



INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

A REVIEW ON RECENT INNOVATION IN INTELLIGENT DRUG DELIVERY SYSTEM

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Accepted Date: 16/01/2017; Published Date: 27/02/2017

Abstract: Intelligent drug delivery systems are the novel innovation invented in recent years to improve the treatment of diseases. These systems are capable of releasing active ingredients at specified rate at specific site in response to the progression of the disease. This system includes pulsatile drug delivery systems, responsive drug delivery, systems utilizing enzymes and antibody interaction, system utilizing chelation and tailor-made medicine designed to perform detection, isolation and release of medicament for the treatment of diseased condition. In pulsatile drug delivery system, a variety of design strategies attempted include single unit capsular system, pulsatile delivery by osmosis, pulsatile delivery by Solubilization and by rupture of membrane. In responsive system various polymers are used which is responsive to body environment. In this system release of drug is controlled by change in temperature, pH or inflammation and sensitive to glucose and other saccharides. In in- situ gelling systems, a viscous liquid is formulated which upon exposure to the physiological conditions convert into gels. Recent innovation in intelligent drug delivery systems are there like programmable devices called microchips for controlled drug delivery, insulin pumps, glucoWatch, microelectronic devices and micro machined silicon membrane implantable bio capsule and Light sensitive intelligent drug delivery systems.

Keywords: Insulin pump, glucoWatch, ophthalmic micro pump, electrolytic pump, implantable device contains hydrogel micro valves, light sensitive liposome.



PAPER-QR CODE

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Access Online On:

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How to Cite This Article:

Vijaykumar J. Gajera, IJPRBS, 2017; Volume 6(1): 1-18

INTRODUCTION

This new class of “intelligent therapeutic” refers to intelligent and responsive delivery systems that are designed to perform various functions like detection, isolation and/or release of therapeutic agent for the treatment of diseased conditions. These systems based on stimuli-responsive polymers which sense a change in a specific variable and activate the delivery.

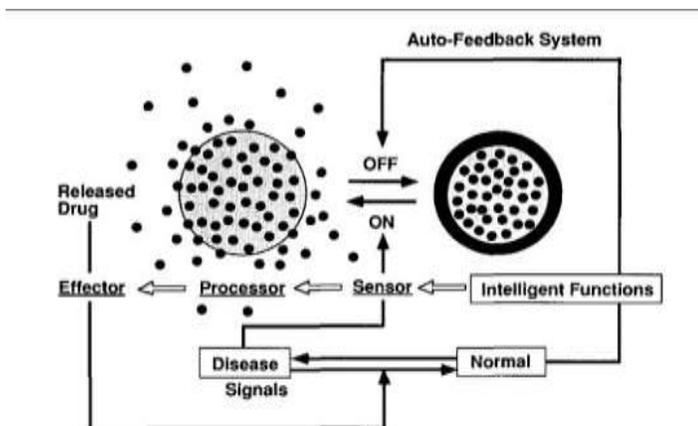


Figure No. 1 Mechanism of IDDS

This review reports on recent advances in the intelligent drug delivery system includes use of responsive polymers, microchips, light sensitive drug delivery, pulsatile drug delivery, responsive drug delivery systems. This technology performs the control release of drug at specific rate to a specific site. This controlled and targeted drug delivery system have lead many complicated ailment with minimum side effects. Intelligent drug delivery system capable to maintain release of medicament in response to physiological needs. This system helps to regulate and maintain localized delivery of therapeutic drug at particular body compartment when needs, preserve the medicament that are rapidly destroyed, improved patient compliance. The aim of this review is to describe the most recent advances in the development of intelligent in situ gel, medical device and light sensitive drug delivery systems.

Classification of intelligent drug delivery system:

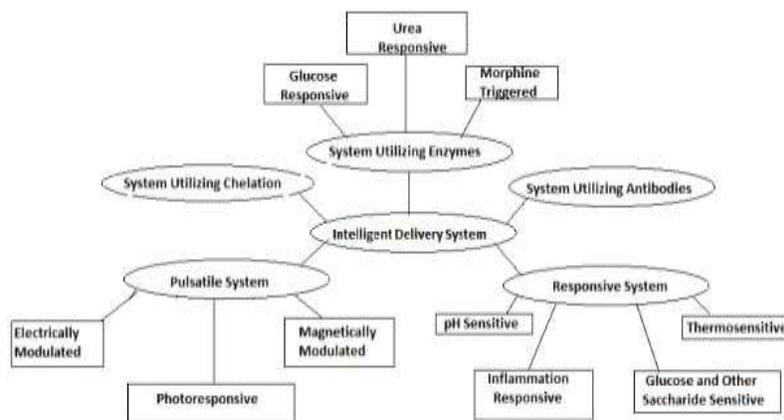


Figure No. 2 classification of IDDS

PULSATILE DRUG DELIVERY SYSTEMS [1,2,3]:

In pulsatile drug delivery systems release of drug is controlled by external stimuli like magnetism, ultrasound, electrical effects and irradiation etc. However, there are certain conditions for which normal release pattern is not suitable it require release of drug after a lag time. In other words, it is required that the drug should not be released at all during the initial phase of dosage form administration. Such a release pattern is known as pulsatile release.

1. Single Unit Capsular System:

This system is mostly developed in form of capsule. In this system contains plug in a capsule. This plug gets swell or erode when contacts with body fluids come and give pulsatile release of medicament.

Pulsincap® system is such a delivery in which a water insoluble body containing the drug formulation is closed with a swellable hydrogel and plugged (insoluble but permeable & swellable) at open end. Upon contact with, gastrointestinal fluid or dissolution medium the plug swells pushing itself out of the capsule after a lag time. For rapid release of water insoluble drug effervescent or disintegrating agents are added.

2. Pulsatile Delivery by Osmosis

This system consists of a semi permeable membrane coated capsule and Inside the capsule, osmotically active agent and the drug formulation. When this system comes in contact with body fluids, water diffuse into capsule that generate the osmotic pressure. This pressure ejects the plug after a specific lag time.

The Port® System is a representative that consists of a gelatin capsule coated with a semi permeable membrane (e.g., cellulose acetate) housing an insoluble plug (e.g., lipidic) and an osmotically active agent along with the drug formulation.

3. Pulsatile Delivery by Solubilization (Erosion of Membrane)

These systems are based upon a drug reservoir surrounded with a soluble or erodible barrier layer that dissolves with time and the drug releases at once after the lag time. When this system comes in contact with the aqueous medium the coat emulsifies or erodes after the lag-time depending on the thickness of coat. The lag time of system is independent of the gastrointestinal motility, pH, enzyme and gastric residence.

Time Clock® system consists of solid dosage form coated with lipid barriers such as carnauba wax and beeswax along with surfactants.

4. Pulsatile Delivery by Rupture of Membrane

These systems are based upon a reservoir system coated with a rupturable membrane. The outer membrane ruptures due to the pressure developed by effervescent agents (or) swelling agent. Citric acid and sodium bicarbonate is incorporated as effervescent mixture in tablet core coated with ethyl cellulose.

When system comes in contact with water it produces carbon dioxide gas, which exerts pressure and after a lag time the membrane ruptures and rapid release of drug occurs.

5. Electrically Regulated Systems: These systems control the release of drug across the membrane by using the electric field. The action of an applied electric field on rate limiting membrane or directly on the solute thereby controlling its transport across the membrane.

Electric field-sensitive polyelectrolyte hydrogels have been developed for use in solute permeation control, artificial muscles and actuators utilizing their swelling-deswelling behaviour.

Insulin was released from poly- (dimethyl aminopropyl acrylamide) (PDMAPAA) gel with chemo mechanical shape change (shrinking) under the influence of electric fields

6. Ultrasonically Modulated Systems:

The ultrasonic-controlled polymeric delivery systems in which release rates of substances can be repeatedly modulated externally. Both Non-erodible as well as Bioerodible polymers can be used for the preparation of drug carrier matrices.

On exposure to ultrasound an enhanced polymer erosion and drug release occurs. The response of system to the ultrasonic triggering is rapid (within 2 min) and reversible in nature.

The enhanced release is also observed in Non-erodible systems exposed to ultrasound where the release is diffusion controlled.

The release rates of zinc bovine insulin from ethylene vinyl acetate copolymer (AVAc) matrices are 15 times higher when exposed to ultrasound. It is also noted that the extent of enhancement can be regulated by the frequency, intensity or duty cycle of the applied ultrasound.

7. Magnetically Modulated Systems:

This approach involves incorporation of magnetic beads in elastic polymers. It has been shown that when oscillating magnetic field is applied, more drug will be released.

Insulin and other macromolecular bioactive can be continuously released by embedding them in a carrier like ethylene vinyl acetate copolymer (EVAc). Another system utilizing EVAc-protein matrices containing magnetic beads exhibit enhanced releases rates when placed in oscillating magnetic field.

SR.NO	BRAND NAME	TECHNOLOGY USED
1.	Verelan ^R PM	CODAS
2.	Propranolol hydrochloride (CRR)	EURANDS
3.	LODOTRA TM	GEOCLOCK
4.	Moxatag TM	PULSYS TM

Table No.1 Marketed products of pulsatile drug delivery systems:

Table No.2 Marketed products controlled release drug systems:

SR.NO	BRAND NAME	DRUG
1.	AbraMag TM	proteins
2.	NanoLink TM	Streptavidin

RESPONSIVE SYSTEMS^[1,2]:

1. pH sensitive systems
2. Thermo-responsive systems
3. Inflammation responsive systems
4. Glucose and other responsive systems
5. Enzymatic and ionic cross linking *in situ* gelling systems
6. Photoresponsive systems (Light sensitive systems)

1. pH sensitive systems^[4]:

Different parts of gastrointestinal track have different pH range and ionic composition of surrounding environment. Alteration in pH of environment cause swelling or deswelling of the polymer. Therefore release of drug depends on pH of surrounding environment. pH-sensitive hydrogels have been synthesized by the addition of ionic monomers to the gel such as acrylic acid (AAc) or aminoethyl methacrylate (AEMA).

Multifunctional pH-sensitive Mesoporous silica nanoparticles MSNs were designed with mixed polymeric coatings, that is, poly (ethylene glycol) (PEG) as a dispersity-enhancer and poly(2-(pentamethyleneimino)ethyl methacrylate) (PPEMA) as an ultra-pH-sensitive gatekeeper. Enhanced dispersity, high drug loading capacity, long-circulation time, pH-triggered targeting, and better cellular uptake of the multifunctional MSNs make them potential candidates for pH-sensitive drug delivery such as tumour therapy.

2. Thermo-responsive systems^[4]:

Thermosensitive hydrogel made by the use of temperature sensitive polymer system. When this system come in contact with body the system turns solution to gel due to physiological temperature of body. This sol-gel transition is known as curing. Curing mainly involves the formation of covalent cross links between polymer chains to form a macromolecular network. Polymers like chitosan and xyloglucan give thermally triggered *in situ* gelling systems.

3. Inflammation responsive systems:

This approach is used to treat patients with inflammatory diseases like rheumatoid arthritis using anti-inflammatory drug. This approach involves dispersion of drug loaded lipid microspheres in to degradable matrices of cross linked hyaluronic acid.

Hyaluronic Acid gel is injected at inflammatory sites which are specifically degraded by hydroxyl radicals produced from inflammation-responsive cells during inflammation. Hyaluronic acid is a linear mucopolysaccharide composed of repeating disaccharide subunits of N-Acetyl-D-glucosamine and D-gluconic acid. The degradation of hyaluronic acid by hydroxyl radicals may be dominant and rapid as compared to that by hyaluronidase if hyaluronic acid is injected in the proximity of inflammatory reactions.

4. Glucose and other responsive system:

In diabetes mellitus there are several systems developed which responds to glucose concentration and maintain blood glucose level. One such include pH sensitive hydrogel with immobilized glucose oxidase enzyme encapsulating saturated insulin solution. As the glucose diffuse into gel glucose oxidase catalysed into gluconic acid. This gluconic acid lowers the pH of surrounding microenvironment of membrane and causes swelling. This approach is currently under investigation.

POLY (HYDROXYETHYL METHACRYLATE) POUCHES (PHEMA) which contain a G-INSULIN-CON a complex suspension

Drawback: Exhibit lag time due to exchange of G-INSULIN & GLUCOSE.

Hydrophobic Nylon Microcapsule showed quick 'ON-OFF' response of insulin release.

Glucose sensitive insulin delivery system based on a sol-gel transition: - A Phenyl boronic acid (PBA) moiety incorporated in poly (N-vinyl-2-pyrrolidone) using radical copolymerization of N-vinyl-2-pyrrolidone with m-acrylamido phenyl boronic acid {poly (NVP-Co-PBA)}. Insulin was entrapped into the polymer gel formed by a complex of poly (vinyl alcohol) with poly (NVP-Co-PBA). PBA forms reversible covalent complexes with molecule having a diol unit, like PVA or glucose. When glucose is added, PVA from the PVA-boronate complex is replaced by glucose. This lead to the transformation of the system from gel to sol state facilitating the release of insulin from the polymeric complex.

5. Enzymatic and ionic cross linking in situ gelling systems

Polymers that are sensitive to ions may go phase transition when it comes into contact with ions.

Gellan gum commercially available as **Gelrite**[®] is an anionic polysaccharide that undergoes in situ gelling in the presence of divalent cations, including Ca²⁺, Mg²⁺. The formulation consists of gellan gum solution with calcium chloride and sodium citrate complex. Cross linking ions can

be provided into formulation in complex form. Xanthan gum has capacity to form gel with the enzyme 'lysozyme' which is present in the tear fluid.

7. photoresponsive systems (Light sensitive systems) [5]:

Photoresponsive technologies are increasing attention to developing materials that is sensitive to photoradiation, which can be applied to the various sites of body. Drug delivery systems (DDS) capable of releasing an active molecule at the appropriate site and at a rate that adjusts in response to the progression of the disease. Biocompatible materials sensitive to certain physiological variables or external physicochemical stimuli (intelligent materials) can be used for achieving this aim. Some light-responsive DDS are of a single use (i.e. the light triggers an irreversible structural change that provokes the delivery of the (Entire dose) while others able to undergo reversible structural changes when cycles of light / dark are applied, behave as multi switchable carriers (releasing the drug in a pulsatile manner). Various chemical mechanisms can cause the rupture of the assembly of the liposomal lipidic components, leading to bilayer destabilization and the release of the liposomal content.

Photosensitive liposomes were prepared for targeting the drug. When light source applied to the liposome its creates rearrangement of lipid bilayer that's creates pores into layer, such pores allow drug molecules to diffuse out of the liposome. Incorporation of polymerizable compounds with reactive dienoyl, sorbyl or styryl groups into the hydrophobic domains of liposomes causes the bilayers to polymerize and assemble into larger clusters when an adequate source of light is applied.

Light-responsive silica nanoparticles (70 nm) were prepared by covalent conjugation of photoactive o-nitrobenzyl bromide molecules with amino groups on the particle surface (86). Drugs with carboxylic, phosphate or hydroxy groups were covalently attached to the o-nitrobenzyl bromide groups. When the resulting particles are irradiated at 310 nm, the o-nitrobenzyl bromide groups transform into o-nitrobenzaldehyde, which causes an irreversible cleavage of the drug-particle bond, leading to drug release. These particles are small enough to penetrate into cells, enabling an external control of the intracellular drug release.

Temperature-induced gel systems with photo controlled release capability may improve the performance of formulations that can be administered as a free flowing fluid that gels in situ due to the temperature change; the viscosity changes under irradiation enable external tuning of drug delivery from the depot. As an example, supramolecular cross-linking of polymers by low-molecular-weight cross-linkers using multiple hydrogen bonds can be used for mediating thermally reversible sol-gel phase transitions.

System utilizing enzyme ^[1,2]:

1. Urea responsive delivery system:

By the action of urease enzyme urea converts into NH_4HCO_3 and NH_4OH that increase the pH. Alteration in pH by immobilization of enzymes that lead to change in erosion rate of polymers. Partially esterified copolymer of methylvinylether and maleic anhydride, this polymer displays release rates that are pH dependent. The polymer dissolves by ionization of the carboxylic acid group. This pH sensitive polymer containing dispersed drug is surrounded by a hydrogel containing urease immobilized by cross linking of urease and bovine serum albumin with glutaraldehyde. Diffusion of urea into hydrogel and

Its subsequent interaction with urease lead to increase in pH which causes erosion of polymer with concomitant drug release.

2. Morphine triggered naltrexone delivery system:

Naltrexone is used for treatment of heroin addiction. It is opiate antagonist that blocks opiate induced euphoria. In this system, naltrexone is dispersed in biodegradable polymer matrices which is covered by Lipid layer that prevents water entry and so retards its degradation. Drug release is initiated by the appearance of morphine (hapten) in the vicinity and dissociation of the enzyme-hapten-antibody complex rendering the enzyme active. This system was developed by entrapping Naltrexone in a Bioerodible polymer.

The system is placed in dialysis bag, which contains lipase enzyme that is covalently attached to morphine and reversibly inactivated by antimorphine complexation. Therefore, when morphine is present in vicinity of the device, morphine diffuses into the dialysis bag and displaces the lipase-morphine conjugate from the antibody allowing now activated enzyme to degrade the protective lipid layer that permits the polymeric core degradation and release Naltrexone into the body.

System utilizing antibody interactions:

System utilizing antibody interactions projected to release of oral contraceptive agents. In this system the β subunit of Human Chronic Gonadotropin (HCG) is grafted on to the surface of the polymer, which in turn is exposed to antibodies to β -HCG. The appearance of HCG in the blood (indication of pregnancy) will cause release of contraceptive drug as HCG competes for the polymer bound antibodies to HCG and initiates the drug release.

System utilizing chelation:

This system include antibody for the treatment of metal poison. The concept is based on the property of metals to accelerate the hydrolysis of carboxylate or phosphate esters and amides. Tagging of the chelator to a polymer chain by a covalent ester or amide link prevents its premature loss by excretion and reduces its toxic effects. In the presence of specific ion, the bound chelating agent forms a complex followed by metal accelerated hydrolysis and subsequent elimination of the metal chelate.

RECENT ADVANCES IN intelligent DRUG DELIVERY SYSTEM:**INSULINE PUMP ^[1,6]:**

In diabetes main goal should be to get your blood glucose (sugar) levels under control in order to increase your chances of a complication-free life. Many people know this, but need to know how to achieve good diabetes management, while balancing the day-to-day demands of diabetes with other life demands.

An insulin pump can help you manage your diabetes. By using an insulin pump, you can match your insulin to your lifestyle, rather than getting an insulin injection and matching your life to how the insulin is working.

When you work closely with your diabetes care team, insulin pumps can help you keep your blood glucose levels within your target ranges. People of all ages with type 1 diabetes use insulin pumps and people with type 2 diabetes have started to use them as well. Insulin pumps deliver rapid- or short-acting insulin 24 hours a day through a catheter placed under the skin. Your insulin doses are separated into: Basal rates, Bolus doses to cover carbohydrate in meals, Correction or supplemental doses.

Basal insulin is delivered continuously over 24 hours, and keeps your blood glucose levels in range between meals and overnight. Often, you program different amounts of insulin at different time of the day and night. When you eat, you use buttons on the insulin pump to give additional insulin called a bolus. You take a bolus to cover the carbohydrate in each meal or snack. If you eat more than you planned, you can simply program a larger bolus of insulin to cover it. You also take a bolus to treat high blood glucose levels. If you have high blood glucose levels before you eat, you give a correction or supplemental bolus of insulin to bring it back to your target range.

The pump, which is about the size of a smart phone or deck of cards, is worn on the outside of your body and delivers insulin through a tube (catheter), connected to a thin cannula, placed into the layer of fat under your skin, typically around your stomach area. The pump can be

worn around your waist in a pump case or attached to a belt or bra, in a pocket, or on an armband. There are a variety of custom-made accessories available so you can carry your insulin pump with style.

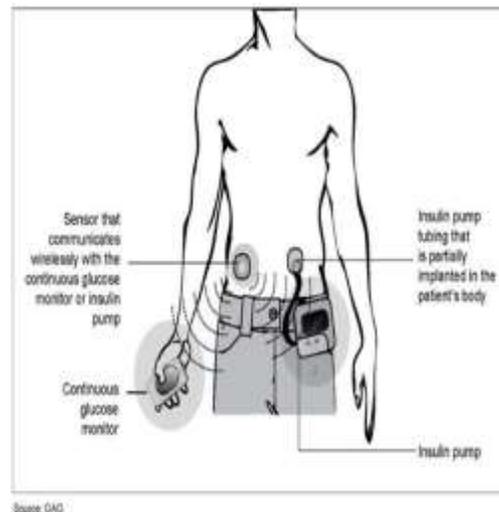


Figure No. 3 Insulin Pump

GLUCO WATCH ^[1]:

The GlucoWatch is a blood sugar (glucose) monitoring device that is worn on the wrist like a watch and does not require drawing blood through a finger-stick. The device takes non-invasive glucose measurements through the skin every 10 minutes for up to 13 hours at a time. These readings are used to supplement finger-stick measurements in detecting and tracking patterns in glucose levels. The device should not be used as a substitute for finger-stick measurements.

The GlucoWatch uses an extremely low electrical current to extract glucose molecules through the skin using patented sampling processes. The glucose is extracted from interstitial fluid that surrounds skin cells, rather than from blood, eliminating the need for multiple finger pricks to provide glucose readings. The Biographer can be worn like a wristwatch and functions like a computer, analysing and responding to data received from the Auto Sensor. The Auto Sensor uses proprietary biosensor technology and snaps into the back of the Biographer. The Auto Sensor is calibrated with a standard blood glucose measurement and takes two hours to warm up. After the warm-up period, the Auto Sensor automatically and non-invasively extracts and measures glucose every 10 minutes for a period of up to 13 hours before requiring replacement. The patient will receive up to six glucose readings per hour.



Figure No. 4 GlucoWatch G2

OPHTHALMIC MICROPUMP [7]:

Localizing drug delivery has the advantage of avoiding systemic side effects, which has been a potential concern with current retinal disease treatments. Both suprachoroidal and intravitreal delivery may eliminate this issue altogether.

The pump provides the capabilities for delivering a programmable microdose direct to the eye. The cannula, inserted through the pars plana, is programmed wirelessly. This version of the device is smaller than the one designed for glaucoma, but it has a larger reservoir volume. As a result, the pump is refilled via a 31gauge needle.

This implantable device uses gas pressure from electrolysis to force its drug through the check valve into the cannula and through the eye wall. It can be reprogrammed and recharged wirelessly, and a needle can be used to refill it. Depending on the location it is mounted to, it can treat glaucoma or deliver drugs intraocular.

The pump has been shown to be capable of use for more than 7 years and further longevity tests are ongoing to determine how much longer it can work. The reservoir can be replenished within 2 minutes in the clinic

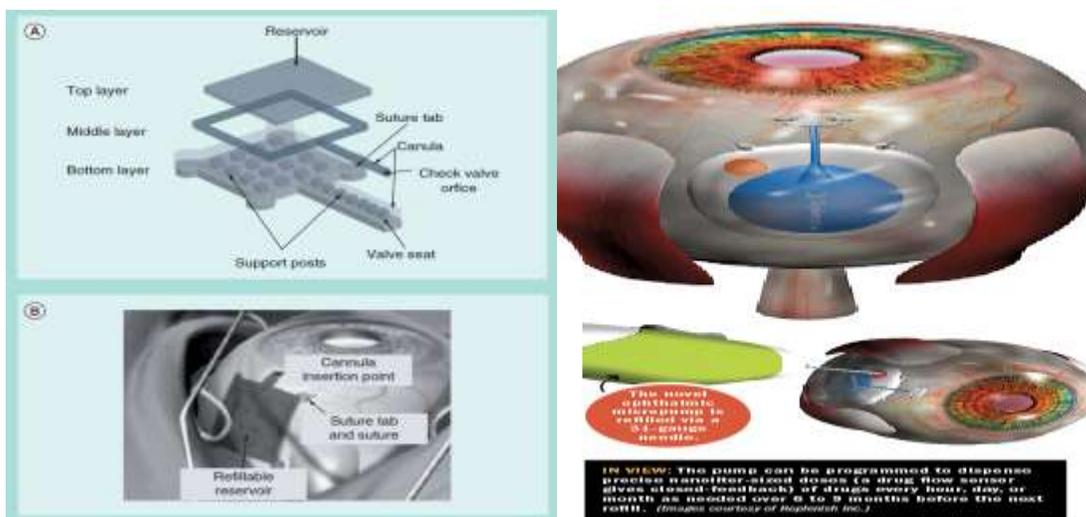


Figure No. 4 (A) Refillable reservoir and cannula Figure No. 5 Ophthalmic Pump

(B) Illustration of device implanted

A WIRELESS IMPLANTABLE DRUG DELIVERY DEVICE WITH HYDROGEL MICROVALVES [8,9]:

Implantable (Micro-Electro-Mechanical Systems) MEMS devices for application are aimed at enabling controlled release of drugs locally at diseased sites through miniaturized devices, offering more effective therapies compared to conventional methods.

This device work on wireless actuation principle above can be applied to different types of temperature-sensitive elements such as temperature-sensitive hydrogels, shape memory alloys, and bimorphs. Hydrogels have been used for a variety of biomedical applications including drug delivery devices. In this effort, poly (N-isopropylacrylamide), or PNIPAM thermoresponsive hydrogels was selected as the microvalve material. PNIPAM exhibits the phase transition temperature called the lower critical solution temperature (LCST) above which it shrinks and deswells the fluid. The PNIPAM microvalves are combined with the L-C resonant heater for their actuation in order to control the drug release through micromachined holes created in a reservoir wall. A photosensitive PNIPAM is used to lithographically form the microvalve structures on the heater circuit, which are designed to plug the release holes in their inactive mode. To initiate drug release, temperature is brought above the LCST by activating the wireless heater by tuning the field-frequency. This causes the shrinkage of the microvalves, thereby unplugging the release holes through which the drug diffuses out of the reservoir. The generated heat also contributes to enhancing the diffusion of the drug. Shifting fM away from fr deactivates the heater and the microvalve, closing the release holes and terminating the drug release.

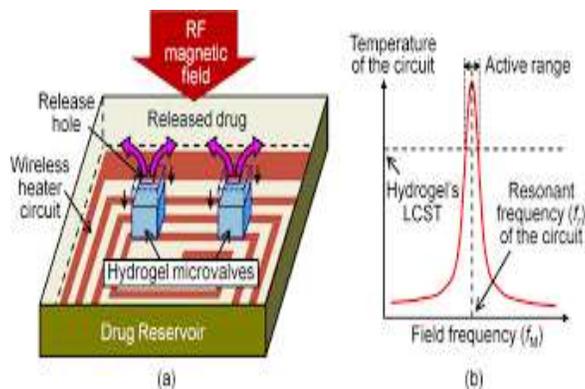


Figure No. 6 A wireless implantable drug delivery device with hydrogel microvalves

MICROFABRICATED DRUG DELIVERY SYSTEMS ^[10,11]:

For the administration of drug into body common routes include the intramuscular, oral, intravenous, subcutaneous, transdermal and rectal each of route has its pros and cons, with the injection route in particular having number of problems such as pain, require skill person and proper and safe disposal of the needles after use.

Working with microfabricated technologies can enable direct application of integrated circuit technology in more traditional systems. Integration of computational system can allow for the development of smart delivery system that can detect changing biological conditions and thus change their responses, starting or stopping the release of medicament, and obtaining optimal and temporal delivery for the best therapeutic effect.

Now a day so many innovations in microfabrication technology are created such as microneedles, insulin patch, implantable devices, Nano patch technology for vaccine delivery system to treat various complicated diseases and improve patient day to day life.

ELECTROLYTIC PUMP ^[12,13,14]:

In contrast to conventional drug delivery systems, implantable drug delivery devices allow for a variety of drugs to be directly delivered through physiological barriers, which is a more efficient use of the medication. The implants also can effectively deliver new pharmaceutical agents, including biologics, biosimilar and other small molecules, which cannot be administered by conventional methods. Once the device is implanted, frequent surgical operations for disease treatment are reduced. Moreover, many implantable drug delivery systems can control the dose at the therapeutic level, as well as sustain a continuous release of drug over an extended periods of time, thus maintaining efficacious levels of drug within patients.

The electrolysis bubble-actuated-pump that included a flat polydimethylsiloxane (PDMS) membrane, an interdigitated Pt/titanium (Ti) electrode with a Nafion coating, and a Pt coated nickel (Ni) metal foam. In order to avoid electrochemical interaction with the drug solution, the pumping chamber is separated from the drug reservoir by the membrane. When power is applied to the electrodes, the deionized (DI) water that serves as the electrolyte is electrolyzed into oxygen (O₂) and hydrogen (H₂); Expansion caused by pressure in the pumping chamber deforms the elastic membrane, which causes the drug solution to be pushed outwards.

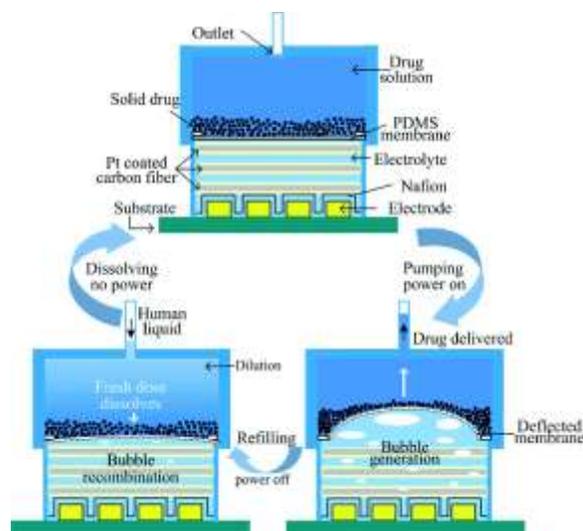


Figure No. 7 Electrolytic pump

In this design, Nafion was uniformly spin coated on the surface of the electrodes in order to protect the electrodes from damage caused by high current electrolysis and to improve the efficiency of bubble generation. During the initial stage, the drug is partly dissolved and forms a saturated solution. When a voltage is applied to the electrodes, electrolysis occurs, and gas expansion pushes the membrane upwards, which ejects the dissolved drug solution through the cannula. Power is applied until the deflection reaches its maximum safe limit, after which the power is removed and the pressure decreases due to gas recombination. The membrane then moves downward, drawing body fluids into the drug reservoir to dissolve more of the remaining solid drug. Power is repeatedly turned on and off to periodically add a further dose.

LIGHT RESPONSIVE LIPOSOME [5]:

The drug is released mainly by passive diffusion. In most cases, this process has been shown to occur too slowly and local drug concentrations required for the optimum therapeutic effect are not reached. Therefore, new approaches to trigger a rapid drug release upon the liposome arrival to the desired body site are being investigated. Destabilization of the liposome structure

by an external source of energy is attracting most interest owing to the spatial and temporal control over the drug release that can be exerted

Incorporation of polymerizable compounds with reactive dienoyl, sorbyl or styryl groups into the hydrophobic domains of liposomes causes the bilayers to polymerize and assemble into larger clusters when an adequate source of light is applied. A consequence of the photopolymerization is that temporal pores in the bilayer are formed around the clusters until the surrounding free mobile lipids rearrange to reconstitute the bilayer. Such pores allow drug molecules to diffuse out of the liposome.

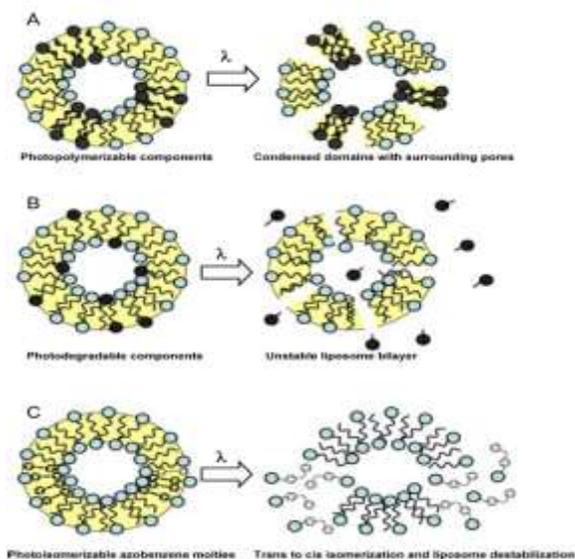


Figure No. 8 Light responsive liposome

CONCLUSION AND FUTURE PERSPECTIVE:

The most of disorders requiring sophisticated precision, dosage and consistent application will continue to influence the production of these innovative devices. Recent advances in the development of intelligent drug delivery by use of micro-and Nano-technologies promise improved treatments of complicated diseases. These intelligent technology controls release profiles of drug by means of an intelligence, fixed structural design, or by using the devices for example, electronic and MEMS. Therefore, this review provides a thorough up-to-date summary of the recent and future intelligent technologies that will capable of controlling release of drug as needed, improve compliance of patients.

As the complexity of the treatments increases due to new knowledge of disease, the complexity of the techniques able to deliver therapies will increase accordingly. In the near future, it can be

expected that the number of intelligent techniques available for different therapies will continue to increase.

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