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Advances in vaginal drug delivery: A nanotechnology-based approach

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A B S T R A C T

Vaginal drug delivery has emerged as a promising route for both local and systemic therapies, offering several benefits over traditional oral and injectable methods. Due to its distinct anatomical and physiological characteristics such as extensive vascularization, a broad surface area and acidic pH the vagina serves as an effective medium for drug absorption. While conventional forms like gels, creams, tablets, and suppositories are still commonly used, they often suffer from issues such as leakage, inconsistent retention and user discomfort. To address these drawbacks, newer technologies such as intra-vaginal rings, bio-adhesive microspheres, liposomes, niosomes and micro-emulsion have been developed, enabling more controlled and sustained drug delivery. Nonetheless, challenges including hormonal variations, user adherence, potential irritation and sociocultural barriers still need to be overcome. Ongoing advancements in drug formulation and delivery technologies are essential to enhance the therapeutic potential of vaginal drug administration.

Keywords: Vaginal drug delivery, Tablets, Vaginal rings, Liposomes, Niosomes.

1. Introduction

The pharmaceutical industry is increasingly exploring mucosal drug delivery pathways to enhance the bioavailability of drugs that perform poorly via the oral route. Among these, the vaginal route has garnered attention for its ability to deliver medications both locally and systemically due to its well-vascularized tissue. Key benefits include avoiding hepatic first-pass metabolism, ease of self-administration and rapid drug uptake, particularly for low molecular weight compounds. Despite these advantages, formulation development for vaginal delivery must consider factors such as variations in epithelial thickness, hygiene practices, gender-specific usage, and sociocultural perceptions. The first vaginal delivery system that allowed controlled release was introduced in 1970, utilizing a ring designed to dispense medroxy progesterone acetate for contraception.[1]

Anatomy and Physiology of the Vagina[2-7]

The human vagina is a flexible, S-shaped muscular canal averaging 6 to 12 cm in length. Structurally, it consists of four histological layers: a stratified squamous epithelium that changes in thickness with hormonal fluctuations; the lamina propria, rich in collagen and blood vessels; a muscular layer composed of circular and longitudinal smooth muscle; and the tunica adventitia, consisting of vascular connective tissue. The presence of rugae increases surface area and elasticity. The pH typically ranges between 3.8 and 4.2, contributing to an antimicrobial environment. These features make the vaginal mucosa highly suitable for drug absorption. Intra-vaginal rings are a notable innovation, offering sustained drug release for periods ranging from weeks to months.

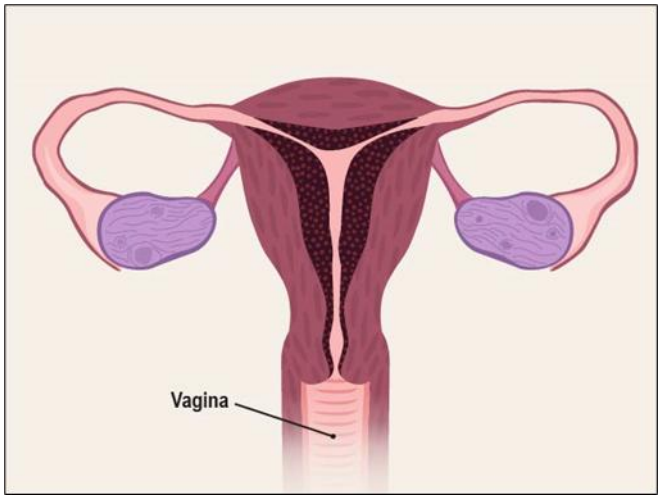

Fig. 1 Vagina

Vaginal drug delivery

Vaginal drug delivery systems have traditionally been employed to administer contraceptives and medications for treating vaginal infections. Due to the rich vascularization of the vaginal wall, drugs delivered via this route are absorbed quickly and efficiently.[8] The concept of controlled-release drug delivery has also been effectively adapted for intravaginal administration targeting systemic circulation. This approach allows for reduced dosing frequency while maintaining optimal therapeutic efficacy.

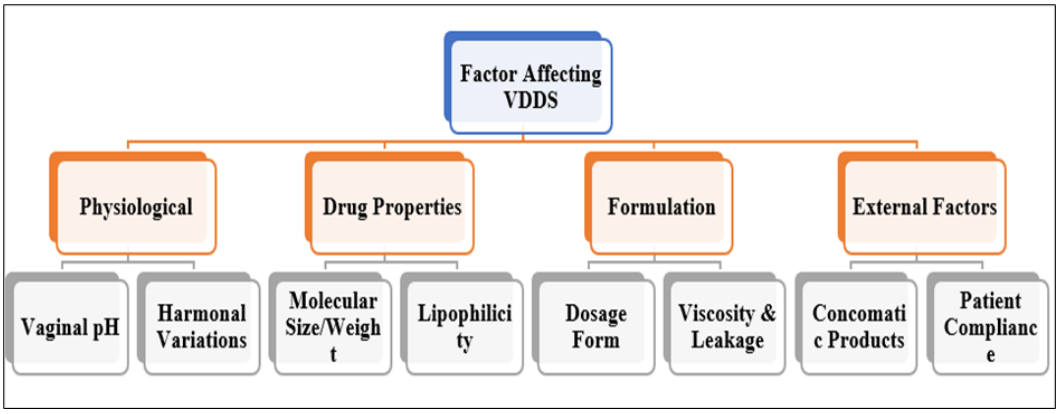

Fig. 2 factor affecting[9]

Mechanisms of Vaginal Drug Absorption[10,11]

Drugs administered vaginally can be absorbed through several mechanisms:

- Trans-cellular diffusion where the drug traverses individual cells.
- Para-cellular transport involving movement between cells through tight junctions.
- Vesicular or receptor-mediated uptake especially for targeted delivery

Advantages of Vaginal Drug Delivery[12,13]

- Circumvents gastrointestinal disturbances like nausea.
- Minimizes gastric irritation and degradation from digestive enzymes.
- Avoids liver metabolism on first pass.
- Drug delivery can be easily halted (e.g., ring removal).
- Suitable for delivering drugs typically given by injection.
- Offers rapid onset and good absorption for small molecules.
- Useful for long-term therapy.
- May enhance macromolecule uptake.

Limitations[14]

- Certain drugs degrade in acidic environments.
- Risk of local irritation.
- Sexual activity may disrupt drug efficacy.

- Hygiene practices and personal habits may influence drug performance.
- Risk of leakage or discomfort.
- Usable only in female patients.

Pharmaceutical Considerations[15,16]

Many pharmaceutical companies are increasingly investing in the innovation of vaginal delivery systems aimed at managing conditions such as vaginal infections, sexually transmitted diseases, contraception and other gynecological disorders. These systems are not only improving therapeutic outcomes but also extending product shelf-life and commercial competitiveness. Advanced formulation techniques include the use of novel excipients and alternative dosage forms. Compatibility between active drugs and excipients is typically evaluated using analytical tools like Differential Scanning Calorimetry (DSC) and stress testing through High-Performance Liquid Chromatography (HPLC).

2. Conventional dosage form

Vaginal Tablets[17]

Vaginal tablets are formulated to disintegrate within the vaginal cavity to release active ingredients effectively. They are often produced using similar excipients and processes as oral tablets, with direct compression being the most common method. To enhance drug release, effervescent agents can be incorporated. Compared to creams and ointments, tablets are more stable and less messy, making them easier to handle. An example includes clotrimazole tablets used for treating fungal infections like candidiasis.

Creams[18]

Vaginal creams are typically employed for local application of antimicrobial or contraceptive agents. While user-friendly and readily available, they can be messy, may cause discomfort and pose challenges in delivering consistent doses. Their tendency to leak can also be inconvenient.

Gels[19]

Vaginal gels, especially those containing antibacterial agents, are widely used to treat infections and symptoms such as irritation or discharge. For example, bacterial vaginos is a common condition caused by an overgrowth of harmful bacteria is effectively treated using these gels.

Suppositories[20]

These solid dosage forms are designed to melt at body temperature and release medication directly into the vaginal cavity. They bypass liver metabolism, are relatively easy to self-administer and are simple to formulate. However, they may lack strong adhesion, can be messy, and are sometimes unsuitable during pregnancy or sexual activity.

3. Novel vaginal dosage forms.

Vaginal Rings[21-23]

These flexible, circular devices provide a reliable means for sustained drug delivery over weeks or months. Initially developed in the 1960s for hormone delivery, they have evolved to deliver both contraceptives and therapeutics systemically. Modern rings are typically made from materials like silicone or ethylene vinyl acetate.

Bio-adhesive Microspheres and Microcapsules[24]

Microsphere-based systems use materials like chitosan for their muco-adhesive and biodegradable properties, allowing prolonged retention in the vaginal environment. These microspheres can be formulated into tablets for sustained release. Traditional cross-linkers used for stabilization, such as glutaraldehyde, can cause toxicity, prompting the search for safer alternatives to enhance biocompatibility.

Liposomes and Niosomes[25]

Lipid-based nanoparticles like liposomes and niosomes have become popular for delivering peptides and proteins vaginally. Formulations with clotrimazole, for instance, have shown promising results in preclinical studies, maintaining drug stability and minimizing irritation while allowing targeted and prolonged release.

Microemulsions[26]

Microemulsion-based systems are especially suited for antifungal agents. These formulations are designed to remain in place without leakage and offer controlled drug release for several hours. Benefits include high drug solubility, ease of preparation, thermodynamic stability, and improved penetration compared to conventional systems. Recent studies show their safety and efficacy in delivering spermicidal compounds.

4. Conclusion

Vaginal drug delivery is a versatile and effective route for both local and systemic therapies. Its distinct advantages-such as bypassing hepatic metabolism, ease of use, and rapid absorption-make it ideal for delivering a wide range of drugs. While traditional formulations like creams and tablets remain in use, advanced systems such as vaginal rings, microspheres, liposomes and microemulsions offer controlled release and improved efficacy. Nevertheless issues such as variability in vaginal physiology, user compliance and cultural acceptance must be addressed during formulation development. Future research and innovation in materials and delivery mechanisms are likely to expand the scope of vaginal drug delivery for chronic and systemic conditions.

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