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Review Article

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EMERGING TRENDS IN IMPLANTABLE DRUG DELIVERY SYSTEM: A OVERVIEW

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Abstract

Implantable drug delivery systems (IDDS) provide precise and sustained medication release at targeted anatomical sites. These systems overcome traditional drug delivery limitations through sophisticated mechanisms including diffusion-controlled release, osmotic pressure gradients, and biodegradable polymer matrices. The evolution of IDDS includes passive polymeric implants, both biodegradable and non-biodegradable, as well as active systems like mechanical and osmotic pumps. Modern manufacturing techniques such as hot melt extrusion, compression modding, and emerging 3D printing technologies have enhanced the precision and scalability of IDDS production. While these systems offer numerous advantages including improved bioavailability, reduced dosing frequency, and targeted therapeutic action, challenges persist regarding surgical implementation, biocompatibility, and reversibility. Clinical applications span multiple therapeutic areas, with notable success in contraception, cancer therapy, and chronic pain management. Recent developments in smart materials and microelectronics have led to more sophisticated systems capable of responsive drug release. IDDS provide regulated medication administration at precise implantation sites, decreasing drug concentrations and side effects while enhancing patient compliance.

Keywords: *Implantable drug delivery, Biodegradable polymers, Recent Technologies.*

1. INTRODUCTION

These systems are designed to deliver medicine and fields directly into the bloodstream, barring the need for frequent needle injections. They are especially suitable for administering insulin, steroids, chemotherapeutic agents, antibiotics, pain relievers, total parenteral nutrition, and heparin. Since the device is fully subcutaneous and does not break the skin's face, the trouble of infection is minimal and it does not intrude with quotidian exertion [1]. An orally administered drug must be shielded against declination in the gastrointestinal [GI) tract and should be efficiently absorbed through the stomach or intestinal stuffing. Once absorbed into the portal gyration, it must also repel breakdown by liver enzymes. To be effective, the drug's absorption and elimination rates should maintain its attention in the blood within the remedial window. These systems eliminate the need for frequent needle injections by delivering medications and fields straight into the bloodstream. They work particularly well for giving insulin, steroids, heparin, antibiotics, chemotherapeutic drugs, painkillers, and total parenteral nutrition. The device has a low risk of infection and does not interfere with daily activities because it is completely subcutaneous and does not rupture the skin [2]. Either chemically altering the drug or creating precise wording that controls its release are two ways to accomplish controlled drug release [3]. The GI tract's relatively lengthy vehicle time of roughly 12 hours limits the effectiveness of oral controlled-release capsule forms, which can last for up to 24 hours. Parenteral routes similar to intravenous injection are used when oral administration is not feasible, particularly for proteins, peptides, and other medications that are susceptible to gastrointestinal disorders [4].

However, intravenous medications typically require frequent dosing and have a brief duration of action. Since injectable controlled-release formulations guarantee both efficacy and safety, they are thought to be more commercially feasible than alternative delivery methods. However, the stratum corneum, the outermost layer of the skin, has limited drug penetration, making topical administration difficult. In contrast, implantable drug delivery systems get around a lot of the drawbacks of topical, intravenous, and oral routes. One particular advantage of subcutaneous implants is that they can be removed if needed [5].

Implants, such as subcutaneous inserts or osmotic pumps, can be inserted into the body via injections or tiny incisions, frequently requiring only a minimal amount of anesthesia and quick procedures. They can also be administered through more involved surgeries, like those required for mechanical pumps, or intravascular techniques, like stents. It's crucial to understand that there can be some ambiguity in the terminology used to describe implantable drug delivery systems (IDDSs). For marketing purposes rather than scientific accuracy, terms like "implant" and "insert" are commonly used interchangeably. In this review, we concentrate on solid implants that are inserted into the body using at least a minimal amount of tissue penetration or incision [6].

Ideal Properties of Implantable Drug Delivery System

Improve case compliance by reducing the dosing frequence during the remedy.

- It should release the medicine in a controlled manner and to maintain a medicine position in the remedial range therefore reducing side goods.
- It should allow easy termination of the remedy by a medical guru.
- It should be and safe and stable with good mechanical strength.
- It should be fluently castrated.
- It should be provident and easy to manufacture.
- It should not present any medical complication.

2. ADVANTAGES OF IMPLANTABLE DRUG DELIVERY SYSTEM:

The advantages of implantation therapy include

2.1. Convenience:

Methods like repeated injections or continuous intravenous infusion can sustain an effective drug concentration in the blood for a longer duration.

2.2. Better drug delivery:

Medications are given out either locally or throughout the system. There are fewer metabolic disturbances that affect blood circulation and metabolism. biological barrier.

2.3. Prolonged Concentration: This system makes it possible to maintain effective drug concentrations over time. However, repeated injections or intravenous infusions require frequent hospital stays for ongoing medical monitoring.

3. DISADVANTAGES OF IMPLANTABLE DRUG DELIVERY SYSTEM:

- Invasive In certain cases, a major surgical procedure is necessary for implantation, leading to scarring at the implant point and discomfort. professed labor force is needed for device implantation.
- Termination non-biodegradable polymeric implants need surgical junking from the body after treatment completion.

4.CLASSIFICATION OF IMPLANTABLE DRUG DELIVERY SYSTEM

Implantable drug delivery system can be classified on the basis of their;

1. Mechanism of drug release 2. Location in the body

1. on the basis of their mechanism of drug release:

These implants are categorized based on how they use energy to deliver drugs. Although it can be difficult to categorize implantable drug delivery systems, they can be separated into different groups of active and passive devices [12,13]. Since osmotic pumps use the passive diffusion releasing method, the passive implantable device is once more broadly divided into two types: the non-biodegradable device and the biodegradable device [14].

Passive drug release:

Simple, homogeneous implants made of compatible materials are known as passive implants. They employ passive diffusion, which is controlled by the type of drug, concentration, polymer, and implant design, to reduce drug release [15].

a. Biodegradable:

Polymers like PCL, PLA, or PLGA are used in implants that are absorbed by the body. These inerted polymers, which include vascular implants and biodegradable stents, fragment into smaller pieces that can be absorbed and removed without a surgical incision, improving patient acceptance and adherence [16].

b. non-biodegradable:

Because of their mechanical strength and long lifespan, polymers such as PEVA, silicone, polyurethanes, and polyacrylates are used in implants. Because of their long battery life, ease of use, non-inflammatory, non-thrombogenic, non-antigenic, and non-carcinogenic qualities, as well as their capacity for local anaesthesia, pumps-including osmotic, peristaltic, and infusion pumps-are recommended [17].

Osmotic pumps:

Osmotic pumps are frequently used in various implant types. To contain medication, these devices use a selectively permeable barrier that allows aqueous fluids to enter through straightforward osmosis. Nevertheless, until the stored load is depleted, the discharge rate stays constant (18).

Infusion pumps:

The medication that was previously stored within the body is administered by infusion pumps using a fluorinated hydrocarbon as a power source. This causes variations in plasma insulin levels, which may result in diabetes-related problems [19].

4. ON THE BASIS OF THEIR LOCATION IN THE BODY:

The implants may be placed in various body parts, organs to release drug with respect to dose and time. On this basis these are classified as follows:

a. Subcutaneous implants:

The devices that are inserted beneath the skin. These are utilized for addressing different issues like pain,

contraception, opioid addiction treatment, hormone replacement therapy, diabetes management, and more.

b. Ocular Implants

These implants are tiny instruments placed in the eye to administer a medication gradually over time. Examples of drug-delivery implants include Ozurdex, used for treating diabetic macular edema and uveitis [20].

d.Intravaginal implants:

The implants that are inserted into the vagina. These implants are low-invasiveness polymeric devices specifically created for the extended and prolonged release of different types of drugs like hormones. [21]

d. Rectal implants:

Rectal implants are surgical devices used to improve bowel movements, deliver drugs, stimulate microbiomes, and treat cancer, allowing direct treatment administration without systemic side effects.

e. Intravascular implants:

Devices implanted into blood vessels for various conditions, either temporary or permanent, mimic artery mechanical and biological functions, determining long-term healing role.

5. METHODS OF PREPARATION OF IMPLANTS

The three primary techniques for implant preparation are covered below. When selecting a manufacturing process for implantable drug delivery devices, several factors must be taken into account, such as cost, efficiency, and variations in the implants' final properties.

5.1 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, after drying overnight at room temperature, the implants were cut to the ideal size and dried at room temperature, the implants were cut to the ideal size and dried at 40 °C.

5.2. Compression Method

The solution was created by dissolving the drug and polymer. To create a consistent cake, the generated solution was freeze-dried. In order for the implant to develop, the cake was compressed.

5.3. Solvent Casting

The polymer is first dissolved in an appropriate solvent, the resulting solution is then poured into a mold, and the solvent is eliminated by evaporation. The implants made using this technique frequently take the form of films or laminar implants.

5.4. Moulding Method

The drug and polymer solution was first made in an appropriate solvent system, then it was lyophilized and turned into a homogenous cake. The finished cake was then shaped into rods using a Teflon sheet that had been heated to between 100 and 120 °C on a hot plate.

5.5. 3D Printing

It is a cheap, reliable, and adaptable process that may be helpful in the future, particularly for the rapid production of standard units for research. Though its suitability improved in 2015, it is not used in mass production.

6. MECHANISM OF IMPLANTABLE DRUGD DELIVERY SYSTEM

The four primary mechanisms of drug release from implantable systems are osmotic pumping, matrix degradation, controlled swelling, and passive diffusion. Controlled swelling systems work best when drugs diffuse from swollen matrices because they limit solvent penetration into the matrix, which slows drug release.

6.1. Matrix degradation:

The process of integrating a drug into a biodegradable polymer matrix that breaks down in the body via enzymatic or hydrolytic action is known as matrix degradation. After being released, the medication permeates the surrounding tissues. Because of their consistent degradation rates and biocompatibility, poly (lactic-co-glycolic acid) (PLGA) and polyanhydrides are frequent utilized polymers. This technique is utilized in biodegradable contraceptive implants for prolonged release without surgical extraction and Gliadel wafers for chemotherapy.

6.2 Controlled swelling

Regulated Swelling Drugs can be released at a controlled rate thanks to regulated swelling systems, which use hydrophilic polymers to absorb water and expand when they come into contact with bodily fluids.

6.3 Osmotic pumping

Osmotic pumping is a method of drug delivery that delivers drugs steadily by using osmotic pressure. Osmotic pump systems are more reliable because they are not impacted by environmental conditions.

6.4. Passive diffusion

Diffusion by Passive Action Drug molecules migrate from high concentrations inside the implant to lower concentrations in nearby tissues through a process known as passive diffusion, which is essential for drug release from implantable systems.

7. CURRENT THERAPEUTIC APPLICATIONS OF IMPLANTABLE DRUG DELIVERY SYSTEM

Implantable drug delivery systems are utilized in various clinical applications, including women's health, cancer treatment, eye conditions, pain relief, infectious diseases, and central nervous system disorders. [23,24].

7.1. Women's health:

Implantable drug delivery systems significantly impact women's health, particularly in contraception. Norplant was the first approved device in 1990, with effective long anti contraceptive

7.2. Cancer treatment

The most popular approach for delivering chemotherapeutic agents is systemic, but this can have

major adverse effects like cardiomyopathy and neutropenia.

7.3. Ocular treatment

Anatomical and physiological barriers make it difficult to administer drugs to the back of the eye. Low medication retention and patient adherence are problems that must be addressed for effective management of eye conditions.

7.4. Central nervous system disorders

In addition to lowering the chance of relapse and hospitalization, these systems can guarantee patient compliance with treatment plans. Antipsychotics delivered parenterally have advantages such as decreased serum drug levels and improved bioavailability.

7.5. Contraception

The FDA recently authorized Norplant, a subdermal implant for the lon Theg-term delivery of the contraceptive drug levonorgestrel, for commercialization.

8. LIMITATIONS OF IMPLANTABLE DRUG DELIVERY SYSTEM:

Despite their advantages, implantable systems face several technical challenges. The semi-permanent nature of some systems can complicate treatment modification or discontinuation when adverse effects occur [25,26].

8.1 Procedure and Medical Risk:

Placement and removal require surgical intervention, which may lead to pain, infection, inflammation, or cosmetic disfigurement.

8.2 Device Failure and Safety

can cause "dose dumping" (rapid, unintended release), leading to toxicity, or insufficient delivery, resulting in therapeutic failure.

8.3 Removal Requirements:

Non-biodegradable implants must be surgically extracted after the drug is depleted to avoid foreign body reactions.

8.4 Drug Compatibility Limitations:

Limited to drugs that is potent, stable for long periods, and capable of diffusing through polymers.

9. FUTURE PROSPECTS AND STRATAGIES

9.1. Active and Smart IDDS:

To build closed-loop systems, future systems will combine sensors and microchips. These gadgets have the ability to automatically release the necessary dosage while also monitoring the patient's physiological condition (such as blood glucose or biomarkers).

9.2. Miniaturization (MEMS and NEMS):

Devices that are even smaller and less intrusive are made possible by Micro-Electromechanical Systems (MEMS). Increasing "volume efficiency "maximizing the size of the drug reservoir

while reducing the overall device foot print is the main goal of future research.

9.3. 3D and 4D printing

Complex geometries for patient-specific implants are made possible by advanced manufacturing. With the addition of "time," which 4D printing introduces, implants can alter their shape or release profiles in reaction to internal body stimuli.

9.4. Smart & Active Delivery Systems

These devices utilize sensors to monitor patient physiology (e.g., glucose levels) and provide feedback-driven or on-demand medication release.

9.5. Bio responsive and Biodegradable Materials:

Implants designed to degrade safely within the body, reducing the need for surgical removal [27].

10. CONCLUSION

Implantable drug delivery system is an innovative approach towards rate-controlled drug delivery at required therapeutic concentrations. This approach has distinct superiority over the traditional administration ways. These systems have evolved from simple matrix devices to sophisticated smart implants capable of responding to physiological signals and delivering medications with precise temporal and spatial control. The combination of advanced polymeric materials, micro/nanotechnology, and smart systems has expanded the possibilities for controlled release mechanisms. Biodegradable systems have eliminated the need for implant removal, while stimuli-responsive materials have enabled dynamic drug delivery in response to physiological needs.

11. AUTHOR CONTRIBUTIONS

All authors are contributed equally.

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