IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Implantable Drug Delivery System

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ABSTRACT

1. Traditional oral administration: Drugs were historically administered orally, but this method posed problems.
2. Need for alternative delivery methods: To address these issues, new dosage forms and delivery systems were developed.

Evolution of Drug Delivery Systems

1. Development of sustained release systems: As technology advanced, sustained release systems were created to maintain a steady release of drugs.
2. Optimizing therapeutic properties: These systems aimed to enhance the safety, efficacy, and reliability of drug products.

Focus on Implantable Drug Delivery Systems (IDDS)

1. IDDS as a therapeutic option: IDDS are a type of sustained release system available for therapeutic use.
2. Advantages of IDDS: These systems offer targeted local delivery, reduced drug requirements, minimized side effects, and improved treatment efficacy.

Purpose of the Review

1. Examining currently available IDDS: This review focuses on the study of existing IDDS.
Highlighting the benefits of sustained release formulations: The development of these formulations has improved treatment outcomes and patient care

INTRODUCTION-

A medication taken orally needs to be able to pass through the intestinal or stomach wall and be protected from denaturation in the gastrointestinal tract. It needs to be resistant to hepatic enzymes once it has been absorbed and entered the portal circulation. Blood levels within the therapeutic range should be guaranteed by the rate of drug absorption and excretion. Furthermore, there should be just enough intact medicine at the site of action to produce the intended therapeutic effect without producing undesirable side effects.Either chemically altering the drug moiety or manufacturing it in a particular way to regulate its release can produce a controlled drug activity.

Assuming that injectable controlled-release dosage forms offer the required safety and efficacy, their commercial success is more likely than that of other delivery methods. Because of the physiological properties of the medications and the existence of a highly impermeable stratum corneum, the majority of pharmaceuticals have limited percutaneous absorption when administered topically.
Comparing implantable drug delivery devices to subcutaneous ones, the former have one distinct benefit over the latter: they do not have the drawbacks of oral, intravenous, or topical drug administration.(1)

The medicinal drug is often contained in a rate-controlling device in implantables. Implantables come in a range of forms and sizes.
Although many medications are best administered orally, other approaches that use pulmonary, infusion, and implantable systems have been developed to get around limitations in drug delivery. For instance, a large number of macromolecules are either poorly absorbed into the bloodstream or broken down in the gastrointestinal system. Additionally, medications that need to take effect quickly might not be suitable for oral delivery. In a similar vein, medications used in pulmonary systems like inhalers must enter the bloodstream through the lungs.Injectable drug delivery has additional drawbacks.

For circumstances when oral drug delivery is not practical or ideal, pulmonary, transdermal, intravenous, or subcutaneous injection or infusion[2], and implantable systems have been developed[3]. In situations where adherence to a prescribed medication schedule is crucial, implantable drug delivery systems are especially preferred. With the use of such devices, a medication can be administered at a predetermined pace without the need for frequent patient or doctor intervention. Depending on whether they distribute the drug passively or actively, the two primary types of drug delivery implants currently on

the market can be separated into two groups. The most used passive medication delivery method is polymer depots.

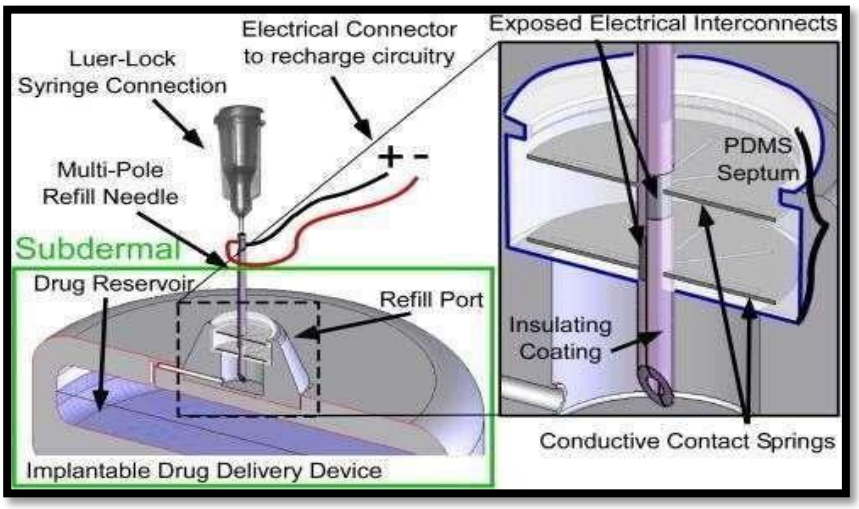

Fig 1- A photo of the front of an assembled microvalve regulateted drug delivery device with the backe side refille port showen inset

As potential answers to these needs, two distinct approaches have been thoroughly examined. One is the creation of a delivery system that releases its payload in pulses of a predefined sequence or at a predefined time. Creating a system that can adapt to changes in the local environment is the other. It has been demonstrated that these systems can change how quickly they distribute drugs in response to a variety of stimuli, such as the presence or absence of a particular molecule, magnetic or electric fields, ultrasound, light, temperature, and mechanical forces.

***ADVANTAGES OF IMPLANTABLE DRUG DELIVERY* SYSTEM :**

1) Convenience : Techniques like repeated injections or continuous intravenous infusion can help maintain an effective drug concentration in the blood for a longer amount of time.
A short-acting medication exacerbates the issue because more injections or infusions are required to maintain a therapeutically effective drug level.
When compared to indwelling catheter-based infusion systems, implantation treatment is further distinguished by a decreased incidence of infection-related issues.

2) Improves Drug Delivery : .
1. Localized or systemic distribution: The drug is delivered directly to the target site or distributed systemically with minimal interference.
2. Minimized metabolic interference: The drug bypasses metabolic barriers, such as the liver, reducing the risk of degradation or inactivation.
3. Reduced biological barriers: The drug is less affected by biological barriers, such as the gastrointestinal tract (GIT), allowing for more efficient absorption and distribution.
4. Improved bioavailability: By bypassing the GIT and liver, the drug is more likely to reach the target site in its active form, increasing its bioavailability.(1)

3) Compliance : 1. Reduced patient involvement: Implantable systems minimize the need for patient-involved dosing, reducing the likelihood of missed doses.
2. No reliance on patient memory: Patients can forget to take their medication, but implantable systems deliver the drug consistently, without relying on patient input.
3. Less frequent dosing: Implantable systems can provide a steady release of medication over an extended period, reducing the need for frequent dosing.

4. Periodic refilling: While some implantable systems may require periodic refilling, this is still less frequent than traditional oral dosing regimens.

Benefits of Improved Compliance

1. Better treatment outcomes: Improved compliance can lead to more effective treatment outcomes and better disease management.
2. Reduced healthcare costs: By reducing the need for frequent dosing and minimizing the risk of missed doses, implantable systems can help reduce healthcare costs.

3. Enhanced patient quality of life: Implantable systems can improve patient quality of life by reducing the burden of frequent dosing and minimizing the risk of treatment-related complications.

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4) Controlled Release

1. Zero-order controlled release kinetics: Implants can deliver drugs at a consistent rate, maintaining a steady therapeutic level.
2. Avoiding peaks and troughs: Zero-order release avoids the toxic peaks and ineffective troughs associated with conventional therapy.
3. Reduced dosing frequency: Controlled release reduces the need for frequent dosing.
4. Increased patient compliance: By minimizing the need for frequent dosing, patient compliance is improved.

A) Bio-Responsive Release

1. Ongoing research: Bio-responsive release, where the implant responds to physiological changes, is an active area of research.
2. Potential for personalized medicine: Bio-responsive release could enable personalized medicine, where the implant adapts to individual patient needs.

B) Intermittent Release

1. Externally programmable pumps: Intermittent release can be achieved using externally programmable pumps.
2. Circadian rhythm-based release: Intermittent release can facilitate drug release in response to circadian rhythms or other physiological changes.
3. Improved efficacy and reduced side effects: Intermittent release can improve efficacy and reduce side effects by delivering drugs in response to specific physiological needs.

5) Flexibility

1. Choice of materials: Various materials can be used to fabricate implantable drug delivery systems, offering flexibility in design and development.
2. Methods of manufacture: Different manufacturing methods can be employed to produce implantable systems, allowing for customization and innovation.

3. Degree of drug loading: The amount of drug loaded into the implantable system can be tailored to specific therapeutic needs.
4. Drug release rate: The rate at which the drug is released from the implantable system can be controlled and adjusted to achieve optimal therapeutic effects.(18- 21)

A) Regulatory Benefits

1. New product designation: Implantable drug delivery systems are considered new products from a regulatory perspective.
2. Market protection extension: The development of an implantable drug delivery system can extend market protection for a drug by:
- 5 years for new drug entries - 3 years for existing drugs

Disadvantages Of Implantable Drug Delivery System :

1) Invasiveness

A) Surgical Requirements

1. Minor or major surgical procedure: Implantable drug delivery systems require a surgical procedure to initiate therapy.
2. Surgical personnel: Trained surgical personnel are necessary to perform the implantation procedure.

B) Potential Complications

1. Time-consuming and traumatic: The implantation procedure can be time- consuming and traumatic for the patient.
2. Scar formation: The implantation site may experience scar formation.
3. Surgery-related complications: A small number of patients may experience surgery-related complications.

C) Patient Discomfort

1. Uncomfortable feeling: Patients may experience discomfort or an uncomfortable feeling while wearing the device.

2) Risk of Device Failure(1)

1. Device malfunction: There is a risk that the implantable device may fail to work as intended.
2. Consequences of device failure: Device failure can lead to inadequate or inconsistent drug delivery, which may compromise treatment efficacy.
3. Surgical intervention required: In the event of device failure, surgical intervention is typically required to correct or replace the device.

A) Implications for Patients

1. Risk of treatment interruption: Device failure can interrupt treatment, potentially leading to worsening of symptoms or disease progression.
2. Need for ongoing monitoring: Patients with implantable drug delivery systems require regular monitoring to ensure device functionality and optimal treatment outcomes.

2) Termination

1. Surgical recovery: These systems require surgical removal at the end of therapy.
2. Controlled termination: Surgical recovery allows for controlled termination of drug delivery.

A) Implications for Therapy

1. Limited control over termination: Biodegradable polymeric implants may not provide the same level of control over termination as osmotic pumps and non-biodegradable polymeric implants.

2. Potential for variable dosing: The biodegradation process may lead to variable dosing, which can impact treatment efficacy and safety.

3) Limitations

A) Size Constraints

1. Small implant size: To minimize patient discomfort, implants are typically designed to be small.
2. Limited loading capacity: The small size of implants limits their ability to carry large amounts of medication.

B) Limited to Potent Drugs

1. Potent medicines only: Due to the limited loading capacity, implantable devices are often restricted to delivering potent medicines.
2. Hormones and other potent drugs: Examples of potent medicines suitable for implantable delivery include hormones and other drugs with high potency.

C) Implications for Therapy

1. Limited treatment options: The size constraints and limited loading capacity of implants limit their use to specific potent medicines.
2. Restricted patient population: Implantable drug delivery systems may not be suitable for patients requiring large doses of medication or those with conditions requiring non-potent medications

4) Biocompatibility Issues

1. Foreign body reactions: The introduction of a foreign substance (the implant) into the body can trigger an immune response, leading to inflammation, tissue damage, and other complications.
2. Biocompatibility concerns: The materials used to construct the implant must be carefully selected to minimize the risk of adverse reactions and ensure compatibility with the surrounding tissue.
3. Safety risks: Biocompatibility issues can compromise the safety of the implant, potentially leading to serious health consequences for the patient.

5) Possibility of Adverse Reactions

1. High drug concentration: Implantable devices can deliver high concentrations of drugs at the implantation site.
2. Local adverse reactions: This high concentration can lead to local adverse reactions, such as:

- Inflammation
- Irritation
- Tissue damage
- Allergic reactions

3. Systemic adverse reactions: In some cases, the high drug concentration can also lead to systemic adverse reactions, such as: - Toxicity

- Organ damage
- Immune system suppression

A) Factors Contributing to Adverse Reactions

1. Drug properties: The chemical and pharmacological properties of the drug can influence the likelihood of adverse reactions.
2. Implant design and materials: The design and materials used in the implantable device can also contribute to adverse reactions.
3. Patient factors: Individual patient factors, such as allergies or sensitivities, can also play a role in adverse reactions.

B) Mitigating Adverse Reactions

Careful device design: Implantable devices should be designed with safety and efficacy in mind.

IMPLANTABLE DRUG DELIVERY DEVICES

1) Field of Controlled Drug Delivery :
Implantable controlled drug delivery techniques are especially helpful for administering medication to areas of the body, such the cornea, that are immunologically separated and inaccessible to conventional drug delivery systems. These days, the field of controlled drug delivery uses techniques including microencapsulation, polymer implants, transdermal patches, and bioadhesive devices.(22-24)

2) Transdermal Patches :
In transdermal patches, the medication is administered beneath the skin using hollow microneedles composed of a biocompatible polymer. Comparing transdermal patches to other drug delivery methods, there are several benefits: the medications are painless, do not break down in the gastrointestinal tract, and provide a consistent dosage without requiring patient compliance [25].The nicotine patch is a well-known example of a transdermal patch.

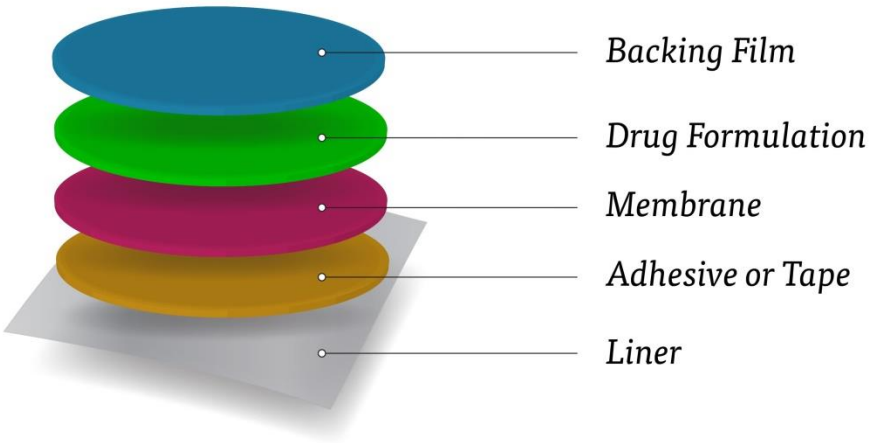

Fig 3 - Transdermal Patches

1) Polymer Implants :
Biodegradable polymers containing medicinal molecules are known as polymer implants. When the polymer interacts with bodily fluids, it breaks down and releases medication molecules. By altering the polymer's characteristics, the rate of degradation and, thus, the drug release can be maximized. The most commonly utilized polymer materials for these purposes include, but are not limited to, polyglycolic acid (PGA), polylactic acid (PLA), polyurethane, and their various mixtures.

2) Bioadhesives :
Materials that create connections with biological surfaces are known as bioadhesives. In this instance, polymer hydrogels are the most often utilized materials. In that they are also filled with medications and release those medications at a predetermined pace when they come into contact with bodily fluids, the principle of operation is comparable to that of polymer implants. Water-swollen networks of polymers are called hydrogels. Covalent crosslinks or physical forces may hold the polymer chains together. The hydrogel's constituents can be engineered to respond to their physical or chemical surroundings. As the temperature rises, the balance of solution and hydrophobic forces changes, causing it to collapse into a denser, more compact form at 35–40 oC.(26) elivery System

1) Microencapsulation :

The technique known as microencapsulation involves encasing the drug molecule in a substance that will delay its resorption, allowing it to stay alive and be released when it reaches its target location.
Microencapsulation can be carried out in a number of ways. Among these are the applications of liposomes, nanoparticles, polymer microspheres, and others [25]. The aforementioned gadgets are known as "passive devices" they precisely administer the medication in extremely tiny doses over time. However, they are unable to provide the medication "on demand" or in a non-linear form. They can't be configured to deliver medication when needed and cease when not.(22,23)

 Some Important Passive Devices Certain medication delivery systems are particularly noteworthy.

1) Microchip Drug Reservoirs :

These gadgets were developed in the MIT lab of Dr. Robert Langer. It is among the first drug delivery systems that are actually based on MicroElectro Mechanical Systems design (MEMS) (Figure 4.1). It has several sealed chambers that can be accessed when a drug dose is needed [24]. In order to fabricate these microchips, prime grade (100) silicon wafers were first coated on both sides with 0.12 mm of low stress silicon nitride using a vertical tube reactor.

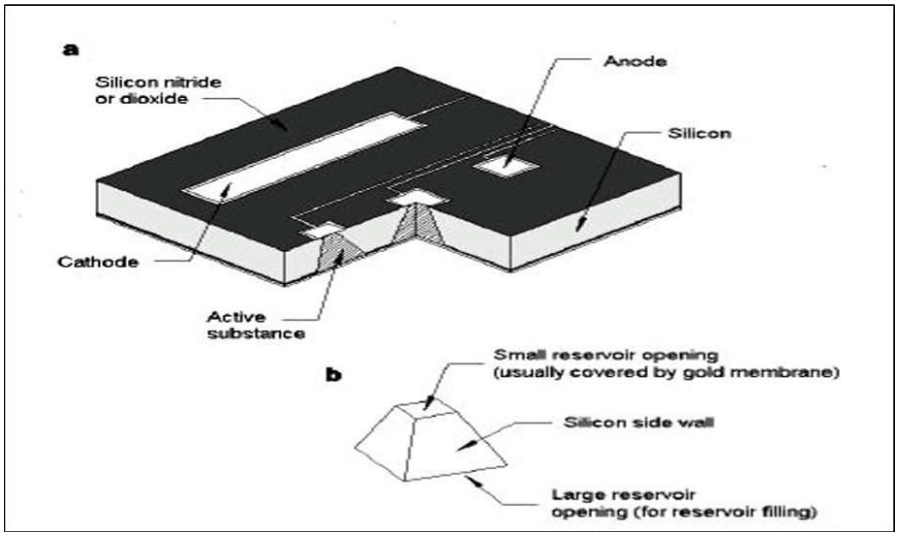

Fig 2- Microchip Drug Reservoirs

Photolithography and electron cyclotron resonance (ECR) enhanced reactive ion etching (RIE) were used to form the silicon nitride layer on one side of the wafer, resulting in a square device (17 mm x 3 mm x 17 mm) with 34,480 square reservoirs. Potassium hydroxide was etched using silicon nitride. The silicon nitride on the opposite side of the wafer was obtained by anisotropically etching square pyramidal reservoirs (Figure 4.1b) into the silicon along the (111) crystal planes using a potassium hydroxide solution at 85.8ºC as an etch mask.

diabetes[27]. The fabrication of nanochannels in the membrane structure consists of two steps. First, surface micromachining nanochannels in a thin film on the top of a silicon wafer. Second, releasing the membrane by etching away the bulk of the silicon wafer underneath the membrane. These nanopore membranes are designed to allow the permeability of glucose, insulin, and other metabolically active products, while at the same time, preventing the passage of cytotoxic cells, macrophages, and complement. The membranes are bonded to a capsule that houses the pancreatic islet cells. Because the difference in the size of insulin, which must be able to pass freely through the pores and the size of the IgGimmunoglobins, which must be excluded, is only matter of a few nanometers, the highly uniform pore distribution provided by micromachine membranes is essential for effective immunoisolation and therapeutic effect. while simultaneously blocking complement, macrophages, and cytotoxic cells from passing through. The
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pancreatic islet cells are housed in a capsule to which the membranes are attached. The highly uniform pore distribution offered by micromachine membranes is crucial for efficient immunoisolation and therapeutic effect because the size difference between insulin, which must be able to pass freely through the pores, and IgGimmunoglobins, which must be excluded, is only a few nanometers.

3) Diffusion Chambers :

A Debiotech Inc. diffusion chamber. They are sealed with a semipermeable membrane and contain a pharmacological cargo. These are used to administer a substantial quantity of medications, sometimes many medications. Higher delivery rates are the result of the membrane's larger surface area than the reservoir. Typically, these reservoirs are not utilized for long-term distribution.(28)

4) Diffusion Controlled Implanted Tubes (29-32)

These give a slow drug delivery rate by using a tiny aperture. They are used to deliver extremely powerful medications over an extended period of time, usually years. The elastomeric tube-based birth control implants that endure for five years are a prime example [33]. The ALZA Corporation's DurosTM osmotic pump serves as a comparable illustration. For systemic or tissue-specific therapy, this nonbiodegradable, osmotically driven system[2] is designed to facilitate the delivery of tiny medications, peptides, proteins, DNA, and other bioactive macromolecules. Using ALZA's exclusive formulation technique, the DUROS® implant is a tiny titanium alloy cylinder that stabilizes and protects the medication inside. A semi-permeable membrane allows water to enter one end of the cylinder, while a port at the other end delivers the medicine at a controlled pace appropriate for the particular medicinal substance. The delivery may take place throughout a 12-month period.

Implantable Pump Systems

The main feature that sets a pump apart from other controlled-release devices is that pressure differences, rather than differences in drug concentration between the concentration and surrounding tissue, are what propel distribution by a pump. Direct mechanical actuation, osmotic action, or pressurizing a drug reservoir can all produce this pressure differential. Early in the 1970s, reports surfaced of the first such gadget to be widely used in clinical settings.Industry and academia, in this case the University of Minnesota and the Infusaid Company, collaborated to develop and market the unit. Freon that had been partially liquefied was used to start a bellows-type pump. With every transcutaneous filling of the implanted device, the Freon was reliquified, and the medicine was administered consistently. The

gadget had no batteries or circuitry. However, Medtronic and the same company's subsequent products included notable improvements. A refillable reservoir, a mechanical pumping/valving mechanism, complex electronics that regulate medication administration and can be programmed telemetrically from outside the body, and a primary lithium battery are some of these more advanced systems [34].There are some qualities that the perfect medicine delivery system should possess. For long periods of time, it must supply a medicine within a range of defined rates (typically the range of drug delivery rates is in tens of µl/min). Features like dependability, chemical, physical, and biological stability should be included. In addition to having overdose protection, the pump needs to be non- inflammatory, non-antigenic, non-carcinogenic, and non-thrombogenic. To justify the surgery involved in implanting the pump, it must be easy to program, have a long reservoir and battery life, be implantable under local precision of distribution over a period of two to five years, and be convenient for both the patient and the healthcare provider. An implantable device must be easy to operate if there are factors like a finite reservoir life, a finite battery life, patient- to-patient variations in medication demands, or long-term changes in a single patient's drug demands.(25)

Examples of important devices currently in use are as follows:

1) Medtronic Synchromed :

The Minimed Medtronic Insulin delivery pump is the most popular implantable medication delivery device. Patients with diabetes mellitus utilize it as an artificial pancreas, as the name implies.The peristaltic minipump[2] of the Minimed pump, which was the manufacturer of the pump that Medtronic eventually purchased, delivers 0.50µl every stroke. Fresh insulin is added to the implantable insulin pump reservoir every two to three months, depending on the patient's insulin needs. A needle is passed into the pump fill port through the skin. Only after the needle has been firmly inserted into the fill port will the pump's

negative pressure mechanically draw the unique U-400 insulin from the syringe into the reservoir, ensuring refill safety. Because titanium is the best material for biocompatibility, it is used to make the implantable pump's body. Carbon monofluoride batteries, which have a minimum lifespan of six to seven years, are utilized. You can use an external communicator to program it. The pump is 2.0 cm in thickness and 8.1 cm in diameter. Negative pressure reservoir with passive filling, pump system fault shutdown, and special code sequencing to synchronize the pump and PPC (Personal Pocket Communicator) are some of the safety features.

THE IDDS SYSTEM :

Conceptual Design :

1) Components

A) Micro Pump
B) Resevior
C) Power Module
D) Control Circuitry and RF Telemetry

A) Micropump : The micropump is an electrically regulated on- demand active device that may provide precise dosages of medicinal substances. The driving mechanism for moving the medication from the reservoir to the catheter is provided by the micropump. High dependability and compact compactness are prerequisites for medicine delivery. The IDDS should be able to administer medication against blood pressure that is between 8 and 12 mmHg in veins or higher than 120 mmHg in arteries. An "in-plane" silicon pump[36] made from silicon-on-insulator (SOI) wafers using the deep reactive ion etching (DRIE) process is used by the IDDS.

B) Reservoir : The size of the implantable device is significantly influenced by the reservoir. The vascular access ports and our reservoir have a similar architecture. It has been shown that these ports have good biocompatibility and biostability [34]. The reservoir should be easily refillable, have smooth curves, and store at least 5 milliliters of the medication. For the IDDS, the port-like reservoir was positioned subcutaneously.While keeping the pump the same size, the reservoir's size can be changed according to necessity. The reservoir will be made of silicone or titanium for biocompatibility concerns. It should be mentioned that there is no specific dosage for chemotherapy continuous infusion. Depending on the needs of the treatment, the dosage, infusion rate, and combination of drugs may change. A catheter connects the port to the implanted device.

C) Power Module : Management of Power The projected power consumption for the intended 10 µl/min delivery rate, excluding the power needed by the RF unit, is between 100 and 500 mW. This amount is an estimate based on the micropump's power usage to produce the necessary diaphragm displacements. Consequently, under 48 hours of continuous use, commercially available small lithium-ion batteries [28, 35] would drain. As a result, the IDDS requires a power management system that uses power source recharge. Using through-skin electrical interconnects to recharge from outside the body is one option.

Using RF coils for wireless power transmission would be a far superior option.

D) Rf Telemerty Test : Five meters separates the telemetry test setup. The received signal is 191 mV, while the broadcast signal is 1.2 mVp-p amplified by a factor of 2000. A 1 KHz sine wave with a 433 MHz carrier is the modified signal [38]. A transmitter unit and a receiver unit make up the telemetry module. In order to provide a fully implanted drug delivery mechanism—including power management, size considerations, and control circuit integration—we aim to combine the telemetry and microfluidic devices.(2,36,37)

FUTURE PROSPECTS

There is now a lot of research being done on implanted drug delivery devices. However, before many of these preparations may be employed, much more work needs to be done in the areas of biodegradable and biocompatible compounds, drug release kinetics, and further development of current methods. Scientists are still hopeful that many of these systems will be able to be prepared with the best zeroorder release kinetics profiles, in vivo, over extended periods of time, enabling sustained usage in patients who are continuously ill.There is a constant preparation of new medications. Many of these drugs are made from proteins and peptides, which are extremely unstable when given orally. It will be feasible to distribute such medications at steady rates by utilizing novel forms of prolonged- release drug delivery devices.(34-36)

Improvements to new implantable devices in the coming years will assist lower drug treatment costs, boost medication efficacy, and improve patient compliance [50–52].

THERAPEUTIC APPLICATIONS OF IDDS

1) Ocular disease : It has been estimated that a wide variety of implanted technologies can provide sustained ocular administration. These include implantable silicone devices, implantable infusion systems, and membrane- controlled devices. An example of a membrane-controlled system is an ocular insert (ocusert) with pilocarpine base and alginic acid in a drug reservoir encircled by an ethylene-vinyl acetate membrane that controls the release rate
[39–41]. The ocusert system provides a near zero order transport of pilocarpine [42] at 20 or 40 μg/h for

seven days after an initial rupture. With appropriate intraocular pressure control and little adverse effects, the device is well tolerated in adults [43–46]. But in older individuals, when the majority of the therapeutic need is present, it appears to be poorly tolerated.Antineoplastic silicone rubber balloons are among the implantables being considered for the treatment of ocular cancer.

1) Contraception : The FDA recently authorized Norplant, a subdermal implant that delivers levonorgestrel, a contraceptive medication, for long-term use. Six silicone membrane capsules, each containing approximately 36 mg of levonorgestrel, make up the device. From a single trocar entry point, the capsules are inserted subcutaneously in a fan-shaped pattern on the inside of the upper arm or forearm. Clinically, at four years, the net pregnancy rate for Norplant users is less than 1.5 per 100 women. By the end of four years, 42% of the women were still using the approach, indicating that it was as acceptable as other methods. Other polymer-based contraceptive methods include silicon rubber vaginal rings that are typically worn for three to seventy-six months, frequently with a removal interval. of one week each month to accommodate menstruation; injections of injectable microspheres or rods made of biodegradable polymers; and the progestasert, an intrauterine drug-releasing device made of ethylenevinyl acetate copolymer that lasts for a year (31)

2) Dental application : Polymeric implants have been tested for a variety of dental uses, including as the local, long-term delivery of fluoride, an antibacterial, and antibiotic. For fluoride distribution with prolonged release, stannous fluoride was included into several dental cements. The drug release rate is limited by another distributed in the hydroxyethyl and methyl methacrylate copolymer hydrogel coated with an outer layer of the same copolymers in a different ratio. Attached to the buccal surface of the maxillary first molar, the device was approximately 8 mm long, contained 42 mg of fluoride in its core, and was intended to release 0.5 mg of fluoride every day for 30 days.(29- 31)

3) Immunization : Research is being done on polymeric implants to improve the immune system's reaction to antigens. The idea here is to administer the antigen continuously or pulsatilely over an extended length of time. Wise et al. used bovine serum albumin as a model antigen to assess the vaccination effectiveness of ethylene-vinyl acetate copolymer pellets. The

immunological response was similar to what was obtained with two injections of complete Freund's adjuvant (an o/w emulsion including microorganisms) in bovine serum albumin.

4) Cancer : Silicone rod implants analogous to those used for delivery of levonorgestrone have been evaluated for delivery ofethinylestradiol or testosterone propionate in persons with prostate cancer. Lupron depot produced by Takeda chemical industries is an implantation system providingonemonth depot release of leuprolide acetate, a synthetic analogue of the gonadotropin- releasing hormone (GhRH). The implant containing biodegradable microspheres made from polylactic – glycolic copolymer at 1:1 compositions having 10% leuprolide acetate for the management of prostate cancer.Zoladexproduced by ICI Pharma provides one month depot release of goserelin acetate from a biodegradable implantable rod for the management of prostate cancer.

5) Narcotic antagonists : A thorough evaluation of naltrexone in implants derived from long-term narcotic antagonist delivery has been conducted. For extended narcotic antagonist activity, naltrexone hydrochloride or the pamoate acid salt has been prepared in a variety of polymers and dosage forms.

6) Other application : Numerous insulin administration methods have already been described , developed and assessed for a biofeedback technique.The drug release rate in these biofeedback-controlled systems is dependent on the body's need for the medicine at a given moment. From a therapeutic standpoint, these systems might be the closest to mimicking a gland's release, like the pancreas. To achieve self-regulated distribution, a variety of methods have been used [2, 41]. A few examples of therapeutic uses for implantable drug delivery systems are the ones listed above.(31)

CONCLUSION :

Recently One of the technological areas that is frequently disregarded in the design, research, and development of novel drug delivery systems in many pharmaceutical companies is implantable drug delivery. Implanted drug delivery systems can distribute the substance in a tailored way and decrease the frequency of patient-driven dosage. Numerous products that use implant delivery technology are being used for a variety of therapeutic purposes, including cancer, ophthalmology, and dentistry. Biocompatibility concerns, like the development of a fibrous capsule surrounding the implant and, in the case of erosion-based devices, the potential toxicity or immunogenicity of the by-products of polymer degradation, must be examined, just like with any implanted material.

The number of products on the market and the number of patents awarded recently demonstrate how many businesses are engaged in the development of novel medication delivery methods. The creation of delivery systems for medications in the future will undoubtedly be more complicated, and pharmaceutical scientists will need to prepare for a demanding work.

REFERENCE

1) ChienYie W; Novel Drug Delivery Systems, Marcel Dekker Inc.;1992, 2nd Ed, 269.

2) Vyas SP and KharRoop K; Controlled Drug Delivery Concepts and Advances, Vallabh Prakashan (Delhi);2008, 1st Ed, 450- 459.

3) Langer R; Where a Pill Won’t Reach,Scientific American; 2003, 288(4): 50– 57.

4) Shah Mitul; Pharmaceutical Implants: http://pharmatips.doyouknow.in; 2010.

5) ChienYie W; Novel drug delivery System, Marcel Dekker Inc.; 1992, 2: 381.

6) Saettone MF, Salminen L; Ocular Inserts for Topical Delivery,Adv Drug Del Rev; 1995, 16:95-106.

7) Khar RK, Vyas SP; Targeted and Controlled Drug Delivery Novel Carrier Systems, CBS Publishers and Distributors: New Delhi; 2002, 1st Ed, 384.

8) Allababidi, S., Shah, J.C.; Efficacy and Pharmacokinetics of Site- Specific Cefazolin Delivery using Biodegradable Implants in the Prevention of Post- Operative Wound Infections, Pharm. Res; 1998; 15: 325–333.

9) Banker RW; In Control Release of Biologically Active Agent. New York: John Wiley & Sons; 1987, 132.

10) Santini JT, Richards AC,Scheidt RA, Cima MJ, Langer RS; Microchip Technology in Drug Delivery, Ann. Med.;2000, 32: 377-379.

11) RanadeVasant V, HollingerMannfred A; Drug Delivery Systems, Boca Raton, Fla. CRC Press; 1996.

12) Mathiowitz Edith, Chickering Donald E, Lehr Claus- Michael; Bioadhesive Drug Delivery Systems: Fundamentals, Novel Approaches, and Development, Marcel Dekker; 1999.

13) Desai TA, Chu WH, Tu JK, Beattie GM, Hayek A, Ferrari M; Microfabricated immunoisolating biocapsules, Biotechnol. Bioeng; 1998, 57: 118120.

14) http://www.debiotech.com

15) Bhatt P Padmanabh; Osmotic Drug Delivery System for poorly Soluble Drug, Pharma Venture Ltd.; 2004.

16) Chein YW; Novel Drug Delivery Systems: Fundamentals Developmental Concept and Biomedical Assessments. Dekker Publisher, New York; 1982, 59- 64.

17) Chein YW; Novel Drug Delivery System. 2nd ed. 270 Madison Avenue Marcel Dekker Publishers, New York; 2005, 87- 95.

18) Jain NK; Advances in Controlled and Novel Drug Delivery, CBS
Publishers & Distributors; 2005, 1st Ed, 204-228.

19) Brissova M, Lacik I, Powers AC, Anilkumar AV, Wang T; Control and Measurement of Permeability for Design of Microcapsule Cell Delivery System, J. Biomed. Mater. Res.; 1998, 39:61-70.

20) Greatbatch W, Holmes CF, Ltd WG, Clarence NY;History of Implantable Devices, IEEE Engineering in Medicine and Biology Magazine; 1991.

21) Shah Mitul; Pharmaceutical Implants: http://pharmatips.doyouknow.in; 2010.

22) Huang Qing-An, Lee Neville; Analysis and design of polysilicon thermal flexture actuator, J. Micromech. Microeng.; 1999, 9: 64-70

23) Theeuwes F, Swanson DR, Guitttard G, Ayer A, Khanna S; Osmotic
Delivery Systems for the βAdrenoceptor Antagonists Metoprolol and Oxprenolol: Design and Evaluation of Systems for Once-Daily Administration, Br. J Clin Pharmacology; 1985, 19: 69-76.

24) Mahdi Rasouli, Soo Jay Phee;Energy Sources and their Development for Application in Medical Devices, Expert Review of Medical Devices; September, 2010, 7(5):693-709(17).

25) Jain NK; Advances in Controlled & Novel Drug Delivery, CBS
Publication, & Distributors; New Delhi;2005, 1st Ed, 219-223.

26) Moddox YF, Bernstein HN; An Evaluation of the Bionite Hydrophilic Contact Lens for Use in a Ocular Drug Delivery System, Ann Ophthalmol; 1992, 4:789.

27) Wentworth JS, Paterson CA, Wells JT,Tilki N, Gray RS, McCartney MD; Collagen Shields Exacerbate Ulceration of Alkali- burned Rabbit Corneas, Arch Ophthalmol; 1993, 111:389-392.

28) Katz IM, Blackman WM; A Soluble SustainedRelease Ophthalmic
Delivery Unit, Am J Ophthalmol; 1977, 83:728-734.

29) Lamberts DW, Pavan-Langston D, Chu W; A Clinical Study of Slow- Releasing Artificial Tears; Ophthalmology; 1978, 85:794-800.

30) BawaR, Dais M, Nandu M, Robinson JR; New Extended Release Ocular Drug Delivery System: Design, Characterization and Performance Testing of Minidisc Inserts, ProcIntSymp Control RelBioact Mater; 1988, 15:106a-b.

31) Koka S; The Implant-Mucosal Interface and Its Role in the Long- Term Success of Endosseous Oral Implants: A Review of the Literature,Int J Prosthodontics; 1998,11(5):421-432.

32) Sennerby L, Roos J; Surgical Determinants of Clinical Success of Osseointegrated Oral Implants: A Review of the Literature,Int J
Prosthodontics;1998, 2(5): 408.

33) RahmanA,Dedi K, Samuel Z, Rashid S, Solakoglu O, Beres F, Cooper
LF;Immediate Placement and Immediate Provisionalization of ITI Implants in Maxillary Non-Restorable Single Teeth. A Preliminary Report; Jun-2004, 13(2):6671.

34) Gupta PK, Hung CT, and Perrier DG; Quantitation of the Release of
Doxorubicin Form Colloidal Dosage Forms using Dynamic Dialysis, J Pharm Sci.; 1987, 76:141–145

35) Robinson DH, and Sampath S; Release Kinetics of Tobramycin Sulphate from Polymethylmethacrylate Implants, Drug Dev. Ind. Pharm; 1989, 15: 2339– 2357.

36) Vyas SP and KharRoop K; Controlled Drug Delivery Concepts and Advances, Vallabh Prakashan (Delhi);2008,1st Ed, 473-474.