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Open Access Review Article

Intravaginal Drug Delivery System: Compherensive Approach to Vaginal Formulations.

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ABSTRACT

Intra-vaginal route of administration is a route of administration where the dosage form is applied vaginally for the convenient release of the dosage form and for better therapeutic action of the medicament, it is usually used in HIV patients. Vaginal route is been used as a traditional delivery system used for the conventional delivery of several locally acting drugs like antimicrobial agents. The various types of formulations as well as the dosage forms are available for intra-vaginal drug delivery system such as tablets gels vaginal rings etc. the disease's such as HIV or other diseases caused into the vaginal area due to causative agents like bacteria fungi etc. For efficient vaginal delivery of drugs, the delivery system should reside at the site of infection for a prolonged period of time.

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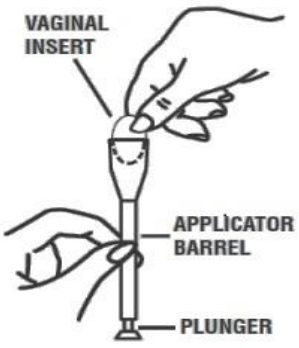
INTRODUCTION:

Vagina is route of administration for Variability in drug absorption related with contraceptives, anti-fungal, and menstrual cycle, menopause and antimicrobials. It is used for the achievement of local or for systemic absorption. The vaginal wall is very well suited for the absorption of drugs for Some drugs are sensitive at vaginal pH systemic use. As it contains a vast network of blood vessels.

Infection with HIV remains an incurable condition. The highest rate of HIV transmission is through the exposure of the vaginal mucosal surface to HIV during sexual intercourse. Microbicides circumvent many of the immunological difficulties associated with HIV vaccine development and make topical formulations a more realistic goal, especially in the short term The most promising strategy currently being pursued is the utilization of intravaginal delivery systems for microbicides. The vaginal route has been rediscovered as a potential route for systemic delivery of various therapeutically important drugs avoid first pass metabolism. However, fruitful delivery of drugs through the vagina remains a challenge because of poor absorption of some drugs across vaginal epithelium. The various factors like vaginal physiology, age of patient, menstrual cycle are affecting the rate of drug absorption after vaginal administration. The future of vaginal drug delivery lies in the bioadhesive tablets, liposomes, niosomes and microparticles, which although relatively new and show great promise in providing truly controlled delivery of drugs.



TYPES OF DOSAGE FORMS USED:

- Vaginal tablets
- Vaginal Gels
- Vaginal creams
- Vaginal rings

- Suppositories.

Vaginal gels and tablets have rapid release rates which, for effective use, ultimately require administration several times a day. Vaginal rings have adequate release rates but have only been formulated for preventing the transmission of HIV and as a contraceptive. The most widely used semi-solid preparations for vaginal drug delivery include creams, ointments, and gels.

Creams and Gels

To date the greatest number of intravaginal drug delivery systems for microbicides, by far, is in the form of creams or gels. Although commonly used for the topical intravaginal delivery of microbicides, these systems are messy, uncomfortable and may not provide an exact dose due to non-uniform distribution and leakage

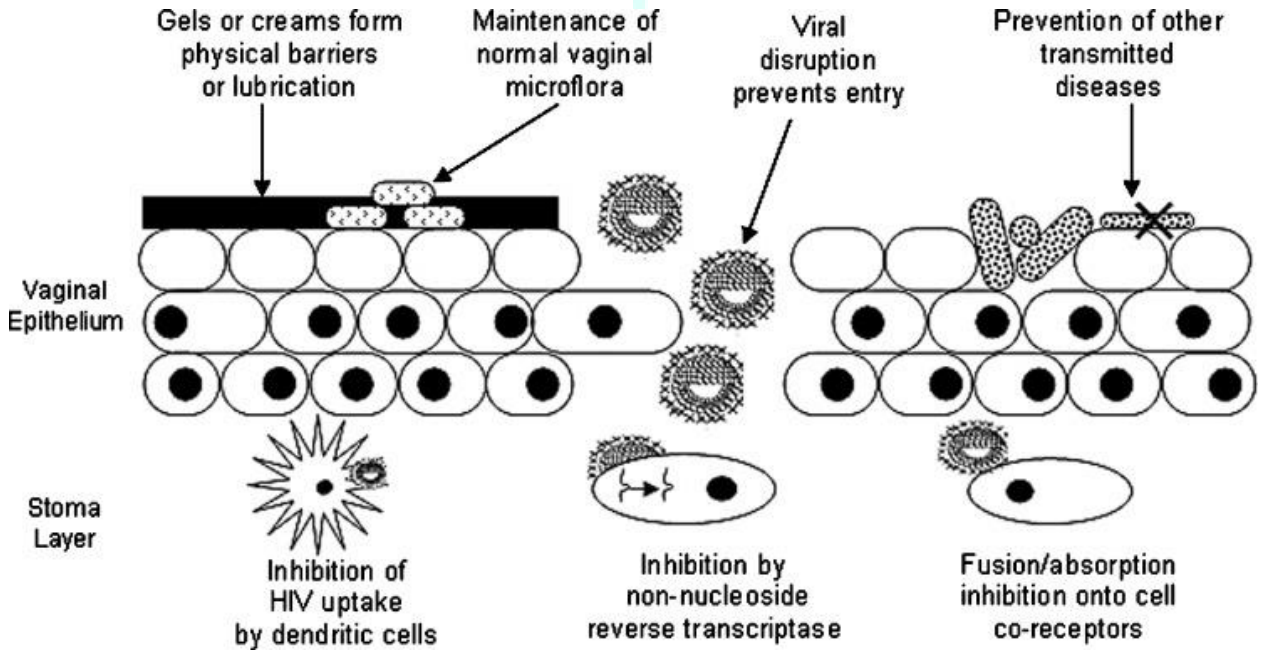
Tablets and Suppositories

A large number of intravaginal delivery systems are also available in the form of tablets or suppositories. Some authors use the terms pessaries and suppositories interchangeably and consider vaginal tablets as a separate dosage form. These formulations are designed to melt in the vaginal cavity and release the microbicide over several hours. Suppositories are most commonly used to administer drugs for cervical ripening prior to child birth and for local delivery of various drugs. Vaginal tablets may contain binders, disintegrants and other excipients that are used to prepare conventional oral tablets. Mucoadhesive polymers are sometimes used in tablet formulations to increase the vaginal residence time of the microbicide been delivered. Other vaginal tablet-like formulations are extrapolations of silicone-based vaginal rings. Research groups have studied the release of microbicides from silicone matrices. Release studies were performed *in vitro* for up to 1 year and *in vivo* in rabbits for up to 52 days. Both *in vitro* and *in vivo* studies showed consistent release profiles over time, showing that microbicide delivery is controlled by diffusion from the silicone delivery device and was not limited by absorption through the vaginal epithelium.

Vaginal Rings

Vaginal rings are circular ring-type drug delivery devices designed to release microbicides in a controlled manner after insertion. The advantages of such a device are that it can be controlled by the user; does not interfere with coitus and allows for the continuous delivery of microbicidal compounds. In simple vaginal rings, the microbicide is homogeneously dispersed within a polymeric ring with the surface of the ring releasing the microbicide faster than the inner layers. The key challenge in development of these systems is finding the optimum dose that will deliver the least amount of microbicide necessary to ensure protection. Advances have been made on the original two-layer ring system by adding a third, outer, rate controlling drug-free elastomer layer to minimize the drug concentration spike.

Mechanism:



Benefits and uses.

- It reduces vaginal burning and vaginal infection.
- It reduces vaginal itching and vaginal discharge.
- Treatment of vaginal dryness.
- Treatment of HIV
- Treatment of yeast infection.
- Contraceptives

TABLE 1: Some of the experimented vaginal drug delivery system9 .

Therapeutic drug	Intended use	Dosage form	Animal model	Comments
Nonoxynol-9	Spermicide/topica l contraceptive	Gel,foam,cream	Rabbit	Detergent type spermicide, irritation and increased risk of infection
Miconazole nitrate	Anti-fungal	Cream, suppository, swelling controlled release system	Invitro	
Prostaglandin E2	Cervical ripenig	Crosslinked PEG hydrogel, suppository	invitro	Onset of labor not always predictable
Lactobacilli strains	Urogenital tract infections	Bi-layered tablet	invitro	Restoration of normal vaginal flora, good bacterial viability in tablets
Progestin, levonorgestrel , orethindrone acetate	contraceptives	Vaginal ring	Human	Uterine bleeding, hormonal side effects, expulsions
estradiol	Harmone replacement therapy	Vaginal ring	Human	Risk of endometrial proliferation
Relaxin	Cervical ripenig	Gel	Human	Decreased incidence of cesarean deliveries, reduced maternal-fetal morbidity
LHRH	Hormone dependent mammary tumors, fertility control	Supposistory	Rat	Suppress secretion of ovarian steroids
Leuprolide	Ovulation inducing activity	Solution suppository,	Rat	Activity increased by 5 times with addition of absorption enhancers
Insulin	Diabetis mellitus	Solution, gel	Rabbit, rat	Low bioavaliabilty

ADVANTAGES

- Simple to manufacture, cost effective and easy to apply thus facilitating patient compliance
- Non-irritative and free from producing any physical discomfort
- Provide immediate and sustained protection by releasing the microbicide in a controlled manner over a prolonged period of timeSolution was transferred into amber colored bottle and sealed till further use and resulting solutions were sterilized by autoclave at 121°C for 20 min at 15 psi.
- Have suitable vaginal retention and distribution
- Be versatile against various pathogens encompassing STIs and HIV

METHOD OF PREPARATION:

TABLETS:-

- the vaginal tablets were prepared by direct compression and direct blending.
- the ingredients were weighed and passed through sive no # 20 ASTM .
- the materials sived was blended into double cone blender at 15 RPM.
- The blended materials were again sifted through #30 ASTM sieve.
- these shifted materials was again blended into the blender for 15 min at 15 RPM.
- the lubricant is sieved through sive no #60 ASTM and addead to above blended mixture and again blended at 15 RPM.
- the direct compression was done for the formation of the vaginal tablet.

GELS:

1. The cold method was used to prepare the vaginal insitu gel.
2. The preferd quantity of drug is weighed and dissolve in saline phospate buffer in aseptic conditions.
3. Preservatives was added at same time.
4. Meanwhile the mixtures of polymers was kept aside for 24 hours for proper mixing.
5. Next the drug and polymeric solution was mixed properly and the intended quantity was added to the isotonic solution .
6. Solution was transferred into amber colored bottle and sealed till further use and resulting solutions were sterilized by autoclave at 121°C for 20 min at 15 psi.

CONCLUSION:

Vaginal preparations, although generally perceived as safer most still associated with number of problems including multiple days of dosing, dripping, leakage and messiness, causing discomfort to users and expulsion due to the self-cleansing action of the vaginal tract. These limitations lead to poor patient compliance and failure of the desired therapeutic effects. For efficient vaginal delivery of drugs, the delivery system should reside at the site of infection for a

prolonged period of time. The vaginal prepartions are explained in short for their convenient use.

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