AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Recent Advances in Vaginal Drug Delivery System: An Overview

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ABSTRACT

The present review highlights human vagina as a valuable route of drug delivery due to its large permeation area, rich vascularization, avoidance of first pass metabolism and relatively low enzymatic activity designed for achieving both local and systemic applications. Vagina is the best route used for administration of drugs like antifungal, contraceptives steroids, peptides and antifungal drugs. The rate and extent of drug absorption through vaginal route may fluctuate depending upon vaginal physiology, age of patients, stage of menstrual cycle, pathological conditions, and formulation factors. This route offers the ease of convenience, good blood supply, absence of GIT and hepatic first pass metabolism and permeability to large molecular weight drugs. Several drawbacks like personal hygiene, gender specificity, cultural sensitivity and local irritation need to be considered while the designing the vaginal formulation. Thus, purpose of this study is to provide the summary of advances undergone in the field of vaginal drug delivery currently available in the market and challenges associated with systemic delivery of drug via vaginal route. This review also highlights the benefits of vaginal route as drug delivery.

Keywords: Vaginal delivery, Vaginal physiology, Antifungal, Contraceptives, Penetration enhancers, Bioadhesion.

*Corresponding Author Email: drgdg@rediffmail.com
Received 14 July 2016, Accepted 27 July 2016

Please cite this article in press as: Kaur R *et al.*, Recent Advances in Vaginal Drug Delivery System: An Overview. American Journal of PharmTech Research 2016.

INTRODUCTION

At present, there is extremely huge interest in the pharmaceutical industry over different mucosal routes for delivering of drugs, which are weakly absorbed after oral administration. Considerable advancement has been made in this research area over few years ago and, at present, the anatomy and physiology, microflora and secretions of the vagina are well understood. The anatomical position, the rich blood supply, good permeability and large surface area of the vagina makes it ideal as an application site for systemic drug delivery alternative to the parenteral and oral route. The vaginal drug delivery route has been known since earliest times and has been rediscovered as a probable route for systemic delivery of macromolecules and other therapeutically important peptides. This route is mainly discovered for administration of antifungal, antimicrobial, antibacterial for vaginal yeast and bacterial infection and for contraceptive. In the case of local treatment it is difficult to design delivery systems providing high drug concentrations in the vagina for extend period of time and to gain high drug bioavailabity. Many drug delivery systems are based on mucoadhesive polymers. Vagina has been intended as a encouraging site for the local and systemic delivery of drugs, for female related conditions. It offers several benefits like avoiding the gut and hepatic first pass metabolism, self medication, easy to formulate, reduce in gastrointestinal and hepatic side effects and local targeting at the site of infection to achieve the prolonged effect to reproductive organs .In postmenopausal woman the reduced epithelial thickness may change the absorption rates of drugs significantly. Conventional vaginal delivery system have some disadvantages like itching, irritation of vagina, messy to apply and low residence time. To overcome all these disadvantages novel formulations like nano drug delivery system (liposome, vaginal niosomes, nano suspensions, nano emulsion, nanofibers) are being formulated. They are increased residence time, localization of formulation to specific sites, cellular targeting and mucoadhesions[1-12].

Benefits of vaginal drug administration

Vagina offers large surface area, rich blood supply, and high permeability for lower molecular weight drugs avoiding hepatic first pass metabolism interference with absorption of medication leading to lesser side effect and greater bioavailability as compare to oral administration. Vaginal administration frequently minimizes side effects associated with the oral route. Example is the administration of Bromocriptine through vaginal in treatment of hyperprolactinemia in women who suffer from vomiting and nausea following oral administration[2]

It has several advantages when compared to conventional dosage forms.

1. Bioadhesive vaginal formulations are readily localized in the area of application thus improving the bioavailability of drugs.
2. Vaginal delivery systems provide responsive contact of the formulation with the essential absorption surface and allows for modification of tissue permeability for absorption of macromolecules such as proteins and peptides.
3. Allow continuous and extended residence of the dosage form at the site of application.
4. Reduces side effects due to avoidance of multiple dosing of drug.
5. These systems are able to swell quickly when placed in aqueous environment and therefore exhibit Inga controlled drug release. The therapeutic efficacy of locally acting drugs can be improved by their increased availability at the target membrane.

Advantages of vaginal drug delivery system[1,2,6,11]

- Easily administered
- Minimum side effects
- Avoids GIT and Hepatic first pass metabolism
- Low enzyme activity
- High vascularization
- Prolonged release
- Minimum systemic side effects
- Increases in bioavailability
- Preferable for drugs that produce GI irritation
- Target site of action with minimal system absorption

Disadvantages of vaginal drug delivery[1,2,6,11]

- Local irritation
- Personal hygiene
- Gender specificity
- Influence of sexual intercourse
- Cultural sensitivity
- Some drugs are sensitive to vaginal pH
- Variability in drug absorption related with menstrual cycle, pregnancy and menopause, can also limit vaginal drug delivery route usage

Vaginal Anatomy and Physiology

Human vagina is slightly S- shaped fibro muscular collapsible tubes approximately 10 cm in length and extended from the cervix of uterus to the vestibule. The vagina is placed between rectum, bladder and urethra. The vagina protects the internal genital organs against rising infections, forms part of the birth canal. The external female reproductive structures are referred to collectively as the vulva. The vaginal opening is located between the opening of the urethra and the anus. Vagina comprised of three different layers; the epithelial layer, the muscular coat and tunica adventitia .The epithelium layer consist of non cornfield, stratified squamous epithelium and it does not contain any gland, but its surface kept moist due to cervical secretion whose composition and volume varies with stage of menstrual, age and degree of sexual excitement. Vaginal rugaes and microridges on epithelial cell surface allow the vagina expands, permit the placement of vaginal formulations and enlarge the surface area of vagina therefore enhancing the drug absorption. Blood supply to vagina through the vaginal branch of uterine artery[1-20].

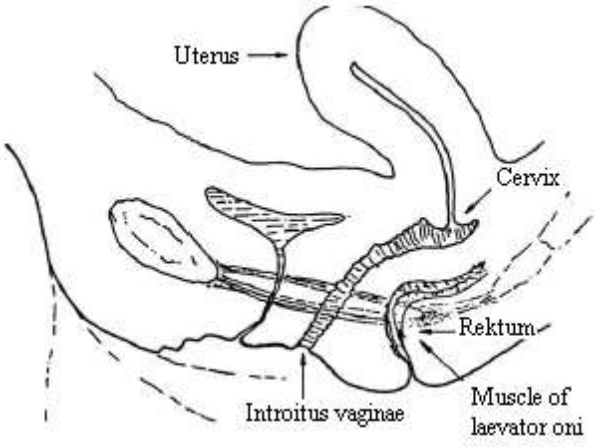

Figure1: Vagina is placed between rectum and bladder

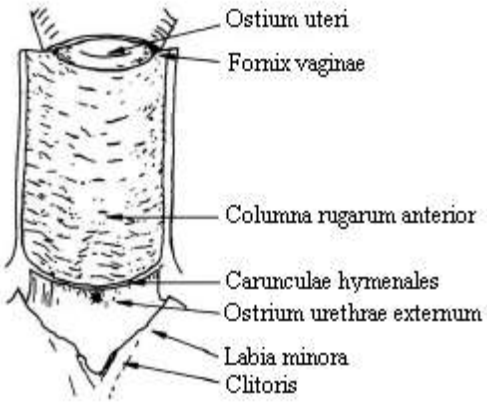

Figure2: Inside upper vaginal wall

Vaginal secretion:

The vaginal release is a mixture of multiple secretions that collects in the vagina from peritoneal, follicular tubal, uterine, Bartholin's and Skene's glands[1-6].

pH:

The vaginal pH of healthy women genital tract is acidic pH 3.5-4.5and maintained that value by bacterial conversion(lactobacilli) of glycogen from exfoliated epithelial cells into lactic acid[1-6].

Cyclic changes:

Changes in hormone (estrogen) level during the menstrual cycle lead to change in the, width of intercellular channels, thickness of epithelial cell layer, secretions and pH[6].

Microflora:

Factors that are influence the ecology of the vagina are glycogen content of epithelial cells, hormonal level, birth control method, glucose, pH and trauma during sexual intercourse, age and antimicrobial treatment[1-6].

Ideal criteria of drug for vaginal delivery[11,12]

- It should melt at vaginal temperature i.e. at 36 °C,
- Non-toxic and non irritating,
- It should not have any meta-stable form,
- Must possess wetting and emulsifying properties.
- Must possess proper viscosity, to avoid the leakage from vagina (in case of semisolid dosage form),
- It should have bioadhesive/ muco-adhesive properties, in order to increase the contact time between the membrane and formulation.

Factors affecting absorption of drug[8]

Various factors that influence drug absorption from the vaginal cavity is crucial in order to design the formulation for intra- vaginal administration.

Physiological Factors:

Factors that are related to the physiology of vagina include pH, effect of the estrous cycle on the permeability of the vagina mucosa, thickness of the vaginal epithelium, viscosity, vaginal fluid volume, pH, chemical composition of fluid, and surface tension, the pressure exerted on the dosage form by the rectal wall, and sexual arousal, mucociliary clearance (MCC), vaginal obstruction, etc. which affect either the ciliary or mucus heating and vaginal blood flow.

Formulation factors affecting vaginal drug delivery:

These factors are related to the dosage forms such as characteristics of the active ingredients, pH, mucosal irritancy; osmolarity, viscosity(solutions, gels) and density (powder, tablets) of the formulation; concentration and volume administrated, particle size of drug molecule, chemical nature, and ionization surface charge and type of dosage form.

Physicochemical Factors affecting Vaginal Drug Delivery:

Physicochemical properties of drugs such as lipophilicity, molecular weight, ionization, chemical nature, surface charges can influence vaginal drug absorption. Vaginal fluid contains a large amount of water; any drug proposed for vaginal delivery requires a certain degree of solubility in water. Peptides and proteins are known to aggregate in the medium due to changes in ionic

strength and pH of the medium or concentration of the substance. The aggregated complex has a different permeation and diffusion coefficient in opposition to the monomer. Metronidazole is a poorly soluble drug has rate limiting dissolution in small volume of vaginal fluid. Vagina permeability of straight chain aliphatic alcohols is depend upon chain length . Lipophillic steroids such as progesterone and estrone permeate the vaginal wall to a greater extent than hydrophilic steroids like hydrocortisone and testosterones. Low molecular weight lipophilic drug having much more absorption than large molecular weight hydrophilic or lipohilic drugs.

Drug release:

Small volume of vaginal fluid makes dissolution as the rate limiting step for systemic absorption of drugs from vaginal dosage form. The type of dosage form affects the rate of dissolution, for instance a drug which is already dissolved in an aqueous vaginal gel, will be more rapidly absorbed than a drug which is in solid form within a vaginal tablet preparation.

Concentration of drug(µg/ml) = (slope x absorbance) ± intercept

Amount of drug released mg/ml = concentration x dissolution bath volume x dilution factor/1000

The effective area of Contact:

The vaginal cavity has an area of approximately 60 cm^2. The total area on which a medicament could get deposited will depend upon the size of the dosage form. The type of formulation influences the size of area over which the drug is deposited. The hydrophilicity of the drug influences the extent of its spreading and distribution throughout the vagina.

Concentration:

With increase in drug concentration in vaginal fluid , the rate of absorption via passive diffusion can be increased. Long term vaginal delivery system are highly concentrated formulations that gradually release the drug in the limited vaginal fluid, ensuring better absorption, making the fluid highly saturated, and sustained drug delivery throughout the intended time of application.

Contact time:

The extent of flow and retention of the medicament within the vaginal cavity depends on the type of formulation and lower vaginal residence time can be improved by a bioadhesive dosage form that results in prolonged contact with the surface and hence a better drug absorption.

Drug absorption mechanism by vagina[5]

Drug transport via vaginal membrane follows three mechanisms

- Trans cellular route: Diffusion through the cell due to a concentration gradient
- Vesicular or receptor mediated transport mechanism

- Intercellular route: Diffusion between cells through the tight junctions

Classification of Vaginal drug delivery system[8]

- Vaginal solid- Tablet
- Vaginal semisolid- creams, gels, ointments, suppositories
- Vaginal liquids- solutions, suspensions, emulsions
- Vaginal aerosols
- Vaginal controlled release formulations- thermosenstive system, bioadhesive system, pH sensitive system

Vaginal tablet:

Vaginal tablet have same composition as conventional oral tablets and it contains binders, disintegrates and other excipients. The advantage of vaginal tablet is insertion and ease of manufacture. Mucoadhesive polymers are used to increase vaginal residence time. Itraconazole, clotrimazole and prostaglandins drugs are administered as vaginal tablets. Presence of hydrophobic or release retarding materials may decrease the absorption of a drug from a vaginal formulation. Highly hydrophobic drugs are not suitable for vaginal tablets. Presence of penetration enhancers like surfactants, bile salts can significantly enhance absorption at the same time the irritation properties of the materials should be taken under consideration[1,3,5,12,21,24].

Vaginal foam:

The contraceptive foams are used to prevent conception and spermicidal is added in it to reduce the chances of preganancy and destroy the sperm. The foam produces a partition between the egg and the sperm. It is very necessary to administer the foam properly and intercourse should be happen within 1 h. It is used as a lubricant during sexual intercourse. The main disadvantages of vaginal foam are they produce messiness, produce inflammation, irritation of vagina not effective against other sexually contagious diseases and should be used with other contraceptive device to make it effective[4].

Vaginal Semisolids:

Vaginal Creams, Gels and Ointment:

Creams, gels and ointment are usually comes under semisolid vaginal formulations used for delivery of contraceptives and antibacterial drugs for local infections. These delivery systems used very regularly and basic qualities of vaginal semisolid formulations should have easy to use, non-toxic and nonirritating to the mucus membrane. Creams and gels may not deliver a correct dose because of non uniform distribution and leakage. In the treatment of bacterial

vaginosis drug like metronidazole and clindamycin vaginal cream are found as effective as orally administered drugs. Chemical entities like anti-infective like Nystatin, clotrimazole, miconazole, clindamycin, and sulfonamides; hormones like progesterone, dinesetroland contraceptives etc. applied through semisolid dosage form. The anti-HIV agents or microbicides currently aimed through topical intravaginal formulations to reduce the mucosal and prenatal virus transmission. Few years ago, significant work has been done on the development of hydrogel drug delivery systems. Hydrogel are swell and retain large volumes of water in their swollen structure and release drug in a control release when placed in an aqueous environment. A swelling controlled miconazole hydrogel delivery system for intravaginal administration has been reported. A 3% alginate gel of nonoxynol-9 has been investigated for intravaginal spermicidal delivery. Now a day, gel microemulsions act as a nontoxic vaginal formulation. A gel microemulsion based formulation of a spermicide with anti-HIV effect, has been developed drugs for cervical ripening and Antibacterial agents are also available as a vaginal gel[1,3,5,12,22,23].

Vaginal Suppositories:

Solid suppositories are the most common dosage forms. Typically, these are of torpedo-shaped dosage forms but incase of vagina oval shape is more preferred. The most commonly base used for vaginal suppositories consist of combination of the various molecular weight polyethylene glycols, preservatives and surfactants. They are buffered to acidic pH about 4.5 and are designed to meltin vaginal cavity to release active constituent over prolong period of time. It is reported that suppository systems are used to administer drugs for cervical ripening prior to childbirth, progesterone for hormonal replacement the rap and local delivery of anti fungal drugs for vaginal candiasis[1,3,5,12].

Vaginal Liquids

Solution, suspension and emulsion:

The vaginal douches and solutions are available in market. They are used for irrigation cleansing of vagina and single dose douches are prepared which are mixed with warm water and applied as inserters in vagina. Vaginal solutions, emulsions and suspensions are liquid formulation used for a local effect, for irrigation and diagnostic purposes. Excipients are mostly used in the formulation to adjust the viscosity of the preparation, to increase the solubility of the active substance or to stabilize the preparation and to adjust the pH of formulation. The excipients do not adversely affect the intended medical action or, cause undue local irritation at the concentrations used. Vaginal emulsions have show phase separation but are easily redispersed on shaking. Vaginal suspensions may show sediment that is easily dispersed on shaking to give a

suspension which remains sufficiently stable to enable homogeneous preparation to be delivered and supplied in single-dose containers. The container is modified to deliver the preparation to the vagina or it is accompanied by a suitable applicator[1,3,5,12].

Vaginal Aerosol:

Aerosols preparations are very common among different vaginal dosage forms. It is popular to deliver estrogenic substances and contraceptive agents. Marketed preparations e.g.povidone-iodine vaginal foam, and other contraceptive foams are available in the market. The vaginal aerosol is used as novel approaches. The foams are used intra vaginally in the same manner as creams. Aerosol package contains an inserter that is filled with foam and the contents placed in the vagina through activation of the plunger. The foams are normally o/w emulsions resembling light creams. They are water miscible and non greasy. Several marketable rectal foams use inserters. Example of vaginal aerosol is Proctofoam (Schwartz), contains pramoxine hydrochloride to reduce inflammatory anorectal disorder[1,3,5,12].

Vaginal route for sustained/controlled-release drug delivery

Controlled and sustained release devices for drug delivery in the vaginal and uterine areas are most often for the delivery of contraceptive steroid hormones.

Vaginal Rings:

Vaginal rings are circular type drug delivery devices designed to release the drug in a controlled way after insertion into the vagina. Vaginal rings comprise a potential revolution in hormone replacement therapy and contraceptive technology. Vaginal ring became popular due to their ease of administration, lack of GIT related symptoms, high efficiency, no interfere with caution, allows continuous delivery of low dose Steroids and does not require a daily intake of pills. They are approximately 5.5 cm diameter with a circular cross section diameter of 4–9 mm. The rate of drug release can be modified by changing the core diameter or thickness of the non medicated coating. Material used for making vaginal ring is usually polymeric in nature. Polymers like Ethylene vinyl acetate are classified by the content of vinyl acetate and addition of vinyl acetate units in the polyethylene provides the advantages such as improved optical properties, increased flexibility, greater adhesion, and increased impact and puncture resistance. Most of the women judged ring easier application. No adverse effects were experienced among the test group during the study period. For most contraceptive rings may placed in the vagina for 21 days followed by a week of ring free period. NuvaRingR is a example of combined contraceptive vaginal ring available in the US market[1,3,5,12].

Figure 3: Vaginal rings

Vaginal Inserts:

Vaginal inserts contains flat rectangular polymeric slab enclosed in a pouch of knitted polyester removal system and buff colored semi transparent hydrogel slab contains drug. The retrieval system is in the shape of long knitted tape that is used to recover the slab. A more common contraceptive device is the intrauterine device (IUD) popularly used to deliver progesterone for cervical ripening and induction of labor. Two types of medicated IUD are generally used, steroid hormones and contraceptive metals. The metal device is exemplified by theCU-7, a polypropylene plastic device in shape of numbers even. Copper is released by a combination of ionization and chelation from a copper wire wrapped around the vertical limb[1,3,5,12].

Vaginal In situ gels:

Mucoadhesive preparations are using temperature sensitive and mucoadhesive polymers, poloxamer and polycarbophil. These are basically semisolid formulations that may introduce in the vaginal cavity by means of suitable inserting device. The water insoluble/ soluble polymers swell in vagina and form bioadhesive gels that adhere on vaginal layer. This allows continuous release up to 25 to 50 hrs. For example: CRIONE GEL[1,3,5,12].

Vaginal microspheres:

These are designed as novel vaginal drug delivery system to inform stability to drug molecules, to produce controlled as well as targeted drug release and improve bioavailability. Mucoadhesive microspheres and Bioadhesive microparticles are used for better prevention of different diseases. It have several advantages such as constant and prolonged therapeutic effect, reduction in dose frequency, mucoadhesion sand better patient compliance. Disadvantages also have been reported like variation in release rates, higher drug loading required, batch to batch non- uniformity, and toxicity. Econazole nitrate polymer– lipid based vaginal mucoadhesive microspheres were prepared by spray congealing method[4,25].

Vaginal nanoparticles:

The effect of administered drugs via vaginal route reduces due to less duration of action and incomplete coverage. Vaginal nano particles have been formulated to obtain cellular targeting, prolong release and for the treatment of several vaginal infectious disorders. To improve the mucoadhesions, nano particles are used because it may contain several mucoadhesive polymers such as chitosan, polycarbophil and achieve better therapeutic efficacy. Example: for vaginal drug delivery mucus penetrating nano particles were used to protect against herpes simplex virus and vaginal liposomes consisting small interfering RNA were prepared to inhibit different vaginal infectious diseases[4].

Other novel approaches[1,3,5,12]

Medicated Vaginal Tampons:

Tampons are those which contains a polymeric delivery system (strips) that absorb menstrual fluid while gradually releasing lactic acid and citric acid. It is approved by the Food and Drug Administration (FDA)

Films:

Vaginal films are shaped as thin sheets, ranging from 220-240μm in thickness and used as vaginal drug delivery system. These systems are colorless, and soft, presenting a homogenous surface. Vaginal films are produced with polymers such as polyacrylates, polyethylene glycol, polyvinyl alcohol, and cellulose derivatives.

Pharmaceutical aspects

Excipients[13]

The choice of an excipient for vaginal formulation is governed by various critical parameters spanning from their origin to their regulatory status. These include

- source, origin, and availability
- functional category
- purity and quality
- impurity levels and extent of characterization
- batch-to-batch consistency
- stability in the pure form and in the formulation
- compatibility with the active ingredient of formulation and packaging material of vaginal formulation
- history of prior human use
- safety and toxicological issues

- cost considerations
- biological activity,
- regulatory status
- patent status

Penetration enhancers:

Penetration enhancers are able to promoting penetration and absorption of drug through vaginal mucosa by declining the penetration barriers. Examples of penetration enhancers are non ionic surface active agents, bile salts, benzalkonium chloride, hyaluronic acid, polyethylene glycol, ethoxydiglycol and interesterified stone oil[2].

Solubility modifiers:

Poor solubility of drug in simulated vaginal fluid may influence the release of drug from dosage form, which effect the onset and therapeutic efficacy of drug. Water soluble drugs are good candidate for vaginal drug delivery and aqueous solubility of drug can be increased by addition of solublizing agent and cosolvency. Commonly used solublizing agents are citric acid , ethylenediamine tetraacetate, sodium meta-phosphate, PVP, sorbitan, tween 80,polyoxyethylene, polyoxyethylene n-alkyl ethers, poloxamers and cyclodextrin[2].

Mucoadhesive agents:

These allow close contact of formulation with vaginal mucosal surface by promoting adherence such as chitosan, pollycarbophil, hyaluronic acid, sodium alginate, tragacanth, cabomer, acacia, sodium carboxy methyl cellulose, cellulose derivatives, Carbopol 974P-NF, Carbopol 971P-NF and acrylic acid. Some polymers are act as site specific bioadhesive properties such as xantham gum and sodium alginate (site specific bioadhesive in simulated vaginal fluid), polycarbophil 934P(pH dependent bioadhesive properties)[2].

Novel concepts in vaginal drug delivery [1,12]

Current vaginal delivery systems include creams, foams, gels, tablets, pessaries and irrigations. The efficacy of these preparations is limited due to their short residence time in the genitourinary tract. Physiological conditions of the genital tract limit long residence times and impair the therapeutic efficacy, requiring multiple and frequent administration of dose for treatment. Improved vaginal therapy can significantly retain the drug at the site of administration for a prolonged period compared to conventional dosage forms. So, novel approaches are designed with desirable distribution, bio-adhesion, maintenance and release characteristics. These includes:

- Bio-adhesive
- Other novel delivery systems.

Bio-adhesive delivery systems

The vaginal route is highly appropriate for bioadhesive drug delivery systems, to retain systems for treating local conditions, or for use in contraception. Bio-adhesive polymer is group of auxiliary agent, based on new designed systems. Bio-adhesive vaginal formulations are able to deliver the active agent for a complete period at a predictable rate. Bio-adhesive formulations have been found to reduce the predictable treatment time of fungal infections by at least 25%. Abio-adhesive formulation has not therapeutic agent and can be used as a moisturizer for the treatment of dry vagina. Tablets that are placed directly between the vaginal mucosalsurfaces have been detected to be excellent bio-adhesive formulations. Bio adhesive micro-particles have also been used for the vaginal delivery. Salmon calcitonin used HYAFF as bioadhesive polymer where microspheres showed increased bio-availability of drug. Water dispersible films are delivered the drugs directly to mucosal surfaces to form close contact with mucosal membrane. Mucoadhesive hydrogels are weakly- cross linked polymer having capacity to swell in contact with water and to spread on to a surface of mucus. Thus their bioadhesive properties may provide controlled drug delivery system with a prolong residence time and intimate contact in vagina. Many hydrophilic polymers and hydrogels are used in vaginal products. Bio-adhesive formulations based on carbomers and polycarbophil give acceptable drug delivery within the vaginal cavity following the application of a single dose. Example is Prochoice TM that is a bio-adhesive gel used in hormone replacement therapy. Replens® is a muco-adhesive gel based on bioadhesive cross-linked polycarbophil designed to be retained in the genital cavity for 3-4 days.

Other novel delivery systems

Phases change polymers such as poloxamers exhibit sol–gel transition in response to body temperature, pH and specific ions and prolong the residence time of the dosage form in the vagina. To provide the prolonged release of active ingredients such as nonoxynol-9, progestins, estrogens, peptides and proteins are formulated that based on thermoplastic graft copolymer in a vaginal environment. An intravaginal therapeutic system made from certain vaginally that is suitable thermoplastic polymeric materials and not absorbable and can be used for the controlled release of drug. Example of a thermoplastic polymer is styrene-butadiene block copolymer. Additional thermoplastic polymers are used for manufacturing novel vaginal delivery systems include polymethylacrylate, polybutylmethacrylate, plasticized polyvinylchloride, plasticized nylon, plasticized polyethyleneterephthalate, polyethylene, polyacrylonitrile, poly trifluorochlor

oethylene, poly-4,4'-isopropylenediphenylenecarbonate, polyethylene vinyl esters and polyvinylchloride-diethylfumarate. A novel medicating system based on thermoplastic polymeric materials that releases effective amounts of progestational and estrogenic steroids, which produce desired anti-fertility effect over a prolonged period. Recently reported amuco-adhesive thermo-sensitive gel that exhibited increased and prolonged antifungal activity of clotrimazole in comparison with conventional PEG-based formulation.

Application of vaginal drug delivery system

- Multi-cycle administration of vaginal contraceptive rings.
- Effective route for the cure of HIV infection.
- Effective route for the cure of local fungal infection.
- Effective for the delivery of hormones.
- Effective for vaginal immunization

Effective for vaginal immunization and cure of HIV infection:

Mostly successful immunization with DNA vaccines administered via various mucosalroutes. A mucosal site, mainly the vaginal route is the primary site of entry of pathogens into the human body and mucosal immunization causes systemic as well as mucosal immunity. In present research several vaginal vaccine preparation are against a variety of pathogens, as well as the Human immunodeficiency virus (HIV). The development of a novel HIV-CCR5 receptor vaccine for the control of human forms of the virus and mucosal simian (SIV). The vaccine have target son both the virus and its CCR5 receptor, was administer in female rhesus monkeys either by the vaginal route or by targeting the iliac lymph nodes. This immunization approach through the vagina was found to considerably inhibit SIV/HIV infection in the animal model and shows a novel approach to prevent of HIV transmission.DNA vaccines are new approach to control of infectious diseases. The female genital tract has the capacity to produce cellular and humoral immune responses against locally antigens. Vaginal immunization of rodents, human and non-human primates has draw out serum and secretory IgA and IgG responses incervico-vaginal washes[3,26,27,28].

Effective for delivery of hormones:

Morimoto, K. et al., (1982)found that polyacrylic acid aqueous gel bases are used to administration of insulin through vaginal mucosa and results showed that when these gels were administered to rats and rabbits, the hypoglycaemic effects were sustained for 30 min and plasma insulin reached at a peak. The improvement of sustained release is necessary to achieve

longer time of hypoglycaemia. Ning, M. et al.,(2005), prepared niosomes with sorbitan monoester as a carrier for vaginal delivery of insulin and Lipid phase evaporation methods with sonication was used to prepared the vesicles by using of span 40 and span 30. The insulin concentrations and hypoglycemic effect after vaginal administration of insulin vesicles into rats were examined and compared with the subcutaneous administration of insulin solution. The insulin-Span 60, Span 40 niosomes had an increasing effect via vaginal delivery of insulin[29].

Administration of vaginal contraceptive rings:

Vaginal ring are polymeric drug delivery device to provide controlled released of drugs for intravaginal administration. The ring is inserted into vagina and provides contraception protection. Leaving the rings in vagina for three weeks slowly release hormones into body, mainly vaginally administered estrogens and progestrons and these hormones are stopping ovulation and thickening the cervical mucus, creating a barrier preventing sperm from fertilizing an egg. Vaginal ring is 91.99% effective at preventing pregnancy and effectiveness depend upon correct use of vaginal ring[1,3,5,12].

Effective route for cure of local fungal infection:

Vaginal yeast infection or candida vaginal infection caused by candida albicans fungus. During lifetime, 75% of all women are likely to have suffer from vaginal candida infection, and upto 45% have two or more. Vaginal yeast infection are due to if their body under stress from poor diet, lack of sleep and illness. vaginal yeast infection can be treated with antifungal agents are inserted into vagina as tablet, creams, suppositories and ointments. For example: Butaoconazole, Clotrimazole, Miconazole, Tioconazole and Terconazole. Bacterial infection, Trichomonal infection and Monilial infection can be treated by Metronidazole, Clindamycin, Clotrimazole, Miconazole nitrate, Ticonazole, Fluconazoleetc[30].

CONCLUSION

It is concluded, that vaginal route is an acceptable choice for drug delivery of most of the antifungals, hormones, anti-bacterial, contraceptives etc. because of its large surface area, rich blood supply and high permeability avoiding limitations of conventional system, leading to non-invasive controlled action which results in improved bioavailability and increase patient compliance.

ACKNOWLEDGEMENT

Authors are thankful to Punjab Technical University Jalandhar, Punjab and ASBASJS Memorial college of pharmacy, Bela, Ropar, Punjab academic support.

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