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Intra-Vaginal Drug Delivery System

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ABSTRACT

Intra-vaginal route of administration is a route of administration where the dosage form is applied vaginally for the appropriate release of the dosage form and better therapeutic action of the dosage form, it is usually used in HIV patients. Vaginal route is been used as an ancient 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 systems such as tablets, gels vaginal rings, etc. The diseases such as HIV or other diseases caused by the vaginal area due to responsible agents like bacteria fungi etc. For better vaginal delivery of drugs, the delivery system should occupy at the site of infection for a prolonged period.

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INTRODUCTION

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

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

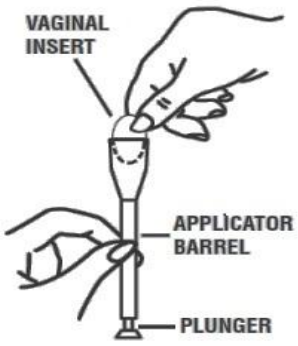

Figure No. 1: Vaginal insert

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, the dosage form is in the form of creams or gels. Whereas commonly used for the topical intra-vaginal delivery of microbes, these systems are confused, uncomfortable, and may not provide an exact dose due to non-uniform distribution and leakage.

TABLETS AND SUPPOSITORIES:

A large number of intra-vaginal delivery systems are also available in the form of tablets and suppositories. Some writers use the terms pessaries and suppositories and consider vaginal tablets as a separate dosage form. These formulations are designed to melt in the vaginal cavity and release the microbes over several hours.

Suppositories are most commonly used to administer drugs for cervical ripening before childbirth and for local delivery of various drugs. Vaginal tablets may contain binders, disintegrants, and other excipients that are used to prepare conventional 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 an estimation 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 constant 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 intercourse 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 challenge in the 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:

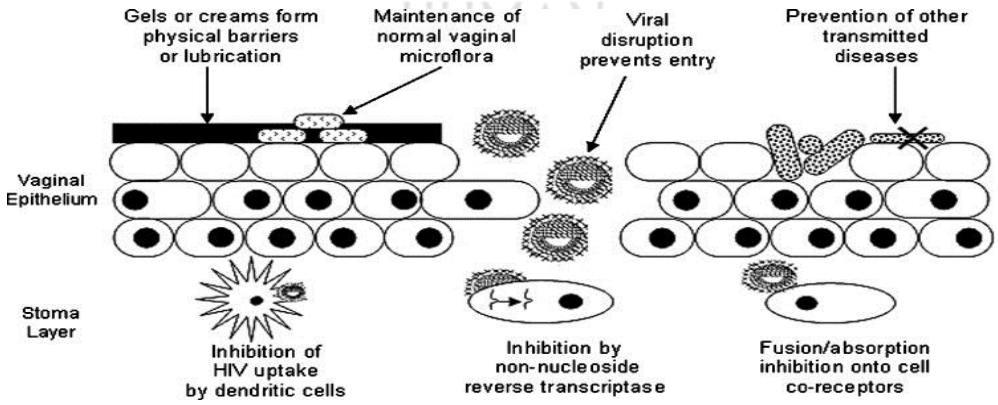

Figure No. 2: Mechanism of inhibition of HIV uptake

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 No. 1: Some of the experimented vaginal drug delivery system[9]

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

ADVANTAGES

1. Simple to manufacture, cost-effective and easy to apply thus facilitating patient compliance

2. Non-irritant and free from producing any physical discomfort

3. Provide immediate and sustained protection by releasing the microbicide in a controlled manner over a prolonged period 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.

4. Have suitable vaginal retention and distribution

5. 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 sieve no # 20 ASTM.
- The materials used were blended into a double cone blender at 15 rpm.
- The blended materials were again sifted through #30 ASTM sieve.
- This shifted material was again blended into the blender for 15 min at 15 rpm.
- The lubricant is sieved through sieve no #60 ASTM and added to the 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 *in-situ* gel.

2. The preferred quantity of drug is weighed and dissolved in saline phosphate buffer in aseptic conditions.

3. Preservatives were added at the same time.

4. Meanwhile, the mixtures of polymers were kept aside for 24 hours for proper mixing.

5. Next, the drug and polymeric solution were mixed properly and the intended quantity was added to the isotonic solution.

6. The solution was transferred into amber-colored bottle and sealed till further use and the 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 many 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 the 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. The vaginal preparations are explained in short for there convenient use.

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