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IMPLANTABLE DRUG DELIVERY SYSTEM

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Abstract:

Historically, medications were often taken orally as liquids or powders. New dosage forms containing the medicine or drugs were produced in order to prevent issues that could arise from using the oral route of drug delivery. Delivery methods that could sustain a consistent medication release to the precise region of action became necessary as time went on. In order to maximize the therapeutic qualities of pharmaceutical goods and make them safer, more effective, and more dependable, drug delivery systems were created. One such system that is accessible for therapeutic use is the implantable drug delivery system (IDDS). This research focuses on the analysis of implanted medication delivery devices that are currently on the market. These systems' main benefits include higher therapeutic efficacy, less medications needed to treat the disease state, reduced likelihood of adverse effects, and focused local drug delivery at a steady rate. The creation of these prolonged release formulations has made it feasible to provide unstable medications that previously required regular daily doses once a week to once a year. These technologies have proven to be more effective than traditional therapy approaches in preliminary investigations. The cost-benefit ratio (cost/benefit) of these recently discovered drug delivery methods is excessively high, which limits their adoption in comparison to traditional dosage forms.

Keywords: *Implantable drug delivery system, implant, recent technology, implant.*

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INTRODUCTION:

Implantable drug delivery systems are a form of innovative drug delivery system that Provides regulated medication delivery at the precise location of the implant. When other delivery methods are neither feasible or preferred, implanted drug delivery devices are ideal. With the help of these devices, medications can be administered at effective rates and places without worrying about patient compliance. In 1938, two scientists named Deansby and Parkes introduced the first implantable medicine delivery method, implanting a compressed pellet via a subcutaneous drug delivery route. (1)

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 administer the drug passively or actively, the two primary kinds of drug delivery implants currently on the market can be distinguished. (2)

Implantable drug delivery systems are currently being used for a variety of therapeutic applications, including the treatment of cancer, dental disease, and contraception. They have the potential to decrease the frequency of patient-driven dosing and to deliver the therapeutic command in a targeted manner. Additionally, the development of this system involves a large number of enterprises, as evidenced by the growing number of implants on the market . (3)

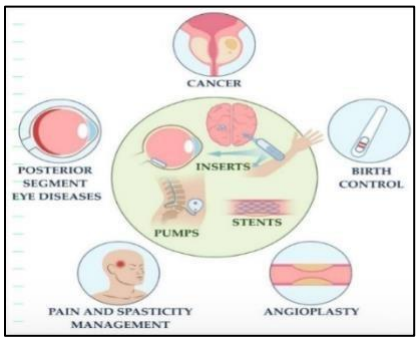

Fig no 1: Implantable drug delivery system

IDEAL PROPERTIES:

- The dosing frequency should be reduced to increase patient compliance and should release the drug during the entire treatment period.
- The implant should be easy to develop and should not be expensive.
- The implant should be easily removable by medical personnel to discontinue treatment.
- The implant should release the drug in a zero-order manner or in a controlled manner that leads to effective treatment and reduced side effects.
- The implantable device should be easy to sterile.
- The implant should be safe, stable, and effective and should have enough mechanical strength.(4)

ADVANTAGES & DISADVANTAGES OF IMPLANTABLE DRUG DELIVERY SYSTEM:

1. ADVANTAGES

- Targeted action.
- Improved Patient compliance.
- Reduced wastage of the drug.
- Minimum dose is required.
- Reduced side effects.
- Convenient therapy.
- Avoid the first-pass metabolism. (5)

DISADVANTAGES:

- Interactions between host and implant.
- Insertion of big size implants requires surgical
- Interventions which can be unpleasant.
- Possibility of inadequate release of drug.
- Predicted danger of device failure.
- Therapy cannot be simply discontinued. (6)

LIMITATIONS:

- Chances of toxicity.

- Painful.
- Need for surgery to insert the device.
- Lower efficacy.
- Practical therapy. (7)

5. CLASSIFICATION OF IMPLANTABLE DRUG DELIVERY SYSTEM

Although classifying IDDS is a challenging procedure, the devices are divided into various active and passive implantable device types. Although the passive implantable device is once more generally separated into two categories the biodegradable process and the non-biodegradable device.

1. Passive diffusion

These are straightforward, homogeneous devices that primarily hold basic medications supplied in biocompatible matrices. They rely on passive diffusion to discharge the drug dose and lack any mobile components or techniques. The two subcategories of passive devices are biodegradable and non-biodegradable. (8)

A. Non-biodegradable polymeric implant systems

The two most popular commercial types are membrane-enclosed reservoirs and matrix controlled or polymeric systems. Commonly utilized polymers include silicones, polyurethanes, poly acrylates, and hetero polymers like polyethylene vinyl acetate (PEVA). Within the matrix-controlled organization, a medication is dispersed evenly throughout the base. A sustained release from the delivery system is provided by the gradual dispersion of the imbedded medication. Although these devices last a long time, they must be replaced after the medication load is depleted to prevent complications like infection, tissue damage, and aesthetic flaws. These kinds of contraceptive methods are commonly used. One of the first and most popular reservoir implants is Norplant . (9) **B. Biodegradable**

polymeric implant systems:

They are becoming widely used since they provide benefits over non-biodegradable ones. Its use of inert polymers that break into tiny pieces and undergo further absorption and elimination inside the body makes it possible to remove the device without making an incision, which increases patient acceptance and compliance However, these systems need the polymer basis to degrade in order to release the medication, which depends on a number of variables such as changes in body temperature or pH and is consequently highly varied among individuals. There are two kinds of biodegradable gadgets. They are monolithic kinds and reservoir systems The design and drug release mechanism of reservoir systems are comparable to those of non-biodegradable systems. (10)

2. Active or dynamic polymeric implants:

These implantable control the release of medication throughout the device using definite propulsion. As such, it provides a high criterion for drug discharge. They control discharge using a variety of energy-dependent positive impulse techniques. Osmotic pressure gradients and electromechanical forces are two examples of power origins. The use of such devices to control the release of drugs from the implant has a beneficial motivation. As a result, they exhibit a greater level of control over drug discharge. The main kind of polymeric effective device is osmotic pumping. This type of device primarily consists of a semi-permeable membrane covering a reservoir of medication. The membrane should have an opening that allows the release of drugs. (11)

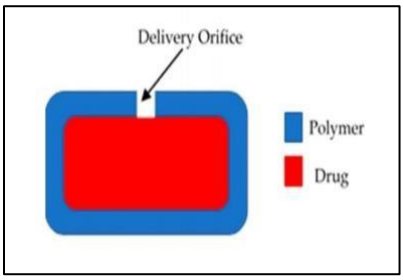

Fig no 2 : Osmotic type implant

6. MECHANISM OF DRUG RELEASE FROM IMPLANT:

Drug release from implantable systems can be categorized into four main mechanisms: matrix degradation, controlled swelling, osmotic pumping, and passive diffusion.

A. Matrix degradation

The process of integrating a drug into a biodegradable polymer matrix that breaks down in the body by enzymatic or hydrolytic activity is known as matrix degradation. After being discharged, the medication

permeates the surrounding tissues. Because of their consistent breakdown rates and biocompatibility, poly (lactic-co-glycolic acid) (PLGA) and polyanhydrides are often utilized polymers. This technique is applied to biodegradable contraceptive implants for prolonged release without surgical extraction and Gliadel wafers for chemotherapy. (12)

B. Controlled swelling

Drugs can release at a controlled rate thanks to regulated swelling systems, which use hydrophilic polymers to absorb water and expand when in contact with body fluids. Materials that retain water and are compatible with biological tissues, such as hydrogels, PEG-based systems, and cross-linked poly (vinyl alcohol), are utilized. These systems are perfect for contemporary drug delivery systems where precision and adaptability are essential since they can be made for intelligent or responsive medication delivery.

C. Osmotic pumping

Osmotic pumping is a method of drug administration that delivers drugs steadily by using osmotic pressure. A core and an osmotic agent encased in a semi-permeable membrane make up the implant. Internal pressure is produced as water from nearby tissues enters the apparatus. This makes it perfect for treating chronic illnesses since it produces a steady, dependable drug release over time. Environmental influences have no effect on osmotic pump systems, increasing their dependability. (13)

D. Passive diffusion

Drug molecules migrate from higher concentrations inside the implant to lower concentrations in nearby tissues through a process known as passive diffusion, which is essential for drug release from implanted systems. The drug can be kept in matrix or reservoir arrangements, and its release rates will follow the kinetics of Fickian diffusion. This technique is frequently utilized for long-lasting, simple diffusion-based distribution in ocular and brain implants as well as long-lasting contraceptives like norplant. (14)

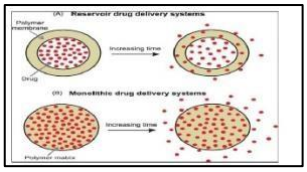

Fig no 3: Drug release from implant

METHOD OF PREPARATION OF IMPLANTS:

The next section discusses the three primary implant preparation techniques.

Extrusion method:

To create a solution, the chosen medication is first dissolved in an appropriate solvent system. The polymer is then gradually added to the solution and left to soak for ten to fifteen minutes. The resulting swelled material was uniformly combined to create a substance that resembled dough. After being moved into the extruder cylinder, the dough was extruded by the assist nozzle into long rods. After drying overnight at ambient temperature, the implants were cut to the ideal size and dried at 40°C (15)

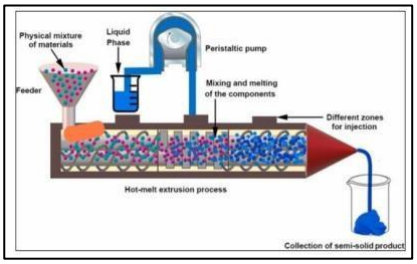

Fig no 4 : Hot melt extrusion

Compression Method:

To create the solution, the medication and polymer were dissolved. To create a consistent cake, the generated solution was freeze-dried. The cake was subjected to compression for the growth of the implant. Implants have been created using a stainless steel system designed for this purpose, consisting of a set of cylindrical punches with a diameter of 1 mm, and a Carver hydraulic press operating at a pressure of 1 metric ton.

Molding Method:
A polymer and drug solution was first made in an appropriate solvent system, then it was lyophilized and turned into a homogenous cake. hat a Teflon sheet heated to between 100 and 120 degrees Celsius on a hot plate was used to form the prepared cake into rods. (16)

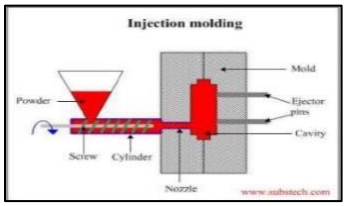

Fig no 5 : Injection molding

3. APPLICATIONS:

Ocular disease:
Use in travitreal implant to deliver medication directly into the eye. Overcoming barrier like the blood- retina barrier to treat condition like macular edema and chronic inflammation.

Contraception:
Several FDA-approved subdermal implants have been used for contraception, with modern versions generally consisting of a single, flexible rod.

Dental application:
For numerous dental applications including local prolonged administration of fluoride antibacterial and antibiotics, polymeric implants have been evaluated. (17)

Cancer:
The implantable drug delivery system has great potential to deliver have great potential to deliver chemotherapeutic drugs safely and effectively the affected side without causing any side effect.

Other application:
Insulin preparations are widely administered via biofeedback operated implantable devices in which drug is released based on pharmacological requirements of body at a specific instance. (18)

CURRENT CHALLENGES:

When developing an IDDS, a number of aspects must be taken into account that affect implant biocompatibility, including implant size, shape, material composition, and surface wettability. Charge and roughness & specific tissue reaction may be triggered by the bulk material's physical and chemical characteristics, and soluble breakdown products may trigger a local tissue reaction of their own. Tissue response is significantly impacted by implant size as well. (19)

The immunological response to biodegradable IDDS used in vivo is also impacted by the degradation products and surface alterations of the biomaterial that result from the degradation process, which can alter the tissue response to synthetic implants. Additionally, local tissue shouldn't physically or chemically alter the substance, and the implant shouldn't cause any inflammation where it is inserted. The World Health Organization states that all implanted materials must pass several stability and compatibility tests (Guidance for Industry and Food and Drug Administration, WHO, 2016). (20)

FUTURE PERSPECTIVES:

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 substances, drug release kinetics, and further enhancement of the current systems. According to the article, scientists are still hopeful that many of these technologies can be set up to be ready for extended use. Many of these medications are constantly being created using protein peptides, which are extremely unstable when taken orally. It will be feasible to distribute such drugs at steady rates over an extended period of time by employing novel forms of prolonged-release drug delivery systems. (21)

It will eliminate the need for repeated dosage. Improvements in new implantable devices are anticipated to lower drug treatment costs, boost

medication efficacy, and improve patient compliance in the years to come. (22)

CONCLUSION:

Drug administration encompasses diverse routes, such as oral delivery, transdermal application, and implantation. Implants play a crucial role in drug delivery systems, offering efficient and sustained release over an extended period. Notably, implantable drug delivery systems exhibit controlled or zero-order release, making them suitable for targeted applications like contraceptive implants. These implants, inserted into the uterus through a minor surgical procedure, gradually release drugs, providing contraception for up to a decade. The advancements in implantable drug delivery systems include features such as zero-order release, reduced toxicity, targeted drug delivery, lower drug quantities, and improved patient compliance. Additionally, these innovations can potentially lead to fewer hospitalizations, opening new avenues in healthcare. The study delves into the mechanisms of drug release from implants, highlighting four distinct methods. It lays the groundwork for future research on implantable drug delivery systems and aids in the selection of appropriate polymers, with a focus on biodegradable and non-biodegradable types. Nonbiodegradable polymers, commonly used in diffusion-controlled implantable systems, are explored in detail.

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