Biosensor-Integrated Drug Monitoring Systems are emerging as a promising new approach for Biomedical Applications

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Abstract: The integration of biosensors with drug monitoring systems is emerging as a highly promising approach in the realm of biomedical applications. This innovative concept combines the power of cutting-edge biosensor technology with drug monitoring capabilities to revolutionize healthcare and enhance patient outcomes. Biosensor integrated drug monitoring systems entail the incorporation of specialized sensors into the body or wearable devices, capable of continuously and non-invasively measuring various physiological parameters. These biosensors can detect biomarkers, metabolites, and even specific drug concentrations within the body, providing real-time data on an individual's health status. This level of precision allows for personalized medicine, tailoring treatments to a patient's unique needs. One of the significant advantages of these integrated systems is the potential for remote monitoring. Data collected by the biosensors can be transmitted to healthcare providers, enabling continuous patient surveillance and timely interventions. This is particularly beneficial for individuals with chronic diseases, offering an improved quality of life and reducing hospitalizations. Moreover, the integration of biosensors with drug monitoring technology holds promise in drug development, by providing a more efficient means of testing the safety and efficacy of new medications. This can accelerate the drug development process and reduce costs. In conclusion, biosensor integrated drug monitoring systems represent a revolutionary advancement in biomedical applications. By harnessing the capabilities of biosensors, this approach has the potential to transform healthcare, making it more precise, patient-centered, and accessible, while also revolutionizing drug development processes

Keywords: Biosensors; drug delivery systems; types of biosensors; biomedical applications;

INTRODUCTION

Biosensor-integrated drug delivery systems have been extensively studied, especially for the treatment of chronic diseases such as cardiovascular diseases (CVD), diabetes mellitus, and cancer, where regular drug administration and continuous monitoring are relevant [1–3]. The conventional modes of treatment have been associated with serious side effects; thus, over the years, controlled drug delivery systems have been explored as a promising alternative to improve the efficacy and safety by optimizing the duration and kinetics of release [4]. Moreover, the use of systems that can initially sense markers associated with regenerative medicine and diseases, and subsequently release their payloads, has shown a great impact on the treatment of chronic diseases [5,6]. Biosensors are analytical devices composed of two main components: a bio-recognition element and a transducer [7]. The bio-recognition element of the sensor identifies the target analyte, while a transducer converts the result of the molecular recognition into an electrical signal. Different biomolecules such as enzymes, nucleic acids, antibodies, proteins, and peptides can be used as a bio-recognition element and biosensors can thus be used to detect specific physiochemical changes in the body (associated with the diseases) with high sensitivity and specificity [8]. Biosensors have been widely utilized for diagnostic and imaging [9–11], however, they are not originally equipped with therapeutics to treat the diseases. Several studies that merge biosensing and drug delivery concepts have been described in the last few decades [12–14]. These systems are a special class of biosensor designed for

the continuous analysis of biological molecules followed by drug release in response to specific signals. These delivery systems, also known as closed loop delivery systems, have proven to be practical tools by tuning drug release as a function of specific signals associated with physiological and pathological processes The closed-loop drug delivery systems usually consist of a monitoring component that senses the surrounding conditions and an actuator component with the capability to trigger drug release. The pairing of the monitor/actuator architecture allows the drug release to be activated at or above a certain signal concentration or threshold, but inhibits such release when the signal level is in normal ranges [15]. A typical example of such systems is the glucose-responsive insulin delivery system, which imitates the pancreatic beta cells to release insulin with a specific dose at a specific time point by responding to the plasma glucose levels [16]. Many biosensor-integrated drug delivery applications utilizing bio microelectrode chanical systems (bioMEMS), electrochemical sensors, and stimulus responsive biopolymer have been described. MEMS are devices with electrical and mechanical components. MEMS designed for biomedical applications are called bioMEMS, which have gained much attention in the biomedical engineering field for biomolecular analyses and sensing. BioMEMS provide many advantages such as short response time, high scalability, and high sensitivity. In bioMEMS, physical, chemical, or biological signals are converted into electrical signals that trigger the drug release. BioMEMS are implanted into the human body and the drug is released according to sensor feedback [17,18]. Electrochemical biosensors have electrodes that convert the chemical signal into an electrical signal. Electrochemical sensors can detect various biomolecules in the human body such as glucose, cholesterol, uric acid, lactate, DNA, hemoglobin, blood ketones and have great potential to treat diseases related to imbalances of biomolecules. Electrochemical sensors are mostly used for biosensing applications, with very few studies relating to biosensing integrated drug delivery applications [19]. Bioresponsive polymers or smart polymers can undergo structural alterations in response to physical, chemical, or biological stimuli. Many microdevices making use of these smart polymers have been described, which respond to external stimuli and deliver drugs when required [20,21]. These smart polymer-based systems, although not true biosensors (as they lack the signal processing unit), have been widely studied for biosensing integrated drug delivery systems. Attachment of the enzyme glucose oxidase and insulin within a hydrogel, which is responsive to pH changes, is a particularly good example of one such system where the smart polymer acts both as a sensor of glucose concentration and as a drug delivery vehicle for insulin [22]. In this review, we have brought together the exciting advances in the field of biosensor integrated closed-loop drug delivery systems. We discuss the bioresponsive smart polymers, bioMEMS, and electrochemical sensors described in the literature, focusing on diabetes, cancer, cardiovascular diseases, and regenerative medicine

TYPES OF BIOSENSORS

The pioneers named Clarke and Lyons began Biosensor in late 1960s. Different kinds of biosensors being utilized based on two elements namely known as sensing element and transduction modes. Enzymes based biosensor, immunosensor which includes antibodies, DNA biosensor, Thermal and piezoelectric biosensor, biological tissues, organelles and microorganisms which can be detected with the help of whole cell biosensor comes under the category of sensing element. Transduction mode relies upon the physiochemical change coming about because of detecting component. Subsequently on the premise of various transducers biosensors can be electrochemical (amperometric, conductometric and potentiometric), optical (absorbance, fluorescence and chemiluminense), piezoelectric (acoustic and ultrasonic) what's more, calorimetric. [23] Biosensors can likewise be arranged in view of their revelation arrange into original which is the easiest approach including direct discovery of either increment of an enzymatically created item or lessening of a substrate of a redox chemicals utilizing characteristic go between for electron exchange e.g., glucose biosensor which utilizes chemical glucose oxidase -and oxygen recognizing diminish in oxygen level or increment in hydrogen peroxide relating to the level of glucose. Second era biosensors utilize manufactured redox middle people like ferrocene, ferricyanide and

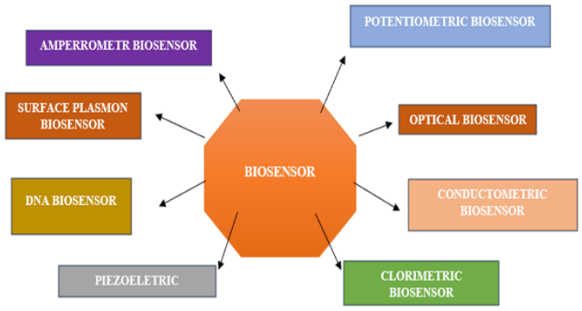

Fig: - [1]

quinones for electron exchange which builds the reproducibility and affectability e.g., self-observing amperometric glucose biosensors. In conclusion, third era in which the redox compounds are immobilized on the cathode surface in such a way, to the point that immediate electron exchange is conceivable between the compound and transducer. It utilizes natural directing material e.g., TTF-TCQN (tetrathiafulvalene tetracyanoquinodimethane). [24] The principal catalyst-based sensor was accounted for by Updike and Hicks in 1967. Catalyst biosensors have been conceived on immobilization techniques, i.e., adsorption of proteins by van der Waals powers, ionic holding or covalent holding. The usually utilized proteins for this reason for existing are oxidoreductases, polyphenol oxidases, peroxidases, and amino oxidases. [25-27] The primary microorganism based or cell-based sensor was realized by Diviès. [28] The tissues for tissue-based sensors emerge from plant and creature sources. The analyte of intrigue can be an inhibitor or a substrate of these procedures. Rechnitz [29] created the main tissue-based sensor for the assurance of amino corrosive arginine. Organelle based sensors were made utilizing layers, chloroplasts, mitochondria, and microsomes. Be that as it may, for this sort of biosensor, the steadiness was high, yet the recognition time was longer, and the specificity was diminished. The primary sorts are examined beneath

1]Amperometric biosensor

Electroactive species present in natural test samples can be easily detected by high affectability biosensor. The oxidation or diminishment of electroactive species is estimated and connected to the centralization of the analyte e.g. glucose biosensors for diabetes checking which produces current due to the potential difference between two electrodes. These anodes limit Eventually Tom's scrutinizing the preparing of a current at plausibility might be associated between two cathodes, the degree from guaranteeing current constantly corresponding of the substrate centralization. The Clarke oxygen cathode for presence of oxygen in the test (analyte) result during reduction is used by these biosensors for facing less difficulty. A main problem of such biosensors is their dependence on the separated O2 fixation in the analyte result. This may be beat Eventually Tom's examining using go between; these particles trade the electrons made Toward the reaction clearly to the cathode as opposed to diminishing those O2 deteriorated on analyte result. Those present-day anodes, in any case, remove those electrons particularly beginning with the diminished proteins without the assistance of arbiters, moreover require help secured with electrically coordinating normal salts. So, the natural test samples may not be characteristically electrodynamic, catalysts are expected to catalyze the generation of radio-dynamic species. For this situation, the deliberate parameter is present. [30]

2] Potentiometric biosensor

In this strategy the scientific data is acquired by changing over the biorecognition procedure into a potential flag which results in oxidation or decreasing capability of biochemical responses. A perm selective particle conductive layer is typically used to gauge the potential flag, which happens when the analyte atom collaborates with the surface e.g., utilization of H+ particles for penicillin discovery utilizing chemical penicillinase, triacyl glycerol utilizing lipase. A high impedance voltmeter is used to check the electrical potential qualification or electromotive power (EMF) between two cathodes. One of the terminals builds up an adjustment in potential as a component of analyte movement or fixation in arrangement and this cathode is known as the pointer anode or now and again called a ion selective electrode (ISE). The potential reaction of an ISE is portrayed by the Nernst condition (i.e., the potential is relative to the logarithm of the centralization of the substance being estimated). The second cathode is the reference and is utilized to finish the electrochemical cell by giving a consistent half-cell potential, which is autonomous of the analyte fixation. ISEs are compound sensors with the longest history and with the biggest number of uses. [31-33] Actually, billions of estimations are played out every year in almost every clinic everywhere throughout the world. This. Shocks no one considering that these

gadgets are outstanding for giving immediate, fast, upkeep free and non-costly estimations. [34]

3] Optical Biosensor

This type of biosensor can be based on the principle of optical diffraction or electro chemiluminescence in which a silicon wafer is covered with a protein by means of covalent bonds which is then presented to UV light through a photograph veil and the antibodies wind up idle in the uncovered areas. At the point when the diced wafer chips are brooded in an analyte, antigen-counter acting agent ties are shaped in the dynamic locales, consequently making a diffraction grinding. This grinding produces a diffraction flag when lit up with a light source. Optical biosensors comprise of a light source, and additionally various optical segments to produce a light bar with particular qualities and to shortcut this light to a balancing operator, an adjusted detecting head alongside a photo detector. [35] These biosensors measure both reactant What's more regular slant reactions. They measure an advance for fluorescence on the other hand on absorbance expedited toward the outcomes created toward reactant reactions. On the other hand, they measure those movements provoked in the inborn optical properties of the biosensor surface in view of stacking on it for dielectric particles, for example, protein (in circumstance from asserting normal slant responses). A vast bit ensuring, biosensor coordinating, including brilliance usage firefly impetus luciferase for recognizable proof of infinitesimal life forms secured close by sustenance then again clinical tests. The minute life forms require help especially lysed should release ATP, which is used Toward luciferase in the region around 02 to plan light which is estimated Eventually Tom's scrutinizing the biosensor. [36]

4] Conductometric Biosensor

The deliberate parameter is the electrical conductance/protection of the arrangement. Conductometric-based biosensors saddle the connection amongst conductance and a biorecognition occasion. Most responses include an adjustment in the ionic species focus and this can prompt an adjustment in the arrangement electrical conductivity or current stream. Basically, a conductometric biosensor comprises of two metal terminals (generally platinum or silver) isolated by a specific separation. Typically, an AC (exchanging current) voltage is connected over the terminals, which makes a present stream be maintained between them. Amid a biorecognition occasion the ionic creation changes and an Ohmmeter (or multimeter) is utilized to quantify the adjustment in conductance between the metal cathodes. Some current investigations have demonstrated that this procedure is prepared to do quickly distinguishing g (<10 mins) different sustenance borne pathogens (i.e Escherichia coli O157:H7, Salmonella). [37- 38] Alocilja and colleagues utilized a conductive polyaniline mark in the sandwich immunoassay plot, which essentially enhanced the affectability by means of the development of a conductive sub-atomic scaffold between the two cathodes. [39] Sadly, one of the significant issues with this strategy is that the affectability is for the most part sub-par contrasted with other electrochemical techniques.

5] Calorimetric Biosensor

Numerous catalysts catalyzed response are exothermic creating heat which is utilized as a reason for estimation of rate of response and consequently analyte focus. The temperature changes are resolved by thermistors e.g. cholesterol biosensors utilizing cholesterol oxidase (warm yield 53 KJmol-1). The analyte game plan is experienced a little stuffed bed area containing immobilized substance; the temperature of the course of action is settled just before section of the game plan into the fragment and also as it is leaving the portion using separate thermistors. This will be those in every way that really matters everything thought about fitting kind of biosensor, utilizing no less than two proteins of the pathway in the biosensor on join two or three responses with broaden those glow yield. On the other hand, multifunctional proteins may a chance to be utilized. An example is the utilization of glucose oxidase for confirmation about glucose. [40]

6] Piezoelectric biosensor

Piezoelectricity can be clarified as a straight cooperation amongst mechanical and electrical frameworks in non-driven gem or comparative structure which initially find by Curie siblings in 1880. [41] Basically, the piezoelectric construct biosensor working in light of the vital that a swaying gem resounds at a characteristic reverberation recurrence. [42-43] The essential components in a biosensor are transducer and biorecognition component. Consequently, in piezoelectric biosensor the transducer is made of piezoelectric material (e.g., quartz) and the biosensing material that secured on the

piezoelectric material which vibrate at the basic repeat. The recurrence is control by the outer electrical flag which delivers a specific estimation of current, when the objective analyte is presented to the detecting material the connection/response will cause the recurrence move which will create changes in current perusing that can be examined to the mass of the analyte of intrigue. There are two essential sorts of piezoelectric sensors: mass wave (BW) and surface acoustic wave (SAW). In any case, writing indicates piezoelectric sensors are not get much consideration and second rate contrasted with electrochemical and optical based biosensing. The bulk wave, quartz precious stone microbalance and surface acoustic wave transducer is on a very basic level in view of the piezoelectric impact. The extraordinary properties of piezoelectric material are used in this sort of detecting. Quartz is the most customarily used piezoelectric since it is unassuming, can be taken care of to yield single valuable stone and can withstand creation, warm and mechanical weight; regardless, there is report that lithium niobate and lithium tantalate can also be used. A current survey has demonstrated that this strategy is exceptionally engaging when coordinate with Microelectromechanical frameworks (MEMS) for biosensing application. [44] Moreover the audit expresses that this kind of transduction is appropriate for touchy, compact and constant biosensing. Piezoelectric transducer has been broadly connected and grasped for immunosensing application. [45-47] Some report recommends that the piezoelectric transducer is sensible for DNA and protein recognizable proof with revelation purpose of constrainment of 1 ng/cm2. [48] A few articles have show up in the writing detailing the utilization of piezoelectric sensor in different application, for example, cholera poison indicative location, hepatitis B, hepatitis C, sustenance borne pathogen recognition and so forth. [49-52] More importantly, it was revealed that piezoelectric is astoundingly sensitive strategy, seeing that a revelation limit of 8.6 pg./l was procured for hepatitis B disease DNA and 25ng/mL for cholera harm area. The favourable circumstances utilizing this sort of transduction are the continuous checking, mark free recognition and straightforwardness of utilization.[53] Be that as it may, there are a few downsides need to defeat, for example, specificity, affectability and in addition obstruction decrease. [54] Likewise, this kind of transducer strategy includes organization and alignment necessity. [55] A current audit by Kim et al. 2011 has survey the guideline and use of nano symptomatic for nanobiosensor. The survey likewise finished up, that application scope of the quartz precious stone has been bit by bit extended, new estimating systems that utilization the quartz gem as a transducer for synthetic sensors and biosensors has been additionally created. [56]

7] DNA Biosensor

The classification of biosensors utilized for DNA discovery is otherwise called biodetectors. The objective is to disengage and measure the nature of single DNA– DNA or immune response antigen bonds, which along these lines has any kind of effect in recognizing and depicting single particles of DNA or antigen. The use of nucleic acids progression for the specific diagnostics application has made since the mid-1953 and up 'til now growing by and large. [57] The astoundingly specific proclivity limiting's reaction between two single strand DNA (ssDNA) chains to shape twofold stranded DNA (dsDNA) is utilized as a part of nucleic acids-based biosensor which designate the nucleic acids as common affirmation segment. This technique has advanced the improvement of DNA based sensor from the conventional technique, for example, coupling of electrophoretic detachments and radio isotropic which are high cost, perilous, tedious and so on. [58] This biosensor working foremost depends on acknowledgment of the corresponding strand by ssDNA to frame stable hydrogen bond between two nucleic acids to end up dsDNA. In request to accomplish this, an immobilized ssDNA is utilized as test in bioreceptor which the base grouping is correlative to the objective of intrigue. Presentation of focus to the test which brings about hybridization of correlative ssDNA to shape dsDNA will bring about creating biochemical response that permits transducer opened up the flag into electrical one. In this manner, writing demonstrates that the present of some linker, for example, thiol or biotin is required in the push to immobilize the ssDNA onto the detecting surface. [59] An imperative property of DNA is that the nucleic corrosive ligands can be denatured to invert authoritative and the recovered by controlling cushion particle fixation. [58] The nucleic corrosive natural acknowledgment layer which consolidates with transducer is effectively synthesizable, profoundly particular and reusable after warm dissolving o the DNA duplex. [60] Furthermore,

this biosensor has an exceptional specificity to give expository instruments that can gauge the nearness of solitary particle animal categories in a complex blend. [61] DNA based biosensor has potential application in clinical indicative for infection and malady recognition. [62-64] In any case, electrochemical transduction is most desert technique used to examining DNA harm and connection which revealed in writing. The improvement of electrochemical DNA biosensor has gotten an incredible arrangement of consideration recently and this has generally been driven by the need to created fast reaction, high affectability, great selectivity and exploratory accommodation. As electrochemical gadgets are extremely helpful for succession particular bio-detecting of DNA. The scaling down of gadgets furthermore, propelled innovation makes them brilliant device for DNA diagnostics. Recognizable proof of electrochemical DNA hybridization all the more frequently excludes checking a current at settled potential. Electrical modes were made for area of both name free and named objects. [65-76] The Fixation of the nucleic destructive test onto the surface of transducer expects a focal part in the general execution of DNA biosensors and quality chips. [77-79] The immobilization step requires a specific depicted test introduction similarly, open to the objective transducer, diverse techniques can be utilized for connecting the DNA test to the strong surface, for example, the utilization of thiolated DNA test for self-gathered monolayers (SEM) onto gold transducers by covalent linkage to the gold surface through practical alkanethiol-based monolayers. The other strategy for connection of DNA test is to biotinylate DNA test and connection through biotin-avidin communication on terminal surface. [65-66,80-81] The avidin altered polyaniline electrochemically stored onto a Pt plate terminal for coordinate identification of E. coli by immobilizing a 5' biotin named test utilizing a differential heartbeat volta metric strategy in the nearness of methylene blue as a DNA hybridization marker. [82] Similarly, electrochemical DNA biosensor in light of polypyrrole-polyvinyl sulfonate covered onto Pt plate terminal was additionally manufactured utilizing biotin-avidin restricting. The revelation of carbon nanotubes (CNTs) in DNA examination plays a critical part by advancement of electrochemical DNA biosensor. CNT empowers immobilization of DNA atoms as well as utilized as effective speaker to enhance flag transduction of hybridization. CNT additionally fills in as novel pointer of hybridization. The use of exhibited CNT into DNA chip requires little measure of test and advancement of CNT construct biosensor assume real part with respect to DNA based diagnostics in clinics or at home. [83] The learning of peptide nucleic corrosive (PNA) has opened another look into region of DNA biosensors. PNA is a DNA copy in which the sugar phosphate spine is supplanted with a pseudo peptide. The hybridization and affirmation of most essential solution phase PNA can be expeditiously extrapolated onto the surface of transducer for maintaining the relationship with the framework of extraordinarily specific DNA biosensors. As such usage of surface kept PNA certification layers gives striking movement specificity onto DNA biosensors involving affirmation of single base confounds. The hybridization is usually distinguished by the expansion in current motion because of redox marker (that perceives the DNA duplex) or from other hybridizationinstigated changes in electro synthetic parameters (e.g. conductivity or capacitance). New redox markers, offering more prominent segregation between single strand (ss) and dsDNA. [84-85,67-68,70-71,86] The utilization of an entomb calators ferro cenyl naphthalene di-imide that ties to the DNA crossover more firmly than regular bury calators and shows little proclivity to the single-stranded test. [87] The electrochemical DNA biosensor might be named based what's more, labeled free.

8] Surface Plasmon Biosensor: -

Surface plasmon reverberation (SPR) biosensor use surface plasmon waves (electromagnetic wave) to recognize changes when the target analyte team up with biorecognition segment on the sensor. On an essential level, when the SPR biosensor is displayed to any movements, it will incite changes in the refractive record which used to measure or viewed the reaction. The SPR transducer is uniting with biomolecule/ biorecognition segment which see and prepared to participate with specific analyte. [88] Consequently when target analyte speak with the immobilized biomolecule on the sensor surface, it makes a modification in the refractive rundown at the sensor surface. [88] This, movements convey an assortment in the spread unfaltering of the surface plasmon wave and this assortment is measure to make examining. A spectrophotometer is used to check the maintenance

scope of test. There been different biorecognition component have been fuses with SPR biosensor, for example, protein, counter acting agent antigen, nucleic acids and compound. [89-93] A critical component of SPR biosensor is that it can give name free detecting without radioactive and fluorescence which makes it exceedingly appealing for continuous checking. [99-95] Moreover, the SPR based transduction can be utilized to and association without show any uncommon properties of fluorescence or trademark retention and diffusing groups. [96] Notwithstanding, a few reports propose that these technique has experience the ill effects of specificity due to non-particular association with biorecognition component which wrongly corresponded by these biosensors. [96] The SPR based transductions are not reasonable for examining little analytes. Since the mass of the material are measured by SPR related to the authority of the sensor's surface whereas small analytes (Mr 3 <1000) give little reactions. [97] The current changes in flag to clamor proportion have made it conceivable to quantify official of such little analytes. [97] SPR biosensors can adequately identify authoritative by atoms as little as around 2 kDa, yet littler particles create deficient changes in bound mass thus can't be specifically estimated satisfactorily. [98] To date, SPR has been broadly utilized as a part of principal organic examinations, wellbeing science investigate, sedate find, clinical conclusion and ecological and horticulture checking. [99] A few articles have showed up in the writing looking into the utilization of SPR based biosensor in pathogen and infection discovery. [100-101]

MARKETED BIOSENSOR

1] MRI Contrast Imaging: -

With the advancements in medical imaging technology and a higher prevalence worldwide, you might have become more familiar with one type of imaging technology known as magnetic resonance imaging (MRI) — and the value it offers to health care. You might be familiar with an MRI machine as a large, cylindrical piece of equipment generating a strong magnetic field around you. It creates highly detailed pictures of your body's soft tissue to provide your doctor with substantial diagnostic and prognostic information.

But, you might not be aware of the crucial role contrast plays in an MRI. MRIs are unique to other imaging methods like CT scans and x-rays because they could involve the use of gadolinium-based contrast agents (GBCAs) , which is a type of MRI contrast dye, to assist in adding clarity and decipherability to your MRI image.

If you need an MRI with and without contrast, and are looking to book your appointment at Envision Imaging, below you can learn more about this technology, its uses and benefits and more.

Brands name: - GE Healthcare, Siemens HealthCare's Philips Healthcare, and canon medical systems

Specification: -

Clinical Application	Whole body
Magnate Type	superconducting
Power Requirements	480 or 380/415
Cooling System Type	Closed-loop water cooled gradients

2] CT scan: -A computerized tomography (CT) scan combines a series of X-ray images taken from different angles around your body and uses computer processing to create cross-sectional images (slices) of the bones, blood vessels and soft tissues inside your body. CT scan images provide more-detailed information than plain X-rays do.

A CT scan has many uses, but it's particularly well-suited to quickly examine people who may have internal injuries from car accidents or other types of trauma. A CT scan can be used to visualize nearly all parts of the body and is used to diagnose disease or injury as well as to plan medical, surgical or radiation treatment.

Brands name: - siemens, Philips, GE, Toshiba

Specification: -

Scan Time:-	Scan Time should be 0.5 sec or less for full 360-degree rotation. Minimum slice thickness should be 0.675 mm or less
Pitch Factor (volume pitch):	freely selectable in auto mode and also manually variable between 0.5 to 1.5 or more. Specify all possible pitch selections.

3[Cardiac monitor: -

Cardiac monitoring is a way of watching the electrical activity of your heart to ensure it is working normally. Five small stickers, called electrodes, are placed on

your body. These are connected either to a small box (a telemetry box) or a large screen on the wall (a wall monitor).

Holter monitors continuously record your heart's activity for 12-24 hours, while event monitors can be worn for up to 30 days and are activated when there are serious rhythm disturbances or when you have symptoms. With both monitors, your heart rhythm is wirelessly transmitted to a monitoring centre for evaluation.

Brand name: -Omron Complete Wireless Upper Arm Blood Pressure Monitor + EKG, Eko DUO + EKG Stethoscope, BioCare 12-Lead ECG Machine, KardiaMobile 6L EKG

specification: -

Type of display	LED.
Display Size	12.1 inch
Input Voltage	220-240 V.
Accuracy	+/- 3 BPM
Number of Channels	2 Channels.
Temperature.	50 Degree C.
Calibration.	+/-1mV.
Sweep Speed.	25 mm/sec.

4] Pulse oximeter: -

A pulse oximeter is a device that is usually placed on a fingertip. It uses light beams to estimate the oxygen saturation of the blood and the pulse rate. Oxygen saturation gives information about the amount of oxygen carried in the blood. The pulse oximeter can estimate the amount of oxygen in the blood without having to draw a blood sample.

Most pulse oximeters show two or three numbers. The most important number, oxygen saturation level, is usually abbreviated SpO_2, and is presented as a percentage. The pulse rate (similar to heart rate) is abbreviated PR, and sometimes there is a third number for strength of the signal. Oxygen saturation values are between 95% and 100% for most healthy individuals, but sometimes can be lower in people with lung problems. Oxygen saturation levels are also generally slightly lower for those living at higher altitudes.

There are two categories of pulse oximeters: prescription use and over the counter (OTC).

Brand name: - Beurer PO30 Pulse Oximeter, Dr Trust Professional Series Fingertip Pulse Oximeter, BPL Smart Oxy Fingertip Pulse Oximeter, Hesley Pulse Oximeter Fingertip

Specification: -

Pulse oximeter - Battery life: lead acid battery; internal, rechargeable; fully charged in 6 hours. Approximately 4-5 hours of continuous use.

Display & indications: -	SpO2: 3-digit LED (light-emitting diodes) display, 10.9mm high. Pulse rate: 3-digit LED display, 10.9mm high. Pulse strength logarithmically scaled; 8 segments remain. Low-battery LED flashes when approximately 30min of battery life remains. Sensors: all reusable LED flashes to alert the operator to check the sensor placement. SpO2: Range 0-100% Accuracy: ±2% at 70-100%, ±3% at 50-69% Averaging: 4.8- or 16-pulse beat average. - Pulse rate: Range 30-254bpm - Accuracy: ±2% at 30-254bpm - Averaging: 8 or 16-second average.
Environmental specifications: -	: Operating temperature 0 to 40°C. Storage Temperature: - 40 to 75°C. Relative humidity: 10-95%, storage (non-condensing) 15-95%, operating. Unit presentation: 1 pulse oximeter with accessories

5] Ultra-sound machine: -

Ultrasound is sound with frequencies greater than 20 kilohertz.[102] This frequency is the approximate upper audible limit of human hearing in healthy young adults. The physical principles of acoustic waves apply to any frequency range, including ultrasound. Ultrasonic devices operate with frequencies from 20 kHz up to several gigahertz.

Ultrasound is used in many different fields. Ultrasonic devices are used to detect objects and measure distances. Ultrasound imaging or sonography is often used in medicine. In the nondestructive testing of products and structures, ultrasound is used to detect invisible flaws. Industrially, ultrasound is used for cleaning, mixing, and accelerating chemical processes. Animals such as bats and porpoises use ultrasound for locating prey and obstacles.[103]

Brand name:- Siemens, GE, Toshiba, Philips, Mindray, and Sonosite

Specification: -Type: Diagnostic ultrasound machine.

Imaging Modes:	B-mode (2D), M-mode, Doppler (color and spectral), 3D/4D Imaging
Frequency Range:	Typically 2-18 MHz for various applications

Transducers:	Multiple transducer probes for different purposes (e.g., linear, convex, phased array).
Display:	High-resolution LCD or LED monitor.
Connectivity:	USB, DICOM, Ethernet for data transfer.
Software:	User-friendly interface with various measurement and analysis tools.
Portability:	Portable or cart-based models available
Power:	Standard electrical outlet.

6] ECG Machine :-

An electrocardiogram (ECG) records the electrical signal from the heart to check for different heart conditions. Electrodes are placed on the chest to record the heart's electrical signals, which cause the heart to beat. The signals are shown as waves on an attached computer monitor or printer. Normal ECG values for waves and intervals are as follows: RR interval: 0.6-1.2 seconds. P wave: 80 milliseconds. PR interval: 120-200 milliseconds. An electrocardiogram (ECG) is a simple, non-invasive test that records the electrical activity of the heart. An ECG can help diagnose certain heart conditions, including abnormal heart rhythms and coronary heart disease (heart attack and angina)

Brand name :-BPL medical ,Contec , Philips , Bpl , Schillerecifi

Specification:

Number of Leads:	ECG machines can have varying numbers of leads, typically ranging from 3 to 12 leads. More leads provide a more comprehensive view of the heart's activity.
Sampling Rate:	The sampling rate determines how many data points are recorded per second. Common rates are 500 Hz or 1000 Hz, ensuring accurate waveform capture.
Display:	ECG machines feature a display screen to view real-time ECG waveforms. Some models may have touchscreen interfaces for ease of use.
Printing Capabilities:	Many ECG machines come with built-in printers to generate hard copies of ECG reports for medical records.
Connectivity:	Modern ECG machines often have connectivity options, including USB, Bluetooth, or Wi-Fi, for transferring data to electronic health records (EHR) systems.

7] Glucose monitoring device:-

A glucose meter, also referred to as a "glucometer",[104] is a medical device for determining the approximate concentration of glucose in the blood. It can also be a strip of glucose paper dipped into a substance and measured to the glucose chart. It is a key element of glucose testing, including home blood glucose monitoring (HBGM) performed by people with diabetes mellitus or hypoglycemia. A small drop of blood, obtained from slightly piercing a fingertip with a lancet, is placed on a disposable test strip that the meter reads and uses to calculate the blood glucose level. The meter then displays the level in units of mg/dL or mmol/L.

Since approximately 1980, a primary goal of the management of type 1 diabetes and type 2 diabetes mellitus has been achieving closer-to-normal levels of glucose in the blood for as much of the time as possible, guided by HBGM several times a day. The benefits include a reduction in the occurrence rate and severity of long-term complications from hyperglycemia as well as a reduction in the short-term, potentially life-threatening complications of hypoglycemia.

Brand name :-

Dexcom, Livongo, One Drop, Bigfoot Biomedical, Levels

Specification: -

Blood glucose is measured in	mmol/L (millimoles per litre) or mg /dL (milligrams per decilitre).
Normal range	4to 6 mmol/L or 72 to 108 mg /dL. Lab based testing is required for the appropriate diagnosis of diabetes mellitus
Impaired fasting glucose range	5.7 to 6.4 mmol/L or 100 to 125 mg/Dl

8] HB-Meter: -

A hemoglobinometer is an instrument used to determine the hemoglobin content of the blood by spectrophotometric measurement. Portable hemoglobinometers provide easy and convenient measurement, which is particularly useful in areas where no clinical laboratories are available.

A hemoglobinometer or haemoglobinometer (British English) is a medical device used to measure hemoglobin concentration in blood.[105] It can operate by spectrophotometric measurement of hemoglobin concentration. Portable hemoglobinometers provide easy and convenient measurement of hematological variables, especially in areas where clinic laboratories are unavailable.[106]

As per guidelines of National AIDS Control Organisation (NACO) for accurate results & mass screening, analysis using hemoglobinometer is a recommended method used for absorbance measurement of whole blood at Hb/HbO2/Isobestic point, based on microcuvette technology such as HemoCue 301[107] and Mokshit-Chanda-AM005A.[108]

Specification: -

Measurement Range:	HP meters typically have a specific range for measuring horsepower, often expressed in horsepower (HP) or kilowatts (kW).
Accuracy:	These meters have a specified accuracy level, which indicates how closely they can measure the true horsepower output.
Display:	They usually feature a digital or analog display to show the measured horsepower in real-time. Input Types: HP meters can be designed for various input types, such as electrical or mechanical, depending on the application.
Mounting:	They may come in different form factors, including handheld devices or panel-mounted meters.
Calibration:	Calibration procedures and intervals may be specified to maintain accurate measurements.

9] Spectrophotometer :-

Spectrophotometry is a method to measure how much a chemical substance absorbs light by measuring the intensity of light as a beam of light passes through sample solution. The basic principle is that each compound absorbs or transmits light over a certain range of wavelength. This measurement can also be used to measure the amount of a known chemical substance. Spectrophotometry is one of the most useful methods of quantitative analysis in various fields such as chemistry, physics, biochemistry, material and chemical engineering and clinical applications.

A spectrophotometer is an instrument that measures the amount of photons (the intensity of light) absorbed after it passes through sample solution. With the spectrophotometer, the amount of a known chemical substance (concentrations) can also be determined by measuring the intensity of light detected. Depending on the range of wavelength of light source, it can be classified into two different types:

- UV-visible spectrophotometer: uses light over the ultraviolet range (185 - 400 nm) and visible range (400 - 700 nm) of electromagnetic radiation spectrum.
- IR spectrophotometer: uses light over the infrared range (700 – 15000 nm) of electromagnetic radiation spectrum.

● Specification:

Wavelength Range:	• Spectrophotometers can have different wavelength ranges, typically from ultraviolet (UV) to visible (VIS) and sometimes into the near-infrared (NIR) spectrum. Common ranges include 190-1100 nm.
Light Source:	• They often use a light source such as a tungsten lamp, deuterium lamp (for UV), or xenon flash lamp. Some advanced models use LEDs or laser diodes.
Detector:	• Detectors can be photodiodes, photomultiplier tubes (PMTs), or charge-coupled devices (CCDs) depending on the model. CCDs are common in modern instruments due to their sensitivity and ability to capture an entire spectrum simultaneously
Resolution:	• Spectrophotometers can have different resolution capabilities, which define how finely they can distinguish wavelengths. Higher resolution instruments provide more precise data.

1.APPLICATIONS IN CANCER TREATMENT: -

Tumor physiology differs markedly from normal tissue physiology. The microenvironment of tumor tissues is associated with areas of O2 depletion, mild acidity, high GSH concentration, and elevated level of hyaluronidase, which can serve as endogenous stimuli. Many bio-responsive drug delivery systems involving pH-, redox-, enzyme-response, and the expression of tumor associated markers (e.g., miRNA, nucleolin) have been described, which show a high potential for cancer treatment [109]. For example, tumor cells show an exaggerated demand for glucose to meet their energy demand for growth compared to normal cells. Glucose oxidase (GOx, which specifically catalyzes beta-D-glucose oxidation into gluconic acid and hydrogen peroxide (H2O2) by using molecular oxygen as an electron acceptor) has thus been strategically studied for noninvasive cancer diagnosis and therapeutics by biosensing glucose levels by measuring the oxygen consumption, pH changes, or production of H2O2 associated with drug release. GOx

has also been combined with other enzymes, hypoxia-activated prodrugs, photosensitizers, or Fenton's reagents to generate multi-modal synergistic cancer therapies [110]. The biosensing integrated drug delivery systems reported for cancer will be described in this section.

3.1. Stimuli-Responsive Polymers

Stimuli-responsive polymers act as an essential constituent of nanoscale sensor-like delivery platforms and have been most extensively explored in the case of cancer. Various chemical (different redox potential of redox couples such as glutathione/glutathione disulphide), physical (temperature and pH), and biological cues (e.g., enzymes, adenosine 5 0 - triphosphate (ATP), and nucleic acids) specific for the tumor microenvironment (TME) have been used to stimulate these polymers to deliver their payload, which will be the focus of this section.

3.1.1. Gox-Based Systems

The presence of gluconic acid because of GOx-catalyzed glucose oxidation increases the acidity of TME; this increase can be used to construct pH-sensitive and glucose-sensitive drug delivery systems. Wang et al. [111] described a self-degradable microneedle patch for the delivery of anti-PD-1 (programmed death-1 pathway). The microneedle was composed of biocompatible hyaluronic acid (HA) integrated with pH-sensitive dextran nanoparticles that encapsulated the anti-PD-1 and GOx-CAT (catalase) enzyme system. GOx in the microneedle converted glucose to gluconic acid to generate an acidic environment, which promoted the self-dissociation of nanoparticles and the release of anti-PD-1. CAT assisted glucose oxidation by the regeneration of O2 and helped consume undesired hydrogen peroxide (H2O2). The patch described by the authors could painlessly penetrate the epidermis and become submerged in the interstitial fluid to efficiently deliver its payload to the tumor microenvironment. In vivo studies using mouse models with melanoma showed that a single administration of the microneedle patch inhibited tumor growth superior to those obtained with intratumor injection of the same dose. Su et al. [112] described glucose oxidase (GOx) triggered gelation of N-hydroxyimide–heparin conjugates to form enzyme-responsive hydrogels for cell-specific drug delivery. N-hydroxy-5-norbornene-2,3- dicarboximide (HONB) can be reduced by D-glucose in the presence of GOx, forming a carbon-centered radical. In this work, the heparin-HNOB conjugate anchored to doxorubicin (DOX) was subjected to GOx mediated polymerization to form a hydrogel at room temperature. Heparin is a highly sulfated polysaccharide belonging to the glycosaminoglycan (GAG) family. Depending on the concentration of heparinase (associated with tumor angiogenesis and metastasis), the DOX bound heparin chain encapsulated in the hydrogel could be cleaved. Close to 46% of the drug release within 60 h was confirmed in the presence of 5 U/mL of heparinase, whilst no release was observed from the control gel. Cell toxicity was analyzed in three cell lines (HeLa, HepG2, and NIH-3T3) and presented positive results in all three cases. Hep (DOX)SN (drug-loaded gel) was able to release the drug in a cell-specific manner by responding to the environmental levels of heparinase. The platform described by the authors could be used to target cancer cells overexpressing heparinase. The use of this gel also minimized the adverse effects of premature drug release on normal cells. These enzyme responsive hydrogels have the potential to serve as smart, multifunctional platforms for targeted cargo and regenerative medicine

2. APPLICATONS IN DIABETES

One of the most recognized diseases worldwide is diabetes. There are currently almost half a billion individuals globally with this disease and this is expected to crest three quarters of a billion by the end of the decade [113]. Traditionally, diabetes is broken into three categories: Type 1 (previously referred to as juvenile); Type 2 (occasion defined as adult onset), and gestational diabetes [114]. Gestational diabetes occurs in ~2–10% of pregnant women with roughly 50% of these cases leading to the mother developing T2D after giving birth [115]. Generally, 5–10% of cases of diabetes are of the T1D form with the remaining 90–95% having T2D [115]. The need to monitor blood glucose, whether for T1D or T2D, is vital for the health and welfare of those afflicted with these diseases. Equally, if not more important, is the need to administer the necessary drug once the knowledge of one's blood glucose is determined. It is this key second part that has led to significant efforts and ultimate successes in bringing closed-loop systems for diabetes management to market.

2.1. Urine-Glucose Testing

Between the 1920s and 1960s, a patient's urine was the only means by which to gauge one's blood glucose. This required taking a few drops of urine and mixing in with Benedict's solution to yield a bright red precipitate as an indicator that there was glucose in the sample

Beyond the lack of practicality of this approach, which was improved on with the "dipstix" [116], it was still only a proxy for blood glucose levels. Currently, there are a number of urine-glucose tests available commercially. However, the technology has its limitations, primarily, it is still simply a proxy for blood glucose. A recent report highlighted this issue, whereby the urine-glucose test was only 14% selective and even failed to identify ~16% of participants with diabetes [117]. A benefit that should not be overlooked with urine-glucose testing is the lack of potential infections that have been reported, albeit minimally, with blood glucose [118]. In developing countries, where blood transmitted pathogenic disease is more prevalent, the cost associated with the lancets themselves are a significant hurdle.

2.2. Blood Glucose Testing

In 1964, Dextrostix, by the Ames-Miles Laboratories, was developed as the first blood glucose test strip [119]. Similar to its predecessor, this approach utilized a colorimetric change, albeit enzymatically. Taken from Clinistix, which was developed in the 1940s, this double sequential enzymatic reaction proceeded by the initial conversion of glucose to gluconic acid (which is in equilibrium with gluconolactone) by glucose oxidase, which also yielded hydrogen peroxide [119]. The hydrogen peroxide acted as a reagent in the oxidation of *o*-toluidine, which was facilitated by peroxidase. The major advance with Dextrostix was the ability to trap the red blood cells by a semipermeable membrane to prevent interference. For its time, it was a revolutionary technology. However, by today's standards, it would be considered somewhat archaic. In addition to requiring 1 min and a relatively large blood sample (30 μL), the results were gauged by the patient's interpretation of a colorimetric change [119]. Fortunately, over the past decades, significant advances within nanotechnology have allowed for the self-monitoring of blood glucose to become a more manageable, less invasive, and expeditious process.

The most instrumental advancement with regard to blood glucose monitoring was the nanotechnology approach for both the creation of enzyme-based circuitry and the miniaturization of the necessary electrodes for the detection of an electrochemical oxidation/reduction potential. Unlike Dextrostix, the majority of today's blood glucose detection devices employ a single enzymatic reaction. With just a single drop of blood, the glucose held within is reacted with a nanolayer of glucose oxidase that is complexed with its redox cofactor, flavin adenine dinucleotide (FAD) [120,121]. In this process, the glucose is oxidized to gluconolactone while the glucose oxidase-flavin adenine dinucleotide (GO_x-FAD^+) is reduced to GO_x-$FADH_2$. Upon the regeneration of GO_x-FAD^+ by the reaction with O_2, also held within the blood, hydrogen peroxide (H_2O_2) is produced. The aforementioned nanolayer of GO_x-FAD^+ is coated on a silver working electrode surface. Thus, when the generated H_2O_2 is oxidized to $2H^+$ and O_2, the corresponding amperometric signal can be correlated with the initial glucose concentration [120,121]. Although this first-generation electrochemical detection technology still dominates the blood glucose monitoring industry, three new generation of devices have been developed

4. APPLICATIONS IN CARDIOVASCULAR DISEASES

Despite the steady developments in invasive cardiovascular interventions and pharmacological therapies, cardiovascular diseases (CVD) remain responsible for the majority of deaths worldwide. The term CVD covers a number of disorders of the circulatory system including atherosclerosis, thrombosis, and their clinical manifestations such as acute coronary syndrome, stroke, peripheral arterial disease, and venous thrombosis. On-demand drug delivery represents an important step toward the development of disease-targeted personalized therapies. Stimuli-responsive drug delivery systems offer the advantages of the disease site-specific treatment localization and a controlled drug release in the affected region, thus reducing off-target effects. Although the stimuli are commonly classified in three categories, namely physical, chemical, and biological, it is necessary to distinguish between the external stimuli (such as light, ultrasound, magnetic or electrical field) and intrinsic stimuli (usually chemical

and biological, related to ionic strength, pH, or enzymatic reactions, but also biomechanical forces). The latter stimuli, being independent of an external trigger and having a higher sensitivity toward pathologic processes, are of particular interest in the biomedical field. Thus far, several stimuli-responsive drug delivery approaches to CVD have been reported including pH-, redox-, hypoxia-, and enzyme-responsive particles, polymers, or hydrogels. This review highlights some of the recently reported "smart" biosensing systems with therapeutic potential in CVD.

4.1. PH-Dependent Drug Delivery The pH of the tissues is an important chemical parameter, changes of which are often related to the disease process. Consequently, this parameter can be exploited for phasetransition in polymer-based drug delivery systems in specific microenvironments or tissue affected by pathological processes. In line with this, DNA-based nanotubes were utilized as a drug carrier system for the pH-dependent delivery of dexamethasone [122]. The nanotubes loaded with glucocorticoid-conjugated oligonucleotides were rapidly internalized by mouse macrophages in vitro, and thanks to the presence of the pH-sensitive i-motif sequence, released dexamethasone in an acidic environment of the end lysosomal compartment. Compared with free dexamethasone, DNA-dexamethasone nanotubes significantly reduced the TNF-α expression in the LPS-stimulated macrophages in vitro. In a mouse model of ischemia-reperfusion, the administration of DNA-dexamethasone nanotubes into the post-ischemic muscle tissue led to reduced leukocyte transmigration and decreased the expression of the endothelial adhesion molecules.

4.2. Hypoxia-Sensing Drug Delivery Systems

Hypoxia is a driving mechanism of cell death in the ischemic tissues. On-demand drug delivery in response to hypoxia thus represents a promising approach to the treatment of myocardial ischemia. An interesting example of hypoxia-sensing drug delivery inspired by mitochondria was recently reported [123]. The double-shell poly (lactic-co-glycolic acid) (PLGA) nanoparticles contained melatonin to scavenge reactive oxygen species (ROS) and prevent apoptosis by activating mitochondrial melatonin receptor I to inhibit cytochrome c release. As a biological oxygen-sensing mechanism, circular DNA was incorporated on the surface of the particles by electrical adsorption. Oxygen-responsive vascular endothelial growth factor (VEGF) expression was realized by binding hypoxia-inducible factor-1α (HIF-1α) with erythropoietin enhancers and was shown to respond to alternating hypoxia– normoxia conditions by up- and downregulating the reporter expression. In a mouse model of myocardial infarction, these particles reduced cell death due to ischemia, improving the structural and functional capacity of the infracted hearts.

4.3. Reactive Oxygen Species-Responsive Drug Delivery

Atherosclerosis and its clinical manifestations including myocardial infarction, ischemia/reperfusion, or stroke are associated with an excessive generation of ROS. ROS have been implicated in the ischemic organ injury by inducing cell damage and apoptosis, but the systemic administration of exogenous antioxidants has proven to be ineffective against oxidative stress-induced injury. In the search for improved strategies of antioxidant delivery and ROS-sensitive targeting, several approaches have been reported. In a study by Li et al. [124], ROS-responsive nanoparticles produced of poly (ethylene glycol) (PEG) and poly (propylene sulphide) (PPS) were used for the encapsulation of a potent plant antioxidant, ginsenoside Rg3 (Rg3). Upon the exposure to ROS, Rg3-loaded PEG-b-PPS nanoparticles injected in the infarcted rat myocardium released Rg3, which improved the cardiac function by reducing the oxidative stress, inflammation, and fibrotic processes via the FoxO3a-dependent mechanism. Another type of ROS-responsive theranostic nanoplatform was developed by Ma et al. in order to detect and treat atherosclerotic plaques. Using a ROS-responsive bond, a fluorophore activated by two-photon aggregation-induced emission was linked to βcyclodextrin. The system was loaded with prednisolone via supramolecular interaction and packed into nanosized micelles based on a ROS-sensitive copolymer poly (2- methylthioethanol methacrylate)-poly (2-methacryloyloxyethyl phosphorylcholine). The resulting micelles, termed TPCDP@PMM, have been shown to accumulate in the atherosclerotic plaques of ApoE−/− mice and disrupt upon contact with ROS, leading to prednisolone release and atherosclerosis inhibition ROS-sensing drug delivery systems have also been developed for the treatment of stroke, which is

responsible for about 10% of deaths worldwide and is a major cause of long-term disability. To achieve the specific targeting of a neuroprotective agent, NR2B9C, to the ischemic site, and improve the controllability of drug release, Lv et al. [125] produced a ROS-responsive nanocarrier. NR2B9C was loaded into dextran cores modified with

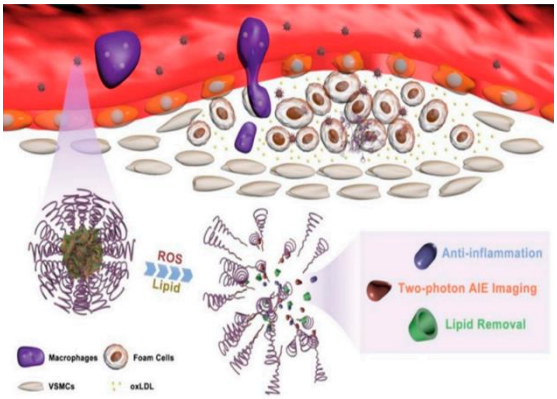

Fig: - [2]

The ROS-responsive polymeric micelles release prednisolone in the lipid-rich environment of atherosclerotic plaque and allow for two-photon aggregation-induced emission imaging. Reproduced from Ma et al. [126], Open Access.

Targeting of the nano system was realized by inserting a stroke homing peptide (CLEVSRKNC) into the shell composed of the erythrocyte membrane [125]. In vitro, the nanocarriers underwent a rapid hydrolysis in the presence of H2O2 and had strong protective effects against glutamate-induced cytotoxicity in the rat adrenal pheochromocytoma cell line PC-12. In a rat model of middle cerebral artery occlusion, ROS-sensing nanoparticles improved the active targeting of NR2B9C to the ischemic area and reduced ischemic brain damage. The ROS-responsive polymeric micelles based on PEG-poly (tyrosine-ethyl oxalyl) (PEG-Ptyr-EO) that respond to the oxidative microenvironment of atherosclerotic plaques were also described [127]. The hyaluronic acid (HA) coating was designed to target CD44- positive inflammatory macrophages. In the presence of ROS, PEG-Ptyr-EO released simvastatin loaded into the particles to reduce the activation of plaque macrophages and additionally contributed to ROS consumption, thus diminishing the oxidative stress. Intravenous administration of ROS-responsive simvastatin-loaded micelles in a mouse model was shown to reduce the plaque cholesterol content and the burden of atherosclerosis.

4.4. Enzyme-Responsive Drug Delivery

Apart from oxidative stress, the microenvironment of atherosclerotic lesions and myocardial infarct tissue is characterized by an increased protease activity. This feature can be utilized to specifically deliver drugs to the regions with increased enzymatic activity if a cleavable, enzyme-responsive linker is introduced to the system. Wang et al. [128] reported a siRNA delivery system that responded to local upregulation in proteolytic activity after myocardial infarction. An injectable shear-thinning and self-healing hydrogel was composed of HA modified with hydrazides or aldehydes and combined with peptide crosslinkers that degrade in response to protease activity. HA was further modified with β-cyclodextrin to sequester cholesterol-modified siRNA against matrix metalloproteinase 2 (MMP2), which was implicated in adverse remodeling after myocardial infarction. In response to protease activity, the hydrogel eroded, releasing siRNA, which effectively silenced MMP2 expression in the cardiac fibroblasts in vitro. Compared to the hydrogels with the control siRNAs, the protease-sensing siMMP2 hydrogel led to significantly increased ejection fraction, stroke volume, and cardiac output in a rat model of myocardial infarction (MI). In parallel, it provided an improved mechanical support to the infarcted heart through reduced hydrogel erosion upon the silencing of MMP2, improving the myocardial thickness in the infarct at 4 weeks post-ischemic injury. An interesting example of combining two distinct biological stimuli for the control of the drug delivery to atherosclerotic lesions was reported by Peters et al. [129]. The authors utilized peptide amphiphiles (PAs) to develop nanocarriers that sensed the increased levels of MMP2, MMP9, and ROS. To this end, the apolipoprotein A1-mimetic peptide was bound to PAs by peptide linkers cleaved by MMPs or ROS. The efficacy of the nanocarriers was tested in vitro on macrophages challenged with interferon gamma or lipopolysaccharide, showing the release of the ApoA1-Ac2–26 peptide and reduced macrophage activation. A dual drug/siRNA delivery system responding to hyaluronidase type II (Hyal-2) was also reported [130]. The designed PLGA nanocarriers encapsulated atorvastatin to control lipid trafficking and reduce inflammation and siRNA against lectin-

like oxidized low-density lipoprotein receptor-1 (LOX-1). The particle cores were clad in three external layers: an innermost lipid bilayer, an intermediate apolipoprotein A1 layer for macrophage targeting, and an outer layer of high molecular weight HA (200 kDa). The outer layer allowed CD44-dependent targeting, and upon Hyal-2 cleavage, led to exposure of the intermediate ApoA1 layer for enhanced entry into the macrophages. The efficacy of this dual-therapy nano system was demonstrated in atherosclerotic mice upon 12-week biweekly administration, showing a significant decrease in plaque size as well as reduced lipid and macrophage accumulation

CONCLUSION

In conclusion, the integration of biosensors into drug monitoring systems is poised to usher in a transformative era in the realm of biomedical applications. This innovative approach holds the promise of revolutionizing healthcare and patient management by combining state-of-the-art biosensor technology with drug monitoring capabilities. First and foremost, biosensor integrated drug monitoring systems offer the potential for highly personalized healthcare. By continuously and non-invasively monitoring a range of physiological parameters and drug concentrations within the body, these systems empower healthcare providers with real-time data. This data-driven approach enables the tailoring of treatments to individual patient needs, leading to more effective and precise interventions. Patients with chronic conditions, in particular, stand to benefit significantly from this approach, as it can lead to improved management of their health, potentially reducing hospitalizations and enhancing their overall quality of life. Additionally, the remote monitoring capabilities of biosensor integrated systems are a game-changer. Data collected by biosensors can be transmitted securely to healthcare professionals, allowing for continuous surveillance of patient health. This feature is invaluable, especially in the context of telemedicine, as it can bridge geographical gaps and provide timely medical interventions. It's a boon for both patients and healthcare systems, as it can alleviate the burden on hospitals and clinics, improving the overall efficiency of care delivery. Beyond its impact on patient care, biosensor integrated drug monitoring systems also hold significant promise in drug development. These systems can streamline the process of testing new medications by providing real-time data on how drugs interact within the human body. This not only expedites drug development but also enhances the safety and efficacy assessment of pharmaceuticals. The result is a potential reduction in the time and cost associated with bringing new medications to market, which can benefit both the pharmaceutical industry and patients eagerly awaiting innovative treatments. In a broader context, the integration of biosensors with drug monitoring systems exemplifies the ever-increasing importance of technology in healthcare. It signifies a shift towards more patient-centric, data-driven, and accessible medical care. As this approach continues to mature and evolve, it has the potential to improve health outcomes, reduce healthcare costs, and enhance the quality of life for individuals around the world. Biosensor integrated drug monitoring systems are indeed a promising and groundbreaking development in the field of biomedical applications.

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