Vaginal suppositories as a novel drug delivery approach

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Abstract- Vaginal suppositories represent an evolving and versatile drug delivery system with applications in both local and systemic therapy. The vaginal route offers unique advantages, including a large absorptive surface area, rich vascularisation, and the ability to bypass hepatic first-pass metabolism, making it highly suitable for drugs with poor oral bioavailability or requiring site-specific delivery. Traditional suppositories were primarily used for the treatment of vaginal infections, contraception, and hormone replacement therapy; however, recent advances in formulation science and material technology have significantly broadened their potential. The incorporation of mucoadhesive polymers, permeation enhancers, thermos-responsive bases, and nanocarrier systems has improved drug solubility, residence time, and controlled release profiles, addressing challenges such as leakage, variability in vaginal physiology, and patient compliance. Emerging innovations, including nanoparticle-loaded suppositories, bio-responsive systems, and 3D-printed personalised inserts, further highlight the potential of this delivery approach. In addition, research into vaginal microbiome interactions and probiotic-loaded suppositories opens new opportunities for disease prevention and women's health management. This review consolidates current knowledge on vaginal suppositories as a novel drug delivery platform, emphasising formulation strategies, therapeutic applications, limitations, regulatory considerations, evaluation, and future perspectives for clinical translation.

Index term- Vaginal suppositories, Novel drug delivery system, Mucoadhesive polymers, Nano-particle loaded formulations, Women's health therapeutics.

NEED FOR STUDY

Vaginal suppositories represent an evolving and versatile drug delivery system with applications in both local and systemic therapy [(1)]. The vaginal route offers unique advantages, including a large absorptive surface area, rich vascularisation, and the ability to bypass hepatic first-pass metabolism [(2), (3)], making it highly suitable for drugs with poor oral bioavailability or requiring site-specific delivery. Traditional suppositories were primarily used for the treatment of vaginal infections, contraception, and hormone replacement therapy. [(3), (4)] However, recent advances in formulation science and material technology have significantly broadened their potential [(5), (6)]. The incorporation of mucoadhesive polymers [(3)], permeation enhancers, thermo-responsive bases, and nanocarrier systems[(5),(7)] has improved drug solubility, residence time, and controlled release profiles, addressing challenges such as leakage, variability in vaginal physiology, and patient compliance[(8)]. Emerging innovations, including nanoparticle-loaded suppositories[(5)], bio-responsive systems[(15)], and 3D-printed personalised inserts[(11),(12)], further highlight the potential of this delivery approach. In addition, research into vaginal microbiome interactions and probiotic-loaded suppositories[(19)] opens new opportunities for disease prevention and women's health management

OBJECTIVES

The objectives of this review article are to:

- Consolidate current knowledge on vaginal suppositories as a novel drug delivery platform[(1),(4),(6)].
- Emphasise formulation strategies[(3),(7)], therapeutic applications[(9),(10)], limitations[(14)], regulatory considerations[(20)], evaluation, and future perspectives for clinical translation[(11),(15)].

INTRODUCTION

ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

The vaginal canal is a muscular, highly vascularized tube lined by a stratified, non-keratinised squamous epithelium (200–300 μm thick in reproductive-age women)[(1),(2)]. Oestrogen levels strongly influence this structure: high oestradiol promotes epithelial proliferation and intracellular glycogen storage, whereas oestrogen deficiency (e.g. menopause) leads to a thinning and atrophy[(3)]. Vaginal cells do not have mucus-secreting goblet cells; instead, lubrication arises from a transudate (plasma exudate) and cervical mucus that flows into the vaginal vault[(6)]. The fluid volume is typically low (a few millilitres per day) and ~95% water, containing mucin glycoproteins (e.g. gel-forming mucins MUC2, MUC5B, etc. from cervical glands), enzymes, immune proteins and exfoliated cells. These mucins form a viscoelastic hydrogel barrier over the epithelium, which protects the tissue and interacts with formulations[(5),(6)] (e.g. binding mucoadhesive polymers).

A hallmark of the healthy vaginal environment is its acidic pH (typically ~3.5–4.5 in premenopausal women). This acidity is maintained mainly by Lactobacillus spp[(3),(6)]. Which dominate (>70%) the bacterial flora in most women. These lactobacilli ferment glycogen breakdown products into lactic acid, creating the low pH that inhibits pathogens. By contrast, other mammals generally have higher vaginal pH, and only humans tend to exhibit the very acidic (≤4.5) environment. Menstrual cycles and hormones cause pH and mucus changes[(6),(7)] (e.g. mid-cycle sperm-friendly mucus); pregnancy induces a thick mucus plug in the cervix. In menopause (low oestrogen), pH rises (toward neutral) and secretions diminish, often leading to dryness and vulnerability to infection[(3)].

Importantly for drug delivery, the vaginal mucosa is permeable and well-vascularized. The epithelium allows drug diffusion into the capillary-rich lamina propria, enabling both local and systemic absorption. Studies suggest vaginal permeability is comparable to or greater than that of the buccal mucosa and exceeds intestinal mucosa for many compounds[(5)]. Even large macromolecules (>300 kDa) can traverse the mucosa more readily than through skin or gut[(5),(8)]. Thus, the vaginal route avoids first-pass metabolism and can rapidly deliver drugs into circulation, as exploited by vaginal rings and gels[(9),(10)].

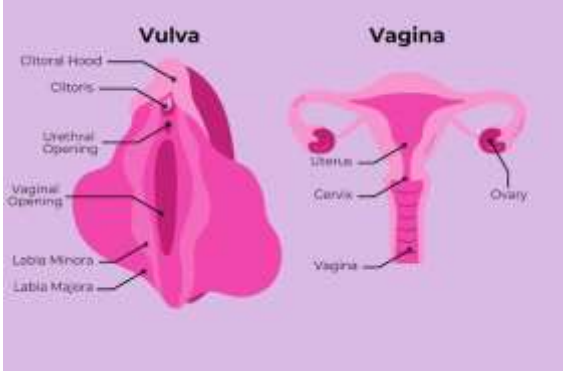

Fig. 1. Structure of Vagina

HISTORICAL BACKGROUND

The origins of vaginal suppositories date back to ancient Egyptian and Greek medicine, where mixtures of honey, plant resins, and oils were used intravaginally for contraception and infection control[(1)]. During the 19th century, suppository technology advanced with the introduction of cocoa butter as a reliable base[(2)]. The 20th century witnessed the commercialisation of clotrimazole suppositories for candidiasis[(3)], which revolutionised self-administered intravaginal therapy. In recent decades, developments in polymer chemistry, nanotechnology, and biotechnology have further redefined vaginal suppositories as precision delivery systems[(4),(6)].

SHAPE OF VAGINAL SUPPOSITORIES.

Usually, the suppositories are oval, conical, bullet-shaped, or cylindrical.

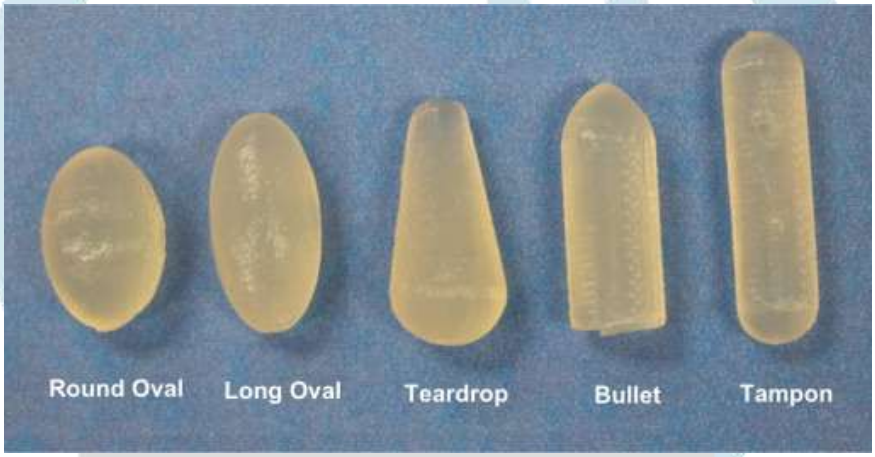

Fig. 2. Shape of Vaginal Suppositories

FORMULATION CONSIDERATIONS

Suppository Bases and Excipients[(2),(3) (6),(7),(8)]

Base selection: Vaginal suppository bases fall into two main classes. **Lipophilic bases** are fat- or oil-based (e.g. cocoa butter, hydrogenated vegetable oils, commercial hard fats like Witepsol). These melt at body temperature and release the drug by diffusion/dispersion in the melted lipid. **Hydrophilic bases** are water-soluble or water-miscible polymers (e.g. polyethene glycol [PEG] mixtures, glycerinated gelatine). Hydrophilic bases require aqueous fluid uptake (which is limited in the vagina) and often dissolve rather than melt. Hydrophilic PEG bases tend to soften and dissolve faster than fatty bases. For example, a comparative study found PEG-based suppositories melted much more quickly (in both acidic and basic media) than a Witepsol wax base; the faster dissolution favoured rapid drug release. In general, hydrophilic bases provide rapid drug availability and uniform release, whereas lipophilic bases may sustain release as they gradually melt. Base choice depends on drug properties (soluble in fat or water?), desired release rate, and stability.

Other base options include **glycerol-gelatine**, a matrix of gelatine, glycerine and water, which is semi-solid and swells to release the drug. Glycerol-gelatine can carry both hydrophilic and lipophilic drugs, but may leak or dry out. Some formulations also employ *in situ* gelling systems (e.g. thermosensitive polymers like poloxamers) that are liquid on insertion but solidify at body temperature, reducing leakage.

Excipients such as surfactants (e.g. lecithin, polysorbates), co-solvents, viscosity modifiers, and preservatives are commonly used to aid drug solubility, stability, and release. Viscosity enhancers like propylene glycol or polyvinylpyrrolidone can slow release and leakage. Chelating agents or pH buffers may be included to maintain drug stability. Colourants and mild fragrances are often avoided to prevent irritation.

Bases suitable for drugs.

Hydrophilic drugs tend to show better release in lipophilic (Hydrophobic) bases.

Hydrophobic drugs tend to show better release in lyophobic (Hydrophilic) bases.

Mucoadhesive Polymers and Permeation Enhancers[3],[5],[7] [15],

To overcome rapid clearance and improve retention, many vaginal formulations incorporate **mucoadhesive polymers**. These materials bond to mucin on the vaginal walls via hydrogen bonding, electrostatic and hydrophobic interactions. Common muco-adhesives include polyacrylic acids (carbomers), cellulose derivatives (HPMC, CMC, HPC), chitosan, alginate, and natural gums (e.g. hyaluronic acid). For instance, semisynthetic celluloses (HPMC/HPC) swell on hydration and adhere to mucus, extending residence time. Valenta (2005) lists poly(acrylates), chitosan, cellulose ethers, sodium alginate, gelatine, pectin, etc., as key vaginal mucoadhesive polymers. Polymers can be used as gel matrices or coatings on tablets/pessaries. The stronger the cohesion, the longer the dosage form will stay in place.

Permeation enhancers may be added to improve the mucosal uptake of poorly absorbed drugs. Common enhancers include surfactants (e.g. sodium lauryl sulphate), fatty acids (e.g. oleic acid), bile salts, or compounds like EDTA that open tight junctions. Some studies highlight chitosan itself as both mucoadhesive and permeation-enhancing. These agents transiently increase epithelial permeability, enhancing systemic delivery of peptides or larger drugs.

MANUFACTURING TECHNIQUES

Traditional manufacturing techniques include moulding and compression. Modern innovations involve hot-melt extrusion, spray congealing, and three-dimensional printing. 3D printing enables personalisation by customising shape, size, and drug loading. These technologies allow combination products, where contraceptives, antivirals, and probiotics can be delivered simultaneously. Manufacturing advancements also aim at improving stability, reducing variability, and lowering costs.[11],[12]

METHOD FOR FORMULATION:

1. Hand mould method or Hand Rolling Method
2. Compression mould (Cold compression) Method
3. Fusion or Melt Mould Method
4. Automatic mould Machine.

Hand mould method or Hand Rolling Method

Hand Rolling is the simplest and oldest method of preparation of vaginal suppositories, in which only a few suppositories are to be prepared in a base using cocoa butter. Its advantage is avoiding unnecessary heating, in which plastics like mass have been prepared by triturating grated cocoa butter with active pharmaceutical ingredients (API) in a mortar. The coherent mass is formed into a ball in the palm, then rolled using a cylinder, then cut into the appropriate number of pieces with a conical shape.

Effective hand rolling requires considerable practice and skill. The major demerit is that the suppository pipe or cylinder tends to crack or hollow in the Centre, which will affect its evaluation.

Fusion or Melt Mould Method

Steps

- Melting the base.
- Mixing medicament.
- Pour the melt into moulds.
- Allow the melt to cool.
- Removing the formed suppositories from moulds.
- Polishing the moulded suppositories.
- Evaluation of suppositories.

Compression mould (Cold compression) Method:

This method involves compressing the bulk mass into moulds without heating. It is beneficial for heat-sensitive ingredients and allows for precise control over the shape and size of the suppositories.

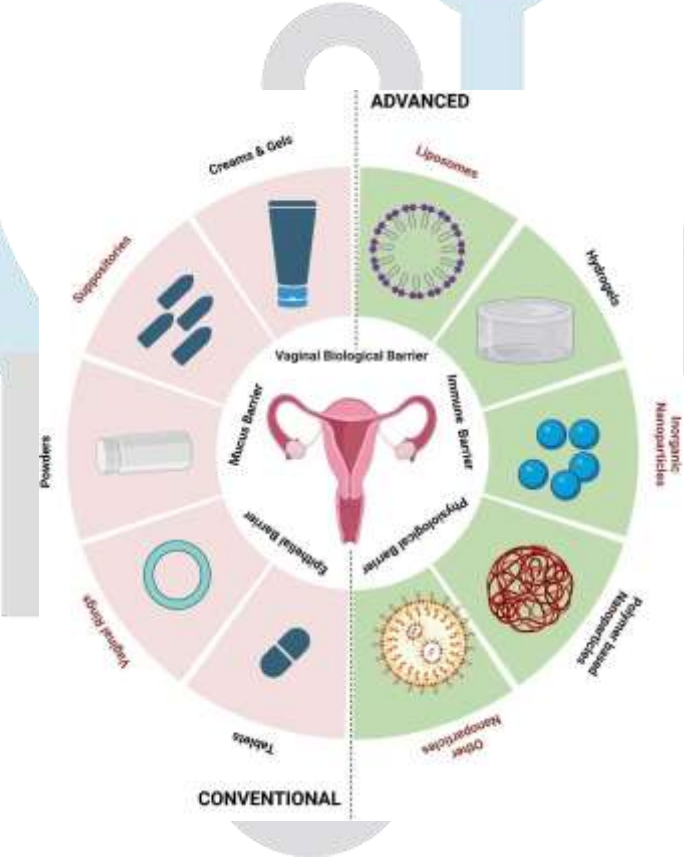

Fig. 3. Conventional and Advanced Vaginal Drug Delivery

ADVANCED DELIVERY VEHICLES

Recent strategies embed novel nanocarriers or smart polymers into vaginal formulations:

- **Nanoparticles:** Polymeric nanoparticles (e.g. PLGA, chitosan NPs), lipid nanoparticles (solid lipid nanoparticles, nano-emulsions) and dendrimers can encapsulate drugs, protecting them and controlling release. Nanoparticles can also be surface-modified for muco-penetration or targeting. For example, nanoparticle-loaded gels have been studied to deliver microbicides or antifungals with prolonged action. Such nano-systems may traverse mucus more readily (muco-inert coatings) and provide extended release[(5),(8)].
- **Liposomes and lipid carriers:** Liposomes can fuse with cell membranes to deliver payloads. Cationic liposomes or transferosomes have been explored to enhance vaginal mucosal delivery of vaccines or hormones. Solid lipid carriers (microparticles or nanoparticles) offer improved stability for volatile or labile drugs[(5)].

- **Thermo-responsive gels (in situ gelling systems):** Poloxamers (triblock PEO–PPO–PEO copolymers) can form liquid-to-gel transitions at body temperature. For instance, Poloxamer 407 mixtures remain liquid in the refrigerator but gel on warming, prolonging contact. Chitosan can also form thermosensitive gels (often with glycerophosphate). Caramella et al. (2015) review poloxamer and chitosan *in situ* gels for vaginal use.[6],[15]
- **Stimuli-responsive and bio-responsive materials:** Advanced systems respond to vaginal stimuli (pH, temperature, enzymes). Examples include pH-sensitive hydrogels that swell or degrade when the acidic environment changes (e.g. during infection). Bio-responsive carriers might release drugs in response to bacterial enzymes (e.g. proteases produced by pathogens). Microbiome-responsive designs are emerging: one could envision probiotic-laden carriers that sense lactobacilli depletion or elicit release under dysbiosis, though such systems are largely experimental[13],[15].
- **3D-printed suppositories:** Recent work has shown that 3D printing allows customizable shapes, multi-layered dosing (immediate plus sustained), and precise control of drug distribution in a pessary. This could enable personalised dosing or combination therapies in a single unit (e.g. separate layers for different drugs). 3D printing also overcomes some compounding limitations of traditional moulding[11],[12].
- **Probiotic-Loaded Suppositories:** Emerging evidence suggests that probiotic vaginal suppositories containing Lactobacillus strains can restore normal microbiota, reduce infections, and improve pH balance. These biotherapeutic formulations represent a promising alternative to conventional antimicrobials[19].
- **Vaginal Microbiome and Drug Delivery:** The vaginal microbiome, dominated by Lactobacillus spp., plays a crucial role in maintaining homeostasis. Disturbances in this microbiota can lead to bacterial vaginosis, yeast infections, or susceptibility to STIs. Suppositories can be designed to restore microbiome balance by delivering probiotics or prebiotics. However, formulations must be carefully optimised to avoid disrupting natural flora. Targeted formulations are being developed to work synergistically with the microbiome for enhanced efficacy.

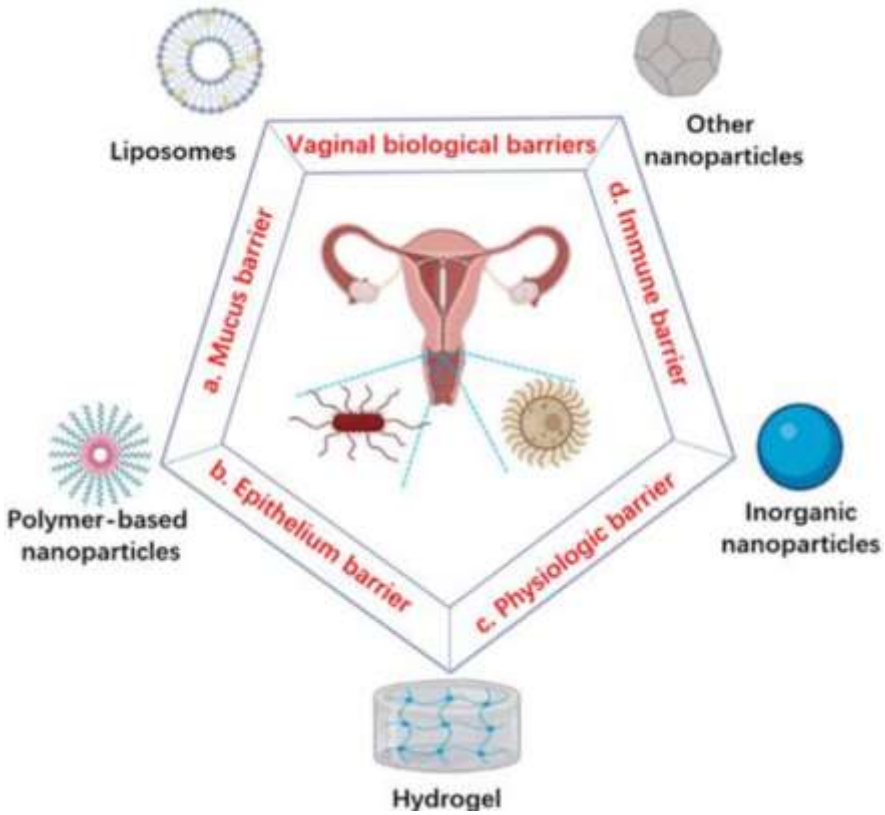

Fig. 4. Barriers for dosage form of Vaginal Drug Delivery

CLINICAL AND PHARMACEUTICAL APPLICATIONS

Vaginal suppositories and pessaries are used for a variety of local and systemic therapies:

- **Antifungal therapy:** Vaginal suppositories for yeast infections are common. Clotrimazole and miconazole suppositories/ovules treat *Candida* vaginitis; these lipid-soluble azoles are released from fatty or PEG bases to act locally on fungal membranes. Nystatin vaginal suppositories are also used. The high local concentration limits systemic exposure and side effects[(3),(4)].
- **Hormonal therapies:** Oestradiol or conjugated oestrogen can be delivered vaginally to treat atrophic vaginitis in menopause. Vaginal oestrogen (in creams, tablets, or rings) improves mucosal thickness, elasticity and lubrication without high systemic doses. Progesterone pessaries are used in assisted reproductive technology for luteal support (in IVF cycles). Some clinicians use vaginal testosterone or dehydroepiandrosterone (DHEA) for hypoactive sexual desire, though these are typically in cream form rather than suppository.
- **Contraception and microbicides:** Spermicidal agents (e.g. nonoxynol-9) have been formulated as vaginal jellies or foams rather than solid suppositories. However, vaginal rings (NuvaRing with etonogestrel/ethinyl oestradiol) and gels (e.g. tenofovir gel for HIV PrEP) represent advanced intravaginal systems. Research is ongoing on multi-purpose prevention technologies (MPTs) that combine contraceptives with antiviral agents in a single vaginal device. Spermicidal suppositories were historically marketed (e.g. para-aminobenzoic acid suppositories), but their use has declined due to messiness and coital timing issues[(9),(10)].
- **Systemic drug delivery:** The vagina is explored for systemic delivery of peptides and small molecules that suffer first-pass metabolism. For example, intravaginal rings have delivered drugs (misoprostol for labour induction, dipivefrine for HIV prevention) effectively. A few studies have tested transvaginal devices (gels or rings) for the delivery of hormones or peptides. While suppositories per se are less common for systemic drug release, in principle, a mucoadhesive suppressive matrix could achieve systemic uptake (as the high vaginal blood flow and permeability might allow)[(9),(10)].
- **Other local indications:** Vaginal suppositories are used for bacterial vaginosis (metronidazole, clindamycin), trichomoniasis, and as delivery vehicles for probiotics (*Lactobacillus* suppositories to restore flora). They can also deliver localised analgesics or anaesthetics, or be used post-surgically to apply antibiotics locally[(19)].
- **Local Therapy**: Widely used in the treatment of bacterial vaginosis, vulvovaginal candidiasis, trichomoniasis, and HPV-related conditions. Vaginal suppositories containing metronidazole, clotrimazole, or miconazole remain first-line local therapies.
- **Contraception:** Spermicidal suppositories (e.g., nonoxynol-9) provide localised contraception, though newer formulations are being developed to improve efficacy and reduce irritation.

CHALLENGES AND LIMITATIONS

While advantageous in many respects, vaginal suppositories face challenges:

- **Leakage and messiness:** Once inserted, bases dissolve or melt and may leak from the introitus, causing discomfort and staining of undergarments. Bulky or non-mucoadhesive formulations are prone to this. To mitigate leakage, mucoadhesive polymers (as noted) can help the dosage form adhere to walls, and in situ gelling formulations can solidify at body temperature. Nappi et al. also note that “pessaries” (bullet-shaped suppositories) tend to avoid leakage better than gels or creams. Careful base choice (e.g. poloxamer gels) and design (shell or coating) can reduce discharge.
- **Dose variability:** The volume of vaginal fluid varies between women and across cycles, affecting how much base dissolves. Excessive fluid (e.g. during menstruation or infections) can dilute drug release. Furthermore, pH shifts (e.g. menstrual blood temporarily raises pH, BV raises pH) can alter

drug ionisation and absorption. These factors introduce variability in effective dose and blood levels if systemic effect is sought.

- **Retention issues:** Sexual intercourse, vigorous activity, or improper placement can dislodge a suppository. Patients must be instructed to lie down after insertion for a few minutes. The need for applicators or specific positions may reduce compliance.
- **Acceptability and comfort:** Some women find inserting suppositories unpleasant or embarrassing. Bases (especially fatty ones) may feel oily. Fragrance-free, neutral-textured formulations are preferred. Also, some ingredients (e.g. SLS surfactant) can irritate sensitive mucosa. Clinically, acceptability studies often find that "messiness" and "film" on tissues are common complaints. Designing formulations (e.g. fast-dissolving, film-forming, or foam applicators) to minimise this is an ongoing effort.
- **Chemical limitations:** The acidic vaginal pH can degrade certain drugs, and enzymes (though fewer than in the GI tract) can metabolise peptides. Also, lipophilic drugs may partition into the base (especially fatty bases) and not release fully. Formulators often use surfactants or cosolvents to keep drugs in solution.
- **Regulatory and stability issues:** Suppositories must be manufactured under strict conditions to ensure uniformity (weight/hardness/content). Many APIs lack specific stability data in base form, and water can promote microbial growth if not preserved. These technical challenges require rigorous pre-formulation work [(2),(3),(4),(6),(14),(20)].

RECENT TECHNOLOGICAL ADVANCES

Several cutting-edge approaches are being applied to vaginal suppositories:

- **Nanomedicine:** Incorporation of nanocarriers within suppositories or gels can enhance delivery. For example, *multipurpose nanoparticles* that carry both antifungal and anti-inflammatory agents are being studied. Lipid nanoparticles or polymeric micelles can solubilise hydrophobic drugs and release them over time. Advances in **muco-inert nanoparticles** (coated with PEG to avoid mucus entrapment) have shown improved distribution throughout the cervicovaginal mucus[(5),(8)].
- **3D Printing:** Emerging work uses 3D extrusion to fabricate suppositories with complex architectures. This allows multi-drug layering (e.g. an outer rapid-release analgesic layer and an inner sustained-release antibiotic core) or personalised dosing. Polymers like PVA and PEG blends can be printed into custom shapes, and this on-demand manufacturing could tailor treatment for patients with unique anatomy or dosing needs[(11),(12),(16)].
- **Bio-responsive materials:** Researchers are developing polymers that respond to vaginal conditions. For instance, pH-sensitive hydrogels (e.g. poly(β-amino ester) networks) that shrink or swell when pH rises (as in infection) to trigger release of antimicrobials. Enzyme-degradable matrices (responding to proteases from pathogens) are being explored. Even systems that sense microbial metabolites (like hydrogen peroxide from healthy lactobacilli) and modulate drug release accordingly are under investigation[(13),(15)].
- **Microbiome-aware systems:** Given the critical role of flora, novel suppositories may include probiotics or prebiotics that favour *Lactobacillus* growth. Designer bacteria producing anti-HIV or anti-inflammatory peptides *in situ* have been conceptualised. The idea of a "vaginal microbiome patch" that both monitors pH and releases buffer or drug is under early development[(19)].

Overall, vaginal suppositories are benefiting from advances in formulation science (e.g. smart polymers, nano formulations) as well as manufacturing (3D printing). These innovations aim to overcome the traditional drawbacks (leakage, short residence) and to expand the range of deliverable therapeutics.

MARKETED PRODUCTS

Several marketed products illustrate the clinical relevance of vaginal suppositories. Clotrimazole[3],[4] suppositories remain a cornerstone in antifungal therapy. Vagifem®[3], delivers oestrogen for menopausal vaginal atrophy. Endometrin®[3] provides progesterone for IVF treatment. Research products include tenofovir-loaded suppositories[9],[10] for HIV prevention. These products demonstrate safety, patient acceptability, and therapeutic efficacy. Market expansion continues with newer bio-enhanced formulations.

COMPARATIVE OVERVIEW WITH OTHER VAGINAL DOSAGE FORMS.

Other vaginal dosage forms include gels, creams, tablets, films, and rings. Suppositories provide controlled release and systemic potential but may suffer from leakage and compliance issues. Rings offer long-term release but can be expensive. Films are discreet but have limited drug loading capacity. Suppositories remain a practical balance between cost, efficiency, and innovation potential. Their ease of manufacture and versatility in formulation make them a widely studied option[3],[4],[9],[13],[14].

Sr no.	Dosage Form	Examples	Advantages	Limitations
1.	Suppositories	Clotrimazole, Oestrogen	Easy manufacturing, Controlled release systemic potential	Leakage, Patient acceptability
2.	Vaginal tablets	Misoprostol, Progesterone	Stable, Convenient packaging	Slower disintegration
3.	Vagina rings	NuvaRing® (etonogestrel/ethinyl oestradiol)	Long-term release (3 weeks – 1 year)	Expulsion risk, Cost
4.	Gels and creams	Metronidazole gel, Clindamycin	Easy application, immediate release	Leakage, Messy application
5.	Films	Anti-viral films	Thin, discreet, fast dissolving	Limited drug load, Fragile

Table. 1. Comparative Overview with Other Vaginal Dosage Forms

REGULATORY CONSIDERATIONS

Vaginal suppositories fall under semisolid/solid dosage forms in both FDA and EMA guidelines. Key regulatory aspects include:

- Quality Control – testing for microbial contamination is mandatory, given the sensitivity of the vaginal environment[3].

- Bioequivalence Studies – challenging due to variability in vaginal physiology; both in vitro release and clinical endpoints are considered[20].
- Patient Safety – excipients must be non-irritant, non-spermicidal (unless intended), and should not disrupt normal vaginal flora[19].
- Standardisation – Need for harmonised protocols (USP, Ph. Eur., WHO) to compare new vaginal formulations[20].

EVALUATION OF VAGINAL SUPPOSITORIES

Evaluation is critical to ensure the safety, efficacy, and patient acceptability of vaginal suppositories. Evaluation includes physicochemical parameters[3],[7] (weight variation, hardness, melting point, disintegration, drug content uniformity) and functional parameters[15] (in vitro dissolution, muco-adhesion strength, permeation studies[5],[6]). Simulated vaginal fluid (SVF) is often employed to mimic in vivo conditions. Ex vivo studies on porcine or bovine mucosa assess adhesion, while animal models evaluate pharmacokinetics and therapeutic efficacy. Clinical trials provide evidence on acceptability, safety, and therapeutic outcomes[9],[10].

- Weight variation and content uniformity: Ensures dosage consistency.
- Hardness and friability: Determine mechanical strength during handling.
- Melting/softening point: Essential for lipophilic bases to ensure uniform drug release.
- Disintegration time: Indicates how quickly the suppository breaks down in vaginal fluids.
- Drug release profile: Studied using a dissolution apparatus modified with simulated vaginal fluid (SVF).
- Mucoadhesion Studies: Ex vivo studies using porcine or bovine vaginal mucosa are performed to evaluate bio-adhesive strength. Polymers like Carbopol or chitosan demonstrate higher adhesion, correlating with prolonged residence time.
- Permeation Studies: Ex vivo diffusion studies using Franz diffusion cells. In vivo pharmacokinetic studies in animal models (e.g., rabbits, sheep) followed by human clinical evaluation.

FUTURE PERSPECTIVES

- Multifunctional formulations combining contraceptive, antimicrobial, and probiotic agents[19].
- Smart biomaterials responsive to pH, enzymes, or temperature changes[13],[15].
- Integration with nanomedicine and gene therapy offers possibilities for treating reproductive tract cancers or viral infections[5],[8].
- Regulatory standardisation of testing protocols (e.g., simulated vaginal fluid, in vitro muco-adhesion models) to improve comparability of formulations across studies.
- Integration with nanomedicine and biodegradable polymers for site-specific delivery.
- Exploration of vaginal microbiome interactions with formulations[19].
- Clinical trials on vaginal vaccines (HIV, HPV, and reproductive tract infections)[9],[10].
- Patient-centred designs with improved acceptability, aesthetics, and convenience.
- Expansion into oncology and systemic peptide delivery.

CONCLUSION

Vaginal suppositories, once considered conventional, are now being reinvented as novel and versatile drug delivery systems**.** Advances in mucoadhesive polymers[3]**,** nanotechnology[5],[8]**,** and 3D printing[11],[12] have opened new possibilities for local and systemic delivery. While challenges[14] such as variability in vaginal physiology and patient compliance remain, ongoing innovations and personalised approaches hold promise to establish vaginal suppositories as a cornerstone in drug delivery, particularly in women's health**,** infectious diseases**,** and systemic therapy.

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