SYSTEMS FOR CONTROLLED DRUG DELIVERY AND DELIVERY MECHANISMS

14. WEEK

INTRAVAGINAL AND INTRAUTERINE SYSTEMS

Vagina is route for administration for contraceptives, anti-fungal, 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 systemic use. As it contains a vast network of blood vessels

- This route offers certain advantages, such as avoidance of gut and hepatic first pass metabolism, reduction in gastrointestinal and hepatic side effects, and local targeting of drugs to the reproductive organs.
- Vaginally administered agents and formulations are mainly being developed to provide “dual prophylaxis” for contraception and protection against microbial infections including Acquired Immune Deficiency Syndrome(AIDS) and other sexually transmitted diseases (STDs).
- Drug delivery technologies that have been used for vaginal drug delivery include the intravaginal ring (IVR) and Vaginal Site bio-adhesive technology.

Benefits of Intravaginal Drug Delivery Systems

- Prolonged release,
- Minimal systemic side effects,
- An increase in bioavailability,
- Use of less total drug than an oral dose,
- First-pass metabolism can be avoided,
- Self medication is possible.
- Contact with digestive fluid is avoided and degradation of drug is minimized.
- Nausea, vomiting, emesis induced through oral administration is avoided.
- Quick onset of action.

Limitations of Intravaginal Drug Delivery Systems

- Gender specificity,
- Patient incompliance,
- Only a few drugs are administered by this route,
- Variability in drug absorption related with menstrual cycle, menopause and pregnancy,
- Influence with sexual intercourse.
- Personal hygiene,
- Some drugs are sensitive at vaginal pH.

Factors Affecting Absorption of Drugs

The drug transport across vaginal membrane mainly takes place by three major ways;

- ✓ Transcellularly- via concentration dependent diffusion through the cells,
- ✓ Paracellularly- mediated via tight junctions and
- ✓ Vesicular or receptor mediated transport.

Drug absorption from vaginal delivery system is mainly takes place in two main steps:

- ✓ Drug dissolution in vaginal lumen and
- ✓ Membrane penetration.

The rate and extent of drug absorption after intravaginal administration may vary depending on following factors:

Physiological Factors

- changes in the thickness of epithelium layer,
- cyclic changes,
- changes in the hormones level,
- volume of vaginal fluid,
- alteration of vaginal pH and
- Sexual arousal can potentially affect drug release from any intravaginal delivery system and also alter its rate of absorption.

For example;

1. Vaginal absorption of steroids is affected by the thickness of vaginal epithelium.
2. Vaginal absorption of estrogen shows high in post menopausal women compare to premenopausal women.

The high volume of vaginal fluid may increase the absorption of poorly water soluble drugs; however the same condition again responsible to remove the drug from the vaginal cavity and subsequent reduction of drug absorption.

Physicochemical Factors

- Lipophilicity,
- Ionization,
- Molecular weight,
- Surface charge and
- Chemical nature can influence the vaginal drug absorption.

In consideration to permeability the lipophilic steroids like progesterone and estrone having better permeability than the hydrophilic one like hydrocortisone and testosterone.

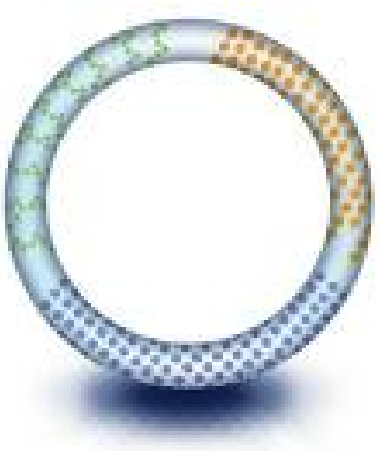
Vaginal Rings

Sustained and controlled-release devices for drug delivery in the vaginal and uterine areas are most often for the delivery of contraceptive steroid hormones.

One such application is the medicated vaginal ring. Medicated vaginal rings fabricated from silastic 382 medical grade elastomer. These are of **‘doughnut-shaped’**. Also known as **intra-vaginal rings** or **V-Rings**.

Vaginal rings provide a means of delivering a drug to the systemic circulation at a controlled release rate.

- **NuvaRing®** is the first-ever marketed vaginal ring; it releases 15 µg ethynyl estradiol and 120 µg etonogestrel, and when used properly, has a failure rate between one and two per 100 woman-years of use.



NuvaRing is inserted into the vagina and left in place for three weeks, after which it is removed for a 'ring-free‘ week to allow menstruation to occur.

Intrauterine Devices

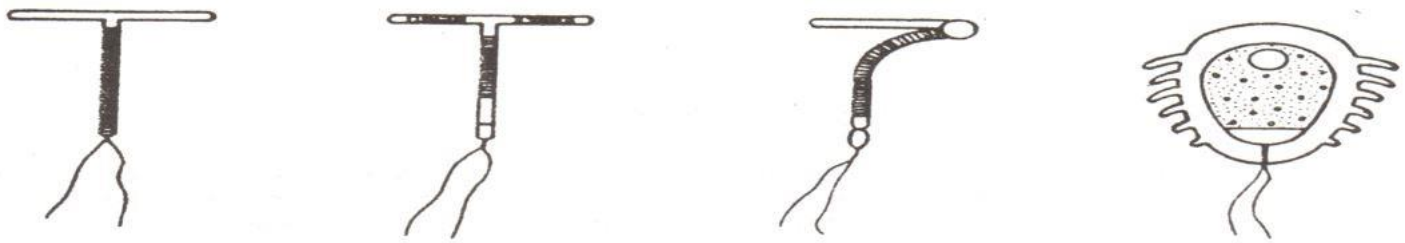
A more common contraceptive device is the intrauterine device (IUD).

Two types of medicated IUD are generally used;

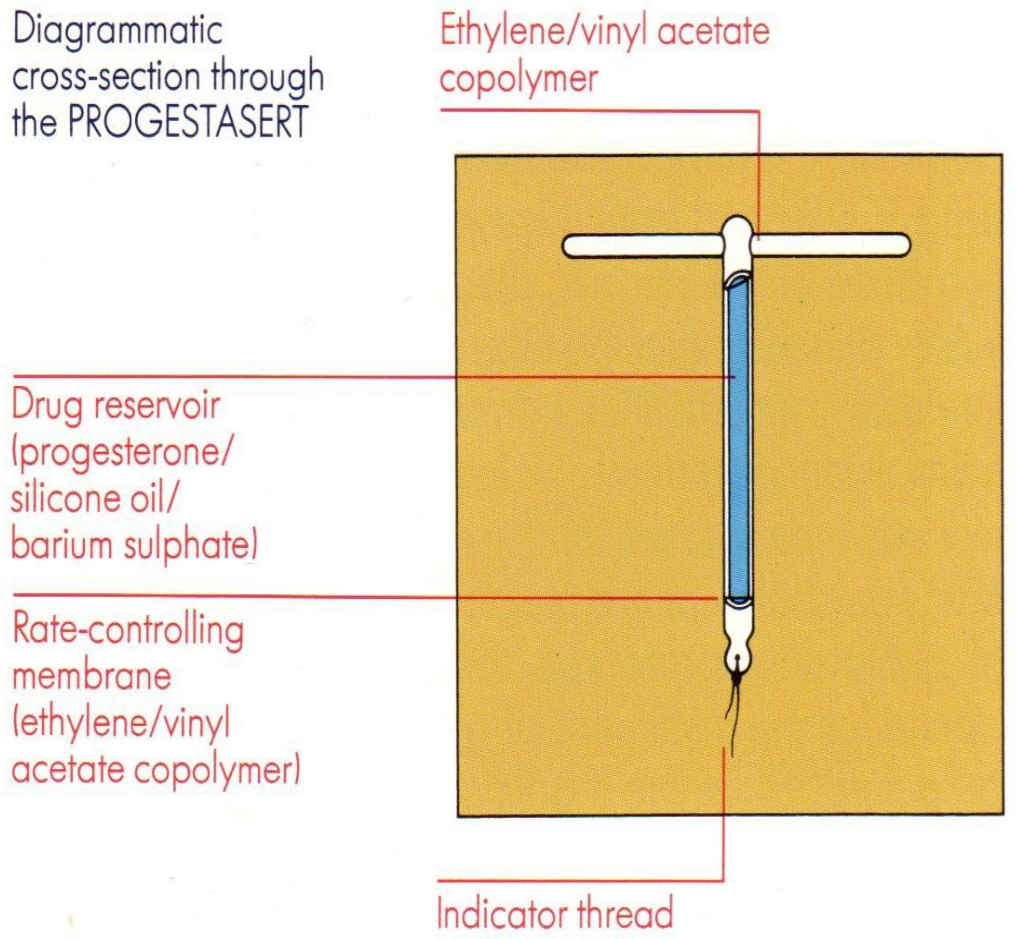
- Contraceptive metals and
- Steroid hormones.

- Efforts to prevent pregnancy have involved inserting objects into the uterus and has been practiced formany years. The first reported use of an intrauterine device (IUD) designed specifically for contraception is 1909.
- However, the first modern use of an IUD was composed of plastic to which barium sulfate was added to make the unit visible under X-rays. While improvements were noted, it was the idea that metals, including copper, could increase the effectiveness of inert, plastic devices.

- The first commercial copper-releasing IUD was the Copper T-200 and the Copper 7.



- **Progestasert®** is the steroid releasing intrauterine device (IUD). The principal example is a T-shaped device composed of a rate-controlling membrane of ethylenevinyl acetate copolymer. Inside this membrane is contained a three-day supply of the amount of progesterone normally taken orally.



- However, since the device delivers progesterone to its target locally at a rate of approximately 65 pg/day, the system lasts for over 1 year. Marketed by ALZA under the trade name Progestasert ®, the system showed comparable pregnancy and expulsion rates to conventional IUDs, often with less menstrual bleeding.