



## REVIEW ON ROUTE OF ADMINISTRATION FOR HIV

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### ABSTRACT:

Sexually transmitted diseases (STDs) and acquired immunodeficiency syndrome (AIDS) have become increasingly significant due to the rapid spread of these diseases, expensive treatment costs, and a heightened risk of transmitting other STDs and AIDS. The current therapies for symptom management are prohibitively costly for the average person and are linked to the emergence of drug resistance. Many individuals with STDs and AIDS are turning to alternative medical systems like Unani, Chinese, Ayurvedic, naturopathy, and homeopathy. Traditionally, medicinal plants have been used to treat infectious diseases without scientific backing. Presently, there is a greater focus on establishing scientific evidence and rationalizing the use of these preparations. Ongoing research aims to identify plants and their active compounds that exhibit activity against sexually transmitted pathogens, including the human immunodeficiency virus (HIV), with the goal of developing effective approaches for prevention and treatment. This review delves into plants reported to have activity or used in traditional medicine for preventing and treating STDs, including AIDS, as well as herbal formulations for vaginal application and topical microbicides of herbal origin.

KEYWORDS: HIV , drug delivery, HIV prevention, microbicides, STI prevention, vaginal drug delivery.

### INTRODUCTION:

In 2007, the global HIV landscape was extensive, with approximately 33.2 million people living with HIV. A concerning aspect was the infection of 2.5 million individuals that year, with almost half in the 15–24 age group. Notably, women constituted nearly 50% of the worldwide HIV-infected population. Heterosexual vaginal intercourse emerged as the primary mode of transmission, disproportionately impacting women. Several factors contribute to women's heightened vulnerability, including physiological susceptibility, social and economic disparities limiting protective measures, and difficulties in negotiating condom use.

Despite continuous efforts, the likelihood of an HIV vaccine within the next decade remains uncertain. Hence, the development of female-controlled HIV prevention strategies, particularly microbicides, is crucial. Microbicides, which are chemical agents intended to prevent or reduce the transmission of sexually transmitted infections, including HIV-1, show potential. Topical microbicides offer a crucial female-controlled preventive method by actively hindering pathogen transmission during intercourse. The vaginal cavity in healthy women maintains a dynamic microenvironment with a diverse array of microorganisms. Disruptions to this ecosystem can result in various infectious conditions and diseases. Sexually transmitted diseases (STDs), also referred to as venereal diseases, encompass infections caused by diverse pathogens such as bacteria, viruses, Chlamydia, and parasites. Current therapies for AIDS and STDs involve drug administration through various routes, including oral, parenteral, and topical methods (vaginal and rectal).

Given that sexual transmission is the primary cause of STDs, there is increasing importance in exploring vaginal and rectal approaches for prevention. In the past decade, considerable advancements have been achieved in the realm of 'microbicides'— compounds or formulations applied topically (vaginally or rectally) to thwart the transmission of STDs, including AIDS. Noteworthy progress includes the development of compounds derived from plants, such as gossypol derivatives, Praneem polyherbal preparations, and medicinal plant extracts. Medicinal plants, widely utilized in both developing and developed nations, offer a logical approach to disease treatment. Their appeal is growing due to benefits like reduced side effects, improved patient tolerance, cost-effectiveness, and a well-established history of usage. Medicinal plants frequently have therapeutic effects that help restore normal physiological functions and target the root causes of disorders. Additionally, they offer renewable and environmentally friendly solutions and can serve as a source of income for impoverished families.

Their local availability, particularly in developing nations, renders them a valuable resource for healthcare and economic empowerment. Moreover, plants exhibit lower susceptibility to drug resistance. Although numerous active agents are accessible for the symptomatic treatment of STDs and AIDS, the emergence of drug-resistant strains and dose-limiting toxic effects pose challenges to treatment efficacy. This situation has spurred the quest for novel antimicrobial substances sourced from various outlets, such as plant extracts and phytochemicals. Numerous plants have undergone screening for their efficacy against STDs, leveraging ethno pharmacological data, with some demonstrating potential as promising candidates. Since at least 1574, medicinal plants have been historically utilized in Europe for the symptomatic treatment of STDs, with 'sarsaparilla' notably introduced as a remedy for syphilis. Throughout the past century, substantial endeavors have been undertaken to carefully select plants, isolate active components, and assess extracts or compounds for their effectiveness against sexually transmitted pathogens, thereby shedding light on their mechanisms of action.

The evolution of HIV prevention via microbicides has seen substantial progress, with the integration of antiretroviral drugs into sustained-release formulations to provide extended protection. Nevertheless, numerous formulations have encountered hurdles, often stemming from insufficient consideration of the characteristics of the vaginal route. Vaginal fluid, a crucial anatomical factor, presents both advantages and challenges. Its aqueous nature and enzymatic activity can hinder drug release and absorption, while its dynamic fluctuations influence drug efficacy. Furthermore, pH fluctuations, especially when seminal fluid is present, could affect the microbicide's protective efficacy. Some microbicides, effective at blocking HIV in laboratory settings, have failed in real-world scenarios due to semen-induced enhancement of virus infection. This underscores the necessity of assessing efficacy in the presence of semen. Preserving the natural barrier of the vaginal epithelium is paramount. For example, a microbicidal gel containing Nonoxonyl-9 resulted in heightened vaginal ulcers during clinical trials. It's essential to consider the role of vaginal microflora, as commensal bacteria uphold a healthy environment. Microbicides must not be toxic to the vaginal microbiota. Common pharmaceutical forms for vaginal drug administration encompass gels, capsules, suppositories, tablets, vaginal rings, and films.

Although initial trials primarily centered on gels, the current trend favors vaginal rings and sustained-release tablets for extended protection. Each dosage form carries its own set of advantages and drawbacks in the realm of microbicide development. The human immunodeficiency virus (HIV) remains one of the most severe epidemics worldwide, with an estimated 36.7 million people living with the virus. Nonetheless, significant strides have been made in accessing antiretroviral therapy over the past decade, leading to a 48% reduction in acquired immunodeficiency syndrome (AIDS)-related deaths. Prevention programs have achieved success in reducing the transmission of the virus in recent years, although it still results in 1.8 million new infections annually. A concerning fact is that the majority of people infected with HIV are women. The data is alarming, with AIDS-related illnesses persisting as the primary cause of death among women of reproductive age. Additionally, it stands as the second leading cause of death among African women aged 15–24. The gender disparity is particularly pronounced among young individuals, with new infections in the 15–24 age group being 44% higher in women.

These statistics underscore the unacceptably high risk of infection among young women. These already staggering figures become even more alarming among women in sub-Saharan Africa, where 75% of new infections in the population aged 15–19 occur in girls. Additionally, this population group has seen little reduction in the incidence of new infections in recent years. While limited access to antiretroviral therapy might seem to be the primary reason for the high prevalence of HIV among women in sub-Saharan Africa, a thorough analysis of the living conditions in this region reveals that the high transmission rate of the virus cannot be attributed to a single cause. It's crucial to acknowledge that this region experiences frequent occurrences of rape and domestic violence. According to the World Health Organization (WHO), women living in these conditions are 50% more likely to contract HIV.

Nevertheless, the primary reason for this prevalence is undoubtedly the lack of access to education and economic independence among women. This hinders their ability to negotiate safe sex with their partners. The harsh reality is that 75% of young women lack the ultimate decision-making power over their own health. Additionally, factors such as polygamy, which remains prevalent in several sub-Saharan countries, and the decline in condom usage observed in countries like Ivory Coast, Niger, Senegal, and Uganda, further compound the challenges. A cycle of HIV transmission has been recently outlined in sub-Saharan Africa to elucidate the minimal decline in AIDS prevalence in this region compared to the global trend. Adult men typically transmit the virus to young women, with approximately 15 million women getting married before the age of 18 each year. As these women mature, they often transmit the virus to men of similar age, perpetuating the cycle. This observation underscores the imperative of empowering women, particularly in sub-Saharan Africa, as a pivotal step toward halting the AIDS epidemic. Promoting societies where gender equality is realized through comprehensive sexual and social education is crucial.

The United Nations (UN) aims to equip young people with the skills, knowledge, and tools necessary to safeguard themselves against acquiring the virus. Indeed, the ability for protection must be bolstered by empowering women and offering them means for preventing HIV transmission that are independent of men, such as vaginal microbicides. This is why research into vaginal microbicides has surged in recent decades. If successful in preventing HIV, they would signify a remarkable advancement in the fight against AIDS.

Vaginal microbicides are defined as "any agent included in a topical formulation designed to prevent the spread of sexually transmitted pathogens either through cell death, inactivation of cell mechanisms, inhibition of viral replication, the formation of a physical barrier between cells and pathogens, or by enhancing the natural protection mechanisms of the cervix and vagina." The strategies employed in developing effective vaginal microbicides in recent decades have been so diverse that they necessitate a preliminary classification to facilitate comprehension. The strategies can be initially categorized into two groups based on whether the microbicides contain antiretroviral drugs. Microbicides without drugs can further be classified into surfactants, polyanions, acidifiers, and glycoprotein 120 neutralizing monoclonal antibodies. The goal of these substances is to deactivate the virus before it encounters the cells, thereby preventing infection. Microbicides containing antiretroviral drugs can be categorized as entry inhibitors or viral enzyme inhibitors. Of particular note in this category is Tenofovir, an inhibitor of the virus's reverse transcriptase. It was included in the first microbicide to demonstrate efficacy in preventing HIV transmission and has since become the most extensively studied drug for this purpose.

Dapivirine, another promising drug for the development of vaginal microbicides against HIV, has also emerged as highly significant. The evolution of microbicide development has progressed significantly over the years. Initially, conventional release formulations typically did not incorporate antiretroviral drugs. However, over time, the potential of antiretroviral drugs for preventing HIV infection was recognized, leading to the gradual emergence of microbicides containing various drugs. The prospect of developing a microbicide without antiretroviral drugs is now scarcely considered, and the current trend in microbicides is to formulate sustained-release formulations for prolonged protection. Regrettably, the overwhelming majority of microbicide formulations developed thus far have failed to provide adequate protection due to their low efficacy or inadequate formulation. This failure often stems from neglecting the characteristics of the vaginal route. The primary anatomical consideration when formulating for vaginal administration is vaginal fluid, which can either aid or hinder our objectives.

**CAUSE OF COMMON NEUROLOGICAL COMPLICATIONS IN HIV PATIENT:-**

Syndrome	Possible aetiology
Meningitis	Cryptococcal meningitis, tuberculous meningitis, bacterial meningitis, syphilitic meningitis, acute HIV infection
Peripheral neuropathy	HIV-associated distal sensory peripheral neuropathy, stavudine, didanosine, zalcitabine, isoniazid, mononeuritis multiplex associated with CMV infection
Haemorrhagic stroke	Poorly controlled hypertension, thrombocytopenia, mycotic aneurysm, cocaine
Subacute encephalitis	HIV encephalopathy, CMV encephalitis, neurosyphilis, acute HIV infection
Polyradiculopathy	HIV polyradiculopathy, CMV polyradiculitis, HSV polyradiculitis, VZV polyradiculitis, cryptococcal meningitis, tuberculous meningitis, lymphomatous
Cerebral mass lesions	Toxoplasmosis, cerebral lymphoma, pyogenic abscess, tuberculoma, cryptococcoma, penicillium abscess, progressive multifocal leucoencephalopathy

**DIFFERENT DOSAGE FORMS :**

Pharmaceutical Dosage Form	Advantages	Drawbacks
GELS	Widely studied and well known. Easy and convenient for women to apply. Low manufacturing cost and easy to mass produce	Unable to retain the drug and provide sustained release. They require an applicator for administration Possible local irritation and leakage. Not particularly stable against adverse environmental conditions
TABLET	Easy and economical to manufacture on an industrial scale. Easy to handle	Possible influence on sexual

	<p>Stable under different environmental conditions</p> <p>Fast-dissolving or sustained-release tablets can be obtained depending on the excipients used in their development</p>	<p>intercourse.</p> <p>Possible local irritation.</p>
FILMS	<p>Discreet use</p> <p>No product leakage during use</p> <p>No applicator required for insertion</p> <p>Minimal packaging and reduced waste</p>	<p>Sustained release still not achieved</p> <p>Possible local irritation</p> <p>Mass production is currently unviable due to the underdevelopment of production resources</p>
VAGINAL RINGS	<p>Sustained release of the drug.</p> <p>Fewer applications.</p> <p>The mass production of this dosage form is becoming increasingly advanced.</p>	<p>They require a higher financial investment.</p> <p>Higher manufacturing cost.</p> <p>Possible influence on sexual intercourse.</p>

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