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REVIEW article

Mucoadhesive vaginal tablet: A novel approach for vaginal drug delivery

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Abstract: The vaginal route has gained significant attention as an effective alternative for local and systemic drug delivery, offering advantages such as avoidance of hepatic first-pass metabolism, enhanced bioavailability, and patient compliance. However, conventional dosage forms like creams and gels often suffer from poor retention and unpredictable drug release. To overcome these limitations, mucosadhesive vaginal tablets have emerged as a promising strategy, capable of adhering to the mucosal surface and providing sustained, localized drug delivery. This review highlights the anatomy and physiology of the vaginal tract, key factors affecting drug absorption, and the mechanistic principles of mucoadhesion. It discusses various formulation methods and polymers, natural and synthetic, such as chitosan, Carbopol, and cellulose derivatives, used to optimize adhesion, swelling, and release characteristics. Furthermore, it explores the therapeutic potential of mucoadhesive vaginal systems in hormonal therapy, contraception, infection control, and targeted cancer therapy. Thus, mucoadhesive vaginal tablets represent a novel and patient-centric approach to vaginal drug delivery, offering enhanced retention, controlled release, and improved therapeutic outcomes. Continued advancements in polymer science and formulation technology are expected to strengthen their clinical applicability and relevance in women's health care.

Introduction

The vagina offers a promising option for local and systemic drug delivery due to its expansive surface area, abundant blood supply, avoidance of the first-pass metabolism, relatively high permeability to various drugs, and the potential for self-insertion. However, this route has not been widely utilized because of significant individual differences in physiological factors, such as pH and the variable levels of vaginal secretions that change based on age and menstrual cycles. While many possibilities are currently under exploration, there are a few vaginal dosage forms available. Existing vaginal delivery systems have drawbacks such as leakage, messiness, and a relatively short residence time due to the self-cleaning nature of the vaginal tract, often necessitating multiple doses per day to achieve the desired therapeutic outcome. The vaginal route seems suitable for bioadhesive drug delivery systems designed to maintain the presence of drugs for treating primarily local conditions or for contraceptive use. Especially important is the need for protection against sexually transmitted infections. To enhance the duration of drug presence in the vaginal cavity, bioadhesive therapeutic systems have been created [1]. The novel systems for vaginal delivery offer several key benefits, including enhanced mucoadhesiveness, prolonged action, and altered drug release profiles. They can be effectively targeted to the specific area of application, thereby increasing drug bioavailability. Various

innovative drug delivery systems, such as liposomes, microemulsions, nanoparticles, microparticles, bio-adhesive gels, bio-adhesive films, bio-adhesive tablets, vaginal rings, and microneedles, have been explored for vaginal use [2]. The pharmaceutical industry and scientific community are currently exploring new methods for administering medications with low oral absorption. Despite the potential for non-invasive drug delivery, the number of scientific articles published in pharmaceutical journals in the last decade indicates that the human vagina remains a relatively understudied option for drug delivery. For various medications, including bromocriptine, propranolol, oxytocin, calcitonin, LHRH agonists, human growth hormone, insulin, and steroids used for hormone replacement or contraception, this pathway provides a more effective alternative to the parenteral method. Administering hormonal contraceptives through the vaginal route is an excellent choice [3].

Classification of an intra-vaginal drug delivery system: Intra-vaginal drug delivery system classified into vaginal rings, vaginal tablets, vaginal powders, vaginal capsules, vaginal ointments, vaginal gels, vaginal creams, and vaginal suppositories [4, 5].

Vaginal tablets are designed to dissolve or break down inside the vagina, releasing the medication into the cavity. A vaginal tablet includes all the inactive ingredients typically found in a standard conventional tablet.

Vaginal ring is made by mixing a contraceptive steroid, like medroxyprogesterone acetate, in the form of micronized solid particles with a thick blend of silicone elastomer and catalyst, then extruding this steroid-polymer mixture into a mold to create the ring. These rings are intended to be inserted into the vagina and sit around the cervix.

Vaginal gels are frequently utilized to introduce substances that tighten the vaginal area by causing the vaginal muscles to contract, which can lead to increased sexual pleasure. In cases of vaginal dryness, these gels serve as a lubricant.

Vaginal foams are contraceptive products designed to prevent pregnancy. A spermicide is incorporated into vaginal foam to kill sperm and lower the likelihood of conception. The foam creates a barrier that separates sperm from the egg.

Factors affecting vaginal drug delivery: The vagina's ecology is affected by various factors, including the glycogen levels in epithelial cells, glucose availability, pH, hormone levels, trauma during intercourse, the method of birth control, age, use of antimicrobial treatments, and childbirth. The vaginal microbiome is a fluctuating system primarily made up of Lactobacillus, the most common organism in the vaginal environment, along with various facultative and obligate aerobes and anaerobes. Vaginal biopsies have proven to be highly effective in showing the distribution of vaginal mucosa. The glycogen content in the superficial epithelial layers of the vagina tends to rise throughout the menstrual cycle and then decrease during the late premenstrual period, correlating with oestrogen levels. As oestrogen production declines during the pre-menopausal and menopausal phases, there is a consistent reduction in vaginal glycogen content [6].

Advantages: Extended/prolonged release, limited systemic side effects, enhanced bioavailability, administration of a smaller overall dose compared to oral intake, first-pass metabolism can be bypassed, self-administration is feasible; contact with digestive fluids is circumvented, reducing drug degradation, nausea, vomiting, and other emesis associated with oral intake are prevented, and rapid onset of action [7]. *Limitations:* This drug delivery system is specific to gender; the vaginal route is generally less favoured due to its inconvenience, the permeability of the vagina is significantly affected by oestrogen levels, which can influence the pharmacokinetics of medications, studies have indicated that the volume of vaginal fluid in an adult female average between 2-3 gram per 24 hours, decreasing with age and potentially impacting drug absorption through the vagina, and the pH level of vaginal fluid is another factor that influences drug absorption, as it affects the uptake of unionized drugs [8].

Mechanism of mucoadhesion: The process can be outlined in the following two phases: *Contact phase:* This phase consists of the interaction between the mucoadhesive substance and the mucus layer, causing the formulation to expand and spread across the mucous membrane. *Consolidation phase:* The mucoadhesive substance is activated by moisture, which further plasticizes the system and enables the adhesive molecules in the mucus to detach and bond through weak van der Waals forces and hydrogen bonds [9].

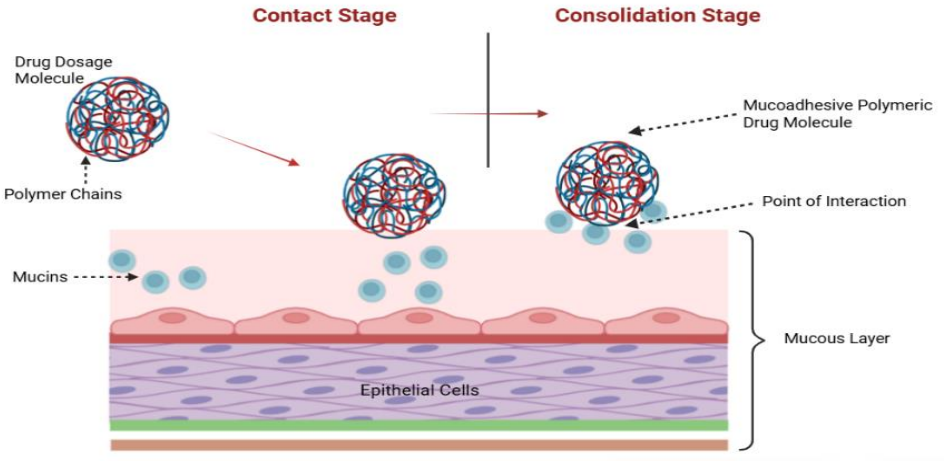

Figure 1: Mechanism of mucoadhesion

Theories of mucoadhesion: There are different theories [10-12].

The wetting theory: This pertains to liquid systems that exhibit an affinity for a surface, allowing them to spread across it. This affinity can be assessed using techniques like measuring the contact angle. As a rule, a smaller contact angle signifies a stronger affinity. For optimal spread ability, the contact angle should be approximately zero. The spread ability coefficient, SAB, can be determined by the difference between the surface energies γB and γA, along with the interfacial energy γAB, as represented in the equation below. This theory highlights the significance of contact angle and the reduction of surface and interfacial energies in achieving a satisfactory level of mucoadhesion.

Electronic theory: The electronic theory posits that mucoadhesive materials and biological substances have contrasting electrical charges. Consequently, when these materials interact, they exchange electrons, resulting in the formation of a double electronic layer at their interface, where the attractive forces within this layer influence the strength of mucoadhesion.

Adsorption theory: The mucoadhesive device sticks to the mucus through secondary chemical interactions, such as van der Waals forces, hydrogen bonding, electrostatic attraction, or hydrophobic interactions. For instance, hydrogen bonds are the dominant interfacial forces in polymers that contain carboxyl groups. These forces are regarded as the most significant contributors to adhesive interactions because, despite their individual weakness, a large number of such interactions can produce a strong overall adhesion.

Fracture theory: This theory explains the force needed to separate two surfaces that are adhered together. The strength of the fracture corresponds to the adhesive strength, represented by the following equation. This theory is beneficial for investigating bioadhesion using tensile equipment. $\sigma = (E \times \varepsilon/L)1/2$, where σ is the fracture strength, ε is the fracture energy, E young modulus of elasticity, and L is the critical crack length.

Diffusion theory: Diffusion theory explains that polymer chains from the bioadhesive interweave with glycoprotein mucin chains, penetrating deeply enough into the opposite matrix to create a semi-permanent bond. This process can be envisioned starting from the initial point of contact. The presence of concentration gradients will drive the polymer chains of the bioadhesive into the mucus network, while the glycoprotein mucin chains will move into the bioadhesive matrix until a balanced penetration depth is reached.

Mucoadhesive polymers: Mucoadhesive agents facilitate intimate contact between the formulation and the vaginal mucosal surface by enhancing adhesion. These agents include polycarbophil, hyaluronic acid, chitosan, sodium alginate, tragacanth, carbomer, acacia, sodium carboxymethyl cellulose, and various cellulose derivatives, as well as Carbopol 974P-NF, Carbopol 971P-NF, and other acrylic acid copolymers. Certain polymers may have bioadhesive properties that are specific to particular sites, such as xanthan gum and sodium alginate in a simulated vaginal environment. Polycarbophil 934-P has shown bioadhesive characteristics that depend on pH levels [13-19].

Cellulose and its derivatives are believed to be the most plentiful organic compounds found on Earth. It consists of a linear arrangement of polysaccharides made up of 3000 to 14,000 glucose units. Pure and unchanged cellulose does not dissolve in water or most organic solvents. The hydroxyl groups in the primary chain can be modified through esterification or etherification to improve solubility and swelling properties. Semisynthetic cellulose derivatives represent a wide and varied group of substances with numerous characteristics. They differ in polarity, water solubility, swelling abilities, and possible pharmacological and biological uses. The most common cellulose derivatives include microcrystalline cellulose, methylcellulose, ethylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, and sodium carboxymethyl cellulose [14].

Pectin and traganth are an invention that comprises a fungicidal or fungistatic agent, a surfactant to enhance penetration, and/or a bioadhesive gum such as tragacanth, pectin, dextran, or xanthan to adhere the medication to the vaginal wall. A solution was created by combining ketoconazole, pectin, nonyl phenol-9, and polyethylene glycol. The bioadhesive tablet made from a 2: 1 mixture of Carbopol-934 and pectin exhibited the strongest bioadhesive properties, the greatest swelling volume, and the least pH decrease among sixteen different formulations utilizing bioadhesive polymers for vaginal use [14, 15].

Alginates are naturally occurring anionic polysaccharides that are biocompatible and biodegradable, primarily found in brown seaweeds (Phaeophyceae). Among all types, sodium alginate is the most utilized for pharmaceutical and biomedical applications. Due to their hydrophilic properties, alginates possess a significant capacity for binding water. When exposed to divalent and multivalent cations, an alginate solution experiences a process known as ionotropic gelation. Alginates are utilized as thickeners and stabilizers in liquid and semisolid pharmaceutical products. They are also studied as binders and agents for forming hydrophilic matrices in solid dosage forms designed for extended release. Additionally, their ability to undergo ionotropic gelation could be beneficial for formulations involving in situ gelling systems [16].

Starch is one of the most plentiful plant polysaccharides and serves as the primary carbohydrate in the human diet. It is made up of two components: linear amylose (25.0%) and branched amylopectin (75.0%), formed from numerous α-D-glucose units. In amylose, the structural elements are connected by α-1,4 bonds, whereas amylopectin features α-1,4, α-1,3, and α-1,6 bonds. Starch is insoluble in cold water, but when heated, it tends to swell and create gels. For vaginal drug delivery applications, starch and its derivatives are primarily studied as components of tablets, micro- or nanoparticles, gels, and so forth [16].

Gelatin: The initial mucoadhesive system intended for vaginal use was formulated with gelatin. In this system, gelatin served as the mucoadhesive polymer within a medicated tampon that contained micronized progesterone as the active ingredient to support pregnancy, especially during in vitro fertilization procedures. However, gelatin's use can sometimes lead to the degradation of moisture-activated drugs, which may limit its effectiveness as an adhesive agent [17].

Chitosan has appealing biological characteristics, including biocompatibility, biodegradability, non-toxicity, and physiological inertness. Chitosan is a polymer that results from the partial deacetylation of chitin. Formulations incorporating this excipient have demonstrated sustained drug release, mucoadhesive properties, inherent antimicrobial activity, and the ability to stimulate the immune response. Specifically, researchers have

studied chitosan independently and in combination with pectin and locust bean gum as excipients for creating mucoadhesive vaginal matrices aimed at the sustained release of tenofovir. The findings indicated that the combination of chitosan and pectin can form polyelectrolyte complexes that create a strong system with prolonged mucoadhesion on the vaginal mucosa and facilitate a controlled release of tenofovir for four days, which aligns with the vaginal turnover period [18, 19].

Anatomy and physiology of the vaginal system: *Vagina:* Historically, this method of administration has been utilized for the delivery of contraceptives and for localized treatments, but it has also been investigated for the systemic delivery of medications. The extensive surface area is attributed to the many folds and microscopic ridges present in the epithelial layer. While the vaginal mucosa does not contain glands, it is typically coated with vaginal fluid, which consists of a combination of fluids from various sources. The primary constituents are cervical mucus and vaginal fluid from the richly supplied mucosa. The volume, thickness, and pH of the cervical mucus fluctuate with age and throughout the menstrual cycle. In fertile women, this fluid is acidic, exhibiting a pH range of 4 to 5 [20]. Vagina is a flexible fibromuscular tube measuring 9 to 10 cm in length in women of reproductive age. It extends upward and backward from the vaginal opening to the base of the uterus. Located between the urethra (and a portion of the bladder) and the rectum, the vagina serves several functions. It allows for the exit of mucous secretions from the upper reproductive organs, menstrual fluid, and products of conception, and it accommodates the penis during sexual intercourse. The vaginal wall consists of four layers: the mucosal layer, the fibrous connective tissue, smooth muscle, and a dense network of vascular connective tissue [21].

Blood supply, lymph drainage, and nerve supply: *Arterial supply* involves the formation of an arterial plexus around the vagina, which is derived from the uterine and vaginal arteries, branches of the internal iliac arteries. *Venous drainage* occurs through a venous plexus located in the muscular wall, which empties into the internal iliac veins. Lymphatic drainage is facilitated by the deep and superficial iliac lymph nodes. *The nerve supply* includes parasympathetic fibers originating from the sacral outflow, sympathetic fibers from the lumbar outflow, and somatic sensory fibers from the pudendal nerves [22]. Human vaginal fluid primarily originates from vaginal and cervical cells, which are rich in enzymes, enzyme inhibitors, proteins, carbohydrates, amino acids, alcohols, hydroxyl-ketones, and aromatic substances. The makeup of these fluids is influenced by hormonal changes and the state of arousal, which can modify the drug release patterns from vaginal drug delivery systems. Throughout the menstrual cycle, the thickness of the vaginal epithelium and the quantity and composition of vaginal fluid change. It is estimated that vaginal cells renew themselves at a rate of 10 - 15 layers every seven days [23].

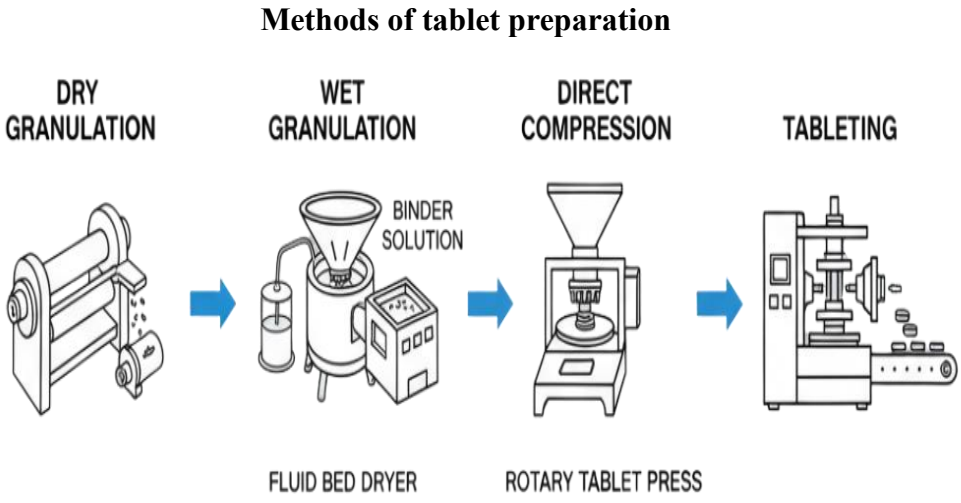

Figure 2: Dry, wet granulation, and direct compression

Tablets are manufactured using three methods: direct compression, wet granulation, and dry granulation.

Direct compression: The direct compression method is often considered the most efficient way to produce tablets. This technique is the simplest and is therefore preferred over alternative methods. Direct compression is the most straightforward and economical means of tablet manufacturing, as it requires fewer processing steps compared to approaches like wet granulation and roller compaction. However, numerous pharmaceutical active ingredients cannot be compressed directly into tablets due to inadequate properties related to flow, cohesiveness, and lubrication. As a result, they must be combined with other directly compressible materials to create acceptable tablets [24]. Direct compression is used when the drug makes up the majority of the tablet's overall weight. For tablets with ≤ 25.0% of the active ingredient, a compatible diluent can be used as a carrier or medium for the drug. Tablets produced using this method are then processed through a compression machine, which can be either a single or multiple-station device [25].

Advantages

Uniformity: Direct compression guarantees a uniform tablet size, shape, and weight.
Convenience: Tablets are simple to administer, and dosage is straightforward.
Cost-effectiveness: Lower manufacturing costs.
Stability: Increased stability and potency of the active pharmaceutical ingredient.
Bioavailability: Improved rates of absorption [26].

Disadvantages

- Stratification can happen because of variations in particle size and bulk density, leading to unsatisfactory content uniformity.
- A drug with a large dosage can create challenges in direct compression, necessitating the use of diluents. This results in larger tablets, which are not only difficult to swallow but also more expensive.
- While handling dry materials, static electricity can develop, hindering the uniform distribution of the drug.
- Additionally, a direct compression diluent may interact with the drug, such as when an amine drug comes into contact with lactose, leading to tablet discoloration [27].

Wet granulation: The method of incorporating a liquid solution into powders entails the weighing of a combination of dry primary powder particles with a granulating liquid. This liquid must consist of a solvent that is volatile, allowing for its removal through drying, and it should also be non-toxic [28]. This method is the most prevalent and widely utilized. It involves several steps, including weighing ingredients, mixing, granulating, screening damp powder, drying, lubricating, and compressing tablets. The primary active ingredient, along with diluents and disintegrants, is combined, after which they are passed through a sieve (sifting). Solutions containing the binding agent are incorporated into the initial mixture while stirring. The quantity of binding agent introduced must be adequate to prevent excessive wetting of the tablet. If the powder is inadequately wetted, the granules may become too soft and can disintegrate during lubrication, which complicates the tablet compression process. Tray drying is the most employed technique for drying tablet granules. Historically, tray drying was the most favored method, though it may gradually be supplanted by fluid-bed dryers as a more modern technique. Once the granules are dried, they are passed through a screen, typically using a 60-100 mesh nylon cloth. After the dry granulation process, a fine powder lubricant is added, which is essential for proper die cavity filling [29]. The primary drawback of wet granulation is its expense. This process incurs high costs due to factors such as labor, time, equipment, energy, and space needs. There is a potential for material loss during different phases of the process. For moisture-sensitive or thermally unstable drugs, stability can be a significant issue. The multiple steps involved lead to increased complexity, making validation and control more challenging [30].

Dry granulation: Dry granulation necessitates the use of drugs or excipients that possess cohesive qualities. This method is more straightforward than wet granulation, leading to reduced costs. It is frequently utilized

when the material being granulated is vulnerable to moisture and heat. The dry granulation process can be performed using a tablet press with slugging tools or on a roller compactor, known as a roll press. This technique often results in a higher proportion of fine granules, which may negatively impact quality or cause yield issues in the tablets. Various response variables are being assessed to evaluate these tablets. Pre-formulation and post-formulation factors are being analysed to ensure the effectiveness of the formulated preparations [31].

Steps: Milling → weighing → screening → mixing → slugging → granulation (dry) → lubrication → compaction [32].

Advantages

- *No solvent residue*: Dry granulation removes concerns associated with solvents.
- *Moisture-sensitive materials*: Appropriate for materials that are sensitive to moisture or heat-sensitive [33].

Disadvantages

- *Elevated compression force*: Necessitates significant compression force, which may lead to tablet imperfections.
- *Restricted binder usage*: Limits the choice and application of binders [33].

Evaluation parameters

Pre-compression tests

- *% Yield* = actual yield / theoretical yield × 100. *Bulk density* = weight of granules/total volume.
- *Tapped density* = Weight of granules / tapped volume.
- *Carr's index* = (tapped density - bulk density) / tapped density × 100.
- *Hausner's ratio* = tapped density/bulk density.
- *Angle of repose (α)* = tan^ (-1) (h/r) where, h = height of the pile, r = base radius of the pile [34].

Post-compression tests

- *Hardness test:* The hardness test is performed with a Pfizer hardness tester or an alternative for three tablets from every batch, and average values are determined.
- *Weight variation test:* A weight variation test is conducted on ten tablets from every batch utilizing an electronic balance, after which the average values are computed.
- *Tablet thickness:* The thickness of each formulation is determined using vernier calipers. An average is calculated by measuring ten tablets from each batch [35].
- *Friability:* Tablet strength can be assessed through friability. The friability of a tablet can be measured using a friabilator (such as Aarson) or similar equipment. It is reported as a percentage. Tablets are placed in a plastic chamber that rotates at 25 rpm for four minutes or until 100 revolutions are completed, dropping the tablets from a height of 6 inches with each turn. Initially, weighed tablets were placed into the friabilator and rotated 100 times. The percentage of weight loss is calculated using the following formula [36].
- *Surface pH studies:* The surface pH of the formulated tablets is assessed by immersing each tablet in 1.0 ml of distilled water for 60 seconds. Once the soaking period is complete, the pH of the damp surface is evaluated by placing the electrode in direct contact with the tablet's surface [37].
- *Ex-vivo mucoadhesion study:* A modified device is utilized for studies on mucoadhesion conducted ex vivo. Ex vivo mucoadhesion experiments use goat vaginal mucosa and a modified two-armed balance. The goat vaginal mucosa is secured to plastic pieces using cyanoacrylate adhesive. A pre-warmed solvent is poured into the beaker containing the mucosa until it reaches the upper surface of the mucosa

to ensure the mucosal viability is maintained. The mucoadhesive tablet is fastened to the upper clamp with adhesive. The beaker is then gradually lowered until the substrate meets the tablet. A preload of 50 grams is applied to the clamp for 5 minutes to allow the adhesive to establish itself. After this period, the preload is removed. Weights are added to another pan until the mucoadhesive tablet detaches from the mucosa, and the amount of weight needed to detach the tablet is recorded [38].

- *Swelling test:* Three tablets are taken from each formulation and accurately weighed, referred to as W1. The selected tablets are then placed into petri dishes containing 5.0 ml of a pH 6.8 phosphate buffer. Afterward, the tablets are removed from the petri dishes, and excess water is eliminated using filter paper. The tablets are weighed again, denoted as W2, and the percentage of hydration for each tablet is calculated using the equation [39].
- *In-vitro dissolution study:* The release of the drug from the tablet is assessed using a dissolution apparatus with a USP paddle type. One side of the tablet is moistened with a citrate/phosphate buffer at pH 4.8 and secured to the bottom of the dissolution vessel. After a duration of two minutes, the vessel is filled with 900 mL of citrate/phosphate buffer at pH 4.8, maintained at 37°C, and stirred at a speed of 50 rpm. At designated time intervals, 5.0 ml samples are taken and replaced with an equal volume of the dissolution medium, which is also kept at 37°C to ensure sink conditions are met. The samples are filtered through a Millipore filter, and the absorbance of the drug is measured using a UV spectrophotometer at a specific λ max. Concentrations are determined based on a calibration curve that was created beforehand, with the citrate/phosphate buffer at pH 4.8 serving as the blank. The percentage of drug released at each time point is expressed as a fraction of the total drug content in the tablets [40].
- *Stability studies:* The stability studies under accelerated conditions are performed in accordance with ICH guidelines. The optimized formulation is enclosed in an amber bottle, with the upper portion sealed using aluminium foil, and this packaged formulation is kept in stability chambers set at 40.0°C ± 2.0°C and 75.0% RH ± 5.0% for a duration of four weeks. The tablets are assessed prior to and following the four weeks for any changes in appearance, drug content, and *in vitro* release [41].

Applications

Mucoadhesive systems to deliver anaesthetics: Viral infections, such as the Human Papilloma virus, can present with painful symptoms, with erosions, ulcers, and scars, often being part of the condition. To address these infections, antiviral medications are combined with anti-inflammatory and pain-relieving drugs like Ketorolac. This substance has properties like opioids and can be utilized to alleviate moderate to severe pain, yet it does not carry the risk of addiction or sedative effects. Its impact is comparable to that of morphine, but it comes with fewer side effects [42].

Hormonal treatment and birth control: Currently, women's health care, particularly regarding sexual health, is being addressed and discussed more openly, allowing for the possibility of administering drugs vaginally. Hormones such as progestogen and oestrogen, alone or in combination, are utilized to alleviate pain and/or infertility linked to this condition. Traditionally, the preferred method for administering these medications has been orally, but lately, vaginal administration is gaining traction to minimize the side effects associated with hormone intake [43].

Cervical cancer treatment: Cervical cancer is the second most prevalent gynecological cancer among women and is known to be resistant to chemotherapy. The creation of mucoadhesive vaginal tablets that contain antivirals is a promising strategy for the treatment and prevention of HPV infections. These formulations facilitate targeted delivery to the infection site, thereby improving drug effectiveness and reducing systemic side effects. Incorporating mucoadhesive polymers in these formulations can prolong the retention time of the drug on the mucosal surface, consequently enhancing the overall effectiveness of the treatment.

Fungal and bacterial infections: Among genital infections, bacterial vaginosis, Trichomonas vaginalis, and vulvovaginal candidiasis are the most prevalent. Chlamydia trachomatis (C. trachomatis) is the primary cause of microbial sexually transmitted infections, leading to significant reproductive health issues in females. Gonorrhea, resulting from the Gram-negative diplococcus Neisseria gonorrhoeae, is a common sexually transmitted infection. Valacyclovir and famciclovir are authorized for treating various clinical forms of HSV infections, such as cold sores and recurrent genital herpes. Acyclovir is the most frequently utilized first-line therapy for Herpes virus infections [44].

Future aspects*:* The latest advancements in mucoadhesive systems have revitalized the understanding of mucoadhesion through innovative mechanisms developed from fundamental research. These cutting-edge mucoadhesive technologies have increasingly captured the attention of researchers focused on targeting specific cells. However, before dosage forms employing these technologies can be used clinically, they require ongoing investigation from biological, industrial, and clinical perspectives. In the coming years, academic and industrial initiatives will likely emerge to explore new possibilities in mucoadhesive systems [47].

Conclusion: Mucoadhesive vaginal tablets offer a promising and patient-friendly approach for localized and systemic drug delivery. Their ability to adhere to the vaginal mucosa ensures prolonged retention, controlled drug-release, and improved therapeutic efficacy. Advances in polymer technology and formulation design have further enhanced their bioadhesive strength and biocompatibility. With ongoing research into novel polymers and smart delivery systems, mucoadhesive vaginal tablets hold significant potential to revolutionize women's healthcare by providing effective, safe, and convenient drug delivery options.

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