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## SHORT REVIEW ON: IMPLANTABLE DRUG DELIVERY SYSTEMS

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### ABSTRACT:

There was a need for delivery systems that could maintain a consistent release of the drug in a specific work environment. Therefore, drug delivery systems are designed to supplement the therapeutic properties of drug products and provide more safe, effective and reliable products. Compared to many other drug delivery systems, implanted pumps and the inclusion of flexible delivery are in the raw stage of development. Although a standard injection pump has different procedures for controlling drug delivery. Benefits usually provided in the dosage form are expected to be 1) Non-invasive resources allow drug administration specific to the area where the drug is most needed. Examples include implants used in the treatment of brain cancer or prostate cancer. This can also allow for very low doses of the drug, which can reduce the potential side effects. 2) Non-fittings allow for continued use of the zero-order release rate of the medical agent. The major advantages of these programs include consistent drug delivery, a few drugs needed to treat the disease, reduce potential side effects, and effective treatment. Due to the development of such released formulas, it is now possible to prescribe non-invasive drugs once a week once a year which in the past required daily anointing.

**KEYWORDS:** Implant, Drug Delivery Systems, Injection Pump, Dose, Target Etc.

### INTRODUCTION

Implantable drug delivery systems allow targeted and localized drug delivery and may achieve a therapeutic effect with lower concentrations of drugs. As a result, they may minimize potential side-effects of therapy, while offering the opportunity for increased patient compliance. This type of system also has the potential to deliver drugs which would normally be unsuitable orally, because it avoids first pass metabolism and chemical degradation in the stomach and intestine, thus, increasing bioavailability.

An ideal implantable parenteral system should possess following properties:

- **Environmentally stable:** Implantable systems should not breakdown under the influence of light, air, moisture, heat, etc.
- **Biostable:** Implantable systems should not undergo physicochemical degradation when in contact with biofluids (or drugs).
- **Biocompatible:** Implantable systems should neither stimulate immune response (otherwise the implant will be rejected) nor thrombosis and fibrosis formation.
- **Removal:** Implantable systems should be removability when required.
- **Non-toxic or non-carcinogenic:** The degradation products or leached additives should be completely safe.
- **Implantable systems should have minimum surface area, smooth texture and structural characteristics similar to the tissue in which it is to be implanted to avoid irritation.**
- **Implantable systems should release drugs at a constant predetermined rate for a predetermined period.**

## ADVANTAGES:

1. **Localized delivery:** - Drug(s) are released in immediate vicinity of implant. Action may be diffusion, limited to the specific location of implantation .
2. **Improved patient Compliance:** - Patient does not need to comply with repeated and timely intake of medication throughout the implantation period. Compliance is limited to one-time implantation (and potential removal in the case of non-biodegradable implants)
3. **Minimized systemic side effects:** - Controlled release for extended periods of time and localized dosing possible with at site of action; adverse effects away from site of action are minimized; peaks and valleys in plasma drug concentration from repeated intermediate release dosing are avoided.
4. **Lower dose:** - Localized implantation of site specific drugs can avoid first pass hepatic effects, thereby reducing dose required to ensure systemic bioavailability
5. **Improved drug stability:** - Protection of drug undergoing rapid degradation in the gastrointestinal and hepatobiliary system
6. **Suitability over direct Administration:** - Hospital stay or continuous monitoring by healthcare staff may not be required for chronic illnesses
7. **Facile termination of drug delivery:** - If allergic or other adverse reaction to drug is experienced, discontinuation of therapy by implant removal is possible.
8. **Potential for intermittent release:** Extremely programmable pumps can facilitate intermittent release in response to various factors such as cardiac rhythm, metabolic needs etc.

9. **Flexibility:** Various types of flexibilities like materials, method of manufactures etc. are available in case of implants. Controlled delivery of both hydrophilic and lypophilic drugs can be obtained from here.

## DISADVANTAGES:

1. **Invasive:** For the insertion of the implants patient has to face either a major or a minor surgical procedure.
2. **Termination:** non-biodegradable polymeric implants can be terminated from the body also with the help of a surgical method at the end of the treatment.
3. **Danger of device failure:** If due to some reason the device fails to operate properly during the treatment then again surgical steps should be taken for removal of the device from the patient's body.
4. **Limited to potent drug:** The size of the device is very small to reduce the patient's discomfort, therefore only the potent drugs which are very small in amount can only be used in this system.
5. **Adverse reaction:** As a high concentration of drug is delivered to the implantation site with the help of the device therefore there is always a chance of adverse reaction due to this local high concentration.

## CONCEPT OF IMPLANTS:

Implants for drug delivery are several types:

### 1. In situ forming implants (In situ depot forming systems):

#### a. In situ precipitating implants:

These implants are formed from drug containing in a biocompatible solvent. The polymer solution form implants after subcutaneous (s.c.) or intramuscular (i.m.) injection and contact with aqueous body fluids via the precipitation of polymers. In situ precipitating implants are formulated to overcome some problems associated to the uses of biodegradable microparticles:

- i). Requirement for the reconstitution before injection
- ii). Inability to remove the dose one injected.
- iii). Relatively complicated manufacturing procedures to produce a sterile, stable and reproducible product.

#### b. In situ microparticle implants:

This type of implants is formed to overcome the disadvantages associated with in situ precipitating implants. These are:

- i). High injection force.
- ii). Local irritation at the injection site.
- iii). Variability in the solidification rates.

- iv). Irregular shape of the implants formed depending on the cavity into which the implants are introduced (implanted).
- v). Undesirable high initial burst release of drugs.
- vi). Potential solvent toxicity.

These in situ implantable systems consist of internal phase (drug-containing polymer solution or suspension) and a continuous phase (aqueous solution with a surfactant, oil phase with viscosity enhancer and emulsifier). The two phases are separately stored in dual-chambered syringes and mixed through a connector before administration.

## 2. Solid implants:

Solid implants are generally cylindrical monolithic devices implanted by a minor surgical incision or injected via a large bore needle into the s.c. or i.m. tissues. Subcutaneous (s.c.) tissue is an ideal location because of its easy access to implantation, poor perfusion, slower drug absorption and low reactivity towards foreign materials. In these implants, drugs may be dissolved, dispersed or embedded in a matrix of polymers or waxes/lipids that control the releasing via dissolution and/or diffusion, bioerosion, biodegradation, or an activation process, such as hydrolysis or osmosis. These systems are generally prepared as implantable flexible/rigid molded or extruded rods, spherical pellets, or compressed tablets. Polymers used are silicone, polymethacrylates, elastomers, polycaprolactones, polylactide-co-glycolide, etc., whereas waxes include glyceryl monostearate. Drugs generally presented in such implantable systems are contraceptives, naltrexone, etc.

## 3. Infusion devices:

Infusion devices are intrinsically powered to release the drugs at a zero order rate and the drug reservoir can be replenished from time to time. Depending upon the mechanism by which these implantable pumps are powered to release the drugs. These are 3 types:

- i). Osmotic pressure activated drug delivery systems
- ii). Vapor pressure activated drug delivery system
- iii). Battery powered drug delivery systems.

## 4. Osmotic pumps:

Osmotic pumps are designed mainly by a semi-permeable membrane that surrounds a drug reservoir (Fig. 1). The membrane should have an orifice that will allow drug release. Osmotic gradients will allow a steady inflow of fluid within the implant. This process will lead to an increase in the pressure within the implant that will force drug release through the orifice. This design allows constant drug release (zero order kinetics). This type of device allows a favorable release rate but the drug loading is limited. The historical development of osmotic systems includes seminal contributions such as the Rose-Nelson pump, the Higuchi-Leeper pumps, the Alzet and Osmet systems, the elementary osmotic pump, and the push-pull or

GITSR system. Recent advances include the development of the controlled porosity osmotic pump, systems based on asymmetric membranes, and other approaches.

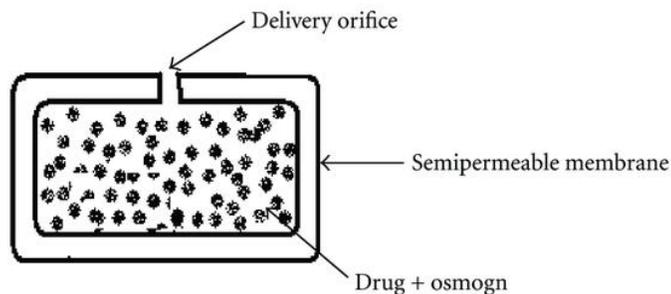


Fig. 1

## OSMOTIC AGENTS:

Osmotic agents are used for the fabrication of the osmotic device maintain a concentration gradient across the membrane by generating a driving force for the uptake of water and assist in maintaining drug uniformity in the hydrated formulation. Osmotic agents usually are ionic compounds consisting of either inorganic salts such as sodium chloride, potassium chloride magnesium sulphate, sodium sulphate, potassium sulphate and sodium bicarbonate. Additionally, sugars such as glucose, sorbitol, sucrose and inorganic salts of carbohydrates can also act as effective osmotic agents.

## CURRENT THERAPEUTIC APPLICATIONS

Implantable drug delivery devices have the potential to be used for a wide variety of clinical applications in areas including, but not limited to: women's health, oncology, ocular disease, pain management, infectious disease and central nervous system disorders. Examples of implantable drug delivery devices for each of these areas are summarized in below table

**Table 1.** Examples of implantable drug delivery devices used in the area of women's health

Product Name	Implant Type	Material	Drug Delivered	Indication
<b>Norplant®</b> <b>Jadelle®</b>	Sub-cutaneous	Silicone	Levonorgestrel	Contraception
<b>Estring®</b>	Intra-vaginal	Silicone	Estradiol	Menopausal symptoms
<b>Nuvaring®</b>	Intra-vaginal	PEVA	Etonogestrel, Ethinyl estradiol	Contraception
<b>Implanon®</b> <b>Nexplanon®</b>	Sub-cutaneous	PEVA	Etonogestrel	Contraception

**Table 2.** Examples of implantable drug delivery devices used for anticancer therapy. ND = not disclosed

Product Name	Implant Type	Material	Drug Delivered	Indication
Zoladex®	Sub-cutaneous	PLGA	Goserelin	Prostate cancer
Prostap®SR	Sub-cutaneous	PLGA	Leuprolide	Prostate cancer
Gliadel Wafers®	Intra-tumoral	Intra-tumoral	Carmustine (BCNU)	Primary malignant glioma
Oncogel®	Intra-tumoral	PLGA-PEG-PLGA	Paclitaxel	Oesophageal cancer

Drug delivery to the posterior segment of the eye is difficult due to the unique anatomical and physiological barriers that the ocular environment presents.

**Table 3.** Examples of implantable drug delivery devices used to treat ocular diseases.

Product Name	Implant Type	Material	Drug Delivered	Indication
Ocusert®	Intra-ocular	PEVA	Pilocarpine, Alginic acid	Open angle glaucoma
Retisert®	Intra-ocular	Microcrystalline cellulose, PVA, Magnesium stearate	Fluocinolone	Non-infectious uveitis
Vitrasert®	Intra-ocular	PVA, PEVA	Ganciclovir	CMV retinitis in AIDS patients

## CONCLUSION

Non-commercial drug delivery is one of the most neglected parts in the field of advancing the distribution of new medicines through the development, research and development of many medicines. Site-specific, medical-oriented releases show an attractive option for companies looking to improve drug product performance or offer additional benefits by integrating an implanted device. , antibiotics, and oncology drugs. Implemented drug delivery technology has the potential to reduce the frequency of patient-centered doses and to deliver space in a targeted manner. This problem should ensure that the high level of interest in the area will extend into the future and lead to significant progress in the drug delivery sector.

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