Makara Journal of Science

Volume 25
Issue 3 *September*

Article 3

9-30-2021

Poly(2-Hydroxyethyl Methacrylate) Hydrogels for Contact Lens Applications–A Review

Kushendarsyah Saptaji
Department of Mechanical Engineering, Faculty of Engineering and Technology, Sampoerna University, Jakarta Selatan 12780, Indonesia, kushendarsyah@sampoernauniversity.ac.id

Nurlaely Rohmatul Iza
Department of Aerospace and Mechanical Engineering, The University of Arizona, Tucson 85721, USA

Sinta Widianingrum
Department of Aerospace and Mechanical Engineering, The University of Arizona, Tucson 85721, USA

Vania Katherine Mulia
Department of Aerospace and Mechanical Engineering, The University of Arizona, Tucson 85721, USA

Iwan Setiawan
Department of Information System, Faculty of Engineering and Technology, Sampoerna University, Jakarta Selatan 12780, Indonesia

Recommended Citation

Saptaji, Kushendarsyah; Iza, Nurlaely Rohmatul; Widianingrum, Sinta; Mulia, Vania Katherine; and Setiawan, Iwan (2021) "Poly(2-Hydroxyethyl Methacrylate) Hydrogels for Contact Lens Applications–A Review," *Makara Journal of Science*: Vol. 25 : Iss. 3 , Article 3.
DOI: 10.7454/mss.v25i3.1237
Available at: https://scholarhub.ui.ac.id/science/vol25/iss3/3

Makara Journal of Science, 25/3 (2021), 145–154
doi: 10.7454/mss.v25i3.1237

Poly(2-Hydroxyethyl Methacrylate) Hydrogels for Contact Lens Applications–A Review

Kushendarsyah Saptaji[1*], Nurlaely Rohmatul Iza[1,2], Sinta Widianingrum[1,2], Vania Katherine Mulia[1,2], and Iwan Setiawan[3]

1. Department of Mechanical Engineering, Faculty of Engineering and Technology, Sampoerna University, Jakarta Selatan 12780, Indonesia
2. Department of Aerospace and Mechanical Engineering, The University of Arizona, Tucson 85721, USA
3. Department of Information System, Faculty of Engineering and Technology, Sampoerna University, Jakarta Selatan 12780, Indonesia

[*]*E-mail: kushendarsyah@sampoernauniversity.ac.id*

Received May 20, 2021 | Accepted July 14, 2021

Abstract

The emerging technology in biomedical engineering requires biocompatible materials, which are also referred to as biomaterials. For a material to be considered biocompatible, it should not interact with human tissues in a harmful way, and vice versa. Various properties of biocompatible materials, such as mechanical and optical properties, have to be considered for different biomedical applications. One of the most popular applications of biomaterials is for contact lenses. Hydrogels, specifically poly(2-hydroxyethyl methacrylate) (PHEMA) hydrogels, are among the most popular ones in ophthalmologic applications, especially in soft contact lenses. This paper reviews the use of PHEMA hydrogels as one of the important biomaterials. The possible applications, properties, and manufacturing process of PHEMA hydrogels, especially in contact lens applications, are addressed. Many studies have shown that PHEMA hydrogels possess many advantages in contact lens applications and have promising development prospects.

Keywords: biocompatible polymer, hydrogel, poly(2-hydroxyethyl methacrylate), PHEMA, soft contact lens

Introduction

Biocompatible materials, which are also referred to as biomaterials, are nonliving materials used as medical devices to interact with biological systems. The nature of this interaction involves biocompatibility properties, which are the capacity of a substance to function with the body, tissues, and organs without causing harmful effects. Biomaterials can be a pure substance or mixture of synthetic substances that may be used as a whole or as part of a system for any period. In addition, the materials may be applied to or substitute for any tissue, organ, or body functions [1]. Biomaterials are expected to be able to improve the quality of life and save human lives.

The development and applications of biomedical devices such as implants, prostheses, and microfluidic devices have increased significantly in recent years. Rapid and real-time diagnosis results such as microfluidic devices are necessary, especially during the COVID-19 pandemic. Therefore, more straightforward, simpler, and cost-effective manufacturing methods to produce biomedical devices are needed, such as the fabrication of burr-free microfluidic mold using micro-milling for creating microfluidic devices [2].

Biomaterials have comprehensive applications, including external and internal human body parts such as joint and limb replacement, artificial skin and arteries, contact lenses, and artificial teeth. Inner body recovery through substitution is known as implantation. Three main aspects exist when using implantation: correct material selection, design, and manufacturing process. Even though a perfect design and manufacturing process are essential, the material selection must meet the required properties, match the desired needs, and be biocompatible [1]. The selected biomaterial must not induce an adverse response from the body, or vice versa. Biocompatible materials need to fulfill several requirements: they should not harm the body, they must have good corrosion resistance, they should be non-toxic and non-carcinogenic, and they must have adequate physical and mechanical properties, especially fatigue strength and toughness. These properties are needed for the materials to function as replacements or multipliers of body tissues [3]. For practical use, the biomaterials

must be easily formed or machined into several shapes. The manufacturing process must not induce surface and subsurface damages such as residual stresses [4]. In terms of economy, biomaterials must be affordable, and their raw materials should be widely available in the market.

One of the applications of biocompatible materials is for contact lenses. The growing number of people suffering from eye diseases such as myopia and astigmatism nowadays has resulted in the rising demand for contact lenses. Contact lenses are also used in the fashion or film industries for cosmetic purposes. Various types of materials have been developed to create contact lenses with enhanced functions, such as good durability and wear time while retaining the comfort of the user. One of the most popular materials for contact lenses is poly(2-hydroxyethyl methacrylate) (PHEMA) hydrogels [5].

This paper mainly focuses on PHEMA hydrogels, especially the characteristics and current development of PHEMA hydrogels in contact lens applications. A brief general review of biocompatible polymers, such as the properties and manufacturing process, is presented first. This work is expected to contribute to a new understanding for researchers who work in the field of biocompatible materials, especially PHEMA hydrogels, by providing a comprehensive discussion on this topic.

Biocompatible Polymers

General types of biocompatible polymers. Biocompatibility is a general term that is used to describe the compatibility of a material introduced into the body or bodily fluids. The material exhibits good performance with a suitable application-specific response to application-specific and is highly dependent on a particular application or environment [6]. A material is biocompatible (in a specific application) if it allows the body to function without complications such as an allergic reaction or other adverse side effects. Biocompatibility is not the same as sterilization. Sterilization is the treatment of a material to release or destroy all living organisms (including bacterial and fungal spores) and is not related to the actual biocompatibility of the material [7].

Lack of biocompatible properties can result in cellular disruption of the normal healing process and additional complications. Therefore, nature biocompatibility is vital for medical equipment. Biocompatibility testing is necessary for all materials to be used in medical devices to minimize any potential hazard to the patient. Any testing of biocompatibility properties requires good characterization of the material to ensure that biocompatibility properties are assessed on well-defined materials. Without sufficient material characterization, testing of biocompatibility properties cannot be related to specific materials, thereby making its use unlikely [6]. Material characterization should be used to the extent that it is possible to identify the material used.

In general, biocompatible polymers can be divided into natural polymers and synthetic polymers. The difference in the properties of the natural and synthetic polymer is based on the polymer structure and the ease of degradation by microbes [8]. Some synthetic polymers are more difficult for microorganisms to break down than natural polymers due to its structural components [9]. Natural polymers are polymers that occur naturally due to the metabolic processes of living things. However, the use of natural polymers is not optimal because the number of natural polymers is limited. In addition, the nature of natural polymers is less stable when heating, absorbs water quickly, and is difficult to form. Natural polymers consist of proteins, polysaccharides (dextran, amylose, cellulose, chitin, and glycosaminoglycans), polynucleotides (DNA and RNA), alginate, hyaluronate, and chitosan [10]. Meanwhile, synthetic polymers are artificially produced in laboratories and are typically derived from petroleum oil [11]. Some examples of synthetic biodegradable polymers are silicone poly-caprolactone, poly(butylene succinate), poly(lactic acid), poly(glycolic acid), poly(butylene succinate-co-adipate), and poly(butylene adipate-*co*-terephthalate) [12, 13].

Applications of biocompatible polymers. Various types of biocompatible polymers are widely used in medical devices. Applications range from artificial faces to throat tubes, from kidneys and parts of the liver to components of the heart and materials for artificial teeth to materials for the groin, knee joints, and other medical devices [14]. Biocompatible polymers are also used for medical adhesives, covers, and coatings for various purposes.

In medical applications, synthetic biocompatible polymers are used more often than metals and ceramics. The main advantage of biocompatible polymers over metals and ceramics is that they are easily manufactured into various forms. Some synthetic polymers applied in medical applications include polyolefin polyethylene, polypropylene (PP), polytetrafluoroethylene (PTFE), polyethylene terephthalate, and silicone [12]. PTFE can be utilized for balloon catheters, face implants, vascular grafts, and hernia patches. Polyethylene can be used for balloon catheters and hip and knee replacements. Silicone can be applied for balloon catheters, face implants, and intraocular lenses. Poly(methyl methacrylate) (PMMA) and 2-hydroxyethyl methacrylate (HEMA) are also used for intraocular lenses.

Hydrogel is also often used in the medical industry. A hydrogel can be described as a polymer network that is three-dimensional, cross-linked, and hydrophilic. It can retain water in its porous structure [15]. The application of hydrogel as biomaterials has several advantages. First, hydrogel has a high-water content, thus giving the

hydrogel a degree of flexibility similar to that of natural tissue. Second, hydrogel is a biocompatible and biodegradable material, and it can be injected. Third, hydrogel has good transfer properties and is easy to modify. In the medical industry, hydrogel is used as a matrix to control the release of active ingredients such as drugs and cells [15]. Furthermore, hydrogels are used as a matrix to repair and regenerate various tissues and organs in the human body. One of the hydrogels used as an optical material is PHEMA hydrogel, which is widely studied as a biomaterial and has been proposed as a soft contact lens material.

Manufacturing of biocompatible polymers. Polymers are synthesized through polymerization. This process occurs when some monomers are bonded (linked chemically) from the low molecular unit to the high molecular mass. Polymerization can be achieved in two on the basis of the form of the molecules. The first method is physical polymerization, and the second is chemical polymerization. Every method has its advantages and disadvantages because it encounters different media.

Polymerization in physical polymerization can be achieved in two ways: ionizing radiation and non-ionizing radiation. In ionizing radiation, the process can be conducted in various media, solids, or liquids with a temperature-independent behavior. Polymerization can be performed at a very low temperature by radiation. The primary process is related to a controlled diffusion reaction in some stages. The stages are the addition of hydroxyl radicals and hydrogen atoms to carbon, the addition of hydrated electrons to the carbonyl groups and radical anion formation with a constant high rate, and the addition of monomer to the growing chain reduces the radicals (Figure 1).

Then, the process utilizes ultraviolet radiation in non-ionizing radiation, which is also called photopolymerization. Ultraviolet light absorption initiated this process. The stages of photopolymerization are generally similar to those of ionizing radiation polymerization. The only difference is in the first stage, which is process initiation. Figure 2 shows the flowchart of the process. The process is commonly used in 3D printing because of ultraviolet light absorption.

In contrast, chemical polymerization occurs when the monomers are bonded and broken by a chemical mechanism known as condensation polymerization, in which the bonding process causes water loss from the monomers. Figure 3 shows the flowchart of chemical polymerization. The media of this chemical polymerization are aqueous only because they are mainly related to water [12].

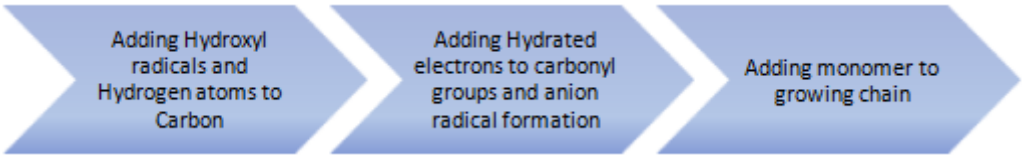

Figure 1. Flowchart of Ionizing Radiation Polymerization

Figure 2. Flowchart of Non-Ionizing Radiation Polymerization

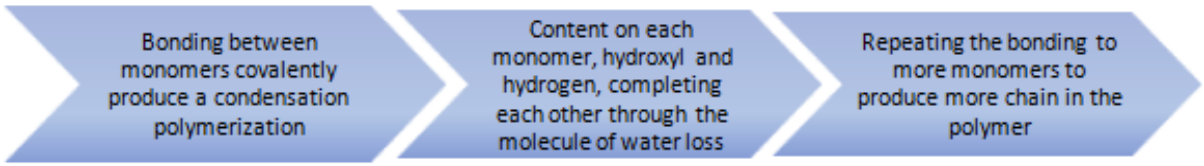

Figure 3. Flowchart of Chemical Polymerization

Poly(2-Hydroxyethyl Methacrylate) Hydrogels

Properties and characteristics of PHEMA hydrogels. One example of biocompatible polymers is PHEMA, which is commonly known as hydrogel materials. In general, hydrogels have superior biocompatibility, ease of manufacture, viscoelastic properties, high hydrophilic polymer networks, low immunogenicity, and similar features with human body soft tissues [16, 17]. They can be made from natural polymer chains such as collagen or alginate or synthetic polymers such as poly(vinyl alcohol), poly(acrylic acid), or PHEMA [18]. Hence, hydrogel materials are suitable for biomedical applications, such as delivering vehicles for cells and drugs due to their cross-linking with more than 90% water [19]. Hydrogels are also used as scaffolds for tissue engineering, artificial articular cartilage, and intelligent devices (that respond to external stimuli, such as pH and temperature), and it may provide initial structural support in defective areas for cell metabolism, growth, differentiation, and new matrix synthesis [17].

PHEMA hydrogel can be defined as a polymer formed by three-dimensional cross-linked polymeric networks based on HEMA, which can retain water content within their structure [20]. From the type of polymers, PHEMA is considered a thermoplastic material. PHEMA hydrogels are inexpensive, have excellent biocompatibility, non-biodegradable, high water content, low thrombogenicity, cytocompatibility, abundant copolymer possibilities, soft materials with excellent temperature stability, acid and alkaline hydrolysis resistance, tunable mechanical properties, and an optically transparent hydrophilic polymer that is desirable for various biomedical applications [16, 21, 22]. PHEMA is hard and brittle material in dry conditions. It becomes soft and flexible and can be cut easily upon swelling when wetted with water [16, 22]. PHEMA has a glass transmission (Tg) temperature and density in the range of 358–393 K and 1.15–1.34 g/mL, respectively [16]. Figure 4 shows the chemical structure of HEMA monomer.

HEMA can be synthesized from methyl methacrylate or methacrylic acid by the reaction of ethylene glycol (transesterification reaction) and ethylene oxide and methacrylic acid [23]. However, these processes contain impurities and need to be refined. The presence of impurities due to cross-linkers such as ethylene

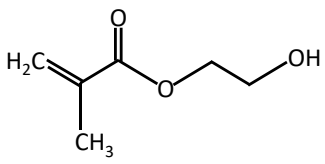

Figure 4. Chemical Structure of HEMA Monomer to form PHEMA Hydrogels

dimethacrylate in HEMA makes the polymer insoluble in water. Therefore, many great efforts have been made to obtain PHEMA hydrogels via copolymerization of HEMA with different hydrophilic methacrylates.

In terms of mechanical properties, PHEMA hydrogels exhibit viscoelastic properties, thereby leading to a slight variation in the mechanical properties. Typically, PHEMA-based hydrogels are very soft and brittle [24]. Surface nanomechanical properties, such as surface stiffness and tip-sample adhesion, depend on cross-linking density and applied load due to its viscoelasticity [20]. Cross-linking density is also related to the water content of the hydrogel. The mechanical properties of hydrogel depend on the water content in the polymer links or the degree of swelling. Thus, mechanical tests such as tensile and compression tests of hydrogels, including PHEMA hydrogels, are usually conducted in an aqueous solution of deionized water [25, 26]. A tensile test in an aqueous solution in a fully swollen state shows that pure PHEMA hydrogels have a tensile strength of around 0.12–0.2 MPa [25]. The elasticity of a PHEMA hydrogel can be analyzed on the basis of their Young's modulus, which mostly ranges between 0.4–1.8 MPa [27].

In terms of optical properties, PHEMA hydrogels exhibit excellent transparency, transmittance, and refraction index suitable for ophthalmologic applications. Choosing a material with optical properties as close to those of natural human eyes is favorable for contact lens applications. Tests that use ultraviolet (UV)-visible spectrophotometer at room temperature show that pure PHEMA hydrogel has a transmittance of about 85% in the visible wavelength region when fully swollen by deionized water [28]. This value is considered more reasonable compared with the transmittance of human corneas (99.7%–99.9%). The refractive index is also a significant consideration in choosing contact lens materials. Tests that use a refractometer show that pure PHEMA hydrogel has a refractive index similar to that of the natural human lens, which is around 1.410 [28]. This value can be increased by copolymerization with other chemicals such as titanium (IV) oxide (TiO_2) for intraocular lens implant applications [29].

Some analysis can be conducted to understand the PHEMA properties. Differential scanning calorimetry (DSC) can be used to understand the kinetic reaction of polymerization. Thermogravimetric/differential thermo-gravimetric analysis proves the excellent dimensional and thermal stability of PHEMA [21]. The swelling test, solubility, and Fourier transform infrared spectroscopy were conducted to examine the existence of strong molecular interaction in the polymer. The presence of physical and chemical reticulations in PHEMA hydrogel is proven, thereby implying that the material has good resistance to chemicals and a high degradation

temperature [21]. The sustainability of PHEMA can be observed using positron annihilation lifetime measurement (PALS). The PALS results show that PHEMA experiences more dehydration in a saline solution than in pure water. In addition, the materials become smaller during the dehydration process in the saline solution [30].

Applications of PHEMA hydrogels. PHEMA hydrogel is utilized mainly for soft contact lens materials and remains a popular material in the market because they are hydrophilic, oxygen-permeable, flexible, and transparent [5, 28]. These characteristics provide comfort for the user; the water content and oxygen permeability prevent dry eyes when the lens is used and allow a long wear time of up to seven days [5]. Hydrogel materials such as PHEMA are suitable to be used for contact lens due to water content in the range of 20% to 80% in volume. The material is also soft and flexible, and has high oxygen permeability, allowing oxygen to pass through the cornea. A soft contact lens made of hydrogel is thin and is used to improve wearing comfort, prevent physiological changes in the cornea, and provide good optical transparency during retinal imaging [31].

In general, contact lenses are utilized for numerous medical purposes, mainly for vision correction such as treating patients with corneal ectasia, ocular surface disease, after ocular surgery, and in the setting of high refractive error [32]. Contact lenses, as an alternative to eye drops in terms of being a drug delivery vehicle for the eye, are desirable because of their potential advantages in dosing regimen, bioavailability, and patient tolerance/compliance [33]. Contact lenses are also used for cosmetic purposes [5], and their use continues to evolve.

Some important soft contact lens properties that mainly related to water and to determine their performance are water content, free-to-bound water ratio, and the extent to which soft lenses dehydrate during wear [19]. A user indicates the necessary contact lens specifications, such as wear time, comfort, durability, handling, vision stability, and cost. Manufacturers also need to meet requirements in terms of material costs, ease of production, and reliability of the contact lenses [5]. Some parameters from a materials science perspective are lens thickness, wettability, oxygen permeability, mechanical properties, and water content. Hence, development of contact lens materials to fulfill these many requirements remains challenging.

PHEMA hydrogel is also utilized in many other ophthalmologic applications. PHEMA hydrogels can be used as a material for intraocular lenses (IOL) to cure cataracts [29]. PHEMA-based contact lenses can also be used as a medium for ophthalmologic drug delivery to cure glaucoma [5, 27]. As a medium for eye drug delivery, PHEMA has some advantages over other methods and materials such as PMMA. Recent studies have also attempted to use PHEMA hydrogel for artificial corneas [34].

In IOL application, PHEMA is considered a good material due to its flexibility and good optical clarity. Usually, the treatment for cataract patients is performed through a surgery called extracapsular cataract extraction, which involves planting a folded IOL implant into the lens capsule through a small incision and letting the implant unfold to replace the natural eye lens. PHEMA is also more resistant to damage during insertion into the lens capsule and does not cause water buildup in the long run, unlike other materials. However, the refractive index of PHEMA is relatively low, and attempts are still being conducted to improve the refractive index [29].

The most significant advantage of PHEMA hydrogels as a contact lens is the flexibility to improve the properties especially via copolymerization [5]. Most PHEMA-based contact lenses in the market today are copolymerized because pure PHEMA is still considered too stiff to be a contact lens material [27]. Mechanical properties such as tensile strength, Young's modulus, and optical properties such as light transmission, oxygen permeability, and water absorption of PHEMA-based hydrogels can be modified and enhanced by various techniques such as polymerization and copolymerization, and different cross-linking rates. Some materials used for modification were surfactants, nanoparticles, and antimicrobial agents. Numerous studies have been conducted to explore more possibilities of copolymers to enhance the functions of contact lenses.

PHEMA hydrogels are commonly copolymerized with ethylene glycol dimethacrylate (EGDMA) to improve mechanical properties. Another common copolymerization method is cross-linked with N-vinylpyrrolidone (NVP) and methacrylic acid to increase the water content. Even after copolymerization with NVP (or PVP as a polymer), a study has shown that pure PVP-PHEMA hydrogel has a tensile strength of only 300 kPa at only 4% strain [24]. However, the downside of this copolymerization is increased protein deposition, which can cause micro-organisms to grow inside the lens and cause infections to its user [5].

A composite with boric acid (BA) to produce contact lenses with higher water content, thermal stability, viscoelasticity, and resistance to Gram-negative and Gram-positive bacteria was created [28]. The cross-linking process can be seen in Figure 5. Another study explored the use of β-cyclodextrin-hyaluronan (β-CD-crHA) as a cross-linker to reduce the tear protein absorption in a contact lens, especially for drug delivery [27].

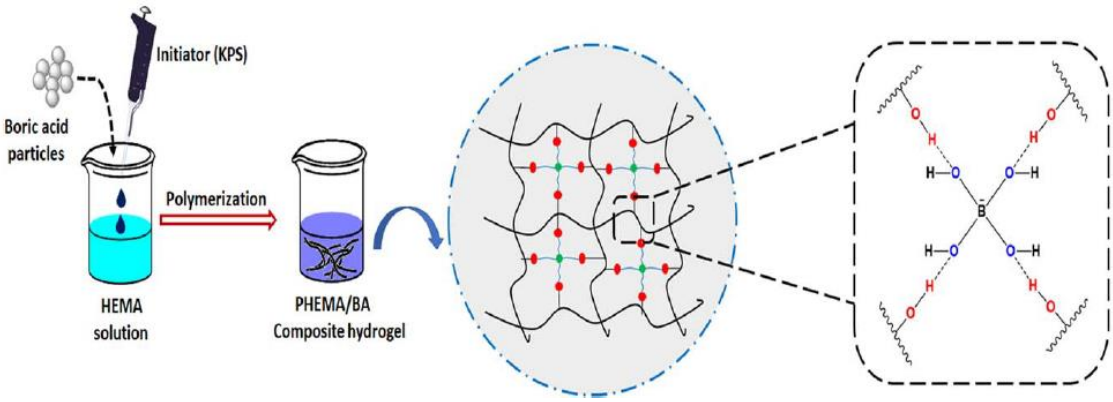

Figure 5. Schematic of the Synthesis of PHEMA/BA Composite Hydrogel [28]

A more sophisticated application of PHEMA hydrogel is to combine it with PMMA. PMMA is also commonly used for contact lenses. However, PMMA-based contact lens is harder and stiffer. PHEMA-PMMA, which is the combination of PHEMA with PMMA, can be used to obtain an artificial cornea [34]. This innovation is one of the ways to reduce the risk of treatment failure. Technology has become more advanced nowadays; thus, keratoprosthetics have experienced some improvement. Keratoprosthetics were first applied to humans in 1859 and featured glass, plastics, or a soft rubber base. Lately, keratoprosthetics are being applied with hydrogels, synthetic polymers, and even a carbo form [34].

PHEMA can also be used for other biomedical applications such as wound healing, bone tissue regeneration, cancer therapy, drug delivery systems, artificial skin, artificial cornea, breast augmentation, catheters, endodontic filling in dentistry, intrauterine inserts, replacement of damaged articular cartilage, implants, and prosthesis [16, 23]. PHEMA hydrogels are especially well suited for usage in biomedical devices and as a basis for drug delivery systems due to their characteristics [35]. However, they also have low oxygen permeability and protein deposition issues [16]. Furthermore, PHEMA materials need to be modified or combined with other materials because pure PHEMA is nondegradable. PHEMA has been combined with hydroxyapatite as a hybrid bio-composite hydrogel in bone tissue regeneration, while PHEMA combined with bacterial cellulose whiskers and silver is used for wound dressing.

The synthesis of artificial hydrogel (PHEMA) and natural hydrogel (bacterial cellulose) was proposed to enhance the toughness and strength of PHEMA [36]. This PHEMA-based nanofiber-reinforced hydrogel can achieve the strength required for scaffold in tissue engineering. The properties of PHEMA hydrogels, especially for drug delivery applications, can also be improved by synthesizing varying amounts of a pluronic (PEO-PPO-PEO). The pluronic was synthesized by bulk polymerization of HEMA in pluronic dimethacrylate under mild photo initiating conditions [22]. The degree of swelling and mechanical strength increased with increased pluronic content in the modified PHEMA hydrogels [22].

An effort to tailor the physicochemical and mechanical properties of PHEMA hydrogels close to healthy articular cartilage was conducted by Bostan *et al*. [18]. Acrylic acid (AA), which is a hydrophilic monomer, was synthesized with PHEMA. HEMA with 5% AA hydrogels is reported to have similar mechanical and tribological properties as articular cartilage [18].

Mezhoud *et al* .[37] synthesized HEMA with a macro-porogenic agent, i.e., NaCl particles, and a porogenic solvent to increase the porosity of the materials. Biporous polymeric PHEMA scaffolds can absorb water as high as ~2500% due to the interconnected higher porosity level [37]. Passos *et al*. [17] improved the cartilage tissue regeneration of PHEMA hydrogel by synthesizing it using an infrared radiation source (ytterbium laser fiber). DSC results showed that glass transition temperature (*T*g) was in the range of 103 °C–119 °C, the maximum swelling was achieved at about 70.8%, and the strain was 56%–85%. This process produced synthesized PHEMA that is compatible with cartilage tissue regeneration with an increase in glycosaminoglycan concentration and DNA content in cells cultured with 40-wt% HEMA.

Manufacturing processes of PHEMA hydrogel contact lens. The stages of manufacturing contact lenses include synthesis of PHEMA hydrogel from its monomers, formation of the lens shape, inspection, and packaging [5]. Polymers are synthesized in a process called free-radical polymerization [38]. Three methods are commonly used to form the contact lens shape: cast molding, spin casting, and lathe cutting or turning [38]. Each method can affect the mechanical properties of the produced lens differently [5].

In cast molding, a mold consists of male and female sections that are usually made of the copolymer of propylene or ethylene. The mold is normally produced by injection molding. The male and female sections are assembled to form a cavity in the contact lens shape when combined. Subsequently, the PHEMA hydrogel is poured on the female section (front curve mold) and covered by the male section (back curve mold) until the hydrogel fills the cavity and is cured until it is solidified to form contact lenses [39]. A diagram of the flow of this process is shown in Figure 6.

In spin casting, a concave mold is placed on a rotatable tube. The mold is filled with liquid HEMA monomer and is then rotated, resulting in the aspheric concave surface of the liquid monomer. The liquid monomer is then cured partially, allowing polymerization and forming a solid aspheric surface. Subsequently, the partially cured polymer is moved to a secondary curing tube where it is rotated again and fully cured, forming the contact lens shape with one concave and one convex surface [40, 41]. A diagram of the flow of this process is shown in Figure 7.

In lathecutting, the dehydrated PHEMA hydrogel is cut into a button shape and turned twice to form the outer and inner surface separately. The machining process for contact lenses is considered a micro turning process that can be conducted using a CNC lathe [38, 42]. In this process, the wettability can be controlled, and the mechanical properties of the hydrogel may be increased [5]. However, as with any machining process, a set of optimum parameters is used to machine the inner and outer surfaces [38, 43]. A diagram of the flow of this process is shown in Figure 8.

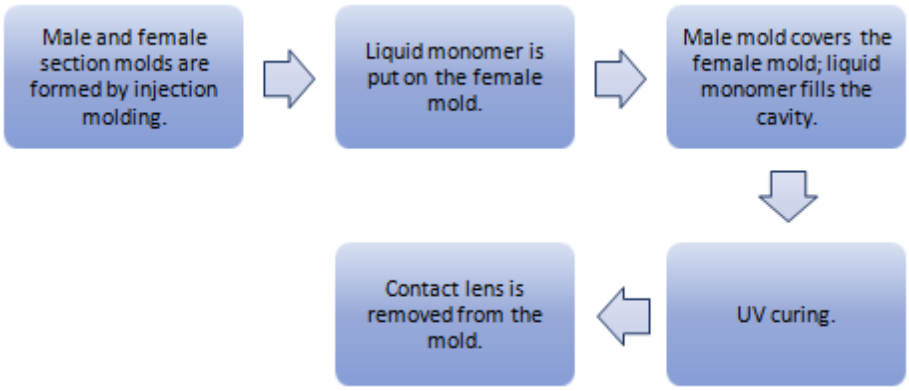

Figure 6. Flowchart of Cast Molding Process for Contact Lens

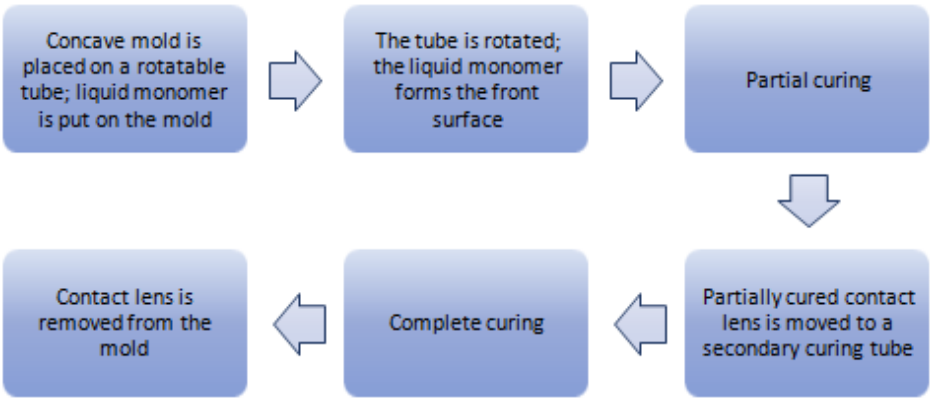

Figure 7. Flowchart of Spin Casting Process for Contact Lens

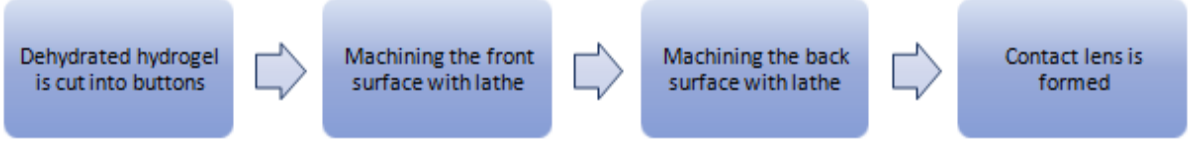

Figure 8. Flowchart of Lathe Cutting Process for Contact Lens

Cast molding is the most popular method of mass-producing contact lenses because it allows multiple lenses to be produced in one process. In contrast, lathe cutting is not favorable for mass production due to its low productivity. In lathe cutting, the contact lenses must be cut one by one, thus increasing the time needed to produce the contact lenses. However, lathe cutting is mainly used for experimental purposes. For IOL implants, diamond turning is a popular method. However, for a hydrogel to be lathed, it must be dried first. A study showed that PHEMA hydrogel, when copolymerized with titanium (IV) oxide (TiO_2), has great machinability when it is dry [29].

Other methods such as injection molding are used to fabricate PP symmetric shell molds of bi-aspheric soft contact lens. The proposed simulation of the injection molding process using Moldex3D software obtained the optimal injection parameters with the Taguchi method [44]. Child *et al*. [31] proposed a simpler and flexible contact lens fabrication method that can be implemented in a laboratory using common tools such as beakers, filter papers, and a UV lamp, and takes about 20 minutes only. The total solution by weight consisted of 63% HEMA, 1% EGDMA, 35% deionized water, and 1% UV initiator [31]. Thin slabs were fabricated by photopolymerizing the HEMA hydrogel solution sandwiched between two glass slides. The lens thickness and curvature were controlled by the two glass slides, and the steel beads were used as eyeball molds. This proposed method successfully produced excellent contact lens properties and reduced the cost and processing time [31].

Recently, a new way to manufacture contact lenses was developed using 3D printing technology. The promising 3D printing manufacturing methods for contact lenses can be used to correct vision, reduce glare, eyestrain, relieve eye allergies, and produce personalized and customized contact lenses based on patient needs and requests. Digital light processing (DLP) is considered the most suitable 3D printing method for manufacturing contact lenses because it enables accurate and uniform layer thickness and surface quality. It also has higher productivity because it allows more than one object to be printed at once. In DLP 3D printing, the polymer is printed on an upside-down print bed and cured by ultraviolet light until it is solidified, forming the contact lenses. However, 3D printing faces the challenge of printing the lenses layer by layer, which risks creating the staircase effect and forming weak attachment points between each layer due to the slicing of a thin, curved object [45].

Conclusion

Polymers are often used in biomedical applications due to their ease of manufacturing and similarities with many living tissues. Among biocompatible polymers, PHEMA hydrogels are advantageous for many ophthalmological applications. Its properties, especially optical properties, are similar to those of the natural human cornea, thus making PHEMA hydrogels excellent materials for soft contact lenses. Furthermore, PHEMA hydrogels provide many copolymerization possibilities to improve their properties, thereby allowing further research and developments in improving the functionality of PHEMA as contact lenses. Many chemicals have been proposed as cross-linkers in the synthesis of copolymerized PHEMA contact lenses. The use of PHEMA for ophthalmologic applications has also evolved. Some studies are still being conducted on a more sophisticated use of PHEMA, such as for drug delivery. PHEMA hydrogel has proven to be a versatile and sustainable biomaterial that is still open to innovations to fulfill broader needs as biocompatible materials.

References

[1] Kalathottukaren, M.T., Kizhakkedathu, J.N. 2018. Mechanisms of blood coagulation in response to biomaterials: Extrinsic factors. In Hemocompatibility of Biomaterials for Clinical Applications, Elsevier. pp. 29–49.

[2] Saptaji, K., Triawan, F., Sai, T.K., Gebremariam, A. 2021. Deburring method of aluminum mould produced by milling process for microfluidic device fabrication, Ind. J. Sci. Technol. 6(1): 123–140, https://doi.org/10.17509/ijost.v6i1.31852.

[3] Golba, B., Benetti, E.M., de Geest, B.G. 2021. Biomaterials applications of cyclic polymers. Biomater. 267(January 2021): 120468, https://doi.org/10.1016/j.biomaterials.2020.120468.

[4] Saptaji, K., Afiqah, S.N., Ramdan, R.D. 2019. A review on measurement methods for machining induced residual stress. Ind. J. Comput. Eng. Des. 1(2): 106–120, https://doi.org/10.35806/ijoced.v1i2.64.

[5] Musgrave, C.S.A., Fang, F. 2019. Contact lens materials: A materials science perspective. Mater. Basel. 12(2): 1–35, https://doi.org/10.3390/ma12020261.

[6] Banerjee, R., Nageswari, K., Puniyani, R.R. 1997. Hematological aspects of biocompatibility-Review article. J. Biomater. Appl. 12(1): 57–76, https://doi.org/10.1177%2F088532829701200104.

[7] Anderson, J.M. 2019. Biocompatibility and Bioresponse to Biomaterials. Elsevier Inc. 675–694, https://doi.org/10.1016/B978-0-12-809880-6.00039-4.

[8] Dhandayuthapani, B., Yoshida, Y., Maekawa, T., Kumar, D.S. 2011. Polymeric scaffolds in tissue engineering application: A review. Int. J. Polym. Sci. 2011(ii): 1–19, https://doi.org/10.1155/2011/290602.

[9] Schink, B., Janssen, P.H., Frings, J. 1992. Microbial degradation of natural and of new synthetic polymers. FEMS Microbiol. Rev. 9(2–4): 311–316, https://doi.org/10.1111/j.1574-6968.1992.tb05852.x.

[10] Ivanova, E.P., Bazaka, K., Crawford, R.J. 2014. Advanced synthetic and hybrid polymer biomaterials derived from inorganic and mixed organic–inorganic sources. New Funct. Biomater. Med. Healthc. 2014: 100–120, https://doi.org/10.1533/ 978178242 2662.100.

[11] Shrivastava, A. 2018. 1 - Introduction to Plastics Engineering. In Plastics Design Library, A.B.T.-I. to P. E. Shrivastava, ed. William Andrew Publishing. pp. 1–16.

[12] Mustafa, N.S., Omer, M.A.A., M.E.M. Garlnabi, Ismail, H.A., Ch, C.H. 2016. Reviewing of General Polymer Types, Properties and Application in Medical Field. Int. J. Sci. Res. 5(8): 212–221, https://doi.org/10.21275/art2016772.

[13] Jiang, L., Zhang, J. 2013. Biodegradable Polymers and Polymer Blends. In Handbook of Biopolymers and Biodegradable Plastics. pp. 109–128.

[14] Chandra, S., Ohama, Y., Chandra, S. 2020. Natural and Synthetic Polymers. In Polymers in Concrete, 1st ed. CRC Press, Boca Raton. pp. 5–25, 2020. https://doi.org/10.1201/9781003068211

[15] Qu, J., Zhao, X., Liang, Y., Zhang, T., Ma, P.X., Guo, B. 2018. Antibacterial adhesive injectable hydrogels with rapid self-healing, extensibility and compressibility as wound dressing for joints skin wound healing. Biomater. 183: 185–199, https://doi.org/10.1016/j.biomaterials.2018.08.044.

[16] Zare, M., Bigham, A., Zare, M., Luo, H., Rezvani Ghomi, E., Ramakrishna, S. 2021. pHEMA: An Overview for Biomedical Applications. Int. J. Mol. Sci. 22(12): 6376, https://doi.org/10.3390/ijms22 126376.

[17] Passos, M.F., *et al*. 2019. PHEMA hydrogels obtained by infrared radiation for cartilage tissue engineering. Int. J. Chem. Eng. 2019: 4249581, https://doi.org/10.1155/2019/4249581.

[18] Bostan, L., *et al*. 2012. Mechanical and tribological properties of poly(hydroxyethyl methacrylate) hydrogels as articular cartilage substitutes. Tribol. Int. 46(1): 215–224, https://doi.org/10.1016/j.triboint. 2011.06.035.

[19] Wang, K., Han, Z. 2017. Injectable hydrogels for ophthalmic applications. J. Contr. Release. 268: 212–224, https://doi.org/10.1016/j.jconrel.2017.10.031.

[20] Li, G., Dobryden, I., Salazar-Sandoval, E.J., Johansson, M., Claesson, P.M. 2019. Load-dependent surface nanomechanical properties of poly-HEMA hydrogels in aqueous medium. Soft Matter. 15(38): 7704–7714, https://doi.org/10.1039/ C9SM01113G.

[21] Passos, M.F., *et al*., 2016. pHEMA hydrogels: Synthesis, kinetics and in vitro tests. J. Therm. Anal. Calorim. 125(1): 361–368, https://doi.org/ 10.1007/s 10973-016-5329-6.

[22] Hong, K.-H., Jeon, Y.-S., Kim, J.-H. 2009. Preparation and properties of modified PHEMA hydrogels containing thermo-responsive pluronic component. Macromol. Res. 17(1): 26–30, https://doi.org/10.10 07/BF03218597.

[23] Montheard, J.-P., Chatzopoulos, M., Chappard, D. 1992. 2-Hydroxyethyl Methacrylate (HEMA): Chemical Properties and Applications in Biomedical Fields. J. Macromol. Sci. Part C(Po): 1–34, https://doi.org/10.1080/15321799208018377.

[24] Li, J., *et al*. 2020. Fibers reinforced composite hydrogels with improved lubrication and load-bearing capacity. Friction. 1–14, https://doi.org/ 10.1007/s40 544-020-0389-9.

[25] Zhao, W., Li, X., Gao, S., Feng, Y., Huang, J. 2017. Understanding mechanical characteristics of cellulose nanocrystals reinforced PHEMA nanocomposite hydrogel: in aqueous cyclic test. Cellulose. 24(5): 2095–2110, https://doi.org/ 10.1007/s 10570-017-1244-7.

[26] Piña-Acosta, J.A., Zizumbo-Lopez, A., Licea-Claverie, A. 2018. Hydrogels of poly(2-hydroxyethyl methacrylate) reinforced with nanocrystalline cellulose as candidates for biomaterials. Polym. Compos. 39: E278–E285, https://doi.org/10.1002/pc.24227.

[27] Li, R., *et al*. 2020. Poly(2-hydroxyethyl methacrylate)/β-cyclodextrin-hyaluronan contact lens with tear protein adsorption resistance and sustained drug delivery for ophthalmic diseases. Acta Biomater. 110: 105–118, https://doi.org/ 10.1016/j.actbio.202 0.04.002.

[28] Ulu, A., *et al*. 2018. Poly(2-hydroxyethyl methacrylate)/boric acid composite hydrogel as soft contact lens material: Thermal, optical, rheological, and enhanced antibacterial properties. J. Appl. Polym. Sci. 135(35): 1–11, https://doi.org/10.1002/ app.46575.

[29] Reinhardt, H.M., Recktenwald, D., Kim, H.C., Hampp, N.A. 2016. High refractive index TiO2-PHEMA hydrogel for ophthalmological applications. J. Mater. Sci. 51(22): 9971–9978, https://doi.org/10.1007/s10853-016-0224-x.

[30] Chamerski, K., *et al*. 2017. Nanoscale observation of dehydration process in PHEMA hydrogel structure, Nanoscale Res. Lett. 12(1): 303, https://doi.org/10.1186/s11671-017-2055-3.

[31] Childs, A., *et al*. 2016. Fabricating customized hydrogel contact lens. Sci. Rep. 6(1): 34905, https://doi.org/10.1038/srep34905.

[32] Jacobs, D.S., *et al*. 2021. CLEAR–Medical use of contact lenses. Contact Lens Anterior Eye. 44(2): 289–329, https://doi.org/10.1016/j.clae.2021.02.002.

[33] Hui, A., Sheardown, H., Jones, L. 2012. Acetic and acrylic acid molecular imprinted model silicone hydrogel materials for ciprofloxacin-HCl delivery. Mater. 5(1): 85–107, https://doi.org/10.3390/ma50 10085.

[34] Hwang, Y., Kim, G. 2016. Evaluation of stability and biocompatibility of PHEMA-PMMA keratoprosthesis by penetrating keratoplasty in rabbits. Lab. Anim. Res. 32(4): 181, https://doi.org/10.5625/lar.2016.32.4.181.

[35] Tomar, N., Tomar, M., Gulati, N., Nagaich, U. 2012. pHEMA hydrogels: Devices for ocular drug delivery. Int. J. Heal. Allied Sci. 1(4): 224, https://doi.org/10.4103/2278-344X.107844.

[36] Zhao, W., Shi, Z., Chen, X., Yang, G., Lenardi, C., Liu, C. 2015. Microstructural and mechanical characteristics of PHEMA-based nanofibre-reinforced hydrogel under compression. Compos. Part B Eng. 76: 292–299, https://doi.org/10.1016/ j.compositesb.2015.02.033.

[37] Mezhoud, S., Le Droumaguet, B., Aimedieu, P., Monchiet, V., Bornert, M., Grande, D. 2021. Investigation of morphology associated with biporous polymeric materials obtained by the double porogen templating approach. Coll. Polym. Sci. 299(3): 537–550, https://doi.org/10.1007/ s00396-020-04747-9.

[38] Mitrovic, A., Stamenkovic, D., Popovic, D., Dragicevic, A. 2020. Manufacturing Process and Thermal Stability of Nanophotonic Soft Contact Lenses. In: Mitrovic N., Milosevic M., Mladenovic G. (eds.), Computational and Experimental Approaches in Materials Science and Engineering. CNNTech 2018. Lecture Notes in Networks and Systems, vol 90. Springer, Cham.

[39] Liu, A.W., Tollefson, N.M., Kosman, D.R. 2011. Method for cast molding contact lenses. EP2340156B1.

[40] Neefe, C.W. 1982. Spin casting of contact lenses. US4416837A.

[41] Newman, S.D. 2017. Systems and methods for the roduction of contact lenses. US2017072649A1.

[42] Saptaji, K., Gebremariam, M.A., Azhari, M.A.B.M. 2018. Machining of biocompatible materials: a review. Int. J. Adv. Manuf. Technol. 97(2018): 2255–2292, https://doi.org/10.1007/s00170-018-19 73-2.

[43] Saptaji, K. 2015. Mechanical Micro-machining. In Nee A. (eds.), Handbook of Manufacturing Engineering and Technology. Springer. London. pp. 1089–1107, https://doi.org/10.1007/978-1-4471-4670-4_12.

[44] Chen, C.-C.A., Vu, L.T., Qiu, Y.-T. 2017. Study on injection molding of shell mold for aspheric contact lens fabrication. Procedia. Eng. 184(2017): 344–349, https://doi.org/10.1016/j.proeng.2017.04.104.

[45] Alam, F., *et al*. 2020. Prospects for additive manufacturing in contact lens devices. Adv. Eng. Mater. 3(2000941): 1–13, https://doi.org/10.1002/adem.202000941.