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Review Article

A Facet Upshot on Parenteral Ocular Implants: in Middle of Updated Perspective

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ABSTRACT

Ocular implants are the devices which released the drug in the body steadily for long time. The subcutaneous implantation of drug pellet is known to be the first medical approach aiming to achieve prolonged and continuous administration of drug. The subcutaneous implantation of drug pellet is known to be the first medical approach aiming to achieve prolonged and continuous administration of drug. This first generation of implantable therapeutics system was produced by simple compression of drug crystal either alone or in combination with small quantity of pharmaceutical adjuvants into tiny cylindrical shaped pellets that can be implanted readily into a subcutaneous tissue. Over the year, a no. of approaches has been developed to achieve the controlled administration of biologically active agents via implantation or insertion in the tissue. The matrix systems are more popular due to simplicity of fabrication and commercialization. The three major type of matrix diffusion control device generally fabricated are insoluble plastics, fatty, and hydrophilic matrices. Insoluble plastic matrices are designed as implants. The drug present with in pore and channel of the polymeric matrix would be released very quickly *In vivo*. Most ocular treatment calls for the topical administration of drug to the tissue around the ocular cavity. Several types of ophthalmic delivery systems are commercially available. Most prescribed dosage form is the eye drop solutions, which are easy to use even though they suffer from inherent disadvantages of immediate dilution and drug loss through the lachrymal drainage. Hence, bioavailability following intraocular administration of drops may hardly be 1.2 % to the aqueous humor and therefore demands suitable intra ocular delivery system to increase bioavailability to a substantial level. However, with the available polymer a reasonably good implant device with minimal tissue interaction, nontoxic, non carcinogenic, have been developed commercially.

Keywords: Polymer matrix, Ocular implant, Subcutaneous tissue

1. INTRODUCTION

Lafarge pioneered the concept of implantable therapeutics system for long term & continuous drug administration in 1861 with the development of subcutaneously implantable drug pellet. Solid pellet containing crystalline hormone were prepared to mimic

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the steady and continuous secretion of hormones from the gland. [1]

Historical development

Potential biomedical applications of silicon elastomer were studied by fabricating a very small capsule shaped implant containing thyroid hormone powder which released the hormone steadily for long time when tested in-vitro. Similar result was obtained with isoproterenol, digitoxin EDTA etc. When encapsulated in silicon [2] capsules. Power (1965) reported the use of silicon containing pyrimethamine to protect chicks from malaria. Use of silicon implants in veterinary medicine for contraception received much attention with the finding by DZINK & COOK. The slow release progesterone over one year period from silicon capsules were lately extended to the control released device for long term contraceptive activity.

Characterstics of ocular parenteral implants:

- Approach zero order kinetics
- Bio stable
- Biocompatible with tissue-implant
- Nontoxic
- Non carcinogenic
- Retrievable
- Release at a constant rate.
- Non immunogenic
- Non mutagenic
- Good mechanical strength
- Free from drug leakage
- Easily sterilizable
- Easy and inexpensive to manufacture

Development of implantable therapeutic system

The subcutaneous implantation of drug pellet is known to be the first medical approach aiming to achieve prolonged and continuous administration of drug. This first generation of implantable therapeutics system was produced by simple compression of drug crystal either alone or in combination with small quantity of pharmaceutical adjuvants into tiny cylindrical shaped pellets that can be implanted readily into a subcutaneous tissue. Over the year, a no. of approaches has been developed to achieve the controlled administration of biologically active agents via implantation or insertion in the tissue. The approaches are outlined as follows:

Type of device based on route of administration

- Subcutaneous implant
- Intra ocular implant

Subcutaneous implants:

Subcutaneous tissue is a basically a sheet of areolar tissue lying directly underneath the skin (dermal tissue).It is rich in fat but poor in nerve network and hemo perfusion therefore, subcutaneous tissue is an ideal location for implantation and prolonged drug administration because of it's ready access, slow drug absorption and low reactivity to the insertion of foreign materials. The methods used to develop reservoir devices include:

(a) Press coating or air suspension coating technique to coat the drug particle reservoir using water insoluble polymeric materials,

(b) Prepared by filling drug reservoir in silicone tubing of a suitable wall thickness and then sealing both the ends securely, and

(c) Preparing films containing drug and polymer by placing the solution on teflon coated surface and allowing the solvent to evaporate to form film.

The matrix systems are more popular due to simplicity of fabrication and commercialization. The three major type of matrix diffusion control device generally fabricated are insoluble plastics, fatty, and hydrophilic matrices. Insoluble plastic matrices are designed as implants. The drug present with in pore and channel of the polymeric matrix would be released very quickly *In vivo*.

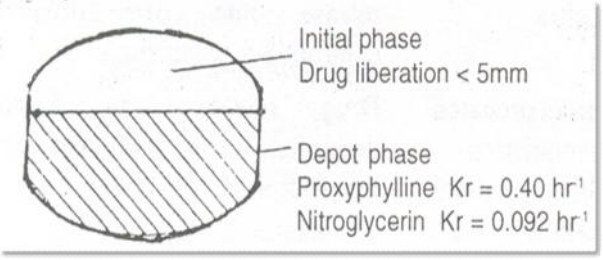


Fig 1: Structure of depot phase

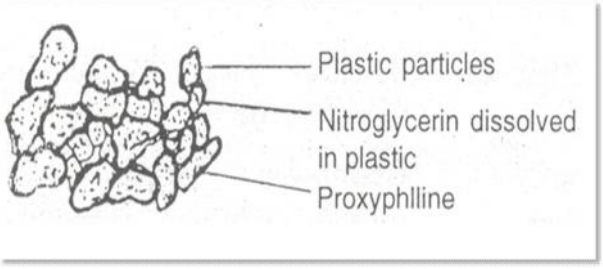


Fig 2: Drug release from depot

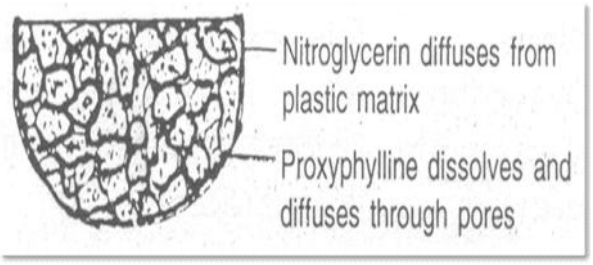


Fig 3: Diagrammatic structure of matrix type controlled release depot formulation

Fatty matrices generally consist of waxes and are prepared by dispersing the drug and excipients in molten wax. This mixture is then congealed, granulated and compressed in to the cores coated.

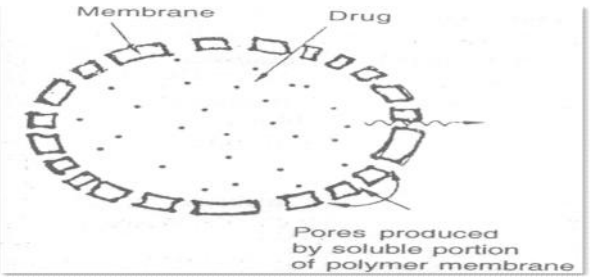


Fig 4: Diagrammatic representation of diffusion control drug release from a coated system

Intra ocular implants

Most ocular treatment calls for the topical administration of drug to the tissue around the ocular cavity. Several types of ophthalmic delivery systems are commercially available. Most prescribed dosage form is the eye drop solutions, which are easy to use even though they suffer from inherent disadvantages of immediate dilution and drug loss through the lachrymal drainage. Hence, bioavailability following intraocular administration of drops may hardly be 1.2 % to the aqueous humor and therefore demands suitable intra ocular delivery system to increase bioavailability to a substantial level.

Biopharmaceutics of ocular drug administration

Topical administration of opthalmic active drug to the eye is the most prescribed route of administration for the treatment of various eye disorders. Unfortunately drug administered to the eye as conventional dosage forms like eye drops show very low bioavailability e.g. Pilocarpine administered in glaucoma as eye drops is available only 2-3% to the aqueous humor. Many factors affect the intraocular bioavailability of topically applied active drugs. [4]

(1) Continual in flow and out flow of lacrimal fluid,

(2) Efficient naso lacrimal drainage,

(3) Interaction of drug with the protein of the lachrymal fluid,

(4) Productive and nonproductive absorption of drug to various ocular tissues notably cornea and conjunctiva.

Taking pilocarpine as example, following instillation of a pilocarpine eye drop dose (50 to 70 microlitre) into the precorneal area of eye , greater part of drug solution (80%of the drug dose) is drained away within 5 minutes by the naso lachrymal drainage system until the solution volume return to the normal resident tear volume of 7.5 microlitre. The remaining drug gets diluted with the tears and the concentration declines and so the uptake by the corneal and conjucntival tissue. This result in to biphasic decline of the drug concentration in the precorneal area; initial rapid decline due to naso lacrimal drainage followed by slow decline due to corneal/conjucntival absorption. The precorneal disposition of pilocarpine eye drop solution by various routes was observed to follow a first order kinetic pattern. Naso lacrimal drainage being the major

route of disposition the volume of the eye drop instilled into the precorneal area of the eye influence greatly the intra ocular bioavailability.

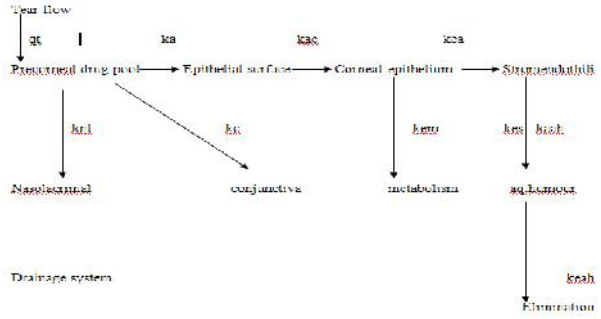
So far, as the trans corneal permeation of drug is concerned the prevailing theories include, all or in part, the following hypothesis

(1) Existence of a permeation barrier in the lipophillic corneal epithelium

(2) Rapid uptake and transport of pilocarpine by the cornea

(3) Release of pilocarpine from the cornea to the anterior chamber is controlled

(4) Existence of pilocarpine depot somewhere in the cornea



Where,
Qt = normal tear fluid production rate (0.66) micro liter/minute)
Knl = composite first order elimination rate constant of naso lacrimal drainage
Kc = apparent rate constant for conjucntival uptake of drug
Ka = apparent rate constant for epithelial uptake of drug
Kae = apparent absorption rate constant into epithelium
Kas = apparent absorption rate constant into stroma endothelium
Kes = apparent elimination rate constant into stroma endothelium
Kaah = apparent absorption rate constant into aqueous humors
Keah = apparent elimination rate constant into aqueous humors
Kem = apparent metabolism rate constant into epithelium

Controlled release ocular device

The control release ocular device is a flexible; oval insert which consists of a medicated core reservoir prepared out of a hydro gel type of material. Based on the mechanism of release and types of construction, the device may be essentially of 3 types:

(a) Diffusion controlled ocular device

This consists of medicated core prepared out of a hydro gel polymer like alginates, sandwiched between two sheets of transparent, lipophillic, rate controlling polymer like ethylene /vinyl acetate copolymer membrane designed to the required geometry suitable for insertion in to the cul-de-sac.[5]

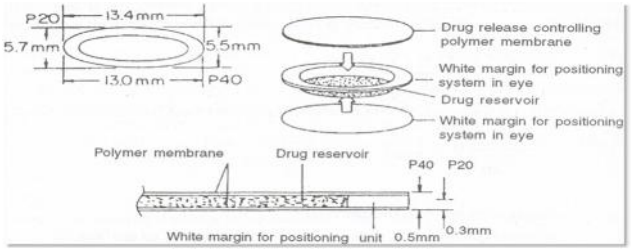


Fig 5: Schematic diagram of an ocusert controlled release drug delivery device

When the device is placed in a cul-de-sac the drug molecule penetrate through the rate controlling membranes at zero order rate process as defined

Dq/dt=dpkm (cr-ct)/dm.

A typical *In vivo* release rate profile of pilocarpine from the ocusert pilo-20 is given in Figure. During the first hour the system releases pilocarpine at a rate, which is three times higher than the programmed rate i.e. 20 microgram per hour. The programme release rate is achieved in approximately six hours and is maintained for seven days. The system administers a total of less than 70% of the pilocarpine loading dose to the eye at the end of seven day medication

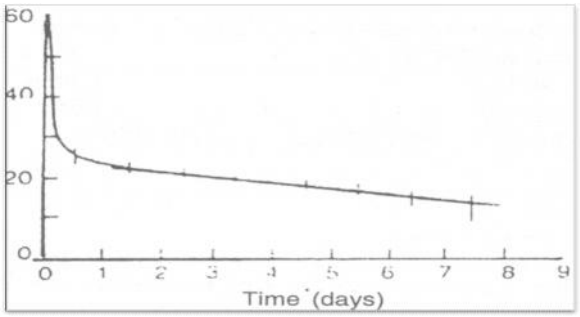


Fig 6: *In-vitro* release pattern of pilocarpine from ocusert pilo-20 system

Ocular inserts of this type have been reported for various other ophthalmic therapeutic agents like carbonic anhydrase inhibitors, epinephrine, anesthetics, antibiotics, anti inflammatory steroids etc.

(b) Hydrophillic matrix type occular device (contact lens type)

This type of device is a matrix prepared out of hydro gel polymers which are generally used to fabricate contact lenses. Even contact lenses can be used to deliver drug at a predominant rate by the selection of a suitable polymer composition. This type of device substantially prolongs the drug /eye contact time and thus increases bioavailability. Some of the polymers that could be used for preparing the device are 2-hydroxyethylmethacrylate, vinyl pyrrolidone acrylic co polymer etc. When contact lenses are used as device, the lenses are presoaked in the drug solution for sufficient time for equibrilliation and are then inserted just like a contact lenses.

Fig 7: Contact lens

[Presoaked hydrophilic contact lenses or ocular drug delivery

Hillman, 1975; Rame R& Gasset 1974]

(c) Erodible device

This type of device is fabricated from bio- erodible or bio- degradable polymer of hydro gel or non hydro gel type. The mechanism of drug release in this system is dependent on rate of erosion or rate of degradation. Several erodible type of ocuserts have been prepared using polymer like carboxymethyl cellulose, poly vinyl alcohol, collagen etc.[6] Containing drug like pilocarpine, gentamicin in etc in the form of disc and wafers. Some of the product are also marketed recently as,

(i) Lacrisert, a cylindrical shaped device made up of hydroxyl propyl methyl cellulose for the treatment of eye in conjunction with artificial teardrops

(ii) Soluble ocular drug insert, (sodi) a small oval shaped wafer containing anti glaucoma drug fabricated out of acryl amide, vinyl pyrridone and ethyl acylate (abe) system. Generally it replaces 4-5 drops instillation

(iii) Ocular therapeutic system or minidisk, is a miniature contact lens with a diameter of 4-5 mm made of silicone based pre polymer

(iv) Corneal collagen shield, prepared by molding collagen mixed with the drug into a contact lens conFiguration is dehydrated and sterilized by gamma radiation and packed. Drugs like antibiotics, steroids have been reported (Bloomfield, 1978)

(d) Implantable silicone devices

A silicone rubber device was developed for the local delivery of an anti-neoplastic drug to the intraocular site and has been tested in animal model. The system was composed of two sheets of silicone rubber glued to the edge with silicone adhesive to form a balloon like sac through which a silicone tubing (0.3 mm dia.) is inserted. The device was tested by implantation into the emperical tissue of rabbit. Such silicone device has significant potential for local controlled delivery of antibacterial, anticancer and antiviral drug to the anterior chamber of eye.

(e) Implantable infusion devices

Patient suffering from dry-eye require frequent instillation of artificial tear preparations. Continuous infusion device containing these solutions was developed by Refojo et. al. (1978) and has been tested successfully in mongrel dog's model. In this device the canalicular system is intubsted with fenestrated silastic tubing, which is subcutaneously tunneled and then attached to miniaturized and computerized pumping device which is capable of pumping a predetermined volume of a solution continuously.

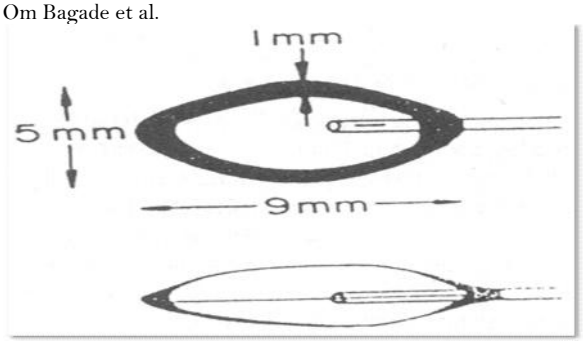


Fig 8: Schematic diagram of an expandable silicone implant type ocular insert

Although controlled release device of another such type is infusaid, where in the energy for pumping is met by an expanding fluid like a fluro carbon in gas-liquid equilibrium at body temperature. The device was tested by implantation in the lumber region of a rabbit whichdelivered drug continuously for six weeks to the rabbit eye.

(f) Future direction

An unusually high number of aggravated ocular condition due to over treatment by repeated instillation have been seen as a result of mechanical injury and sensitivity reactions.[7] This is the case like anti-viral therapy, which demands instillation every hour. Besides being cytotoxic these agent have both mutagenic and oncogenic potential therefore, such treatment modalities should be intervened with controlled release device to minimize the toxic potential and could be more useful in the management of many ophthalmic conditions. They are not very much popular because such device has to be put in place and taken out from under the eyelid periodically.

2. CASE STUDIES

A. *In vitro* and *In vivo* evaluation of Gellan based ocular inserts of Phenylephrine [17]

Ocular inserts of phenylephrine (1.5 mg/insert) were prepared by solvent casting Method using mercury as the substrate. Gellan gum based ocular inserts of phenylephrine were prepared by solvent casting method, and Evaluated for uniformity of thickness, weight, drug content, surface ph, *in vitro* release and *In vivo* mydriatic response in rabbits. The inserts were found to release drug following Higuchi square root release kinetics. *In vivo* comparison of the inserts with three times dosing of the conventional eye drop formulation revealed a comparable intensity and extent of mydriatic response produced by inserts. The present investigation was undertaken with the objective of preparing a Sustained release ocular delivery system of phenylephrine using gellan gum as the Biopolymer. *In vitro* release studies revealed that the sustained release of phenylephrine followed the higuchi square root release pattern. *In vivo* comparison of the optimized batch of inserts with the three time dosage regimen of the conventional eye drop formulation revealed a comparable mydriatic response of the ocular insert. It can be concluded from the study that gellan gum based ocular inserts of phenylephrine can be effectively used for sustained topical ocular delivery. Reverse phase HPLC method was used for analysis of phenylephrine. The study indicates potential usefulness of the gellan gum based ocular insert for controlled ocular delivery of phenylephrine.

B. Ocular inserts for controlled delivery of pefloxacin mesylate:

Preparation and evaluation [18]

Pefloxacin mesylate is a flouroquinolone antibacterial drug. Ocular inserts were prepared by the film casting technique in teflon coated. All formulations carried 0.72 mg pefloxacin mesylate, 2.69 mg polyvinyl pyrrolidone (pvp) k-30, plasticizers, propylene glycol (10% m/m) and dibutyl phthalate (15%, m/m). The reservoir type of the ocular insert consisted of three layers of films, the inner Reservoir film containing the drug and two-rate controlling films surrounding the reservoir. The release rates were found to decrease by increasing the concentration Of eudragit rs 100 and decreasing the concentration of eudragit rs. 100 in rate-controlling membranes.

The UV absorption maximum for the pure drug and the medicated formulation was found to be at 273 nm. Reservoir type ocular insert consisting of a polyvinyl pyrrolidone reservoir with Pefloxacin mesylate and rate-controlling membranes of eudragit rs 100 and eudragit Rl 100 mixtures demonstrated sustained release of the drug in the eye for 5 days. The *In vivo* results suggest that the lower hydrophilicity of rate-controlling membrane plays an important role in retarding the release of the drug from reservoir ocular inserts. The drug remained intact and stable in the ocular insert on storage, with no apparent chemical interaction between the drug and the excipients.

C. *In vitro* and *In vivo* evaluation of ocular inserts of ofloxacin [19]

Ofloxacin is a broad-spectrum antibacterial agent with activities against gram-negative bacteria (E.coli, Klebsiela pneumonias, Serratia species, Proteus species, Pseudomonas aerogenosa and H. influenzae) and, Gram-positive bacteria (Staphylococcus species, Streptococcus enterococci). It is used in the treatment of kerato-conjunctivitis, blepharo-conjunctivitis, corneal ulcer, preoperative prophylaxis and other ocular infections. It has a plasma half-life of 5.7±1 hours (1, 2). The weight and thickness of the inserts were in the range of 57.3-126.0 mg and 55.6-99.3 microns. Moisture vapor transmission through films followed zero-order kinetics and decreased with increase in film thickness. The drug content varied from 99.53-99.86%. The method of exposure to uv radiation was used for sterilization of ocular inserts. Ocular insert f3 with rate-controlling membrane of eudragit rs100, when inserted into the eye of rabbit showed controlled release up to 24 hours. The ocular inserts of ofloxacin were prepared by solvent casting technique employing mercury as substrate and characterized on the basis of interaction studies, physico-chemical characteristics, microbiological studies, *in vitro* and *In vivo* release studies.

Ocular inserts of ofloxacin prepared in pva matrix and cast with rate-controlling membranes prepared from ethyl cellulose, eudragit rs100 and eudragit rs 100 in combination with pvp ocular inserter of ofloxacin 145 were smooth, flexible and transparent.

Approaches to the development of parenteral implantable therapeutic system

Over the years a number of approaches have been developed to achieve the controlled administration of biologically active agents. These approaches are outlined as follows:

A. Diffusion controlled system

1**. Membrane permeation –controlled system containing**

i. Non porus membranes
ii. Microporus membrane
iii. Semipermeable membranes

2. Matrix diffusion controlled system containing

i. Lipophilic polymer
ii. Hydrophillic swellable polymers
iii. Porous polymer

3. Microreserviour dissolution controlled system containing

i. Hydrophilic reservoir/lipophillic matrix
ii. Lipophillic matrix / hydrophilic matrix

B. Activation controlled systems

i. Osmotic pressure activated
ii. Vapor pressure activated
iii. Magnetically activated
iv. Ultra sound activated
v. Hydrolysis activated

A. Diffusion controlled system

1. Membrane permeation –controlled system

In this, the drug reservoir is encapsulated in a compartment totally enclosed by a rate controlling polymeric membrane.[8] The drug reservoir can be either drug solid particles or dispersions of drug solid particles in a liquid or a solid type dispersing medium. The polymeric membrane can be fabricated from a homogenous or heterogeneous nonporous polymeric material or a micro porous membrane and can be accomplished by molding capsulation, microecapsulation, or other techniques.

2. Matrix diffusion controlled system

In this, the drug reservoir is formed by homogeneous dispersion of drug solid particle throughout a lipophillic or hydrophilic polymer matrix

The dispersion of drug solid particle in the polymer matrix can be accomplished by bending drug solid with a viscous liquid polymer or a semi solid polymer at room temperature, followed by cross linking of polymer chains. This drug polymer dispersion is then extruded to form drug delivery device of various shapes and sizes.

The rate of drug release from this matrix diffusion controlled delivery device is not constant.

3. **Microreservior dissolution controlled system**

In this, the drug reservoir which is suspension of drug crystals in an aqueous solution of a water miscible polymer forms a homogeneous dispersion of millions of discrete, unleacheable, microscopic drug reservoirs in a polymer matrix drug in liquid compartment, polymer coating membrane, and elution solution, respectively.

Release of drug from the micro reservoir-type drug delivery system can follow either an interfacial partition or a matrix diffusion control process.

B. Activation controlled system

Several implantable pumps for the sustained release of drug have been developed utilizing activated system to mechanically push the medication into body at a controlled rate. Among many such systems the following category of product has received much attention and some of them have also undergone commercialization.

1. Osmotic pressure driven device

Osmosis is defined as the passage of solvent into a solution through a semipermiable membrane.

Osmotic pressure can be measured with the help of osmometer one side of which contains a pure solvent, while the other contains a solution. A semipermiable membrane separates the two sides.

Osmotic pressure is defined as the excess pressure, or pressure greater than that above the pure solvent, which must be applied to the solution to prevent the passage of the solvent through a perfect semipermiable membrane.

A. Classification of implantable osmotic pumps [11]

1. **The Rose Nelson pump**:- The two Australian physiologists reported the first osmotic pump . The pump consisted of three chambers a drug chamber with an orifice, a salt chamber with elastic diaphragm containing excess solid salt and water chamber.
2. **Higuchi – Leeper pump**: - The first simplified version of the rose nelson pump. It contains a rigid housing and semipermeable membrane, which is supported on a perforated frame. Rigid hosing is divided into two chambers by a movable separator. The benefit is that it does not have a water chamber, and a device is activated by water imbedded from the surrounding environment. This means the pump can be prepared and loaded with drug and then stored for weeks or month prior to use.

3. **Higuchi – Theeuwes pump**: - In early 1970s, Higuchi and Theeuwes developed a simpler form of the rose nelson pump. Semipermeable wall itself acted as a rigid outer casing of the pump. The device is loaded with drug prior to use. When the device is placed in aqueous environment, release of the drug follows a time course set by the salt used in the salt chamber and the permeability of the outer membrane casing.
4. **Implantable mini osmotic pump**: - This is the most advanced version in the category of implantable pump developed by 'Alza corporation. It is composed of three concentric layers – the drug reservoir, the osmotic sleeves and the rate controlling semipermiable membrane. The additional component called flow moderator is inserted in to the body of the osmotic pump after filling.

The innermost drug reservoir which is surrounded by osmotic sleeve is a cylinder containing high concentration of osmotic agent. The pumps are available with variety of delivery rates between 0.25 to 10ml per hour and drug delivery duration between 1 day and 4 weeks.

2. Vapour presssure activated infusion pumps

In this mode of controlled drug delivery, the drug reservoir, in a solution formulation, is contained inside an infuscate chamber, which is physically separated from the vapor pressure chamber by a freely movable bellows. The vapor chamber contain a vaporizable fluid e.g. Fluorocarbon which vaporizes at body temperature and creates a vapor pressure. Under the vapor pressure created the bellows move upward and force the drug solution in the infusate chamber to release, through a series of flow regulators and delivery cannula, in to the blood circulation at a constant flow rate. A typical example is the development of infusaid, an implantable infusion pump, for the constant infusion of heparin for anticoagulation therapy, of insulin as antidiabetic medication and of morphine for patient suffering from the intensive pain of terminal cancer.

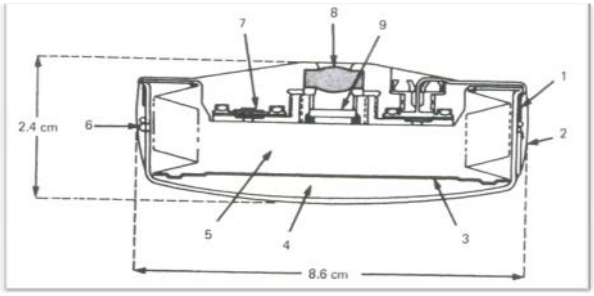


Fig 9: Cross-sectional view of a vapor pressure-activated drug delivery system,

(1) flow regulator, (2) silicon polymer coating, (3) bellows, (4) fluorocarbon chamber (5) infusate chamber, (6) fluorocarbon fluid filling tube, (7) filter, (8) inlet septum, (9) needle stop.

3. Magnetically activated drug delivery

Macro molecular drug, such as peptides, have been known to release only at a relatively low rate from a polymeric drug delivery devices. The device is fabricated by positioning a donut shaped magnet at the center of biocompatible polymer matrix which contains a homogeneous dispersion of a macro molecular drug at a rather high drug: ratio, to form a hemispheric magnet pellet. The pellet is then coated with polymer like ethylene-vinyl acetate copolymer or silicone elastomer on all sides except the cavity at the center of the flat surface, to permit the release of the macromolecular drug under pressure. Hemispheric magnetic device can release macromolecular drug at controlled basal rate, by diffusion process.

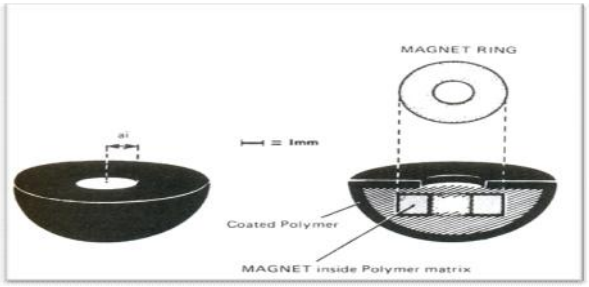


Fig 10: Magnetically activated drug delivery

4. Ultra sound activated drug delivery

It was recently discovered that ultrasonic wave can also be utilized, as an energy source to facilitate the release of drug at a higher rate from polymeric drug delivery devices containing a bio-erodible polymer matrix e.g. Polyalkane anhydride. [13] The potential application of ultrasonic wave for the modulation of drug release is still undergoing evalution.

Medical aspects of implantation

The environment of living tissue, in which the device is implanted, determines the release rate of the drug.

1. Reaction of implant to host

Inflammation is a defensive reaction of living body to any irritant, whether physical, chemical, or bacterial. The presence of a surgically implantable device calls for major adoption by the host tissue unless the device is absorbable. The reaction in the body can be minimized by:

a. The polymer device should have minimum surface area,
b. The device should have smooth surface finish.
c. Ideally the implant should posses the same structural characteristic as the tissue in which it embedded, and
d. As far as possible the polymer used should be flexible as, a rigid plastic material inserted into a soft tissue often becomes infected and rejected.

Silicon capsules were found to show least degree of reaction among synthetic polymer implants particularly when implanted in the subcutaneous or intra-peritoneal space.

2. Reaction of host to implant

No polymer is totally impermeable to the body fluid. Even highly lipophillic polymers like silicone elastomer absorb fat-soluble substances of the blood like cholesterol and steroids. Most important in the clinical use of polymeric device are the effects of tissue enzyme and free radicals as well as hydrolysis caused by the absorption of body fluids.[16] Change in physical property of the device seen often may be due to environmental stress or a result of chemical change. Carbon-carbon bond cleavage may account for the loss of tensile strength in hydrophobic polymers.

Drawback of parenteral implants:

- The primary one is that release profile of drug from pallet is not costant .it can npt be readily controlled.
- In term of precision of release rate and duration of action
- The fact has triggered the research and development of novel controllable implantable therapeutic system to replace pallet for long term continuous administration of drug.

3. CONCLUSION

In conclusion the ideal implantable therapeutic system should be bio stable, biocompatible with minimal tissue-implant interaction, nontoxic, non carcinogenic, retrievable and should release the drug at a constant programmed rate for a predetermined duration of medication.

The concept of implant delivery system though conceived long back was commercialized only after the uses of bio-compatible polymer were developed. Implants with diffusion controlled delivery system were mainly used for subcutaneous and intradermal delivery of many drugs for extended duration of action. Out of these, polymer based matrix delivery systems have become popular, particularly for drug like naltraxone and other anti abuse drugs. Application of medicated implant device for dental therapeutics is the recent development which has immense commercial potential treating dental infection, particularly of anaerobic organisms. In spite of this investigation development of an ideal and bio-compatible polymer free from toxic and allergic manifestation is yet to be brought about. However, with the available polymer a

reasonably good implant device with minimal tissue interaction, nontoxic, non carcinogenic, have been developed commercially.

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