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Review Article
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DESIGN AND ADVANCEMENTS OF IMPLANTABLE DRUG DELIVERY SYSTEM

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Abstract

Conventional drug delivery systems often provide limited control over drug release profiles, resulting in fluctuating plasma concentrations, reduced therapeutic efficacy, and increased adverse effects. To overcome these limitations, Novel Drug Delivery Systems (NDDS) have been developed, among which Implantable Drug Delivery Systems (IDDS) represent a promising approach for controlled, targeted, and sustained drug administration. The reviewed studies highlight the design, materials, mechanisms, and applications of implantable systems, including polymeric implants and advanced magnetically actuated soft capsule robots. These systems enable zero-order or programmable drug release directly at the site of action, minimizing systemic exposure and improving patient compliance. Shape-programmable and magnetically controlled capsules demonstrate the potential for gastric retention, safe tissue interaction, and controlled drug release, followed by safe elimination from the body. IDDS are particularly beneficial for drugs with poor oral bioavailability, enzymatic degradation, or narrow therapeutic windows, such as insulin, steroids, and anticancer agents. Applications span multiple therapeutic areas including oncology, ophthalmology, dentistry, and contraception. Despite their advantages-such as reduced dosing frequency, improved efficacy, and targeted delivery-high cost, complex design, and the need for extensive clinical validation remain significant challenges. Continued research and technological refinement are essential to enhance safety, affordability, and large-scale clinical adoption of implantable drug delivery systems.

KEYWORDS: *Implantable drug delivery system, Implantable drug delivery devices, Implantable polymeric drug delivery system, Implantable pumps, Implants.*

1. INTRODUCTION

The concept of implantable drug delivery systems (IDDSs) in modern medicine may be traced to Deansby and Parkes who, in 1938, subcutaneously (SC) implanted compressed pellet of crystalline estrone to study their effect up on castrated male chickens. In the year 1861, Lafarge introduced the concept of implantable system for sustained release drug administration. Implantable drug delivery systems are placed under the skin and designed to release medicines into the bloodstream without the reprise insertion of needles. Oral route is the most accepted route for delivery of medicines, but it possesses disadvantages due to declination of the medicines by the acidic/alkaline conditions of stomach and intestine. Implantable drug delivery systems have potential superiority in regional administration with better pharmacologic outcomes at minimum doses [1].

In recent years, rapid scientific and technological developments have led to a significant increase in research output across various disciplines. As a result, it has become increasingly challenging for researchers and practitioners to stay updated with the latest findings. Review articles serve as an essential tool in organizing scattered information, evaluating the reliability of available data, and presenting structured insights. They also support evidence-based decision-making and contribute to academic learning and innovation [2].

1. Ideal Requirements

A sterile medication delivery system for a subcutaneous implantation that includes a rod- shaped inner matrix with an elongated body and two ends is capable delivering the medications over time at a predetermined rate. Implantable medicine delivery system (IDDS) was initiated by Lafarge in 1861, in bullet form for long term nonstop administration of crystalline hormone, but the release profile, couldn't be controlled, with duration of ctio' and wasn't constant also danckwert et al in 1930, by introduced SR implantable delivery system to be administered by subcutaneous route [3].

- Improve patient compliance by reducing the dosing frequency during the therapy.

- It should be and safe and stable with good mechanical strength.
  - It should be economical and easy to manufacture.
  - It should be chemically inert, non-carcinogenic and hypoallergenic in nature.

Benefits

- Provides controlled and sustained drug release.
- Reduces dosing frequency.
- Improves patient compliance.
- Maintains constant plasma drug concentration.
- Minimizes peak and trough effects.

CLASSIFICATION OF INPLANTABLE POLYMERIC DRUG DELIVERY SYSTEM:

Polymers are the key elements in implantable systems as they provide extended and optimised drug release. They act as rate-limiting membrane in implant system and the choice of which must be done in keeping view of host biocompatibility and ease of sterilization [4].

PASSIVE POLYMERIC IMPLANTS

Passive polymeric implants are simple devices that do not contain any moving parts or energy source. Drug release occurs mainly by diffusion, swelling, or polymer degradation. These systems are widely used due to their simplicity, reliability, and safety. Passive polymeric implants are further classified into non-biodegradable and biodegradable implant systems.

NON-BIODEGRADABLE POLYMERIC IMPLANT SYSTEMS

The most common commercial forms are matrix-controlled or polymeric system and membrane enclosed reservoir. The dynamics of expulsion and release rate of medicament is inconstant and relies on amount of substance in the base [5].

BIODEGRADABLE POLYMERIC IMPLANT SYSTEMS

These systems offer advantages over non bio-degradable ones and hence are more popular. Polymeric substances such as polycaprolactone (PCL), polylactic acid (PLA), or polylacetocoglycolic acid (PLGA) are typically used for formulation. Their formulation is furthermore intricate than that of nonbiodegradable ones.

ACTIVE OR DYNAMIC POLYMERIC IMPLANTS

Active polymeric implants utilize internal or external energy sources to precisely regulate drug release. These systems contain mechanical, electrical, magnetic, or osmotic control mechanisms that allow programmable and adjustable drug delivery. Common examples include osmotic pumps, infusion pumps, peristaltic pumps, and electromechanical micro-pumps [6].

Implantable Pumps

The presence of sophisticated microsystems have made easy in designing pumps as little adequate that it can be implanted hypodermally to deliver drugs. The pumps should possess desirable properties like noninflammatory, non-thrombogenic, nonantigenic, noncarcinogenic, convenience, long reserve and battery life, easily organisable, and can be inserted using local anaesthesia. Presently five groups of implant pumps are present.

Infusion Pumps

Infusion pumps distribute the stored medicament inside the body with the help of a fluorinated hydrocarbon as energy source. The pump contains disc-like container constructed by lightweight bio composite titanium that comprises of foldaway that divides the container interiorly in two isolated compartments [7].

Osmotic Pumps

Osmotic pumps are extensively prevalent of all implant types. These devices involve medication confined in a selectively permeable membrane that permits an inward movement of aqueous fluids in the device by simple osmosis. The pace of discharge remains persistent or zero order till stored load is been exhausted [8].

Peristaltic Pumps

Peristaltic pumps work by external source of power mainly by batteries and consist of cylindrically rotating apparatus. They made of a rubber membrane of silicone and their duration of use is dependent on the battery as energy source used.

MECHANISM OF DRUG DISCHARGE FROM IMPLANTABLE DEVICES

Drug discharge from implantable devices occurs through diffusion, polymer degradation, swelling, and osmosis. In diffusion-controlled systems, the drug moves slowly from the polymer matrix or reservoir into the surrounding tissue. In degradation-controlled systems, the polymer gradually erodes, leading to controlled release of the drug. Swelling-controlled systems release the drug when the polymer absorbs body fluids and expands.

METHODS OF PREPARATION OF IMPLANTS

The preparation of implantable drug delivery systems involves techniques that ensure uniform drug distribution, controlled release, and suitable mechanical strength. Common methods include hot melt extrusion, compaction, moulding, and 3D printing. In hot melt extrusion, the drug and polymer are melted and extruded to form rod-shaped implants [9].

Extrusion Method

The extrusion method is a commonly used technique for the preparation of implantable drug delivery systems, especially rod-shaped implants. In this method, the drug is mixed uniformly with a thermoplastic polymer, and the mixture is heated until it becomes soft and plastic.

Compression Method

The compression method is used for the preparation of implantable drug delivery systems by directly compressing a uniform mixture of drug and polymer into solid implants using a tablet compression or hydraulic press machine.

Moulding Method

The moulding method is used for the preparation of implantable drug delivery systems by melting the polymer and mixing it uniformly with the drug, followed by pouring the molten mass into suitable moulds. After cooling and solidification, the implants are removed from the mould and cut into the required sizes.

3D Printing

3D printing is a modern technique used in the preparation of implantable drug delivery systems, which allows precise fabrication of implants with customized shapes and sizes [10].

EVALUATION PARAMETERS OF IMPLANTS

After the preparation by any suitable method, an implant is subjected to the evaluation that is Shape and size, Uniformity of thickness, Weight variation, and stability studies also [11].

Size and shape

Implants are evaluated under light and the size of the implant was determined with the help of Vernier Caliper.

Uniformity of thickness

Implants are separately subjected to determine the thickness with the help of Vernier Calipers, which gives a precise reading of thickness and tells about the difference in the thickness of every implant. Minimum three samples should be evaluated to get the mean value.

Uniformity of weight

This test is also known as the weight variation test. It is performed to determine the uniformity of the weight of every implant. 7.4 Swelling Index:

A specimen is placed in swelling solution of phosphate buffer pH 7 for an hour and the weight is estimated. The remaining solution is cautiously removed by gently cleaning with dry sheet. The magnitude of swelling for every unit at any instant is determined by given

$$Swelling\ Index = \frac{W2-W1}{W1} X\,100$$

formula:

Where, W2 and W1 represent the specimen's mass at specified instant and in dried form, correspondingly.

7.5 Stability testing:

This test is done to detect disparities in standard of drug accompanied by time and storage characteristics like temperature, moisture, light, shelf life, etc.

ADVANTAGES [12].

- Provides controlled and sustained drug release over a long period.
- Improves patient compliance by reducing dosing frequency.
- Maintains constant plasma drug concentration, reducing peaks and troughs.
- Enables targeted and localized drug delivery, minimizing systemic side effects.

DISADVANTAGES [13]

- Requires surgical procedure for implantation, which may cause pain and risk of infection.
- Removal of non-biodegradable implants requires additional surgery.
- Dose adjustment is difficult once the implant is placed.
- High cost of devices and surgical procedures.

LIMITATIONS [14]

- Painful.
- Need for surgery to insert the device.
- Increased effectiveness and efficiency
- The system must be implanted via microsurgery.

THERAPEUTIC APPLICATIONS [15].

Implantable drug delivery systems are widely used to provide controlled, sustained, and targeted drug delivery for various medical conditions. Their major therapeutic applications include:

Contraception

Implants are commonly used for long-term contraception by releasing hormones such as levonorgestrel and etonogestrel in a controlled manner.

Cancer Therapy

Implantable systems are used for localized and sustained delivery of anticancer drugs, minimizing systemic toxicity and improving therapeutic outcomes. Examples include implants delivering goserelin, leuprolide acetate, and paclitaxel for prostate and other cancers.

Ocular Drug Delivery

In ophthalmology, implants are used to deliver drugs directly to the eye for prolonged periods. These systems are effective in the treatment of glaucoma, uveitis, and cytomegalovirus (CMV) retinitis. Examples include Ocusert, Vitrasert, and Retisert.

Diabetes Management

Implantable pumps and insulin delivery devices provide continuous and controlled insulin release, helping maintain normal blood glucose levels and reducing fluctuations associated with multiple daily injections.

FUTURE ASPECTS

Smart & Programmable Implants

Smart and programmable implants are advanced implantable drug delivery systems designed to release drugs in a controlled and adjustable manner. These implants contain microchips, sensors, and programmable pumps that allow precise control over drug dosage and timing.

Nanotechnology Integration

Nanotechnology integration in implantable drug delivery systems involves the use of nanoparticles, nanofibers, and nano-coatings to improve targeted and controlled drug release. These nano-materials enhance drug stability, solubility, and bioavailability. Biodegradable Implant. Biodegradable implants are implantable drug delivery systems made from polymers that gradually break down inside the body after releasing the drug. They do not require surgical removal, which reduces patient discomfort and medical costs.

CONCLUSION

Implantable drug delivery system is an innovative approach towards rate-controlled drug delivery at required therapeutic concentrations. The drug can be administered by different routes like oral drug delivery, transdermal, and implant etc. the maturity of drugs are responsible for all the drug delivery systems One of the innovative components that is sometimes overlooked in the advancement of new medicine delivery through formulation, research, and development in many pharmaceuticals is implantable drug delivery. The market for polymeric implantable drug delivery devices is one that is growing. These devices have more benefits than drawbacks, including the capacity to improve patient compliance, stabilize medications inside, and be removed in the event of an unpleasant reaction. The therapeutic uses of implanted drug delivery systems are discussed. Implantable drug delivery systems represent a promising and innovative approach to controlled and sustained drug administration.

AUTHOR CONTRIBUTIONS

All authors are contributed equally.

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The authors have no conflicts of interest to declare.

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