulations, and easier-to-take options	Enhanced patient adherence due to more convenient, user-friendly OC formulations, reducing missed doses and improving treatment outcomes
Combination therapies	Combining OCs with other dermatological treatments (e.g., topical therapies, laser treatments) for comprehensive skin management	Multimodal approaches that combine OCs with topical or procedural treatments may provide better results for conditions like acne and hirsutism
Global accessibility	Efforts to make OCs more affordable and accessible in low- and middle-income countries, as well as broader insurance coverage	Increased global access to OCs, ensuring equitable treatment options for women worldwide, especially in underserved populations
Patient education and awareness	Focus on educating both healthcare providers and patients about the dermatological benefits of OCs, beyond contraception	Reduction in stigma and better understanding of OCs' non-contraceptive benefits, leading to broader acceptance and usage in dermatology

hormone profiling may enable dermatologists to predict individual responses to specific contraceptives, leading to personalized treatment plans that minimize trial-and-error prescribing. Patients with genetic predispositions to adverse effects, such as a high risk of VTE or poor metabolism of certain progestins, could be identified and offered safer alternatives.

Educational initiatives and public awareness campaigns will also play a critical role in the future. As more women and physicians become educated on the non-contraceptive benefits of OCs and their relative safety when used appropriately, the stigma surrounding their use for dermatologic purposes may diminish. Greater awareness could also encourage earlier diagnosis and treatment of conditions like PCOS, where OCs can be a cornerstone of therapy.

In summary, while challenges such as side effects, variability in response, and accessibility persist, the future of OCs in dermatology is bright. With advancements in hormone formulations, targeted therapies, and personalized medicine, OCs are likely to remain a cornerstone in the management of androgen-driven skin conditions, offering safer and more effective options for patients worldwide.

Conclusions

OCs have become an essential tool in dermatology, providing significant benefits in managing conditions like acne, hirsutism, and androgenetic alopecia. By modulating hormonal imbalances and reducing androgenic activity, particularly through anti-androgenic progestins such as drospirenone and cyproterone acetate, OCs can dramatically improve skin health. Their ability to regulate sebum production, reduce acne lesions, and control excessive hair growth has made them a cornerstone treatment for patients with androgen-driven dermatologic concerns, especially for those with conditions like PCOS. The versatility and effectiveness of OCs in dermatology continue to make them a preferred option for many women seeking both contraception and dermatologic relief.

Despite their widespread use, the selection of the right OC requires careful consideration of individual health profiles, including potential risks of side effects such as VTE and cardiovascular issues. As advancements in hormonal formulations and personalized medicine continue, the future of OCs in dermatology looks promising. More targeted therapies, reduced side effects, and a better understanding of individual responses will likely improve patient outcomes and adherence. With ongoing research and improved public education, OCs will continue to offer safe, effective solutions for managing androgenic skin conditions, enhancing the quality of life for many women.

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Conflict of Interest

None.

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