Review Article

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A Review Of Smart Contact Lenses For Biological Applications

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1. Abstract

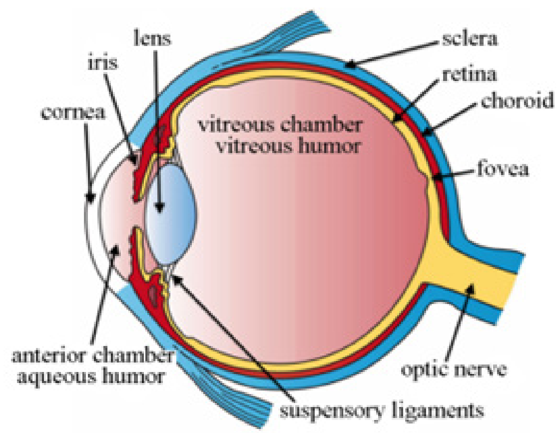
Contact lenses are used to correct eye defects such as farsighted ness, myopia, presbyopia and astigmatism. Recently, biosensors and contact lenses are used as an excellent platform for diagnosing eye diseases and drug delivery. In this research, a history of the development of lenses, types of manufacturing methods, biomaterials and their characteristics, the use of lenses in drug release, UV light reflection, focal length adjustment and antibacterial lenses, existing challenges and a look for future applications of this type. The lenses are covered.

2. Keywords:
Smart contact lenses, eye, drug delivery, light, eye defects.

3. Introduction

The sense of sight is the most important sense in humans, so that 30% of human brain cells are involved in the processing of visual information [1]. The eye is the organ of human vision. The structure of the eye lens is convex and is placed inside a bony cavity called the eyeball and is protected from the outside by the upper and lower eyelids. While the eye is placed inside the eye socket, it is surrounded by a layer of fatty tissue, which of course, the membrane surrounding the eye ball separates it from this fatty tissue, and thus the movements of the eyeball are made more easily accept [1]. The structure and anatomy of the eye is shown in Figure 1.

Figure 1: Eye structure and anatomy [1].



The principles of optics are that light rays are reflected when passing from one environment to another environment with different density, except when they meet perpendicularly to the surface of the interface between the two environments. Parallel rays of light strike a convex lens and are reflected, then converge or converge to a point behind the lens (primary focus). The principal focus is located on a line that passes through the center of curvature of the lens and is called the principal axis. The main focal length refers to the distance from the lens to the focal point. For practical purposes, light rays striking the lens from an object at a distance greater than 6 m are considered parallel. The rays that are reflected from the object with a distance less than 6 m are divergent and converge on a point on the main axis at a distance far from the main focus. Concave lenses cause the parallel rays of light to move away from each other. The retina is the first part that receives visual information. The structure of the sclera changes as the protective layer of the eyeball in front and the cornea becomes transparent and light enters the eye through it. The structure of the retina is shown in Figure 2. The point that can be taken from the figure is that when light shines on the eye, it must pass through other cells to reach the photoreceptors, which are located in the last, deepest and farthest layer of the retina from the surface of the eye, and this issueIt can cause refraction of light and reduce the power and accuracy of vision.

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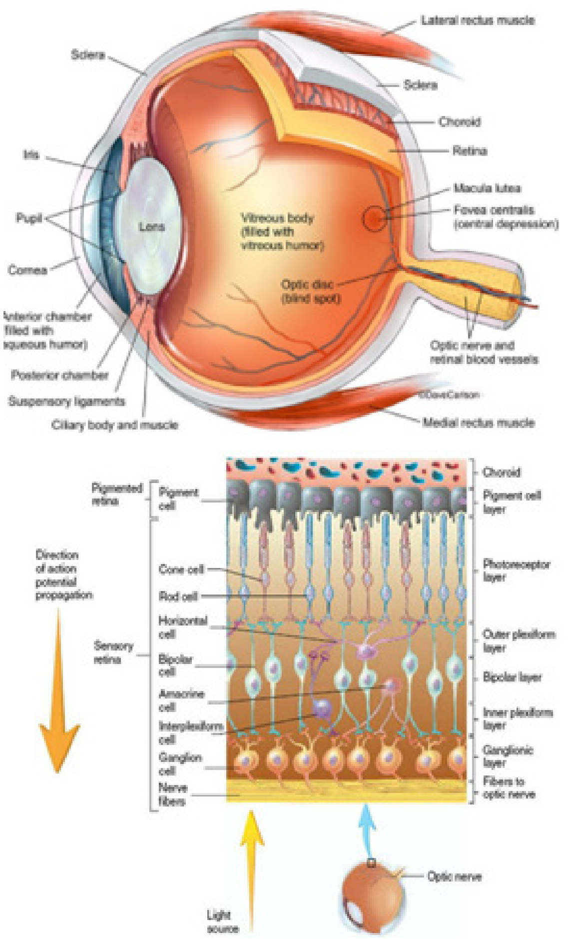
Figure 2: The structure of the retina and the way light passes through the eye [2].



Incorrect refraction of light in the eye causes us to not have a clear and real view of objects. There are usually four types of defects that are related to the incorrect refraction of light in the eye. These defects are:

- **Farsightedness:** The focus of the rays that enter the eye is formed behind the retina.
- **Myopia:** The focuses of the rays that enter the eye are formed in front of the retina, but because eventually a non-focal image is formed on the retina and a clear image is not formed.
- **Presbyopia:**Usually occurs due to the hardening of the lens and also the limitation of the space in which the lens can change its shape.
- **Astigmatism:** Usually there is no single focus [1].

In order to remove these defects and to see objects clearly, auxiliary lenses (glasses, lenses) should be used. The methods of making lenses and using them as an environment for the release of drugs and biosensors are mentioned.

4. Eye Lens Engineering

4.1. Introduction to the History of Lenses

The history of making lenses goes back to the end of the 18th century. British and John presented a design of the lens in 1832. The first glass eye lenses were made in 1887. The first polymer lenses using polymethyl methacrylate plastic were made in 1934 due to the durability, optical properties and lack of physiological activity of this material along with the ease of making it with existing methods. Polymer contact lenses were designed to cover the cornea of the eye in 1948, and finally in 1971, soft lenses were developed.

4.2. Types of Eye Lenses

Eye lenses are divided into two groups:

1. Contact lenses
2. Intraocular lenses

4.3. Contact Lenses

In these types of lenses, the main emphasis is on the development of materials with greater stability, more appropriate flexibility, more oxygen permeability and better biocompatibility. In general, it can be said that the raw materials of contact lenses must have the following characteristics:

1. To be biologically ineffective.
2. Have a strong adhesive force.
3. The friction between the surface of the lens and the tissue of the eye should be low.
4. It has good permeability to gases.
5. It does not lose its characteristics in the eye-friendly environment.
6. Do not stimulate the body's defense system.

It should also be noted that the polymer materials used in making contact lenses must have a high degree of purity. In terms of flexibility, lenses can be divided into three groups, which include:

1. Hard lenses
2. Flexible lenses
3. Soft hydrogel lenses.

Flexible and hydrogel lenses are considered as soft eye lenses, and based on this, the polymers used to make lenses can be generally divided into two groups, which are:

1. Hard materials
2. Flexible, soft and hydrophilic materials.

4.4. Intraocular Lenses

These lenses are used in eye surgeries and especially in cataract treatment. Recently, a new UV absorber has also been designed for such lenses.

4.5. Properties Affecting the Performance of Lenses

The most important properties that affect the performance of lenses are:

1. Density
2. Refractive index
3. The passage of light
4. Surface properties
5. Blue content
6. Dimensional stability according to heating time and elasticity
7. Mechanical properties

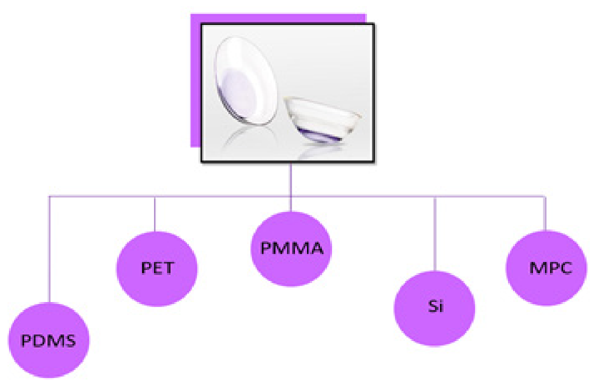
8. Permeability to oxygen
9. Compatibility with the eyes
10. Chemical stability and non-toxicity
11. Method and ease of sterilization

The importance of these issues varies depending on the type and duration of use [2].

4.6. Biomaterials used in Lenses

Different biomaterials (Figure 3) can be used to design and produce lenses. In medical applications, lenses made of hydrogel polyhydroxyethyl methacrylate, Silion (Si) are of special interest. For example, Ulu et al. used poly hydroxy ethyl methacrylate and boric acid lenses to treat eye infection [3]. Kazemi et al designed lenses for drug release using polyhydroxyethyl methacry late. Chitosan was used to modify the surface of the lenses. Antibacterial property was observed in these lenses [4]. Various biomaterials are used to make lenses, whose properties and characteristics are mentioned below.

Figure 3: Materials for making contact lenses.



4.7. Polymethyl Methacrylate (PMMA)

PMMA contact lenses were among the first eye lenses and were in the first instance created of glass and were widely used for a long time. Polymerization of PMMA is done in attendancea series of agents like ethylene glycol dimethyl acrylate to make hard contact lenses. Polymethyl methacrylate is used as an ideal material for making hard contact lenses due to its good features such as very good visual transparency, low light and electromagnetic wave deviation, good optical properties, no difficulty manufacturing and sterilization, weightless and small cost. They are also a hyaloid and durable ther moplastic biomaterial, but it has significant disadvantages such as hardness and lack of oxygen permeability, because if oxygen is not received on the surface of the cornea, the production of lactic acid increases and causes the cornea to swell, so these lenses Made of this material are only used for short periods of time. Today, these lenses are used less. The permeability to oxygen and other properties of PMMA can be improved by copolymerizing it with other monomers such as styrene or alpha-methylstyrene, and these materials have higher transparency and refractive index than PMMA alone.so, expansion in contact optical glass biomaterials with excellent O2 permeance differentiate to hard gas (RPG) biomaterials is needed [5]. Currently, PMMA is used as a substrate and coating in smart contact lenses due to its durability and ease of manufacture [5-7].

4.8. Polyethylene Terephthalate (PET)

PET is a thermoplastic homopolymer from the polyester family, which is created by a one-step polymerization method of reaction between pure terephthalic acid and ethylene glycol monomer. PET is a polymer that is exerted in almost all states to build polyester fibers (70%), bottle resin (22%), film (6%) and engineering polyester resins (2%), however in Iran this biopolymer is mostly used forIt is used to make all kinds of drinking bottles [8]. Polyethylene terephthalatehas nice chemical and thermal stability but has a little glass pass temperature (85°C), it is simple to thermally convert it into several films with intricate conformations [9]. In PET smart contact lenses, it lacks gas permeability and is very harderthan normal hydrogel substances, as a conclusion, inconvenience caused by lengthful-timeerosion and inflationingof the cornea may occur. That better biocompatibility, gas permeance and hydrophilic, Poly ethylene terephthalate together of Polydimethylsiloxane can be used to make sharp contact optical glass [6].

4.9. Poly (2-hydroxyethyl Methacrylate)

Polyhima for intraocular lenses is synthesized with emixture polymerization of 2-hydroxyethyl methacry late as crude substance, ammonium persulfate and sodium pyrosulfite as catalyst, and triethylene glycol dimethacrylate as cross-link increasable [8]. This polymer was make known as an artificial hydrogel with strength and mechanical and biocompatible properties suitable to contact optical glass utilizations [3]. They may distend non-aqueous dilutions and shape hydrogels. It should be noted that this type of polymer was also used in the first generation of soft contact optical glass. This polymer may be combined by other monomers to produce optical glass with unique properties. To instance, combined polyhydroxyethyl methacry late by methacry late and glyceryl methacry late for production hydrophilic hydrogels by top O2 permeance. Otto and co-workers prepared poly hydroxy ethyl methacry late for biological applications, which could absorb up to 40% water while being transpicuous [8].

4.10. Polydimethylsiloxane (PDMS)

In the structure of PDMS, two methyl groups are located on the silicon atom. PDMS is also known as dimethylpolysiloxane and dimethic one. PDMS is known as veryextensively used silicon-basis natural polymer due to its properties and versatility that result to it’s a lot of usages. Also, PDMS be an organosilicic polymer compound that is optically transparent and generally neutral, non-toxic and non-flammable [8] and has the properties of elasticity, transparency, biocompatibility and air permeability [10]. This polymer is one of the most widely used silicone- basis polymers. This polymer is used in biological tissues what need close touch. Because it has excellent biocompatibility [11]. Present intelligentcontact optical glassare usually manufactured using this polymer as a layer or coating material [12,13]. To instance, Hossein and colleagues produced an

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intelligent contact optical glassconsume this polymer. As a contact optical glassmaterial, this polymer not only places the recorder in a curved shape on the cornea, but also provides the patient with normal view [14].

5. Silicon

Silicone is one of the synthetic polymers that are often synthesized through a three-step process (chlorosilane synthesis, chlorosilane hydrolysis, and polymerization and condensation) using ring-opening polymerization. The main chain of this polymer includes oxygen and silicon atoms, and depending on the type of alkyl chain attached to the silicon atom, they will have different properties. The siloxane bonds in the main skeleton of this polymer are more stable than the carbon bonds, and therefore, silicone rubbers have unique thermal resistance, chemical stability, and insulating properties compared to organic polymers [8]. Si hydrogels are natural macromolecules which comprising the building ingredients from silicone rubber. In 1999, soft silicone hydrogel optical glasswere expanded. then many works were done on their surface hydrophilization [15]. O2 carrier in normal hydrogels beconfined into water canals, so O2 permeability mayjust be completed withadding water [16]. Si hydrogels possess H2O and siloxane channels that very much increase the oxygen permeance of contact optical glass [13]. These hydrogels have prominent features such as O2 permeability, translucence, biocompatibility, weak oxidation, for this reason, they are widely used [16].

6. Methacryloxyethyl Phosphorylcholine

MPC is a natural material by a phosphorylcholine category that is biologically ineffective. It is highly regarded in various medical usage because it is stable to protein absorption, cell adherence and blood coalescence [17,18]. Implantable blood pumps [19], artificial hip joints [20], and diagnostic systems [21] are among the applications of MPC. Shimizu and colleagues synthesized a silicone hydrogel. This hydrogel showed well elasticity, great optical transparency, great O2 penetrance and little protein attraction valence contrasted to tradflexible contact optical glass biomaterials. A biosensor for monitoring ophthalmic fluid glucose was also placed in these hydrogels [22]. chart 1 display the biomaterials used to prepare lenses along with their molecular formula and chemic building [13] and with the increment in the numeral of universal users using contact lenses, search on contact lenses bequickly improving and improving user comfort, breathability, biocompatibility and how to make them.It is developing. Overall, contact optical glass biomaterials must be lucid, hydrophilic, oxygen permeable, biocompatible, and mechanically soft [7].

7. Technology for the Manufacture and Analysis of Intelligentoptical Glass

7.1. Microliquids

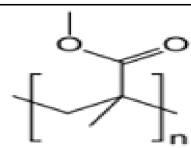
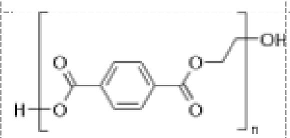
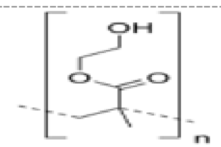
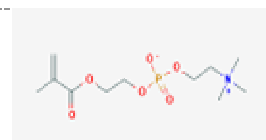
Microfluidic process includes the knowledge and technologic by systems inunified canals at micro scale, through which a small amount of liquid (typically from 10-9 to 10-18 L) can be controlled and systematically manipulated in designed shapes.to be Contact lens design due to the principles governing microfluids tooptical glass, tiny powers soliquid area energy, capillary force, vigor loss, resistor to liquids make the use of this method desirable. During blinking, tears cover level of the lens and because of capillary force, tears arrive the channels and thus they can be collected. The specifications of microliquids technology such as size, image, current rate should be improv for lens plan [28]. Wu et al. measured and presented a model to analyze fluid velocity and flow in intraocular contact lenses by directly integrating the internal channels of the sensor using MEMS technology. They used micro thermal sensors to measure the amount of liquids. The results showed that the deviation of the droplet movement path in the channels of contact lenses largely depends on the swelling of the microchannels [29,30].

7.2. Photolithography

Many microelectronic components and microchannels in smart contact lenses are made indirectly or directly by photolithography Technique. Photolithography is one method in which shapes are created using light transmitted of photomask in the areaby silicon wafer. The operation flow is explain In the following: one silicon wafer is spin-covered by monotonic slim layer from photoresist. A cover is often placed on the wafer to increase resistance to light adhesion. After manufacturing the pre-wafers and coating them to remove excess solvents, they are placed under an optical device that is similar to microcanalgeometry the optic projection machine, and with turning on the UV beam, a part of the coated wafer that is exposed to lightundergoes a chemical change. To increase the resistance of coated wafers that were exposed to light, a series of developers with specific chemical compounds were used [28].

7.3. Infusion Method

Infusion methodis procedurewith inject fused substances at the moled to make composites. Sections from Infusion method development are shown in Smart contact optical glasses may mass-Production in the Infusion method development, leading to expense reductions [28]. In 2009, Siegel designed a microdevice for making contact lenses using a mold to inject materials into it. This microdevice was called cofabrication, which could be an alternative to multilayer microfabrication. This method is adaptable to a variety of labconfigures. They usegadgets. they are minor costly toward multi-step tools to micro manufacturing. In addition, the method need salone little Level from a light-fast lawful and an expensive chemic to photolithography. Materials with high or down melting spots, fluid metals, fluid crystals, molten sodium chlorides, foams, gases, polymers, etc., which cannot be easily manipulated, can be easily changed after the production stage in this method. Removed and replaced. Also, for the production of contact lenses, after the material is injected into the mold, a kind of bond is created between the materials, and with conversion foreign statusfor example: temperature, radiation, etc, considering the operational efficiency and repeatability of this method, the cost of productionmuch can be reduced [31]. Lin et al. designed a sensor that is a non-invasive method to replace lactate measurement and calibration of continuous lactate contact lenses. L-lactate is significant biomarker to clinical assessment, measurement of O2 shortage, increased salt concentration because of intense practice. Tear drop have been identified non-invasive sampling perimeter to eschew the grievous and uncomfortable current blood experiment method for evaluateing lactate planes. Although, lactate oxidase is sensitive at fluctuations lack O2, causing incorrect lactate mensurationsin teardrop. A new tear lactate sensor was tested using lactate oxidase, which was recently released by protein engineering and

Materials	molecular formula	Chemical structure	Advantages/disadvantages	reference
PMMA	$(C_5H_8O_2)_n$		Outstanding optical properties, low oxygen permeability, high hardness and toughness.	[23]
PET	$(C_{10}H_8O_4)_n$		Low glass transition temperature, low hardness, low surface energy, hydrophobic, excellent chemical and thermal resistance.	[24]
PHEMA	$(C_6H_{10}O_3)_n$		Adjustable mechanical properties, relatively high water content, good thermal and chemical stability.	[25]
PDMS	$(C_2H_6OSi)_n$		Flexibility and high oxygen permeability.	[26]
MPC	$C_{11}H_{22}NO_6P$		Low protein absorption, good surface wettability, high oxygen permeability, low mechanical properties.	[27]

7.4. Shaping with a Mold

Shaping with a moldis popular simplest procedure for patterning hydrogel actuators on a large scale with different dimensions from cm to mm, but this method must be composed byanother techniques for make a special template toany desired geometric form [33]. For example, hydrogels can be used to make energy-inspired lenses because hydrogels can undergo rapid and reversible spontaneous deformation due to swelling and reduction of solution caused by pH changes. These hydrogels can be turned into rings, tubes, etc. by precisely modelling the geometric form and measure through the Shaping with a mold methods [34]. A 2016 study was conducted on active hydrogel actuators bywell compatibility, biodegrad ability for regenerative medicine. These hydrogel biostimulants were made from the two-layer structures of chitosan and cellulose-carboxymethyl cellulose solution in an aqueous alkaline urea system comprising epichlorohydrin as crosslinker and strong adherence among two sheets because of powerful electrostatic gravitation and chemic crosslinking. Double-layered hydrogels by well mechanic attributes can quickly return to their original state with pH changes and swelling, and thus designs with complex shapes and specific geometric sizes can be achieved. Layers of chitosan with positive charge and cellulose with negative charge change the swelling behavior of the hydrogel, and by applying sufficient force to the hydrogel, it can be used as soft receptors, smart capsules, and bioinspired lenses [35].

7.5. Soft Lithography

Soft lithography can create three-dimensional and layered microstructures on the surface except for the main microstructure of the surface. In addition, in the soft lithography process, broad Number of substances mayusedto create microstructures [28].

7.6. Lithography

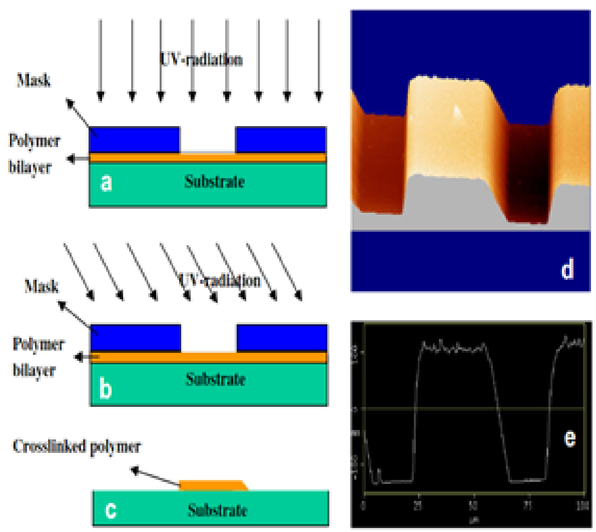
the initiative of the spot-contact transistor and need for littler and in expensiversemiconductor apparatuses, multiple momentous Technique process so lithography were quickly established. In addition, lithography method expending a rotation-covered polymer film substratum was also developed. In lithography procedure, first the desirable microstructure is created inside a resistant substrate, and then the favorable microstructure is transmissive to the bottom layerthrough processes such as etching, ion implantation, or the use of a wall. Depending on several kinds microstructure transition on the substrate, different types of lithography like uv-vis lithograph, full electron lithography, x-ray lithographare created. By using lithography, it is always possible to control and produce hollow enclosures bydetailed, repeatable format and gauge with self-folding actuators. By using rotating and inclined coating, very uniform polymer films with nm thicknesses can be created on the substrate [33]. Kumar et al designed a photolithographic route (Figure 4) to fabricate many number uniform and nice modality polymer microtubes.

eliminated oxygen interference [32].

Table 1: Molecular formula, chemical structures and material properties of typical contact lenses.

The significant facture for assign the size of pipes is their thickness. By increasing the thickness of the two layers, the diameter of the pipes increases. Kinetics of tube organization was studied according to solution acidity and UV dose. The amount of rolling augment by the acidity of the dilution. The diameter and rolling speed of the tube reduce by increasing UV exposure time. Microtubes have possibly useingwithin microfluidic machines and the string of biotechnology, in other words, they form self-rolling double-layer polymer microtubes [35].

Figure 4: Photolithography process and schematic method of a symmetric pattern formation. (a-c) exposed to UV radiation in a natural state, (b) sample exposed to UV light at a high incidence angle and (c) pattern development after washing of uncrosslinked polymer, (d) 3D AFM image of asymmetric polymer ribbons,and (e) AFM image section prediction [35].



7.7. Laser Ablation
Laser ablation is a method that is usually used in the fabrication of microfluidic devices, and in this method, elevated-severitylaser rayis used for specialpositions material so that the beam energy can be absorbed at the point of contact with the material destroy them. with shake the laser fount glow on under coat conforming kind of article, laser severity and wavelength, a microstructure is acquired. Thermic force created with laser some when remodels the chemical attributes area substance. One of the ways to overcome this problem is to use femtoseconds or CO2 laser [28].

7.8. 3D Printing Technology
3D printing (Figure 5) is a growing digital manufacturing method that benefits from precise computer-aided model control by complex actuators with less manufacturing time, less cost, and the least amount of waste materials [33].

Figure 5: 3D printing technology

7.9. Ionic Inkjet Printing
Ionic inkjet print as computer-aided print technology and ink is well consumed in daily job and in diurnal living.This process is used byexpansion computer-helping printing plansand equipment, traditional inkjet printin scientific fields as modern technology such as pattern substances for microfluidic analytic systems and print tissues such as pattern printing or complex cross-linking on hydrogel is placed [33].

7.10. Ionic Printing
Ion printing is another method for hydrogel patterning containing polyelectrolytes.Compared to inkjet printing, ion printing not only allows correction of the hydrogel at the external layer, but also causes variations in material volume, eventuate profound ion printing templates. The axiom of the ion printing procedure is based on the introduction of metal Positive ions to hydrogels through help electrical marks, and the ion regions printed by metal Positive ions excite the ionic cross-linking of metal Positive ions and polyelectrolytes, which leads toThe water content of the hydrogel and its volume are reduced.In addition, the deformation of the structure changes with the current of the ion printer and the printing depth [33].

8. Smart Contact Optical Glass Sensors and Their Usage

Persontear drops comprise very chemicals including proteins, lipids, electrolytes, urea, ascorbic acid, L-lactic acid, cholesterol, etc [36]. Timely measurement of the concentration of these substances Createsprecious physiologic datato betterment, therapy andprevent of several illness.

8.1. Evaluation Glucose Concentration
Glucose concentration is significant parameter diagnosis of diabetes mellitus. Although, an usual method to alone-spot blood glucose evaluation is to usage grievous finger prick draw a blood instance.Many studies and informationshave shown than concentration of glucosinteardrop is positively associate by blood glucose concentration [37]. Smart contact lenses with tear glucose sensor basis the mixture of GOD, CAT withprove GOD in graphene canals usage pyrene linkages through π-π stacking detect the tear concentration of glucosin when glucose passes through the

graphene sensor channel, and sends the discover data to a show machine similar LED display via correction and amplification. Then detect the concentration of glucose in teardrop and until it is upper the sill, the pixel turns off [38]. Momentous is for physicians to obtain unremitting mensurationsof teardrop glucose monitoring. Dynamic changes in glucose levels cause blood and tear glucose concentration to be measured by sensors. Empirical consequence displayed that surface of glucose in teardrop starts to increment ten minutes then the increase of glucose surface in the blood, and the biosensor had a quick reaction to teardrop glucose and a suitable calibration range [38,39]. To Supervision the glucose concentration in the eye liquid, Google designed contact optical glass that associate by the blood glucose concentration in diabetic sicks [40,41]. The advantages of these smart contact lenses with biological sensors consist intermittent monitoring, top precision, and convenience in longsome -time use. various types of glucose-sensitive lenses by electrical root were designed with Park and Colleagues [38].

8.2. IOP Measurement

High IOP fluctuations are one of the reason of glaucoma [33]. however, repeated measurement of IOP by Goldman tonometer, which is Normal clinical mensuration instrumentation andintricate. Contact optical glass sensors to monitoring IOP are divided into 4 categories: capacitive sensors, resistive circular force sensors, tonometer sensors, and microinductive sensors [43]. The curvature of the cornea also changes by IOP, and as aeffect the capacitance of the IOP sensor on the contact optical glass too variation, that is measured as aalteration in split between the upper and lower pages of the sensors. Green et al. designed pressure sensors equipped with a hydrogel contact optical glass that allow attached IOP evaluation. This sensor maymeasurement variation in IOP with detecting changes in the meridional angle of the connector among cornea and sclera. In this sensor, radius curvature of the cornea and the capacitance of the cornea increases when high IOP occurs, and as a result, readout materiel to wireless IOP measurement may discover alteration in frequency intensification [44,45].

8.3. Mensuration of Lactic Acid Condensation

Lactate is significant biomarker to clinical fault diagnosis and safety monitoring that may be apply to detect increased sodium chloride concentration owing to physiologic causes. In general, human blood lactic acid levels of more than two mili moles per litermay be arranged as lactic acidosis. There are clinical manifestations that canresult to lactic acid toxication Comme: toxins, turbulence, anaemia, member defeat. Currently, teardrop areapply as a possibly sampling mediocre byeasiness of derivation forchange the ache and discomfort of blood sampling. is usedactual -term monitoring of lactate condensation in vivo using contact optical glass sensors has become aunder taking string.Thomas and Partnersschemed and proposaledan amperometric L-lactic acid sensor embedded in a contact optical glass. This electrochemical sensor converts to analytical stream emblems via redox responses on the outer layer of the electrodes. They consumed glutaraldehyde for cross-link lactate oxidase to the electrode outer layer and L-lactate was selectively detected while the substrate was coated with medical grade and biocompatible polyurethane. The sensor was designed by a reference electrode, a platinum working electrode, and an ancillary platinum numerator electrode to provide a constant reference voltage among the reference electrode and the counter. The sensor demonstrated sufficient Clarity in the physiologic periphery of lactic acid concentration, rapid answer epoch of 35 seconds, and moderate allergy in the lineal range to measuring L-lactate concentration in teardrop liquid [32].

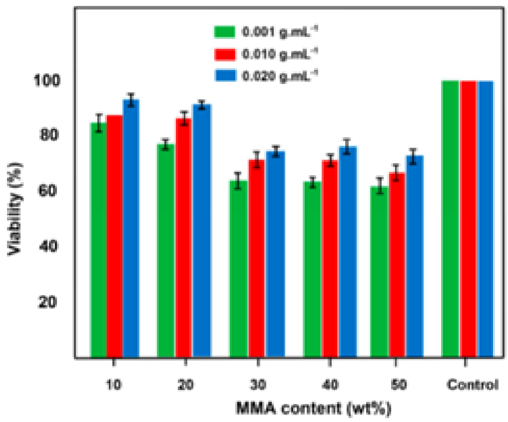
8.4. Drug Releaseby Usingcontact Optical Glass

Most of the eye medications are currently injected locally via eye drop, but, the effectiveness of the drop is endangerdue to patient non-admission. Also, the effectiveness of these therapies is finite to persistent illnesses as glaucoma and dry eye. Afavorable drug releasedevice can easily hand over the necessary drugs to the eye tissues sans intervening by the patients' natural physiologic operations. With embedding a drug releasedevice in contact optical glass and abandoning the drug in the teardrop layer, the effectiveness of the drug may be augmented up to 50%. The layout of a practical optical glass to drug releaseshould have the ability for load single or more drugs in them and liberation the medicines at remedial surfaces and in the favorable period of time in such a way as to cause undesirable systemic factors for the eye self do not.

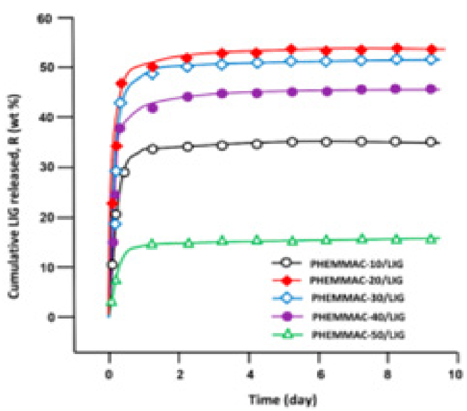
Based on this, Mehtal et al designed PNIPAM by integrating the nanotechnology of smart silicone hydrogel contact lenses with the anti-glaucoma drug timolol malate using PVP polymer nanofibers. The release of timolol malate drug was investigated based on pseudo-Fickian or Fickian diffusion and using Higuchi and Korsmeyer-Peppas models, and the results of drug release in the laboratory environment showed that about 86.7% of the drug was released after 24 hours. This study focused on designing daily lenses that can be worn during the day and removed at night. This design also overcomes the problems of multiple doses and limitations associated with drug unavailability [46]. Tayyab et al prepared a series of copolymer composites (2-hydroxyethyl methacrylate, methyl methacrylate, ethylene glycol dimethyl methacrylate) along with the medicine lignocaine using solvent evaporation. This hydrophobic-hydrophilic composite packed with particles can release drugs with a therapeutic dose of more than a week. Cytotoxicity test using MTT method (Figure 6 (a)) did not show any considerable toxicity of Polyhydroxyethyl methyl methacrylate bearer. These may be used as suitable and secure candidacy for medication release. The publication of lignocaine via the copolymer Background pursue the Fick pattern and the dynamic diffusion was lightly controlled by the content of methyl methacrylate in the hydrophilic-hydrophobic copolymer. The release of drugs (Figure 6 (b)) loaded in these composites in an aqueous medium with neutral pH is satisfactory and promising [47].

Figure 6: (a) Graph of in vitro cytotoxicity test of PHEMMAC samples with L929 cells after 24 h incubation, (b) Cumulative LIG of released PHEMMAC drug carrier systems [47].

(a)

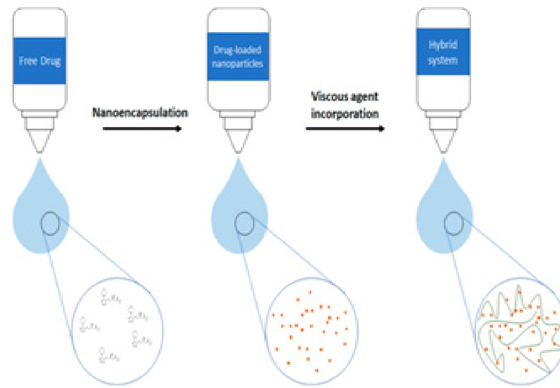


(b)



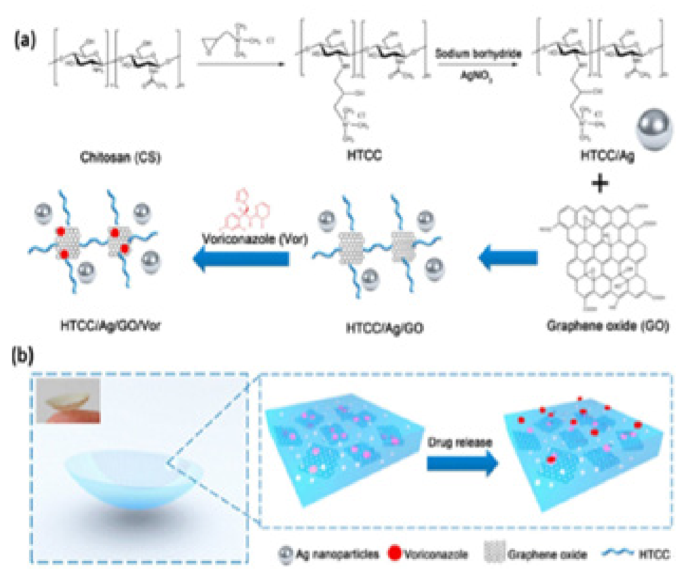
Esteban et al investigated the potential of gelatin nanoparticles loaded with timolol malate contained in hydroxypropyl methylcellulose and a beta-adrenergic blocker (Figure 7), which is widely used in the clinic for the treatment of glaucoma.Studies were performed in rabbits with elevated IOP. Gelatin nanoparticles are able to reduce and control IOP pressure. By comparing commercial formulations and gelatin nanoparticles filled with timolol malate with the same drug dose, it was observed that: nanoparticles increase e-Cacy by increasing IOP pressure from 21% to 30% and disintegrating 1.7 times under the AUC curve to be. Statistically, combining nanoparticles with timolol and viscous polymer reduces IOP up to 30% (0.65 mmHg) along with the maximum recovery time and speed.In addition, the amount of IOP pressure drop was observed for another four hours, and then the drug activity took 12 hours to release the drug, and this IOP reduction is 2.5 times more than the samples available in the market. There fore, gelatin nanoparticles alone or in combination with viscous polymer solutions are a promising option for delivering beta-blockers to control intraocular pressure in glaucoma [48].

Figure 7: General structure of the combined system of timololminate and gelatin-hydroxypropyl methylcellulose nanoparticles [48].



Fungous keratitis is aearnest eye sickness and one of the main reason of death and eye blindness in the cosm, but it is mostly neglected, especially in expanding nations. A group of researchers designed a hybrid contact lens based on chitosan hydrogel, silver nanoparticles, graphene oxide, and the antifungal drug Voriconazole as antimicrobial agents (Figure 8 (a)). Voriconazole was loaded onto graphene oxide to protect the drug and promote its maintain liberation (Figure 8 (b)) in hydrogel-based contact lenses. Person corneal mucous cells were weakly inhibited in these contact lenses, but corneal cell growth was not inhibited because graphene oxide is negatively load, allowing the whole optical glass to become more neutrally charged. Also, human corneal epithelial cells can multiply in these types of lenses due to the positive charge of chitosan. This contact lens-based on Drug releasedevice may be a promising remedial method to the fast and efficient therapy of fungous keratitis [49].

Figure 8: (A) (a) Synthesis of chitosan hydrogel, silver nanoparticles, graphene oxide and antifungal drug Voriconazole; (b) Schematic representation of medicated contact lenses and controlled drug release, (B) Cumulative release curve of Vor in PBS solution [49].



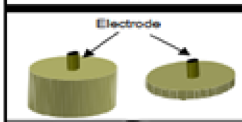
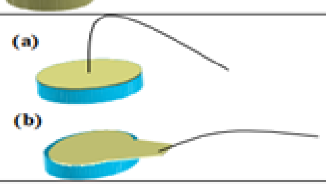
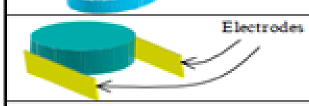
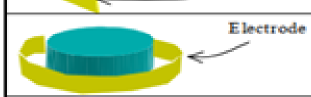
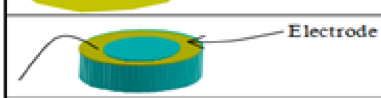
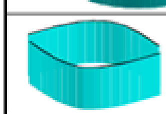
8.5. Adjusting the Focal Length Using Smart Lenses

Paxtona and colleagues connect two or three centraloptical glass for untanglethe difficult of presbyopia byvarious central distances and form a single optical glass. GRIN graded optical glasses with refractive index and variable focal length can be used.As with any possible optical glass substances, 2 of the most significant perspectives to consider are visual clarity and structural strength. There fore, a pliable and self-stable gel byanvisual transparency of more than 70% was produced to light in the range of 700-400 nm. In general, poly (acrylic) acid-sodium acrylate hydrogels as substances in the modern descendant of smart optical glasses swell with an electric string, and this swelling is repeatable and remainder almost stable [50]. Paxtona et al investigated the possibility of using electrically active hydrogels as substances in aoptical glass that has the ability to change the focal length. Table 2 shows the materials that are unsuitable for the electrode.Because they react with the hydrogel or its surrounding environment. Table 3 shows the shape of the used electrodes along with their results. Two promising materials as electrodes are silver and aluminum, where silver is used as the cathode and aluminum as the anode. Forexperiment electrical answer, the gel disks were exposed an electric field with a voltage of 5 volts and a current range of 200 mA for 5 minutes. Also, the resultant displayed that the further the crosslinker concentration in the hydrogel, the fewer the transparency of the hydrogel [51].

Table 2: Electrode materials [51].

Material	Purity	Dimensions	Obtained from
Copper foil	99%	Thickness : 0.1 mm	BDH Chemicals
Carbon	unknown	Diameter: 6.1 mm Weight: 3.1862 g	Standard laboratory supply
Surgical-grade stainless steel	unknown	Diameter: 1 mm	unknown
Zinc foil	99%	Thickness: 0.1 mm	BDH Chemicals
Silver foil	99.9%	Thickness: 0.025 mm	Aldrich Chemical Company
Aluminum foil	unknown	Thickness: 0.1 mm	RS Components

Table 3: Electrode shapes [51].

Diagram	Name	Summary
	"Rod" electrode	Frequently used by other authors, although not suited for applications where the gel *surface* is required. Charge enters the gel at *one centralised* point.
	"Disk" electrode "Spoon" electrode	Electrode shapes developed by the DCRC. Spoon electrode used frequently in experimentation, due to ease of attachment. Disk electrode slightly more difficult to attach. Offers the advantage of "distributed charge".
	"Sheet" electrode	Least-used design, but may offer some advantages as the entire surfaces of the gel is left uncovered.
	"Ring" electrode	An idea first mentioned by Salehpoor [9]. Utilised frequently in this research, as it leaves the gel surface uncovered.
	"Circular" electrode	Overcomes the problem of "centralised charge" whilst still allowing most of the surface to remain uncovered.
	"Conducting sheath" electrode	Perhaps the ultimate electrode, but also the most difficult to design. Will require significant future research to be fully realised.

9. Different Strategies for Designing Antimicrobial Contact Lenses

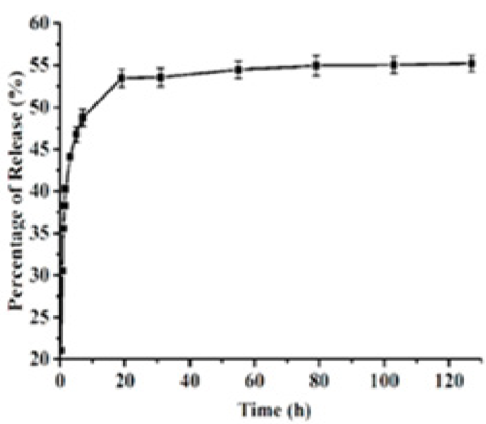
9.1. Chemical Strategies

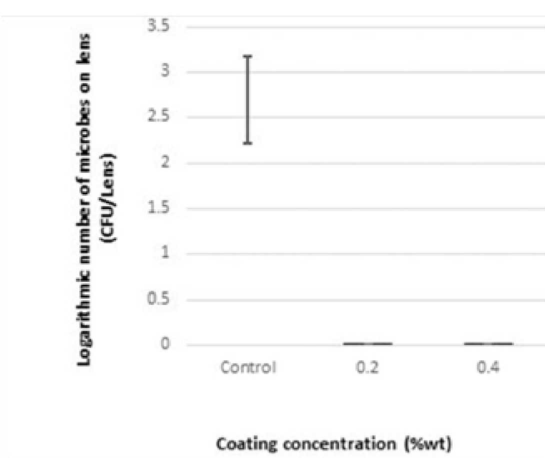
In important microbial cell processes, antimicrobial chemicals can be used and by them adhesion of microorganisms occurs and the death and killing of cells is directly reduced. Of course, some of these chemicals produce superoxide and are toxic to microbial cells[52].

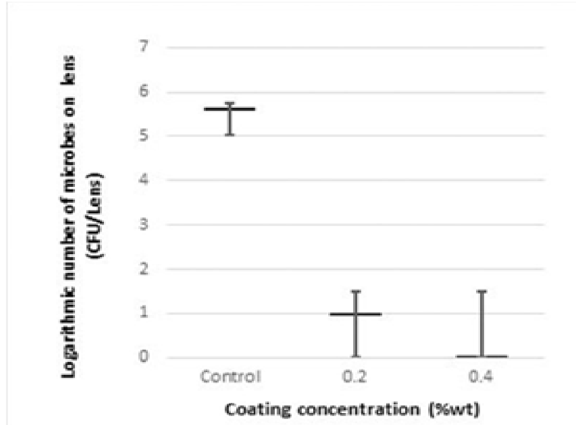
9.1.1. Silver: Silver is used as a biomaterial with antimicrobial properties due to multiple mechanisms of action, physical disturbances in microbial metabolism, changing surface properties and reducing microbes' adhesion to the surface, and formation of a protective layer as a biomaterial with antimicrobial properties. For example, in 2006, a case of silver-impregnated contact lenses was investigated in laboratory conditions to reduce the contamination of eye contact lenses. The silver ion was added to the mixture plastic at the molding stage, so the lens quality and silver distribution are uniform. By adding the solution, Ag+ ions react slowly with the soluble ions and by this reaction prevents the proliferation and bacteria [53].

9.1.2. Silver Nanoparticles: A major problem in the use of silver ions is the inactivation of the complex and precipitation, and for this reason, silver nanoparticles are used in research, which is a more suitable alternative. Many studies have been done in this field. Also, the effects of these silver nanoparticles in combination with other antimicrobial molecules to strengthen the antimicrobial effect of contact lenses have also been investigated [52]. For example, R. Tuby et al used Zn-CuO nanoparticles in hydrogel contact lenses as an antimicrobial agent. Nanoparticles were placed as a coating on the lenses. Also during the coating process, active nanoparticles are formed on the surface. Antimicrobial properties of coated lenses against Gram-positive and Gram-negative bacteria showed that coating process leads to reduced particle size and better antibacterial activity of lenses. The antimicrobial property of these coated lenses is suitable and the reduction of microbes on the surface of the lenses was observed (Figure 9 (a, b)) [54].

Figure 9: (A) Adhesion of P. aeruginosa to coated contact lenses. Presented are the medians and ranges. (B) Adhesion of S. epidermidis to coated contact lenses. Presented are the medians and ranges [54].







9.2. Factors Producing Free Radicals

Superoxide ions and nitric oxide reactive intermediates damage the microbial DNA and cause oxidative stress [52].

9.2.1. Selenium: Selenium is one of the substances that produces free radicals and is therefore used as a catalyst in reactions. Because the superoxide they produce is toxic to viruses and bacteria [52]. For example, P. Tran and colleagues stated that bacterial layers on the surface of the lenses can lead to the possibility of corneal infection and acute eye redness. Coating on contact lens prevents formation of these layers and reduces these important clinical problems. Selenium-containing compounds can catalyze the formation of superoxide radicals, which are the site of bacterial cytotoxicity [55,56].

9.2.2. Organozinum: Organozinome was studied as an additive in contact lenses. For example, Tran and colleagues stated that the tergentinium polymer completely prevents biofilm formation by aeruginous aureus, maitophilia, and marcescens. This type of lens has antimicrobial properties because organozonum does not leave the polymer and prevents biofilm formation and can even be a better alternative than silver [52].

9.2.3. Nitric Oxide Releasing Polymers: Nitric oxide releasing polymers are other biomaterials that can be used to design lenses with antimicrobial properties. These types of polymers produce active nitrogen oxide intermediates such as nitrite peroxide and dioxide, that can damage the structure of DNA, proteins and cells. These polymers have cytostatic and cytotoxic properties and affect protozoa, fungi and bacteria [52].

9.3. Blockers of Quorum Estimation

One way of signaling cells is quorum, which is secreted by messenger molecules, allowing bacteria to alter gene expression and generate adaptive phenotypic responses [52].

9.4. Use of Antimicrobial Peptides

Host defense peptides such as defensins and catelicidins are also used as a natural antimicrobial agent. This property of antimicrobial peptides comes from their net charge, which is usually positive and amphipathic, allowing for interaction with gram-negative bacteria [52].

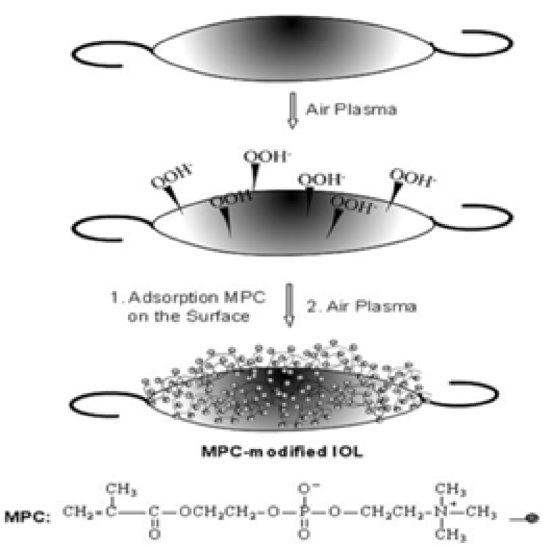
10. Use of Non-Steroidal Anti-Inflammatory Medicines

Anti-inflammatory drugs prevent the production of bacterial layers outside the cell. For example, Jose Fernando Rosa dos Santos and colleagues designed acrylic hydrogels with a high proportion of cyclodextrins. These lenses are able to improve the ability to insert or insert drugs into the hydrogel and control the rate at which they are released. The results showed that these hydrogels prevent leakage and release of drugs into the common protective fluid of soft contact lenses. It also protects the loaded drugs for two weeks [57].

11. Use of Passive Antimicrobial Agents

This method, unlike chemical strategies, actively kills microbes. Inactive and non-passive factors change the properties of the surface of the material and prevent the entry of microbes and their adhesion to the lenses[52]. For example, Ke Yao et al investigated the hydrophilic of silicone intraocular lenses later covalent bonding escorted by 2-methacryloyloxyethyl phosphorylcholine. To improve the surface biocompatibility of intraocular lenses, 2-methacryloyloxyethyl phosphorylcholine was placed on the IOL through air plasma (Figure 10). Hydrophilicity of IOL lenses is significantly and permanently improved after attachment to MPC. Platelet, macrophage, and LEC adhesion on the IOL surface were clearly suppressed, indicating increased biocompatibility of the surface. Also, thinfilm evolution decreased later 1080 minutes of incubation. These lenses keep low wettability, protein absorption, and low epidermal and arachnoid bacteria adhesion [58].

Figure 10: Schematic representation of connecting MPCon silicon objects with plasma process [58].



12. Challenges and Prospects

Most optical glass mayalone discover single biomarker as glucose, lactic acid in eye. With the passage of time and expansion and progress in the field of contact optical glasses, they can be used as a strong medical gadget to diagnose several diseases and chemical ingredients in factual moment. Also, for their better efficiency in distinction, electrical sensors can be used to registration physical signals (pressure, temperature) and electrical stimulation of optical neurons pending assessment [59]. In addition to the effect of optical glassesin successive and minimally invasive detection of maladies, they too play a effect in the behavior of eye illnesses. By the advance of techniques and micro-scale materials, contact optical glasses mayat present be planedby thecapability to liberation medicines contiguous [60,61]. Lucidity of optical glasses because of the tuneable biologic and physicochemic attributes of hydrogels, it is envisaged that they may greatly better the efficiency of smart contact optical glasses in medicine transfer. The expansion of contact optical glasses by a medicine transfer device wherein medicines can be reloaded maintain behest to the expansion of reusable contact lenses tolong-range usage. Most available sensorial devices are not mighty of self-reinforcing. Pliable photovoltaic technique maychange the customary authority Source method in contact optical glasses since normal sunlight is simple to transform into energy [62]. It may greatly decrease the connector line of interior machines and the convolution of electronic machines. These attributes will manufacture photovoltaics a trend in pliable and stretchable electronics in futurity [63]. The nanogenerators are tiny and may be used as a potency source module tooptical glasses. The product mechanical energy from the contiguous blinking move of the eyelids and transform it into electricity [64]. With exert the triboelectric efficacy, a structurally ordinary, down-Price, and environmentally compatible nanotriboelectric generator to contact optical glasses may be productioned [65].

Fictitious intelligence mayso be used to better the remedial efficacy of optical glasses.In specific, device acquisition algorithms may be used in optical glasses to recognize person safety situation with lengthy-time monitoring and provide personated the rapies to different species of illnesses [66]. Information accumulated of persones may be uploaded to a lattice and cumulative in cloud databases. These plural Information will flourish significantly and must be analysedusing device acquisition algorithms to foretell the safety situation of personesin clinical assessment and behavior. Forameliorate the efficiency and diversity of optical glasses, it is essential to add more chips and connectoresto the machine. These things may cause challenges because ofstream plan and construction need miniaturization, inflexionity, visual transparency, and resistor to frequented wear. The original reasons for these obstacles are: checkmate conjoining wires, the hardness of the chips and the measure of the sensor electrodes. The small connectoresintrant smart contact optical glasses are traditionally builteof copper, silver, gold, and platinum, that are checkmate and maydistrict Human's view. These substances may be changed and improve with bright biomaterials as graphene, carbon nanowires or indium tin oxide. Miniaturization of optical glass-embedded chips toinformation storage, information transferion, and circuit electricity has found increasingly significant, scholaresand artful selleresto expand future -descendant chips with many taskes. Also, the sensibility of the device reductions significantly with the decrease of the scale of the all currente, especially by the scale of the sensitive electrodes. To dissolve the aforesaid obstacles, one approachis to use energetic sensors, Likefield-

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effect transistors and supplementary metal oxide semiconductor sensors, which show excellent sensibility notwithstanding possess micrometer sizes [67]. Increases the compression of energetic ingredients in a machine means more energy expenditure, that becoming other large difficulties. Many efforts have been made to increment the authority reserve valence of circuits in optical glasses, containing inductive, visual, RF authority, and supercapacitors [68], however these procedures cannot continuously provide the authority reserve meeting the prescriptions of actual -time health monitoring. Realize that this difficult may be dissolved withlocating biofuel cells in optical glassesbecause these cells transform chemic energy by the chemicals in the teardrop liquid into electricity. Enzymes necessaredto comfort biochemical responses may beindigenous biologic liquids from foreign dilutiones. The obstacle of demolition of enzymes after a certain term of time may be dissolved with replenishing new enzyme dissolutiones. The mechanical resistance and biocompatibility of contact optical glassesis other agent affecting their capability to monitor persistent health, thatmay be addressed via advanced materials and technologies. For example, the presentationof oxygen conduits in Polydimethylsiloxane optical glasses mayameliorate the gas permeance of the lenses in the lengthy time and thus increment its biocompatibility [23]. Meliorated biocompatibility underestimate the protected response and enhances the therapeutic functions without causing harmful, negative physiological, allergic reactions and brings convenience to the users.

13. Result

Smart contact lenses have significant potential in medical applications because they have features such as non-invasiveness, intelligent drug delivery, automatic color detection and focal length adjustment. These types of lenses are used to detect and check glucose concentration in tears, glaucoma, hypoxia, eye diseases, drug delivery. Also, these versatile and integrated lenses can be more effective in collecting information about eye diseases and thus facilitate the diagnosis and treatment process. We believe that to improve the properties and efficiency of these new lenses from biomaterials and new methods can be used to design it

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