Chapter 7

Castor Oil Polyurethanes as Biomaterials

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Additional information is available at the end of the chapter

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Abstract

Medical application of polyurethane (PU) elastomers has been contributed significantly to the quality and effectiveness of health care systems. Applications such as nasogastric catheter, sutures, wound dressing, drug delivery system, and insulation on the leads of electronics pacemakers are already in the market. Properties of polyurethanes such as thermal and chemical stability, mechanical performance, and low degradation rate make an outstanding material for that kind of application. More recently, castor oil as polyol source has been investigated due to the needs of friendly environmental sources. In this chapter, we want to approach the advances in polyurethane area from castor oil for application in medicines. A review of castor oil-based polyurethanes, chemical modification, processing techniques, and applications in tissue engineering and medical devices will be made with the objective to understand the current situation, limitations, challenges, and perspective of this type of material.

Keywords: castor oil, polyurethane, biomaterial, elastomer, medicine

1. Introduction

Polyurethanes are an important class of polymers which are used in a surprising array of commercial applications [1]; this special group of heterochain polymers is characterized by the presence of urethane groups, which are esters of carbamic acid, but they are not containing primarily those groups [2]. The polyurethanes include those polymers containing a plurality urethane groups in the molecule backbone, regardless of chemical composition of the rest of the chain. A type of polyurethane may contain aliphatic and aromatic hydrocarbons, esters, ethers, amides, urea, and isocyanurate groups [1]. In **Figure 1**, we can see the variety of functional groups in a polyurethane structure from castor oil and methylene diphenyl diisocyanate against the structure of polyethylene glycol.

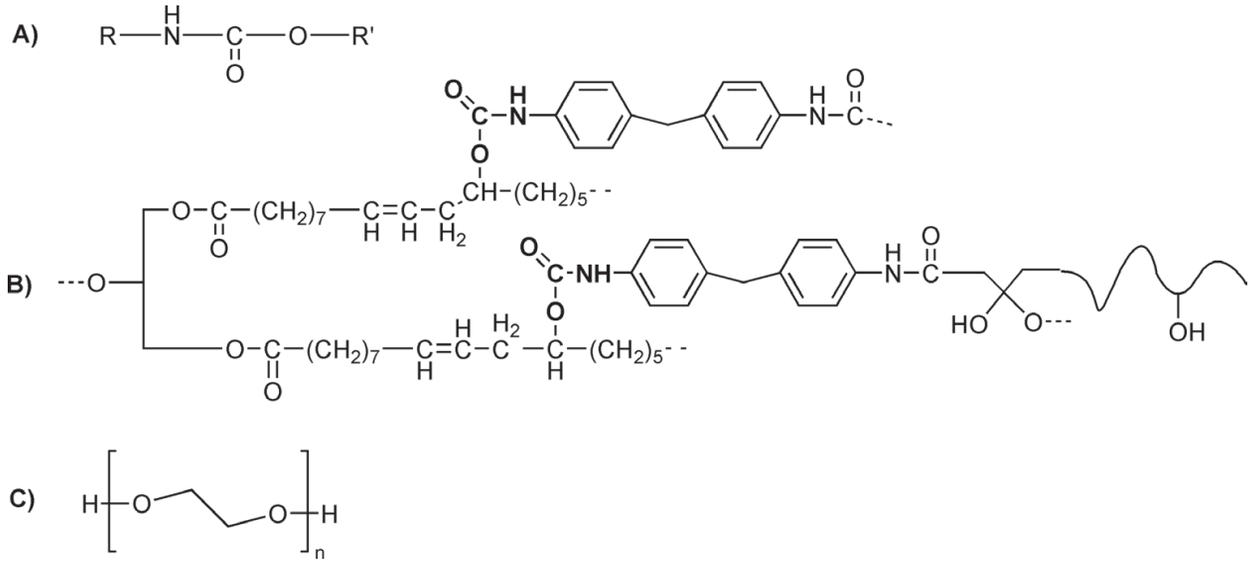

Figure 1. (A) Basic structure of urethane bond. (B) Structure of polyurethane synthetized by the reaction between modified castor oil and diphenylmethane diisocyanate. (C) Structure of polyethylene glycol. Polyurethane structure shows the variety of functional groups in its structure.

The use of polyurethane in the medical field has been documented since 1965 [3]; these products range from nasogastric catheters to insulation on electronic pacemakers. The versatility of being rigid, semirigid or flexible, biocompatible, and hydrolytic stable has abrasion resistance, good physical strength, thermoplasticity or thermosetting and also polyurethanes have been described to resist gamma radiation, oil, bases, and acid. These are some properties which made this type of polymer as an important resource in the medical devices industry [1].

However, current researches have focus on the design of biodegradable formulation for the tissue and organ engineering, drug delivery, and resorbable implants. Biodegradable polyurethanes have a set of design requirements that include the use of biocompatible monomer, tissue-like mechanical response, bioactivity, appropriate degradation rate, and so on [3]. The strong structure-properties relationship of this kind of materials is a good characteristic that allows structure modification to include biodegradable and cell response linkage or functional groups to accommodate the designed criteria.

In this way, the use of castor oil as polyol source has been proved outstanding because it is a biocompatible and hydrophobic monomer which is composed of 90% ricinoleic fatty acid—the unique natural fatty acid with hydroxyl groups in its chain [4]. This characteristic made the polyurethane synthesis easy and also, the reported noncytotoxic activity, elastomeric behavior, and tunable mechanical properties can mimic tissue performance.

According to all information above, in this chapter, we are going to study the recent advances in medical applications of castor oil polyurethanes; first, a brief review of the chemistry of polyurethanes to understand the qualities of these outstanding materials is discussed. Second, an overview of castor oil's applications and advantages is discussed. Next, a review of castor oil chemical modification, filler agents, and scaffold fabrication techniques is discussed. At the end of the chapter, a reflection about perspectives and new challenges of castor oil polyurethanes applications in medicine is described.

2. Chemistry of polyurethanes

The chemistry of urethanes makes use of the reaction of organic isocyanates with compounds containing active hydrogens. For example, hydroxyl groups, amines, and water react to produce urethane linkage, urea groups, and carbon dioxide, respectively.

It is possible to synthesize the urethane groups by various methods, but the most popular one is the reaction between an isocyanate and an alcohol as shown in **Figure 2**. This route was first reported by Wurtz in 1849. But in 1937, Dr. Otto Bayer synthesized the first polyurethane from a diisocyanate and polyester through a polyaddition reaction where the reaction product is exclusively the polymer [2].

As mentioned previously, polyurethanes are an extremely versatile group produced in wide range of densities, cross-link densities, and stiffness. For that reason, the polyurethanes are classified in two main groups: elastic polyurethanes (e.g., flexible foams, elastomers, coating, and adhesive) and rigid polyurethanes (e.g., rigid foams, structural foams, and wood substitutes). This classification is based on the polyol structure. The molecular weight and the number of hydroxyl groups/mol or polyol functionality are two important properties for the arrangement of the structure. Low functional polyol (2–3 hydroxyl groups/mol) and high molecular weight (over 2000 daltons) produce an elastic polyurethane; on the contrary, low molecular weight and high functionality produce a rigid cross-linked polyurethane [1, 2].

Because urethane groups can generate hydrogen bounds, they form a *hard segment* and the rest of the polyol chain is a *soft segment*. The increase in functionality also increases the hydrogen bound interaction and reduces the soft segment mobility, and further reduces the flexibility of the polymer. In **Figure 3**, a representation of the arrangement of each elastic polyurethane and rigid polyurethane has been shown.

Polyurethanes can be prepared by mixing diisocyanates with liquid diol or polyol at fixed NCO/OH ratio being casted in a mold. Isocyanate-terminated prepolymer can be made by mixing with excess of diisocyanate, to further addition of low molecular weight molecules to chain extension. This molecule is usually called *chain extender*. A brief explanation of these components is discussed in the following sections.

2.1. Polyol

Polyols are reactive substances containing at least two reacting groups. These compounds can be hydroxyl or amine-terminated. There are four types of polyols.

2.1.1. Polyether polyols

Polyether polyols are the products of reaction between a simple molecule called initiator and an alkylene oxide. The hydroxyl-terminated polyether polyol functionality depends on the

Figure 2. Scheme of reaction between isocyanate and alcohol.

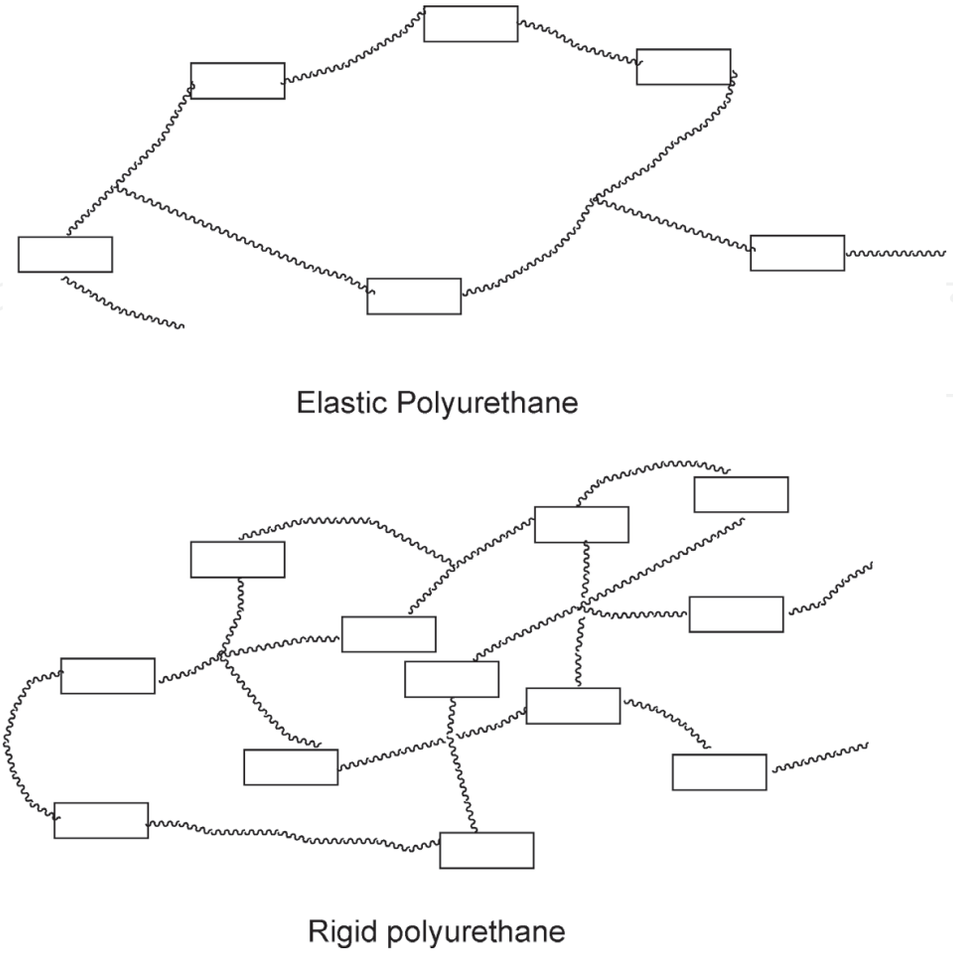

Figure 3. Scheme of elastic and rigid polyurethanes arrangement of hard and soft segments. Adapted from Ref. [2].

functionality of the initiator. If the initiator is a diol, the product will have a functionality of two and, in the same way, if the initiator is a triol, the resultant functionality will be of three [1].

This type also includes active hydrogen-containing polymers such as acrylonitrile or styrene, and also polyureas prepared from the reaction of polyisocyanates and diamines, or polyurethanes prepared by the reaction of polyisocyanates and polyalkanol amines such as triethanol amine. Polyether polyols produce high quality polyurethane foams and elastomers [1]. **Figure 4** shows some structures of reported polyether polyols.

2.1.2. Polyester polyols

Figure 5 shows some structures of polyalkylene glycol esters. They are prepared by condensation polymerization of alkylene glycol and the corresponding diester or diacid.

Vegetable oil-based polyols are included in this category; however, these are produced in most cases by reacting saturated bonds to add hydroxyl groups. Castor oil is a natural vegetable oil-based polyester, and more related information is given in the next section [1].

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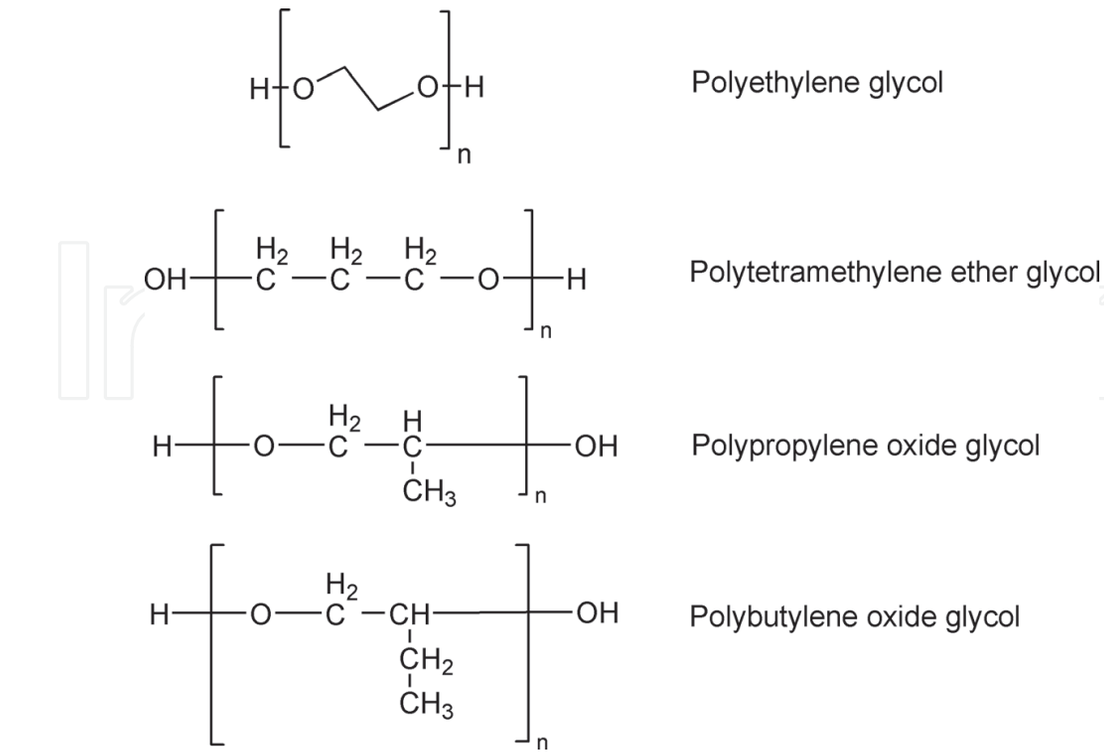


Figure 4. Examples of polyether polyols.

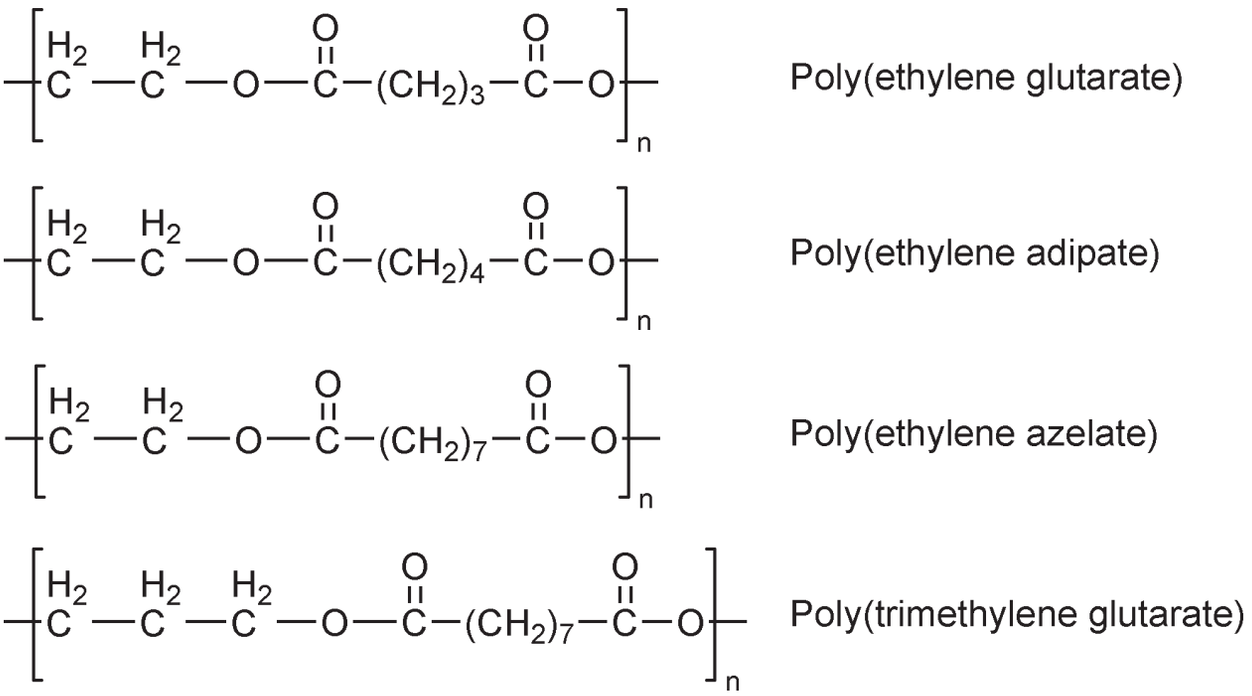


Figure 5. Examples of polyesters polyols.

2.1.3. Polycarbonates

Polycarbonates are prepared by condensation of phosgene or alkylene glycol carbonates. This chemistry is controlled to ensure that resultant contain terminal hydroxyl groups [1]. Polycarbonates-based polyols are characterized by high polarity and strong carbonate bond expecting polyurethanes with good mechanical properties and phase separation [5]. Also, more stability has been observed toward oxidative and hydrolytic biodegradation than polyesters polyols [6]. However, production cost of polycarbonate-based polyols is greater than polyether and polyester. Polycarbonates synthesis is strongly dependent on petroleum. But recently, a new generation of polycarbonates from carbon dioxide has been studied [7].

One important property for polyol analysis is called the hydroxyl value. The quantification of that is described in ASTM D1957 standard.

2.2. Isocyanate

Isocyanate is an important and high reactive organic functional group which is involved in a surprisingly diverse range of chemical reactions. Commercially available organic isocyanates include aliphatic, cycloaliphatic, araliphatic, aromatic, and heterocyclic polyisocyanates [1]. Some examples are presented in **Figure 6**.

The high reactivity of this group can be explained by the electron density among atoms. **Figure 7** shows that how oxygen, which has the highest electron density, has negative charge and carbon with the lowest density has positive charge. Nitrogen is an intermediate negative charge [2].

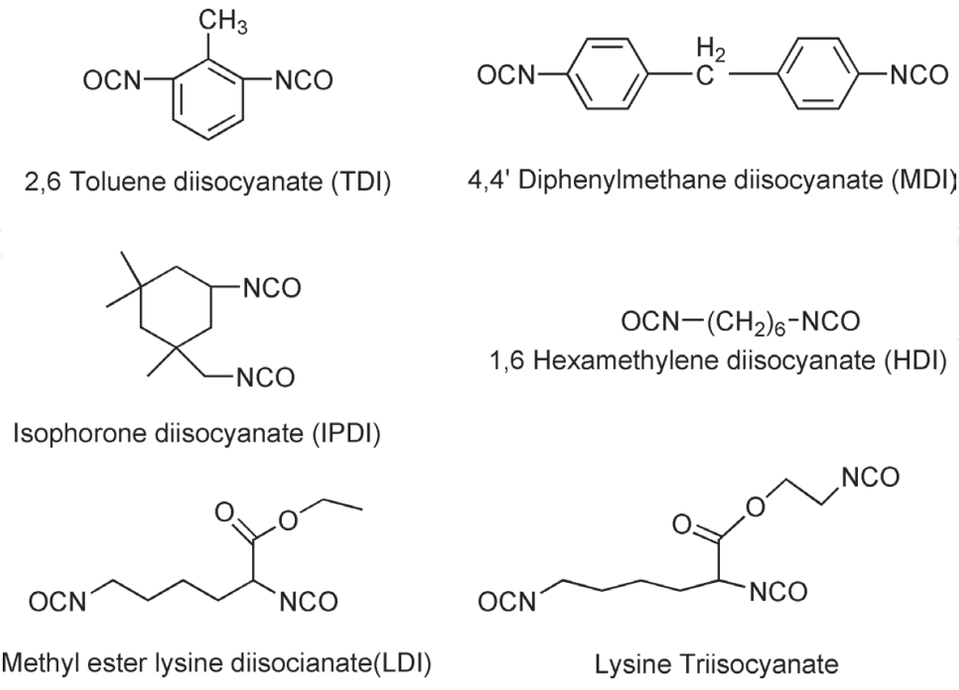


Figure 6. Some commercially available diisocyanates.

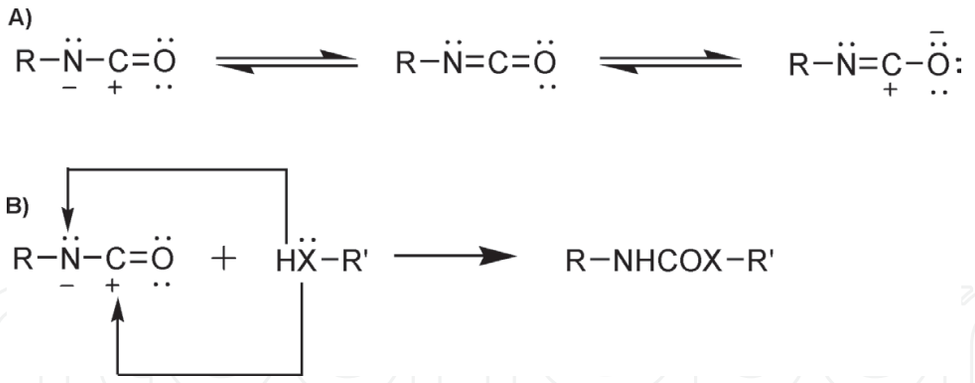


Figure 7. (A) Electron density of isocyanate group, and (B) nucleophilic reaction between isocyanate and active hydrogen compounds. Adapted from Ref. [2].

The reaction between an isocyanate group and active hydrogen is an addition at the carbon-nitrogen double bond. The nucleophilic center of the active hydrogen compounds attacks the electrophilic carbon and the hydrogen is added with the nitrogen atom [2] (**Figure 7**).

As shown in **Figure 6**, there are a lot of commercial isocyanates. However, 4,4-diphenylmethane diisocyanate (MDI) and 2,6-toluene diisocyanate (TDI) are the mostly used compounds in the polyurethane industry [1]. Mechanical performance of MDI- or TDI-based polyurethanes is superior against aliphatic diisocyanates and also, they are more reactive because of their aromatic structure. Despite of this, aromatic structures are not desired in materials for medical applications due to the fact that they could produce toxic degradation products. Recent researches are more focused toward aliphatic diisocyanates for polyurethane synthesis with medical purpose [8].

2.3. Chain extenders

They are low molecular weight reactants that produce familiar elastomeric behavior of the polyurethanes. Chain extenders have molecular weight in the range of 40–300 daltons and can be classified as hydroxyl-terminated or amino-terminated. However, only dysfunctional compounds are considered as chain extender; higher functionalities are considered as crosslinkers [1]. Introduction of those compounds allows to build block copolymer with alternating blocks of hard and soft segments [3].

Introduction of high hard-segment content in the polyurethane backbone determinates the final properties and performance of the polymer. Hard-segment content controls the mechanical properties such as modulus and ultimate strength, in addition to the thermal and hydrolytic stability of the finished product [1].

2.4. Catalyst

Polyurethane synthesis can be catalyzed in the form of any chemical reaction. A catalyst is a material that affects the rate of a reaction but emerges from the reaction unchanged. The catalyst can be considered as the controlling agent of the reaction. It is widely used in urethane

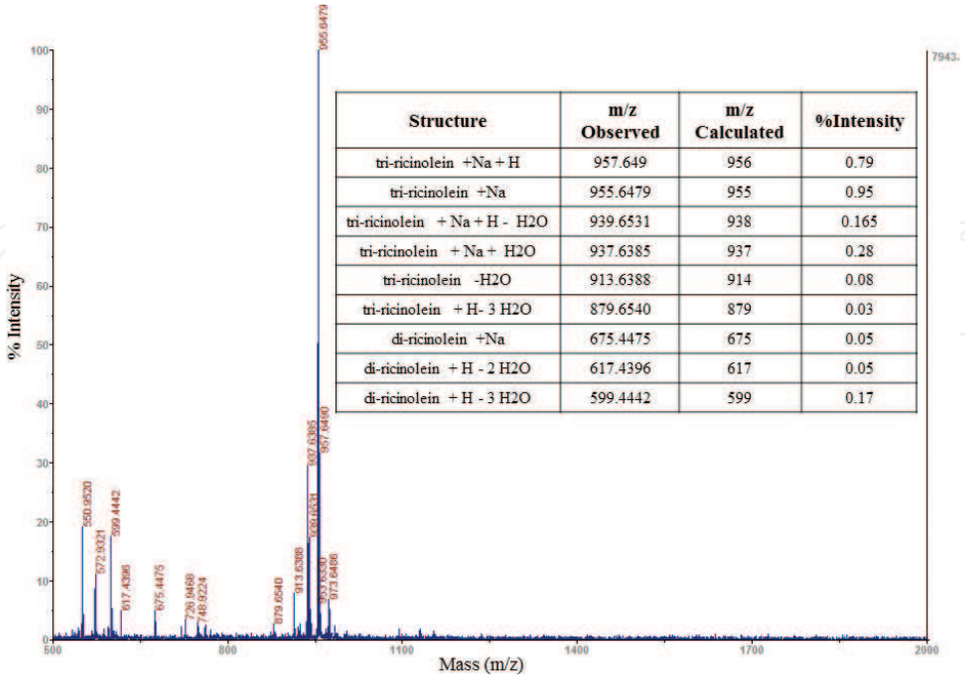
foam production; its primary job is to provide the desired reaction profile, which can be measured by cream, rise, gel, and tack-free times to obtain the desired properties of the foam [1]. The science of the catalytic process is out of range in this chapter; please see reference [1] to enhance your knowledge about the effect of catalyst in the process of polyurethane manufacturing.

Catalysts in polyurethanes are tertiary amines and some of them are organotin, lead, and mercury organometallics. Some tertiary amines used as catalyst are: triethylenediamine, dimethylcyclohexylamine, bis(dimethylaminoethyl) ether, and N-methyl-N′-(2-dimethylaminoethyl)-piperazine. And some commonly used as organotin are dibutyltin dilaurate, stannous octoate, and tin(II) 2-ethylhexanoate.

To summarize, chemical composition of polyurethanes is a factor that determinates the final properties response such as mechanical properties, abrasion resistant, and hydrolytic degradation. Also, as we can observe that the variety of sources opens infinite possibilities to design new and alternative polyurethanes which show the important role of this type of materials in the medical field and the potential to be applied in new fields to improve the health system.

3. Castor oil polyol

Castor oil is extracted from seed of *Ricinus communis*. Its chemical composition has been well described by many authors in the past. All of them agree that around 90% is ricinoleic acid triglyceride [9, 10]. In **Figure 8**, we can observe the distribution of compounds in castor



Structure	m/z Observed	m/z Calculated	%Intensity
tri-ricinolein +Na + H	957.649	956	0.79
tri-ricinolein +Na	955.6479	955	0.95
tri-ricinolein + Na + H - H2O	939.6531	938	0.165
tri-ricinolein + Na + H2O	937.6385	937	0.28
tri-ricinolein -H2O	913.6388	914	0.08
tri-ricinolein + H- 3 H2O	879.6540	879	0.03
di-ricinolein +Na	675.4475	675	0.05
di-ricinolein + H - 2 H2O	617.4396	617	0.05
di-ricinolein + H - 3 H2O	599.4442	599	0.17

Figure 8. Mass spectroscopy of castor oil. Adapted from Ref. [9].

Component	Composition
Ricinoleic acid Triglyceride	77%
Ricinoleic acid di and monoglyceride	14%
Minor components	9%

Table 1. Chemical composition of castor oil determinate by mass spectrometry.

oil obtained from mass spectrometry. In **Table 1**, a summary of the results forming mass spectrometry is shown. Only 9% of the sample is having minor components such as stearic and palmitic acid.

Ricinoleic acid is the unique naturally occurring fatty acid with hydroxyl functional group in its structure. The abundance of castor oil makes it as friendly environmental alternative for polyurethane synthesis. The results of polyurethanes are characterized by being flexible and elastomeric due to the long fatty acid chain and these results lead polyurethanes as a thermosetting material because of their trifunctional functionality nature [10].

Recent studies have shown the potential of castor oil in polyurethane industry applications such as flame retardancy foams [11, 12], adhesives [13, 14], surface coating [15, 16], and, of course, biomaterials [8, 17]. For example, castor oil was used for the synthesis of rigid foams with flame retardancy properties; castor oil was alcoholyzed with glycerol and epoxidation of glyceride castor oil was then carried out to react with diethyl phosphate to get the flame retardancy polyols. Improvement in mechanical strength, thermal stability, and limiting oxygen index at low concentration of phosphate compounds was observed [12]. Also, Zhang et al. [11] used castor oil-based glycerides from transesterification reaction with glycerol and pentaerythritol condensed with phthalic anhydride and ammonium polyphosphate as filler flame retardancy agent. Mechanical properties and thermal stability during pyrolysis were enhanced to obtain better results than the commercially available polyol PS-3152-based polyurethane foams.

In the adhesive field, Moghadam et al. [13] developed a group of castor oil polyester polyols by condensation with difference carboxylic acid. These green adhesive showed superior bonding properties like wood to wood specimen and also, some of them showed good chemical resistance. Polyurethane adhesive based on modified castor oil through transesterification reaction with pentaerythritol was reported; this type of adhesive showed better response with regard to properties like physico-mechanical and anticorrosive with the modification, also improvement in properties was observed with the increase of pentaerythritol in the structure [14].

Above examples of castor oil application demonstrated the flexibility of this source; authors used the advantage of hydroxyl groups for urethane formation and also, they made additional modification to enhance polymer performance. In castor oil structure, there are other functional groups susceptible for chemical modification through easy organic and well-reported reactions. In **Figure 9**, we can observe the structure of castor oil highlighting three important parts: ester bond, double bound, and hydroxyl group.

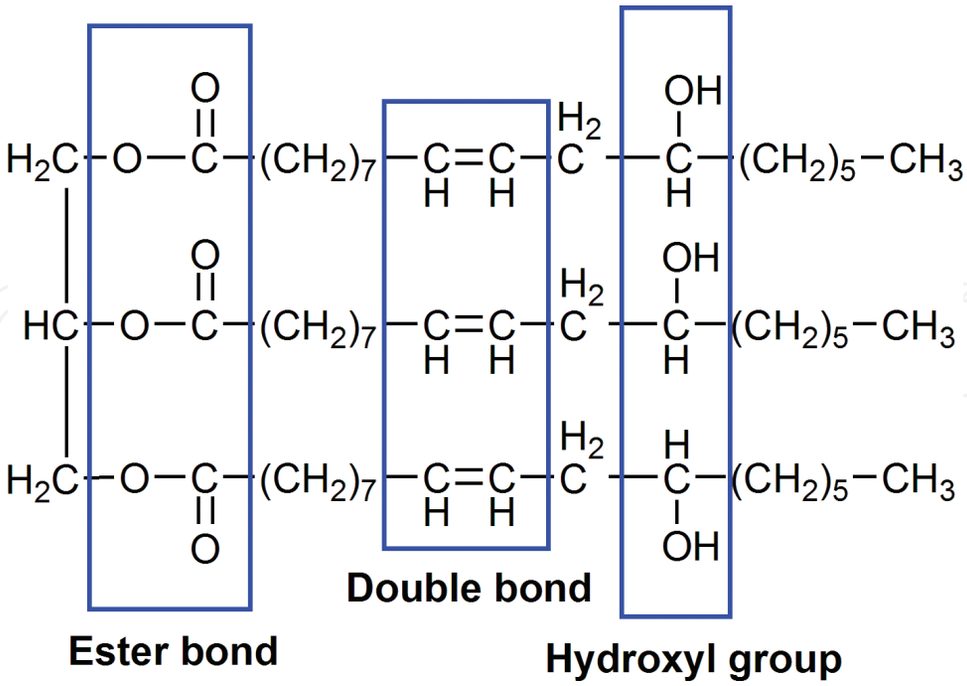


Figure 9. Chemical structure of castor oil. Highlighted are the three main groups related with many chemical reactions. Those groups have been modified by several authors to add desired functional groups and enhance performance of materials.

One of the commons reactions, which has been studied involving the characteristic ester bond of triglyceride, is the transesterification reaction. This type of reaction is widely described in biodiesel manufacturing process where a vegetable oil reacts with a low molecular weight alcohol such as methanol and ethanol. Instead of long linear chains for fuel applications, the aim of castor oil transesterification is to increase the hydroxyl group content, branching of polyols, and finally to increase the hard segments content and network formation of polyurethane structure. For those reasons, polyalcohol compounds such as glycerol, pentaerythritol, and triethanolamine are used in this field.

Application of glycerol in transesterification showed an enhancement on tensile properties, hardness, and chemical attack resistance due to higher increase of cross-linking density. Published works demonstrated an increase of hydroxyl value in glycerides of castor oil [18]. As mentioned above, more hydroxyl groups produce more urethane bonds and these are related with the hydrogen interaction determining cross-linking density. Also, products of transesterification generate more branched polyurethanes which tend to form network arrangements. However, those polymers characterize by low thermal stability [9]. Other works synthesized polyurethanes from modified castor oil obtained by transesterification reaction. Those materials exhibited better mechanical response and thermal stability against glyceride castor oil derivatives. Pentaerythritol by-products have higher hydroxyl value and also higher cross-linking density [18] which is related with an improvement of the performance of the material. In the same way, Dave and Patel [10] use triethanolamine as polyhydroxyl agent in transesterification for interpenetrating networks.

There are few instances that reported the involvement of the saturated bond in castor oil [12]. However, many reactions such as oxidation, polymerization, hydrogenation, epoxidation, halogenation, sulfonation, and other addition reactions could carry out. Additionally, many authors have reported the use of filler agents to enhance some properties [8, 11, 15, 19, 20], these agents are physically bonded with the castor oil and they do not react.

Exploring the chemical structure of the castor oil, we can realize the potential of this source for innovation in the polyurethane field. With the biocompatibility character, it seems obvious why it has excelled in the biomedical field. In the next section, we will study some described approaches of castor oil-based polyurethanes and their derivatives.

3.1. Medical applications

As mention above, medical applications of polyurethanes have contributed significantly to the quality of the care system. More recently, the study of biodegradable formulations for tissue and organ engineering and resorbable implants has been outperformed.

In the context of castor oil, several researches have been carried out studying applications such as wound healing, bioadhesive, cardiac, and bone tissue engineering. To reach adequate degradation rate, mechanical performance, antimicrobial activity, cell-biomaterial interaction, cell viability, and proliferation techniques such as composite reinforced, segmented polyurethane, and scaffold manufacturing are applied. Following a little review of some applied castor oil-based polyurethanes will present highlighting chemical modifications, composites, and scaffolds structures used to achieve desired properties.

Nguyen Dang et al. [21] developed a castor oil-segmented thermoplastic polyurethane with controlled mechanical properties mixing difference soft segments like castor oil, poly(tetrahydrofuran) polyol, and poly(dimethylsiloxane) polyol. They demonstrated that mechanical properties and flexibility of polyurethane can be significantly altered by both incorporated castor oil and poly(dimethylsiloxane)/poly(tetrahydrofuran) polyol ratio during the synthesis. Polyurethanes, also, exhibited a good biocompatibility in 3T3 fibroblast culture. In the same way, Miao et al. [22] synthetized smart polymers with shape memory using castor oil and polycaprolactone triol. Full shape recovery was reached at physiological temperature with various recovery speeds according to the polymer composition. These examples show the use of segmented polyurethanes or block copolymer to control mechanical behavior of materials.

Combining polyester with polyether is a good option for controlled behavior too. Not only mechanical behavior is affected by block copolymerization, adding hydrophilic monomer at reactive mixture could also modify the degradation. Ganji et al. [20] used polyethylene glycol with castor oil to improve degradation rate, because it is a hydrophilic polyol which increases the permeability in bulk as well as surface and makes the material more susceptible to degradation.

Though, there are many different ways to achieve criteria design. As we have already described, alcoholyzed castor oil is an interesting alternative to increase mechanical performance.

Products of transesterification of castor oil with glycerol and pentaerythritol have been used for medical purposes. Du et al. [17] worked with glyceride of castor oil to enhance the mechanical strength of hydroxyapatite/polyurethane scaffolds for bone tissue engineering. Compared to castor oil, the glyceride can provide more hydroxyl groups (from 155 to 288 of the hydroxyl value) resulting in an increase of the scaffold compressive strength (from hundreds of kPa to 4.6 MPa). Likewise, Li et al. [23] reported that the molecular modification of soft segments by glyceride of castor oil can increase the scaffold compressive strength by 48% and the elastic modulus by 96%. Those materials also demonstrated promising prospects for bone repair and regeneration. Also, using pentaerythritol for castor oil modification, Uscategui et al. [24] compared polyurethanes from transesterification reaction with castor oil-based polyurethanes. Though mechanical behavior was increased in alcoholyzed castor oil due to increase of cross-linking density, cell viability of those polymers had lower values than castor oil. But, the observed viability was above 70% which was comparable to commercial polypropylene suture used as positive control producing no toxic effects of materials on L-929 fibroblast.

Introduction of specific bounds or functional groups by chemical modification of castor oil is possible to regulate other properties rather than only mechanical stretch. For example, Sathiskumar et al. [25] had reacted castor oil with sebacic acid, citric acid, and D-mannitol by melt condensation polymerization to introduce ester linkages which are easily cleavable in aqueous medium. The contact angle measurement and hydration test results indicated that the surface of the polymer was hydrophilic and *in vitro* degradation of polymer in PBS solution carried out at physiological conditions indicated that the degradation goes to completion within 21 days. Physical, mechanical, and degradation can be tuned varying the curing conditions of the polyurethanes accordingly to the desired application in human body.

Similarly, Yari et al. [26] synthetized epoxy-terminated polyurethane prepolymer based on castor oil and glycidyltriethylammonium chloride (GTEAC) as a reactive bactericidal agent for wound dressing. Membranes could maintain for a long period the moist environment over the wounds with low exudates. Cytotoxicity analysis of samples against mouse L929 fibroblast and MCA-3D keratinocyte cells showed good cytocompatibility. The membrane containing 50% GTEAC exhibited an effective antibacterial activity while showing acceptable cytocompatibility.

Also, polyols from castor oil transesterification with glycoside starch obtained by glycosylation with ethylene glycol were used to synthetize polyurethanes type bioadhesives with methyl ester lysine diisocyanate (LDI) and isophorone diisocyanate (IPDI). It was determined that polyurethanes obtained from LDI have lower mechanical properties and adhesion, and a higher degree of cross-linking compared to homologs obtained from IPDI. The results of the biodegradable character (contact angle and weight loss) showed that these LDI polyurethanes materials had a greater hydrophobic character due to the presence of the ester bonds in the structure of the hard segment. It was also found that the polyurethanes obtained from LDI have lower cytotoxicity [27].

On the other hand, reinforced composite is another option, wide reported, to achieve design criteria. This process is based on adding some compounds with specific characteristic to get a

desired response of materials. These components are not involved in reactions, but are physically bounded with the polyurethane matrix. **Figure 10** shows a method for composite polyurethanes preparation.

In that context, Uscategui et al. [24], additionally, studied the effect of polycaprolactone diol (PCL) incorporation into modified castor oil-based polyols, obtained from transesterification reaction with pentaerythritol. They studied the effect of three concentrations of PCL (5, 10, 20% w/w). Mechanical test shows performance enhancement in some polymers with PCL, however in some cases, largest concentration of PCL (20%) reduces by phase separation of soft and hard segments. At cell viability test, PCL concentration did not have any effect on modified castor oil-based polyols but 20% of PCL reduced the cell viability and lower concentration did not affect significantly in castor oil-based polyurethanes.

Also, Arevalo et al. [8] studied the effect of chitosan on the physico-chemical, mechanical properties, and biological activity on mixtures of PCL and polyurethanes obtained from castor oil. They studied three concentrations of chitosan (0.5, 1, 2% w/w) and two of PCL (5 and 10%). It was found that the incorporation of chitosan enhances the ultimate tensile strength of the polyurethanes and does not affect the strain at fracture in polyurethanes with 5% of PCL. Mechanical stretch suggested applications on the aorta and the skin. Water absorption was increased with the concentration of chitosan in the matrix due to the hydrophilic behavior of chitosan. The results of *in vitro* biocompatibility suggested that polyurethanes do not cause risks to cell viability and can be used in biomedical applications.

Nowadays, with the enhancement of nanotechnology, nanocomposites have become a new field to study in the biomaterials area. In this case nanoparticles can induce morphological and structural changes in the hard and soft segment, also some nanoparticles give additional bioactivities such as antibacterial [19] and cell adhesion or proliferation [28]. Like this, some studies related with bone and cardiac tissue engineering with castor oil-based polyurethanes have been published.

Li et al. [23], also, studied the effect of nanoparticles of hydroxyapatite (HA) into glycerides of castor oil, when nanoHA particles were incorporated into the matrix, the compressive

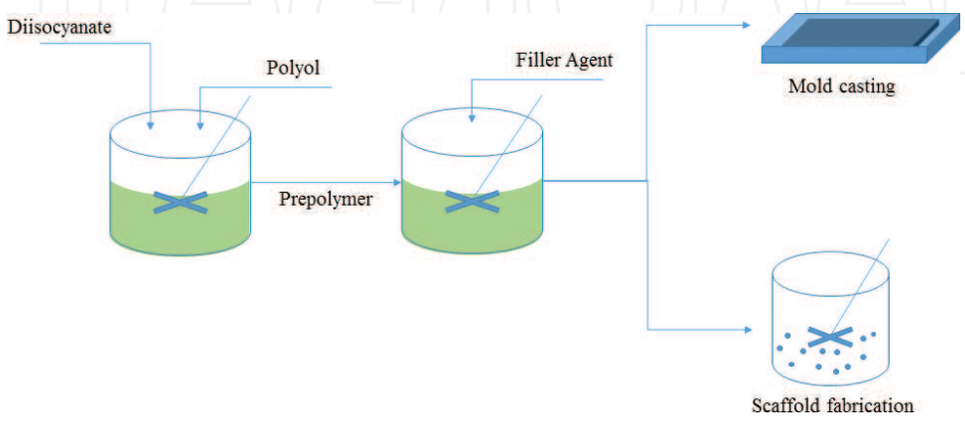


Figure 10. Scheme of composite polyurethane preparation.

strength and elastic modulus further increased by 49–74%, from 2.91 to 4.34 MPa, and from 95 to 165.36 MPa, respectively. Particles improved the interface bounding with the polyurethane and provided effective bioactivity for bonding with bone tissue.

Ganji et al. [20] fabricated nanocomposite scaffolds made of gold nanotubes/nanowires incorporated into biodegradable castor oil-based polyurethanes as alternative for cardiac patches to treat postmyocardial infarction. By incorporating gold nanotubes/nanowires into polyurethane scaffolds, the wired material structure can mimic the electromechanical properties of the myocardium. Cardiomyocyte adhesion and proliferation were strongly increased in response to electrical stimulation on composites. After 4 days of incubation and electrical stimulation on the scaffolds, cardiomyocytes on polyurethane scaffolds samples showed a more native morphology and enhanced proliferation compared to gold-free PU-0. A concentration of 50 ppm of nanoparticles induced optimum cell distribution and spreading, as well as the largest up-regulated expression levels of genes relevant to cardiac differentiation and hypertrophy. In another work, Ganji et al. [29] fabricated porous composite scaffolds for biomedical application based on gold nanotubes/nanowires and mixed with castor oil–polyethylene glycol-based polyurethanes. Addition of 50 or 100 ppm nanostructures had significant effects on thermal, mechanical, and cell attachment of fat-derived mesenchymal stem cells of polyurethanes. Higher cross-link density and better cell attachment and proliferation were observed in polyurethane containing 50 ppm. The results revealed that gold nanotubes/nanowires formed hydrogen bonding with the polyurethane matrix and improved the thermomechanical properties of nanocomposites, as compared with pure PU.

The word "scaffolds" has been mentioned several times in this chapter. Scaffolds are considered as three-dimensional porous structure with the main goal to provide appropriate base for tissue growth and cell proliferation [30]. A lot of techniques are well described in the literature. Some of them are particle leaching, solvent casting/particle leaching, thermally-induced phase separation, melt molding, gas foaming, emulsion freeze-drying, solvent casting/solvent evaporation, electrospinning, 3D printing, and rapid prototyping. However, few of these methods can be applied to castor oil-based polyurethanes because of the cross-linking and thermoset nature of these types of materials, it is not possible to solubilize in any organic solvent so techniques that involve solvents like solvent casting/particle leaching, thermally-induced phase separation are discarded. Additionally, methods such as 3D printing and melt molding require thermoplastic behavior. The pore size of the scaffold should mimic the size of the specific type of cell accordingly with the application; also, pore interconnectivities are desired to allow fluid exchange and cell proliferation.

Methods like particle leaching, gas foaming, and 3D printed sacrificed mold are used to fabricate castor oil-based polyurethane scaffolds.

3.1.1. Particle leaching

Specified diameter particles are added to prepolymer solution; particles remain embedded throughout the polymer matrix after curing period. After immersion in water, particles are leached out leaving a porous structure (**Figure 11**). The shape and size of pores are directly determined by the shape and dimensions of the leachable particles used. Tablet salt, sugar,

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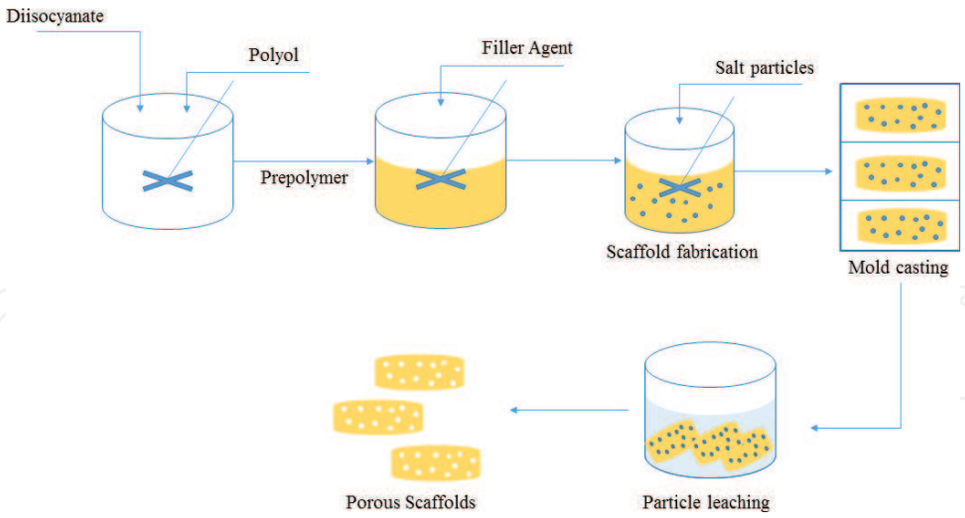

Figure 11. Scheme of particle leaching polyurethane scaffolds preparation.

ammonium chloride, sucrose, starch particles, gelatine and paraffin microsphere have been used. However, it is important to know that particles must be inert during all manufacturing process. Another parameter that influences the structure is the amount of particles added. If the salt content is insufficient, the polymer solution will surround the particles and isolated pores will appear. On the other hand, if the amount of salt added is too high, a deficient structure with voids will be formed due to close geometric packing [30].

This technique was used to obtain porous size between 355 and 600 μm using sieved tablet salt. Scaffolds show cell attachment of H9C2 cardiomyocyte cells [20] and fat-derived mesenchymal stem cells [29]

3.1.2. Gas foaming

Gas foaming is a process that is widely used in industry for the preparation of e.g., expanded polystyrene, polyvinyl chloride foams, but it can also be applied for the preparation of scaffolds. Foaming can be carried out by reacting the components or releasing the gas which is a product of the thermal degradation of the gas-foaming agent. In polyurethanes, water can be added to polyol and isocyanate mixture. Water reacts with an excess of isocyanate producing carbon dioxide which is the foaming agent. This technique is rarely used for the fabrication of scaffolds, because it is hard to control pore diameter and the average pore diameter is too large to allow adequate cell proliferation [30]. However, some authors reported the use of nonreactive foaming agents like cyclopentane [11]. It evaporates with the heat of urethane reaction creating the foam. Most of the applications of this method are related with bone tissue engineering. Like this, Du et al. [17] used gas foaming to develop their HA/glyceride of castor oil-based polyurethane scaffolds with an *in situ* reaction with water. Sixty percent of porosity and 500 μm of interconnectivity were reached with that technique. Also, Li et al. [23] used similar process for scaffold fabrication. They reached a porosity between 52 and 57%. They discussed that a porous structure with a pore size of approximately 200–800 μm and a porosity of 57% are appropriate for the growth of cells in bond tissue engineering.

3.1.3. 3D printed sacrificed mold

This technique required a 3D printer. In this technique, basically, a mold is printed with the desired characteristics of pore size and porosity. Then the prepolymers are casted in the mold allowing curing. After that, mold is removed by dissolving the printed mold with a compatible solvent.

One advantage of 3D printing is to directly print porous scaffolds with designed shape and interconnected porosity from a CAD file with a variety of materials such as ceramic, metallic, polymeric, and composites. And the use of sacrificed mold is an opportunity for thermoset polymers. Generally, this technique contain inherent difficulties to form small-sized tubular channels around 250 mm; the pores in the printed scaffold from the guided approach here are actually the shape of the extruded fiber, which can be readily adjusted by shaping the size and geometry of the nozzle [22].

In this context, Miao et al. [22] use 3D printed PLA scaffold serving as a sacrificial mold to get PCL-castor oil-based polyurethanes with shape memory and with a gradient pore structure to biomimic the tissue structure. The pores had a gradient distribution from the top to the bottom as the distance between pores increased from 240 to 560 mm. These authors used the term four-dimensional printing to include the additional shape memory property of their polyurethanes. Four-dimensional (4D) printing is an emerging new concept that refers to the ability of 3D printed objects to change form and/or function after fabrication, thereby offering additional capabilities and/or performance-driven applications. For example, hydrophilic materials have been utilized to 4D fabricate self-evolving structures that perform geometric folding, curling, expansion, and various other programmed shape changes after submersion in water

In this chapter, we have been discussing how the polyol affects the materials response; however it is important to dedicate a place to talk about isocyanates. There are a lot of commercial available isocyanates and the mostly used in polyurethane industry are MDI and TDI because they are high reactive aromatic structure and also, as we described, they produce superior mechanical response. Aromatic structures should be avoided in medical applications because they are related to toxic degradation products. Many studies have demonstrated carcinogenic potential of aromatic diamines under *in vivo* conditions; these diamines are characteristic degradation products of MDI and TDI [8]. In biomedical fields, there are many researches carried out with aliphatic isocyanates as an alternative, for example Valero et al. [31] compared the mechanical and degradation response of castor oil-based polyurethanes from three difference isocyanates: isophorone diisocyanate (IPDI), methyl ester lysine diisocyanate (LDI), and lysine triisocyanate (LTI). Mechanical stretch was similar in IPDI and LDI but higher in LTI-based polyurethanes, due to high functionality isocyanate, and degradation rate was higher in LDI-based polyurethanes because LDI introduces additional ester bound, as we mention, it is high susceptible to hydrolytic degradation.

It can be realized that many authors were introduced in each section of this chapter. It is because they used different methods to study the effect on several properties, so they can identify the right method for the better performance.

To summarize, castor oil-based biomaterials have been tested at *in vivo* models, especially for bone tissue regeneration. This means that castor oil-based polyurethanes achieve many requirements for real medical applications. It is another proof of the potential of this material in the biomaterials and tissue engineering field. Further, some reported examples of animal's model are presented.

Du et al. [17] used female sprague dawley rats with a defect in region of femoral condyle to test the osteogenesis of HA/glyceride of castor oil-based polyurethanes scaffolds. They conclude with the histological studies that the newly formed bone tissue had appeared around the scaffold and in the pores of scaffold. After 8 weeks, there were more new bone formations around and within the porous scaffold, and no adverse inflammatory response could be noticed. In contrast, the amount of new bone was more in cell-seeded scaffold than unseeded scaffold. Although the cell seeded group seemed to perform slightly better than unseeded group, both scaffolds showed good *in vivo* osteogenesis.

Li et al. [23] tested the *in vivo* osteogenesis of HA/glyceride of castor oil-based polyurethanes scaffolds too with New Zealand white rabbits with a defect in femoral condyles. New bone with high density had formed in the surface region, and a bone matrix and trabecula had also grown into the scaffold porous structure. The quantity of new bone at 24 weeks is substantially greater than the quantity of new bone at 12 weeks. New bone preferentially forms on the surface and subsequently grows inward following an osteoconductive pathway.

Nacer et al. [32] used male *rattus norvegicus albinus*, Wistar lineage submitted to bone defect filled with castor oil-based polymer. Three experimental groups were formed with (1) castor oil polymer containing only calcium carbonate; (2) castor oil polymer with calcium carbonate and doped with 5% of silica nanoparticles; and (3) castor polymer with calcium carbonate doped with 10% of silica nanoparticles. The results showed that there was bone growth in all the studied groups, with a greater tendency of growth in the group 1. After 30 days, all the groups presented similar results. After 60 days, a greater amount of fibroblasts, osteoblasts, osteocytes, and osteoclasts in group 3 were observed, with integrated activity of three kinds of cells involved in the bone activation-reabsorption-formation.

4. Conclusion and perspectives

In this chapter, we studied the chemistry of polyurethanes and we understood the versatility of these types of polymers and their importance in industry. Also, we reviewed the properties that made it an outstanding material for biomedical applications. Additionally, we explored the potential of castor oil-based polyols for biomaterials and tissue engineering applications. It is clear that castor oil have many qualities such as biocompatibility, biodegradability, naturally occurring hydroxyl groups, and easy chemical modification which call the attention for this particular field. However, it is clear too that medical devices and tissue engineering require multiples criteria design, as we observed in the review, from several points of view such as mechanical performance, adequate 3D structure, and adequate degradation rate accordingly with the application, nontoxic degradation products, specific hydrophilic

and hydrophobic behavior, and so on. These requirements could be satisfied combining as many techniques of chemical modification, composite reinforced, scaffold manufacturing, and polyol-isocyanate composition, as need to achieve all the criteria designs for biomaterials. Also, new technologies advances, like 4D printing, are helping to solve the requirements.

Particularly, castor oil-based polyurethanes have a huge way for innovation in the biomaterials fields. As we saw, many of the applications are related with bone tissue engineering. New fields such as skin, vascular tissues, eyes, and connective tissues could explore and, also, for fabrication of medical devices, sutures, catheters, and wound dressing. Also, in the age of bioactive biomaterials, it is important to include the design criteria with additional properties like antibacterial activity which can increase the performance and the value of the material.

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References

[1] Szycher M. Szycher's handbook of polyurethanes. 2nd ed. Boca Raton, FL: CRC Press; 2013.

[2] Ionescu M. Chemistry and technology of polyols for polyurethanes. 1st ed. Shrewsbury: Rapra Technology; 2005.

[3] Touchet TJ, Cosgriff-Hernandez EM. 1 – Hierarchal structure–property relationships of segmented polyurethanes. Advances in Polyurethane Biomaterials. 2016;3-22

[4] Medeiros AMMS, Machado F, Rubim JC. Synthesis and characterization of a magnetic bio-nanocomposite based on magnetic nanoparticles modified by acrylated fatty acids derived from castor oil. European Polymer Journal 2015;**71**:152-163. [Internet]. Elsevier Ltd. Available from: http://dx.doi.org/10.1016/j.eurpolymj.2015.07.023

[5] Jofre-Reche JA, García-Pacios V, Costa V, Colera M, Martín-Martínez JM. Role of the interactions between carbonate groups on the phase separation and properties of waterborne polyurethane dispersions prepared with copolymers of polycarbonate diol. Progress in Organic Coatings. Nov 2015;**88**:199-211. [Internet, cited 5-March-2017]. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0300944015300412

[6] Fernández-d'Arlas B, Alonso-Varona A, Palomares T, Corcuera MA, Eceiza A. Studies on the morphology, properties and biocompatibility of aliphatic diisocyanate-polycarbonate polyurethanes. Polymer Degradation and Stability. Dec 2015;**122**:153-160. [Internet, cited 5-March-2017]. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0141391015301221

[7] Orgilés-Calpena E, Arán-Aís F, Torró-Palau AM, Orgilés-Barceló C. Novel polyurethane reactive hot melt adhesives based on polycarbonate polyols derived from CO2 for the footwear industry. International Journal of Adhesion and Adhesives. 2016;**70**:218-224. [Internet, cited 5-March-2017]. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0143749616301440

[8] Arevalo F, Uscategui YL, Diaz L, Cobo M, Valero MF. Effect of the incorporation of chitosan on the physico-chemical, mechanical properties and biological activity on a mixture of polycaprolactone and polyurethanes obtained from castor oil. Journal of Biomaterials Applicatons. 2016;**31**(5):708-720

[9] Valero MF, Pulido JE, Ramírez Á, Cheng Z. Polyurethanes sintetized of polyols obtained from castor oil modified by transesterification with pentaerythritol. Quimica Nova. 2008;**31**(8):2076-2082. [Internet. SBQ; cited 31-March-2014]. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422008000800031&lng=pt&nrm=iso&tlng=pt

[10] Dave VJ, Patel HS. Synthesis and characterization of interpenetrating polymer networks from transesterified castor oil based polyurethane and polystyrene. Journal of Saudi Chemical Society. 2017;**21**(1):18-24. [Internet, King Saud University]. Available from: http://dx.doi.org/10.1016/j.jscs.2013.08.001

[11] Zhang M, Pan H, Zhang L, Hu L, Zhou Y. Study of the mechanical, thermal properties and flame retardancy of rigid polyurethane foams prepared from modified castor-oil-based polyols. Industrial Crops and Products. 2014;**59**:135-143. [Internet, cited 17-Feburary-2016]. Available from: http://www.sciencedirect.com/science/article/pii/S0926669014002817

[12] Zhang L, Zhang M, Hu L, Zhou Y. Synthesis of rigid polyurethane foams with castor oil-based flame retardant polyols. Industrial Crops and Products. 2014;**52**:380-388. [Internet, Elsevier B.V.]. Available from: http://dx.doi.org/10.1016/j.indcrop.2013.10.043

[13] Moghadam PN, Yarmohamadi M, Hasanzadeh R, Nuri S. Preparation of polyurethane wood adhesives by polyols formulated with polyester polyols based on castor oil. International Journal of Adhesion and Adhesives. 2016;**68**:273-282.

[14] Valero MF, Gonzalez A. Polyurethane adhesive system from castor oil modified by a transesterification reaction. Journal of Elastomers and Plastics. 2012;**44**(5):433-442. [Internet, cited 23-March 2014]. Available from: http://apps.webofknowledge.com.ezproxy.unisabana.edu.co/full_record.do?product=UA&search_mode=Refine&qid=8&SID=1DukxKeCqDaN613PBmH&page=1&doc=8&cacheurlFromRightClick=no

[15] Valero MF, Ortegón Y. Polyurethane elastomers-based modified castor oil and poly(e-caprolactone) for surface-coating applications: synthesis, characterization, and *in vitro* degradation. Journal of Elastomers and Plastics. 2015;**47**(4):360-369

[16] Gite VV., Kulkarni RD, Hundiwale DG, Kapadi UR. Synthesis and characterisation of Polyurethane coatings based on trimer of isophorone diisocyanate (IPDI) and monoglycerides of oils. Surface Coatings International Part B Coatings Transactions. 2006;**89**(2):117-122

[17] Du J, Zou Q, Zuo Y, Li Y. Cytocompatibility and osteogenesis evaluation of HA/GCPU composite as scaffolds for bone tissue engineering. International Journal of Surgery. 2014;**12**(5):404-407. [Internet, Elsevier Ltd]. Available from: http://dx.doi.org/10.1016/j.ijsu.2014.03.005

[18] Valero MF, Pulido JE, Ramírez Á, Cheng Z. Determination of crosslink density of polyurethanes obtained from castor oil modified by transesterification. Polímeros. 2009;**19**(1):14-21. [Internet]. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0104-14282009000100008&lng=es&nrm=iso&tlng=es

[19] Macocinschi D, Filip D, Paslaru E, Munteanu BS, Dumitriu RP, Pricope GM, et al. Polyurethane-extracellular matrix/silver bionanocomposites for urinary catheters. Journal of Bioactive and Compatible Polymers. 2015;**30**(1):99-113. [Internet]. Available from: http://jbc.sagepub.com/cgi/doi/10.1177/0883911514560661

[20] Ganji Y, Li Q, Susanne E, Böttner M, Selhuber-unkel C, Kasra M. Cardiomyocyte behavior on biodegradable polyurethane / gold nanocomposite scaffolds under electrical stimulation. Materials Science and Engineering C: Biomimetic Materials, Sensors and Systems. 2016;**59**:10-18. [Internet, The Authors]. Available from: http://dx.doi.org/10.1016/j.msec.2015.09.074

[21] Nguyen Dang L, Le Hoang S, Malin M, Weisser J, Walter T, Schnabelrauch M, et al. Synthesis and characterization of castor oil-segmented thermoplastic polyurethane with controlled mechanical properties. European Polymer Journal. 2016;**81**:129-137. [Internet]. Available from: http://dx.doi.org/10.1016/j.eurpolymj.2016.05.024

[22] Miao S, Zhu WJ, Leng J, Castro N, Zhang LG. Four-Dimensional printing hierarchy scaffolds with highly biocompatible smart polymers for tissue engineering applications. Tissue Engineering Part C Methods. 2016;**22**(10):952-963. [Internet]. Available from: http://online.liebertpub.com/doi/10.1089/ten.tec.2015.0542

[23] Li L, Zuo Y, Zou Q, Yang B, Lin L, Li J et al. Hierarchical Structure and Mechanical Improvement of an n-HA/GCO–PU Composite Scaffold for Bone Regeneration. ACS Applied Materials & Interfaces. 2015;**7**(40):22618-22629.

[24] Uscátegui Y, Arévalo F, Díaz L, Cobo M, Valero M. Microbial degradation, cytotoxicity and antibacterial activity of polyurethanes based on modified castor oil and polycaprolactone. Journal of Biomaterials Sciences, Polymer Edition. 2016;**27**(18):1860-1879. [Internet, Taylor & Francis]. Available from: http://dx.doi.org/10.1080/09205063.2016.1239948

[25] Sathiskumar PS, Madras G. Synthesis, characterization, degradation of biodegradable castor oil based polyesters. Polymer Degradation and Stability. 2011;**96**(9):1695-1704. [Internet, Elsevier Ltd]. Available from: http://dx.doi.org/10.1016/j.polymdegradstab.2011.07.002

[26] Yari A, Yeganeh H, Bakhshi H, Gharibi R. Preparation and characterization of novel antibacterial castor oil-based polyurethane membranes for wound dressing application. Journal of Biomedical Materials Research - Part A. 2014;**102**(1):84-96

[27] Valero MF, Díaz LE. Bioadhesive polyurethane obtained from polyols derived of castor oil and starch modified candidates in biomedical applications. Revista Latinoamericana de Metalurgia y Materiales. 2016;**36**(1):9-19. [Internet, Universidad Simón Bolívar; cited 21-Feburary-2017]. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-84964070312&partnerID=40&md5=381ffd43402c9686bf8d4b9fd59bbc68

[28] Depan D, Venkata Surya P, Girase B, Misra R. Organic/inorganic hybrid network structure nanocomposite scaffolds based on grafted chitosan for tissue engineering. Acta Biomaterialia. 2011;**7**(5):2163-2175.

[29] Ganji Y, Kasra M, Salahshour Kordestani S, Bagheri Hariri M. Synthesis and characterization of gold nanotube/nanowire-polyurethane composite based on castor oil and polyethylene glycol. Materials Science and Engineering: C Materials for Biological Application. 2014;**42**:341-349. [Internet, cited 24-May-2016]. Available from: http://www.sciencedirect.com/science/article/pii/S0928493114003063

[30] Janik H, Marzec M. A review: Fabrication of porous polyurethane scaffolds. Materials Science and Engineering C: Biomimetic Materials, Sensors and Systems. 2015;**48**:586-591. [Internet, Elsevier B.V.]. Available from: http://dx.doi.org/10.1016/j.msec.2014.12.037

[31] Valero MF, Díaz LE. Polyurethane networks from pentaerythritol-modified castor oil and lysine polyisocyanates: Synthesis, mechanical, and thermal properties and in vitro degradation. Quimica Nova 2014;**37**(9):1441-1445. [Internet, SBQ; cited 21-Feburary-2017]. Available from: http://www.gnresearch.org/doi/10.5935/0100-4042.20140228

[32] Nacer RS, Poppi RR, Carvalho P de TC de, Silva BAK da, Odashiro AN, Silva IS, et al. Castor oil polyurethane containing silica nanoparticles as filling material of bone defect in rats. Acta Cirurgica Brasileira. 2012;**27**:56-62. [Internet, scielo]. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-86502012000100010&nrm=iso

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