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Microchip: New Approach In Novel Drug Delivery System

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ABSTRACT

Now days there is need of using novel drug delivery systems to avoid side effects of conventional drug delivery systems and to achieve more significant effects from drug delivery system. Microchip is a new approach in the novel drug delivery system. It is a device act as an implant and delivers required quantity of drug on the site of action at specific time. This method is beneficial in chronic diseases which having long time therapy. Device has substrate, reservoirs, reservoir cap, microprocessors, battery, antenna, biocompatible coating etc. There are different types to deliver drug from the reservoirs. Diffusion method, electro thermal method, diamond electrophoretic method, electrochemical degradation method, polymer degradation method. By using one of these methods optimum drug can deliver. This device having so many advantages like it stores the drug for long period of time and also protects the drug. Effective concentration of drug can be maintained in blood for long period of time. This system is more beneficial to treat chronic diseases. Chronic diseases require therapy for long period of time which improves patient non-compliance. Chronic diseases like diabetes, cancer, and osteoporosis can be treated by using microchip.There are some limitations in this type of drug delivery system which can be overcome in future research study. This type of drug delivery system can take new era in the world of medicine and technology.

Keywords-microprocessor, electrophoretic, biocompatible, osteoporosis

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INTRODUCTION

Proper drug delivery system can give proper results to therapy. It gives significant effect on the drugs therapeutic efficacy. Conventional drug delivery systems produce a sharp initial increase in drug concentration to a peak above the therapeutic range followed by fast decrease in concentration to level below the therapeutic range. Additionally, repeatable dosing of medication may be difficult to patient due to their noncompliance. In controlled drug delivery systems (CDS), drug delivery is mainly focused on achieving a constant release of drug over long periods of time with minimum side effects and the improvements in these delivery systems are elimination of side effects, optimized therapy and better patient compliance.

In case of orally administered drug, before absorption drug must be protected against denaturation in GIT and should be able to absorb across the wall of stomach or intestine. Next it should be protected from hepatic enzymes. Then from the dosage form required amount of drug should be reached at the site of action. These disadvantages can be covered in oral controlled release dosage form, but main drawback of oral dosage form is the long transit time of approximately 12 hours through the GIT. Alternative for oral rout is parenteral route. Due to short duration of action of some drug and therapy for chronic diseases frequent injections are required.

Daily injections decrease patient compliance. Some therapies like cancer, osteoporosis required repeated administration of drug to the patient for long period of time. This may increase patient non- compliance. In case of potent drug they require such dosage form through which drug can be released in required amount, at specific site of action and at specific time. This avoids many side effects of drug. Dosage form which is capable to release drug in controlled, pulsatile and continuous manner is required in such type of therapies. Best alternative for this is implanted drug delivery system

Now a day's microchip is a new approach in novel drug delivery system. Microchip is an implant used to give modified release of drug. It can give continues or pulsatile or control release of drug. Microchip has many advantages which covers the drawbacks of other drug delivery systems. It is better option for daily injections which may cause patient non- compliance. Use of microchip improves the patient compliance.

Microchip has many advantages like it stores the drug for long period of time and also protects the drug. Effective concentration of drug can be maintained in blood for long period of time. Microchip can also characterized by a lower occurrence of infections associated problems in

comparison to indwelling catheter based infusion system. It improves drug delivery step by delivering drug at the site of action at specific time. It minimizes side effects by releasing drug at the site of action. It releases only precise amount of drug from chip, simple to use and manufacture. Patient compliance is also increased by allowing a reduction or a complete elimination of drug. Patient has less involvement in delivering the required medication. Other advantages in case of controlled release kinetics, it release drug in zero order with avoiding peaks (toxicity) and troughs (ineffectiveness) of conventional therapy and dosing frequency also reduced. These microchips can store drug in solid, liquid, semi-solid form. Microchip can store one or more than one drug at a time.

IMPLANTABLE CONTROLLED DRUG DELIVERY SYSTEM[7]

The controlled drug delivery systems are used to release therapeutic agent at predictable rate in vivo. Most of controlled drug delivery systems are designed for implantable devices, transdermal, subcutaneous, or intramuscular uses. Implantable devices can deliver drug which cannot be delivered via the oral route or are irregularly absorbed via GIT. These devices deliver drug in to blood stream. This replaces daily injections and repeated insertion of IV catheters. This is beneficial to the treatment of chronic diseases.

This system is particularly suitable for drug delivery requirements of insulin, steroids, chemotherapeutics, antibiotics, analgesics, heparin and contraceptives. These devices are placed under skin which reduces side effects caused by traditional administration techniques. Implantable devices can control release by electrical power source to achieve zero order or manipulated non-zero release profile. Figure 1 shows drug levels in the blood with (a) traditional drug dosing and (b) controlled-delivery dosing.

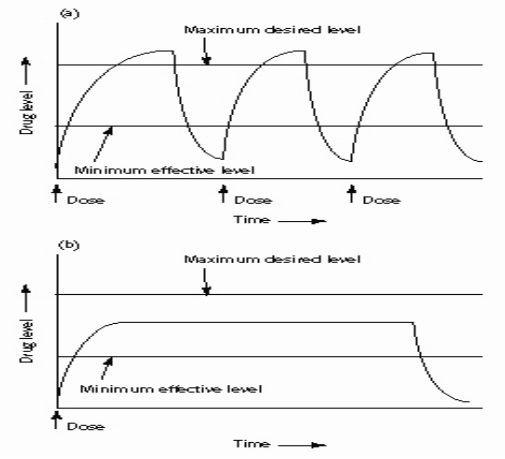

Figure 1: Drug levels in the blood with (a) traditional drug dosing (b) controlled-delivery dosing

Design of Microchip Device

Device contain one substrate that act as support. This substrate having pores called as reservoirs. Reservoirs are for holding drug molecules. It can hold drug in solid liquid or gel form. Reservoirs are covered with a metal plate called as reservoir cap. This is conductive membrane and wired with final circuit which is controlled by microprocessor. Metal used for reservoir cap may be gold, platinum, or titanium. Metal layer get dissolved and drug is released. Release of drug, its exact time, and amount of drug release is controlled by central processor.

Substrate

Before choosing material for the substrate some factors should be considered. It should be impermeable to the drug molecules and surrounding fluid, it should be biocompatible and non-degradable. In case if it is non-biocompatible then it is enclosed in biocompatible material like silicon. Reservoirs are patterned in to the substrate generally by using microfibrication technique. By using photolithography, chemical vapor deposition (or) microfibrication process, these microchips are fabricated.

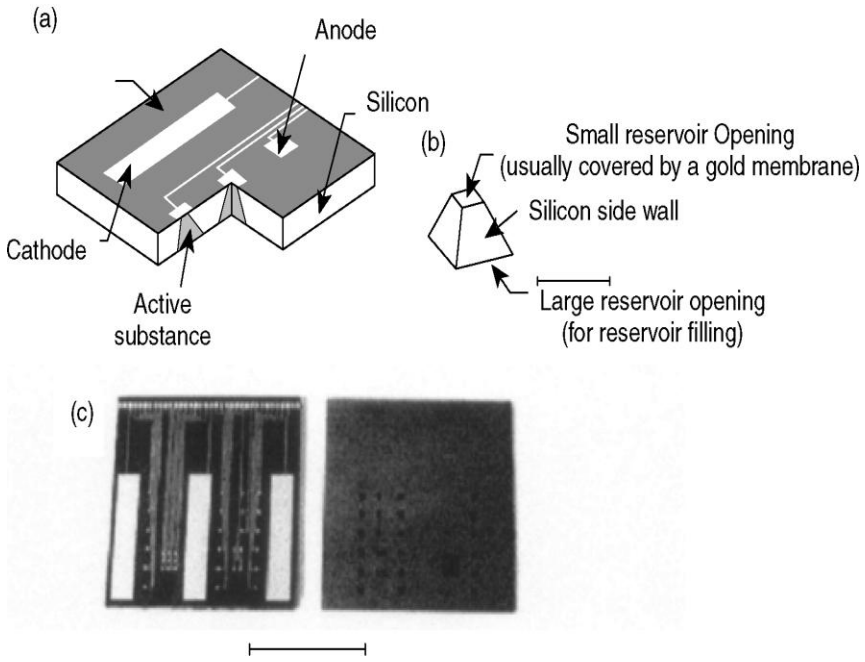

Figure 2.Typical controlled release microchip – a) cut section showing anode, cathode, and reservoir b) shape of individual reservoir c) Photograph of a prototype microchip: the electrode-containing front side and the backside with openings for filling the reservoirs.[7]

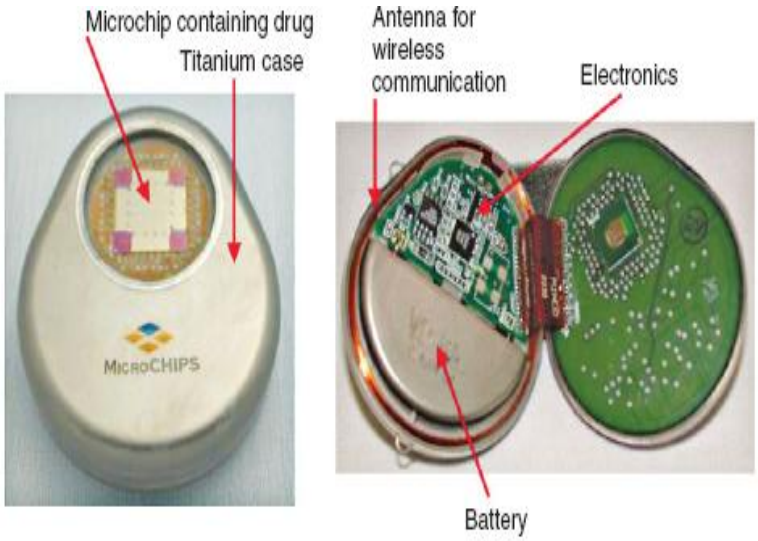

Figure 3: Exterior (left) and interior (right) views of assembled system: Implantable multi reservoir microchip drug delivery device[15]

Reservoir cap

Reservoir cap is made up of thin conductive metal film. Over this film anodes are patterned surrounded by cathodes. Material used to fabricate anodes and cathodes should be electrically conductive. Material can get dissolve and oxidized upon application of electric potential. Anode is an electrode where oxidation occurs. As shown in figure anode is placed exactly above the reservoir which oxidizes and get dissolve in surrounding solution upon the application of electric potential between anode and cathode. This process is responsible for the release of drug from the reservoir by exposing system to the surrounding fluids.

For reservoir cap generally material used are gold, platinum or titanium but gold is preferable and generally chosen as model membrane because it is easily deposited and patterned, it has low reactivity with other substances. It is resistant to corrosion.

Working of Microchip and Drug Release Mechanism[3,4,5,6,10,14]

There are many mechanisms for the release of drug from microchip. Diffusion mechanism is one of them. Drug is stored in micro channels. These micro channels are fabricated by using poly (methyl methacrylate). Drug is diffused from these micro channels. [10]

Second one is electro thermal mechanism. Drug containing micro channels are covered with thin layer of metal. By passing current through this thin layer heat is generated in metal layer. By dissolving metal layer drug is released from the microchip.[9]

Third mechanism is diamond electrophoretic mechanism. To avoid problem of high voltage and time of biochemical analysis in electro thermal mechanism microchips are manufactured by

mold technique. In this technique polycrystalline layer of diamond is used because it is material having highest known thermal conductivity. And drug is released by electrophoretic mechanism.[4,5]

Other mechanism is electrochemically reduction of membrane. This membrane is covered to micro channels which stores the drug. This membrane may be prepared by metal (gold, titanium, platinum, silicon etc.) or may be made up of drug loaded poly propylene film.

Microchip implants can be embedded inside the body of humans for the purpose of acting as unique lifetime identifiers (ULI). This is act as personal identifier for patient.[8]

Polymers used for the construction of a microchip[10,]

Only biodegradable polymers are used in microchip device. The polymer degrades when it comes in contact with body fluid and due to degradation of polymer, drug is released from the reservoirs. Drug release from reservoirs can be modified by degradation properties of polymer. Polymers used in the construction of microchips are Polymerized type of anhydride crossed with sebacic acid. Rate of release could be changed with the amounts of sebacic acid. Polyurethane, Cellulose Acetate, polyethylene glycol, polylactic acid, polyglycolic acid, polyurethanes and combinations of these in different proportions are used.

Human Trial of Microchip[11,12]

Robert Farra carried out a clinical trial of implanted microchip. Human parathyroid hormone fragment (hPTH) was delivered in vivo from this device, for the treatment of osteoporosis. In this therapy patient must has to inject daily. This daily injection can be replaced by pulsatile or intermittent drug delivery system. Microchip is best option for daily injections.

Robert studied on 8 postmenopausal osteoporotic women for 4 months. Lyophilized hPTH was placed in microchip and it is implanted to release drug for 20 days.

The pharmacokinetic, bioavailability, safety and tolerability were studied and it is as same as the injectable dosage form. Pharmacokinetic profiles were studied by withdrawing blood sample periodically. Changes in bone formation is evaluated by measuring serum type I collagen pro peptide and bone reabsorption were studied by measuring serum type I collagenolysis fragments.

MIT (Massachusetts Institute of Technology) scientists Michael Cima and Robert Langer were called as creators of a microchip based drug delivery system that has passed a trial treating 8 patients. They have been tested microchip in 8 osteoporotic women and delivered a drug for 20 days. Result obtained was there were no adverse effect and it is effective for therapy.

This microchip was implanted by giving anesthesia. Microchip contained 20 reservoirs which hold 600 Nano liter of drug solution in each reservoir. These reservoirs are covered with

platinum or titanium. By giving current to this metal layer this layer is melted and allowed for drug release. "Microchip announces clinical results for first successful human clinical trial of implantable wireless microchip drug delivery device." This microchip study was published in online edition of the journal "science translational medicine."

Microchip is approach to multiyear drug delivery without giving daily injections. Again Robert Farra, microchip president and chief operating officer said that microchip can improve managements of chronic diseases

Future Developments In Microchip[2]

There are some drawbacks in microchip drug delivery system. By changing or developing some parts in microchip we can avoid these drawbacks. Adsorption of material on microchip inside the body is a big problem to release drug. In future research study this problem may solve. In some case there is need to cover microchip by biocompatible material. But this covering may alter the release of drug from chip. This problem may solve in future research study. One more limitation is electric breakdown of material used for microchip. This problem can solve by using good quality material.

CONCLUSION

From the study of microchip we can conclude that microchip is a new approach in novel drug delivery system. It having many advantages and avoids many disadvantages caused by other delivery systems. In future it will be best choice of delivery system for chronic diseases. Treatment of chronic diseases is big trouble for doctors, pharmacist, and patient. But microchip can solve all problems in therapy of chronic diseases. Microchip can deliver drug to patient for long period of time. Therapeutic level of drug can be maintained in body for years. Drug can be protecting from degradation in side body. Delivery of drug is depends on patient need. Drug can deliver in prescribed manner on the site of action. Microchip is prepared by microfibrication technique. Materials used for the preparation of microchip are metal parts, battery, drug which is to be deliver and polymer. If there is need of coating of biocompatible material then and then only microchip is covered with biocompatible material. This type of delivery system eliminates the need of patients or doctors which improves patient compliance. It is best option for daily injections and long term treatment of chronic diseases like cancer, diabetes, osteoporosis etc. Finally we can conclude that microchip is an implant is more beneficial for the patients suffering from chronic diseases.

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