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Medication Delivery Using Hydrogels to Treat Vaginal Infections

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INTRODUCTION

In terms of anatomy, the ovaries, fallopian tubes, cervix, ectocervix, and vagina make up the majority of the female reproductive system. The 9 cm long distensible organ known as the vagina is made up of stratified epithelium, a fibromuscular layer, lamina propria, and adventitia. Beyond that, cervical mucus protects it, which aids in drug absorption. About 90% of cervical mucus is made up of several substances, including water, urea, carbohydrates, mucins, fatty acids, salts, and proteolytic enzymes. The major purposes of mucus are to lubricate and protect the vagina from infections, and the cervical mucus in the vagina is constantly regenerated. Age, hormone levels, and the menstrual cycle all have an impact on the anatomy and physiology of the vagina, which can disrupt the natural vaginal flora and affect the pH, makeup, and volume of the vaginal fluids. For instance, during the follicular phase of the menstrual cycle, the rate of mucus formation might be lowered by as much as 50%. All of these things may encourage the development of vaginal infections.

DESCRIPTION

Due to the vagina's significant benefits, including its large contact surface area, good permeability, and high vascularization in addition to overcoming issues with first pass metabolism and gastrointestinal degradation, the vagina has been extensively investigated as an alternative route of drug administration. Additionally, it offers a high drug concentration at the site of action, which favours a decrease in adverse effects.

Due to the high prevalence of vaginal infections in adult women—which account for 70% of complaints and requests for medical consultation—this condition has been deemed a public health issue. Commercially, a variety of traditional formulations, including capsules, lotions, solutions, gels, and vaginal suppositories, are utilised for local management of various vaginal infections (ovules). However, these pharmaceutical forms are limited by vaginal route due to leakage, drug stability, short residence time, poor release and distribution of drugs in the vaginal cavity. The usage of hydrogels designed for vaginal drug delivery has been highlighted among the pharmaceutical alternatives investigated in light of the constraints of the vaginal route and conventional dosage forms. Three-dimensional polymer networks known as hydrogels have the capacity to swell, absorb water, and deliver controlled medication release, among other properties. They have the potential for vaginal application because they favour the formulation's staying power on the vaginal mucosa, which enables dosage reduction and, as a result, higher therapeutic efficacy, especially when compared to conventional dosage forms.

The increased residence duration at the site of action is a result of the mucoadhesive characteristics' favourable interaction with the mucosa lining the vaginal cavity. This mucoadhesive feature is directly correlated with the molecular weight, functional groups, spatial conformation, swelling level, porosity, degree of cross-linking, etc. of the polymers. Therefore, the hydrogel's three-dimensional structure, interaction with mucin found in mucus, and subsequent mucoadhesion are all influenced by the type of polymer that makes up the hydrogel. Electrostatic interactions, hydrogen bonds, Van der Waals forces, and hydrophobic interactions can all be used to establish the mucoadhesion process between hydrogel and mucin. In terms of the thermo-responsive property, the gelation process happens as a result of the sol-gel phase transitioning to the physiological temperature, allowing for prolonged system permanence and drug distribution into the vaginal mucosa. In this regard, natural and/or synthetic polymers can typically be combined to create polymeric blends in order to get such features and control the biological performance of hydrogels. The most widely studied polymers and their properties with a view to designing hydrogels for the treatment of vaginal infections were reported.

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In an effort to create therapeutic approaches for the treatment of vaginal infections, hydrogels have been extensively investigated as medication and/or nanocarrier vehicles. In fact, numerous studies have demonstrated that the usage of hydrogels is crucial in enhancing the therapeutic efficiency when administered vaginally. This study therefore concentrated on the key developments in the use of hydrogels as drug or nanosystem carriers for vaginal delivery, highlighting the benefits and difficulties of these systems in treating vaginal infections, with a focus on trichomoniasis, candidiasis, and bacterial vaginosis.

Hydrogel use in treating vaginal infections

According to their etiologic agent, vaginal illnesses can be classified as bacterial, fungal, or parasitic infections. Therefore, it's crucial to comprehend the clinical and pathological characteristics as well as the primary difficulties in treating each vaginal infection. In this regard, we suggested to talk about a general overview of vaginal infections, followed by the use of hydrogels as vaginal medicine delivery techniques.

Bacterial vaginosis, which affects women between the ages of 15 and 44 and has a high incidence rate worldwide (21.2 million), is thought to be the most common cause of irregular vaginal discharge. Due to a change in the vaginal flora's composition—a decrease in the quantity of protective lactobacilli and an increase in the growth of harmful bacteria—this condition is classified as a polymicrobial infection. Gardnerella vaginalis, Atopobium vaginae, Mycoplasma hominis, Mobiluncus spp., *Prevotella* spp., *Peptostreptococcus* spp., *Bacteroides* spp., among others, are typical anaerobes or microaerophiles responsible for the majority of cases.

Most studies that target vaginal administration have been conceived and created employing polymers with mucoadhesive and/or stimuli-responsive properties to accomplish the desired biological impact. According to numerous publications, the concentration of these polymers can modify the properties of hydrogels including viscosity, spreadability, hardness, and mucoadhesive ability. It can also provide suitable functionality like the extension of formulation residence time and drug release. Additionally, the development of these systems should take into account how the vaginal environment changes when bacteria are present (for example, a less acidic pH), as this can affect the *in situ* gelation process. Finally, the combination of hydrogels and nanocarriers led to synergistic effects and new vaginal medication delivery techniques for the treatment of bacterial vaginosis. Most studies that target vaginal administration have been conceived and created employing polymers with mucoadhesive and/or stimuli-responsive properties to accomplish the desired biological impact. According to numerous publications, the concentration of these polymers can modify the properties of hydrogels including viscosity, spreadability, hardness, and mucoadhesive ability. It can also provide suitable functionality like the extension of formulation residence time and drug release. Additionally, the development of these systems should take into account how the vaginal environment changes when bacteria are present (for example, a less acidic pH), as this can affect the *in situ* gelation process. Finally, the combination of hydrogels and nanocarriers led to synergistic effects and new vaginal medication delivery techniques for the treatment of bacterial vaginosis [1-6].

A vaginal infection called vulvovaginal candidiasis, which affects 70–75% of women of childbearing age and has a high recurrence rate (40–50%), is brought on by the genus *Candida* spp., particularly *C. albicans*. Vulvovaginal candidosis is caused by a number of risk factors, including age, sexual activity, hormones, corticosteroids, antibacterial drugs, contraceptives, and diabetes mellitus. These yeasts typically live in the lower female genital tract and are a component of the human mycoflora. Due to an imbalance in the vaginal microbiota and the adhesion of yeasts to epithelial cells, the infection process changes from asymptomatic to symptomatic and involves virulence factors like the production of enzymes, toxins, and phospholipase as well as blastoconidia and pseudohyphae that can destroy the vaginal epithelium.

CONCLUSION

There is currently a lack of effective prevention and therapy for vaginal infections like bacterial vaginosis, candidiasis, and trichomoniasis. With the aim of improving local therapy for vaginal infections, hydrogels continue to be a potential approach to get beyond the limitations of the vaginal route and conventional formulations. It is possible to modify a system's properties and create stimuli-responsive hydrogels with mucoadhesive and/or antibacterial capabilities by using particular polymers. The majority of studies conducted to date in this regard have taken use of the aforementioned characteristics to enable drug distribution on the vaginal environment and enhance therapeutic efficacy, with a focus on the usage of chitosan, poloxamer, and carbopol polymers.

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