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Review Article

ORAL CONTRACEPTIVES: RECENT ADVANCES, MECHANISM, AND CLINICAL APPLICATIONS

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Oral contraceptives (OCs) are one of the most commonly used reversible contraceptive methods worldwide. These hormonal treatments function by thickening the cervical mucus, altering endometrial receptivity, and inhibiting ovulation. They include synthetic estrogen and/or progestin. Between 2021 and 2025, new advances such as low-dose formulations, drospirenone-only pills, and over-the-counter availability increased accessibility and safety. OCs have a number of non-contraceptive benefits in addition to contraception, such as managing menstruation, reducing acne, and lowering the risk of endometrial and ovarian cancer. However, there are still concerns regarding potential risks such as thrombosis and cardiovascular disease. This article reviews oral contraceptives' mechanism of action, pharmacology, clinical applications, recent advancements, and public health concerns.

Keywords: Progestin-only pills (POPs), oral contraceptives, combined oral contraceptives (COCs), hormonal contraception, ovulation inhibition, ethinylestradiol, drospirenone, cervical mucus, Endometrial thromboembolism; contraceptive efficacy; reproductive health; pharmacokinetics, pharmacodynamics, and family planning

INTRODUCTION

One of the most popular and successful forms of reversible contraception in the world is oral contraceptives (OCs). They have transformed reproductive health since their inception in the 1960s by giving women a dependable and practical way to avoid getting pregnant. These hormonal preparations contain synthetic versions of progestin and/or estrogen that affect the female reproductive system by changing the endometrial lining, altering cervical mucus, and inhibiting ovulation, all of which hinder conception and implantation.

The creation of oral contraceptives was a significant development in public health and medicine. Early formulations included comparatively high hormone dosages, which were linked to more adverse consequences. Modern low-dose formulations, however, are safer, more effective, and more tolerated thanks to ongoing research and technical developments. In addition to being used for birth control, oral contraceptives are now crucial in the treatment of a number of hormonal and gynecological conditions.

Oral contraceptives have a number of non-contraceptive health advantages in addition to their main contraceptive purpose. These include controlling menstrual cycles, treating acne, managing polycystic ovarian syndrome (PCOS), reducing dysmenorrhea (painful menstruation), and lowering the risk of

endometrial and ovarian malignancies. These advantages have made them a useful therapeutic tool in women's healthcare, extending their clinical applications beyond family planning.

The improvement of oral contraceptives' safety profile and accessibility has been the main focus of recent developments between 2021 and 2025. Over-the-counter (OTC) availability, drospirenone-only formulations, and ultra-low-dose estrogen pills are examples of innovations that have improved user compliance and decreased the possibility of side effects. Furthermore, in contemporary clinical practice, the idea of individualized contraception—where a person's choice of contraception is based on their lifestyle, risk factors, and health status—has drawn more attention.

Oral contraceptives have many advantages and are widely used, but they also have some hazards. Nausea, headaches, mood swings, and in rare instances, major consequences like thrombosis and cardiovascular events are possible side effects, especially in high-risk groups. Therefore, to guarantee safe and efficient use, proper patient selection, counseling, and monitoring are crucial.

In general, oral contraceptives continue to be a fundamental component of family planning and reproductive health initiatives worldwide. They continue to develop as a result of continuous research and innovation, providing enhanced safety, efficacy, and other therapeutic advantages. The goal of this article is to give a thorough summary of oral contraceptives' mechanism of action, pharmacology, clinical applications, new developments, and effects on public health. [1-15]

2. Types of Oral Contraceptives

There are two types of Oral contraceptives and they are:-

2.1 Combined Oral Contraceptives (COCs)

Figure 1: Combined Oral Contraceptives (COCs)

Estrogen (ethinylestradiol) and progesterone are found in COCs.

Mechanism:

- Ovulation is prevented by inhibiting FSH and LH.
- Cervical mucus thickening
- Changes in the endometrium

Advantages

- High effectiveness (>99%)
- Control of the menstrual cycle
- decreased risk of endometrial and ovarian cancer

Disadvantages

- Thromboembolism risk

- Unsuitable for smokers older than 35

2.2 Progestin-Only Pills (POPs)

Figure 2: Progestin-Only Pills (POPs)

Mechanism:

- Increases cervical mucus thickness.
- Partially inhibits ovulation
- Modifies the endometrium

Indications:

- Women who are nursing
- Women who shouldn't take estrogen.[16-25]

3. Mechanism of Action

Oral contraceptives (OCs) work by affecting several stages of the female reproductive process through a mixture of hormonal effects. These processes mainly include endometrial lining alterations, cervical mucus alteration, and ovulation suppression. High contraceptive efficacy is ensured by the combined effect of these acts.

3.1 Suppression of Ovulation

Ovulation inhibition is the main way that combination oral contraceptives (COCs) work. The anterior pituitary gland and hypothalamus are negatively impacted by the estrogen and progestin components. As a result, the pituitary gland secretes less luteinizing hormone (LH) and follicle-stimulating hormone (FSH) while the hypothalamus decreases the release of gonadotropin-releasing hormone (GnRH).

Consequently:

- Inhibition of follicular development
- There is no ovulation and the mid-cycle LH surge is avoided.

Pregnancy is prevented since fertilization cannot occur without the release of an ovum.

3.2 Alteration of Cervical Mucus

The consistency of cervical mucus is significantly altered by progestin. In order to make it easier for sperm to enter the uterus during ovulation, cervical mucus normally becomes thin and watery.

But when progestin is present:

- Cervical mucus thickens and becomes viscous.
- Sperm penetration is greatly decreased.
- Sperm motility is compromised.

Even if ovulation takes place, this produces a physical barrier that keeps sperm from getting to the ovum.

3.4 Effects on Fallopian Tubes (Tubal Motility)

The fallopian tubes' motility and secretions are also impacted by oral contraceptives. Changes in hormones can affect how the ovum and sperm move through the reproductive system.

his results in:

- Decreased ovum and sperm transit coordination
- Reduced chance of fertilisation

3.5 Overall Effect

Several mechanisms work together to make oral contraceptives effective, including:

- Ovulation prevention
- Sperm entrance inhibition
- Avoiding implantation

When used properly, oral contraceptives are among the most dependable reversible methods of contraception due to their overlapping mechanisms. [26-34]

4. Pharmacokinetics of Oral Contraceptives

The processes by which a medication is absorbed, distributed, metabolized, and removed from the body are referred to as pharmacokinetics. The hormonal components of oral contraceptives (OCs), progestins and estrogen (often ethinylestradiol), are the primary determinants of their pharmacokinetics.

4.1 Absorption

When used orally, oral contraceptives are quickly absorbed from the digestive system, primarily in the small intestine.

- The liver's first-pass metabolism of ethinylestradiol lowers its bioavailability.
- The oral bioavailability of progestins is typically higher (about 90–100%).
- In the majority of contemporary formulations, food has no impact on absorption

4.2 Distribution

The bloodstream carries the hormones throughout the body when they are absorbed.

- 97–98% of ethinylestradiol is linked to proteins, mostly albumin.
- Sex hormone-binding globulin (SHBG) is bound by certain progestins.
- These hormones readily pass through cell membranes and disperse throughout different tissues because they are lipophilic.

4.3 Metabolism

- Cytochrome P450 enzymes, particularly CYP3A4, are responsible for the metabolism of both progestins and estrogen.
- While some metabolites may have some moderate hormonal function, most metabolites are inert.
- Drug interactions are crucial.
- Rifampicin and phenytoin are examples of enzyme inducers.
- Hormone levels with enzyme inhibitors (like ketoconazole)

4.4 Excretion

Oral contraceptive metabolites are removed by:

- Renal excretion, or urine
- Feces (via bile)

Additionally, enterohepatic circulation prolongs the effects of ethinylestradiol. [35-43]

5. Pharmacodynamics of Oral Contraceptives

The effects of a medicine on the body and the processes by which these effects take place are referred to as pharmacodynamics. The hypothalamic-pituitary-ovarian (HPO) axis and regular hormonal management of the menstrual cycle are the main ways that oral contraceptives (OCs) produce their pharmacodynamic effects.

5.1 Suppression of the Hypothalamic–Pituitary–Ovarian (HPO) Axis

The ovulation inhibition via hormonal feedback mechanisms is the primary pharmacodynamic effect of oral contraceptives.

- The hypothalamus receives negative feedback from progestin and estrogen.
- Gonadotropin-releasing hormone (GnRH) is released less frequently as a result.
- As a result, the anterior pituitary secretes less FSH and LH.

Effects:

- Follicular development inhibition (FSH)
- LH surge prevention
- There is no ovulation.

5.2 Effect on Cervical Mucus

Cervical mucus is significantly altered by progestin.

- Mucus thickens, thickens, and becomes less permeable.
- Inhibition of sperm entry into the uterus
- Decreases the likelihood of fertilization. [44-51]

6. Clinical Uses of Oral Contraceptives

Oral contraceptives are regarded as one of the most dependable and efficient reversible methods of contraception and are mostly used to prevent unwanted pregnancies. They work by interfering with several stages of the reproduction process through a mixture of hormonal activities. Ovulation suppression is the main way that oral contraceptives prevent pregnancy. The hypothalamus and anterior pituitary gland are negatively impacted by the estrogen and progestin components included in combined oral contraceptives. Gonadotropin-releasing hormone (GnRH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) are all secreted less as a result. Because of this, the ovary is unable to release an egg, which prevents fertilization, and the mid-cycle LH surge necessary for ovulation does not take place.

Oral contraceptives not only stop ovulation but also stop fertilization by changing the properties of cervical mucus. Progestin causes the cervical mucus to thicken, thicken, and become less permeable. Sperm have a much harder time entering the uterus and getting to the fallopian tubes as a result of this physical barrier. The chances of fertilization are further reduced since, even if sperm are able to penetrate, their motility and survival are

compromised.

The impact of oral contraceptives on the endometrium is another significant method of contraception. The endometrial lining becomes thinner, less vascular, and less amenable to implantation as a result of the hormonal components. This implies that the likelihood of the fertilized ovum successfully implanting in the uterus is significantly decreased, even in the event of fertilization. Oral contraceptives also affect fallopian tube motility, which can interfere with the ovum and sperm moving in unison. By inhibiting their appropriate interaction, this further reduces the likelihood of conception.

Additionally, by enabling individuals and couples to regulate the timing and spacing of pregnancies, oral contraceptives play an important part in family planning. By lowering the dangers connected with closely spaced pregnancies, this improves the health of mothers and children. From the standpoint of public health, their use aids in minimizing unsafe abortions, decreasing maternal mortality, and reducing unwanted pregnancies. [52-60]

7. Drug interaction

As they might have a substantial impact on the safety and effectiveness of oral contraceptives (OCs), drug interactions are a crucial factor to take into account. The cytochrome P450 enzyme system, specifically the CYP3A4 isoenzyme, is principally responsible for the liver's metabolism of oral contraceptives, especially those that contain ethinylestradiol and progestins. The plasma concentration of contraceptive hormones can be changed by any medication that stimulates or inhibits these enzymes, which may result in decreased efficacy or a higher chance of side effects.

Enzyme-inducing medications have one of the most clinically significant interactions. These drugs speed up the body's metabolism and removal of contraceptive hormones by increasing the activity of hepatic enzymes. Consequently, there is a drop in the plasma levels of progestin and estrogen, which may result in contraceptive failure and an elevated chance of unwanted pregnancy. Certain antitubercular treatments like rifampicin and rifabutin, antiepileptic pharmaceuticals like phenytoin, carbamazepine, and phenobarbital, and various antiretroviral drugs used to treat HIV are common examples of drugs that induce enzymes. Additionally, herbal remedies like St. John's Wort can dramatically lower the efficacy of oral contraceptives by acting as enzyme inducers. Additional or other non-hormonal methods of contraception are frequently advised in these situations.

Medications that impact gastrointestinal function may also interact with one another. Oral contraceptives' effectiveness can be diminished by medications that increase

gastrointestinal motility or induce vomiting and diarrhea. Additional contraceptive measures are advised in these circumstances.

Moreover, oral contraceptives can affect how other medications are metabolized. For instance, they might change the plasma levels of some drugs, like anticoagulants, benzodiazepines, and corticosteroids, which could increase or decrease their effects. This reciprocal relationship emphasizes how crucial it is to thoroughly evaluate a patient's medication history before administering oral contraceptives. [61-69]

8. Recent Advances of oral contraceptive

The development and use of oral contraceptives have advanced significantly in recent years, with a particular emphasis on enhancing accessibility, safety, and efficacy. The creation of ultra-low-dose estrogen formulations is among the most noteworthy. Higher estrogen dosages found in earlier oral contraceptives were linked to a higher risk of side effects such thrombosis and cardiovascular problems. Nowadays, substantially lower levels of ethinylestradiol are used in modern formulations to preserve the effectiveness of contraception, which lowers the frequency of adverse effects and increases user tolerability.

The creation of more recent progestins, including drospirenone, which provide extra therapeutic advantages, is another significant breakthrough. Due to its anti-androgenic and anti-mineralocorticoid qualities, drospirenone helps lessen premenstrual syndrome symptoms, acne, and fluid retention. The development of drospirenone-only pills is a significant advancement because these formulations effectively suppress ovulation without the use of estrogen, making them appropriate for women who are contraindicated for estrogen, such as those who have a higher risk of cardiovascular disease or thromboembolism.

Enzyme-inhibiting medications, on the other hand, raise blood levels of contraceptive hormones by reducing the metabolic activity of hepatic enzymes. This may improve the pharmacological effects of oral contraceptives, but it may also raise the risk of side effects like headache, nausea, breast tenderness, and, in certain situations, serious problems like thrombosis. Antifungal medications like ketoconazole, several antiviral medications, and some antibiotics like erythromycin are examples of enzyme inhibitors. Careful monitoring is necessary due to the elevated hormone levels linked to these interactions, particularly in women who have cardiovascular disease risk factors.

Recent improvements in the use of oral contraceptives have also been attributed to digital health technologies. These days,

telemedicine platforms and mobile health apps offer education, medication reminders, and simpler access to medical professionals. These tools increase oral contraceptive effectiveness overall, decrease missed doses, and improve adherence.

Moreover, studies is being done to develop male contraceptive pills and non-hormonal oral contraceptives, which could transform family planning in the future. These developments seek to increase both partners' responsibility for contraception and offer efficient contraception with less hormonal side effects. [70-81]

9. Public Health Impact

By greatly enhancing reproductive health outcomes and promoting social and economic development, oral contraceptives have had a major impact on public health globally. The decrease in unwanted pregnancies is one of the most significant benefits of oral contraceptives. Oral contraceptives help women and couples plan the timing and number of children, preventing unintended pregnancies and lowering the need for risky abortions by offering a dependable and easily accessible means of contraception. As a result, maternal morbidity and mortality are significantly reduced, especially in low- and middle-income nations where access to safe abortion services may be restricted.

Oral contraceptives promote maternal and child health in addition to lowering unwanted pregnancies. Effective contraceptive use enables women to space out their pregnancies appropriately, allowing them to recuperate both physically and nutritionally in between pregnancies. Complications include low birth weight, maternal anemia, and premature birth are less likely as a result. Maternal and infant survival rates increase as a result, underscoring the value of oral contraceptives in public health initiatives.

Additionally, oral contraceptives are essential for advancing gender equality and women's empowerment. Giving women autonomy over their reproductive decisions allows them to participate more actively in social, professional, and educational endeavors. Pregnant women who are able to plan their pregnancies are more likely to seek higher education and professional possibilities, which improves their independence and financial security. This empowerment has a wider social impact, supporting local and national economic development and prosperity.

The widespread use of oral contraceptives lessens the strain on healthcare resources from the standpoint of the healthcare system. By lowering the need for maternal healthcare services, such as prenatal, postnatal, and delivery care, unwanted pregnancies can be avoided, which lowers healthcare expenses. Additionally, by reducing the burden of disease,

oral contraceptives' non-contraceptive health benefits—such as a lower risk of some malignancies and the management of gynecological disorders—contribute to general public health.

Oral contraceptives are also a crucial part of international family planning initiatives and population management plans. They support sustainable development and more equitable distribution of resources like food, healthcare, and education by assisting in the control of population growth. In highly populated areas, where rapid population development may put a strain on limited resources, this is especially crucial.

By lowering unwanted pregnancies, enhancing maternal and child health, empowering women, and promoting social and economic advancement, oral contraceptives have a profound effect on public health. Achieving global health objectives and raising the standard of living for people and communities everywhere depend on their ongoing development and greater accessibility. [82-85]

10. Future Perspectives of Oral Contraceptives

The development of safer, more efficient, and user-friendly oral contraceptives that cater to the various needs of people is the main goal for the future. The goal of ongoing research is to reduce negative effects while preserving high contraceptive efficacy. The creation of hormone-free oral contraceptives is one of the main areas of interest. By focusing on particular stages of the reproductive process, such as ovulation or fertilization, these innovative drugs seek to prevent conception without affecting the body's hormonal balance. By greatly lowering the possibility of hormone-related side effects, such strategies could make contraception safer for a larger group of people.

The development of male oral contraceptives is another encouraging avenue. Although women have historically been primarily responsible for contraception, current research is investigating hormonal and non-hormonal male contraceptive pills that can successfully inhibit sperm function or production. Male oral contraceptives could transform family planning by encouraging shared responsibility between spouses if they are developed and generally accepted.

In the future, personalized contraception is anticipated to be very important. Healthcare professionals may be able to customize contraceptive options depending on a person's genetic composition, hormonal profile, and risk factors thanks to the expanding discipline of pharmacogenomics. By choosing the best formulation for each person, this method would increase efficacy and lower the possibility of adverse consequences.

To improve ease and compliance, new developments in drug delivery systems are also being investigated. Even while oral

contraceptives are now simple to use, new developments could include formulations with longer half-lives, fewer doses, or better absorption characteristics. These advancements may contribute to fewer missed doses and increased adherence, both of which are essential for preserving the efficacy of contraceptives.

Additionally, it is anticipated that digital health technology will become more significant in the future of contraception. Wearable technology, telemedicine platforms, and mobile apps can track menstrual periods, give individualized advice, and remind users to take their pills. Particularly in remote or disadvantaged locations, these tools can improve access to reproductive health information and services and increase user adherence.

Additionally, efforts are being made worldwide to increase the affordability and accessibility of oral contraceptives. In the upcoming years, policies promoting community-based distribution, over-the-counter availability, and educational initiatives are probably going to grow. The goal of these programs is to guarantee that everyone has access to safe and efficient contraception, irrespective of their financial situation.In conclusion, innovation, customization, and accessibility are key components of the future of oral contraceptives. It is anticipated that oral contraceptives will become safer, more accessible, and more tailored to individual needs as a result of continued research and technology developments. Their contribution to enhancing reproductive health and advancing international public health objectives will only grow as a result of these advancements. [86-94]

Conclusion

Because of their great efficacy, reversibility, and several therapeutic advantages, oral contraceptives continue to be a mainstay of family planning and reproductive health around the world. Since their inception, they have greatly enhanced women's quality of life by giving them control over their reproductive choices and preventing unwanted births. Oral contraceptives have various significant non-contraceptive advantages in addition to its core contraceptive function, including as managing hormonal imbalances, controlling menstrual cycles, and lowering the risk of several malignancies.

The safety, efficacy, and accessibility of oral contraceptives have been considerably improved by recent developments. User compliance has increased and side effects have decreased thanks to the development of low-dose formulations, novel progestins, and over-the-counter availability. Better adherence and more specialized care have also been made possible by innovations like digital health support systems and personalized contraception. Oral contraceptives are now

more widely accepted and appropriate due to these advancements.

Despite these benefits, there are hazards associated with oral contraceptives. Individual health problems, possible side effects, and drug combinations must all be carefully considered. To guarantee their safe and efficient use, appropriate counseling, frequent observation, and knowledge of proper usage are crucial.In conclusion, oral contraceptives continue to be essential to contemporary healthcare since they combine the effectiveness of contraception with a variety of therapeutic advantages. Their impact on global reproductive health will be further strengthened by ongoing research, increasing public knowledge, and enhanced accessibility, making them an essential tool for improving health outcomes and enabling people to make educated reproductive decisions.

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Conflict of Interest

The authors declare that they have no conflict of interest