This is the authors' version of the article published in European Polymer Journal. The final version is available at https://doi.org/10.1016/j.eurpolymj.2025.113985

Non-Isocyanate Polyurethanes: Perspectives as Biomaterials

Anna Pierrard[a], Sofia F. Melo[b,c], Cécile Oury[c], Christophe Detrembleur[a,d], Christine Jérôme*[a]

[a] Center for Education and Research on Macromolecules (CERM), CESAM Research Unit, Department of Chemistry, University of Liège, Allée du six août 11, Building B6c, 4000 Liège, Belgium. E-mail: c.jerome@uliege.be

[b] Faculty of Medicine, University of Liège, Avenue Hippocrate 15, Quartier Hôpital, 4000 Liège, Belgium.

[c] GIGA Cardiovascular Sciences - Laboratory of Cardiology, University of Liège, Avenue de l'Hôpital 11, Quartier Hôpital, Building B34, 4000 Liège, Belgium.

[d] WEL Research Institute, 1300 Wavre, Belgium.

*Corresponding author **: E-mail: c.jerome@uliege.be**

Abstract

Polyurethanes (PUs) are used in many applications, including in the medical sector (e.g., breast implants, vascular access and cardiac assist devices) due to their remarkable mechanical performances combined with proven in vivo biocompatibility. However, their industrial synthesis from toxic isocyanate precursors poses environmental and health concerns. With regulations increasingly restricting the isocyanate use, exploring greener alternatives has become imperative. Extensive research of health-friendlier synthesis processes triggered the emergence of a new family of PUs called Non-Isocyanate Polyurethanes (NIPUs). Recent developments have shown that NIPUs are already competitive with PUs, for example in the adhesives and coatings field, and new opportunities emerged in biomedical applications. This review highlights recent breakthroughs regarding NIPUs development, emphasizing their appealing properties for biomedical applications as well as their biocompatibility. By shedding light on the close relationship between their peculiar structure and specific properties, we highlight the potential of NIPUs to engineer biomaterials and we position them as unprecedented options for the design of future medical devices.

This is the authors' version of the article published in European Polymer Journal. The final version is available at https://doi.org/10.1016/j.eurpolymj.2025.113985

Introduction

Biomaterials are materials engineered to be used in contact with living systems for medical applications, either for therapeutics such as implants, medical devices or treatments of diseases or injuries, or for diagnostics as sensors. This implies that a material used as biomaterial must demonstrate biocompatibility, meaning that it or its degradation products should not induce undesirable host tissue response when in contact with the body. A first aspect to define a material as biocompatible is to demonstrate the absence of toxicity or inflammatory reactions (also called "negative" biocompatibility). Different aspects of biocompatibility, depending on several factors according to the specific use and the type of application envisaged, must be validated before considering clinical use of the biomaterial.[1–3]

Polymer materials offer a wide diversity of mechanical properties from stiff thermosets to soft elastomers and hydrogels, combined with tunable chemical properties giving control of their stability, ranging from fast degradation to long-term stability. They are thus particularly attractive to meet specific medical needs. While some bio-based polymers like alginate, starch, chitosan, cellulose or even collagen find applications as biomaterials[4,5], the development of synthetic polymers for biomedical purposes (such as devices, wound dressings, therapeutics, drug delivery, diagnostics, …) has also accelerated given that the fine control of their structure during synthesis allows the tailoring of their final properties (mechanical, degradation, etc.) depending on the function targeted in the final application.[5,6] In view of the increasingly important advances in current medicine, the demand of more sophisticated and innovative biomaterials is therefore growing.

In this context, polyurethanes (PUs), constituting one of the most widely produced polymer families in the world (particularly in the form of foams, coatings and adhesives) thanks to their ease of synthesis, low cost, and tunable mechanical properties, have been used in various applications, including in the highly demanding biomedical market.[7] Indeed, the high stability of the urethane bonds gives them remarkable mechanical properties and easily adaptable structures, and consequently makes them suitable for diverse medical applications, such as in various implants, drug delivery systems, catheters, or even wound dressings. They have therefore been used clinically for many years and their suitability for biomedical applications no longer needs to be proven.[8–15] Nevertheless, these PUs are industrially produced from very toxic isocyanate reagents that are responsible for serious environmental and health problems (notably respiratory diseases of exposed workers) and are themselves produced from the even more toxic phosgene gas, which is becoming less and less acceptable today.[16–20] Therefore, alternative PU synthesis routes, which are more environmental and health friendly, are rapidly developing to avoid the use of these dangerous and harmful isocyanates, leading to the emergence of so-called non-isocyanate polyurethanes (NIPUs).[21–26] From these greener and safer newly

developed chemistries, some novel PU structures emerge, such as poly(hydroxy-urethanes) (PHU)s[7,17,26,26–28] and poly(hydroxy-oxazolidones) (PHOx)s[29–32] that, in addition to the urethane bond, exhibit an additional hydroxyl group. The latter impart specific properties to these NIPUs, which constitute new opportunities for engineering (bio)materials.[33]

Given the importance and the fast development of NIPUs, several reviews have already been dedicated to them. However, most of these reviews focus mainly on the variety of synthesis routes[17,26–28,34,35], and the range of potential monomers[35–37]. As a result, NIPUs applications have received relatively little attention in existing literature reviews.[17,22,38] The present review is the first to explore and discuss the potential of NIPUs as promising (bio)materials for medical applications. In addition to describing the main characteristics of the synthesis and the structures of PUs, that have led to their positioning as biomaterials currently marketed for the medical field, this review thus mainly aims to highlight recent developments in NIPU materials, in particular PHUs and PHOxs, and emphasize their attractive properties for biomedical applications. By shedding light on the close relationship between their peculiar structures and valuable specific properties, we review all the current available reports on their specific design and use as biomaterials for diverse biomedical applications, namely tissue engineering, drug delivery systems, antibacterial materials, and blood-contacting devices. This review focuses for the first time on NIPU biomaterials and demonstrates their significant potential, positioning them as unprecedented candidates for the design of future medical devices.

1. Polyurethanes from isocyanates

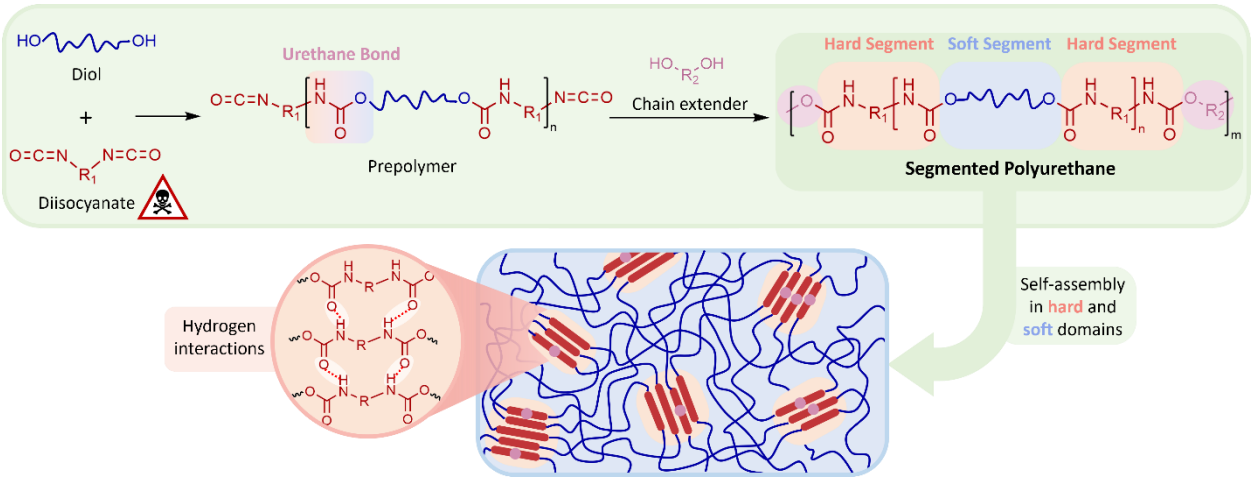
2.1. History and development of polyurethanes from isocyanates

Polyurethanes, originally invented by Otto Bayer in the 1930s[39], refer to a family of polymers containing organic segments linked by urethane (carbamate) bonds. This urethane group is exceptionally stable and rigid and has a cohesive energy similar to that of the amide function.[40,41] This confers to polyurethanes excellent mechanical properties, even though these urethane groups might represent only a small fraction of their macromolecular structure. While PUs can be prepared by chain-growth polymerization of cyclic carbamate monomers, the step-growth process based on the reaction of easily accessible diols and/or polyols with a diisocyanate is widespread (**Scheme 1**). In this step-growth synthesis process, PUs can be manufactured to achieve a wide variety of hardness, from stiff thermoplastics to soft elastomers simply by varying the structure of the monomers used. This triggered their development in numerous applications and nowadays, they are thus used in different forms such as adhesives, coatings, and flexible or rigid foams, which constitutes the majority of their use.[26] In

2023, due to their high demand, the global polyurethane market size was estimated to be USD 78.90 billion and is even expected to reach USD 104.99 billion by 2028.[42]

The large diversity of high-performance PUs available results from the easy synthesis of segmented PUs by step-growth polymerization from a wide range of readily available monomers and prepolymers. First, a diol (mainly macromolecular) reacts with a diisocyanate compound in the presence of a tin-based catalyst to form a prepolymer. In a second step, this prepolymer is elongated by reaction with a chain-extender, usually a diol (or a diamine) of low molar mass, to form additional urethane (or urea) linkages and obtain the final segmented PUs. As shown in **Scheme 1**, not only the structure of the macromolecular diol (macrodiol, shown in blue) but also that of the R_1 group of the diisocyanate (red) and of the R_2 group of the second diol (pink) can be varied to tailor the PU structure depending on the targeted properties. The resulting segmented PUs are generally phase-separated due to the immiscibility of the macrodiol and the polyurethane segments, as the latter tend to self-associate by hydrogen bonding and crystallize. When the macrodiol has a low glass-transition temperature (T_g) and is thus viscous or rubbery, the microphase-separation of the macrodiol soft segments and polyurethane hard segments in different domains results in PU thermoplastics with remarkable elastomer properties.[43–45] The broad choice of possible macrodiols such as polydimethylsiloxane (PDMS), polyether (polytetrahydrofuran (PTHF)/ poly(tetramethylene oxide) (PTMO), polyethylene glycol (PEG),…), or even polyester (polycaprolactone (PCL), …) diols, leads to segmented PUs that can for instance be either rigid or soft, hydrophilic or hydrophobic, (bio)degradable or not, and thus suitable for a wide range of applications. In addition to fossil-sourced precursors, the synthesis of PUs starting from bio-based compounds (generally polyols) from renewable sources further expands the diversity of PU structures and properties, such as using lignin as polyol to improve the flame resistance of the resulting PUs.[46,47] Therefore, due to their remarkable properties and numerous advantages, PUs are currently present on multiple markets, including automotive, construction and insulation, furniture, textile, sports, packaging, electronics and health sectors.[26,39]

This is the authors' version of the article published in European Polymer Journal. The final version is available at https://doi.org/10.1016/j.eurpolymj.2025.113985

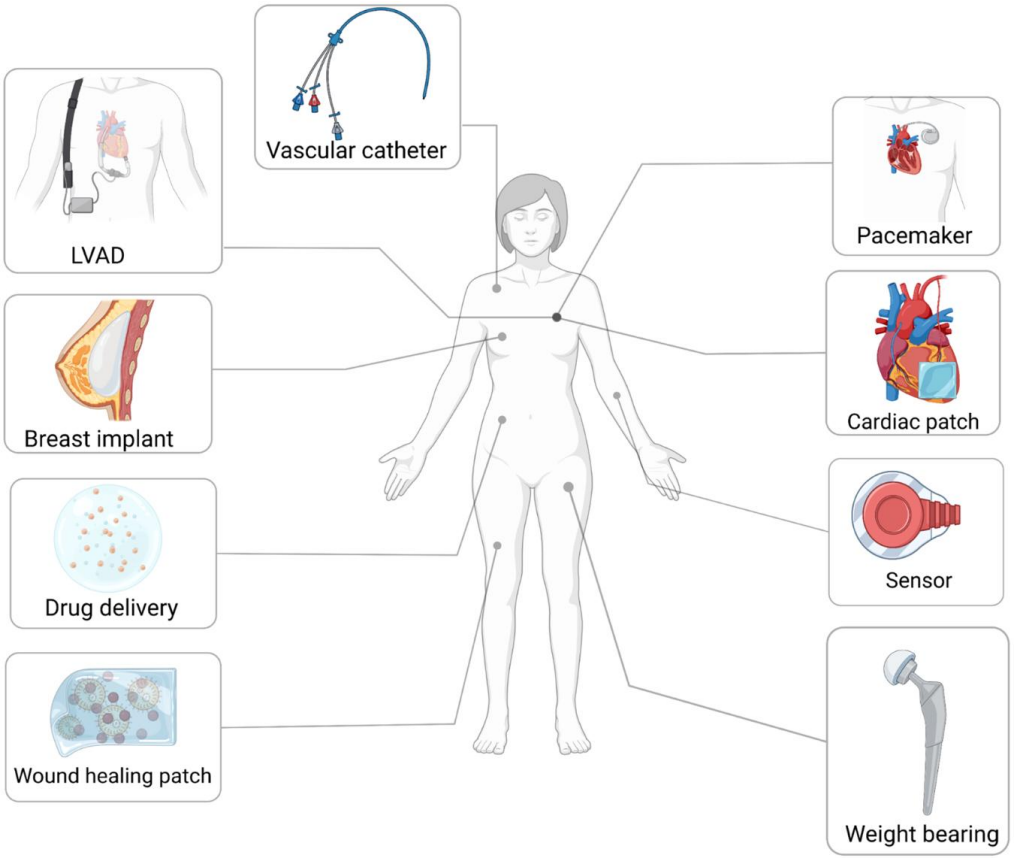


Scheme 1. Synthesis of segmented polyurethanes and representation of the phase-separation between hard and soft domains when a soft macromolecular diol is used.

2.2. Biomedical applications of polyurethanes

Regarding their use in the biomedical field, PUs were first introduced in this type of application in the late 1950s and have since been largely used for these purposes. Indeed, the chemical structure of PUs can be easily modulated and tailored to combine high mechanical strength with other valuable properties such as elasticity, chemical stability, wear resistance, hydrophobicity or even anti-bacterial activity (e.g., by the incorporation of bactericidal groups in their structure, such as quaternary ammonium salts).[4,48,49] The biocompatibility of PUs, obtained either from petro- or bio-sourced precursors, such as those deriving from vegetable oils,[50] has also been extensively reported in the literature. Many *in vitro* and *in vivo* tests demonstrated their bio/cytocompatibility towards several cell types. PUs hemocompatibility has also been described, although less often, and some PUs could even display anti-thrombogenic properties.[5,10,51] Medical grade segmented PUs have thus been commercialized by several companies, such as BASF, DSM, Bayer or Lubrizol, most of them using the aromatic 4,4′-methylene diphenyl diisocyanate to insure hard segments of high strength and stability with a melting temperature generally ranging between 150 and 250 °C.[10] As for the choice of the macrodiol precursor, it depends on the type of targeted application. Indeed, when biodegradability is required (which is the case for most scaffolds used in tissue engineering approaches, wound dressings, or drug-delivery systems), polyester-based PUs are chosen, since the ester bonds are easily hydrolyzed by esterase enzymes.[15] On the contrary, for implantation applications requiring long-term stability of the PU mechanical properties, more stable soft segments have been developed, generally either polyether (e.g., Pellethane®, Elasthane®, …), polycarbonate (Corethane®, Carbotane®,

…) or silicone (Pursil®, Carbosil®, Elast-Eon® …).[15] The mechanical properties of such PUs are particularly suitable for prosthetic materials such as weight-bearing, breast, ocular, or even heart valve prostheses, as well as intravascular catheters and stents. PUs are also part of diverse cardiac assist devices, such as pacemakers (leads), heart assist pumps, Left Ventricular Assist Devices (LVAD) and total artificial hearts (housing and chambers).[4,10,39,44,49,52–54] Finally, they also find applications in sensors[51], e.g., as a membrane to cover implantable biosensors in order to ensure their biocompatibility.[55] The **Scheme 2** shows the main applications of segmented PUs currently used clinically.[44] As illustrated, they play a significant role in many medical fields. In pharmacology, they are found in a variety of injectable or implantable drug-delivery systems[56,57], in dermatology, they are used as patches insuring wound healing[51,58]), in reconstructive surgery as breast implants, in orthopedics, they are relevant in weight-bearing prostheses, in cardiology, they are used for various cardiovascular devices (such as pacemakers, cardiac patches, sensors and catheters [11,13,51,56]), etc.[8,10]



Scheme 2. Current reported biomedical applications of polyurethanes.[44] Copyright Elsevier Ltd (2025).

For long-term applications such as the latter, the urethane bond has been found to display excellent hydrolysis resistance.[15] However, even if the urethane bond is considered

stable regarding hydrolysis, *in vivo* long-term biostability issues associated with PUs have been reported in the literature, as they may be subject to biodegradation and oxidative-, aging-, or environmental stress cracking phenomena due to their daily use, leading to the deterioration of their mechanical performances. Strategies have therefore been developed to improve the biostability of segmented PUs, notably by the replacement of polyether and polycarbonate soft segments, which play an important role in the shortening of the stability duration, by more stable chains such as polysiloxanes or polyolefins.[10,13,14,44,51,59–65] For example, Simmons et al.[66] tested and compared the biostability of a siloxane-based polyurethane (Elast-Eon®) and two types of Pellethane® containing different amounts of the poly(tetramethylene glycol) soft segment, namely 2363-80A and 2363-55D, of different stiffness and commonly used for catheters. While the softer Pellethane® sample (2363-80A), i.e. with the larger content of polyether soft segment, showed signs of substantial and deep degradation after 3 months and fractured after 6 months of *in vivo* implantation, the Pellethane® 2363-55D and the siloxane-based PUs showed respectively minor and little to no degradation at both implantation times.

Thanks to their easy and low-cost synthesis, their exceptional mechanical properties mimicking those of soft-tissues, their biocompatibility, and their versatility of physico-chemical properties arising from the wide range of possible monomers employed, segmented PUs have thus become materials of first choice for use as biomaterials for high-performance medical systems. They have therefore been developed and used in numerous biomedical applications throughout the years and are still used as of today.

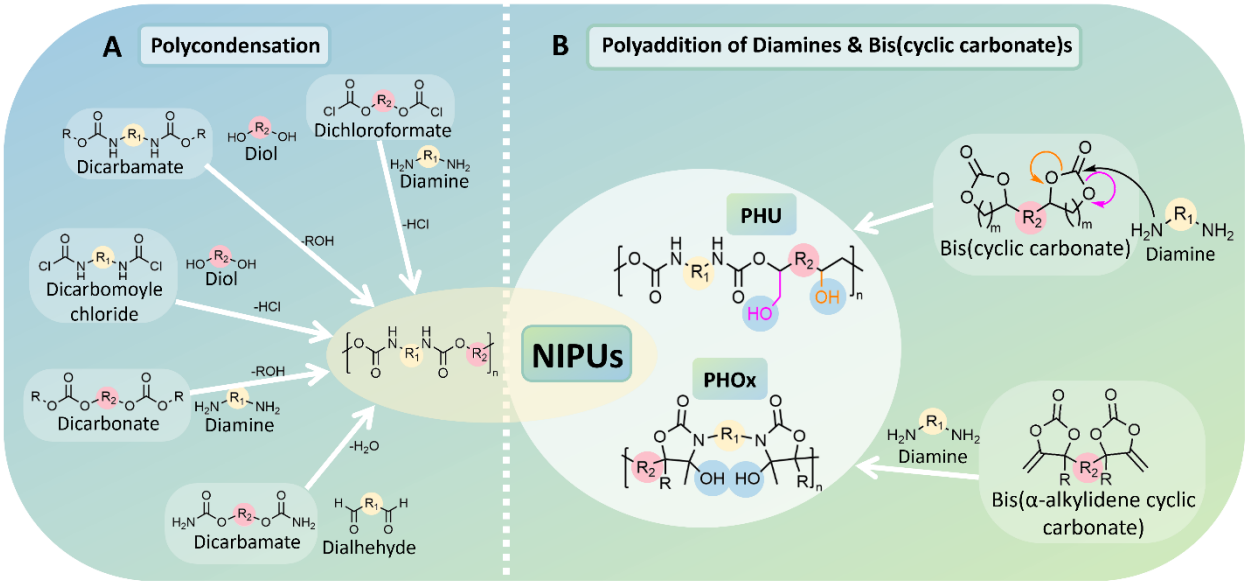
2. Non-Isocyanate Polyurethanes

3.1. History and development of non-isocyanate polyurethanes

Although PUs are materials of choice for highly demanding biomedical applications, their industrial synthesis has a major drawback. Indeed, serious safety concerns have arisen due to the high toxicity of the isocyanate compounds required to efficiently generate the urethane bonds. These isocyanates are responsible for severe environmental and human health damages, such as asthma and lung injuries, dermal and eye-related irritations and acute poisoning, to which workers are exposed.[4,16,18,19,67–69] In addition, isocyanate compounds are synthesized from phosgene ($COCl_2$), an even more toxic gas used as lethal and harmful chemical weapon during World War I, but still intensively produced due to its low cost and ease of synthesis. Regulations from official organizations have therefore been developed to limit their use, such as the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) legislation made by the European Parliament and Council.[27,70] Precautions are thus taken at industrial levels, but

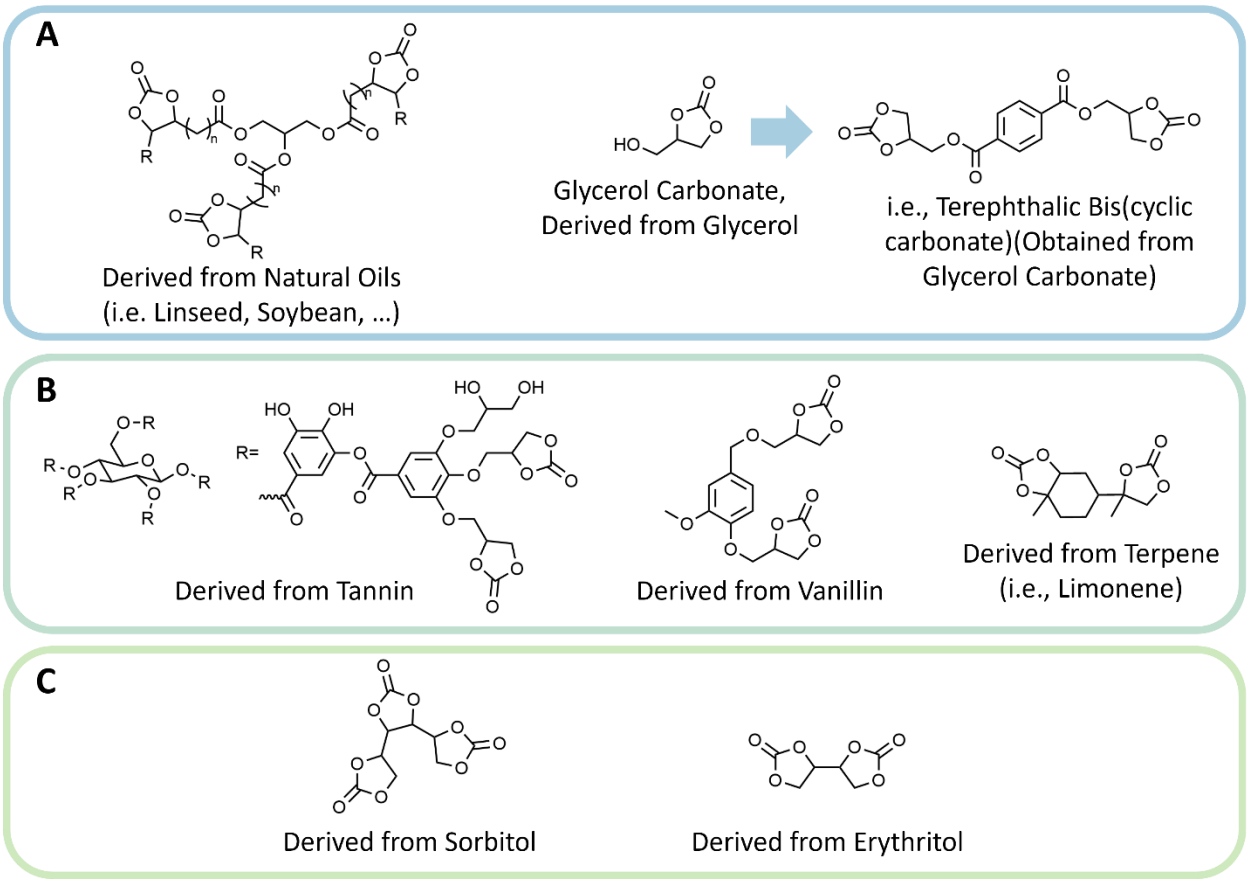
accidental exposure can happen, like the infamous example of the catastrophic accident of Bhopal in India in 1984, where thousands of people died due to the release of gases containing methyl isocyanate and phosgene, thereby also polluting the region.[71,72,70] These limitations are thus likely to be expanded in the future to increasingly restrict the use of isocyanates with the aim of making industrial syntheses safer.

The production of isocyanate-free PUs by more environmental- and health-friendly alternative routes has therefore become a growing area of research.[17,24,26,28,73–75] Several alternative synthesis pathways have thus been developed to exclude these hazardous and moisture-sensitive isocyanate compounds, leading to so called non-isocyanate polyurethanes (NIPUs).[17,28,38,47,73] Among them, polycondensations (for example of dichloroformate and diamine) have been investigated to replace the conventional isocyanate polyaddition to diol derivatives of traditionally synthesized PUs. These various polycondensation processes, shown in **Scheme 3.A** (adapted from Cornille et al.[26]), lead to NIPUs with structures similar to those of isocyanate-based PUs and advantageously allow the synthesis of segmented NIPUs that could particularly be used in biomedical applications, which is not the case of another alternative pathway, i.e., the ring-opening polymerization of cyclic carbamates or aziridine. However, they have the inconvenience of generating toxic by-products (volatile or toxic compounds) which contaminate the materials obtained. Moreover, some of the used precursors are also derived from harmful phosgene.[28,75]



Scheme 3. Synthesis pathways and structures of non-isocyanate polyurethanes (NIPUs) obtained by polycondensation (**A**) and polyaddition of diamines and bis(cyclic carbonate)s (**B**).

In this context, a new isocyanate-free route to NIPUs was born, namely the polyaddition between diamines and bis(cyclic carbonate)s (**Scheme 3.B**), as the ring-opening of the latter by primary amines is a facile way to produce urethane bonds in safer conditions than by the isocyanate chemistry. Actively investigated, this relevant procedure is easy to implement, safe, quite cost-effective, does not release any by-products, and valorizes carbon dioxide to easily produce the cyclic carbonates. Indeed, this emblematic waste product responsible for global warming is currently valorized as an abundant and cheap carbon source for the synthesis of organic compounds, and notably in this case, 5-membered cyclic carbonates by the quantitative catalyzed coupling to epoxides.[29,37,76–85] Moreover, as already shown for PUs[46,47], it is possible to synthesize NIPUs from bio-sourced derivatives, either (poly)cyclic carbonates or (poly)amines, which makes the synthesis of these new polymers even greener by limiting fossil-sourced raw materials. The epoxides needed to produce cyclic carbonates can be partially or totally of bio-origin, and a wide range of possible cyclic carbonate precursors has already been reported in the literature, for example starting from natural vegetable oils (triglycerides, such as linseed or soybean oil[36,86–94], whose unsaturations are easily oxidized into epoxides, from glycerol to produce glycerol carbonate[95,96]), from wood derivatives (such as cellulose[97], tannin[98–100], lignin[101–103], vanillin[104–106] or terpene[107,108] derivatives), or even from starch and sugar (i.e. sorbitol[109] or erythritol[110,111]). Some examples of these different bio-sourced cyclic carbonates are shown in **Scheme 4**.[35,75,112–114] Additionally to the epoxides, a broad range of bio-based poly(amine)s can also be employed, such as 1,4-butanediamine, lysinol[115], or 1,10-decanediamine[116].[75,117–119] It is therefore possible to prepare NIPUs of high bio-based content by combining both bio-based monomers.[109] For example, Hu et al.[88] developed reprocessable PHUs by combining carbonated soybean oil and sorbitol ether carbonate with Priamine 1074, a bio-based diamine derived from oleic and/or linoleic acid to reach a biobased content of up to 100%. Since the reactivity of the 5-membered cyclic carbonates[120] is quite low, it most often requires a thermal treatment for the polymerization to occur at decent rates and/or the use of some catalysts, e.g. organic (such as TBD, MTBD, thiourea, DBU, TEA …)[23,121,122], salts (Lewis acids such as lithium-based salts or strong bases such as quaternary ammonium salts)[123–125], or organo-metallic catalysts (zinc, tin or chrome-based).[26,28,78,79,126] Polymerizations were also accelerated by using 5-membered cyclic carbonates bearing electron withdrawing groups such as ether or ester groups (which increase the carbonyl electrophilicity)[127,128] or by utilizing more reactive six-, seven- or eight-membered cyclic carbonates.[129–135]



Scheme 4. Examples of bio-sourced cyclic carbonates used for the synthesis of NIPUs: (**A**) originating from natural vegetable oils, (**B**) from wood, and (**C**) from starch and sugar.

This side-product-free process keeps the advantage and versatility of the step-growth polymerization by allowing the production of segmented NIPUs with a wide range of possible structures and properties by changing the R_1 (in pale red) and R_2 groups (in pale yellow) represented on the **Scheme 3**, which is of special interest for biomedical applications. Indeed, various bis-amino end-capped polymers, such as bis-amino-polysiloxanes, or bis-amino-polyethers (like Jeffamine®) are available and make possible the synthesis of segmented polymers by copolymerization with small bis(cyclic carbonate) monomers.[52,53,103,136] Moreover, the opposite approach, i.e., the synthesis of cyclic carbonate end-capped macromonomers has also been reported, such as for PDMS[137,138], or for several polyethers like PEG[139], poly(propylene glycol) (PPG)[140–142] or PTHF[43,142], leading to a diversity of NIPU structures by combination with various small size diamine compounds. As examples, Nanclares et al.[43] successfully synthesized segmented PU elastomers by using bis(cyclic carbonate)s of both bisphenol A and PTHF as precursors for hard and soft segments, respectively, and *m*-xylylenediamine as chain extender. Rossi de Aguiar et al.[137]

developed a hybrid non-isocyanate PDMS-urethane for the coating of biomedical grade metals used for orthopedic and dental implants. To do so, a PDMS-based bis(cyclic carbonate) and either 3-aminopropyltriethoxysilane or 5-amino-1,3,3-trimethylcyclohexanemethylamine were mixed before being deposited by drop casting on metals (titanium alloy and stainless steel). Physical treatments were then applied to improve the adhesion of these coatings, which also prevented the corrosion of the metals in contact with physiological medium by acting as a hydrophobic physical barrier. Hydrogels were also developed by Gennen et al.[139] by the solvent-free step-growth polymerization of a CO_2-sourced hydrophilic PEG-based bis(cyclic carbonate) and several polyamines, one acting as crosslinker. These networks once immersed in water were able to absorb and retain large amounts of water, leading to soft hydrogels of interest for biomedical applications such as wound dressings or scaffolds for cell culture. The compression strength of these hydrogels could also be increased, with strain at break ranging from 61 to 85% and stress at break ranging from 43 to 1366 kPa by incorporating inorganic nanoclay in the formulations before the polymerization step, demonstrating the tunability of their mechanical properties. Later on, by using hydrosoluble precursors, Bourguignon et al. also developed various NIPU hydrogels with high water-swelling ability. These are synthesized in water at room temperature, without any catalyst and from commercially available poly(amine)s.[143,144] By using poly(vinyl amine) in the formulations, these waterborne NIPUs have proved capable of capturing formaldehyde, a toxic product contributing to indoor air pollution, through the formation of methylene bridges.[145]

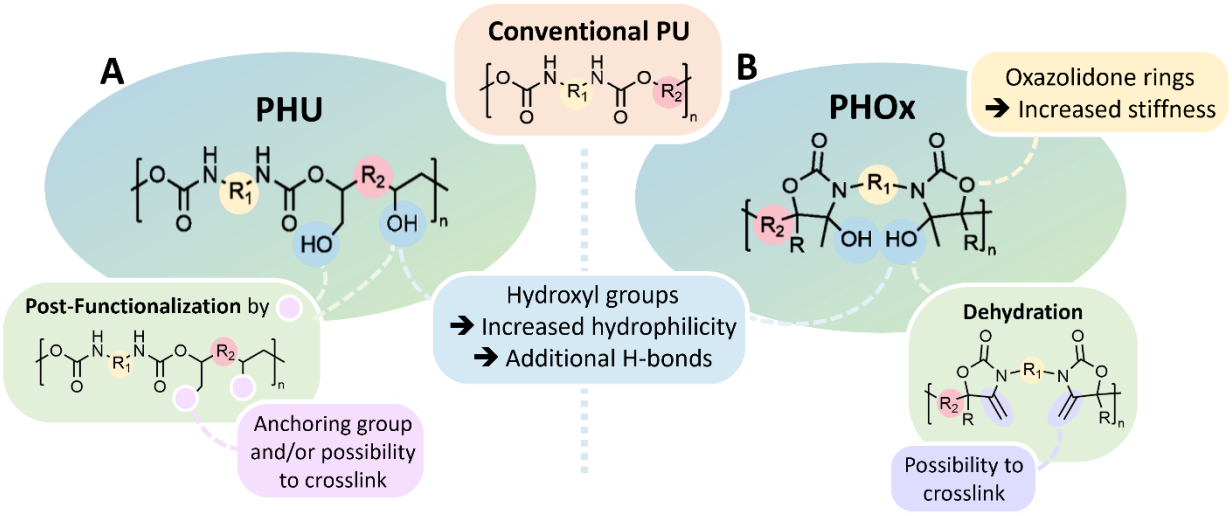
Remarkably, this polyaddition strategy also leads to NIPUs with structures that differ from those of conventionally synthesized PUs by the presence of additional pendant primary and secondary hydroxyl groups (shown in blue in **Scheme 3.B**) that result from the non-regioselective aminolysis of the cyclic carbonate monomers. The NIPUs synthesized by this process are therefore also called poly(hydroxyurethane)s (PHUs) and have specific properties due to the presence of these hydroxyl groups along their polymer backbone. First, these polymers exhibit increased hydrophilicity and water uptake compared to their PU counterparts, which can be favorable for (biomedical) applications that require this behavior, e.g. for hydrogels[43,146,147], and which, in addition, could facilitate their impregnation with drugs to achieve controlled drug delivery. The hydrolytic stability of these materials, when used for long-term applications, can also be impacted as absorbed water can act as plasticizer[148], changing the properties of the material over time or even causing irreversible hydrolysis and/or cracking, which can increase under elevated temperatures. To investigate this potential effect, Kotanen et al.[146] analyzed the hydrolytic stability of hybrid PU/PHU adhesives and saw that their water absorption was rapidly followed by a quasi-equilibrium, and that increasing the water temperature to 50 or 70 °C produced a second faster water uptake step. While the PU/PHU material was not

dramatically affected by short water immersion time, even when increasing the temperature to 50 °C, a longer immersion period of one month at elevated temperature was proven damaging as the adhesive started to lose its integrity at 50 °C and eventually solvate at 70 °C. Magliozzi et al.[149] also developed biobased PHU networks with shape memory properties at body temperature and hydrolysable after a few months of immersion in D_2O (to be directly analyzed by ^1H nuclear magnetic resonance), which can be valorized for several biomedical applications. Fanjul-Moisterín et al.[53] synthesized PEG-based hydrogels that were found to be stable in an aqueous medium when their water content was low, while gels with higher water contents (above 90 wt%) were hydrolyzed after a few months.

Moreover, these hydroxyls can also be responsible for additional interactions with surfaces which can be exploited to improve the adhesion performance of PHUs used as coatings and adhesives (generally in the form of thermosets).[33] These groups are also capable of forming inter- and intramolecular hydrogen bonds (H-bonds) with urethane groups, increasing their chemical resistance[22,150] and also, in the case of linear NIPUs, the viscosity of the polymers during their synthesis, which is the main cause of their lower molar masses.[120,151] In some cases, they can also form H-bonds with other segments such as polyethers (in polyether-PHUs), preventing the nanophase separation which traditionally occurs in conventional PUs between these soft segments and the urethane parts constituting the hard segments. As a result, linear PHUs generally flow under the force of gravity and obtaining thermoplastic PHUs can be very challenging. To solve this problem, some groups have developed various strategies, such as incorporating more steric hindrance in the polyether segment (e.g., replacing PEG by PPG)[152], diluting the oxygen atom content (i.e., replacing PEG by PTHF)[43,152], and/or combine this soft segment with a rigid and aromatic *m*-xylylenediamine as chain-extender to bring harder segments[43], a rigid and aromatic divinylbenzene- or resorcinol bis(cyclic carbonate)[153], and/or a diamine-diamide chain extender.[154]

Additionally, the presence of these hydroxyl groups gives the interesting possibility to post-modify the polymers, e.g. by post-functionalizing PHUs by various anchoring groups, which can be of great interest to target specific applications, especially in the biomedical field (**Scheme 5.A**).[26,43,49,155,156] Indeed, these anchoring groups can be used to introduce specific functions such as esters, silyl ethers, acrylates or olefins, which can affect the PHU thermo-mechanical properties but might also be exploited for post-crosslinking reactions (for instance by thiol-ene reaction).[155,157–160] This post-crosslinking ability is of particular interest for example to reinforce the mechanical properties of the polymers, improve their stability or even give them the ability to be 3D printed (i.e., by photo-crosslinking). As an example, the specific intermolecular interactions (multiple H-bonds between the urethane groups, the hydroxyl groups and the

polyether segments) occurring in a PPG-PHU led to viscosities particularly well-adapted for nozzle-based 3D photoprinting process. Accordingly, a photocurable ink consisting in a PPG-PHU end-capped with allyl groups mixed with a crosslinker bearing three thiol groups and a photoinitiator were printed into networks by photo-induced thiol-ene reaction, and various elastomer structures, which can be used in biomedical applications, such as a vaginal ring, were thus easily 3D printed.[140] Some PHUs have therefore already demonstrated their high potential to substitute isocyanate-based conventional PUs in numerous current applications, such as foams[161–167] or adhesives and coatings.[92,168–173] Furthermore, their particular structures and properties, described above, prove that they offer new opportunities that could also be interesting for the development of biomedical applications, not only in the form of foams, adhesives or coatings, more widely described, but also as alternative bulk elastomers for implantation.



Scheme 5. Structures and properties of PHUs (**A**) and PHOxs (**B**) and possible post-modifications.

Most recently, another family of NIPUs has been reported, namely poly(hydroxy-oxazolidone)s (PHOx)s, produced by the polyaddition of diamines with bis(□-alkylidene cyclic carbonate)s (**Scheme 3.B** and **Scheme 5.B**). In contrast to the previous 5-membered cyclic carbonates prepared from epoxides, these novel cyclic carbonates compounds are produced by the organocatalyzed carboxylative coupling of CO_2 to the corresponding bis(propargylic alcohol)s, and contain an exocyclic olefinic function that enables a regiocontrolled ring-opening while strongly enhancing their reactivity towards the amines.[29,30,124,125,174–186] With this new process, fast reactions are therefore obtained at room temperature and under catalyst-free conditions, which consist first in the formation of an oxo-urethane linkage by ring-opening of the cyclic carbonate, followed by a spontaneous cyclization into a hydroxy-oxazolidone ring.[29,31] In contrast to PHUs,

PHOxs are thus characterized by cyclic urethane linkages that increase the chain stiffness, leading to polymers characterized by a high glass transition temperature (up to 130 °C).[31] Various bis(□-alkylidene cyclic carbonate)s have already been synthesized with linear, cyclic, or even aromatic spacers,[29,32,37,175,179,187–189] and the scope of PHOx has been further expanded by varying the nature of the diamine.[31] Like PHUs, the presence of hydroxyl groups on their structures gives them a relative hydrophilic site as well as the ability to be post-modified, for example by introducing alkylidene groups by facile dehydration[31,190,191], which can be interesting to prepare networks (**Scheme 5.B**). Finally, some promising PHOxs have already shown high potential as adhesives[189] and coatings[190], or in high temperature applications[31,32], and their novel structures and properties could also open new possibilities. Future innovative applications can be envisioned, as their higher stiffness (compared to PHUs) could extend the range of possible uses of NIPUs.

3.2. NIPUs in biomedical applications: advantages and limitations

Given the novel structures and properties of NIPUs, researchers naturally began to study their biological properties. In this review, we particularly address PHUs, since the biological properties of PHOxs have not yet been reported in the literature. The first studies reported on PHUs intended for such biomedical applications date from 2016[137,139] and the first biocompatibility tests performed on this family of polymers were reported in 2017.[4] Since then, the performances of various NIPUs tailored for diverse medical applications have been more widely investigated. In this review, they will be discussed in regard to their biomedical use, divided into four categories, as schematized in **Scheme 6** and summarized in **Table 1** (tissue engineering), **Table 2** (drug-delivery and antimicrobial) and **Table 3** (blood-contacting devices), also describing the structures of their precursors.

3.2.1. Tissue engineering applications

To foresee the use of new materials that have not yet been used in a commercial medical device, their biocompatibility first needs to be assessed by *in vitro* cytotoxicity tests. It is recommended to consider both a direct contact test, where cells are put in the presence of the new material, and an indirect contact test, where it is the extracts from the material that are in contact with the cells. According to ISO 10993-5, a threshold of 70% in the percentages of metabolic activity (relative percentage compared to a negative control – usually cells incubated in their normal culture medium) must be reached to define a material as non-cytotoxic.[192]

As an illustrative example, the absence of cytotoxicity of PHU networks obtained from a tannic acid precursor was accordingly demonstrated by Esmaeili et al.[100], who designed bio-based NIPU networks by curing of either diethylenetriamine or diaminodiphenylmethane and a monomer bearing cyclic carbonate functions prepared by chemical fixation of CO_2 of a tannic acid-based epoxy resin. Indeed, by performing a 3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide (MTT) assay on fibroblasts exposed to the extracts of the PHU networks (indirect contact test) for 72 h, these cells showed a viability of 84 ± 1%, thus confirming the biocompatibility of these biomaterials and showing promising signs for their future use in tissue engineering scaffolds without releasing toxic products. Interestingly, these PHU networks comprising tannic acid derivatives in their structure were specially chosen given the antioxidant, antimicrobial, anti-inflammatory and anticarcinogenic properties of this natural polyphenolic waste, given that these are all valuable properties for tissue engineering approaches.[193] Since the antioxidant properties derive from the number of phenolic groups present in the structure of tannic acid[194,195], the antioxidant activity of these group-bearing NIPU networks was evaluated by measuring their 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals scavenging ability and comparing it to that of guaiacol, a common commercial antioxidant. These studies proved that the NIPU networks effectively trapped the DPPH radicals and therefore confirmed their antioxidant activity. These networks, by combining biocompatibility and antioxidant properties, demonstrated strong promise for temporary tissue engineered scaffolds able to locally decrease cellular oxidative hassle. Another example is that of Ghosal et al.[196], who recently took advantage of the hydroxyl groups formed during the aminolysis of ethylene carbonate to synthesize diurethane-diol monomers valuable for the synthesis of polyester-urethanes by polycondensation with different renewable acids. Various scaffolds for soft tissue engineering applications were thereby prepared by reaction between low-cost renewable precursors and recycled poly(ethylene terephthalate) (PET) waste (bottles) through a catalyst- and solvent-free melt polycondensation process. These biodegradable materials, via hydrolysis of their ester bonds, and their degradation products are reported as non-cytotoxic towards mouse fibroblasts (cell viability >95% after 1 day of indirect contact), proving their potential for these biomedical applications.

Tissue engineering approaches generally require the manufacturing of scaffolds which are usually porous. To produce them, one of the most attractive techniques is electrospinning, as it allows the production of nonwoven fiber mats with a high surface-to-volume ratio and high porosity, advantageous to help cells to penetrate and grow inside. These mats can then be used as scaffolds for tissue regeneration by mimicking the structure and the properties of the host tissue, provided that the fibers have suitable mechanical strength. Aduba et al.[52] have synthesized a segmented poly(amide-

hydroxyurethane) by one-pot melt polymerization of a renewably sourced 9,10-cyclic carbonate-methyl decanoate, 1,12-diaminododecane, and Jeffamine THF-100. This PHU thermoplastic was then successfully electrospun in fiber mats characterized by a Young's modulus of 6-9 MPa and a stress at break of ≈ 1.5 MPa, that are similar to values reported for electrospun PU fibers.[197] They also showed that these poly(amide-hydroxyurethane)-based fibrous mats exhibited higher water uptake than their synthesized thermoplastic PU counterparts (control), which is of interest when applications as wound dressing or drug delivery systems are foreseen. The biocompatibility of these mats was assessed through the evaluation of the viability of primary human fibroblasts after 24 h and 72 h of exposure to the fibrous mat degradation byproducts. Results confirmed the non-cytotoxicity of the polymeric meshes. These fibrous mats are therefore promising not only to be used as scaffolds for tissue engineering but also for wound dressings, and drug delivery applications. Carbajo-Gordillo et al.[198] also synthesized PHU-based porous multicomponent hydrogels with improved rheological properties in a single-step process. To do so, they combined two polymers, namely crosslinked PHU synthesized (by reaction between diethylenetriamine and/or 1,6 hexamethylenediamine and a bis(cyclic carbonate) derived from 1-thioglycerol or 1,2-dithioglycerol along with tris(2-aminoethyl)amine) *in situ* within a colloidal solution of either poly(vinyl alcohol) or gelatin derived from porcine skin. These semi-interpenetrating polymer networks (SIPNs), whose chains are entangled with each other, formed porous and stable three-dimensional scaffolds that are particularly interesting for drug delivery and tissue engineering applications, although no biological tests have yet been carried out on these biomaterials.

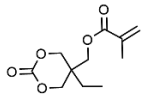
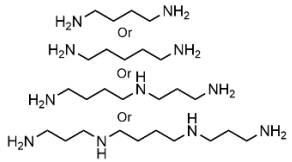
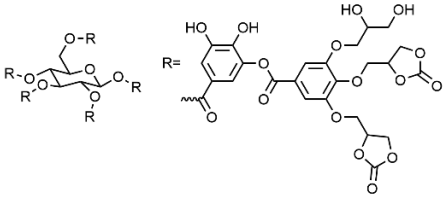
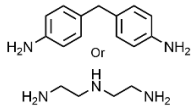
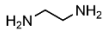
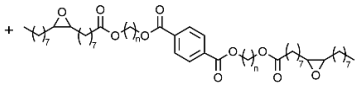
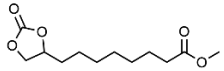
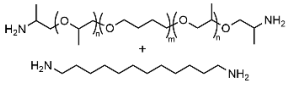
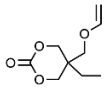
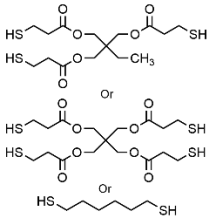
Additive manufacturing, or 3D printing, is another emerging technology, encompassing various techniques, and particularly suited to the processing of biomaterials since it can meet the current needs of personalized medicine by allowing the on-demand creation of customized objects (e.g. implants adapted to a specific patient). In particular, the 3D printing of PUs has already been reported in the literature[199–204], even though these approaches mostly concern isocyanate-based PUs and usually lack printing resolution, which is crucial in the case of biomedical applications. Indeed, surface irregularities can contribute to unwanted structural stresses, flow dysfunctions, or the adhesion of bacteria.[205] Pyo et al.[4] first reported the continuous optical (UV-light based) 3D printing of photopolymerizable NIPUs. To prepare them, photocurable diurethane monomers were first synthesized from different biogenic amines and six-membered cyclic carbonates bearing a methacrylate group. These monomers were then UV-crosslinked by a rapid continuous optical printing technique to build biologically relevant 3D printed objects with smooth contours, user-defined geometries, and tunable stiffness gradients. The cytocompatibility of the NIPUs was then assessed by measuring the cell viability of fibroblasts directly seeded on the round shaped printed structures (2.5 mm in diameter),

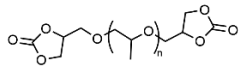
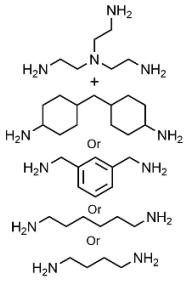
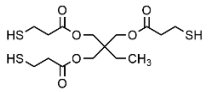
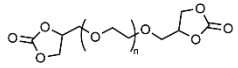
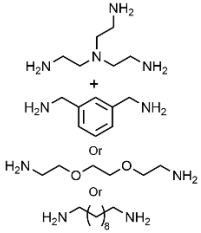
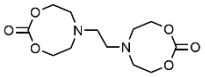
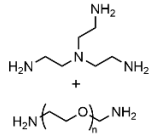
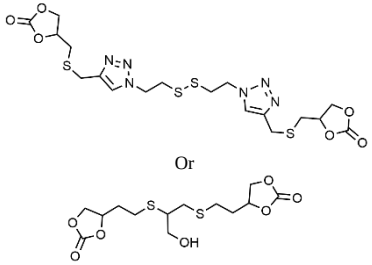
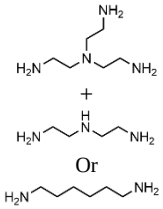
showing high viability rates (>95% after 3 and 7 days of incubation). The fibroblasts normal morphology and good adhesion also highlighted the possible use of these NIPUs as biomaterials in contact with living cells, such as scaffolds for tissue engineering, medical implants, microfluidic or lab-on-a-chip devices, diagnostic probes or even monitoring systems. Warner et al.[206] then developed 3D printable NIPUs with tunable properties using a two-step process. First, a diurethane monomer end-capped by allyl functions was synthesized by a thermal catalyst-free ring opening reaction of trimethylolpropane monoallyl ether cyclic carbonate with a bio-based diamine (cadaverine). Then, the allyl functional groups of this monomer were reacted with variable branched thiol crosslinkers (which allowed the tunability of the NIPUs properties) by a UV-induced thiol-ene reaction that also enables their 3D printing by a light-based process. They were therefore able to print the NIPUs into new biocompatible structures such as slab constructions for cells. The cytocompatibility of these structures was tested by seeding and growing high-density cell sheets of murine myoblasts (C2C12) on them. Cell sheets were analyzed by cell imaging, which showed lower cell death (around 3%) than the control, therefore demonstrating no acute toxicity. Building vascular anti-coagulation and anti-biofouling structures or coatings could therefore be considered with those NIPUs. Fanjul-Mosteirín et al.[53] also developed 3D-printable semicrystalline hydrogels made of PEG-PHUs. These thermosensitive hydrogels were synthesized by ring-opening of highly reactive N-substituted eight-membered bis(cyclic carbonate) by poly(ethylene glycol) diamine (bringing thermosensitive semicrystalline domains at low-water contents) and multifunctional tris(2-aminoethyl)amine, acting as crosslinking agent. They showed that the crystallization-induced gelation of low-water content networks led to adequate rheological and mechanical properties, which allowed the extrusion-based printing of the pre-formed hydrogels because their storage modulus could be tuned up to 3 orders of magnitude as a function of temperature and therefore give them the ability to flow during the 3D-printing conditions. The cytotoxicity studies demonstrated the absence of toxicity of these hydrogels towards HeLa epithelial cells, which displayed normal morphology after contact with the hydrogels extracts and high metabolic activities in the presence of the hydrogels, similar to the control group. These 3D-printed pre-formed biocompatible hydrogels allow cell propagation and proliferation and thus appear as good candidates to replace soft tissues thanks to their suitable water content and mechanical properties.

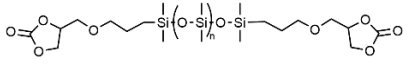
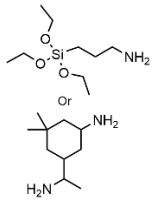
These different results therefore demonstrate that PHUs are capable of competing with conventional PUs with regard to tissue engineering applications, the most compelling example being the electrospun PHU developed by Aduba et al.[52], which showed mechanical properties similar to PU, but higher hydrophilicity, which is an advantage over traditional PUs for wound dressing applications.

This is the authors' version of the article published in European Polymer Journal. The final version is available at https://doi.org/10.1016/j.eurpolymj.2025.113985

Table 1. Summary of cited PHUs and their precursors developed for tissue engineering applications.

Specific application and required general properties	(Poly) Cyclic carbonate precursor	(Poly) Amine precursor	Additional component	Notes	Ref.
Tissue Engineering					
For degradable scaffolds, use of degradable segments (i.e., ester bonds)			/	Photocrosslinking of diallyl diurethane monomers for 3D-printable scaffolds, implants, probes…	Pyo et al.[4] (2017)
			/	Networks for scaffolds	Esmaeili et al.[100] (2018)
			 to form the intermediate + Citric acid/sebacic acid/ mannitol to form poly(ester-urethanes)	Degradable crosslinked poly(ester-urethanes) for scaffolds	Ghosal et al.[196] (2023)
For implants or coatings, use of more biostable segments (i.e., polypropylene			/	Electrospun scaffolds of poly(amide-hydroxyurethane)	Aduba et al.[52] (2018)
				3D-printable objects with variable thiol crosslinkers for slab constructions for cells or coatings	Warner et al.[206] (2019)

glycol segments)			/	Thermally crosslinked networks for implants or coatings	Pierrard et al.[140] (2023)
				3D-printable photocrosslinked networks for implants	
For hydrogels, use of hydrophilic segments (i.e., polyethylene glycol segments)			/	Crosslinked hydrogels	Gennen et al.[139] (2016)
			/	3D-printable crosslinked hydrogels	Fanjul-Mosteirín et al.[53] (2021)
			poly(vinyl alcohol) or gelatin (intertwined)	Crosslinked multicomponent SIPN hydrogels	Carbajo-Gordillo et al.[198] (2024)

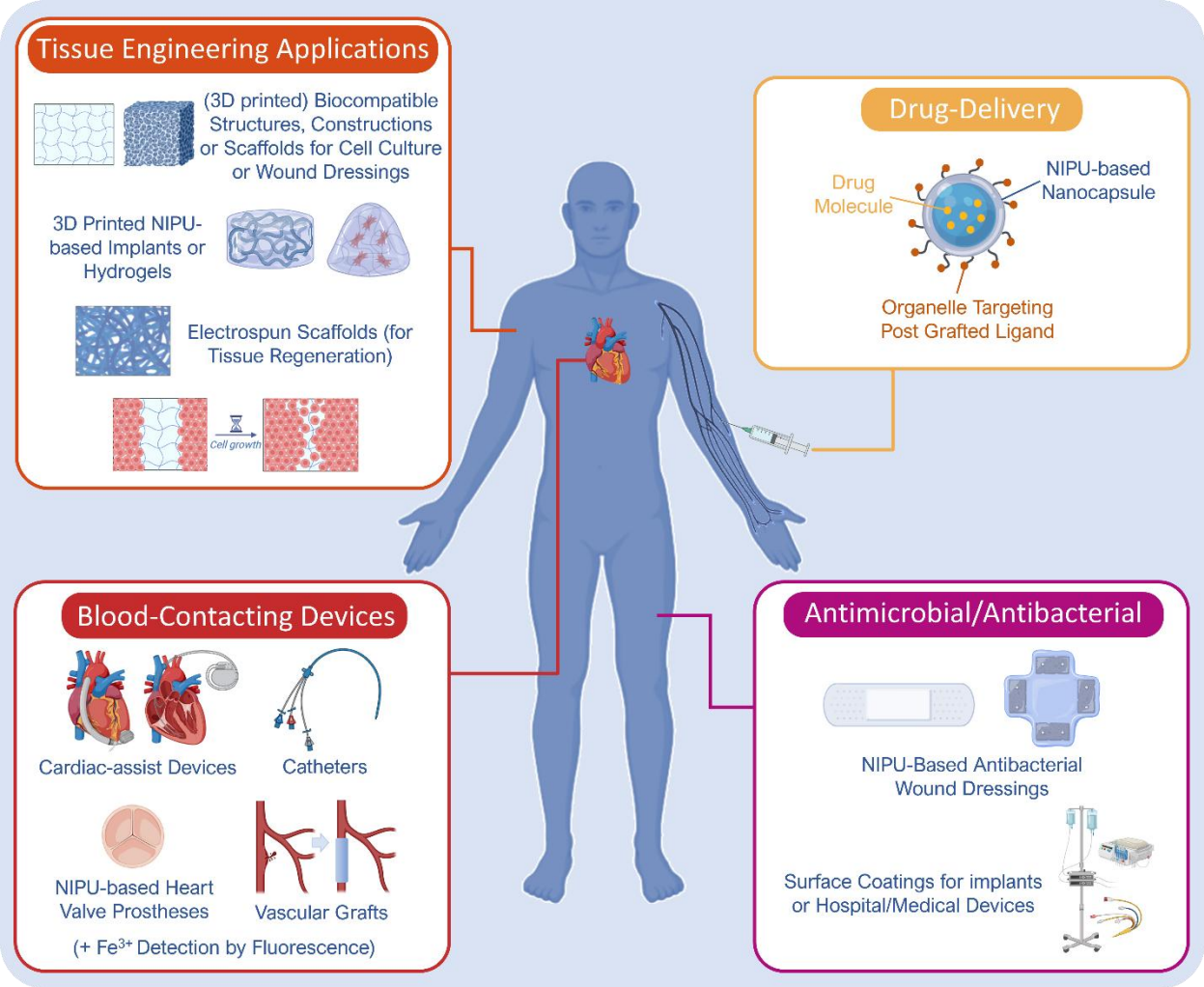
For coatings or adhesives			/	Surface modification of biomedical metals by polydimethylsiloxane-urethane	Rossi de Aguiar et al.[137] (2016)

3.2.2. Drug-delivery applications

Polymer-based nanocapsules are already used in drug release systems due to their many advantageous properties such as superior stability and controlled release profiles arising from the relative thickness, robustness, and low permeability of their membranes. They can potentially encapsulate compounds like hydrophobic and hydrophilic drugs, inorganic nanoparticles, small RNAs, and imaging/contrast agents, protect them from their external environment and *in vivo* degradation, and provide site specificity for their controlled release. Usually, the polymers chosen to serve as nanocapsules are synthetic biodegradable and biocompatible polymers, such as aliphatic polyesters: poly(ε-caprolactone), poly(lactide), poly(lactide-co-glycolide), or segmented polyester-PUs. Additionally, playing on a polyester-segmented structure allows to control the degradation mechanism by the programmed cleavage of the polymer chain (by biochemical transformation of esterase enzymes, acting as external stimulus), and leads to the controlled release of drugs.[45,49,207–214]

In this context, Pramanik et al.[49] developed mitochondria targeting NIPU-based nanocarriers with repetitive ester functions, capable of encapsulating small drug molecules like doxorubicin inside their hydrophobic core. These NIPU-based drug carriers were prepared by an *in-situ* reaction between 1,8-diaminooctane and adipate bis(cyclic carbonate) at a droplet interface (inverse mini-emulsion technique). Thanks to the pendant hydroxyl groups of PHUs, organelle-specific targeting ligands were post-grafted onto the surface of the particles by esterification reaction, so that the drug could be specifically delivered to mitochondria while avoiding non-specific uptake in other organelles. Given that mitochondria play a role in several biological processes and that their dysfunction is associated with various diseases such as cancer or Alzheimer's, these NIPU nanocarriers, with increased efficacy compared to conventional treatments, offer a promising new therapeutic approach for the biological imaging and drug delivery related to these illnesses. *In vitro* studies on cancer cells (glioblastoma) showed that the specific release of doxorubicin into mitochondria caused higher cytotoxicity and cell death than the free drug alone, while MTT assays performed with solutions at different concentrations of these nanocapsules confirmed their biocompatibility. Finally, the controlled release of the encapsulated dye was demonstrated and confirmed *in vivo* in a live zebrafish model.

This work, by taking advantage of the hydroxyl groups of NIPUs for the post-grafting of specific ligands, highlights the new opportunities of NIPUs to obtain functional nanocapsules targeting different organelles, compared to traditional PUs which do not contain these easily functionalizable groups.



Scheme 6. Current reported biomedical applications of non-isocyanate polyurethanes (developed at the academic research level).

3.2.3. Antimicrobial and antibacterial properties

Microbial invasion can lead to skin and soft tissue infections and cause severe tissue damage, which translates into millions of hospitalizations every year.[215] This problem is also encountered in the case of tissue engineered implants, even after fastidious sterilization, as complications arising from bacterial infections remain one of the main causes of implant rejection and lead to repetitive surgical procedures.[196] Indeed, bacteria can adhere and proliferate on the surface of an implant/device and form a biofilm, which allows them to escape the host's immune response and hampers antibiotic efficacy.[216,217] To prevent and/or treat these infections, several antimicrobial approaches have thus been developed over the years. Some examples include

antimicrobial wound dressings, which, in addition to the desired antimicrobial activity, need to maintain a suitable moist environment, physically protect the wounds, be chemically and physically stable, non-toxic towards dermal cells, and finally, easily detachable from the wounds.[218–221] Among antimicrobial agents, quaternary ammonium salts are particularly attractive as they combine high efficacy against a wide spectrum of bacteria with low toxicity against mammalian cells. In addition, it is possible to generate long-lasting bactericidal activity by binding chemically these agents to the polymer backbone of the dressings or coatings.[216,222–224]

Since the preparation of PUs for the production of wound dressings had already been reported in the literature[58,225–228] and that PU wound dressings are even currently sold in pharmacies, Gholami et al.[229] developed wound dressings composed of both PHU and PU parts. To do so, they first synthesized a hybrid PHU prepolymer from cyclic carbonated soybean oil and dimethylethylenediamine. This amine-terminated prepolymer was then quaternized, leading to a PHU carrying quaternary ammonium salts. This PHU bearing the bactericidal ammonium salts was then used as polyol and mixed with castor oil (which carries hydroxyl groups) and isophorone diisocyanate to form the final hybrid PHU ammonium-polyurethane used as antibacterial wound dressings. The cytocompatibility of the dressings was then first evaluated by studying the interactions between the materials and L929 fibroblasts, which showed normal morphology and good adhesion to the culture plate at borderline or beneath the dressings. An MTT assay was also performed to measure the metabolic activity of these cells and those cultured in medium containing the dressings extracts, which showed a viability >95%. These results thus demonstrated the cytocompatibility of the prepared dressings. A concentration range of ~6–9 wt% of $(CH_3)_3N^+$ moieties inserted in the backbone of the membranes was determined to be below the toxicity threshold for fibroblasts. Their antimicrobial activity was then assessed through viable colony-forming unit (CFU) counting detached from the prepared wound dressings, which revealed remarkable antimicrobial activity. In some cases, bactericidal effect was observed against several bacteria (*Staphylococcus aureus (S. aureus)*, *Pseudomonas aeruginosa*, and *Candida albicans*). *In vivo* antimicrobial activity was also evaluated for the materials that had the best physical and mechanical properties and showed that the latter could maintain a nearly microbial-free environment over the injured tissue without having any deleterious effect on normal cells. However, it should be underlined that these membranes are partly composed of conventional PUs based on isocyanates.

Using another antimicrobial additive, namely silver nanoparticles, Li et al.[103] designed antimicrobial silver-NIPU foams derived from lignin for wound healing purposes. Indeed, (conventional) PU foams have also already been used to treat chronic wounds due to their suitable properties (external and internal pores can have better antimicrobial agent

release characteristics as well as long-lasting effects).[230] In this approach, a lignin-based NIPU was obtained by oxyalkylation reaction of enzymatically hydrolyzed lignin with glycerol carbonate (also acting as solvent), followed by reaction of this cyclic carbonated lignin with polyether-based diamines of two different molecular weights, acting as curing agents. Then, in a final step, a blowing agent (poly(methylhydrosiloxane)) was added to induce the foaming, while silver nanoparticle solutions were also added during this process to increase the antimicrobial activity of the final foams, knowing that lignin itself has already demonstrated antimicrobial activity.[231] The *in vitro* evaluation of the antimicrobial performance of these silver-NIPU foams, carried out by CFU counting, showed a bactericidal effectiveness superior to 95% against both *Escherichia coli* (*E. coli;* Gram-negative) and *S. aureus* (Gram-positive) (within 4 h), while hemolysis tests, performed on mouse blood, and indirect contact cytotoxicity tests, performed on 3T3 mouse fibroblasts, showed low hemolysis rates (<3%) and high cell survival rates (100%), respectively. Finally, the *in vivo* evaluation of wound closure using these foams as dressings in mice, as well as the histological analyses of these wounds, showed that this material rapidly improved healing and repaired damaged tissues. Quan et al.[232] also designed similar foams by preparing cyclic carbonated lignin likewise. The latter was then reacted with bis(3-aminopropyl) ether (blowing agent) to form lignin-based NIPU foams, subsequently immersed in copper chloride solutions and NaOH to obtain copper hydroxide-loaded ($Cu(OH)_2$) foams. In the final step, the $Cu(OH)_2$-loaded foams were placed in a H_2O_2 solution to synthesize NIPU foams loaded with copper peroxide (CuO_2). These wound dressing foams are pH responsive as they can release Cu^{2+} ions along with strong oxidizing •OH radicals in acidic conditions, which can potentially be useful for destroying cancer cells[233], as well as for sterilization.[234–236] Copper ions are also proven to prevent the production of microorganisms and bacteria.[237,238] The antimicrobial activity towards *E. coli* and *S. aureus* highlighted the high antibacterial performance of the foams (up to >95% for both bacteria in the case of the foam loaded with the higher concentration of CuO_2), the copper peroxide content being proportional to the antimicrobial activity due to its capacity to produce reactive oxygen species capable of effectively inhibiting bacterial growth. However, the authors noted that too high a dose may induce drug resistance, leading to decreased long-term antimicrobial performance. Hemocompatibility tests using rat blood showed a hemolysis rate <3% and therefore indicated a slightly hemolytic effect (see Blood-Contacting Devices section). Cytotoxicity tests, by direct contact after 24 h, were performed with NIH-3T3 mouse fibroblasts as these cells play a role in wound healing. It was observed that the cell viability decreased slightly with increasing CuO_2 concentrations, although it remained >80%, proving the biocompatibility of the composite foams. Skin wound healing in mice was observed with a control and the foams, the latter closing faster than with the control, thereby demonstrating their healing effect, also confirmed by histological analyses. Among all synthesized foams, the NIPU foam loaded in 100 mM of CuO_2 performed better and combined good physico-

chemical properties and water absorption (important to absorb wound exudates), high antibacterial activity against *E.coli* and *S. aureus*, and *in vitro* and *in vivo* biocompatibility that make it a promising scaffold for the treatment of chronic wounds. These two studies therefore demonstrate that biobased and degradable NIPU foams are very promising for wound dressing applications.

Lately, Laurén et al.[239] also developed antimicrobial and biocompatible 3D-printed porous NIPU-based hydrogels, another type of scaffolds for wound healing applications. For that purpose, they first prepared a hydrophilic PEG-PHU by reacting a bis(cyclic carbonate) poly(ethylene glycol) with cystamine as diamine. Different NIPU-based hydrogels were then obtained by simply mixing together the obtained PEG-PHU with various ratios of double-quaternized chitosan (DQC), considering the antiviral and antibacterial properties of this agent[240], as well as TEMPO-oxidized cellulose nanofibrils (TCN). The resultant gel network being based on H-bond interactions between the pendant functions of its constituents, these TCN reinforce these interactions, controlling the hydrogel rheological properties and thus providing them with 3D-printability by direct ink writing. Indeed, this 3D printing technology, particularly well-suited for temperature-sensitive materials, requires hydrogels with reversible shear-thinning behavior. Hydrogel scaffolds with controlled porous architecture were then successfully 3D-printed. The cytotoxicity of these hydrogels was then assessed *in vitro* in order to ensure the biocompatibility of the printed scaffolds and find the optimal ratio of DQC to incorporate, considering its potential toxicity (depending on its concentration) despite its antibacterial activity. MTT cell viability tests demonstrated the non-acute toxicity of the scaffolds towards NIH-3T3 mouse fibroblasts cultured on their surfaces, as they remained viable even though their proliferation was slower than on the control surface. Moreover, this cell proliferation increased with the DQC concentration in the hydrogels without negatively impacting cell viability, which suggests a decrease of the slight cytotoxic effects of DQC when inserted in the NIPU matrix. These hydrogels made of DQC, cellulose nanofibrils and PEG-PHU, therefore appear as promising biomaterials to form 3D-printable porous hydrogels with excellent swelling properties, and capable to prevent the passage of impurities/bacteria into a wound when used as dressings. It is however important to specify that no antimicrobial/antibacterial activity test was carried out in this work. Using the electrospinning technique, Ge et al.[241] also developed nanofibrous membrane dressings, as these scaffolds are particularly suitable for wound treatments due to their micro/nanopores that can prevent exogenous microorganisms invasions and therefore, reduce the dressing replacement frequency, and their high surface area which can efficiently absorb wound exudates.[242] They synthesized NIPUs end-capped with alcohols using ethylene carbonate, 1,6-hexanediamine, and PEG 1000 (in different proportions) using a tin-based catalyst. Then, they used the polycondensation approach with a dicarbamate and sebacyl chloride (chain extender) to obtain NIPU-co-polyglycolic

acids. One of them was then electrospun with or without additional curcumin, and they investigated the antimicrobial activity of these two nanofiber mats along with a bare NIPU membrane against *S. aureus* and *E. coli*. The NIPU-co-polyglycolic acid mat showed an antibacterial activity against *S. aureus* after 3 h of >75 %, compared to >90% for the one with curcumin, which is mainly attributed to the proven antibacterial effect of curcumin itself.[242–244] The results against *E.coli* were not satisfactory, as well as those of the NIPU membrane, which did not show any antimicrobial activity against both bacteria. The cytotoxicity of the nanofibrous NIPU-based mats (without curcumin) were evaluated by direct contact with L929 cells and showed >89 % and >93% of cell viability after 1 and 3 days, respectively. Finally, they evaluated the *in vivo* hemostatic property, the wound granulation tissue thickness of the nanofibrous membranes, and the wound regeneration (histological and biomarker analyses) in mice and saw that the composite dressings effectively stopped the bleeding, prevented wounds from turning into chronic ones, protected the wounds against harmful bacteria and had healing effects.

Additionally, Tam et al.[245] introduced for the first time water-soluble and dispersible phosphate-containing NIPUs, called NIPU phosphate monoesters, by the polymerization of two different bio-derived bis (cyclic carbonates) with the bio-based 1,5-pentanediamine (cadaverine) using green solvents. Their following functionalization by selective phosphorylation using tetrabutylammonium dihydrogenphosphate as a phosphate source resulted in a phosphate functionality (pendant groups) of up to 50%. They displayed oil-in-water emulsion stabilization and biodegradability (between 56 and 75% in 28 days), promoted by their water solubility and the presence of easily hydrolysable functions (i.e., phosphates and esters). Since phosphate source groups had been previously reported to have antivirulence properties[246], antimicrobial activity tests against *E. coli* and *Bacillus subtilis* were performed. Some NIPU phosphate monoesters showed considerable antimicrobial effect against both bacteria, contrary to the non-functionalized NIPU. Cytotoxicity tests by direct contact with human keratinocyte HaCaT cells after 24 h demonstrated the non-toxicity of the polymers at concentrations up to 0.5 mg mL^{-1} (cell viability >80%), and *in vitro* skin irritation tests, performed on reconstructed human epidermis (EpiSkin), proved their non-skin irritant features. These polymers are promising as multifunctional additives in personal care, dental, tissue engineering and drug-delivery applications, as the biocompatibility of phosphorus-containing polymers is well known and described in the literature.[247,248]

Hospital infections resulting from the colonization of bacteria on medical device surfaces are considered as one of the six leading causes of death in western-industrialized countries, particularly for vulnerable patients.[249] There is therefore a need to produce effective antibacterial surface coating formulations for hospital appliances to limit the spread of these infections. For this purpose, the preparation of bactericidal coatings

(polymers) used in the case of implants/devices is a very efficient strategy. With this goal in mind, Karami et al.[250] synthesized a NIPU network starting from diethylenetriamine and a star-shaped macromonomer prepared from the bio-based glycerol and succinic acid, then epoxidized using epichlorohydrin and carbonated by CO_2 fixation. During this synthesis, tetrabutylammonium bromide (TBAB) was used as a catalyst and was not removed by any purification step, which is quite unusual for materials intended for biomedical use since they can induce side reactions potentially dangerous for health. The latter was therefore still present in the final network structure. Considering the established antibacterial property of organic cations and the antimicrobial properties of quaternary ammonium salts having N^+ functionalities[251–253], the NIPU network was thus expected to exhibit antibacterial properties due to the presence of TBAB, even though the physical blending of polymers with cationic compounds is less advantageous than the modification of polymers with them.[252] The antibacterial activity of the NIPU film was thus evaluated against *S. aureus* and *E.coli* by zone of inhibition assays. A notable effect of the amount of TBAB present in the network on the inhibition of bacterial growth was shown. Their group also noticed that this antibacterial activity became more effective by doubling the dosage of TBAB. The antibacterial properties of these NIPU films against *S. aureus* and *E. coli* therefore proved their potential use in surface coating formulations for hospital and medical devices as antiseptic agents.

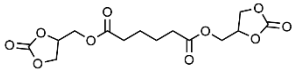
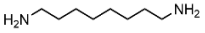
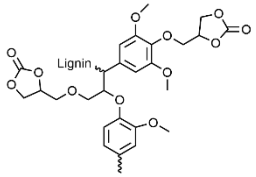
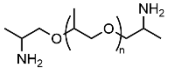
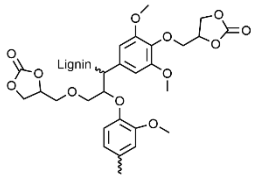
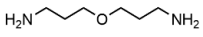
Gharibi et al.[216] also designed non-leaching bioactive and biocidal NIPU-siloxane coatings by sol-gel process. To do so, carbonated soybean oil was reacted with 3-(dimethylamino)-1-propylamine to form a tertiary amine intermediate, followed by its simultaneous quaternization and functionalization by alkoxysilane groups to produce curable prepolymers comprising methoxysilane, quaternary ammonium, and urethane moieties. Lastly, the final organic-inorganic coatings were prepared by the sol-gel crosslinking of this prepolymer on a metallic substrate. These NIPU-based coatings containing quaternary ammonium moieties showed a 100% contact-active antibacterial activity against *E. coli* and *Bacillus subtilis* (*B. subtilis*; Gram-positive), led to high cell viability (>90%, performed by direct and indirect MTT assays on L929 fibroblasts), as well as a low hemolysis ratio (around 1.8%), and good cell adhesion and proliferation, which confirmed their cytocompatibility. Interestingly, the antibacterial activity of the coatings did not decrease for at least 21 days, which seems to indicate their long-lasting antibacterial action to coat devices such as implants, catheters, or stents. Moreover, no antibacterial agent leached from the films during this period either, as both types of bacteria could grow in the medium containing the coating extracts, thus confirming their proper anchoring in the coatings. More recently, Maya et al.[136] also developed antibacterial NIPU coatings derived from sunflower oil. They first epoxidized sunflower oil, an oil with a high level of unsaturations, which allows to obtain a high conversion degree of both precursors employed for the synthesis of the PHU coating, namely carbonated sunflower oil and

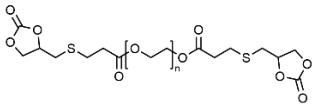
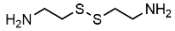
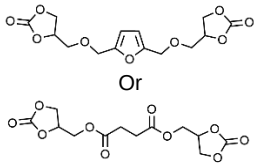
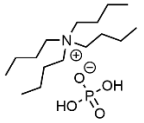
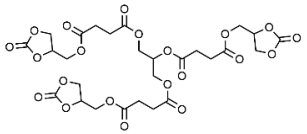
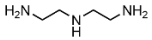
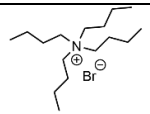
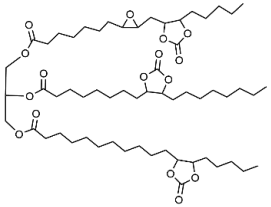
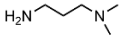
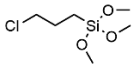
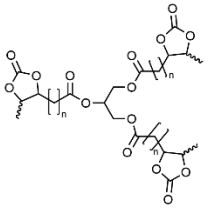
polyamine-polyol (obtained by reaction with ethylenediamine). This coating formulation entirely based on renewable sunflower oil does not require the use of solvent nor catalyst. Nevertheless, the bare NIPU film did not show the expected antibacterial properties against *E. coli* and *S. aureus* nor high cell viability towards Detroit 551-CCL 110™ fibroblasts (≈ 60%). The surface of this coating was therefore grafted by acrylic acid by UV-initiated radical modification, enhancing the surface hydrophilicity by incorporating carboxylic acid functions. This acid modified coating showed a higher cell viability of around ≈ 75% (measured by MTT assays), as well as a significant antibacterial effect towards *S. aureus.*

The majority of the aforementioned examples highlight the beneficial role of the additional hydroxyl groups of the PHUs involved in these antibacterial materials, which allow their functionalization with various bactericidal ammonium salts, reinforce coatings through their multifunctionality allowing crosslinking, and provide necessary H-bonds to composite hydrogels to make them suitable for 3D printing technologies. This further demonstrates the usefulness of their structural differences (compared to conventional PUs) for medical applications.

This is the authors' version of the article published in European Polymer Journal. The final version is available at https://doi.org/10.1016/j.eurpolymj.2025.113985

Table 2. Summary of cited PHUs and their precursors developed for drug delivery and antimicrobial applications.

Specific application and required general properties	(Poly) Cyclic carbonate precursor	(Poly) Amine precursor	Additional component	Notes	Ref.
Drug-delivery					
For degradable nanocarriers, use of cleavable bonds (i.e., ester bonds)			Doxorubicin (drug) entrapped in the nanocapsule + post-grafting with organelle-targeting ligand	Cleavage of nanocapsules by esterase enzymes	Pramanik et al.[49] (2018)
Antimicrobial- Antibacterial					
General presence of antimicrobial/ antibacterial agents (additional component)			Ag nanoparticles + poly(methylhydrosiloxane) (blowing agent)	Foams with antibacterial effect against *E. coli* and *S. aureus* (hemolysis tests also performed)	Li et al.[103] (2024)
			CuCl2 and NaOH to form $Cu(OH)_2$ loaded foams + H_2O_2 to form CuO_2 loaded foams	Foams with antibacterial effect against *E. coli* and *S. aureus* (*in vivo* tests performed)	Quan et al.[232] (2025)

			Double-quaternized chitosan + TEMPO-oxidized cellulose nanofibrils (enhancing the 3D printability and swelling behavior)	3D printable hydrogels	Laurén et al.[239] (2024)
	 Or		 (For functionalization by phosphorylation)	Biodegradable and dispersible polymer with antibacterial effect against *E. coli* and *Bacillus*	Tam et al.[245] (2024)
			 Catalyst, still present in the final polymer	Coatings with antibacterial effect against *E. coli* and *S. aureus*	Karami et al.[250] (2019)
			 (For quaternization)	Coatings with antibacterial effect against *E. coli* and *B. subtilis* (hemolysis tests also performed)	Gharibi et al.[216] (2022)
		Polyamine polyol (mix of secondary and primary amines) obtained by reaction between epoxidized sunflower oil and ethylenediamine[254]	Acrylic acid (grafting agent)	Coatings with antibacterial effect against *E. coli* and *S. aureus*	Maya et al.[136] (2024)

3.2.4. Blood-Contacting Devices

Blood-contacting medical implants or devices are used for many applications but are known to be prone to infection, foreign body reaction and/or surface-induced thrombosis. Particularly, circulating blood is in direct contact with the surface of the implant/device in the cardiovascular system. Plasma proteins are rapidly adsorbed onto the implant/device surface, which leads to platelet adhesion, contact phase activation of the coagulation and thrombus formation.[255,256] Prescribed to avoid this, anti-thrombotic agents are rarely effective and bleeding complications can occur.[257,258] As a result, in view of developing implantable medical devices which sometimes need suitable surface modifications, the best approach remains prevention, notably by evaluating the compatibility of the newly designed devices/implants with different blood components through an array of tests. Such an assessment is called blood compatibility or hemocompatibility, as it refers to a part of biocompatibility regarding implantation in the specific case of the cardiovascular system.

Very few studies have been reported in the literature regarding the hemocompatibility of NIPUs, the first one being that of Xu et al.[138], published in 2018, on a fluorescent PHU (FPHU) produced by the addition of a bis(cyclic carbonate) obtained from the CO_2 carbonatation of 1,3-bis-(3-glycidoxypropyl tetramethyldisiloxane) with 1,6-hexanediamine. This new non-traditional FPHU-based material exhibited strong blue fluorescence and revealed to be selectively sensitive to Fe^{3+} ions with a low detection limit (4.56 µM), thus providing a simple alternative method for the detection of iron concentration. Indeed, as an essential element of the body's metabolism, iron plays a key role in various biological processes. Therefore, too little or too much iron in the body can lead to several health issues, such as iron deficiency anemia, or Parkinson's and Alzheimer's diseases.[138,259] Monitoring iron ions could therefore provide information on these diseases. The biocompatibility of the FPHU was first assessed through MTT assays performed on L929 mouse fibroblasts after indirect contact with the materials. Results showed that the sample with 100% of FPHU extract presented slight toxicity after 24 h of incubation, although the cell viability remained significantly higher than that with PU extracts. In that work, all cells in contact with self-produced-PU leachates were dead after 48 h, while the cell viability of the FPHU group was still above 60%. These results were in line with the observation of cell morphology, which also demonstrated that FPHU had less toxic effect compared to PU. The flow cytometry analyses performed to examine the cycles of the cells growing in different FPHU extracts concentrations for 24 h were also consistent with the MTT results, as the FPHU did not seem to induce cell necrosis or apoptosis, contrary to what has been reported in the literature for PUs.[260] Then, the cytotoxicity of the FPHU towards THP-1 macrophages was tested by indirect MTT assay, which revealed cell viabilities > 80% after 6 h. In addition, they also evaluated the

immunotoxicity of the FPHU by measuring the concentrations of cytokine release of macrophages, as it reflects the duration and intensity of the inflammatory response to the biomaterials. The latter was lower than for some PU-based materials. Finally, hemolysis tests, i.e., the evaluation of the release of hemoglobin into plasma owing to the damage of red blood cells (RBCs), were performed by direct and indirect contact methods, which showed hemolysis ratios of 1.76% and 3.95%, respectively. It should be noted that the hemolysis rate of biomaterials should ideally be below 2% for biomedical applications (according to ISO 10993-4[261], a material which induces less than 2% of hemolysis is considered non-hemolytic, and slightly hemolytic for 2%-5% of hemolysis). Since conventionally synthesized PUs do not display fluorescence and are not able to detect iron, this biocompatible and hemocompatible FPHU seems very promising.

As cited before, Gharibi et al.[216] also performed an hemolysis test on a biocidal NIPU-siloxane coating, which revealed a low hemolysis rate (<2%). Zhao et al.[141] also worked on the thermoresponsive behavior of PHUs designed for biomedical composite materials. These linear polymers were synthesized by reaction between a cyclic carbonated polypropylene glycol and polyoxyethylene bis(amine), and their thermoresponsive behavior was evaluated during a heating and cooling run by a series of characterization techniques. Hemolysis assays were then performed using RBCs obtained from fresh blood, collected from rabbit hearts. RBCs were added to solutions of PBS buffer with different concentrations of PHU and incubated for 4 h at 37 °C. Results showed low hemolysis ratios (max. 2.8%), which suggests the hemocompatibility of this PHU. Their biocompatibility was also checked through an MTT assay performed with mouse L929 fibroblasts, by incubating the cells with culture medium containing various concentrations of this PHU for 1, 2, and 3 days at 37 °C. The results showed high cell viability values for all concentrations (from >75% to >95% of cell viability). This confirmed the non-cytotoxicity of these promising materials for cardiovascular applications, which was also corroborated by cell imaging.

Among all the cardiac assist devices or cardiovascular implants that have been developed until now, heart valve prostheses are of prime importance. Indeed, valve replacement through the implantation of prosthetic heart valves is currently the only effective treatment for aortic stenosis, a widespread heart valve disease from which 3-6% of the population over 65 suffers and which represents about 300,000 valve replacement interventions per year.[142,262–264] Two types of heart valve prostheses are currently clinically employed: mechanical and biological valves (also called bioprostheses). Unfortunately, both options involve serious drawbacks, such as high risks of thromboembolism and early degeneration for mechanical and biological prostheses, respectively. Polymer-based heart valve prostheses have therefore been developed as alternatives that could avoid these disadvantages, with particular focus on PU-based materials, given its suitable

mechanical and biological properties.[11,44,265,266] But despite showing promising results, these PU-based prostheses have never been used clinically. Indeed, conventional PU has been associated with long-term implantation issues, such as thrombotic complications in blood-contacting devices, but also calcification and/or sub optimal valve geometry problems in the case of heart valves.[267–269] The latest studies are thus focusing on PU modifications to solve these issues, by developing synthetic valves made of segmented polycarbonate urethane, silicone polycarbonate urethane, or PU composite materials, for instance.[44,270–274] NIPUs, however, could also represent promising candidates for this type of prosthesis, as their structural differences may bring an answer to the problems mentioned above.

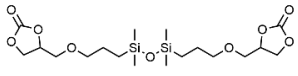
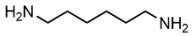
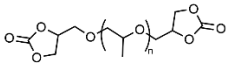
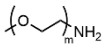
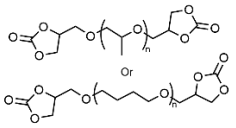
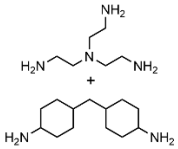
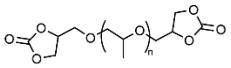
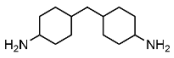
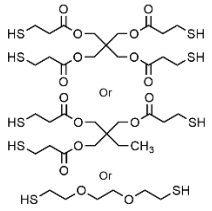
Our research team (Melo et al.[142]) developed the first customized NIPU-based heart valve prostheses by the polyaddition between 4,4′-methylenebis(cyclohexylamine), PPG or PTHF bis(cyclic carbonate)s and a triamine as crosslinker.[140] The *in vitro* cytocompatibility, hemocompatibility, thrombogenicity and calcification susceptibility of these NIPU networks were assessed and compared to medical grade PU. Human fibroblasts and endothelial cells (HUVECs) displayed normal morphology after indirect contact with these NIPU-based elastomers, which also showed no hemolytic effects (max. 0.5%). NIPU surfaces surprisingly presented drastically reduced platelet adhesion and contact activation-induced coagulation, demonstrating their exceptionally low thrombogenicity and indicating that NIPUs could outperform PUs at this level. An ideal tri-leaflet valve design was then modeled in 3D by fluid structure interaction computations, and valves of this defined design, produced by injection molding using a 3D printed stainless steel mold, were then tested in the aortic position of a pulse duplicator, showing ISO-compliant hydrodynamic performances (similar to those of currently used bioprostheses). NIPU patches did not calcify over a period of 8 weeks, contrary to bovine pericardium patches used as control. Additionally, these NIPU networks reinforced with a medical-grade PET mesh displayed mechanical properties similar to those of native valve leaflets, further proving their potential for this type of applications.

Finally, since PHUs carry additional hydroxyl groups compared to PUs, our team also took advantage of them to functionalize and crosslink a polyether-based PHU into elastomers.[155] The hydroxyl groups of a PPG-PHU precursor were quantitatively functionalized by a CO_2-sourced cyclic carbonate molecule bearing a pendant allyl group to bring unsaturations allowing the photocrosslinking of the material in presence of various polythiols by thiol-ene reaction. Elastomers exhibiting a range of mechanical properties mimicking different natural tissues were obtained from the same unsaturated PPG-PHU precursor only by playing with the polythiol functionality. The rheological properties of these formulations rendered them suitable for light-based 3D-printing processes, and small objects (millimeter to micrometer scale) were subsequently printed by Digital Light

Processing, opening the possibility to print various designed objects for personalized medicine, such as custom prostheses or implants. *In vitro* hemocompatibility with different blood components was then assessed by performing hemolysis tests with RBCs, quantifying the adhered platelets on the NIPU surfaces, and measuring the clotting times upon contact with these materials. Results revealed no hemolytic effects, as well as the absence of increased platelet adhesion or coagulation activation. The biocompatibility of these NIPU networks was also evaluated *in vitro* by quantifying their cytotoxic effects through direct and indirect contact tests towards human primary fibroblasts, which confirmed their remarkable cytocompatibility.

These results thus demonstrate the great potential of these materials for biomedical applications, including in the cardiovascular system, such as blood-contacting vascular grafts, drug eluting implants or heart valve prostheses. The most notable examples are the development of a PHU demonstrating fluorescence properties that are not present in conventional PUs[138], as well as PHUs showing hemocompatibility performances that have in some cases outperformed conventional PUs[142].

Table 3. Summary of cited PHUs and their precursors developed for blood-contacting devices.

Specific application and required general properties	(Poly) Cyclic carbonate precursor	(Poly) Amine precursor	Additional component	Notes	Ref.
Blood-Contacting Devices					
Monitoring of some diseases			/	Fluorescent PHU for Fe^{3+} ion detection	Xu et al.[138] (2018)
			/	PHUs with thermoresponsive behavior as component for composite materials	Zhao et al.[141] (2022)
For valve or vascular prostheses, elastomer properties are required, use of soft segments (i.e., polyethers)			PET mesh reinforcement	NIPU networks for heart valve prostheses	Melo et al.[142] (2024)
			Functionalization of the PHU with  + crosslinking with various polythiols 	3D-printable networks for vascular grafts, drug eluting implants or heart valve prostheses	Pierrard et al.[155] (2024)

Conclusions

PUs are among the most produced polymers worldwide. Out of the many applications in which they are found, biomedical applications have an important place, given that they are already widely used in clinics and marketed in this field. However, their production is increasingly impacted by restrictions related to the use of one of their two main reagents, i.e., isocyanates. These compounds are indeed very harmful not only to the environment, but also to humans. To avoid their use, non-isocyanate PUs (NIPUs) have been developed by using safer alternative syntheses, in particular by the promising polyaddition of poly(cyclic carbonate)s with (poly)amines. This synthetic route gave birth to unprecedented polymer structures different from PUs, called PHUs or PHOxs, depending on the cyclic carbonate functionality, offering new opportunities, notably by taking profit of their additional pending hydroxyl groups.

In this review, we focused on the works reporting NIPUs developed for medical applications (particularly PHUs, since biomedical PHOxs have not yet been reported), and we collected and categorized for the first time all the available papers mentioning biocompatibility tests on these polymers. The latter are all encouraging and show promising results regarding the biocompatibility and even the hemocompatibility (although less often described) of PHU materials. PHUs are therefore proven suitable for a wide range of biomedical applications, from drug delivery systems and tissue engineered implants to blood-contacting devices and are thus of particular interest for the future. This review sheds light on the beneficial presence of the hydroxyl group of the PHUs: (i) they bring additional H-bond interactions leading to NIPUs with specific rheological behavior particularly well-adapted to processes such as electrospinning or various 3D printing technologies, opening the field to personalized medicine; (ii) they can be used for diverse post-functionalization reactions which are valuable for anchoring antibacterial moieties, for further crosslinking of the PHU materials, or for anchoring targeting ligands for drug delivery systems; and (iii) they also increase the hydrophilicity of PHUs scaffolds, which generally favors cell adhesion. Moreover, in a specific case, a PHU even showed non-conventional fluorescence properties allowing the detection of iron ions, an interesting characteristic that has not been reported for PU. It should be noted that the aforementioned reported antibacterial properties of NIPUs seem to arise either from the presence of antibacterial/microbial additives such as silver nanoparticles, curcumin or quaternary ammonium salts (which can already be present as catalyst during the synthesis step), or from the functionalization of these salts on the polymers (by quaternization) and is therefore not an antibacterial property which is intrinsic to the urethane bonds. It would thus be interesting to carry out more antibacterial tests on biocompatible NIPUs that do not contain these antimicrobial additives to determine whether they exhibit any antibacterial activity or not.

To date, biocompatibility studies of the more recently developed PHOxs (synthesized from cyclic exovinylene carbonates) have not yet been reported, although these materials also exhibit specific properties of interest for the biomedical field, such as pendant hydroxyl groups that can also be functionalized, their easy crosslinking, and their cyclic structure that gives them increased stiffness compared to PHUs, which would allow to broaden the range of possible applications of NIPUs. Their particular features are therefore certainly going to trigger their exploitation for biomedical applications and initiate studies of their biological properties in the near future. Overall, NIPUs have the potential to replace and even surpass PUs in several biomedical applications, but to affirm this, long-term NIPU aging and/or biocompatibility studies (*in vitro* or *in vivo*) should also be performed. Yet, to the best of our knowledge, except for a few hydrolysis studies in aqueous media, notably performed on PEG-based PHUs, such studies are not yet reported in the literature. Degradation tests under accelerated aging conditions and in-depth studies of the fate of the biomaterials after long-term implantation should be carried out in the future to identify the nature of the degradation products and their formation rate and to assess the absence of toxicity of potential degradation products associated with these materials. Long-term *in vitro* and *in vivo* studies should therefore be performed in the future to better understand the biocompatibility, degradation and stability of these promising NIPUs structures.

Conflict of interest

There are no conflicts of interest to declare.

Acknowledgements

The authors would like to thank the "Fonds de la Recherche Scientifique" F.R.S.-FNRS in the frame of the FRIA project of S. F. Melo and the Research Director positions of C.D. and C.O.. S. F. Melo obtained additional financial support from the GIGA Doctoral School for Health Sciences and the "Fondation Léon Fredericq".

Bibliography

[1] J.H. Lee, J.W. Lee, G. Khang, H.B. Lee, Interaction of cells on chargeable functional group gradient surfaces, Biomaterials 18 (1997) 351–358. https://doi.org/10.1016/S0142-9612(96)00128-7.

[2] Y. Tamada, Y. Ikada, Effect of Preadsorbed Proteins on Cell Adhesion to Polymer Surfaces, Journal of Colloid and Interface Science 155 (1993) 334–339. https://doi.org/10.1006/jcis.1993.1044.

[3] A.K. Pearce, R.K. O'Reilly, Polymers for Biomedical Applications: The Importance of Hydrophobicity in Directing Biological Interactions and Application Efficacy, Biomacromolecules 22 (2021) 4459–4469. https://doi.org/10.1021/acs.biomac.1c00434.

[4] S.-H. Pyo, P. Wang, H.H. Hwang, W. Zhu, J. Warner, S. Chen, Continuous Optical 3D Printing of Green Aliphatic Polyurethanes, ACS Appl. Mater. Interfaces 9 (2017) 836–844. https://doi.org/10.1021/acsami.6b12500.

[5] W.-H. Chen, Q.-W. Chen, Q. Chen, C. Cui, S. Duan, Y. Kang, Y. Liu, Y. Liu, W. Muhammad, S. Shao, C. Tang, J. Wang, L. Wang, M.-H. Xiong, L. Yin, K. Zhang, Z. Zhang, X. Zhen, J. Feng, C. Gao, Z. Gu, C. He, J. Ji, X. Jiang, W. Liu, Z. Liu, H. Peng, Y. Shen, L. Shi, X. Sun, H. Wang, J. Wang, H. Xiao, F.-J. Xu, Z. Zhong, X.-Z. Zhang, X. Chen, Biomedical polymers: synthesis, properties, and applications, Sci. China Chem. 65 (2022) 1010–1075. https://doi.org/10.1007/s11426-022-1243-5.

[6] E.J. Bolívar-Monsalve, M.M. Alvarez, S. Hosseini, M.A. Espinosa-Hernandez, C.F. Ceballos-González, M. Sanchez-Dominguez, S.R. Shin, B. Cecen, S. Hassan, E. Di Maio, G. Trujillo-de Santiago, Engineering bioactive synthetic polymers for biomedical applications: a review with emphasis on tissue engineering and controlled release, Mater. Adv. 2 (2021) 4447–4478. https://doi.org/10.1039/D1MA00092F.

[7] G. Rokicki, P.G. Parzuchowski, M. Mazurek, Non-isocyanate polyurethanes : synthesis , properties , and applications, Polym. Adv. Technol. 26 (2015) 707–761. https://doi.org/10.1002/pat.3522.

[8] S. Wendels, L. Avérous, Biobased polyurethanes for biomedical applications, Bioactive Materials 6 (2021) 1083–1106. https://doi.org/10.1016/j.bioactmat.2020.10.002.

[9] P. Alves, P. Ferreira, M.H. Gil, Biomedical Polyurethanes-Based Materials, in: Polyurethane: Properties, Structure and Applications, Nova Publishers, New York, 2012: pp. 1–25.

[10] W. Wang, C. Wang, Polyurethane for biomedical applications: A review of recent developments, in: The Design and Manufacture of Medical Devices, Elsevier, 2012: pp. 115–151. https://doi.org/10.1533/9781908818188.115.

[11] M. Kütting, J. Roggenkamp, U. Urban, T. Schmitz-Rode, U. Steinseifer, Polyurethane heart valves: Past, present and future, Expert Review of Medical Devices 8 (2011) 227–233. https://doi.org/10.1586/erd.10.79.

[12] J.V. Cauich-Rodriguez, L.H. Chan-Chan, F. Hernandez-Sanchez, J.M. Cervantes-Uc, Degradation of Polyurethanes for Cardiovascular Applications, in: Advances in Biomaterials Science and Biomedical Applications, 2013: pp. 51–82. https://doi.org/10.5772/53681.

[13] G.M. Bernacca, T.G. Mackay, R. Wilkinson, D.J. Wheatley, Polyurethane heart valves : Fatigue failure , calcification , and polyurethane structure, 34 (1997) 371–379.

[14] T. Al Kayal, P. Losi, M. Asaro, S. Volpi, W. Bonani, M. Bonini, G. Soldani, Analysis of oxidative degradation and calcification behavior of a silicone polycarbonate polyurethane-polydimethylsiloxane material, Journal of Biomedical Materials Research Part A 110 (2022) 1109–1120. https://doi.org/10.1002/JBM.A.37357.
[15] F. Xie, T. Zhang, P. Bryant, V. Kurusingal, J.M. Colwell, B. Laycock, Progress in Polymer Science Degradation and stabilization of polyurethane elastomers, Progress in Polymer Science 90 (2019) 211–268. https://doi.org/10.1016/j.progpolymsci.2018.12.003.
[16] C.A. Krone, T.D. Klingner, Isocyanates, polyurethane and childhood asthma, Pediatric Allergy Immunology 16 (2005) 368–379. https://doi.org/10.1111/j.1399-3038.2005.00295.x.
[17] G. Rokicki, P.G. Parzuchowski, M. Mazurek, Non-isocyanate polyurethanes: synthesis, properties, and applications: Non-Isocyanate Polyurethanes: Synthesis, Properties, and Applications, Polym. Adv. Technol. 26 (2015) 707–761. https://doi.org/10.1002/pat.3522.
[18] C.A. Redlich, M.H. Karol, Diisocyanate asthma : clinical aspects and immunopathogenesis, 2 (2002) 213–224.
[19] D.C. Allport, D.S. Gilbert, S.M. Outterside, MDI and TDI : Safety , Health and the Environment . A Source Book and Practical Guide, John Wiley & Sons Ltd., Chichester (2003).
[20] D. Heederik, P.K. Henneberger, C.A. Redlich, on behalf of the ERS Task Force on the Management of Work-related Asthma, Primary prevention: exposure reduction, skin exposure and respiratory protection, European Respiratory Review 21 (2012) 112–124. https://doi.org/10.1183/09059180.00005111.
[21] L. Maisonneuve, O. Lamarzelle, E. Rix, E. Grau, H. Cramail, Isocyanate-Free Routes to Polyurethanes and Poly(hydroxy Urethane)s, Chem. Rev. 115 (2015) 12407–12439. https://doi.org/10.1021/acs.chemrev.5b00355.
[22] M.S. Kathalewar, P.B. Joshi, A.S. Sabnis, V.C. Malshe, Non-isocyanate polyurethanes : From chemistry to applications, RSC Adv. 3 (2013) 4110–4129. https://doi.org/10.1039/C2RA21938G.
[23] H. Sardon, A. Pascual, D. Mecerreyes, D. Taton, H. Cramail, J.L. Hedrick, Synthesis of Polyurethanes Using Organocatalysis : A Perspective, Macromolecules 48 (2015) 3153–3165. https://doi.org/10.1021/acs.macromol.5b00384.
[24] P. Stachak, I. Łukaszewska, E. Hebda, K. Pielichowski, Recent Advances in Fabrication of Non-Isocyanate Polyurethane-Based Composite Materials, (2021).
[25] J. Guan, Y. Song, Y. Lin, X. Yin, M. Zuo, Y. Zhao, X. Tao, Q. Zheng, Progress in study of non-isocyanate polyurethane, Industrial and Engineering Chemistry Research 50 (2011) 6517–6527. https://doi.org/10.1021/ie101995j.
[26] A. Cornille, R. Auvergne, O. Figovsky, B. Boutevin, S. Caillol, A perspective approach to sustainable routes for non-isocyanate polyurethanes, European Polymer Journal 87 (2017) 535–552. https://doi.org/10.1016/j.eurpolymj.2016.11.027.
[27] A. Gomez-lopez, F. Elizalde, I. Calvo, H. Sardon, Trends in non-isocyanate polyurethane (NIPU) development, Chem. Commun. 57 (2021) 12254–12265. https://doi.org/10.1039/d1cc05009e.

[28] L. Maisonneuve, O. Lamarzelle, E. Rix, E. Grau, H. Cramail, Isocyanate-Free Routes to Polyurethanes and Poly(hydroxy Urethane)s, Chem. Rev. 115 (2015) 12407–12439. https://doi.org/10.1021/acs.chemrev.5b00355.
[29] S. Gennen, B. Grignard, T. Tassaing, C. Jérôme, C. Detrembleur, CO 2 -Sourced α-Alkylidene Cyclic Carbonates: A Step Forward in the Quest for Functional Regioregular Poly(urethane)s and Poly(carbonate)s, Angew. Chem. Int. Ed. 56 (2017) 10394–10398. https://doi.org/10.1002/anie.201704467.
[30] C. Ngassam Tounzoua, B. Grignard, C. Detrembleur, Exovinylene Cyclic Carbonates Multifaceted CO2-Based Building Blocks for Modern Chemistry and Polymer Science, Angewandte Chemie International Edition 61 (2022) 1–25. https://doi.org/doi.org/10.1002/anie.202116066.
[31] T. Habets, F. Siragusa, B. Grignard, C. Detrembleur, Advancing the Synthesis of Isocyanate-Free Poly(oxazolidones)s: Scope and Limitations, Macromolecules 53 (2020) 6396–6408. https://doi.org/10.1021/acs.macromol.0c01231.
[32] A.R. Wong, M. Barrera, A. Pal, J.R. Lamb, Improved Characterization of Polyoxazolidinones by Incorporating Solubilizing Side Chains, Macromolecules 55 (2022) 11006–11012. https://doi.org/10.1021/acs.macromol.2c02104.
[33] H. Asemani, F. Zareanshahraki, V. Mannari, Design of hybrid nonisocyanate polyurethane coatings for advanced ambient temperature curing applications, J of Applied Polymer Sci 136 (2019) 47266. https://doi.org/10.1002/app.47266.
[34] E. Delebecq, J.-P. Pascault, B. Boutevin, F. Ganachaud, On the Versatility of Urethane/Urea Bonds: Reversibility, Blocked Isocyanate, and Non-isocyanate Polyurethane, Chem. Rev. 113 (2013) 80–118. https://doi.org/10.1021/cr300195n.
[35] C. Carré, Y. Ecochard, S. Caillol, L. Avérous, From the Synthesis of Biobased Cyclic Carbonate to Polyhydroxyurethanes: A Promising Route towards Renewable Non-Isocyanate Polyurethanes, ChemSusChem 12 (2019) 3410–3430. https://doi.org/10.1002/cssc.201900737.
[36] M. Rayung, N.A. Ghani, N. Hasanudin, A review on vegetable oil-based non isocyanate polyurethane: towards a greener and sustainable production route, RSC Adv. 14 (2024) 9273–9299. https://doi.org/10.1039/D3RA08684D.
[37] B. Grignard, S. Gennen, C. Jérôme, A.W. Kleij, C. Detrembleur, Advances in the use of CO 2 as a renewable feedstock for the synthesis of polymers, Chem. Soc. Rev. 48 (2019) 4466–4514. https://doi.org/10.1039/C9CS00047J.
[38] H. Khatoon, S. Iqbal, M. Irfan, A. Darda, N.K. Rawat, A review on the production, properties and applications of non-isocyanate polyurethane: A greener perspective, Progress in Organic Coatings 154 (2021) 106124. https://doi.org/10.1016/j.porgcoat.2020.106124.
[39] A. Das, P. Mahanwar, A brief discussion on advances in polyurethane applications, Advanced Industrial and Engineering Polymer Research 3 (2020) 93–101. https://doi.org/10.1016/j.aiepr.2020.07.002.
[40] E. Yılgör, I. Yilgör, Hydrogen bonding: a critical parameter in designing silicone copolymers, Polymer 42 (2001) 7953–7959. https://doi.org/10.1016/S0032-3861(01)00293-2.
[41] D.J. Buckwalter, J.M. Dennis, T.E. Long, Amide-containing segmented copolymers, Progress in Polymer Science 45 (2015) 1–22. https://doi.org/10.1016/j.progpolymsci.2014.11.003.

[42] Polyurethane Market Size & Share Analysis - Growth Trends & Forecasts (2023 - 2028), Mordor Intelligence, 2023.
[43] J. Nanclares, Z.S. Petrović, I. Javni, M. Ionescu, F. Jaramillo, Segmented polyurethane elastomers by nonisocyanate route, J. Appl. Polym. Sci. 132 (2015) 42492. https://doi.org/10.1002/app.42492.
[44] M. Crago, A. Lee, S. Farajikhah, F. Oveissi, D.F. Fletcher, F. Dehghani, D.S. Winlaw, S. Naficy, The evolution of polyurethane heart valve replacements: How chemistry translates to the clinic, Materials Today Communications 33 (2022) 104916. https://doi.org/10.1016/j.mtcomm.2022.104916.
[45] W. Liu, S. Li, B. Wang, P. Peng, C. Gao, Physiologically Responsive Polyurethanes for Tissue Repair and Regeneration, Advanced NanoBiomed Research 2 (2022) 2200061. https://doi.org/10.1002/anbr.202200061.
[46] H. Vahabi, H. Rastin, E. Movahedifar, K. Antoun, N. Brosse, M.R. Saeb, Flame Retardancy of Bio-Based Polyurethanes: Opportunities and Challenges, Polymers 12 (2020) 1234. https://doi.org/10.3390/polym12061234.
[47] A. Delavarde, G. Savin, P. Derkenne, M. Boursier, R. Morales-Cerrada, B. Nottelet, J. Pinaud, S. Caillol, Sustainable polyurethanes: toward new cutting-edge opportunities, Progress in Polymer Science 151 (2024) 101805. https://doi.org/10.1016/j.progpolymsci.2024.101805.
[48] J. Kucinska-Lipka, I. Gubanska, H. Janik, M. Sienkiewicz, Fabrication of polyurethane and polyurethane based composite fibres by the electrospinning technique for soft tissue engineering of cardiovascular system, Materials Science and Engineering: C 46 (2015) 166–176. https://doi.org/10.1016/j.msec.2014.10.027.
[49] S.K. Pramanik, S. Sreedharan, H. Singh, M. Khan, K. Tiwari, A. Shiras, C. Smythe, Jim.A. Thomas, A. Das, Mitochondria Targeting Non-Isocyanate-Based Polyurethane Nanocapsules for Enzyme-Triggered Drug Release, Bioconjugate Chem. 29 (2018) 3532–3543. https://doi.org/10.1021/acs.bioconjchem.8b00460.
[50] S. Miao, P. Wang, Z. Su, S. Zhang, Vegetable-oil-based polymers as future polymeric biomaterials, Acta Biomaterialia 10 (2014) 1692–1704. https://doi.org/10.1016/j.actbio.2013.08.040.
[51] M. Cui, Z. Chai, Y. Lu, J. Zhu, J. Chen, Developments of polyurethane in biomedical applications: A review, Resources Chemicals and Materials 2 (2023) 262–276. https://doi.org/10.1016/j.recm.2023.07.004.
[52] D.C. Aduba, K. Zhang, A. Kanitar, J.M. Sirrine, S.S. Verbridge, T.E. Long, Electrospinning of plant oil-based, non-isocyanate polyurethanes for biomedical applications, J. Appl. Polym. Sci. (2018) 1–11. https://doi.org/10.1002/app.46464.
[53] N. Fanjul-Mosteirín, R. Aguirresarobe, N. Sadaba, A. Larrañaga, E. Marin, J. Martin, N. Ramos-Gomez, M.C. Arno, H. Sardon, A.P. Dove, Crystallization-Induced Gelling as a Method to 4D Print Low-Water-Content Non-isocyanate Polyurethane Hydrogels, Chem. Mater. 33 (2021) 7194–7202. https://doi.org/10.1021/acs.chemmater.1c00913.
[54] D. Visser, H. Bakhshi, K. Rogg, E. Fuhrmann, F. Wieland, K. Schenke-Layland, W. Meyer, H. Hartmann, Green Chemistry for Biomimetic Materials: Synthesis and Electrospinning of High-Molecular-Weight Polycarbonate-Based Nonisocyanate

Polyurethanes, ACS Omega 7 (2022) 39772–39781. https://doi.org/10.1021/acsomega.2c03731.

[55] C. Baj-Rossi, E.G. Kilinc, S.S. Ghoreishizadeh, D. Casarino, T.R. Jost, C. Dehollain, F. Grassi, L. Pastorino, G. De Micheli, S. Carrara, Fabrication and packaging of a fully implantable biosensor array, in: 2013 IEEE Biomedical Circuits and Systems Conference (BioCAS), IEEE, Rotterdam, Netherlands, 2013: pp. 166–169. https://doi.org/10.1109/BioCAS.2013.6679665.

[56] J.O. Akindoyo, M.D.H. Beg, S. Ghazali, M.R. Islam, N. Jeyaratnam, A.R. Yuvaraj, Polyurethane types, synthesis and applications – a review, RSC Adv. 6 (2016) 114453–114482. https://doi.org/10.1039/C6RA14525F.

[57] M. Lowinger, S. Barrett, F. Zhang, R. Williams, Sustained Release Drug Delivery Applications of Polyurethanes, Pharmaceutics 10 (2018) 55. https://doi.org/10.3390/pharmaceutics10020055.

[58] J.G. Lundin, G.C. Daniels, C.L. McGann, J. Stanbro, C. Watters, M. Stockelman, J.H. Wynne, Multi-Functional Polyurethane Hydrogel Foams with Tunable Mechanical Properties for Wound Dressing Applications, Macromol. Mater. Eng. 302 (2017) 1600375. https://doi.org/10.1002/mame.201600375.

[59] A. Gostev, I. Shundrina, V. Pastukhov, A. Shutov, V. Chernonosova, A. Karpenko, P. Laktionov, In Vivo Stability of Polyurethane-Based Electrospun Vascular Grafts in Terms of Chemistry and Mechanics, Polymers 12 (2020) 845. https://doi.org/10.3390/polym12040845.

[60] K. Stokes, R. McVenes, J.M. Anderson, Polyurethane Elastomer Biostability, J Biomater Appl 9 (1995) 321–354. https://doi.org/10.1177/088532829500900402.

[61] R. Ward, J. Anderson, R. McVenes, K. Stokes, In vivo biostability of polysiloxane polyether polyurethanes: Resistance to biologic oxidation and stress cracking, J. Biomed. Mater. Res. 77A (2006) 580–589. https://doi.org/10.1002/jbm.a.30555.

[62] J. Kang, G. Erdodi, C.M. Brendel, D. Ely, J.P. Kennedy, Polyisobutylene-based polyurethanes. V. Oxidative-hydrolytic stability and biocompatibility, J. Polym. Sci. A Polym. Chem. 48 (2010) 2194–2203. https://doi.org/10.1002/pola.23989.

[63] E. Briganti, P. Losi, A. Raffi, M. Scoccianti, A. Munaò, G. Soldani, Silicone based polyurethane materials: a promising biocompatible elastomeric formulation for cardiovascular applications, J Mater Sci: Mater Med 17 (2006) 259–266. https://doi.org/10.1007/s10856-006-7312-4.

[64] Q. Zhao, N. Topham, J.M. Anderson, A. Hiltner, G. Lodoen, C.R. Payet, Foreign-body giant cells and polyurethane biostability: *In vivo* correlation of cell adhesion and surface cracking, J. Biomed. Mater. Res. 25 (1991) 177–183. https://doi.org/10.1002/jbm.820250205.

[65] R.W. Hergenrother, H.D. Wabers, S.L. Cooper, Effect of hard segment chemistry and strain on the stability of polyurethanes: in vivo biostability, Biomaterials 14 (1993) 449–458. https://doi.org/10.1016/0142-9612(93)90148-U.

[66] A. Simmons, A.D. Padsalgikar, L.M. Ferris, L.A. Poole-Warren, Biostability and biological performance of a PDMS-based polyurethane for controlled drug release, Biomaterials 29 (2008) 2987–2995. https://doi.org/10.1016/j.biomaterials.2008.04.007.

[67] E. Dendooven, K. Foubert, T. Naessens, L. Pieters, J. Lambert, O. Aerts, Isocyanates may contribute to allergic contact dermatitis from diabetes devices and

wound dressings, Contact Dermatitis 87 (2022) 414–419. https://doi.org/10.1111/cod.14187.

[68] N. Sheibani, Simulation and experimental study on the incompatibility issue between ADN and isocyanate, J Mol Model 28 (2022) 405. https://doi.org/10.1007/s00894-022-05399-y.

[69] S. Gagné, J. Lesage, C. Ostiguy, H. Van Tra, Determination of unreacted 2,4-toluene diisocyanate (2,4TDI) and 2,6-toluene diisocyanate (2,6TDI) in foams at ultratrace level by using HPLC-CIS-MS-MS, Analyst 128 (2003) 1447–1451. https://doi.org/10.1039/B310463J.

[70] Commission Regulation (EC) No 552/2009 of 22 June 2009 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards Annex XVII, Official Journal of the European Union (2009) L164/7-L164/31.

[71] M. Gutch, N. Jain, A. Agrawal, S. Consul, Acute accidental phosgene poisoning, Case Reports 2012 (2012) bcr1120115233–bcr1120115233. https://doi.org/10.1136/bcr.11.2011.5233.

[72] W.W. Holmes, B.M. Keyser, D.C. Paradiso, R. Ray, D.K. Andres, B.J. Benton, C.C. Rothwell, H.M. Hoard-Fruchey, J.F. Dillman, A.M. Sciuto, D.R. Anderson, Conceptual approaches for treatment of phosgene inhalation-induced lung injury, Toxicology Letters 244 (2016) 8–20. https://doi.org/10.1016/j.toxlet.2015.10.010.

[73] A. Gomez-Lopez, F. Elizalde, I. Calvo, H. Sardon, Trends in non-isocyanate polyurethane (NIPU) development, Chem. Commun. 57 (2021) 12254–12265. https://doi.org/10.1039/D1CC05009E.

[74] B. Bizet, E. Grau, J.M. Asua, H. Cramail, Hybrid Nonisocyanate Polyurethanes (H-NIPUs): A Pathway towards a Broad Range of Novel Materials, Macro Chemistry & Physics 223 (2022) 2100437. https://doi.org/10.1002/macp.202100437.

[75] M. Ghasemlou, F. Daver, E.P. Ivanova, B. Adhikari, Bio-based routes to synthesize cyclic carbonates and polyamines precursors of non-isocyanate polyurethanes: A review, European Polymer Journal 118 (2019) 668–684. https://doi.org/10.1016/j.eurpolymj.2019.06.032.

[76] H. Blattmann, M. Fleischer, M. Bähr, R. Mülhaupt, Isocyanate- and Phosgene-Free Routes to Polyfunctional Cyclic Carbonates and Green Polyurethanes by Fixation of Carbon Dioxide, Macromol. Rapid Commun. 35 (2014) 1238–1254. https://doi.org/10.1002/marc.201400209.

[77] H. Büttner, L. Longwitz, J. Steinbauer, C. Wulf, T. Werner, Recent Developments in the Synthesis of Cyclic Carbonates from Epoxides and CO2, Top Curr Chem (Z) 375 (2017) 50. https://doi.org/10.1007/s41061-017-0136-5.

[78] P.P. Pescarmona, M. Taherimehr, Challenges in the catalytic synthesis of cyclic and polymeric carbonates from epoxides and CO2, Catal. Sci. Technol. 2 (2012) 2169. https://doi.org/10.1039/c2cy20365k.

[79] A.J. Kamphuis, F. Picchioni, P.P. Pescarmona, CO2 -fixation into cyclic and polymeric carbonates: principles and applications, Green Chem. 21 (2019) 406–448. https://doi.org/10.1039/C8GC03086C.

[80] C. Martín, G. Fiorani, A.W. Kleij, Recent Advances in the Catalytic Preparation of Cyclic Organic Carbonates, ACS Catal. 5 (2015) 1353–1370. https://doi.org/10.1021/cs5018997.

[81] Y. Ecochard, S. Caillol, Hybrid polyhydroxyurethanes : How to overcome limitations and reach cutting edge properties ?, European Polymer Journal 137 (2020). https://doi.org/10.1016/j.eurpolymj.2020.109915.
[82] M. Alves, B. Grignard, R. Mereau, C. Jerome, T. Tassaing, C. Detrembleur, Organocatalyzed coupling of carbon dioxide with epoxides for the synthesis of cyclic carbonates: catalyst design and mechanistic studies, Catal. Sci. Technol. 7 (2017) 2651–2684. https://doi.org/10.1039/C7CY00438A.
[83] F. de la Cruz-Martínez, M. Martínez de Sarasa Buchaca, J. Martínez, J. Fernández-Baeza, L.F. Sánchez-Barba, A. Rodríguez-Diéguez, J.A. Castro-Osma, A. Lara-Sánchez, Synthesis of Bio-Derived Cyclic Carbonates from Renewable Resources, ACS Sustainable Chem. Eng. 7 (2019) 20126–20138. https://doi.org/10.1021/acssuschemeng.9b06016.
[84] V. Aomchad, À. Cristòfol, F. Della Monica, B. Limburg, V. D'Elia, A.W. Kleij, Recent progress in the catalytic transformation of carbon dioxide into biosourced organic carbonates, Green Chem. 23 (2021) 1077–1113. https://doi.org/10.1039/D0GC03824E.
[85] A. Rehman, F. Saleem, F. Javed, A. Ikhlaq, S.W. Ahmad, A. Harvey, Recent advances in the synthesis of cyclic carbonates via CO2 cycloaddition to epoxides, Journal of Environmental Chemical Engineering 9 (2021) 105113. https://doi.org/10.1016/j.jece.2021.105113.
[86] M. Alves, B. Grignard, S. Gennen, C. Detrembleur, C. Jerome, T. Tassaing, Organocatalytic synthesis of bio-based cyclic carbonates from CO2 and vegetable oils, RSC Adv. 5 (2015) 53629–53636. https://doi.org/10.1039/C5RA10190E.
[87] C.V. Rajput, N.V. Sastry, N.P. Chikhaliya, Vegetable oils based precursors: modifications and scope for futuristic bio-based polymeric materials, J Polym Res 30 (2023) 159. https://doi.org/10.1007/s10965-023-03534-8.
[88] S. Hu, X. Chen, J.M. Torkelson, Biobased Reprocessable Polyhydroxyurethane Networks: Full Recovery of Crosslink Density with Three Concurrent Dynamic Chemistries, ACS Sustainable Chem. Eng. 7 (2019) 10025–10034. https://doi.org/10.1021/acssuschemeng.9b01239.
[89] W. Zhang, T. Wang, Z. Zheng, R.L. Quirino, F. Xie, Y. Li, C. Zhang, Plant oil-based non-isocyanate waterborne poly(hydroxyl urethane)s, Chemical Engineering Journal 452 (2023) 138965. https://doi.org/10.1016/j.cej.2022.138965.
[90] M. Bähr, R. Mülhaupt, Linseed and soybean oil-based polyurethanes prepared via the non-isocyanate route and catalytic carbon dioxide conversion, Green Chem. 14 (2012) 483. https://doi.org/10.1039/c2gc16230j.
[91] L. Poussard, J. Mariage, B. Grignard, C. Detrembleur, C. Jérôme, C. Calberg, B. Heinrichs, J. De Winter, P. Gerbaux, J.-M. Raquez, L. Bonnaud, Ph. Dubois, Non-Isocyanate Polyurethanes from Carbonated Soybean Oil Using Monomeric or Oligomeric Diamines To Achieve Thermosets or Thermoplastics, Macromolecules 49 (2016) 2162–2171. https://doi.org/10.1021/acs.macromol.5b02467.
[92] S. Panchireddy, B. Grignard, J.-M. Thomassin, C. Jerome, C. Detrembleur, Bio-based poly(hydroxyurethane) glues for metal substrates, Polym. Chem. 9 (2018) 2650–2659. https://doi.org/10.1039/C8PY00281A.

[93] J. Catalá, I. Guerra, J.M. García-Vargas, M.J. Ramos, M.T. García, J.F. Rodríguez, Tailor-Made Bio-Based Non-Isocyanate Polyurethanes (NIPUs), Polymers 15 (2023) 1589. https://doi.org/10.3390/polym15061589.
[94] A. Centeno-Pedrazo, Z. Freixa, R. Feola, F. Lunzer, E.J. Garcia-Suarez, P. Ortiz, Bringing non-isocyanate polyurethanes closer to industrial implementation using carbonated soybean oil-based amino hardeners, Progress in Organic Coatings 185 (2023) 107925. https://doi.org/10.1016/j.porgcoat.2023.107925.
[95] C. Carré, H. Zoccheddu, S. Delalande, P. Pichon, L. Avérous, Synthesis and characterization of advanced biobased thermoplastic nonisocyanate polyurethanes, with controlled aromatic-aliphatic architectures, European Polymer Journal 84 (2016) 759–769. https://doi.org/10.1016/j.eurpolymj.2016.05.030.
[96] C. Muzyka, S. Renson, B. Grignard, C. Detrembleur, J.M. Monbaliu, Intensified Continuous Flow Process for the Scalable Production of Bio-Based Glycerol Carbonate**, Angew Chem Int Ed 63 (2024) e202319060. https://doi.org/10.1002/anie.202319060.
[97] D. Trojanowska, F. Monie, G. Perotto, A. Athanassiou, B. Grignard, E. Grau, T. Vidil, H. Cramail, C. Detrembleur, Valorization of waste biomass for the fabrication of isocyanate-free polyurethane foams, Green Chem. 26 (2024) 8383–8394. https://doi.org/10.1039/D4GC01547A.
[98] M. Thébault, A. Pizzi, S. Dumarçay, P. Gerardin, E. Fredon, L. Delmotte, Polyurethanes from hydrolysable tannins obtained without using isocyanates, Industrial Crops and Products 59 (2014) 329–336. https://doi.org/10.1016/j.indcrop.2014.05.036.
[99] M. Thébault, A. Pizzi, H.A. Essawy, A. Barhoum, G. Van Assche, Isocyanate free condensed tannin-based polyurethanes, European Polymer Journal 67 (2015) 513–526. https://doi.org/10.1016/j.eurpolymj.2014.10.022.
[100] N. Esmaeili, M.J. Zohuriaan-Mehr, A. Salimi, M. Vafayan, W. Meyer, Tannic acid derived non-isocyanate polyurethane networks: Synthesis, curing kinetics, antioxidizing activity and cell viability, Thermochimica Acta 664 (2018) 64–72. https://doi.org/10.1016/j.tca.2018.04.013.
[101] A. Lee, Y. Deng, Green polyurethane from lignin and soybean oil through non-isocyanate reactions, European Polymer Journal 63 (2015) 67–73. https://doi.org/10.1016/j.eurpolymj.2014.11.023.
[102] A. Salanti, L. Zoia, M. Orlandi, Chemical modifications of lignin for the preparation of macromers containing cyclic carbonates, Green Chem. 18 (2016) 4063–4072. https://doi.org/10.1039/C6GC01028H.
[103] J. Li, X. Xu, X. Ma, M. Cui, X. Wang, J. Chen, J. Zhu, J. Chen, Antimicrobial Nonisocyanate Polyurethane Foam Derived from Lignin for Wound Healing, ACS Appl. Bio Mater. 7 (2024) 1301–1310. https://doi.org/10.1021/acsabm.3c01257.
[104] C. Aouf, J. Lecomte, P. Villeneuve, E. Dubreucq, H. Fulcrand, Chemo-enzymatic functionalization of gallic and vanillic acids: synthesis of bio-based epoxy resins prepolymers, Green Chem. 14 (2012) 2328. https://doi.org/10.1039/c2gc35558b.
[105] E.A.B.D. Silva, M. Zabkova, J.D. Araújo, C.A. Cateto, M.F. Barreiro, M.N. Belgacem, A.E. Rodrigues, An integrated process to produce vanillin and lignin-based polyurethanes from Kraft lignin, Chemical Engineering Research and Design 87 (2009) 1276–1292. https://doi.org/10.1016/j.cherd.2009.05.008.

[106] M. Fache, E. Darroman, V. Besse, R. Auvergne, S. Caillol, B. Boutevin, Vanillin, a promising biobased building-block for monomer synthesis, Green Chem. 16 (2014) 1987–1998. https://doi.org/10.1039/C3GC42613K.
[107] A. Brandolese, D.H. Lamparelli, M.A. Pericàs, A.W. Kleij, Synthesis of Biorenewable Terpene Monomers Using Enzymatic Epoxidation under Heterogeneous Batch and Continuous Flow Conditions, ACS Sustainable Chem. Eng. 11 (2023) 4885–4893. https://doi.org/10.1021/acssuschemeng.3c00370.
[108] M. Bähr, A. Bitto, R. Mülhaupt, Cyclic limonene dicarbonate as a new monomer for non-isocyanate oligo- and polyurethanes (NIPU) based upon terpenes, Green Chem. 14 (2012) 1447. https://doi.org/10.1039/c2gc35099h.
[109] S. Schmidt, B.S. Ritter, D. Kratzert, B. Bruchmann, R. Mülhaupt, Isocyanate-Free Route to Poly(carbohydrate–urethane) Thermosets and 100% Bio-Based Coatings Derived from Glycerol Feedstock, Macromolecules 49 (2016) 7268–7276. https://doi.org/10.1021/acs.macromol.6b01485.
[110] V. Salvado, M. Dolatkhani, É. Grau, T. Vidil, H. Cramail, Sequence-Controlled Polyhydroxyurethanes with Tunable Regioregularity Obtained from Sugar-Based Vicinal Bis-cyclic Carbonates, Macromolecules 55 (2022) 7249–7264. https://doi.org/10.1021/acs.macromol.2c01112.
[111] S. Schmidt, F.J. Gatti, M. Luitz, B.S. Ritter, B. Bruchmann, R. Mülhaupt, Erythritol Dicarbonate as Intermediate for Solvent- and Isocyanate-Free Tailoring of Bio-Based Polyhydroxyurethane Thermoplastics and Thermoplastic Elastomers, Macromolecules 50 (2017) 2296–2303. https://doi.org/10.1021/acs.macromol.6b02787.
[112] K. Błażek, H. Beneš, Z. Walterová, S. Abbrent, A. Eceiza, T. Calvo-Correas, J. Datta, Synthesis and structural characterization of bio-based bis(cyclic carbonate)s for the preparation of non-isocyanate polyurethanes, Polym. Chem. 12 (2021) 1643–1652. https://doi.org/10.1039/D0PY01576H.
[113] O. Lamarzelle, G. Hibert, S. Lecommandoux, E. Grau, H. Cramail, A thioglycerol route to bio-based bis-cyclic carbonates: poly(hydroxyurethane) preparation and post-functionalization, Polym. Chem. 8 (2017) 3438–3447. https://doi.org/10.1039/C7PY00556C.
[114] K. Błażek, J. Datta, Renewable natural resources as green alternative substrates to obtain bio-based non-isocyanate polyurethanes-review, Critical Reviews in Environmental Science and Technology 49 (2019) 173–211. https://doi.org/10.1080/10643389.2018.1537741.
[115] P.S. Metkar, M.A. Scialdone, K.G. Moloy, Lysinol: a renewably resourced alternative to petrochemical polyamines and aminoalcohols, Green Chem. 16 (2014) 4575–4586. https://doi.org/10.1039/C4GC01167H.
[116] G. Hibert, O. Lamarzelle, L. Maisonneuve, E. Grau, H. Cramail, Bio-based aliphatic primary amines from alcohols through the 'Nitrile route' towards non-isocyanate polyurethanes, European Polymer Journal 82 (2016) 114–121. https://doi.org/10.1016/j.eurpolymj.2016.07.007.
[117] A. Cornille, V. Froidevaux, C. Negrell, S. Caillol, B. Boutevin, Thiol-ene coupling: An efficient tool for the synthesis of new biobased aliphatic amines for epoxy curing, Polymer 55 (2014) 5561–5570. https://doi.org/10.1016/j.polymer.2014.07.004.

[118] V. Froidevaux, C. Negrell, S. Caillol, J.-P. Pascault, B. Boutevin, Biobased Amines: From Synthesis to Polymers; Present and Future, Chem. Rev. 116 (2016) 14181–14224. https://doi.org/10.1021/acs.chemrev.6b00486.
[119] C. Carré, L. Bonnet, L. Avérous, Original biobased nonisocyanate polyurethanes: solvent- and catalyst-free synthesis, thermal properties and rheological behaviour, RSC Adv. 4 (2014) 54018–54025. https://doi.org/10.1039/C4RA09794G.
[120] V. Besse, F. Camara, F. Méchin, E. Fleury, S. Caillol, J.-P. Pascault, B. Boutevin, How to explain low molar masses in PolyHydroxyUrethanes (PHUs), European Polymer Journal 71 (2015) 1–11. https://doi.org/10.1016/j.eurpolymj.2015.07.020.
[121] R.H. Lambeth, T.J. Henderson, Organocatalytic synthesis of (poly)hydroxyurethanes from cyclic carbonates and amines, Polymer 54 (2013) 5568–5573. https://doi.org/10.1016/j.polymer.2013.08.053.
[122] C. Bakkali-Hassani, D. Berne, P. Bron, L. Irusta, H. Sardon, V. Ladmiral, S. Caillol, Polyhydroxyurethane covalent adaptable networks: looking for suitable catalysts, Polym. Chem. 14 (2023) 3610–3620. https://doi.org/10.1039/D3PY00579H.
[123] C. Wulf, M. Reckers, A. Perechodjuk, T. Werner, Catalytic Systems for the Synthesis of Biscarbonates and Their Impact on the Sequential Preparation of Non-Isocyanate Polyurethanes, ACS Sustainable Chem. Eng. 8 (2020) 1651–1658. https://doi.org/10.1021/acssuschemeng.9b06662.
[124] B. Grignard, C. Ngassamtounzoua, S. Gennen, B. Gilbert, R. Méreau, C. Jerome, T. Tassaing, C. Detrembleur, Boosting the Catalytic Performance of Organic Salts for the Fast and Selective Synthesis of α-Alkylidene Cyclic Carbonates from Carbon Dioxide and Propargylic Alcohols, ChemCatChem 10 (2018) 2584–2592. https://doi.org/10.1002/cctc.201800063.
[125] R. Méreau, B. Grignard, A. Boyaval, C. Detrembleur, C. Jerome, T. Tassaing, Tetrabutylammonium Salts: Cheap Catalysts for the Facile and Selective Synthesis of α-Alkylidene Cyclic Carbonates from Carbon Dioxide and Alkynols, ChemCatChem 10 (2018) 956–960. https://doi.org/10.1002/cctc.201701567.
[126] M. Blain, L. Jean-Gérard, R. Auvergne, D. Benazet, S. Caillol, B. Andrioletti, Rational investigations in the ring opening of cyclic carbonates by amines, Green Chem. 16 (2014) 4286–4291. https://doi.org/10.1039/C4GC01032A.
[127] A. Cornille, M. Blain, R. Auvergne, B. Andrioletti, B. Boutevin, S. Caillol, A study of cyclic carbonate aminolysis at room temperature: effect of cyclic carbonate structures and solvents on polyhydroxyurethane synthesis, Polym. Chem. 8 (2017) 592–604. https://doi.org/10.1039/C6PY01854H.
[128] O. Lamarzelle, P.-L. Durand, A.-L. Wirotius, G. Chollet, E. Grau, H. Cramail, Activated lipidic cyclic carbonates for non-isocyanate polyurethane synthesis, Polym. Chem. 7 (2016) 1439–1451. https://doi.org/10.1039/C5PY01964H.
[129] H. Tomita, F. Sanda, T. Endo, Reactivity comparison of five- and six-membered cyclic carbonates with amines: Basic evaluation for synthesis of poly(hydroxyurethane), J. Polym. Sci. A Polym. Chem. 39 (2001) 162–168. https://doi.org/10.1002/1099-0518(20010101)39:1<162::AID-POLA180>3.0.CO;2-O.
[130] H. Tomita, F. Sanda, T. Endo, Polyaddition of bis(seven-membered cyclic carbonate) with diamines: A novel and efficient synthetic method for

polyhydroxyurethanes, J. Polym. Sci. A Polym. Chem. 39 (2001) 4091–4100. https://doi.org/10.1002/pola.10058.

[131] R.H. Lambeth, S.M. Mathew, M.H. Baranoski, K.J. Housman, B. Tran, J.M. Oyler, Nonisocyanate polyurethanes from six-membered cyclic carbonates: Catalysis and side reactions, J of Applied Polymer Sci 134 (2017) 44941. https://doi.org/10.1002/app.44941.

[132] L. Maisonneuve, A.-L. Wirotius, C. Alfos, E. Grau, H. Cramail, Fatty acid-based (bis) 6-membered cyclic carbonates as efficient isocyanate free poly(hydroxyurethane) precursors, Polym. Chem. 5 (2014) 6142–6147. https://doi.org/10.1039/C4PY00922C.

[133] T.M. McGuire, E.M. López-Vidal, G.L. Gregory, A. Buchard, Synthesis of 5- to 8-membered cyclic carbonates from diols and CO2: A one-step, atmospheric pressure and ambient temperature procedure, Journal of CO2 Utilization 27 (2018) 283–288. https://doi.org/10.1016/j.jcou.2018.08.009.

[134] J.L. Hedrick, V. Piunova, N.H. Park, T. Erdmann, P.L. Arrechea, Simple and Efficient Synthesis of Functionalized Cyclic Carbonate Monomers Using Carbon Dioxide, ACS Macro Lett. 11 (2022) 368–375. https://doi.org/10.1021/acsmacrolett.2c00060.

[135] A. Yuen, A. Bossion, E. Gómez-Bengoa, F. Ruipérez, M. Isik, J.L. Hedrick, D. Mecerreyes, Y.Y. Yang, H. Sardon, Room temperature synthesis of non-isocyanate polyurethanes (NIPUs) using highly reactive N-substituted 8-membered cyclic carbonates, Polym. Chem. 7 (2016) 2105–2111. https://doi.org/10.1039/C6PY00264A.

[136] M.D.P. Maya, S. Torres, C. Gartner, Synthesis and surface modification of sunflower oil-based non-isocyanate polyurethane: Physicochemical and antibacterial properties, J of Applied Polymer Sci (2024) e55181. https://doi.org/10.1002/app.55181.

[137] K.M.F. Rossi de Aguiar, U. Specht, J.F. Maass, D. Salz, C.A. Picon, P.-L.M. Noeske, K. Rischka, U.P. Rodrigues-Filho, Surface modification by physical treatments on biomedical grade metals to improve adhesion for bonding hybrid non-isocyanate urethanes, RSC Adv. 6 (2016) 47203–47211. https://doi.org/10.1039/C6RA05397A.

[138] W. Xu, B. Liu, X. Cai, M. Zhang, X.-H. Zhang, P. Yu, Fluorescent poly(hydroxyurethane): Biocompatibility evaluation and selective detection of Fe(III), J Appl Polym Sci 135 (2018) 46723. https://doi.org/10.1002/app.46723.

[139] S. Gennen, B. Grignard, J.-M. Thomassin, B. Gilbert, B. Vertruyen, C. Jerome, C. Detrembleur, Polyhydroxyurethane hydrogels: Synthesis and characterizations, European Polymer Journal 84 (2016) 849–862. https://doi.org/10.1016/j.eurpolymj.2016.07.013.

[140] A. Pierrard, A. Aqil, C. Detrembleur, C. Jérôme, Thermal and UV Curable Formulations of Poly(propylene glycol)–Poly(hydroxyurethane) Elastomers toward Nozzle-Based 3D Photoprinting, Biomacromolecules 24 (2023) 4375–4384. https://doi.org/10.1021/acs.biomac.2c00860.

[141] Y. Zhao, X. Xia, J. Zhou, Z. Huang, F. Lei, X. Tan, D. Yu, Y. Zhu, H. Xu, Thermoresponsive behavior of non-isocyanate poly(hydroxyl)urethane for biomedical composite materials, Adv Compos Hybrid Mater 5 (2022) 843–852. https://doi.org/10.1007/s42114-021-00379-x.

[142] S.F. Melo, A. Nondonfaz, A. Aqil, A. Pierrard, A. Hulin, C. Delierneux, B. Ditkowski, M. Gustin, M. Legrand, B.M.E. Tullemans, S.L.N. Brouns, A. Nchimi, R. Carrus, A. Dejosé, J.W.M. Heemskerk, M.J.E. Kuijpers, J. Ritter, U. Steinseifer, J.C. Clauser, C. Jérôme, P. Lancellotti, C. Oury, Design, manufacturing and testing of a green non-isocyanate polyurethane prosthetic heart valve, Biomater. Sci. 12 (2024) 2149–2164. https://doi.org/10.1039/D3BM01911J.

[143] M. Bourguignon, J.-M. Thomassin, B. Grignard, C. Jerome, C. Detrembleur, Fast and Facile One-Pot One-Step Preparation of Nonisocyanate Polyurethane Hydrogels in Water at Room Temperature, ACS Sustainable Chem. Eng. 7 (2019) 12601–12610. https://doi.org/10.1021/acssuschemeng.9b02624.

[144] M. Bourguignon, J. Thomassin, B. Grignard, B. Vertruyen, C. Detrembleur, Water-Borne Isocyanate-Free Polyurethane Hydrogels with Adaptable Functionality and Behavior, Macromol. Rapid Commun. 42 (2020) 2000482. https://doi.org/10.1002/marc.202000482.

[145] M. Bourguignon, B. Grignard, C. Detrembleur, Introducing Polyhydroxyurethane Hydrogels and Coatings for Formaldehyde Capture, ACS Appl. Mater. Interfaces 13 (2021) 54396–54408. https://doi.org/10.1021/acsami.1c16917.

[146] S. Kotanen, M. Poikelispää, A. Efimov, T. Harjunalanen, C. Mills, T. Laaksonen, E. Sarlin, Hydrolytic stability of polyurethane/polyhydroxyurethane hybrid adhesives, International Journal of Adhesion and Adhesives 110 (2021) 102950. https://doi.org/10.1016/j.ijadhadh.2021.102950.

[147] I. Łukaszewska, A. Bukowczan, K.N. Raftopoulos, K. Pielichowski, Examining the Water–Polymer Interactions in Non-Isocyanate Polyurethane/Polyhedral Oligomeric Silsesquioxane Hybrid Hydrogels, Polymers 16 (2023) 57. https://doi.org/10.3390/polym16010057.

[148] I. Łukaszewska, A. Bukowczan, K.N. Raftopoulos, K. Pielichowski, Water-polymer interactions and mechanisms of water-driven glass transition decrease in non-isocyanate polyhydroxyurethanes with varying hydration sites, Polymer 302 (2024) 127060. https://doi.org/10.1016/j.polymer.2024.127060.

[149] F. Magliozzi, A. Scali, G. Chollet, D. Montarnal, E. Grau, H. Cramail, Hydrolyzable Biobased Polyhydroxyurethane Networks with Shape Memory Behavior at Body Temperature, ACS Sustainable Chem. Eng. 8 (2020) 9125–9135. https://doi.org/10.1021/acssuschemeng.0c02610.

[150] O. Figovsky, L. Shapovalov, F. Buslov, Ultraviolet and thermostable non-isocyanate polyurethane coatings, Surface Coatings International Part B: Coatings Transactions 88 (2005) 67–71. https://doi.org/10.1007/BF02699710.

[151] M. Blain, A. Cornille, B. Boutevin, R. Auvergne, D. Benazet, B. Andrioletti, S. Caillol, Hydrogen bonds prevent obtaining high molar mass PHUs, J. Appl. Polym. Sci. 134 (2017) 44958. https://doi.org/10.1002/app.44958.

[152] E.K. Leitsch, G. Beniah, K. Liu, T. Lan, W.H. Heath, K.A. Scheidt, J.M. Torkelson, Nonisocyanate Thermoplastic Polyhydroxyurethane Elastomers via Cyclic Carbonate Aminolysis: Critical Role of Hydroxyl Groups in Controlling Nanophase Separation, ACS Macro Lett. 5 (2016) 424–429. https://doi.org/10.1021/acsmacrolett.6b00102.

[153] G. Beniah, X. Chen, B.E. Uno, K. Liu, E.K. Leitsch, J. Jeon, W.H. Heath, K.A. Scheidt, J.M. Torkelson, Combined Effects of Carbonate and Soft-Segment

Molecular Structures on the Nanophase Separation and Properties of Segmented Polyhydroxyurethane, Macromolecules 50 (2017) 3193–3203. https://doi.org/10.1021/acs.macromol.6b02513.

[154] G. Beniah, D.J. Fortman, W.H. Heath, W.R. Dichtel, J.M. Torkelson, Non-Isocyanate Polyurethane Thermoplastic Elastomer: Amide-Based Chain Extender Yields Enhanced Nanophase Separation and Properties in Polyhydroxyurethane, Macromolecules 50 (2017) 4425–4434. https://doi.org/10.1021/acs.macromol.7b00765.

[155] A. Pierrard, S.F. Melo, Q. Thijssen, S.V. Vlierberghe, P. Lancellotti, C. Oury, C. Detrembleur, C. Jérôme, Design of 3D-Photoprintable, Bio-, and Hemocompatible Nonisocyanate Polyurethane Elastomers for Biomedical Implants, Biomacromolecules 25 (2024) 1810–1824. https://doi.org/10.1021/acs.biomac.3c01261.

[156] S.V. Zubkevich, M. Makarov, R. Dieden, L. Puchot, V. Berthé, S. Westermann, A.S. Shaplov, D.F. Schmidt, Unique Method for Facile Postsynthetic Modification of Nonisocyanate Polyurethanes, Macromolecules 57 (2024) 2385–2393. https://doi.org/10.1021/acs.macromol.3c02232.

[157] H. Buchheit, B. Bruchmann, K. Stoll, R. Mülhaupt, Functionalized acrylic polyhydroxy urethanes as molecular tool box for photocurable thermosets and 3D printing, Journal of Polymer Science 59 (2021) 882–892. https://doi.org/10.1002/pol.20210115.

[158] Mhd.Abd.C. Mhd. Haniffa, K. Munawar, Y.C. Ching, H.A. Illias, C.H. Chuah, Bio-based Poly(hydroxy urethane)s: Synthesis and Pre/Post-Functionalization, Chem. Asian J. 16 (2021) 1281–1297. https://doi.org/10.1002/asia.202100226.

[159] G. Beniah, W.H. Heath, J.M. Torkelson, Functionalization of hydroxyl groups in segmented polyhydroxyurethane eliminates nanophase separation, J. Polym. Sci. Part A: Polym. Chem. 55 (2017) 3347–3351. https://doi.org/10.1002/pola.28722.

[160] B. Ochiai, S. Inoue, T. Endo, One-pot non-isocyanate synthesis of polyurethanes from bisepoxide, carbon dioxide, and diamine, J. Polym. Sci. A Polym. Chem. 43 (2005) 6613–6618. https://doi.org/10.1002/pola.21103.

[161] F. Monie, B. Grignard, J. Thomassin, R. Mereau, T. Tassaing, C. Jerome, C. Detrembleur, Chemo- and Regioselective Additions of Nucleophiles to Cyclic Carbonates for the Preparation of Self-Blowing Non-Isocyanate Polyurethane Foams, Angew. Chem. 132 (2020) 17181–17189. https://doi.org/10.1002/ange.202006267.

[162] F. Monie, B. Grignard, C. Detrembleur, Divergent Aminolysis Approach for Constructing Recyclable Self-Blown Nonisocyanate Polyurethane Foams, ACS Macro Lett. 11 (2022) 236–242. https://doi.org/10.1021/acsmacrolett.1c00793.

[163] A. Cornille, C. Guillet, S. Benyahya, C. Negrell, B. Boutevin, S. Caillol, Room temperature flexible isocyanate-free polyurethane foams, European Polymer Journal 84 (2016) 873–888. https://doi.org/10.1016/j.eurpolymj.2016.05.032.

[164] A. Cornille, S. Dworakowska, D. Bogdal, B. Boutevin, S. Caillol, A new way of creating cellular polyurethane materials: NIPU foams, European Polymer Journal 66 (2015) 129–138. https://doi.org/10.1016/j.eurpolymj.2015.01.034.

[165] M. Bourguignon, B. Grignard, C. Detrembleur, Water-Induced Self-Blown Non-Isocyanate Polyurethane Foams, Angew. Chem. Int. Ed. 61 (2022) e202213422. https://doi.org/doi.org/10.1002/anie.202213422.
[166] B. Grignard, J.-M. Thomassin, S. Gennen, L. Poussard, L. Bonnaud, J.-M. Raquez, P. Dubois, M.-P. Tran, C.B. Park, C. Jerome, C. Detrembleur, CO_2 -blown microcellular non-isocyanate polyurethane (NIPU) foams: from bio- and CO_2 -sourced monomers to potentially thermal insulating materials, Green Chem. 18 (2016) 2206–2215. https://doi.org/10.1039/C5GC02723C.
[167] M. Bourguignon, B. Grignard, C. Detrembleur, Cascade exotherms for rapidly producing hybrid non-isocyanate polyurethane foams from room temperature formulations, Chemistry, 2023. https://doi.org/10.26434/chemrxiv-2023-t48bf.
[168] A. Gomez-Lopez, S. Panchireddy, B. Grignard, I. Calvo, C. Jerome, C. Detrembleur, H. Sardon, Poly(hydroxyurethane) Adhesives and Coatings: State-of-the-Art and Future Directions, ACS Sustainable Chem. Eng. 9 (2021) 9541–9562. https://doi.org/10.1021/acssuschemeng.1c02558.
[169] A. Gomez-Lopez, N. Ayensa, B. Grignard, L. Irusta, I. Calvo, A.J. Müller, C. Detrembleur, H. Sardon, Enhanced and Reusable Poly(hydroxy urethane)-Based Low Temperature Hot-Melt Adhesives, ACS Polym. Au 2 (2022) 194–207. https://doi.org/10.1021/acspolymersau.1c00053.
[170] A. Gomez-Lopez, B. Grignard, I. Calvo, C. Detrembleur, H. Sardon, Accelerating the Curing of Hybrid Poly(Hydroxy Urethane)-Epoxy Adhesives by the Thiol-Epoxy Chemistry, ACS Appl. Polym. Mater. 4 (2022) 8786–8794. https://doi.org/10.1021/acsapm.2c01195.
[171] A. Cornille, G. Michaud, F. Simon, S. Fouquay, R. Auvergne, B. Boutevin, S. Caillol, Promising mechanical and adhesive properties of isocyanate-free poly(hydroxyurethane), European Polymer Journal 84 (2016) 404–420. https://doi.org/10.1016/j.eurpolymj.2016.09.048.
[172] S. Panchireddy, J.-M. Thomassin, B. Grignard, C. Damblon, A. Tatton, C. Jerome, C. Detrembleur, Reinforced poly(hydroxyurethane) thermosets as high performance adhesives for aluminum substrates, Polym. Chem. 8 (2017) 5897–5909. https://doi.org/10.1039/C7PY01209H.
[173] Y.R. Sulthana, S.A. Gurusamy Thangavelu, Development of nonisocyanate polyurethane–MWCNT nanocomposites: coatings with enhanced antifouling, corrosion resistance and UV protection properties, New J. Chem. 49 (2025) 404–417. https://doi.org/10.1039/D4NJ04917A.
[174] Y. Yuan, Y. Xie, C. Zeng, D. Song, S. Chaemchuen, C. Chen, F. Verpoort, A recyclable AgI/OAc^- catalytic system for the efficient synthesis of α-alkylidene cyclic carbonates: carbon dioxide conversion at atmospheric pressure, Green Chem. 19 (2017) 2936–2940. https://doi.org/10.1039/C7GC00276A.
[175] C. Qiao, P.D. Engel, L.A. Ziegenhagen, F. Rominger, A. Schäfer, P. Deglmann, P. Rudolf, P. Comba, A.S.K. Hashmi, T. Schaub, An Organocatalytic Route to *endo* -Vinylene Carbonates from Carbon Dioxide-Based *exo* -Vinylene Carbonates, Adv Synth Catal 366 (2024) 291–298. https://doi.org/10.1002/adsc.202301374.
[176] A. Boyaval, R. Méreau, B. Grignard, C. Detrembleur, C. Jerome, T. Tassaing, Organocatalytic Coupling of CO_2 with a Propargylic Alcohol: A Comprehensive

Mechanistic Study, ChemSusChem 10 (2017) 1241–1248. https://doi.org/10.1002/cssc.201601524.

[177] Y. Hu, J. Song, C. Xie, H. Wu, T. Jiang, G. Yang, B. Han, Transformation of CO_2 into α-Alkylidene Cyclic Carbonates at Room Temperature Cocatalyzed by CuI and Ionic Liquid with Biomass-Derived Levulinate Anion, ACS Sustainable Chem. Eng. 7 (2019) 5614–5619. https://doi.org/10.1021/acssuschemeng.8b05851.

[178] Z. Zhang, J. Li, R. Zhang, X. Sun, L. Wang, J. Zhang, Transformation of CO2 into α-alkylidene cyclic carbonates at room temperature and atmospheric pressure by phthalimide based ionic liquids with inert cation and moderate basicity, Journal of Molecular Structure 1299 (2024) 137133. https://doi.org/10.1016/j.molstruc.2023.137133.

[179] S. Dabral, U. Licht, P. Rudolf, G. Bollmann, A.S.K. Hashmi, T. Schaub, Synthesis and polymerisation of α-alkylidene cyclic carbonates from carbon dioxide, epoxides and the primary propargylic alcohol 1,4-butynediol, Green Chem. 22 (2020) 1553–1558. https://doi.org/10.1039/C9GC04320A.

[180] A. Cervantes-Reyes, K. Farshadfar, M. Rudolph, F. Rominger, T. Schaub, A. Ariafard, A.S.K. Hashmi, Copper-catalysed synthesis of α-alkylidene cyclic carbonates from propargylic alcohols and CO_2, Green Chem. 23 (2021) 889–897. https://doi.org/10.1039/D0GC03990J.

[181] M. Li, S. Abdolmohammadi, M.S. Hoseininezhad-Namin, F. Behmagham, E. Vessally, Carboxylative cyclization of propargylic alcohols with carbon dioxide: A facile and Green route to α-methylene cyclic carbonates, Journal of CO2 Utilization 38 (2020) 220–231. https://doi.org/10.1016/j.jcou.2020.01.024.

[182] G. Shi, R. Zhai, H. Li, C. Wang, Highly efficient synthesis of alkylidene cyclic carbonates from low concentration CO_2 using hydroxyl and azolate dual functionalized ionic liquids, Green Chem. 23 (2021) 592–596. https://doi.org/10.1039/D0GC03510F.

[183] L. Ouyang, X. Tang, H. He, C. Qi, W. Xiong, Y. Ren, H. Jiang, Copper-Promoted Coupling of Carbon Dioxide and Propargylic Alcohols: Expansion of Substrate Scope and Trapping of Vinyl Copper Intermediate, Adv Synth Catal 357 (2015) 2556–2565. https://doi.org/10.1002/adsc.201500088.

[184] Y. Zhao, L. Tian, J. Qiu, Z. Li, H. Wang, G. Cui, S. Zhang, J. Wang, Remarkable synergistic effect between copper(I) and ionic liquids for promoting chemical fixation of CO 2, Journal of CO2 Utilization 22 (2017) 374–381. https://doi.org/10.1016/j.jcou.2017.10.017.

[185] J. Qiu, Y. Zhao, Z. Li, H. Wang, M. Fan, J. Wang, Efficient Ionic-Liquid-Promoted Chemical Fixation of CO_2 into α-Alkylidene Cyclic Carbonates, ChemSusChem 10 (2017) 1120–1127. https://doi.org/10.1002/cssc.201601129.

[186] Y. Wu, Y. Zhao, R. Li, B. Yu, Y. Chen, X. Liu, C. Wu, X. Luo, Z. Liu, Tetrabutylphosphonium-Based Ionic Liquid Catalyzed CO_2 Transformation at Ambient Conditions: A Case of Synthesis of α-Alkylidene Cyclic Carbonates, ACS Catal. 7 (2017) 6251–6255. https://doi.org/10.1021/acscatal.7b01422.

[187] F. Ouhib, B. Grignard, E. Van Den Broeck, A. Luxen, K. Robeyns, V. Van Speybroeck, C. Jerome, C. Detrembleur, A Switchable Domino Process for the Construction of Novel CO_2 -Sourced Sulfur-Containing Building Blocks and

Polymers, Angew. Chem. Int. Ed. 58 (2019) 11768–11773. https://doi.org/10.1002/anie.201905969.
[188] F. Siragusa, E. Van Den Broeck, C. Ocando, A.J. Müller, G. De Smet, B.U.W. Maes, J. De Winter, V. Van Speybroeck, B. Grignard, C. Detrembleur, Access to Biorenewable and CO2-Based Polycarbonates from Exovinylene cyclic carbonates, ACS Sustainable Chem. Eng. 9 (2021) 1714–1728. https://dx.doi.org/10.1021/acssuschemeng.0c07683.
[189] C. Chauveau, S. Fouquay, G. Michaud, F. Simon, J.-F. Carpentier, S.M. Guillaume, α,ω-Di(vinylene carbonate) telechelic polyolefins: Synthesis by metathesis reactions and studies as potential precursors toward hydroxy-oxazolidone-based polyolefin NIPUs, European Polymer Journal 116 (2019) 144–157. https://doi.org/10.1016/j.eurpolymj.2019.03.052.
[190] M. Razavi-Esfali, T. Habets, F. Siragusa, B. Grignard, H. Sardon, C. Detrembleur, Design of functional isocyanate-free poly(oxazolidone)s under mild conditions, Polym. Chem. 15 (2024) 1962–1974. https://doi.org/10.1039/D4PY00101J.
[191] T. Habets, G. Seychal, M. Caliari, J.-M. Raquez, H. Sardon, B. Grignard, C. Detrembleur, Covalent adaptable networks through dynamic N,S-acetal chemistry: toward recyclable CO2-based thermosets, Journal of the American Chemical Society 145 (2023) 25450–25462. https://doi.org/10.1021/jacs.3c10080.
[192] ISO 10993-5:2009 - Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity, (2009).
[193] N. Sahiner, S. Sagbas, N. Aktas, Preparation and characterization of monodisperse, mesoporous natural poly(tannic acid)–silica nanoparticle composites with antioxidant properties, Microporous and Mesoporous Materials 226 (2016) 316–324. https://doi.org/10.1016/j.micromeso.2016.02.012.
[194] N. Sahiner, S. Sagbas, N. Aktas, Preparation of macro-, micro-, and nano-sized poly(Tannic acid) particles with controllable degradability and multiple biomedical uses, Polymer Degradation and Stability 129 (2016) 96–105. https://doi.org/10.1016/j.polymdegradstab.2016.04.010.
[195] M. Azadfar, A.H. Gao, M.V. Bule, S. Chen, Structural characterization of lignin: A potential source of antioxidants guaiacol and 4-vinylguaiacol, International Journal of Biological Macromolecules 75 (2015) 58–66. https://doi.org/10.1016/j.ijbiomac.2014.12.049.
[196] K. Ghosal, P. Sarkar, D. Chakraborty, S. Das, K. Sarkar, Green Synthesis of Nonisocyanate Poly(ester urethanes) from Renewable Resources and Recycled Poly(ethylene terephthalate) Waste for Tissue Engineering Application, ACS Sustainable Chem. Eng. 11 (2023) 13688–13708. https://doi.org/10.1021/acssuschemeng.3c03566.
[197] C. Xu, Y. Huang, J. Wu, L. Tang, Y. Hong, Triggerable Degradation of Polyurethanes for Tissue Engineering Applications, ACS Appl. Mater. Interfaces 7 (2015) 20377–20388. https://doi.org/10.1021/acsami.5b06242.
[198] A.I. Carbajo-Gordillo, E. Benito, E. Galbis, R. Grosso, N. Iglesias, C. Valencia, R. Lucas, M.-G. García-Martín, M.-V. de-Paz, Simultaneous Formation of Polyhydroxyurethanes and Multicomponent Semi-IPN Hydrogels, Polymers 16 (2024) 880. https://doi.org/10.3390/polym16070880.

[199] P.C. Caracciolo, N.J. Lores, G.A. Abraham, Polyurethane-based structures obtained by additive manufacturing technologies, in: Materials for Biomedical Engineering: Hydrogels and Polymer-Based Scaffolds, Elsevier, 2019: pp. 235–258. https://doi.org/10.1016/B978-0-12-816901-8.00008-0.

[200] K.-C. Hung, C.-S. Tseng, S.-H. Hsu, 3D printing of polyurethane biomaterials, in: Advances in Polyurethane Biomaterials, Elsevier, 2016: pp. 149–170. https://doi.org/10.1016/B978-0-08-100614-6.00005-6.

[201] K.-C. Hung, C.-S. Tseng, L.-G. Dai, S. Hsu, Water-based polyurethane 3D printed scaffolds with controlled release function for customized cartilage tissue engineering, Biomaterials 83 (2016) 156–168. https://doi.org/10.1016/j.biomaterials.2016.01.019.

[202] J. Herzberger, J.M. Sirrine, C.B. Williams, T.E. Long, Polymer Design for 3D Printing Elastomers: Recent Advances in Structure, Properties, and Printing, Progress in Polymer Science 97 (2019) 101144. https://doi.org/10.1016/j.progpolymsci.2019.101144.

[203] J. Park, D. Tahk, C. Ahn, S.G. Im, S.-J. Choi, K.-Y. Suh, S. Jeon, Conformal phase masks made of polyurethane acrylate with optimized elastic modulus for 3D nanopatterning, J. Mater. Chem. C 2 (2014) 2316. https://doi.org/10.1039/c3tc32194k.

[204] F.-Y. Hsieh, H.-H. Lin, S. Hsu, 3D bioprinting of neural stem cell-laden thermoresponsive biodegradable polyurethane hydrogel and potential in central nervous system repair, Biomaterials 71 (2015) 48–57. https://doi.org/10.1016/j.biomaterials.2015.08.028.

[205] W. Zhu, J. Li, Y.J. Leong, I. Rozen, X. Qu, R. Dong, Z. Wu, W. Gao, P.H. Chung, J. Wang, S. Chen, 3D-Printed Artificial Microfish, Adv. Mater. 27 (2015) 4411–4417. https://doi.org/10.1002/adma.201501372.

[206] J.J. Warner, P. Wang, W.M. Mellor, H.H. Hwang, J.H. Park, S.-H. Pyo, S. Chen, 3D printable non-isocyanate polyurethanes with tunable material properties, Polym. Chem. 10 (2019) 4665–4674. https://doi.org/10.1039/C9PY00999J.

[207] S. Mura, J. Nicolas, P. Couvreur, Stimuli-responsive nanocarriers for drug delivery, Nat Mater. 12 (2013) 991–1003. https://doi.org/10.1038/nmat3776.

[208] C.-K. Chen, W.-C. Law, R. Aalinkeel, Y. Yu, B. Nair, J. Wu, S. Mahajan, J.L. Reynolds, Y. Li, C.K. Lai, E.S. Tzanakakis, S.A. Schwartz, P.N. Prasad, C. Cheng, Biodegradable cationic polymeric nanocapsules for overcoming multidrug resistance and enabling drug–gene co-delivery to cancer cells, Nanoscale 6 (2014) 1567–1572. https://doi.org/10.1039/C3NR04804G.

[209] M. Yan, J. Du, Z. Gu, M. Liang, Y. Hu, W. Zhang, S. Priceman, L. Wu, Z.H. Zhou, Z. Liu, T. Segura, Y. Tang, Y. Lu, A novel intracellular protein delivery platform based on single-protein nanocapsules, Nature Nanotech 5 (2010) 48–53. https://doi.org/10.1038/nnano.2009.341.

[210] X. Wang, J. Hu, G. Liu, J. Tian, H. Wang, M. Gong, S. Liu, Reversibly Switching Bilayer Permeability and Release Modules of Photochromic Polymersomes Stabilized by Cooperative Noncovalent Interactions, J. Am. Chem. Soc. 137 (2015) 15262–15275. https://doi.org/10.1021/jacs.5b10127.

[211] W.-C. Liao, I. Willner, Synthesis and Applications of Stimuli-Responsive DNA-Based Nano- and Micro-Sized Capsules, Adv. Funct. Mater. 27 (2017) 1702732. https://doi.org/10.1002/adfm.201702732.
[212] H. He, Y. Chen, Y. Li, Z. Song, Y. Zhong, R. Zhu, J. Cheng, L. Yin, Effective and Selective Anti-Cancer Protein Delivery via All-Functions-in-One Nanocarriers Coupled with Visible Light-Responsive, Reversible Protein Engineering, Adv. Funct. Mater. 28 (2018) 1706710. https://doi.org/10.1002/adfm.201706710.
[213] S. Sharma, U. Paiphansiri, V. Hombach, V. Mailänder, O. Zimmermann, K. Landfester, V. Rasche, Characterization of MRI contrast agent-loaded polymeric nanocapsules as versatile vehicle for targeted imaging, Contrast Media Mol. Imaging 5 (2010) 59–69. https://doi.org/10.1002/cmmi.364.
[214] B. Kang, T. Opatz, K. Landfester, F.R. Wurm, Carbohydrate nanocarriers in biomedical applications: functionalization and construction, Chem. Soc. Rev. 44 (2015) 8301–8325. https://doi.org/10.1039/C5CS00092K.
[215] J.P. Burnham, J.P. Kirby, M.H. Kollef, Diagnosis and management of skin and soft tissue infections in the intensive care unit: a review, Intensive Care Med 42 (2016) 1899–1911. https://doi.org/10.1007/s00134-016-4576-0.
[216] R. Gharibi, M.B. Teimouri, S. Safavian, Biocidal organic-inorganic urethane-siloxane coating by facile polymerization of single component soy-based prepolymer, Surface and Coatings Technology 429 (2022) 127925. https://doi.org/10.1016/j.surfcoat.2021.127925.
[217] J.W. Costerton, P.S. Stewart, E.P. Greenberg, Bacterial Biofilms: A Common Cause of Persistent Infections, Science 284 (1999) 1318–1322. https://doi.org/10.1126/science.284.5418.1318.
[218] D. Simões, S.P. Miguel, M.P. Ribeiro, P. Coutinho, A.G. Mendonça, I.J. Correia, Recent advances on antimicrobial wound dressing: A review, European Journal of Pharmaceutics and Biopharmaceutics 127 (2018) 130–141. https://doi.org/10.1016/j.ejpb.2018.02.022.
[219] J. Boateng, O. Catanzano, Advanced Therapeutic Dressings for Effective Wound Healing—A Review, Journal of Pharmaceutical Sciences 104 (2015) 3653–3680. https://doi.org/10.1002/jps.24610.
[220] E. Rezvani Ghomi, S. Khalili, S. Nouri Khorasani, R. Esmaeely Neisiany, S. Ramakrishna, Wound dressings: Current advances and future directions, J. Appl. Polym. Sci. 136 (2019) 47738. https://doi.org/10.1002/app.47738.
[221] V. Vivcharenko, A. Przekora, Modifications of Wound Dressings with Bioactive Agents to Achieve Improved Pro-Healing Properties, Applied Sciences 11 (2021) 4114. https://doi.org/10.3390/app11094114.
[222] H. Shadmon, A. Basu, L.H. Eckhard, A.J. Domb, N. Beyth, Synthesis, characterization and antibacterial activity of heterocyclic quaternary ammonium polymers, New J. Chem. 42 (2018) 15427–15435. https://doi.org/10.1039/C8NJ03392G.
[223] Y. Jiao, L. Niu, S. Ma, J. Li, F.R. Tay, J. Chen, Quaternary ammonium-based biomedical materials: State-of-the-art, toxicological aspects and antimicrobial resistance, Progress in Polymer Science 71 (2017) 53–90. https://doi.org/10.1016/j.progpolymsci.2017.03.001.

[224] M.C. Jennings, K.P.C. Minbiole, W.M. Wuest, Quaternary Ammonium Compounds: An Antimicrobial Mainstay and Platform for Innovation to Address Bacterial Resistance, ACS Infect. Dis. 1 (2015) 288–303. https://doi.org/10.1021/acsinfecdis.5b00047.
[225] H. Gholami, H. Yeganeh, S.B. Burujeny, M. Sorayya, E. Shams, Vegetable Oil Based Polyurethane Containing 1,2,3-Triazolium Functional Groups as Antimicrobial Wound Dressing, J Polym Environ 26 (2018) 462–473. https://doi.org/10.1007/s10924-017-0964-y.
[226] A. Yari, H. Yeganeh, H. Bakhshi, R. Gharibi, Preparation and characterization of novel antibacterial castor oil-based polyurethane membranes for wound dressing application: Preparation and Characterization of Novel Antibacterial Co-Based Polyurethane Membranes, J. Biomed. Mater. Res. 102 (2014) 84–96. https://doi.org/10.1002/jbm.a.34672.
[227] A. Rezapour-Lactoee, H. Yeganeh, S.N. Ostad, R. Gharibi, Z. Mazaheri, J. Ai, Thermoresponsive polyurethane/siloxane membrane for wound dressing and cell sheet transplantation: In-vitro and in-vivo studies, Materials Science and Engineering: C 69 (2016) 804–814. https://doi.org/10.1016/j.msec.2016.07.067.
[228] R. Gharibi, H. Yeganeh, H. Gholami, Z.M. Hassan, Aniline tetramer embedded polyurethane/siloxane membranes and their corresponding nanosilver composites as intelligent wound dressing materials, RSC Adv. 4 (2014) 62046–62060. https://doi.org/10.1039/C4RA11454J.
[229] H. Gholami, H. Yeganeh, Vegetable oil-based polyurethanes as antimicrobial wound dressings: *in vitro* and *in vivo* evaluation, Biomed. Mater. 15 (2020) 045001. https://doi.org/10.1088/1748-605X/ab7387.
[230] Y. Ding, Z. Sun, R. Shi, H. Cui, Y. Liu, H. Mao, B. Wang, D. Zhu, F. Yan, Integrated Endotoxin Adsorption and Antibacterial Properties of Cationic Polyurethane Foams for Wound Healing, ACS Appl. Mater. Interfaces 11 (2019) 2860–2869. https://doi.org/10.1021/acsami.8b19746.
[231] Y.-H. Xu, P. Zeng, M.-F. Li, J. Bian, F. Peng, γ-Valerolactone/water system for lignin fractionation to enhance antibacterial and antioxidant capacities, Separation and Purification Technology 279 (2021) 119780. https://doi.org/10.1016/j.seppur.2021.119780.
[232] M. Quan, J. Li, M. Cui, G. Sha, Y. Wang, B. Wu, J. Zhu, J. Chen, Copper peroxide-loaded lignin-based non-isocyanate polyurethane foam for wound repair applications, International Journal of Biological Macromolecules 288 (2025) 138733. https://doi.org/10.1016/j.ijbiomac.2024.138733.
[233] X. Renaudin, Reactive oxygen species and DNA damage response in cancer, in: International Review of Cell and Molecular Biology, Elsevier, 2021: pp. 139–161. https://doi.org/10.1016/bs.ircmb.2021.04.001.
[234] M.Y. Memar, R. Ghotaslou, M. Samiei, K. Adibkia, Antimicrobial use of reactive oxygen therapy: current insights, Infection and Drug Resistance 11 (2018) 567–576. https://doi.org/10.2147/IDR.S142397.
[235] Y. Ding, G. Yang, S. Zheng, X. Gao, Z. Xiang, M. Gao, C. Wang, M. Liu, J. Zhong, Advanced photocatalytic disinfection mechanisms and their challenges, Journal of Environmental Management 366 (2024) 121875. https://doi.org/10.1016/j.jenvman.2024.121875.

[236] T. Barkhade, K. Nigam, G. Ravi, S. Rawat, S.K. Nema, Plasma Sterilization for Bacterial Inactivation: Studies on Probable Mechanisms and Biochemical Actions, Plasma Chem Plasma Process 44 (2024) 429–454. https://doi.org/10.1007/s11090-023-10429-5.

[237] B. Božić Cvijan, J. Korać Jačić, M. Bajčetić, The Impact of Copper Ions on the Activity of Antibiotic Drugs, Molecules 28 (2023) 5133. https://doi.org/10.3390/molecules28135133.

[238] I. Salah, I.P. Parkin, E. Allan, Copper as an antimicrobial agent: recent advances, RSC Adv. 11 (2021) 18179–18186. https://doi.org/10.1039/D1RA02149D.

[239] I. Laurén, A. Farzan, A. Teotia, N.C. Lindfors, J. Seppälä, Direct ink writing of biocompatible chitosan/non-isocyanate polyurethane/cellulose nanofiber hydrogels for wound-healing applications, International Journal of Biological Macromolecules 259 (2024) 129321. https://doi.org/10.1016/j.ijbiomac.2024.129321.

[240] S. Borandeh, I. Laurén, A. Teotia, J. Niskanen, J. Seppälä, Dual functional quaternary chitosans with thermoresponsive behavior: structure–activity relationships in antibacterial activity and biocompatibility, J. Mater. Chem. B 11 (2023) 11300–11309. https://doi.org/10.1039/D3TB02066E.

[241] F. Ge, T. Wan, L. Kong, B. Xu, M. Sun, B. Wang, S. Liang, H. Wang, X. Zhao, Non-isocyanate polyurethane-co-polyglycolic acid electrospun nanofiber membrane wound dressing with high biocompatibility, hemostasis, and prevention of chronic wound formation, Heliyon 10 (2024) e33693. https://doi.org/10.1016/j.heliyon.2024.e33693.

[242] H.T. Bui, O.H. Chung, J. Dela Cruz, J.S. Park, Fabrication and characterization of electrospun curcumin-loaded polycaprolactone-polyethylene glycol nanofibers for enhanced wound healing, Macromol. Res. 22 (2014) 1288–1296. https://doi.org/10.1007/s13233-014-2179-6.

[243] A. Kumari, N. Raina, A. Wahi, K.W. Goh, P. Sharma, R. Nagpal, A. Jain, L.C. Ming, M. Gupta, Wound-Healing Effects of Curcumin and Its Nanoformulations: A Comprehensive Review, Pharmaceutics 14 (2022) 2288. https://doi.org/10.3390/pharmaceutics14112288.

[244] Z. Fu, J. Zou, J. Zhong, J. Zhan, L. Zhang, X. Xie, L. Zhang, W. Li, R. He, Curcumin-Loaded Nanocomposite Hydrogel Dressings for Promoting Infected Wound Healing and Tissue Regeneration, International Journal of Nanomedicine 19 (2024) 10479–10496. https://doi.org/10.2147/IJN.S479330.

[245] E.K.W. Tam, N.X. Chong, P.S. Choong, B. Sana, A.M. Seayad, S. Jana, J. Seayad, Phosphate functionalized nonisocyanate polyurethanes with bio-origin, water solubility and biodegradability, Green Chem. 26 (2024) 1007–1019. https://doi.org/10.1039/D3GC03379A.

[246] A. Zaborin, J.R. Defazio, M. Kade, B.L.D. Kaiser, N. Belogortseva, D.G. Camp, R.D. Smith, J.N. Adkins, S.M. Kim, A. Alverdy, D. Goldfeld, M.A. Firestone, J.H. Collier, B. Jabri, M. Tirrell, O. Zaborina, J.C. Alverdy, Phosphate-Containing Polyethylene Glycol Polymers Prevent Lethal Sepsis by Multidrug-Resistant Pathogens, Antimicrob Agents Chemother 58 (2014) 966–977. https://doi.org/10.1128/AAC.02183-13.

[247] S. Hiranphinyophat, Y. Iwasaki, Controlled biointerfaces with biomimetic phosphorus-containing polymers, Science and Technology of Advanced Materials 22 (2021) 301–316. https://doi.org/10.1080/14686996.2021.1908095.
[248] S. Monge, B. Canniccioni, A. Graillot, J.-J. Robin, Phosphorus-Containing Polymers: A Great Opportunity for the Biomedical Field, Biomacromolecules 12 (2011) 1973–1982. https://doi.org/10.1021/bm2004803.
[249] M. Cloutier, D. Mantovani, F. Rosei, Antibacterial Coatings: Challenges, Perspectives, and Opportunities, Trends in Biotechnology 33 (2015) 637–652. https://doi.org/10.1016/j.tibtech.2015.09.002.
[250] Z. Karami, K. Kabiri, M.J. Zohuriaan-Mehr, Non-isocyanate polyurethane thermoset based on a bio-resourced star-shaped epoxy macromonomer in comparison with a cyclocarbonate fossil-based epoxy resin: A preliminary study on thermo-mechanical and antibacterial properties, Journal of CO2 Utilization 34 (2019) 558–567. https://doi.org/10.1016/j.jcou.2019.08.009.
[251] L.A.T.W. Asri, M. Crismaru, S. Roest, Y. Chen, O. Ivashenko, P. Rudolf, J.C. Tiller, H.C. Van Der Mei, T.J.A. Loontjens, H.J. Busscher, A Shape-Adaptive, Antibacterial-Coating of Immobilized Quaternary-Ammonium Compounds Tethered on Hyperbranched Polyurea and its Mechanism of Action, Adv. Funct. Mater. 24 (2014) 346–355. https://doi.org/10.1002/adfm.201301686.
[252] E.-R. Kenawy, S.D. Worley, R. Broughton, The Chemistry and Applications of Antimicrobial Polymers: A State-of-the-Art Review, Biomacromolecules 8 (2007) 1359–1384. https://doi.org/10.1021/bm061150q.
[253] S. Shahi, M.J. Zohuriaan-Mehr, H. Omidian, Antibacterial superabsorbing hydrogels with high saline-swelling properties without gel blockage: Toward ideal superabsorbents for hygienic applications, Journal of Bioactive and Compatible Polymers 32 (2017) 128–145. https://doi.org/10.1177/0883911516658782.
[254] Z. Wang, X. Zhang, R. Wang, H. Kang, B. Qiao, J. Ma, L. Zhang, H. Wang, Synthesis and Characterization of Novel Soybean-Oil-Based Elastomers with Favorable Processability and Tunable Properties, Macromolecules 45 (2012) 9010–9019. https://doi.org/10.1021/ma301938a.
[255] M. Weber, H. Steinle, S. Golombek, L. Hann, C. Schlensak, H.P. Wendel, M. Avci-Adali, Blood-Contacting Biomaterials: In Vitro Evaluation of the Hemocompatibility, Front. Bioeng. Biotechnol. 6 (2018) 99. https://doi.org/10.3389/fbioe.2018.00099.
[256] C.A. Siedlecki, Hemocompatibility of Biomaterials for Clinical Applications: Blood-Biomaterials Interactions, Elsevier, 2018. https://doi.org/10.1016/C2014-0-04140-8.
[257] P. Li, R. Yin, J. Cheng, J. Lin, Bacterial Biofilm Formation on Biomaterials and Approaches to Its Treatment and Prevention, Int. J. Mol. Sci. 24 (2023) 11680. https://doi.org/10.3390/ijms241411680.
[258] D.A. Fitzmaurice, ABC of antithrombotic therapy: Bleeding risks of antithrombotic therapy, BMJ 325 (2002) 828–831. https://doi.org/10.1136/bmj.325.7368.828.
[259] N.C. Andrews, Iron Metabolism: Iron Deficiency and Iron Overload, Annu. Rev. Genom. Hum. Genet. 1 (2000) 75–98. https://doi.org/10.1146/annurev.genom.1.1.75.
[260] C. Gretzer, K. Gisselfält, E. Liljensten, L. Rydén, P. Thomsen, Adhesion, apoptosis and cytokine release of human mononuclear cells cultured on degradable

poly(urethane urea), polystyrene and titanium in vitro, Biomaterials 24 (2003) 2843–2852. https://doi.org/10.1016/S0142-9612(03)00097-8.

[261] ISO 10993-4:2017 - Biological evaluation of medical devices - Part 4: Selection of tests for interaction with blood, (2017).

[262] A. Timmis, P. Vardas, N. Townsend, A. Torbica, H. Katus, D. De Smedt, C.P. Gale, A.P. Maggioni, S.E. Petersen, R. Huculeci, D. Kazakiewicz, V. De Benito Rubio, B. Ignatiuk, Z. Raisi-Estabragh, A. Pawlak, E. Karagiannidis, R. Treskes, D. Gaita, J.F. Beltrame, A. McConnachie, I. Bardinet, I. Graham, M. Flather, P. Elliott, E.A. Mossialos, F. Weidinger, S. Achenbach, European Society of Cardiology, L. Mimoza, G. Artan, D. Aurel, M. Chettibi, N. Hammoudi, K. Vardanyan, S. Pepoyan, H. Sisakian, D. Scherr, P. Siostrzonek, B. Metzer, I. Mustafayev, T. Jahangirov, Y. Rustamova, N. Mitkovskaya, N. Shibeka, V. Stelmashok, M. De Pauw, P. Lancellotti, M. Claeys, Z. Kušljugić, A. Džubur, E. Smajić, M. Tokmakova, V. Traykov, D. Milicic, M. Pasalic, S. Pavasovic, T. Christodoulides, I. Papasavvas, C. Eftychiou, A. Linhart, M. Táborský, M. Hutyra, J.T. Sørensen, M.J. Andersen, S.D. Kristensen, M. Abdelhamid, K. Shokry, P. Kampus, M. Laine, M. Niemelä, B. Iung, A. Cohen, C. Leclercq, D. Trapaidze, K. Etsadashvili, A. Aladashvili, K. Bestehorn, S. Baldus, A.M. Zeiher, J. Kanakakis, A. Patrianakos, C. Chrysohoou, Z. Csanádi, D. Becker, Z. Járai, Þ.J. Hrafnkelsdóttir, V. Maher, J. Crowley, B. Dalton, A. Wolak, E.B. Assa, B. Zafrir, A. Murrone, C. Spaccarotella, S. Urbinati, B. Salim, S. Orazbek, A. Ayan, G. Bajraktari, D.A. Poniku, M. Erkin, A. Saamay, K. Kurban, A. Erglis, S. Jegere, I. Bajare, M. Mohammed, A. Sarkis, G. Saadeh, R. Šlapikas, T. Lapinskas, J. Čelutkienė, K. Ellafi, F. El Ghamari, J. Beissel, C. Banu, T. Felice, R. Xuereb, M. Popovici, D. Lisii, V. Rudi, A. Boskovic, M. Rabrenovic, S. Ztot, S. Abir-Khalil, J.G. Meeder, A.C. Van Rossum, M. Elsendoorn, J. Kostov, E.S. Kostovska, S. Kedev, K. Angel, O.C. Mjølstad, Ø. Bleie, M. Gierlotka, R. Dąbrowski, P. Jankowski, S.B. Baptista, J. Ferreira, V. Gil, E. Badila, D. Gaita, B.A. Popescu, E. Shlyakhto, N. Zvartau, E. Kotova, M. Foscoli, M. Zavatta, S. Stojkovic, M. Tesic, S. Juricic, G. Kaliská, R. Hatala, P. Hlivák, Z. Fras, M. Bunc, A. Pernat, Á. Cequier, M. Anguita, J. Muñiz, B. Johansson, P. Platonov, D. Carballo, M. Rüdiger-Stürchler, F.C. Tanner, H.E. Shebli, S. Kabbani, L. Abid, A. Faouzi, S. Abdessalem, V. Aytekin, I. Atar, V. Kovalenko, E. Nesukay, A. Archbold, U. Tayal, C. Wilkinson, R. Kurbanov, K. Fozilov, M. Mirmaksudov, D. Boateng, G. Daval, G. Momotyuk, D. Sebastiao, European Society of Cardiology: cardiovascular disease statistics 2021, European Heart Journal 43 (2022) 716–799. https://doi.org/10.1093/eurheartj/ehab892.

[263] L.J. Davidson, C.J. Davidson, Transcatheter Treatment of Valvular Heart Disease: A Review, JAMA 325 (2021) 2480. https://doi.org/10.1001/jama.2021.2133.

[264] O.M.J.A. Stassen, D.E.P. Muylaert, C.V.C. Bouten, J. Hjortnaes, Current Challenges in Translating Tissue-Engineered Heart Valves, Curr Treat Options Cardio Med 19 (2017) 71. https://doi.org/10.1007/s11936-017-0566-y.

[265] M.A. Rezvova, K.Y. Klyshnikov, A.A. Gritskevich, E.A. Ovcharenko, Polymeric Heart Valves Will Displace Mechanical and Tissue Heart Valves: A New Era for the Medical Devices, IJMS 24 (2023) 3963. https://doi.org/10.3390/ijms24043963.

[266] K. Navas-Gómez, M.F. Valero, Why Polyurethanes Have Been Used in the Manufacture and Design of Cardiovascular Devices: A Systematic Review, Materials 13 (2020) 3250. https://doi.org/10.3390/ma13153250.

[267] T.G. Mackay, G.M. Bernacca, A.C. Fisher, C.S. Hindle, D.J. Wheatley, In Vitro Function and Durability Assessment of a Novel Polyurethane Heart Valve Prosthesis, Artificial Organs 20 (1996) 1017–1025. https://doi.org/10.1111/j.1525-1594.1996.tb04589.x.

[268] G.M. Bernacca, T.G. Mackay, R. Wilkinson, D.J. Wheatley, Calcification and fatigue failure in a polyurethane heart valve, Biomaterials 16 (1995) 279–285. https://doi.org/10.1016/0142-9612(95)93255-C.

[269] G.M. Bernacca, B. O'Connor, D.F. Williams, D.J. Wheatley, Hydrodynamic function of polyurethane prosthetic heart valves: influences of Young's modulus and leaflet thickness, Biomaterials 23 (2002) 45–50. https://doi.org/10.1016/S0142-9612(01)00077-1.

[270] S.K. Singh, M. Kachel, E. Castillero, Y. Xue, D. Kalfa, G. Ferrari, I. George, Polymeric prosthetic heart valves: A review of current technologies and future directions, Front. Cardiovasc. Med. 10 (2023) 1137827. https://doi.org/10.3389/fcvm.2023.1137827.

[271] S.H. Daebritz, J.S. Sachweh, B. Hermanns, B. Fausten, A. Franke, J. Groetzner, B. Klosterhalfen, B.J. Messmer, Introduction of a Flexible Polymeric Heart Valve Prosthesis With Special Design for Mitral Position, Circulation 108 (2003). https://doi.org/10.1161/01.cir.0000087655.41288.dc.

[272] A. Cavallo, E. Gasparotti, P. Losi, I. Foffa, T. Al Kayal, E. Vignali, S. Celi, G. Soldani, Fabrication and in-vitro characterization of a polymeric aortic valve for minimally invasive valve replacement, Journal of the Mechanical Behavior of Biomedical Materials 115 (2021) 104294. https://doi.org/10.1016/j.jmbbm.2020.104294.

[273] A.G. Kidane, G. Burriesci, M. Edirisinghe, H. Ghanbari, P. Bonhoeffer, A.M. Seifalian, A novel nanocomposite polymer for development of synthetic heart valve leaflets, Acta Biomaterialia 5 (2009) 2409–2417. https://doi.org/10.1016/j.actbio.2009.02.025.

[274] B. Rahmani, S. Tzamtzis, R. Sheridan, M.J. Mullen, J. Yap, A.M. Seifalian, G. Burriesci, In Vitro Hydrodynamic Assessment of a New Transcatheter Heart Valve Concept (the TRISKELE), J. of Cardiovasc. Trans. Res. 10 (2017) 104–115. https://doi.org/10.1007/s12265-016-9722-0.