



Combination of polylactide with cellulose for biomedical applications: a recent overview

Aneta Kopańska · Marek Brzeziński ·
Zbigniew Draczyński

Received: 8 December 2022 / Accepted: 14 November 2023 / Published online: 9 December 2023
© The Author(s) 2023

Abstract This review summarizes the use of cellulose and polylactide for medical applications with particular emphasis on modern dressings. Although classic cotton and viscose dressings are still available and popular, the usefulness of new forms of cellulose (Cel) and its derivatives opens new wound treatment options. Therefore, trends in functionalizing traditional cellulose dressings, including products made of bacterial cellulose, and dressings from cellulose derivatives, are discussed. Polylactide (PLA), in turn, is a biodegradable and biocompatible polyester that fulfills plenty of tasks in many medical fields, from surgery to modern diagnostic methods. However, polylactide dressings can still be advantageous to the market. Thus, the next part of the article contains a recent update of available knowledge about PLA and its applications in regenerative medicine and drug-delivery systems. The last part is devoted to the possibilities of combining both materials in dressings and related problems and benefits. Methods for compatibilization with the surface of both polymers and new

techniques for producing Cel/PLA composite materials are also described.

Keywords Smart dressings · Regenerative medicine · Polylactide · Cellulose

Abbreviations

BA	Butyl acrylate
BC	Bacterial cellulose
CA	Cellulose acetate
CAB	Cellulose acetate butyrate
CA-g-PLA	Cellulose Acetate-grafted-Poly(L-lactic Acid)
CAP	Cellulose acetate phthalate
CAT	Cellulose acetate trimellitate
CDA	Cellulose diacetate
CDDA	Dimethyl dodecyl [3-(trimethoxysilyl) propyl] ammonium chloride
Cel	Cellulose
Chol	Cholesterol
CMC	Carboxymethyl cellulose
CNCs	Cellulose nanocrystals
CNFs	Cellulose nanofibrils
COX	Cellulose oxalate
DNA	Deoxyribonucleic acid
E100-PLGA	Methacrylic acid copolymer (Eudragit 100)-poly(D,L-lactide-co-glycolide)

A. Kopańska (✉) · Z. Draczyński
Institute of Material Science of Textiles and Polymer Composites, Lodz University of Technology, Żeromskiego 116, 90-924 Lodz, Poland
e-mail: aneta.kopanska@dokt.p.lodz.pl

M. Brzeziński
Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Sienkiewicza 112, 90-363 Lodz, Poland

EC	Ethylcellulose	PLA- <i>b</i> -PEG	Poly(lactic acid)-block-poly(ethylene glycol)
Gal-PEG-PLA	Galactosamine-modified poly(ethylene glycol)-poly(lactide)	PLA-g-CNFs	Poly(lactic acid) grafted cellulose nanofibers
HEC	Hydroxyethylcellulose	PLA-HPG	Poly(lactic acid)-hyperbranched polyglycerol
HEMC	Hydroxyethylmethylcellulose	PLA-PEG-ACUPA/TPP	Poly(lactide)-poly(ethylene glycol)-2-(3-((S)-5-amino-1-carboxypentyl)-ureido) pentanedioate/triphenylphosphonium
HFBMA	2,2,3,4,4,4-Hexafluorobutyl methacrylate	PLGA	Poly(D,L-lactide-co-glycolide)
HPC	Hydroxypropyl cellulose	PLL	ϵ -Poly-L-lysine
HPC	Hydroxypropylcellulose	PLLA	Poly-L-lactic acid
HPMC	Hydroxypropyl methylcellulose	PLLA-g-CNCs	Poly(lactic acid) grafted cellulose nanocrystals
HPMC	Hydroxypropylmethylcellulose	PMAA	Poly(methacrylic acid)
HPMCAS	Hydroxypropyl methylcellulose acetate succinate	PTFE	Polyfluortetraethylene
HPMCP	Hydroxypropylmethylcellulose phthalate	PTMC	Polytrimethylene carbonate
MA-g-PLA	Maleic anhydride grafted PLA	PVA	Poly(vinyl alcohol)
MC	Methylcellulose	Quat 188	3-Chloro-2-hydroxypropyl trimethyl ammonium chloride
MC	Methylcellulose	RNA	Ribonucleic acid
MCC	Microcrystalline cellulose	SA	Sodium alginate
MFC	Microfibrillated cellulose	Span 60	Sorbitan monostearate
mPEG- <i>b</i> -PLA	Methoxypoly(ethylene glycol)-block-poly(DL-lactic acid)	TCP/PLLA	β -Tricalcium phosphate/poly(L-lactic acid)
NaCMC	Sodium carboxymethylcellulose	TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
OC	Oxidized cellulose	TMC	Trimethylene carbonate
OLA	Oligo(lactic acid)	TPGS	E-tocopheryl poly(ethylene glycol) succinate
pAC	Plasticized cellulose acetate	TPU	Thermoplastic polyurethane
PAE	Polyacrylic ester		
PAMAM G4.5	Polyamidoamine dendrimers, generation 4.5		
PCL	Poly(ϵ -caprolactone)		
PDLA	Poly-D-lactic acid		
PDLAG	Poly (D-lactic acid-co-glucose) copolymer		
PDLLA	Poly-D,L-lactic acid		
PEG	Poly(ethylene glycol)		
PEG-PLA	Poly(ethylene glycol)-poly(lactide)		
PHA	Poly(3-hydroxyalkanoate)		
PHEMA	Poly(2-hydroxyethylmethacrylate)		
PLA	Poly(lactide)		

Introduction

Cellulose dressings as a form of wound treatment are present in medical practice since antiquity. Ancient literature presents dressings as one of the stages of wound care (Nicoli Aldini et al. 2008). Textiles made of natural vegetable fibers, such as linen bandages, often soaked with therapeutic and antibacterial substances, were already used in ancient Egypt (Sipos

et al. 2004; Thomas and Uzun 2019; Wilkins 1964). In the twentieth century, the development of plastics industry resulted in the introduction of synthetic fibers, in parallel with an increase of the wound-treating materials available, from classic woven, knitted and nonwoven dressings up to modern foams (Fogh and Nielsen 2015; Salisbury et al. 2022), hydrogels (Francesco et al. 2018; Shu et al. 2021; Wu et al. 2023; Zhang et al. 2019), hydrocolloids (Stoica et al. 2020b; Thomas 2008) and thin membranes (Graça et al. 2021). Composite dressings combine multiple functions in one product and their form varies depending on the raw materials used and the expected functionality (Gupta and Edwards 2019).

This work focuses on analyzing materials for modern products supporting regenerative medicine composed of cellulose and polylactide. It contains present-day state of knowledge about these two polymers and their combination for medical applications, however, with strong emphasis on wound dressings. It may also help with establishing whether polylactide/cellulose (PLA/Cel) systems have some unique advantages over these polymers acting alone. To understand their mutual interactions, many points are discussed, including structural, functional, and engineering issues. One of the biggest problems related to combining PLA and cellulose is their different affinity to water. Polylactide is hydrophobic and cellulose is hydrophilic, so the goal is to modify them in such way that will enhance interphase PLA/Cel interactions and improve mechanical properties of their composites.

Cellulose is the most classic and well-known natural polymer. From the earliest beginnings of wound healing, it has been present as a part of medical equipment and until this day it has not lost its great significance in the scientific world. As one can see, the versatility of cellulose applications has strongly increased with the material and chemical engineering development, although classical cotton fabrics are not forgotten in medicine and hospital environment (Graça et al. 2021). The aim of developing new solutions leads from the activation of medical products, which were previously passive like cotton gauzes and bandages (Graça et al. 2021; Lumbreras-Aguayo et al. 2019b), constructing cotton-reinforced modern forms of dressings (Lumbreras-Aguayo et al. 2019b), to pure nanoscale cellulose and its derivatives as healing materials (Alavi and Nokhodchi 2020; Cidreira et al.

2021; Liu et al. 2020). In addition, bacterial cellulose has also been considered as a smart material with some advantages over plant-based cellulose (Portela et al. 2019; Rathinamoorthy 2022).

In the face of a long history of cellulosic dressings, polylactide occurs as a quite new product, however, it has been known for years. Polylactide (PLA) is a biodegradable and biocompatible polymer (Basu et al. 2016; Gupta and Kumar 2007; Michalski et al. 2019) and is recognized as safe by the U.S. Food and Drug Administration. Therefore, PLA has attracted considerable attention as a candidate capable of replacing petroleum-based polymers due to its good processing and mechanical properties (Raquez et al. 2013). PLA is proposed for various applications in industrial, pharmaceutical, and environmental fields. Among these multiple fields of PLA utilization, biomedical usage is one of the most frequently proposed for PLA-based materials (Sinha Ray 2012).

It seems that both cellulose and polylactide as materials for medical applications can now have similar functionalities. However, traditional cellulose dressings still have a strong market position, also for economic reasons. Enriching them with a polylactide in active form, for example as a medium for drugs, could be a relatively cheap and effective way to modernize them and at the same time to meet the specific needs of patients. This can be the simplest way to launch PLA on the market, as the use of dressings in everyday life does not require medical consultation but they need to be affordable and easy to apply. The combination of both polymers in one material (for example via grafting or polymerization) may provide a possibility for new modifications, considering their different physical and chemical properties, the capability to perform different chemical reactions with other compounds, as well as the ability to degrade with all the consequences. Finally, it is worth examining whether the characteristics of the PLA/Cel systems are a simple sum of the features of their components or, on the contrary, the ingredients complement each other, presenting an improved quality, not available when they perform separately.

The structure and properties of cellulose

The main building block of a cotton fiber is cellulose, whose quality and structure determine its most

important properties. Cotton has the highest content of cellulose from all-natural sources, reaching up to 96% dry matter (Segal and Wakelyn 1985), followed by sisal and pineapple leaf fibers (Gas-san et al. 2001). Cellulose, a polysaccharide with a summary formula $(C_6H_{10}O_5)_n$, is a large molecular structure polymer resulting from a natural polycondensation. The cellulose macromolecule chain is made of β -D-glucopyranosyl units connected with 1,4- β -glycosidic bonds. The repeated unit is the glucose residue (French 2017). The non-reducing end of a cellulose chain is composed of a hydroxyl group, whereas the reducing end is a hemiacetal. The presence of hydroxyl groups in the molecule determines the reactivity of cellulose, although these groups, due to the location in the spatial structure, are not just as reactive. The most reactive group is the one located at C2, then with C6 carbon. Hydroxyl groups, as they are characterized by polarity, form hydrogen bonds between macromolecules, which in turn causes stiffening of the chain and the formation of strongly ordered spatial structures—the so-called crystalline phase in fiber.

To describe the properties of the cellulose polymer, specify such features as:

- average polymerization degree;
- average degree of crystallinity;
- construction of the elementary cell in the crystalline phase.

High dispersity of molar mass is a typical feature of cellulose isolated from natural sources. Native cellulose consists of macromolecules with different polymerization degrees, while the average polymerization degree is different for cellulose materials of different origins (e.g., for cotton cellulose and cellulose from wood). Similar diversity can be observed in the degree of crystallinity. Various sources give the following value: according to Urbańczyk (1985), the degree of crystallinity in cellulose derived from plant fibers reaches 60–80%; according to "Handbook of Polymers", it is 75% for cotton (which is the cleanest source of cellulose I), while according to "Comprehensive Cellulose Chemistry" it is about 60%, with this applying to cotton fibers undergoing initial physicochemical treatment (Klemm et al. 1998). However, as in the case of all cellulosic materials, crystallinity values have considerable dependence on the

exact methods, even just considering X-ray diffraction (French 2020).

A crystal's unit cell is the smallest unit of the crystal that can be used figuratively to construct the structure of the crystal by simple repetition of the unit cell along the X, Y, and Z axes of the crystal. The six basic parameters are in the XYZ axis system of the lattice, (a, b, c)—the distances at which the cell elements are repeated, and the angles between the axes (α , β , γ). However, the Miller indicators (h, k, l) define crystallographic planes that result in the various peaks of photon intensity on a diffraction pattern. These characteristics are different for every polymorph (French 2014). Chemical and physicochemical treatment has a significant impact on the form of an elementary cell, a crystallographic variety, as well as the content of crystalline material in fiber. An example would be the mercerization process, where under specific conditions native cellulose I is converted to cellulose II, whose parameters of the structure of the elementary cell of crystalline differ from the output material (Takahashi and Takenaka 1987). A different shape of the elementary cell carries, therefore, a change in physical and chemical parameters, such as changing the density of the material, differences in mechanical properties, as well as the ability to bind dyes. Other polymorphic forms of cellulose are cellulose III, which can be obtained as a result of ammonia swelling cellulose I or II, and cellulose IV, an effect of force and heat to other cellulose varieties (Klemm et al. 1998). The degree of cellulose crystallinity changes with the origin of the material and the processing it was subjected to, moreover, the properties of converted polymorphs depend on their parental structures (Wada et al. 2004). A different question is whether these conversions are reversible. Hindi (2016) lists seven interconvertible polymorphs of cellulose, namely, I_α , I_β , II, III_I, III_{II}, IV_I, and IV_{II} and states that celluloses III_I and III_{II} revert to their previous forms in a high temperature and humid environment. The reversion is possible also in the case of cellulose IV.

Bacterial cellulose

Although cellulose II is typically the result of mercerization with NaOH or dissolution and regeneration as in the viscose or NMMO processes for making rayon or lyocell, its natural sources are known. This material

Table 1 Parameters of bacterial cellulose, plant cellulose and PLA nanofibers. Details on PLA enantiomers have been already shown (Brzeziński and Biela 2014)

	Bacterial cellulose	Plant Cellulose	PLA (nanofibers)
Tensile strength (MPa)	20–300	25–200	50–192
Young's modulus (MPa)	130,000	2.5–0.170	1000–3900
Water holding capacity (%)	> 95	25–35	-
Size of fibers (nm)	20–100	micrometer scale	50–943
Crystallinity (%)	74–96	40–85	5–35
Degree of polymerization	14,000–16000	300–10000	1300–230000
Porosity (%)	> 85	< 75	< 92 (depends on electrospinning process)
Total surface area (m ² /g)	> 150	< 10	Corresponds to fiber diameter; e.g. 4,7 for 282 nm
References	Wang et al. (2019a, b)		Hrib et al. (2015), Inai et al. (2005), Maleki et al. (2022), Shen et al. (2018)

occurs in the sea algae from *Halicystis* species, under certain rare conditions. Mutant bacteria have also produced cellulose II. The bacterial cellulose in the form of cellulose II is most often produced by the strain of *Gluconacetobacter xylinus* (Dufresne 2017). However, the typical bacterial and algal cellulose is cellulose I, and more precisely I α (Picheth et al. 2017; Rusdi et al. 2022; Wada et al. 2001), whereas, as the research on *Acetobacter xylinum* ATCC23769 indicated, the crystallographic structure of cellulose (I or II) can be modified the culture conditions (Hirai et al. 1997). Other bacteria strains used for cellulose production are *Agrobacterium*, and *Sarcina*. The quality of bacterial cellulose can be diversified by controlling nutrient sources (meaning carbon sources) and culture conditions of bacteria strains (Abeer et al. 2014; Gullo et al. 2017). The influence of pH, temperature, and access to UV light was studied by Lazarini et al. (2018) on the *Gluconacetobacter hansenii*. The *G. hansenii* variants grown under different pH and UV conditions showed lower capacity to BC production when compared to original *G. hansenii* ATCC 23769 (Lazarini et al. 2018). In the review of bacterial cellulose for wound healing applications (Ahmed et al. 2020), BC in general is characterized by greater purity, the ability to absorb water, and porosity (Table 1). The authors discuss also mechanical properties of BC, and its Young's modulus and tensile strength which are comparable to aramid fibers, and indicate it as a reinforcement in composites. Moreover, BC is a promising medical material that does not require initial, time-consuming and expensive purification. Naomi et al. (2020) describes bacterial and

plant cellulose in detail. According to that work, the main BC differences compared to vegetable cellulose are:

1. Purity of the material (without the presence of hemicellulose, lignin, waxes, and other impurities).
2. Mechanical properties (Young's modulus, tensile strength) beneficial for tissue scaffolding structure, e.g. bone tissue (Torgbo and Sukyai 2018)
3. The higher degree of crystallinity (over 80%) (Revin et al. 2021).
4. High water absorption, but relatively low Water Vapor Transmission Rate.
5. No immune response, no inflammatory reaction after contact with live tissue.
6. Ease of shaping due to the high flexibility module.
7. Much higher porosity, as well as a larger size of pores.
8. Higher hydrophilicity.

However, these differences, especially mechanical properties and water absorption, depend on production medium composition, for example the concentration of sugar. As reported, BC from sago liquid waste showed a tensile strength of 44.2–87.3 MPa, Young's Modulus of 0.86–1.64 GPa and water holding capacity of 85.9–98.6 g g⁻¹. It could also be observed that the increased mechanical strength is linked to lower water holding capacity (Yanti et al. 2021). It is also worth mentioning that mechanical modifications influence BC properties as well as cultivation

methods (Betlej et al. 2021). As one can see, many factors affecting the final form of BC determine its versatility for various applications. Usefulness for therapeutic purposes and biocompatibility with human tissues, however, seems to be at a similar level as plant cellulose—the effectiveness of improving processes of regeneration, cell adhesion and hemostatic effects depend mainly on the modifications and the presence of additional medicinal compounds. Some authors, nevertheless, emphasize that its natural structure also closely mimics many biological tissue properties (e.g. collagen fibers of bone and skin tissue), it has an ability to regulate cell adhesion, and its antigen immobilization capability for biosensor applications (Abazari et al. 2021).

Currently, bacterial cellulose is used in various aspects of regenerative medicine, from wound treatment, through the use of drug delivery systems, to tissue reconstruction (Table 2). BC occurs in various forms, both on a micro and nanoscale—as membranes, fibers (and materials made of them, usually nonwoven), hydrogels and composites. A commercial example is Dermafill® (previously known as Biofill®) membrane dressing that acts as a temporary skin substitute (Castro et al. 1988), but there are more products on the market and even more solutions under research, proving usefulness of this material (Zhong 2020).

Natural cellulose materials and traditional dressings

Fibrous dressings, regardless of the type of fibers found in them (both natural and artificial/synthetic) are manufactured in the woven and non-woven form. Structures such as cotton wool were made use of relatively late (compared to the world history of wound dressings)—around 200 years ago. Cotton wool consisted of washed, loose and combed cotton fibers. Therefore, it was supposed to replace the traditional linen ripped strips or unraveled threads made of old clothing (Elliott 1957).

Although the last few dozen years have allowed for the development of advanced technologies of dressings supporting wound treatment, still the most typical and widely available cellulose dressing is gauze, bleached fabric, loosely woven with canvas weave. Initially, it was produced only from natural cotton fibers, but currently on the market there are also gauzes made of artificial cellulose fibers or cotton/

viscose mix. Gauze dressings only fulfill basic tasks, like protecting the wound against the external environment and absorbing exudate. Their properties are determined by the number of warp threads—the greater the number, the more the dressing absorbs. A sufficiently strong twist of yarn and other parameters of spinning are also important to prevent the dressing from being undesirably distributed when removing it from the wound. Gauze as a compress absorbs blood and bodily fluids. While in the form of a bandage, it is also used as a secondary dressing, holding and covering the primary (or, in other words, active) dressing, which has therapeutic properties and needs to be secured from moving and/or from external environment. An example of primary dressing that is combined with topical cover is non-adherent HELIX3-CM® Collagen Matrix, suitable for burns, sores, blisters, ulcers, and wounds. Simplicity and the relatively low cost of the production of the standard gauze, as well as the ease of adapting to the patient's specific needs, mean that its high popularity will probably last long.

An interesting attempt to enrich the functionality of gauze to a wide extent was presented by Said (2021). The designed gauze was first pre-modified by chitosan cationization or anionic carboxymethylation. Then, by successively applying hydroxyapatite, silver nanoparticles and ginger oil, it gained anti-inflammatory, antimicrobial and anti-UV properties. Another strategy was to modify the surface of the gauze by grafting the poly(Methacrylic Acid) (PMAA), which was followed by testing the implementation of ZnO nanoparticles to obtain the antibacterial and antimicrobial functions and by investigation of the drug releasing profile after loading it with nalidixic acid. Compared to an unmodified gauze, the antibacterial effect was the result of PMAA grafting itself. The results were due to bactericidal properties of acrylic acid polymers. The explanation is that acidic environment disturbs cytoplasmic homeostasis pH, while acid groups reduce bacterial adhesion. However, 100% inhibition effect for *S. epidermidis* bacteria was achieved only by adding ZnO (Lumbreras-Aguayo et al. 2019a). The process of hemostasis is to be supported by gauze with grafted carboxymethyl chitosan and covered with gelatin and alginate using the Layer-By-Layer method, a technique of fabrication of thin films made by depositing respectively oppositely-charged materials (Zheng et al. 2021). A relatively

Table 2 Areas of BC application in regenerative medicine

Application of BC in regenerative medicine	Action	Characteristics	Final use	References
Drug delivery	Anti-inflammatory	BC with diclofenac sodium	Hydrogel	Adepu and Khandelwal (2020)
		BC with ibuprofen	Membrane (transdermal delivery)	Ossowicz-rupniewska et al. (2021)
	Anticancer	BC with Cisplatin	Drug carrier	Lee et al. (2012)
		Antiseptic	BC with octenidine	Nonwoven wound dressing
	BC chemisorbed with antiseptic molecules: octenidine, polyhexanide, povidone-iodine, chlorhexidine, ethacridine lactate, and hypochlorous solutions,		Wound dressing for chronic wounds	Dydak et al. (2021)
	Antioxidant		BC with entrapped fireweed (<i>Epilobium angustifolium</i> (L.) extract	Membrane (transdermal delivery)
	Antimicrobial	Papain immobilized on pure BC and BC cross-linked with glutaraldehyde (BG)	Composite membrane dressing	Asanarong et al. (2021)
			BC with lignin derived dehydrogenative polymer of coniferyl alcohol (DHP))	Composite hydrogel
		In situ synthesis of silver nanoparticles simultaneously with the production of BC	Nanocomposite hydrogel	Fadakar Sarkandi et al. (2021)
		4,6-diamino-2-pyrimidinethiol (DAPT)-modified gold nanoparticles (Au-DAPT NPs)	Membrane dressing	Ying Li et al. (2017)
Tissue regeneration	Supporting moist environment	BC with glycerin as plasticizer with improved moisturising properties	Membrane	Almeida et al. (2014)
		BC crosslinked with citric acid along with catalysts, such as disodium phosphate, sodium bicarbonate, ammonium bicarbonate	Super-absorbent wound dressing	Ciecholewska-Juško et al. (2021)
	Improved biocompatibility	BC with vaccarin promoting the endothelial tissue proliferation	Membrane	Qiu et al. (2016)

Table 2 (continued)

Application of BC in regenerative medicine	Action	Characteristics	Final use	References
	Promoting cell proliferation and tissue regeneration	Collagen reinforcement	Composite scaffolds	Noh et al. (2019)
		BC with <i>b</i> -glucan, hydroxyapatite nanoparticles and graphene oxide	Scaffolds with antibacterial activity	Umar Aslam Khan et al. (2021)
		BC oxidized into dialdehyde bacterial cellulose (DBC) by regioselective oxidation, and then composited with collagen peptide (Col-p)	Composite membrane	Wen et al. (2015)
		Surface micropatterning of BC with low-energy CO ₂ laser lithography, and targeted immobilization of a tetrapeptide consisting of Arginine-Glycine-Aspartic acid-Serine (H-Arg-Gly-Asp-Ser-OH, RGDS)	Scar-free wound healing hydrogel	Hu et al. (2019)

simple way to improve functionality is to use cotton gauze, present on the market (classic and covered with anti-adhesive wax) to apply 2-deoxy-D-ribose (2dDR) which would support angiogenesis (Andleeb et al. 2020). In the case of a hydrophobic wax dressing, it was necessary to construct a carrier using paraffin, ethanol, and poly(ethylene glycol) (PEG) in various configurations or implement 2dDR in a partly diluted wax cover. Another way of modifying conventional cotton fabric was grafting L-cysteine (Cys) on the surface and then implementing copper nanoparticles in the presence of citric acid. Such material exhibited satisfactory activity against bacteria *S. aureus* and *E. coli* and excellent washing fastness (Qingbo Xu et al. 2018a, b).

In recent years, the greige cotton, which is unbleached cotton as a dressing material conducive to hemostatic processes in open wounds, has become the object of wider interest. In the work of Edwards et al. (2022), it occurred that highly cleaned and sterile unbleached cotton, due to its constituents, may produce hydrogen peroxide at a certain level. Moreover, it can be modulated with ascorbic acid by impregnation with classical pad-dry method, resulting in antimicrobial properties. It is beneficial from

the ecological and economic point of view to omit the cotton bleaching stage and avoid the use of chemicals necessary for this process (such as wetting agents, and whitening agents based on hydrogen peroxide or chlorine compounds). It is worth emphasizing that naturally occurring substances remain on the fibers—pectins, proteins, waxes, hemicellulose, fats, as well as vestigial amounts of inorganic compounds called ash. Leaving them on the fiber affects the hydrophobicity and polarity of the surface and creates an environment conducive to blood clotting. On the other hand, dressings consisting only of greige cotton may not absorb exudate sufficiently for exactly the same reasons (Vincent Edwards et al. 2020).

Apart from cotton, attempts are made to adapt other natural cellulose fibers to the needs of wound treatment. As in the case of greige cotton, cellulose material with a natural addition of specific substances supporting treatment is linen (*Linum L.*). Recent research shows that linen dressings have healing effects on wounds not only because of cellulose material and polymers naturally occurring with it (hemicellulose, lignin, pectin), but also because of the presence of potentially bioactive substances, such as vanillin, 4-hydroxybenzoic acid, ferulic acid,

coumaric acid, syringaldehyde, olyhydroxybutyrate/hydroxybutyrate, and polyamines. By examination on cellular line of mouse BALB/3T3 fibroblasts and normal human dermal fibroblast (NHDF), and normal human epidermal keratinocytes (NHEK) line, human dermal microvascular endothelial (HMVEC) cell line, epidermal carcinoma cancer A431, and monocyte THP-1 cell line, it has been shown that genetically modified linen fibers, differing from unmodified fibers with increased content of the above-mentioned compounds, accelerated the proliferative activity of damaged tissues (Gębarowski et al. 2020).

Cellulose derivatives for dressings

The presence of hydroxyl groups in cellulose macromolecules results in high reactivity of the polymer and great possibilities for modification for medical purposes. Typical reactions with OH groups are etherification, esterification, acetalization, and oxidation. Some of the obtained derivatives (especially esters and ethers) are well known and have been produced commercially for a long time (Klemm et al. 1999).

In an overview of cellulose and its derivatives for wound healing, Tudoroiu mentions: cellulose esters, cellulose acetate (CA), cellulose acetate butyrate (CAB), cellulose acetate phthalate (CAP), cellulose acetate trimelitate (CAT), hydroxypropylmethylcellulose phthalate (HPMCP), and hydroxypropyl methylcellulose acetate succinate (HPMCAS). Among ethers, there are sodium carboxymethylcellulose (NaCMC), hydroxypropylmethylcellulose (HPMC), methylcellulose (MC), hydroxyethylcellulose (HEC), ethylcellulose (EC), hydroxypropylcellulose (HPC), hydroxyethylmethylcellulose (HEMC), and benzylcellulose. They appear also in combinations of two or more and usually contain active pharmaceutical ingredients (Tudoroiu et al. 2021). Usually, most reports also mention bacterial cellulose, although its production is significantly different.

Cellulose derivatives due to their specific properties influencing the easy forming of various forms of dressing and healing process (alone or with other components) are versatile and flexible materials. The main advantage over pure cellulose is improved solubility in water with some exception of, for example, ethylcellulose or cellulose acetate. Moreover, the properties of cellulose-based nanoparticles can

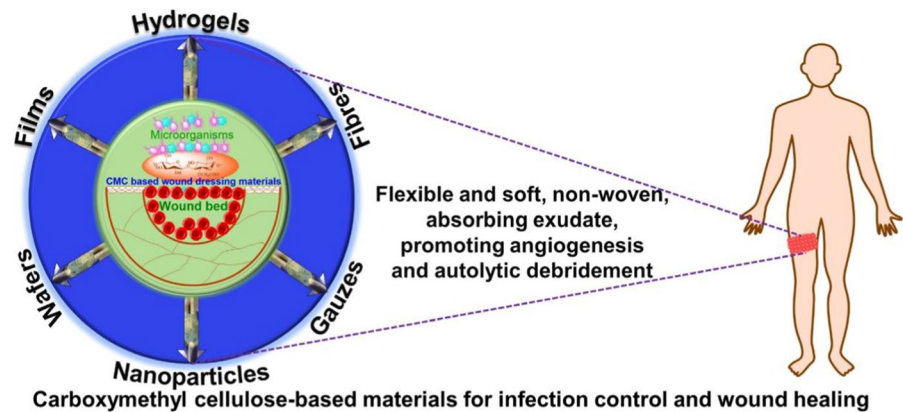
prolong circulation of drug carriers in organism by increasing drug solubility and stability and thus enhance their bioavailability, or perform as biosensors and as a tool of targeted therapy thanks to easy customization for specific tasks (Hosny et al. 2022). Biosensors based on oxidized or carboxylated cellulose nanomaterials promote amide linkage between amide groups of proteins and nucleic acids, and carboxyl groups grafted onto cellulose molecules which increases their resistance to external environment (Teodoro et al. 2021). As biosensors, they might be useful for detection of such bio-molecules as urea, lactate, glucose, genes, amino acids, cholesterol, and proteins (Kamel and Khattab 2020). Cellulose derivatives, in particular carboxymethyl cellulose (CMC), cellulose acetate and bacterial cellulose were also discussed from a clinical point of view. Some advantages are as follows:

1. cellulose acetate—excellent scaffolding biomaterial for implementation of drugs and other compounds with anti-microbial, antioxidant, anti-inflammatory, and antiviral activity
2. carboxymethyl cellulose—the ability to construct hydrogels in the presence of metallic ions,
3. bacterial cellulose – highly effective surface area, and a hydrophilic nature that gives it a high liquid loading capacity, ability to drug carrying, good mechanical properties and breathability (Abazari et al. 2021)

In recent years, (CMC)-based wound dressing materials have been strongly discussed due to their biocompatibility, biodegradability, low cost, and other properties such as tissue resembling and non-toxicity (Kanikireddy et al. 2020). Various forms and practical use of dressings are possible (Fig. 1).

Some CMC dressings are already present on the market, such as Aquacel®, which was proven to encapsulate potentially pathogenic bacteria in its gel structure when it covers the wound (Walker et al. 2003). The basic Aquacel® is composed only of sodium carboxymethylcellulose spun into fibers and then shaped into dressing form. Put into the wound, it absorbs exudation inside of the fibers, keeping it away from the tissue. At the same time, it changes the structure to the gel and maintains the moist wound environment for optimal healing (Williams 1999). Attempts were made to use cotton cellulose

Fig. 1 CMC-based dressings. Reprinted from (Kani-kireddy et al. 2020) with permission from Elsevier



from waste remaining after production processes to produce CMC and create hydrogel wound dressing. Recovered cotton fibers were cut and pretreated with 20% sodium hydroxide solution to remove impurities, and then bleached in 6% solution of sodium hypochlorite. In the next step, CMC was synthesized by the etherification with various amounts of sodium monochloroacetate (SMCA). Hydrogel was obtained through the cross-linking reaction in the presence of epichlorohydrin (ECH). Different combinations of cellulose and CMC were used to achieve desired results- suitable exudate absorption, wound dehydration, and tissue regeneration environment (Jirawitch-alert et al. 2022).

Hydroxypropyl cellulose (HPC) was a matrix for nanocomposite films enriched with graphene oxide (GO) grafted silver-coated zinc oxide nanoparticles (Ag/ZnO) (Fig. 2). These so-called AGO nanofillers positively influenced mechanical strength, UV resistance, and antibacterial performance (Wang et al. 2019a, b). Another solution for antibacterial properties was Polyhexamethylene guanidine hydrochloride (PHMG) grafted to cellulose diacetate (CDA) wound dressing surface through an amide reaction. The dressing had a nanofibrous structure made by electrospinning, which additionally enhanced hydrophilicity. Such prepared materials were tested for water absorption, and absorbing capacity (or, in different words, water holding capacity). In the first case, the weight of samples soaked with saline solution for 10 s was compared to the weight of lyophilized ones. Secondly, the weight of samples previously immersed in saline overnight was measured to determine water retention over a certain period of time. Results showed that increasing amount of PHMG has

significantly influenced all those parameters (Xiao et al. 2022). Cellulose diacetate wound dressing also supports hemostasis and counteracts excessive blood loss (Liang et al. 2021).

Hydroxypropyl methylcellulose (HPMC) combined with collagen enriched with povidone-iodine and formed into scaffolds effectively facilitated the proliferation of fibroblast cells with no toxic effects (Kesavan et al. 2022). A combination of ethylcellulose/hydroxypropyl methylcellulose nanofibers was loaded with aloe vera extract and formed into a wound healing dressing mat, which exhibited enhanced cell proliferation, adhesion, and antibacterial activity (Mohebian et al. 2022).

Poly lactide

In this part of the review, the focus will be on the application of PLA-based materials for regenerative medicine and drug delivery systems. Since there are numerous reviews about PLA-based materials in drug delivery, describing PLA safety (Pawar et al. 2014; Ramot et al. 2016) and biomedical applications of its copolymers (Bawa and Oh 2017; Jain et al. 2016; Oh 2011), stereocomplexes (Bertin 2012; Brzeziński and Biela 2015; Tsuji 2016), hydrogels (Basu et al. 2016), and nanoparticles (NPs) (Casalini et al. 2019; Kumari et al. 2010; Tyler et al. 2016). Moreover, the clinical applications of PLA were also summarized (DeStefano et al. 2020). There are also some examples of PLA-based NPs under clinical trials (Niza et al. 2021; Prabhu et al. 2015), for instance, Genexol-PM or BIND-014®. Therefore, this part presents only recent achievements in this field which were published last

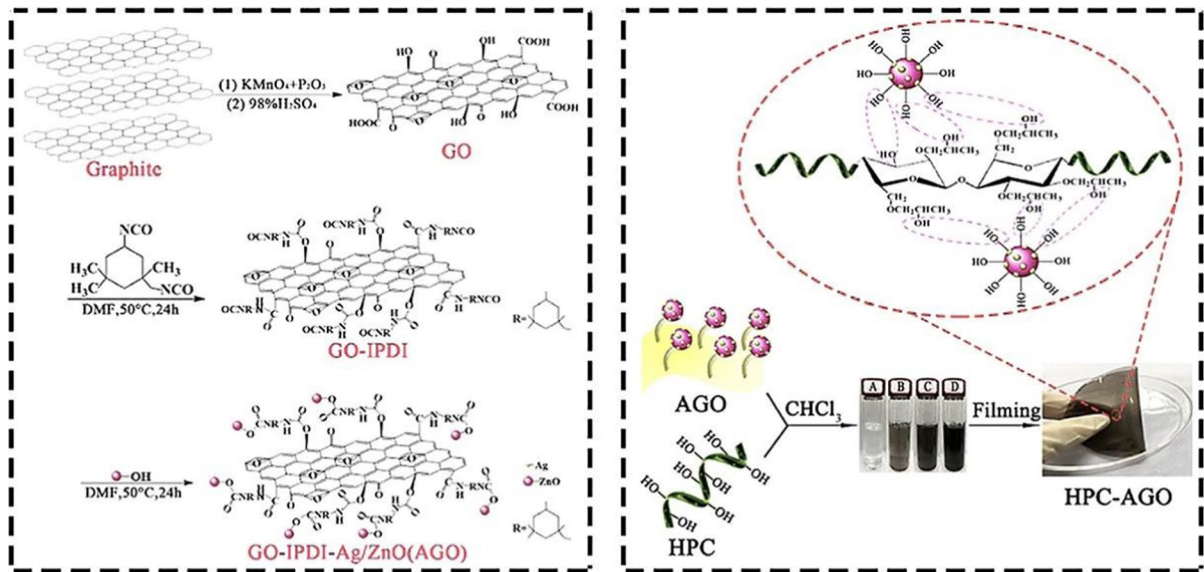


Fig. 2 Synthetic Route for AGO/hydroxypropyl cellulose nanocomposite films. Reprinted with permission from (Wang et al. 2019a, b), source. Copyright 2019 American Chemical Society

or this year. However, there is also intention to outline wider use of polylactide in form of fibers, its modifications and perspectives.

Polylactide (PLA) is a biocompatible polyester that can be obtained by polycondensation of lactic acid or the ring-opening polymerization (ROP) of lactide. (Slomkowski et al. 2014). The building block of PLA can be composed both from optically active L- and D-enantiomers. Therefore, pure poly-L-lactic acid (PLLA) or poly-D-lactic acid (PDLA) can be produced from L-lactic and D-lactic acid, respectively (Zibiao Li et al. 2016). Moreover, the polymerization of a racemic mixture of both enantiomers leads to the preparation of poly-D,L-lactic acid (PDLLA). The structure of the PLA chain determines the properties of the resulting macromolecule and, as consequence, PLLA/PDLA are semi-crystalline polymers whereas the PDLLA is an amorphous polymer. In addition, the equimolar mixture of PLLA and PDLA forms a supramolecular complex which is called stereocomplex (Tsuji 2005). The formation of this complex improves the mechanical and thermal resistance for degradation of PLA-based materials (Zibiao Li et al. 2016).

The PLAs are typically obtained via polycondensation or polymerization (Slomkowski et al. 2014). The first method uses the reaction between hydroxyl

and carboxyl groups of lactic acid to form ester bonds and obtain the desired polymer (Cheng et al. 2009). The ring-opening polymerization (ROP) of lactide (cyclic dimer of lactic acid) is the most popular method for PLA synthesis because it allows for the preparation of high molecular weight polymers with the absence of the side products typically observed during polycondensation. Moreover, the stannous octoate ($\text{Sn}(\text{Oct})_2$) as catalyst and alcohol as initiator are used for the PLA synthesis (Kowalski et al. 2000). However, various new catalysts both for coordination, cationic, and organocatalyzed polymerization were recently proposed (Kamber et al. 2007; Mezzasalma et al. 2017; Sebai et al. 2018). In addition, the star-shaped, hyper-branched, and dendritic PLAs can be prepared from the appropriate initiators of LA polymerization (Bednarek 2016; Michalski et al. 2019).

Polylactide in regenerative medicine

Research on the use of polylactide in medicine, including regenerative medicine, has been conducted with high intensity for several decades (Li et al. 2020). At the end of the twentieth century, Bendix (1998) presented an application for PLA and its copolymers (such as glycolide, trimethylene carbonate, and caprolactone) mainly in the form of screws,

pins (which means surgical accessories intended for bone fixation), plates in surgery and orthopedics (homopolymers, PDLLA, L- and D,L-lactide copolymers), chopped drug release systems, surgical thread components and other medical textile materials (PLA and its copolymers with glycolide and TMC). Currently, the scope of polylactide applications has expanded significantly. As reported in 2016, Tyler (2016) mentions such fields of medicine as:

- Orthopedics (bone regeneration, resorbable screws),
- Neurology (peripheral nerves, spinal cord),
- Cardiology (stents),
- Dentistry (tissue regeneration, fillers),
- General and plastic surgery (hernial nets, surgical threads, lifting threads, fillers),
- Gynecology (stabilizing nets),
- Radiology (theranostic imaging),
- Oncology (drug delivery systems, vaccines).

Until recently, polyesters (both aromatic and aliphatic) were not the main component of broadly understood dressings but were used as a strengthening add-on. An example is the Silflex® dressing made of a polyester mesh, whose functionality is based on the outer, coating silicone layer. There are already dressings on the market with polylactide. Suprathel® is a flexible and permeable to gases and liquid membrane, with such components as polylactide, trimethylene carbonate, and ϵ -caprolactone. Suprathel® is intended for treating burns, and thanks to the ability to biodegrade, it avoids painful changes of the dressing because it degrades directly in the wound. The conducted research among patients suffering from chronic wounds associated with diabetes (for example diabetic foot) also indicated its effectiveness in reducing the size of treated chronic wounds, at the same level as in the case of non-diabetic wounds (Nischwitz et al. 2021). The positive effect of polylactide on wounds is also confirmed by other studies in which nanofibrous polylactide nonwovens were subjected to tests on the porcine model (Menclová et al. 2021a, b). It has also been shown in vivo that PLA product strengthened the proliferative phase in the treatment of wounds compared to chitosan fabrics of similar structure (Menclová et al. 2021a, b). This shows that in the case of dressing materials, polylactide is still a relatively new material and the

possibilities of the use of polylactide dressing materials are still to be learned and require further research.

Attempts are being made to modify its properties without the participation of additional substances, for example by plasma. In the 2015 examination, two types of non-woven fabrics, spun-bonded and needle-punched, both made of D-lactide, were put under the low-temperature plasma. The action of plasma was tested in two variants, in the presence of atmospheric air and C₆F₁₄ (perfluorohexane). The operation of the plasma from the air has increased the sorption properties of polylactide fibers, which according to the authors of the study predestines the received material for the category of superabsorbents. In turn, as a result of plasma treatment, perfluorohexane increased its hydrophobicity. The disadvantage of modification may be its impermanence, because the changes in the surface activity of the fibers disappeared after a few months (Urbaniaik-Domagala et al. 2016).

The subject of interest is polylactide and its copolymers, most often in the form of nanofibers produced by the electrospinning method (Kanmaz et al. 2018). Nanofibers, due to the specific dimensions and significant advantage of the surface above the volume, are materials with increased surface activity affecting interactions in the treated area and can imitate the properties of external cell matrix (Extracellular Matrix, ECM), in particular, peptide and hyaluronic acid nanofibers (Mohiti-Asli and Lobo 2016).

Polylactide nonwovens can be modified for special applications already at the production stage, through production parameters, or by changing the parameters of the spinning solution, including the addition of active substances and drugs. Several factors influence the final form and functionality (Sharifi et al. 2020; Antoniya Toncheva et al. 2014). Production parameters determine the physical, thermal, and mechanical properties of fibers, while the additives primarily give medicinal, antiseptic, and antibacterial properties, although above a certain concentration production also requires adaptation of spinning conditions due to the impact on the properties of a spinning solution (by changing viscosity, the presence of dispersion agents). The form of fibers, porosity, and transverse dimensions are also affected by the presence of copolymers. It is also known that copolymers affect the effectiveness of dressings. It has been shown in in vitro and in vivo research that

Table 3 Recent examples of fibrous PLA materials for wound dressings and tissue regeneration

Function	Structure
Antimicrobial and anti-inflammatory	Poly(ϵ -caprolactone[PCL])/ Poly(lactic acid [PLA]) with <i>Nigella Sativa</i> extract (Sharifi et al. 2020) Quaternization of PMTA in PLA/PMTA fibers (Echeverría et al. 2019) Fibers Loaded with Birch Bark Triterpene Extract (Fan and Daniels 2021) Fibers with propolis extract and silver nanoparticles (Adomavičiūtė et al. 2017) PDLLA nanofibers encapsulating amoxicillin (Ho et al. 2021) Porous PLA membranes with sulfated chitosan, polydopamine and gentamicin (Yu et al. 2023)
Supporting regeneration process	Core-shell nanofibers based on PLA and γ -PGA (Fang et al. 2019) PVP/PLA-PEO fibers containing encapsulated collagen and cefazolin (Hajikhani et al. 2021b, a)
Antioxidant	Nanofibers of PLA with other copolymers loaded with lycopene (Hajikhani et al. 2021b, a) Polylactide/poly[(R,S)-3-hydroxybutyrate] (PDLLA/a-PHB) blend mats with proanthocyanidins (Zięba et al. 2021)

the membrane from the polylactide/poly(vinyl alcohol)/sodium alginate (PLA/PVA/SA) mix improves fibroblast proliferation and reduces the inflammatory response at an early stage of healing compared to membranes of pure PLA, while the effect of collagen deposition is clearer in the case of the latter (Bi et al. 2020). However, the effectiveness of releasing drugs is influenced by the crystallinity of the polymer due to the difficult access of water molecules to the crystalline phase. The use of nanofibers with active medical compounds for the treatment of wounds is already the subject of several studies (Ambekar and Kandasubramanian 2019; Arida et al. 2021; Liu et al. 2017). Typical active additives for the spinning solution used in various combinations are natural extracts, metal nanoparticles, peptides, antibiotics, growth factors, both in molecular form and encapsulated, or mixture of copolymers and it is summarized in Table 3.

Surface modification of PLA fibers

The polylactide products, such as nanofibers, foams, and films, regardless of whether they have been enriched in the production process, undergo further modifications. In tissue engineering, the change in surface properties is often aimed at increasing an affinity to the human tissues. Cells' adhesion is influenced by the polymer surface wettability, free surface energy, surface charge (an electric charge present on the surface of the material), as well as the chemical structure of the outer layer and its morphology. Generally, highly adhesive tissue material is hydrophilic with a surface charge with the opposite charge to the surface of the cells. Specific needs determine the values of the above parameters (Wang et al. 2005).

However, it is worth mentioning that some results show that the cells are able to adhere and proliferate either on hydrophilic and hydrophobic surfaces, although the number of cells on hydrophobic surface initially decreases to finally increase after time (Ishizaki et al. 2010). Another research on superhydrophobic materials and their interactions with proteins and cells highlights the importance of surface topology in protein and cell adhesion (Lourenço et al. 2012). In this study, protein adsorption was higher on smooth surfaces than textured. The relationship between cell adhesion and surface roughness was also relevant, as cell adhesion and proliferation were inhibited on rough surfaces; however, cells remained viable and active. This means that good tissue affinity is a complex phenomenon and cannot be easily determined (Ferrari et al. 2019). Increasing the hydrophilicity of polylactide products is the subject of great interest. It is usually achieved with physical and chemical methods, through γ -ray irradiation (Qi et al. 2019), surface hydrolysis (Lee and Yeo 2016; Liu et al. 2019; Tham et al. 2014), plasma or laser treatment (Kudryavtseva et al. 2017; Mohsenimehr et al. 2020; Rytlewski et al. 2012; Stoleru et al. 2016; Wan et al. 2004), and the choice of the method also affects other surface properties such as roughness (surface morphology) or cell affinity. Plasma is the most versatile method and its impact causes various interactions with the material: cleaning, etching, activation by creating functional groups, grafting, and polymerization (Cools et al. 2014). At the stage of spinning the fibers, admixtures of hydrophilic copolymers, including poly(ethylene glycol), are used in the spinning solution (Hendrick and Frey 2014; Suzuki et al. 2018). In the wetting tests (by contact angle measurement), it has been

shown that the value of the wetting angle decreases proportionally as the PEG percentage in the mixture increases (Athanasoulia et al. 2019; Athanasoulia and Tarantili 2017). Another solution is to impregnate polylactide material with poly(ethylene glycol) copolymers. PDLLA membranes saturated with an amphiphilic monomethoxyl poly(ethylene glycol)-*b*-poly(D,L-lactide) (PEG-PDLLA) showed changes in the wetting angle from 74.5° to 50°, depending on the solution concentration (Yang et al. 2018). The PEG connection method to PLA (mixing or grafting to the surface) is important from the point of view of the mechanical properties and parameters of the spinning solution, because the PEG add-on causes a reduction of the strength of the mixture and increases the viscosity of the spinning solution (Kruse et al. 2018; Toncheva et al. 2016). Zhu modified films from high molecular weight poly-L-lactide by immersing them with poly-D-lactide with low molecular weight and poly (D-lactic acid-co-glucose) copolymer (PDLAG) dissolved in chloroform (Zhu et al. 2021). The submersion in a solution for more than 3 min resulted in swelling of the foil, and in a further step its destabilization. As a result, stereocomplexed crystals are formed on the surface of the foil, and homogeneous crystals inside the foil, and hydrophilicity improved because of the presence of glucose. The next method of connecting the PEG hydrophilic groups is to create a three-element structure (scaffolding), in which the PLA-*b*-PEG block copolymer is a kind of "glue" bonding with a hydrophobic PLA and hydrophilic PEG. The dissolved mixture was slowly poured into the powdered NaCl which then, after the polymer's solvating and thermal recrystallization, was washed out and thus obtained a porous scaffolding structure (Zhu et al. 2015).

PLA as matrix for drug delivery systems, a recent update

PLA-based NPs with anticancer properties

The PLA-based NPs are widely used as a carrier of anti-cancer drugs to enhance their stability and efficiency. The recent trends are focused on the design of the stimuli-responsive polymers that can recognize the difference between the tumor and healthy tissues since there is a distinct difference between pH

around the tumor site. Moreover, the co-delivery of two or more active agents is proposed to enhance the effectiveness of nanotherapies. Therefore, this section is describing recent strategies of improvement in the delivery of chemotherapeutics by PLA-based nanosystems. It is divided by the applied drug or their combination, however with one exception for photodynamic therapy since it was excluded from this classification and described separately.

Doxorubicin

Doxorubicin (DOX) is a drug from a group of anthracycline antibiotics and its mode of action is related to the blocking of the topoisomerase II. Since PLA does not possess any functionalities in the backbone that allows for its sensitivity to the external stimuli, therefore one possible strategy could be its copolymerization with appropriate monomers. For instance, the stimuli-responsive PLA copolymers with allylglycidyl ether (AGE) (Kost et al. 2021), L-proline derivative (Brzeziński et al. 2021) were proposed for the preparation of PLA-based NPs loaded with DOX. Both nanoformulations exhibit pH-dependent DOX release, however the cross-linking by supramolecular interactions between enantiomeric PLA chains decrease the release from obtained NPs. Their efficiency has been proven in vitro against AGS (human gastric adenocarcinoma) and HeLa (human epithelioid cervix carcinoma) cell lines. In addition, the copolymers of poly(2-hydroxyethylmethacrylate)-*g*-poly(lactide)-*b*-poly(ethyleneglycol)-*b*-poly(2-hydroxyethylmethacrylate)-*g*-poly(lactide) (PHEMA-*g*-PLA)-*b*-PEG-*b*-(PHEMA-*g*-PLA) were obtained via combination of reversible addition fragmentation chain (RAFT) and ring-opening polymerization (ROP) methods (Ghamkhari et al. 2021). Subsequently, these copolymers were used for the covering of graphene oxide surface and, as a result, the DOX-loaded nanocomposites were obtained. The pH-triggered drug release from nanocomposites was shown and their efficiency has been proved against mouse breast cancer (4T1) cell line.

Docetaxel

Docetaxel (DTX) is classified as a plant alkaloid and it could bind to the Bcl-2 protein that is responsible for the stopping of apoptosis in cancer cells or inhibit

the microtubular depolymerization. To efficiently encapsulate DTX, two different macromolecules were utilized for the preparation of nanoparticles: disulfide-crosslinked star-PLGA nanoparticles (HA-sPLGA XNPs) and hyaluronic acid combined with PDLLA (Wang et al. 2021). For this purpose, the nanoprecipitation was used to prepare DTX-loaded NPs that were cross-linked and compared with those un-crosslinked ones. Moreover, the release of DTX could be accelerated by the addition of glutathione. The NPs can be also effectively uptaken by the human lung carcinoma (A459) cells. However, the *in vivo* tests against A549 tumor-bearing mice models revealed prolonged half-life elimination of cross-linked NPs and indicated that the decrease of tumor growth can be achieved after their administration.

Paclitaxel and cis-platin

Paclitaxel (PTX) originates from the Pacific yew tree and its mode of action is related to inhibition of spindle bodies formation during mitosis. The microfluidic technique was employed for the preparation of NPs composed of PLLA macromolecules (Zhang et al. 2021a, b). This method relies on the mixing of NPs solutions in a solvent with non-solvent in the microfluidic channels that leads to the nanoprecipitation of the polymeric matrix (Brzeziński et al. 2019). The PTX-loaded particles were prepared by applying a commercially available microfluidic chips and dichloromethane was used as solvent of PLLA dissolution. However, SDS was added to the formulation to stabilize the obtained NPs. The benefits of microfluidic preparation of nanocarriers could be mainly related to their sustained drug release characteristic in comparison to those prepared by traditional nanoprecipitation. It was also shown that the slower release can be achieved by embedding the PTX-loaded NPs in microparticles. Moreover, magneto-sensitive PLA-based NPs were prepared by film rehydration and further modified with maghemite to introduce sensitivity to a magnetic field (Pigareva et al. 2021). The obtained particles were stable in different pH values; however NPs can be slowly decomposed by enzymatic hydrolysis after 7 days due to the stabilization effect of PEG-corona. Finally, the efficiency of NPs was proved against human breast adenocarcinoma cells (MCF7).

Curcumin

Curcumin (Cur) is a hydrophobic natural compound that has been investigated for cancer treatment since it inhibits cancer growth by downregulating cyclin B1 or activating the caspase-9/3 cascade. For its encapsulation, the copolymers composed of galactosamine-modified poly(ethylene glycol)-poly(lactide) (Gal-PEG-PLA) and D- α -tocopherol poly(ethylene glycol) 1000 succinate (TPGS) and micelles were synthesized by thin-film dispersion method (Sun et al. 2021a, b, c). The size of micelles was ranging from 80 to 120 nm, and their biocompatibility was proven by MMT assay in Caco-2 (human colon adenocarcinoma) cells. Most importantly, the micelles were distributed mainly in the jejunum and ileum and the maximum concentration in plasma (C_{max}) was enhanced by encapsulation of Cur in nanocarriers. Moreover, due to the presence of galactosamine moiety, the micelles possess the liver-targeting ability.

Camptothecin

Camptothecin (CPT) is a well-known topoisomerase inhibitor used for cancer treatment with CPT-loaded NPs. In this regard, poly(lactic acid)-hyperbranched polyglycerol (PLA-HPG) was prepared and used as a matrix for CPT encapsulation (Hu et al. 2021). The main aim was to prolong intratumoral drug retention and enhance nonsurgical treatment of skin cancer. Moreover, two types of NPs were prepared since PLA-HPG NPs were also treated with sodium periodate and non-adhesive NPs were transformed into bioadhesive particles due to the formation of aldehydes in the polymeric backbone. The NPs release their payloads within 100 h, however the bioadhesive NPs can efficiently enter the interior of the cell by clathrin-mediated endocytosis. The intradermal transplantation of mice carcinoma squamous cells (PDVC57 SCC) into syngeneic C57BL/6 strain of laboratory mice allows to show the enhanced biodistribution of bioadhesive NPs within the tumor parenchyma by confocal microscopy. In addition, co-delivery of bioadhesive NPs with immunostimulating CpG oligodeoxynucleotides induce the reduction of tumor growth.

Poly(lactic acid)-block-poly(ethylene glycol) (PLA-*b*-PEG) NPs were produced by flash nanoprecipitation hand-made confined impinging jet mixer

(Wilson et al. 2021). To enhance the properties of CPT, it was conjugated with an acid derivative of α -tocopherol (vitamin E), yielding the novel prodrug molecule. The NPs with the size around 100 nm were further encapsulated in PEG microgel microparticles to achieve the prolonged release of the prodrug.

Imiquimod (R837)

Imiquimod (R837) is a compound responsible for the activation of immune system response against cancer. This molecule was grafted on the mPEG-*b*-PLA backbone by an acid-sensitive bond (Li et al. 2021a, b, c). This approach allows for the release of R837 in the acidic environment of the tumor. The in vitro activation of macrophages by P-R837 was tested in human umbilical vein endothelial cells (HUVECs) and the results clearly showed their pH-triggered activation.

Ursolic acid

Ursolic acid (UA) is a naturally derivate triterpene that could inhibit cancer proliferation. This compound was encapsulated in the interior of the PLA-based NPs covered by chitosan with a size between 300 and 350 nm (Antonio et al. 2021). The release of UA occurs in a sustainable way for 144 h. Moreover, due to the presence of chitosan on the surface of NPs, the mucoadhesive properties of the carriers were improved. The obtained NPs exhibit good hemocompatibility, low cytotoxicity, and bioavailability after oral delivery to model rats.

Mithramycin

Mithramycin (MTM) is another example of an anti-biotic natural product used against testicular cancer, glioblastoma, or Ewing sarcoma. It is proposed that MTM could bind to GC-rich sequences in DNA which results in the disfunction of transcription factors. To enhance its stability, MTM was encapsulated in the hydrogel, PLA, and liposomal NPs and tested against sarcomas (Estupiñán et al. 2021). These three materials release MTM with different velocities, nonetheless the most sustained release was observed from liposomes. The myxoid liposarcoma models MSC-5 H-FC and T-5 H-FC#1 were utilized and similar effect was observed for all proposed formulations

of the drug. In addition, all prepared drug-delivery systems were able to reduce the growth of CSC-enriched 3D clonal sphere cultures (tumorspheres) of T-5 H-FC#1 cells. Finally, their high efficiency has been also proven (liposomal nanocarriers) by the in vivo assay mice carrying T-5 H-FC#1 cells without the presence of side effects.

Co-delivery of two anticancer drugs

The co-delivery of two different active compounds in one nanocarrier is done to increase their therapeutic effect. It was implemented to modulate different signaling pathways, reduce the dose of anticancer drugs, and overcome intrinsic drug resistance of cancer. However, to fully utilize this potential, those drugs should be encapsulated in the polymeric nanocarriers, since this approach enhances their bioavailability and stability. Moreover, the embedding in the polymeric matrix allows for control over the drug release kinetics. In this section, the different strategies of the co-delivery are briefly summarized:

- (a) A combination of sorafenib (inhibitor of multi-kinase) and paclitaxel was encapsulated in the poly(lactide) and hyaluronic acid co-modified half-generation of PAMAM G4.5 dendrimers (sPA) matrix (Ma et al. 2021). The pH-dependent release of the drug and enhanced efficiency in killing of human hepatocyte carcinoma (HepG2) cells by the co-delivery of two different drugs (in vitro) was observed.
- (b) Sophisticated copolymers composed of lactide and modified lactides were used for conjugation of sulfobetaine, paclitaxel, and gemcitabine (inhibition of DNA synthesis) (Sun et al. 2021a, b, c). These copolymers self-assemble in water to form the desired NPs. The cytotoxicity assay at Paca-2 (human pancreatic ductal adenocarcinoma) cells in vitro and in vivo on mouse model revealed their superior properties in comparison to a combination of pure drugs.
- (c) PLGA matrix was used for the delivery of gemcitabine and erlotinib (epidermal growth factor receptor (EGFR) inhibitor) due to its positive effect during clinical trials (Cai et al. 2021a, b). Their ability to decrease the cancer cells viability was proven against human pancreatic cancer (PANC-1) cells line. Most importantly,

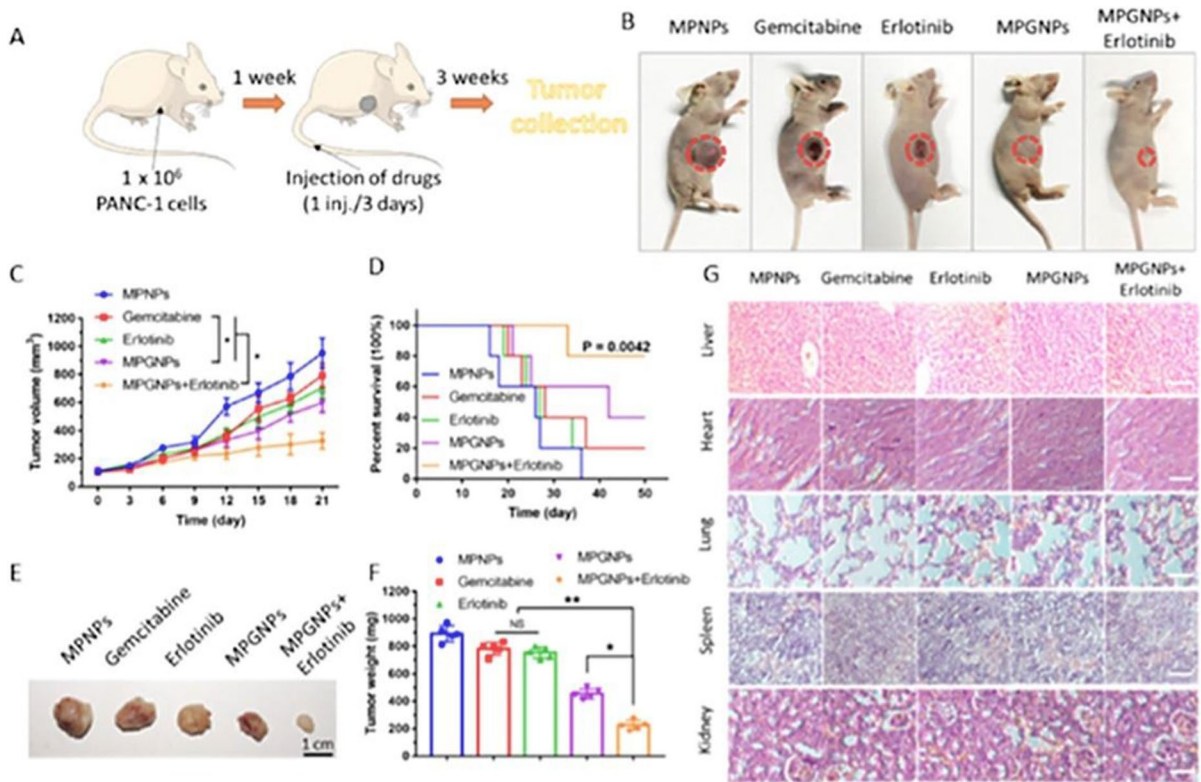


Fig. 3 In vivo antitumor effect of MPGNPs combined with erlotinib. **A** The PANC-1 pancreatic cancer tumor model was established. Drugs were intravenously injected every 3 days, and the tumor was collected after 3 weeks. **B** Representative photographs of mice with the tumor circled in each group. **C** Tumor growth curve of the differentially treated mice. **D** Survival curves of the mice in the different groups calculated

by the Kaplan–Meier estimate for 50 days. **E** Image and **F** weight of the tumor. **G** Representative images of H&E-stained liver, heart, lung, spleen, and kidney. Scale bar = 50 μ m. Data are shown as the mean \pm SD. * $P < 0.05$; ** $P < 0.01$; NS, no significance ($n = 5$ for each group). Reprinted with permission from (Cai et al. 2021a, b). Copyright 2021 American Chemical Society

the tumor growth can be efficiently inhibited, as well as, the percent of mice survival significantly increased after treatment of drug combination delivered by NPs, as shown in Fig. 3. The authors concluded that this was a proof-of-concept for the potential clinical applications of their drug delivery system.

- (d) Commercially available PLA–PEG functionalized with biotin (targeting moiety) was used for the preparation of micelles co-loaded with epothilone B (apoptosis inducer, cytotoxic for cells overexpressing P-glycoprotein) and rapamycin (mTOR inhibitor) (Zajdel et al. 2021). Their co-encapsulation in polymeric matrix decreases the survival of human breast cancer (MCF-7 and MDA-MB-231) cells exposed

to the NPs with both drugs in their interior in comparison to single-loaded NPs.

- (e) Star-shaped PLAs with cholic acid core were mixed with E-tocopheryl poly(ethylene glycol) succinate (TPGS) and curcumin (Cur), yielding the polymeric micelles (Guan et al. 2021). The combined effect was related to downregulating P-gp expression of tumor cells due to the presence of TPGS moiety, with the simultaneous effect of Cur as an anticancer drug. Their efficiency was tested against MCF-7/ADR (breast cancer) cells and it was concluded that the utilization of obtained nanocarriers allows for reversal of tumor immunosuppression mediated by CD47 and PD-L1.
- (f) Poly(ethylene glycol)–polylactide (PEG–PLA) copolymers were used for the delivery

of tumor-associated antigen vaccine (antigen agent) with chemotherapeutic DBPR114 (quinazoline-based, multi-kinase inhibitor for the treatment of myeloid leukemia) (Huang et al. 2021a, b, c). The experiments on the tumor-bearing mouse demonstrated the synergistic effect of co-delivery of antitumor drug/antigen agents slowing down the tumor growth.

- (g) The copolymer with pendant functions such as polylactide-poly(ethylene glycol)-2-(3-((S)-5-amino-1-carboxypentyl)-ureido) pentanedioate/triphenylphosphonium (PLA-PEG-ACUPA/TPP) can be used for encapsulation of ingenol-3-angelate and DOX (Wang et al. 2022). The dual-drug-loaded particles were obtained via nanoprecipitation to induce effective immunogenic cell death (ICD). As expected, the tumor growth was suppressed most efficiently by the administration of NPs loaded with the mixture of both active compounds. Interestingly, due to the treatment by NPs, the increase of CD8⁺ T cells and CD4⁺ T cells indicates the inhibition of the immune response of cancer.
- (h) Ag-TiO₂/poly(lactic acid) nanohybrid was prepared by loading of norfloxacin (NOR) and tenoxicam (TENOX) on the surface of Ag-TiO₂ which was finally covered by PLA layer by solution casting (Salahuddin et al. 2021). Such approach allows for the preparation of nanocarriers effective against different bacteria strains (Ag) and simultaneously against cancer cells (the co-delivery of the drugs). Interestingly, the release of both drugs was faster at the physiological conditions than in the acidic medium typically observed near tumors. This was explained by the more effective shedding effect of PLA and the difference in the ionic interactions in these two distinct pH environments, nevertheless, this feature may limit their applications. Subsequently, their antimicrobial activity was tested against several bacteria strains and it was proved their efficiency against *gram-positive* and *gram-negative* bacteria. However, the nanohybrids were able to decrease the viability of different cancer cells, their cytotoxicity was lower in comparison to DOX.

Photodynamic and photothermal therapy

Photodynamic (PDT) and photothermal (PTT) therapies are based on the utilization of molecules that can be activated by light to annihilate the cancer cells. The advantage of this type of therapy is its low invasiveness and selectivity against cancer cells. To address this challenge, indocyanine green (ICG) loaded PLA-based NPs were prepared via nanoprecipitation (Güney Akkurt and Gülsoy 2022). NPs with a size of 300 nm embedded approximately 8.3 µM of ICG per 1 mg of nanocarriers and 70% of the drug was released after 96 h. The cell viability of PC-3 (human prostatic adenocarcinoma) cells was assessed in the dark and after light irradiation to show the light-triggered action of ICG, the results clearly indicated that a high decrease in the cell viability can be only achieved upon laser light irradiation. A similar approach was proposed by Santos-Oliveira et al. however the combination of two active substances (dacarbazine and zinc phthalocyanine) encapsulated in the PLA and poly(vinyl alcohol) matrix (do Reis et al. 2021). The NPs were prepared by emulsion-based method and their morphology was shown by atomic force microscopy (AFM), interestingly their adhesion properties increase significantly after drug encapsulation. The MTT assay performed on human amelanotic melanoma (MV3) cells line indicated that the combination of chemotherapeutic drug dacarbazine with photosensitive zinc phthalocyanine gives the best results and inhibits the cancer cells recovery. Jin and Lo et al. followed the approach of a combination of a drug and photoactive compounds in one nanocarrier (Guo et al. 2021a, b, c). However, the main difference was that they conjugate both DOX and zinc phthalocyanine to one macromolecule. Subsequently, the NPs were fabricated by nanoprecipitation, however the addition of PEG5000-PDLLA5000 was necessary for the stability of the obtained ZnPc–Dox@micelles. As expected, the ZnPc–Dox@micelles more efficiently kill cancer cells in comparison to DOX-loaded NPs after laser irradiation. Most importantly, the obtained nanocarriers were localized at the tumor site in the mice model and were able to decrease the tumor growth after light irradiation.

In addition, the micelles composed of the chitosan-*g*-polylactide loaded with photoporphyrin IX were also proposed for photodynamic therapy (Sibarani et al. 2021). However, apart from their size,

morphology, and cytotoxicity, there was no example of the light-triggered enhancement of their efficiency. It might be assumed that this will be shown in the follow-up work.

Antimicrobial nanomaterials

Poly lactide NPs loaded with 1,2-benzisothiazolin-3-one (BIT) were covered with chitosan to induce their antimicrobial activity and enhance the activity of the drug (Yao et al. 2021). The particles were fabricated by oil/water (o/w) solvent evaporation, dried, re-suspended in the acetic acid aqueous solution of chitosan to prepare the desired nanospheres. The release kinetics revealed that the coating by chitosan decreased the drug release from nanospheres, in addition, the chitosan-modified nanospheres were the most effective against *E. coli* and *S. aureus*. Their improved efficiency was correlated with their efficient cellular uptake and disruption of a cellular structure due to membrane damage. Moreover, micelles obtained by self-assembly of PLA-*b*-PEG copolymers were used to cover a coverslip glass surface (Caruso et al. 2021). To introduce the antimicrobial properties, the photosensitizer (PS) was encapsulated in the interior of the micelles which was able to generate reactive oxygen species (ROS). The release of PS strongly depends on the degree of branching of block copolymers and the most stable micelles that can release PS in 48 h were subsequently utilized for the coating of the surface. As expected, the micelles were inactive in the dark, however the dose-dependent killing of *S. aureus* after the irradiation was observed. Similarly, the strategy of using PLA- or PLGA-based copolymers was proposed for the treatment of biofilm-relevant infections associated with acidity (Guo et al. 2021a, b, c). To prepare pH-sensitive micelles poly(β -amino ester) block was introduced to the copolymer backbone, as shown in Fig. 4. Finally, triclosan (TCS) was loaded and their antimicrobial properties were tested. Due to the pH-sensitivity of obtained micelles, their interactions with the negatively charged component of bacteria can be greatly enhanced. This feature affects the TCS release from the micelles and the enhanced release was observed in the acidic pH. Moreover, the micelles showed superior killing efficiency against bacteria in comparison to free TCS. This was explained by their good penetration and accumulation in bacteria biofilm due

to the charge switch at pH 5. This was also proven by the in vivo test on the subcutaneously implanted catheters covered with *E. coli* biofilms.

A different approach was proposed by Kammann et al. (2021) since both microparticles (MPs) and NPs loaded with cholesterol (Chol) were tested against *S. pneumoniae* induced lung damage. Three different formulations of MPs and NPs were prepared from PLGA, E100–PLGA blends (methacrylic acid copolymer (Eudragit 100) and poly(D,L-lactide-co-glycolide), 40:60 w/w), and PLA–Chol, however, they also varied after encapsulation of cholesterol. Among all tested cholesterol carriers, the NPs composed of cationic Eudragit and PLGA exhibited the most efficient uptake by cells with results in the high intracellular level of cholesterol. This allows for the cellular defense action which results in neutralizing the pneumolysin (PLY) level to protect the cells from damage caused by toxins. It was concluded that polymeric cholesterol carriers can be used as a supply to enhance the cell defense mechanism against bacterial infections.

NPs for brain treatment

An interesting approach was proposed by Higazy et al. (2021), in which polylactide-co-caprolactone-based nanoparticles were loaded with lamotrigine (LTG), which is used for the treatment of epilepsy. The prepared formulation was stabilized by the addition of different amounts of PVA to the aqueous phase. After centrifugation and drying, the size and stability of re-dispersed NPs were tested. It was shown that the size decreased with the increasing amount of PVA. In addition, the presence of PVA on the NPs surface also decreased their zeta potential. The release of LTG varied between different formulations, nonetheless in all cases the burst release was observed, after which the sustained release of the drug occurred. Most importantly, the comparison of the effectiveness of LTG-loaded NPs with Lamictal® (lamotrigine, an anti-epileptic medication) tablets indicated that NPs more efficiently target the brain, and as result the drug targeting efficiency or direct transport percentage values were significantly higher for NPs.

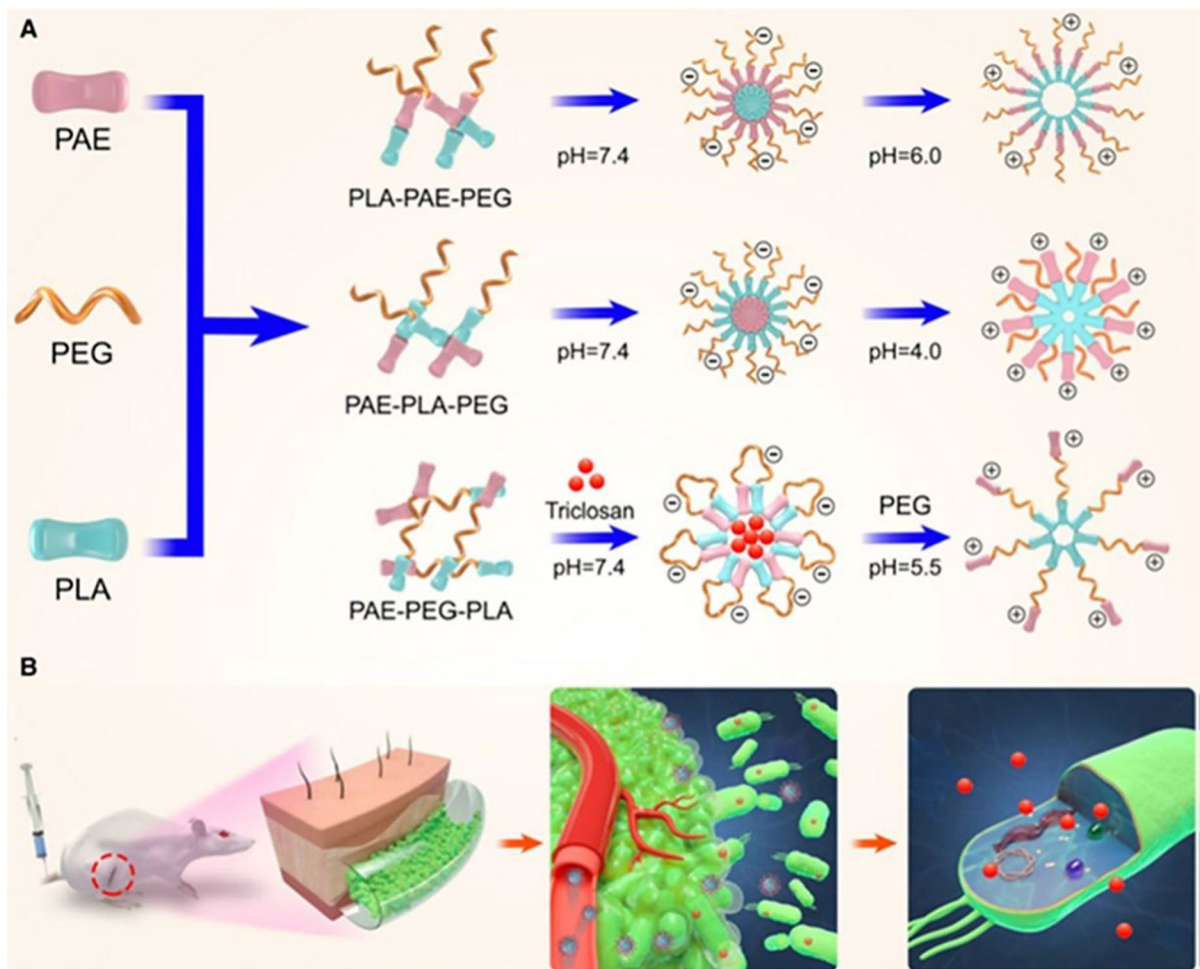


Fig. 4 Elaboration on the architecture of pH-sensitive copolymers with proper pH (A). The mechanism for targeting delivery of encapsulated drug into bacteria deep into biofilms using

SCAMs for treatment of implant-related biofilm infections (B). Reprinted from (Guo et al. 2021a, b, c) CC BY 4.0

NPs for DNA and RNA delivery

PLA-based NPs can be used as vehicles for the delivery of DNA, RNA, and genes (Mendes et al. 2022). Since these materials can be very easily degraded in the human body or cannot cross the cell membrane, therefore the encapsulation of genetic materials in NPs is a perfect solution. To understand the interactions between PLA and DNA, Maiti et al. performed multiple experiments of their binding interactions, as well as, the DNA release from the nanocarriers (Senapati et al. 2021). The addition of DNA to PLA increases the size of obtained NPs. Moreover, it also alters the surface charge of NPs due to the presence

of free phosphate groups. For instance, UV–vis analysis revealed a blue shift of DNA after the formation of the complex with PLA which indicates their strong dipolar interactions. The release of DNA from NPs followed the Korsmeyer–Peppas model and the non-Fickian diffusion mechanism. The MTT assay showed good biocompatibility of such carriers. Finally, the simulation of their interactions indicated that PLA can more effectively interact with the AT-rich region of DNA in comparison to the GC-rich region.

Moreover, the PLGA NPs were used as carriers of interfering RNAs (siRNAs) or short hairpin RNAs (shRNAs) for the treatment of inflammatory bowel disease (IBD) (Bao et al. 2021). The NPs were

prepared by the emulsion-based method and their size ranged from 265 to 285 nm. The NPs prepared by this method exhibit high load of SNX10-shRNA plasmids (SRP). To assess their efficiency *in vivo*, the chronic IBD mice were treated with SRP-loaded NPs and a control. The IL-1 β , TNF- α , and IL-23 levels were decreased, therefore, it prevents reduction in the mice body weight. The authors proposed that the anti-inflammatory effect of NPs induced by signaling pathways in epithelial cells.

NPs for peptide delivery

Peptides are an important class of bioactive compounds that required encapsulation for the preservation of their biological activity. For this purpose, core-shell NPs composed of poly(ethylene oxide)-poly(lactide) were used for encapsulation of glutamyl-cysteinyl-glycine (GSH), and their properties were compared with particles made from cholesterol and sorbitan monostearate (Span 60) (Ghorbanizamani et al. 2021). The particles were prepared by dispersion of copolymers or lipid with surfactant dissolved in the proper solvent, in phosphate-buffered saline (PBS). The size of GSH-loaded particles was 148 and 90 nm for copolymeric and cholesterol/Span 60, respectively. The high encapsulation efficiency was achieved, however the release of GSH was relatively low, both in the physiological and acidic conditions. As a result of NPs action in HeLa (cervical cancer) and U87 (human glioblastoma astrocytoma) cells, a significant decrease of glycation end products and beta-sheet formation was observed, nevertheless more efficient were those built from cholesterol/Span 60.

In addition, the copolymers of zwitterionic poly(D-glucose carbonate) and semicrystalline polylactide were used for encapsulation of insulin and insulin glargine (Elsabahy et al. 2021). The authors proposed an interesting approach in which the control over the morphology of nanoassemblies was achieved by varying the block length in copolymers. As a result, three distinct morphologies could be obtained: spherical, cylindrical, and platelet-like. The binding of insulin to the nanoparticles was confirmed by gel retardation assays and the highest value was obtained for platelet-like NPs. The obtained NPs were biocompatible, and their uptake depended on their size and shape, notwithstanding the cell type also should be considered.

The *in vivo* test in diabetic rats indicated that insulin-loaded NPs exhibit better hypoglycemic activity than free insulin. However, the cylindrical NPs were the most effective ones. Therefore, the control over the morphology of NPs could be a good tool for the improvement of the pharmacological availability of insulin.

PLA for bone regeneration

PLA is often chosen as a matrix for bone repair purposes (Naseem et al. 2021). In this regard, β -tricalcium phosphate/poly(L-lactic acid) (TCP/PLLA) scaffolds with incorporated zinc ions were proposed for bone healing (Huang et al. 2021a, b, c). The *in vitro* and *in vivo* assays confirmed that the presence of Zn²⁺ from the scaffolds was able to promote differentiation of periosteum-derived progenitor cells (PDPCs) and transition from M1 to M2 macrophages. As a result, the implanted scaffolds (5% Zn group) participate in bone regeneration *in vivo*. Moreover, the scaffolds were biocompatible and no side effects in organs were observed. In addition, the PLA composite fracture fixator with the addition of vancomycin cationic liposome was tested for its ability to suppress the bacterial growth and for reduction of antibiotics toxicity (Cai et al. 2021a, b). The *in vitro* drug release test showed sustained vancomycin release that could decrease the damage to fibroblasts. The inhibition zone of composite against *E. coli* and *S. aureus* showed their beneficial antimicrobial properties. The cell adhesion studies on MC3T3-E1 (mouse bone) cells revealed superior properties of the composite in comparison to pure PLA, and as a result, increased proliferation was observed. Additionally, the composite exhibits a better osteogenic effect due to lowering of the inflammatory effect after implantation of the scaffold. The multi-component composite system consisting of chitosan (CS)-coated poly(trimethylene carbonate) (PTMC)/polylactic acid (PLLA)/oleic acid-modified hydroxyapatite (OA-HA)/vancomycin hydrochloride (VH) was proposed by Zhang et al. (He et al. 2021). In this contribution, the VH-loaded microspheres were prepared by emulsion technique, and their properties were compared with PTMC/PLLA, PTMC/OA-HA composite microspheres. The sustained release of the drug was obtained and almost all of the drug was released from the interior of the microspheres after 30 days. The

incubation of microspheres with osteoblast cells indicated their favorable biocompatibility. The alkaline phosphatase (ALP) activity of MC3T3-E1 preosteoblast cells cultured on the obtained scaffolds showed the increased activity. Therefore, it could be postulated that the proposed microspheres can promote bone regeneration. Although, the *in vivo* tests were not performed.

The copolymers of PLA with ϵ -caprolactone (Radwan et al. 2021) with poly(ethylene glycol) (Tang et al. 2021) were also used as materials for enhancing bone regeneration. In the first contribution, drug-loaded poly (L-lactide-co- ϵ -caprolactone)/calcium phosphate (CaP) composite was prepared via *in situ* formation of composites powder, in addition, the composite without polymer and blank composite powder was also prepared. As a drug, the antibiotic moxifloxacin hydrochloride (MOX) was added as it is used for the treatment of chronic osteomyelitis (OM). The obtained material exhibits suitable porosity and sustained release of the drug. The prepared scaffolds exhibited all typically required properties for the materials for bone regeneration, such as improved proliferation and differentiation of osteoblast cells, antimicrobial effect, and induction of new bone-cell formation. Therefore, the authors recommended their clinical experiments on humans (Radwan et al. 2021). A different approach was proposed by Zhu et al (2021) in which platelet lysate (PL) used for cartilage tissue engineering was embedded in PDLA-PEG-PDLA hydrogel. To enhance its delivery, PL was encapsulated in NPs composed of heparin (Hep) and ϵ -poly-L-lysine (PLL) and added to the hydrogel. This allows for the release of drug-loaded NPs, followed by the PL diffusion from the hydrogel matrix. The test against IL-1 β induced human chondrocytes showed that the obtained biomaterials exhibit anti-inflammatory properties. Finally, ACLT-Induced osteoarthritic rats were treated with PL-loaded hydrogel and it was shown that the presence of the hydrogel allows repairing of the cartilage defect in rats since it was filled with soft and friable tissue (Tang et al. 2021).

Micro-sized systems

Microparticles of PLLA were prepared by the emulsion-based method for diabetes treatment in animals, such as equids, dogs, cats, and rabbits (Bouriche et al.

2021). Metformin hydrochloride was chosen as an active ingredient for diabetes treatment. Due to the fact that microparticles were prepared by emulsification, the obtained particles exhibit a high dispersity index, and their size was ranging from 1 to 55 μm . The size distribution can highly influence the drug release, thus an alternative methods of particles preparation should be considered in the future. Finally, the concentration of the drug in plasma after single-dose administration in rabbits was determined after intravenous, oral, and oral microparticles solution administration. The results indicated that PLA microparticles showed optimal, sustained release of the drug and its increased half-life.

Moreover, the microrods of poly(lactide-co-glycolide) copolymers were used as DOX carriers (Xu et al. 2021). To obtain such morphology of PLGA particles, the one-step electrospray method was used. In addition, the DOX-loaded microspheres were also prepared to compare the effect on particles morphology. Nevertheless, the alteration in processing parameters allows for the preparation of different particles with varying lengths and diameters; DOX was only added to microrods with 16 μm in length and 1 μm in diameter and microspheres with a diameter of 2.95 μm . The cell viability examination indicated the superior efficiency of microrods against microparticles, yet the free drug exhibit higher killing ability than microcarriers. The difference in efficiency between two distinct particles morphology was explained by the faster drug release and larger specific surface area of microrods.

Micro-film

Poly(L-lactide)-co-poly(ϵ -caprolactone) copolymers were used for the preparation of the micro-film that is flexible enough to fit the sclera (Wu et al. 2021). Those films were loaded with triamcinolone acetonide (TA) which is used for adjunctive intraocular or peri-ocular steroid for the treatment of posterior globe trauma. The blank and drug-loaded films were made by spraying on the polyfluortetraethylene (PTFE) plate and the obtained materials were dried before peeling off the template. The encapsulation of the drug in the film allows for its sustained release over 200 days. Histology images revealed that there was no inflammatory cell infiltration around the film.

Subsequently, the *in vivo* tests indicated that TA-loaded film can be implanted during the first phase of globe trauma repair and induce the healing of the eye with simultaneous degradation of the polymeric matrix.

Hydrogels as a drug and DNA/RNA depots

Hydrogels are soft materials that due to their porous structure can preserve a large portion of water or aqueous solution (Li et al. 2021a, b, c). Among all studied hydrogels, those composed of polyesters are widely used since the ester bond can be hydrolyzed in an aqueous solution. Typically, the amphiphilic block copolymers of hydrophobic lactide or glycolic acid with hydrophilic ethylene glycol are proposed for their preparation (Basu et al. 2016). In this regard, such hydrogels were recently proposed for photodynamic nitric oxide (NO) (Sun et al. 2021a, b, c) or gene carriers (Kim et al. 2021) for cancer therapy and colitis treatment (Guo et al. 2021a, b, c). In the first contribution, the poly(lactic-glycolic acid) (PLGA) NPs loaded with NO donor L-arginine (L-Arg) photosensitizer indocyanine green (ICG) were added to the poly(ϵ -caprolactone)-poly(ethylene glycol)-poly(ϵ -caprolactone) (PCL-PEG-PCL) hydrogel to obtain thermosensitive hydrogels (Sun et al. 2021a, b, c). The rheological test showed that hydrogels possess shear-thinning properties that allow for their facile injection with syringe. Moreover, encapsulation of NPs in the hydrogel matrix could prolong the ICG release which results in increased drug retention *in vivo*. Most importantly, after NIR irradiation the formation of reactive oxygen species (ROS) is induced which subsequently lets to oxidization of the L-Arg to produce NO gas. Nevertheless, the hydrogels exhibit low cytotoxicity against 4T1 cells; it was dramatically changed after NIR irradiation, cell apoptosis and necrosis were observed. These superior properties were further confirmed by *in vivo* antitumor study which showcased the inhibition of tumor growth. Likewise, due to the formation of ONNO⁻ at the tumor site, the degradation of collagen was observed which is responsible for tumor progression. In the second contribution, the sophisticated spermine-grafted copolymer was synthesized (MPEG-*b*-[polycaprolactone-ran-poly(spermine-L-lactide)]) to prepare hydrogels as gene depots (Kim et al. 2021). This pendant cationic group can form a

complex with tat3-small hairpin RNA (St3-shRNA) which may induce the downregulation of the signal transducer and activator of transcription 3. This complex was further used for the *in situ* forming hydrogel gene depot since the obtained copolymers exhibit sol-gel transition at 37 °C. Due to the macromolecules amphiphilic structure, the formed complex was stable even after incubation with serum, DNase or heparin for a long time. Moreover, the cytotoxicity of the obtained copolymer with St3-shRNA was significantly lower in comparison with St3-shRNA/polyethylene amine (PEI) which is typically used to form a complex with RNA or DNA. The antitumor activity was tested after intratumoral injection into mice and the volume of the tumor rapidly decreased, especially after multiple injections at 3, 6, 9, 12, and 15 days.

Thermosensitive hydrogels composed of poly(D,L-lactic acid)-poly(ethylene glycol)-poly(D,L-lactic acid) (PDLLA-PEG-PDLLA) block copolymers were suggested for colitis treatment (Guo et al. 2021a, b, c). At the concentration exceeding 11% these copolymers form a gel at a body temperature and can be used as a depot for mesalazine (5-aminosalicylic acid) which is used for the treatment of ulcerative colitis (UC). This strategy allows to avoid the burst release of the drug and more than 70% of the drug was released after 40 h, independently from the hydrogel structure. The cytotoxicity test revealed good biocompatibility of the obtained materials. Additionally, hydrogel can preserve its structure even after 25 days after injection. This reflects in its long-term shielding function for the used drug and efficient treatment of UC. As a result, the treatment of UC mouse model with the PDLLA-PEG-PDLLA hydrogels loaded with mesalazine induces weight gain and symptom relief which confirms that it is a good strategy for the improvement of the UC treatment in the future.

In summary, there is an enormous need for the design and implementation of PLA-based materials in biomedical applications. Notwithstanding the fact that these materials have been investigated for a decade, there is a still place for improvement and novel ideas. As it was reported in this review, the main effort is put into the applications of PLA-based NPs in cancer therapy. The increasing number of *in vivo* investigations paved the way for PLA-based NPs for pre-clinical and clinical applications. Nevertheless, their utilization for drugs delivery to the brain

or applications as gene carriers should be constantly developed. Due to their biocompatibility, the PLA and its copolymers are also frequently used as materials for bone regeneration. Moreover, antimicrobial agents are also encapsulated by PLA biodegradable matrix. However, this usually required the modification of the PLA backbone to overcome the drawbacks of PLA such as brittleness or low sensitivity to external stimuli. Although great progress has been achieved, there is still a lot of goals that need to be achieved for the implementation of this technology in the real life, therefore combined efforts from scientist from different fields are needed to truly achieve the development of PLA-based materials applications.

PLA/Cel systems

Surface modification of cellulose materials

The reactivity of cellulose is associated with the presence of hydroxyl groups in a macromolecule and their availability to reaction which depends on the degree of polymer crystallinity. A densely packed structure prevents access to the entire volume of reagents, so often the basic task before the main modification of cellulose is to convert it into swollen form and then, possibly, into a dissolved state. The basic and most versatile compound that allows to modify the shape of macromolecules in cellulose is sodium hydroxide, due to which with the right selection of modification time, solution concentration and temperature, the process of relaxing and rebuilding cellulose structure can be controlled. A wide review regarding cellulose solvents based on aqueous sodium hydroxide solutions was published by Budtova and Navard (2016). One of the effects of NaOH processing is a change of the form of crystalline cellulose into the crystalline form of cellulose II, which is also called regenerated cellulose. The process of treating textiles with aqueous solutions of sodium hydroxide is called mercerization and can be conducted with or without tension, which involves different physicochemical properties, such as mechanical strength, gloss, crystalline degree, internal fiber orientation, dyeing ability, and susceptibility to enzymatic hydrolysis (Roy Choudhury 2017). For these reasons, clothing made of mercerized cotton fibers is characterized by greater durability and comfort of use. During the mercerization, due to the effect of

relaxation (swelling) of the fiber, there is also a possibility to implement active substances inside the fibers and thus obtain functional textiles. With this method, chitosan was entrapped (Grgac et al. 2020). In this paper a standard cotton woven fabric and cotton/polyester blended fabric were utilized. In the first stage, a bath in an aqueous solution of 20% sodium hydroxide was used with a surfactant at 25 °C. In the second stage, the bath consisted of chitosan powder with the addition of citric acid, sodium hypophite monohydrate, and detergent was prepared. Subsequently, the fabrics were rinsed and neutralized to neutral pH. The last stage was drying and conditioning (curing). Fabrics prepared in this way and washed 5 times continued to show antimicrobial effects. Interestingly, the efficiency in fighting *Candida* was observed only in the case of blended fabric, which suggests that not only chitosan and accompanying agents have an impact on the activity of created material, but also its base structure, the presence of both polyester and hydrolysis products of polyester fibers, which probably appeared as a result of NaOH processing.

The mercerization process can be developed with cationization, the method widely described in the literature (Correia et al. 2020). It is a chemical process using quaternary ammonium compounds (called QACs or quats), which causes a change in the surface load from negative to positive, which is mainly used to increase the efficiency of dyeing textiles with anionic dyes and allows for reduction of the amount of salt (sodium chloride, NaCl) during the process. It applies to both native and regenerated cellulose fibers (Periyasamy 2016; Dong et al. 2020). Cationization during mercerization means affecting textile material with ammonium salt without prior flushing from a mercerizing solution and then put off for aging in plastic bags for 24 h (Tarbuk et al. 2014a). As a result of combined mercerization and cationization processes, etherification of cellulose II and significantly increased water adsorption occur, and surface-active agents and dyes indicate that the number of available hydroxyl groups exceeds the results of mercerization alone (Tarbuk et al. 2014b).

In the above examples, the authors focus on ammonium compounds mainly as auxiliary agents in the dyeing industry, whereas quats play a significant role in medicine as disinfectants, antibacterial, antifungal, and antiviral (Rutala and Weber 2015). For this reason, attempts are made to use their properties

to modify textiles and assess their functionality, although the use of quats in wound dressing can be disputable due to a strong, negative impact on the environment and living organisms (Nalecz-Jawecki et al. 2003; Zhang et al. 2015). H. Han developed a cotton fabric cover with Dimethyl Dodecyl [3-(Trimethoxysilyl) propyl] Ammonium Chloride (CDDA) and showed that the antibacterial activity of cotton increases with CDDA concentration. At the same time, it was stated that the comfort of use is reduced, including increased hydrophobicity of the surface, stiffness, and roughness of the fabric. What is more, the antibacterial effect systematically decreases after washing in anionic detergents. To avoid undesirable effects, modified L-Arginine with Carbon–Carbon double bond (M-Arg) was added. Both compounds, CDDA and M-Arg were grafted on the surface of cotton as a result of polycondensation and free radical polymerization respectively, thus covers resistant to multiple laundries were obtained (Han et al. 2020).

Ammonium salts are used as agents for preparing material for further modification. Research from 2017 on modified gauze cationically and anionically with the addition of silver nanoparticles and oxytetracycline hydrochloride showed the usefulness of pretreated gauze with a cationizing agent for wounds, while gauzes modified anionically worked on inflammation of the skin (Rehan et al. 2017). This was due to the different behavior of the material in different pH environments. In addition, the profile of releasing the drug from "cationic" gauze was characterized by the lack of initial rise as opposed to the "anionic" version. These results were used by Montaser to prepare gauze modified with 3-chloro-2-hydroxypropyl trimethyl ammonium chloride (Quat 188), nanosilver and oxytetracycline hydrochloride and then covering it with salicyl-imine-chitosan biopolymer by exhausting method (Montaser et al. 2020). In vivo studies in rats have shown that although a cationized gauze with the addition of silver and oxytetracycline has greater efficiency in the treatment of burns than classic gauze (area of damaged skin after 12 days of therapy decreased by respectively- 50.8% and 32%), but it is still less effective than ointment available on the market (Dermazin®). However, it was matched by a gauze covered with a biopolymer (change of burns- 91.2%).

The modification of the cotton surface of gauze cationically and anionically was an introduction to

applying hydroxyapatite (Hap) and silver nanoparticles (Ag NP) with ginger oil (Said et al. 2021). Cationic modification is based on the ultrasonic bath of gauze samples with the addition of chitosan and then conditioning them at increased temperature. The anionic modification method consists of partial carboxymethylation using monochloroacetic acid preceded by mercerization. These procedures improved HAp and Ag NP deposition on the cotton gauze. Notwithstanding, increased color, UV protection, and antimicrobial features were obtained by deposition of silver nanoparticles contrary to hydroxyapatite, and the study showed that the pretreatments influenced uniformity of silver active layer and number of implemented NPs.

Compatibilization of cellulose materials with a hydrophobic polymer

To introduce hydrophilic cellulose material compatibility with a hydrophobic polymer, cellulose surface properties are modified, both in the form of macro and nanocellulose (Bledzki 1999; Ng et al. 2017). The expected durability of the combination of both materials decides the choice of modifications. In the case that the composite is to be used under mechanical load, compatibility based on chemical reactions and the production of durable covalent bonds between polymers will ensure more durability. In the case of materials with a short life cycle and used in a non-destructive environment (not only mechanically, but also chemically), probably simple physical methods of joining polymers, such as impregnation, are sufficient. The second issue to consider is the purity of the material for medical applications, which can be achieved by using only safe substances for the production and depriving it of the remains of auxiliary agents, which with longer exposure can show an irritating or pathogenic effect. Therefore, not every solution used in the production of composites and combining cellulose with a hydrophobic polymer is suitable for regenerative medicine due to the lack of compatibility with the living organism.

Physical methods include stretching, calendaring, thermal energy interaction, electrical discharges (crown, low-temperature plasma), mercerization, adsorption using the layer-by-layer method or liquid or gels—impregnation from dispersion or polymer solution compatible with a hydrophobic surface.

Chemical methods include:

- Anionic and cationic modifications to give specific electrostatic properties and improving the durability of the then-applied functional layers (Kittinaovarat et al. 2012; Sharma and Sayed 2016)
- Esterification with compounds containing acetyl groups.
- Applying coupling agents—substances forming network interfacial areas increasing wetting by changing the surface tension of substrates or creating covalent bonds simultaneously with cellulose fiber and hydrophobic polymer.
- Hydrophobization of cellulose material
- Grafted copolymerization.

The division of methods was based on classifications available in the literature, despite that it is worth noting that it is largely conventional, because often the same modification technique can be classified into more than one method (Table 4).

Compatibilizers and compatibilizing agents are layers with intermediate properties between polymers. Through their presence, the properties of interfacial space in mixtures of materials of various characteristics change. Such materials can be copolymers consisting of two polymers intended for connection in the composite. Coltelli presented a proposal for the comb-like synthesis of copolymers of cellulose acetate (AC) and oligo(lactic acid) with different OLA proportions using a binding agent with diepoxide (EJ40). The study has shown that cellulose in compatibilizer has been partially deacetylated, and the proportion of OLA is not that significant for the copolymer properties, but more for the ease of obtaining it. The activity of the compatibilizer in blends of PLA and AC fibers was confirmed in endurance tests. Change in strength was based on a significantly increased Young module, which suggests increased adhesion of composite components (Coltelli et al. 2021).

The coupling agents, similarly to compatibilizers, operate in the interface spaces of composites. In this case, the increase in matrix adhesion and strengthening are obtained due to the presence of functional groups and their ability to produce chemical bonds with substrates. In cellulose-poly lactide composites, silanes are the most common for medical purposes (Ghalia and Dahman 2017).

Chitosan is a common, natural polymer used to modify the surface of cellulose materials. Due to the antibacterial, antimicrobial, antioxidant, and anti-inflammatory properties, as well as the ease of modification due to the presence of hydroxyl and amine functional groups, it is a source of interest in the area of regenerative medicine, and is also considered as a drug carrier (Aranaz et al. 2021). When playing a role of a surface modifier chitosan and its derivatives is most often implemented by impregnation or pad-dry-cure method (Said et al. 2021), as well as cellulose esterification (QingBo Xu et al. 2017, 2018a, b, 2019). The coating technique has been used in a chitosan hydrogel deposition as a functional layer on cotton fabric (Bentoufa et al. 2020). The cotton substrate has been pretreated cationically and anionically. The cationic groups were created by dyeing the samples with a polyazo dye and then reducing with sodium dithionite in an alkaline environment. The anionization occurred through the acetylation of cellulose with chloroacetic acid.

Role of the TEMPO

TEMPO, or (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl, is radical for the production of nanocellulose by the "top-down" method by changing the load of electrostatic forces occurring between microfibrils (Wąchala et al. 2011). As a result of cellulose oxidation, carboxylic groups are formed in the C6 position, which opens the way for further modifications. In the medical industry, oxidized cellulose (OC), both type I (natural) and II (regenerated) is produced by oxidation with nitric oxide and is used, among others, to produce absorbable haemostatic gauze and absorbable surgical threads. The haemostatic effect appears because the acid carboxylic group combines with the Fe₃₊ ion in hemoglobin, and thus accelerates the formation of a clot and clogging of bleeding (Lao and Deng 2021). TEMPO-oxidized cellulose, and above all TEMPO-oxidized bacterial cellulose can be a medium to implement antibacterial substances, such as silver nanoparticles (Ifuku et al. 2009; Wu et al. 2018) or silver sulfadiazine (AgSD) (Khattak et al. 2020); for the silver cations can permanently connect ionically with the anionic surface of cellulose. Cheng et al. (2017) gives the method of producing TEMPO-oxidized cellulose nanocrystals: the CN water dispersion is subjected to ultrasound bathing for 15 min.

Table 4 Recent development of compatibilization of cellulose with polylactide and other hydrophobic polymers for different approaches

Recent development of compatibilisation of cellulose with polylactide and other hydrophobic polymers for different approaches		References
Chemical	Cationisation and anionisation	QUACs acting as surfactant (Pal et al. 2019) Viscose fabrics oxidized with TEMPO or coated with TEMPO-oxidized cellulose nanofibrils (Korica et al. 2021) Bacterial cellulose modified anionically with poly(acrylic acid) using “grafting from” technique to crosslink with cationic chitosan (Khamrai et al. 2017)
	Esterification	Cellulose nanocrystals esterified with maleic anhydride (CNC _{MA}) which resulted in higher stability of the cellulose nanoparticles in aqueous suspensions, lower thermal stability and higher surface hydrophilicity of created Cel/PLA composite (Parize et al. 2017) Cellulose nanocrystals (CNCs) modified using immobilized lipase (Novozyme 435) to catalyze the formation of laurate ester groups on the CNC surface (Yin et al. 2020) One-step modification of both Fischer esterification and acid hydrolysis of cellulose (Spinella et al. 2015) Cellulose nanofibrils (CNFs) modified by catalyzed lactic acid esterification in an aqueous medium with SnCl ₂ as a catalyst (Lafia-Araga et al. 2021) Esterification using valeric acid (Shojaeiarani et al. 2019) A site-specific reaction between the primary surface hydroxyl groups (C6-OH) of cellulose and acyl imidazoles (Beaumont et al. 2021)
	Compatibilizers	Cellulose triacetate/PLLA graft polymers synthesized in the presence of 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) (Volokhova et al. 2019) Long-chain hyperbranched polymers (LCHBPs) (Huang et al. 2022) oleic acid as compatibilizer in a catalyst-free esterification of cellulose oxalate (COX) and microcrystalline cellulose (MCC) (Huang et al. 2021a, b, c) Cellulose Acetate-grafted-Poly(L-lactic Acid) (CA-g-PLA) (Choi et al. 2020) Comb-like copolymers of cellulose acetate (AC) and oligo(lactic acid) OLA prepared by chemical synthesis in solvent or reactive extrusion in the melt, using diepoxide as the coupling agent for compatibilizing poly(lactic acid)/plasticized cellulose acetate PLA/pAC blends (Coltelli et al. 2021) Methylenediphenyl diisocyanate (MDI) in microfibrillated cellulose (MFC)/PLA composite (Lee et al. 2019) Bamboo flour grafted lactide (Xin-yu Song et al. 2017)
	Coupling agents	Bamboo nanowhiskers modified by silanes (Ma et al. 2019) Bacterial cellulose nanofibers modified by silanes in PEG/PLA matrix (Abu Ghalia and Dahman 2017) Microcrystalline cellulose coated with titanate coupling agent as a reinforcement of PLA filament for 3D printing (Murphy and Collins 2018) Maleic anhydride (MA) grafted PLA (MA-g-PLA) (Mohd Ghazali and Pickering 2021) SiO ₂ /silanes coupling compounds for jute/PLA composites (Xueyang Song et al. 2022)
	Grafting	Oligoesters containing reactive end groups based on poly(DL-lactic acid) PDL-LA, poly(ϵ -caprolactone) PCL and poly(3-hydroxyalkanoate)s PHA grafted on cellulose via esterification (Samain et al. 2011) Grafting of polylactide (PLA) onto the cellulose nanofiber (CNF) (CNF-g-PLA) prepared by in situ reactive extrusion using dicumyl peroxide (DCP) as a free radical initiator (Li et al. 2021a, b, c) CNC's surface modified by TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl radical) oxidation method followed by surface grafting of TEMPO-oxidized CNC (TOCNC) performed with poly(ethylene glycol) (Pal et al. 2019)

Table 4 (continued)

Recent development of compatibilisation of cellulose with polylactide and other hydrophobic polymers for different approaches

	References
Hydrophobisation	Alkyl ketene dimer (AKD) as bonding agent between cellulosic fiber and PLA matrix (Caylak et al. 2021) Octyl gallate (OG), dodecyl gallate (DG), and octadecyl gallate (OCG) grafted onto the jute fabric, which were mediated by horseradish peroxidase (Dong et al. 2021) Alkylation of cellulose nanocrystals with alkyl bromide (Lee et al. 2020) Hydrophobisation of bamboo nanocellulose using rarasaponins for drug carrying (Wijaya et al. 2020) Modification of jute fabrics via horseradish peroxidase (HRP)-catalyzed covalent grafting of butyl acrylate (BA) and 2,2,3,4,4,4-Hexafluorobutyl methacrylate (HFBMA) (Huimin Wu et al. 2017) Microcrystalline cellulose (MCC) modified using toluene-2,4-diisocyanate (TDI) in tetrahydrofuran (THF) (Olonisakin et al. 2021)
Physical Mixing	Blends prepared by mixing polylactic acid (PLA) in Cellulose triacetate and foamed by supercritical CO ₂ (ScCO ₂) (Zhang et al. 2021a, b) PLA/cellulose nanofibrils composite nanofibers made from chloroform solution by electrospinning (Yang et al. 2019) Cellulose nanofibers CNF/PEG masterbatch as a compatibilizing medium for melt-mixing with PLA (Safdari et al. 2017) An aqueous CNF-based suspension in the presence of poly(ethylene glycol) for melt compounding with PLA (Cailloux et al. 2019)
Coating	Sisal fibres coated with bacterial cellulose nanofibres through dipping method (Lee et al. 2012) PLA coated on the Surface of alkaline or silane-treated flax fiber surfaces via a solution dipping process (Kodal et al. 2015) The surface modification of flax fibers by lignin and tannin solutions performed using a dip-coating method (Bayart et al. 2020) Bacterial cellulose coated with PLA and benzalkonium chloride for acute wound healing approaches (Foong et al. 2018)
Plasma treatment	Cellulose thin layers treated with oxygen plasma and immersed in a L-lactide solution for grafting under different conditions (Couturaud et al. 2015)
Additive manufacturing (3D printing)	PLA filament printed directly on washed and unwashed cotton fabric of various structures (Gorlachova and Mahltig 2021)

Then, the aqueous solution of the TEMPO and sodium bromide gradually drops into the liquid with cellulose, and subsequently, a 12% solution of NaClO sodium hypochlorite is added to start oxidation. The pH of the mixture (10.8) is controlled using NaOH. The reaction ends with the addition of 1 ml ethanol and hydrochloric acid reducing the pH value to 7. Finally, modified crystals are rinsed several times in distilled water and dried to the form of powder. Such modified material was used to produce composite dressings with sodium alginate to support hemostasis processes. The evaluation was carried out on a rabbit model of a liver wound and an ear wound by measuring the volume of lost blood and coagulation time. Pure alginate dressing and classic gauze were used as reference points. Both in the case of dressings in the

form of a film and dressings in the form of sponges, new composites have shown significantly better effectiveness in stopping blood loss compared to gauze and pure sodium alginate, regardless of the percentage of modified nanocrystals in the dressing volume. The volume of bleeding was correlated, also time of bleeding was significantly shorter in the case of composite dressings. On the other hand, the differences in effectiveness in relation to the dressing structure (sponge/film) turned out to be relatively small, so it can be assumed that the presence of TEMPO-oxycellulose plays the greatest role in hemostatic processes.

Grafting and polymerization

An interesting idea is the combination of cellulose and polylactide in a simple way, by grafting of polymer or monomer polymerization on surface of the other, thus obtaining a durable, hybrid material with resultant properties of both components. In the previous chapter, several examples of such materials are given as compatible with PLA/Cel composites, however they can be used as the main product subjected to subsequent functionalization, both structural and surface. Due to the ease of creating polylactide polymer, it is usually cellulose that is the basis for the polymerization of lactide and the grafting of polylactide. The function of the polymerization initiator is most often performed by hydroxide groups of cellulose molecules. On the other hand, a typical catalyst for the polymerization of a lactide is the stannous octoate (SnOct_2), although its use in medical applications can be a problem due to cytotoxicity and difficulty with rinsing out of the resulting material (Tanzi et al. 1994). Hence, new catalysts are proposed, such as zinc L-proline (Giram 2021), zinc guanidine (Hermann et al. 2020), or complexes of other metals (Bhattacharjee et al. 2021). Cellulose as a base occurs in various forms: nanoparticles (crystals and fibrils), fibers (for example cotton fibers), yarn, mat, foil, and woven or knitted textiles. The higher the degree of cellulose processing, the greater the challenge is to connect a polylactide to it without a byproduct in the form of a free polymer. An emphasis on cellulose modification for grafting was placed by Zhou in a short overview (Zhou et al. 2021).

In the last decade, there were few publications about modeling PLA/Cel material using grafting and/or polymerization. Y. Zhang conducted in situ graft copolymerization of cellulose-g-PLA and then directly melt-spun fibers to investigate their mechanical properties. The reaction medium was 1-allyl-3-methylimidazolium chloride ([AMIM]Cl) and tin(II) octoate worked as an initiator (Zhang et al. 2014). Cellulose in form of nanocrystals was surface modified by grafting L-lactide in toluene for better dispersion in hydrophobic polymer matrices. The shape of nanocrystals remained unchanged after modification (Peltzer et al. 2014). Another example is poly(lactic acid) grafted cellulose nanofibers (PLA-g-CNFs) achieved via ring opening polymerization in toluene/acetone dispersion,

also with tin(II) octoate as initiator. The main goal was an improvement of tensile and strength properties of such fibers blended with pure PLA matrix for the purpose of filaments for 3D printing (Dong et al. 2017). In a previous study, Braun et al. (2006) shows that better mechanical properties are obtained when at the stage of polymerization, lactide is mixed with already-made polylactide. The experiment contained three variants: (1) cotton fiber mixed with a commercial PLA without additional polymerization of lactide, (2) fiber on which the lactide was polymerized, (3) fiber at the same time mixed with a high molecular weight PLA and polymerized with lactide. The catalyst was tin (II) octoate with co-catalysts titanium (IV) isopropoxide (TIP) and triphenylphosphine, (PPh_3). The polymerization process was preceded by 6-h pretreatment of cellulose fibers in the 8 WT solution of sodium hydroxide at 37 °C. The fibers were partially destroyed, but at the same time increased porosity and thus increased availability of hydroxyl groups on the surface was obtained.

At the nanoscale CNC-PLLA nanomaterials were synthesized via in situ ring-opening polymerization of L-lactide in the presence of CNC, resulting in a hydrophobic, homogeneous mixture of PLLA-grafted-CNC and free PLLA homopolymer. Free PLLA acted as an agent against aggregation of PLLA-g-CNC and compatibilizer in mixtures with other polymers (Miao and Hamad 2016). In this case, the catalysts were SnOct_2 or ZnO and the initiator was benzyl alcohol.

When discussing mixing cellulose derivatives and polylactide, Luan et al. (2013) proposes a "one-pot" thermoplastic cellulose acetate-graft-poly(L-lactide) copolymer using unmodified cellulose. In this process, firstly cellulose is acetylated with acetic anhydride in an ionic liquid 1-allyl-3-methylimidazolium chloride (AmimCl), secondly, in the same solution, ring-opening graft copolymerization of L-lactide is carried out from the residual hydroxyl groups of CA as initiators using 4-dimethylaminopyridine (DMAP) as the catalyst. The same environment of all processing stages can simplify the modifications, reduce costs, and improve control over reaction conditions.

3D printing

Both cellulose and its derivatives and polylactide can be a medium to 3-dimensional printing (3DP), alone or with other components. Although dressings and formulations for topical skin management made with 3DP technology have strong representation in scientific literature, there is still a lack of solutions based on polylactide alone or PLA/Cel systems. Nonetheless, there are available filaments for Fused Deposition Modelling (FDM), which are in fact cellulose reinforced polylactide composites (Wang et al. 2018). De Oliveira in his review dedicated to 3DP dressings describes only the printing of nanocellulose and does not mention polylactide (de Oliveira et al. 2021). As mentioned in previous chapters, PLA at the moment seems not to be a first-choice dressing material, although it is worth emphasizing that it serves well in other fields of regenerative medicine. The effectiveness of the use of 3D objects made of polylactide has already been summarized and evaluated clinically, although long-term assessments are still needed. The trials were mainly aimed at surgical purposes (Diment et al. 2017). Despite all of the above, there are new solutions in 3DP for wound healing with PLA playing an important role. For example, in composition with flexible thermoplastic polyurethane (TPU), it was proposed as filament for the production of antibacterial wound dressings using the Fused Filament Fabrication (FFF) with the addition of antibiotic (amikacin) (Szarlej et al. 2021). Mesh made of PLA filament pre-mixed with lignin, tetracycline, and the addition of curcumin was designed for wound dressing and showed the influence of structural dimensions on curcumin permeation. These observations may allocate mesh for custom-made dressings (Domínguez-Robles et al. 2019). Another solution for tissue engineering is a composite scaffold, where different amounts of polylactic acids are printed on bacterial cellulose membranes to precisely construct PLA layer structure. Controlling printing parameters would result in better cell adhesion and proliferation (Wu et al. 2022).

On the other hand cellulose and its derivatives such as methylcellulose, hydroxypropyl cellulose (HPC), ethylcellulose (EC), hydroxypropyl methylcellulose acetate succinate (HPMCAS), and microcrystalline cellulose were reviewed as suitable polymers for applications in 3DP drug delivery systems (Giri et al. 2021). In the case of dressing or wound

healing, nanocellulose, methylcellulose, and their blends with other components are bioinks/resins serving as a printable base for active additives in smart hydrogel bandages (Tsegay et al. 2022).

When discussing binding PLA with cellulose in one hybrid dressing material, where one serves as ink and the other as a substrate, the adhesion between these two polymers is still under consideration. Gorlachova and Mahltig (2021) tested the adhesive properties of 3D objects made of polyamide 6.6 (Nylon) and polylactide applied on 6 different cotton fabrics. The samples were characterized by determining roughness by laser scanning microscopy and hydrophilicity by drop test. To determine adhesion, a perpendicular test was used, by measuring the force needed to separate printed objects from a substrate. In the case of polylactide, the results show that the speed of printing influences adhesion, which rises after a lower speed, whereas the temperature of the filaments is significantly opposite to the relatively low impact of the temperature of the printing table. Adhesion also changes depending on the preparation of the initial fabric (by washing or not), as well as the thickness and structure of the sample—thicker cotton shows greater binding to the polylactic filament, which is related to the distance of the substrate from the printing head. Thicker samples are compressed during printing, which makes a liquid polymer mechanically stick into the fabric structures. A similar correlation occurs in the case of substrate weight per area parameter. The greater mass promotes the increase in adhesivity. To summarize, the authors indicate that in each case of Nylon, the adhesion of print was greater compared to PLA printing, due to the greater hydrophobicity of PLA, and thus less compatibility with hydrophilic cotton.

The direction of printing is also important in obtaining a better binding of printed polylactide with a cotton substrate. In tests of filling directions, the force needed to break the coating printed at an angle of 45° was 75% greater compared to the coating printed at an angle of 90° (Redondo et al. 2020).

PLA/Cel nanocomposites

The term nanotechnology has been known since the 1970s and is used to consider materials and material engineering methods that can be achieved with nanometric precision. From the beginning of the 90 s,

Table 5 Plants for implementation in wound dressings

Types of plants for implementation in wound dressing (according to Fatehi)

Extracts	<i>Centella asiatica</i> , sorghum, spirulina, green tea, <i>Coptis chinensis</i> , <i>Hypericum perforatum</i> , soursop, <i>Melilotus officinalis</i> , gum arabic and <i>C. Officinalis</i> , gymnema, henna, <i>Tridax procumbens</i> , grape seed, <i>Aloe vera</i> , moringa, mangosteen, <i>Zataria multiflora</i> , <i>Quercus infectoria</i> , German chamomile, <i>Juniperus chinensis</i> , <i>Beta vulgaris</i> , β -Glucan, <i>Biophytum sensitivum</i> , <i>Azadirachta indica</i> , Nile, <i>Memecylon edule</i> , and <i>Myristica andamanica</i>
Essential oils	Lavender, cinnamon, <i>Zataria multiflora</i> , lemongrass, peppermint
Compounds	Curcumin, shikonin, alkannin, astragaloside, thymol

a part devoted to the treatment of people and maintaining health separated and was called nanomedicine (Freitas Jr 1999). In the case of the treatment of wounds, nanotechnology proposes NPs with properties supporting wound treatment to classic dressings, the production of controlled drug carriers, as well as completely new structures such as scaffolds, nanofibers, foams, and thin films (Stoica et al. 2020a). Cellulose nanocrystals and cellulose nanofibrils were discussed as hydrogels for medical applications such as drug delivery, tissue engineering, and wound healing (Du et al. 2019). Nanofibers and products made of them, such as non-woven, have special properties, a large external surface in relation to volume, therefore they are an active product and capable of absorbing relatively large amounts of liquid from the wound, as well as enabling air flow. In this way, the extracellular matrix (ECM) can mimic. They are produced mainly by electrospinning, and the raw material can be both natural and synthetic polymers, the requirement is to obtain a solution/spinning fluid with appropriate parameters. In nanofibers dressings, substances from plants such as oils, extracts, or clean compounds are often implemented (Table 5) (Fatehi and Abbasi 2020). This mainly improves antimicrobial and antibacterial protection. Other active substances implemented in the nanofibrous membranes are peptides and metals (gold, copper oxide, silver, zinc oxide), and their performance can reduce the consumption of antibiotics (Zhang et al. 2022). However, antibiotics are still in use. PLA nanofibers containing hydroxypropyl methylcellulose (HPMC) and tetracycline hydrochloride (THC) were solution-blow spun to create material effective against bacteria *E. Coli* and *Listeria monocytogenes*. Interestingly, the addition of HPMC improved the antibacterial activity of the

material compared to neat PLA nanofibers (Bilbao-Sainz et al. 2014)).

An example of nanocomposite dressing is nanofibrous mats made of a mixture of polylactide and cellulose acetate. In addition, the antimicrobial agent, thymoquinone (TQ) was implemented into the scaffolds for protection from infections and acceleration of healing properties (Gomaa et al. 2017). Nanocomposite coating of PLA matrix and 3 active materials (zinc oxide and copper nanoparticles and tranexamic acid) were developed on conventional sterile cotton gauze and investigated for inhibiting the growth of bacteria *S. aureus* and *E. coli* (Molapour Rashedi et al. 2021). In another study, asymmetric multilayer polylactide nanofiber (AMPN) mats were prepared and a one-sided and prolonged release profile of hydrophilic dye or oxaliplatin was observed. Such a solution was aimed at post-surgical anti-cancer therapy (Liu et al. 2015). Multilayers were designed and objected to delaying drug release and one external PLA film prevented the dressing from adhering to the tissue. This non-porous film also protects from undesirable drug release and its unintended spread.

Conclusions

Present-day needs for wound treatment have increased with growing knowledge of the human body and developing technology. The importance is not only in protection from external factors, and just absorbing exudation with some antimicrobial additives, but in full replacement of lost tissue and an environment that would be friendly for recovery. Multiple solutions are offered for these purposes, including attempts to create custom-made products, answering individual issues, or semi-finished

products, which are enriched with medications just before use. To summarize, these are supposed to be strictly matched dressings with the highest control of treated areas of the human body. Therefore, efforts are made to make old known materials take a new form on a quite different scale, measuring in macroscale to nanometers, and easy for modification. There are two different ways of development. One is to improve classical dressings like cotton gauze with specific covering layers, the second is to create nanomaterial and start building dressing from the smallest molecules, gaining unique properties, not available previously. Cellulose goes both ways, so it becomes more versatile than ever before, being an active part of drug-releasing systems, scaffolds, and wound healing. Moreover, its versatility is enhanced by the possibility of producing bacterial cellulose, independent from cotton and other plants cultivation, which can burden natural environment. Since polylactide is a synthetic polymer with a great advantage of being biodegradable and biocompatible, it can cover them mostly with the exception of conventional dressings. However, this may change because research is still being conducted on dressings made mainly of a polylactide and its behavior in clinical conditions is assessed. As this review pointed out, today PLA plays a significant role as drug carrier, especially in cancer therapy, as a scaffolds builder, and tissue enhancer, although it performs often with other polymers like poly(ethylene glycol), which improves its hydrophilicity. Important results showed that it can give additional advantages when left in a wound, even for biodegradation.

The question is if there are reasons for joining polylactide and cellulose in one product for medical purposes. Firstly, both can supplement mutual deficiencies, which is often seen in composites. However, the difficulty appears when thinking about the permanent binding of these two polymers due to their different affinity to water and sometimes due to the need for auxiliaries used for coupling or polymerization. The main issue is medical purity and the non-toxicity of all components. Secondly, their combination can probably enhance mutual performance, as showed in described research with cotton/polyester fabrics. This may be an opportunity for new dressings trends, where polylactide will partly replace also conventional cotton products,

and enhance their properties to a more proactive side.

Acknowledgments During completing this article, the first author was a Doctoral Candidate in the Interdisciplinary Doctoral School at the Lodz University of Technology, Poland.

Author contributions All authors contributed equally to the study conception, design and content. All authors drafted, revised, and approved the final manuscript.

Funding The authors declare that no funds, grants, or other support were received during the preparation of this manuscript. The idea for the article: A.K. Literature search and analysis: all authors. Drafting and revising: all authors.

Availability of data and materials Non applicable.

Declarations

Competing interests The authors declare no competing interests.

Ethics approval Non applicable.

Consent for publication Figures 1, 2, 3 and 4 are reused from other articles with permissions from publishers.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

- Abazari MF, Gholizadeh S, Karizi SZ, Birgani NH, Abazari D, Paknia S, Derakhshankhah H, Allahyari Z, Amini SM, Hamidi M, Delattre C (2021) Recent advances in cellulose-based structures as the wound-healing biomaterials: a clinically oriented review. *Appl Sci*. <https://doi.org/10.3390/app1117769>
- Abeer MM, Mohd Amin MCI, Martin C (2014) A review of bacterial cellulose-based drug delivery systems: their biochemistry, current approaches and future prospects. *J Pharm Pharmacol* 66(8):1047–1061. <https://doi.org/10.1111/jphp.12234>

- Abu Ghalia M, Dahman Y (2017) Fabrication and enhanced mechanical properties of porous PLA/PEG copolymer reinforced with bacterial cellulose nanofibers for soft tissue engineering applications. *Polym Test* 61:114–131. <https://doi.org/10.1016/j.polymertesting.2017.05.016>
- Adepu S, Khandelwal M (2020) Ex-situ modification of bacterial cellulose for immediate and sustained drug release with insights into release mechanism. *Carbohydr Polym* 249:116816. <https://doi.org/10.1016/j.carbpol.2020.116816>
- Adomavičiūtė E, Pupkevičiūtė S, Juškaitė V, Žilius M, Stanys S, Pavilonis A, Briedis V (2017) Formation and investigation of electrospun PLA materials with propolis extracts and silver nanoparticles for biomedical applications. *J Nanomater* 2017:1–11. <https://doi.org/10.1155/2017/8612819>
- Ahmed J, Gultekinoglu M, Edirisinghe M (2020) Bacterial cellulose micro-nano fibres for wound healing applications. *Biotechnol Adv* 41:107549. <https://doi.org/10.1016/j.biotechadv.2020.107549>
- Alavi M, Nokhodchi A (2020) Antimicrobial and wound treatment aspects of micro- and nanoformulations of carboxymethyl, dialdehyde, and TEMPO-oxidized derivatives of cellulose: recent advances. *Macromol Biosci* 20(4):e1900362. <https://doi.org/10.1002/mabi.201900362>
- Almeida IF, Pereira T, Silva NHCS, Gomes FP, Silvestre AJD, Freire CSR, Sousa Lobo JM, Costa PC (2014) Bacterial cellulose membranes as drug delivery systems: An in vivo skin compatibility study. *Eur J Pharm Biopharm* 86(3):332–336. <https://doi.org/10.1016/j.ejpb.2013.08.008>
- Ambekar RS, Kandasubramanian B (2019) Advancements in nanofibers for wound dressing: a review. *Eur Polym J* 117:304–336. <https://doi.org/10.1016/j.eurpolymj.2019.05.020>
- Andleeb A, Dikici S, Waris TS, Bashir MM, Akhter S, Chaudhry AA, MacNeil S, Yar M (2020) Developing affordable and accessible pro-angiogenic wound dressings; incorporation of 2 deoxy D-ribose (2dDR) into cotton fibres and wax-coated cotton fibres. *J Tissue Eng Regen Med* 14(7):973–988. <https://doi.org/10.1002/term.3072>
- Antonio E, dos Reis Antunes Junior O, Marcano RGDJV, Diedrich C, da Silva Santos J, Machado CS, Khalil NM, Mainardes RM (2021) Chitosan modified poly (lactic acid) nanoparticles increased the ursolic acid oral bioavailability. *Int J Biol Macromol* 172:133–142. <https://doi.org/10.1016/j.ijbiomac.2021.01.041>
- Aranaz I, Alcántara AR, Civera MC, Arias C, Elorza B, Caballero AH, Acosta N (2021) Chitosan: an overview of its properties and applications. *Polymers*. <https://doi.org/10.3390/polym13193256>
- Arida IA, Ali IH, Nasr M, El-Sherbiny IM (2021) Electrospun polymer-based nanofiber scaffolds for skin regeneration. *J Drug Deliv Sci Technol* 64:102623. <https://doi.org/10.1016/j.jddst.2021.102623>
- Asanarong O, Minh Quan V, Boonrunsiman S, Sukyai P (2021) Bioactive wound dressing using bacterial cellulose loaded with papain composite: Morphology, loading/release and antibacterial properties. *Eur Polym J* 143:110224. <https://doi.org/10.1016/j.eurpolymj.2020.110224>
- Athanasoulia IG, Tarantili PA (2017) Preparation and characterization of polyethylene glycol/poly(L-lactic acid) blends. *Pure Appl Chem* 89(1):141–152. <https://doi.org/10.1515/pac-2016-0919>
- Athanasoulia IGI, Christoforidis MN, Korres DM, Tarantili PA (2019) The effect of poly(ethylene glycol) mixed with poly(l-lactic acid) on the crystallization characteristics and properties of their blends. *Polym Int* 68(4):788–804. <https://doi.org/10.1002/pi.5769>
- Bao WL, Wu Q, Hu B, Sun D, Zhao S, Shen X, Cheng H, Shen W (2021) Oral nanoparticles of snx10-shrna plasmids ameliorate mouse colitis. *Int J Nanomed* 16:345–347. <https://doi.org/10.2147/IJN.S286392>
- Basu A, Kunduru KR, Doppalapudi S, Domb AJ, Khan W (2016) Poly(lactic acid) based hydrogels. *Adv Drug Deliv Rev* 107:192–205. <https://doi.org/10.1016/j.addr.2016.07.004>
- Bawa KK, Oh JK (2017) Stimulus-responsive degradable polylactide-based block copolymer nanoassemblies for controlled/enhanced drug delivery. *Mol Pharm* 14(8):2460–2474. <https://doi.org/10.1021/acs.molpharmaceut.7b00284>
- Bayart M, Adjallé K, Diop A, Ovlaque P, Robert M, Elkoun S, Bayart M, Adjallé K, Diop A, Ovlaque P, Barnabé S (2020) PLA/flax fiber bio-composites : effect of polyphenol-based surface treatment on interfacial adhesion and durability. *Compos Interfaces* 00(00):1–22. <https://doi.org/10.1080/09276440.2020.1773179>
- Beaumont M, Otoni CG, Mattos BD, Koso TV, Abidnejad R, Zhao B, Kondor A, King AWT, Rojas OJ (2021) Regioselective and water-assisted surface esterification of never-dried cellulose: nanofibers with adjustable surface energy. *Green Chem* 23(18):6966–6974. <https://doi.org/10.1039/D1GC02292J>
- Bednarek M (2016) Branched aliphatic polyesters by ring-opening (co)polymerization. *Prog Polym Sci* 58:27–58. <https://doi.org/10.1016/j.progpolymsci.2016.02.002>
- Bendix D (1998) Chemical synthesis of polylactide and its copolymers for medical applications. *Polym Degrad Stab* 59(1–3):129–135. [https://doi.org/10.1016/s0141-3910\(97\)00149-3](https://doi.org/10.1016/s0141-3910(97)00149-3)
- Benltoufa S, Miled W, Trad M, Slama RB, Fayala F (2020) Chitosan hydrogel-coated cellulosic fabric for medical end-use: antibacterial properties, basic mechanical and comfort properties. *Carbohydr Polym* 227:115352. <https://doi.org/10.1016/j.carbpol.2019.115352>
- Bertin A (2012) Emergence of polymer stereocomplexes for biomedical applications. *Macromol Chem Phys* 213(22):2329–2352. <https://doi.org/10.1002/macp.20120143>
- Betlej I, Salerno-Kochan R, Jankowska A, Krajewski K, Wilkowski J, Rybak K, Nowacka M, Boruszewski P (2021) The impact of the mechanical modification of bacterial cellulose films on selected quality parameters. *Coatings* 11(11):1–12. <https://doi.org/10.3390/coatings11111275>
- Bhattacharjee J, Sarkar A, Panda TK (2021) Alkali and alkaline earth metal complexes as versatile catalysts for

- ring-opening polymerization of cyclic esters, pp 1–15. <https://doi.org/10.1002/tcr.202100148>
- Bi H, Feng T, Li B, Han Y (2020) In vitro and in vivo comparison study of electrospun PLA and PLA/PVA/SA fiber membranes for wound healing. *Polymers*. <https://doi.org/10.3390/POLYM12040839>
- Bilbao-Sainz C, Chiou BS, Valenzuela-Medina D, Du WX, Gregorski KS, Williams TG, Wood DF, Glenn GM, Orts WJ (2014) Solution blow spun poly(lactic acid)/hydroxypropyl methylcellulose nanofibers with antimicrobial properties. *Eur Polym J* 54(1):1–10. <https://doi.org/10.1016/j.eurpolymj.2014.02.004>
- Bledzki A (1999) Composites reinforced with cellulose based fibres. *Prog Polym Sci* 24(2):221–274. [https://doi.org/10.1016/S0079-6700\(98\)00018-5](https://doi.org/10.1016/S0079-6700(98)00018-5)
- Bouriche S, Alonso-García A, Cárceles-Rodríguez CM, Rezgui F, Fernández-Varón E (2021) An in vivo pharmacokinetic study of metformin microparticles as an oral sustained release formulation in rabbits. *BMC Vet Res* 17(1):1–11. <https://doi.org/10.1186/s12917-021-03016-3>
- Braun B, Dorgan JR, Knauss DM (2006) Reactively compatibilized cellulosic polylactide microcomposites. *J Polym Environ* 14(1):49–58. <https://doi.org/10.1007/s10924-005-8706-y>
- Brzeziński M, Biela T (2015) Micro- and nanostructures of polylactide stereocomplexes and their biomedical applications. *Polym Int* 64(12):1667–1675. <https://doi.org/10.1002/pi.4961>
- Brzeziński M, Socka M, Kost B (2019) Microfluidics for producing polylactide nanoparticles and microparticles and their drug delivery application. *Polym Int* 68(6):997–1014. <https://doi.org/10.1002/pi.5753>
- Brzeziński M, Kost B, Gonciarz W, Krupa A, Socka M, Rogala M (2021) Nanocarriers based on block copolymers of L-proline and lactide: the effect of core crosslinking versus its pH-sensitivity on their cellular uptake. *Eur Polym J* 156:10. <https://doi.org/10.1016/j.eurpolymj.2021.110572>
- Brzeziński M, Biela T (2014) Stereocomplexed polylactides BT - encyclopedia of polymeric nanomaterials. In: Kobayashi S, Müllen K (eds). Springer Berlin Heidelberg, pp. 1–10. https://doi.org/10.1007/978-3-642-36199-9_394-1
- Budtova T, Navard P (2016) Cellulose in NaOH–water based solvents: a review. *Cellulose* 23(1):5–55. <https://doi.org/10.1007/s10570-015-0779-8>
- Cai H, Wang R, Guo X, Song M, Yan F, Ji B, Liu Y (2021a) Combining gemcitabine-loaded macrophage-like nanoparticles and erlotinib for pancreatic cancer therapy. *Mol Pharm* 18(7):2495–2506. <https://doi.org/10.1021/acs.molpharmaceut.0c01225>
- Cai W, Liu J, Zheng L, Xu Z, Chen J, Zhong J, Song Z, Xu X, Chen S, Jiao C, Guo J, Yi Y, Zhang Y (2021b) Study on the anti-infection ability of vancomycin cationic liposome combined with polylactide fracture internal fixator. *Int J Biol Macromol* 167:834–844. <https://doi.org/10.1016/j.ijbiomac.2020.11.039>
- Cailloux J, Raquez J, Lo G, Santana O, Bonnaud L, Dubois P, Lluís M (2019) Melt-processing of cellulose nanofibril/polylactide bionanocomposites via a sustainable polyethylene glycol-based carrier system. *Carbohydr Polym* 224:115188. <https://doi.org/10.1016/j.carbpol.2019.115188>
- Caruso E, Orlandi VT, Malacarne MC, Martegani E, Scanferla C, Pappalardo D, Vigliotta G, Izzo L (2021) Bodipy-loaded micelles based on polylactide as surface coating for photodynamic control of staphylococcus aureus. *Coatings* 11(2):1–14. <https://doi.org/10.3390/coatings11020223>
- Casalini T, Rossi F, Castrovinci A, Perale G (2019) A perspective on polylactic acid-based polymers use for nanoparticles synthesis and applications. *Front Bioeng Biotechnol* 7:1–16. <https://doi.org/10.3389/fbioe.2019.00259>
- Castro OC, Ribeiro Filho AS, Nogueira V (1988) Cellulose membrane a temporary skin substitute. In: HFA: publicação técnico-científica, Brasília, Vol 3, Issue 3, pp 209–232
- Caylak S, Ertas M, Donmez Cavdar A, Angin N (2021) Mechanical characteristics and hydrophobicity of alkyl ketene dimer compatibilized hybrid biopolymer composites. *Polym Compos* 42(5):2324–2333. <https://doi.org/10.1002/pc.25980>
- Cheng Y, Deng S, Chen P, Ruan R (2009) Polylactic acid (PLA) synthesis and modifications: a review. *Front Chem China* 4(3):259–264. <https://doi.org/10.1007/s11458-009-0092-x>
- Cheng F, Liu C, Wei X, Yan T, Li H, He J, Huang Y (2017) Preparation and characterization of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO)-oxidized cellulose nanocrystal/alginate biodegradable composite dressing for hemostasis applications. *ACS Sustain Chem Eng* 5(5):3819–3828. <https://doi.org/10.1021/acssuschemeng.6b02849>
- Choi HS, Lee Y, Kim YH (2020) Characteristics of cellulose acetate-g-Poly(L-lactic Acid) (CA-g-PLA) and its application as a compatibilizer for CA/PLA blends. *Polym Korea* 44(3):309–317. <https://doi.org/10.7317/pk.2020.44.3.309>
- Cidreira ACM, de Castro KC, Hatami T, Linan LZ, Mei LHI (2021) Cellulose nanocrystals-based materials as hemostatic agents for wound dressings: a review. *Biomed Microdevice* 23(4):43. <https://doi.org/10.1007/s10544-021-00581-0>
- Ciecholewska-Juško D, Żywicka A, Junka A, Drozd R, Sobolewski P, Migdał P, Kowalska U, Toporkiewicz M, Fijałkowski K (2021) Superabsorbent crosslinked bacterial cellulose biomaterials for chronic wound dressings. *Carbohydr Polym* 253:10. <https://doi.org/10.1016/j.carbpol.2020.117247>
- Coltelli MB, Mallegni N, Rizzo S, Fiori S, Signori F, Lazzeri A (2021) Compatibilization of poly(Lactic acid) (PLA)/plasticized cellulose acetate extruded blends through the addition of reactively extruded comb copolymers. *Molecules*. <https://doi.org/10.3390/molecules26072006>
- Cools P, De Geyter N, Morent R (2014) PLA enhanced via plasma technology: a review. In: New developments in polylactic acid research (Issue December)
- Correia J, Rainert KT, Oliveira FR, de Cássia Siqueira Curto Valle R, Valle JAB (2020) Cationization of cotton fiber: an integrated view of cationic agents, processes variables, properties, market and future prospects.

- Cellulose 27(15):8527–8550. <https://doi.org/10.1007/s10570-020-03361-w>
- Couturaud B, Baldo A, Mas A, Robin JJ (2015) Improvement of the interfacial compatibility between cellulose and poly(l-lactide) films by plasma-induced grafting of l-lactide: The evaluation of the adhesive properties using a peel test. *J Colloid Interface Sci* 448:427–436. <https://doi.org/10.1016/j.jcis.2015.02.035>
- de Oliveira RS, Fantaus SS, Guillot AJ, Melero A, Beck RCR (2021) 3d-printed products for topical skin applications: From personalized dressings to drug delivery. *Pharmaceutics*. <https://doi.org/10.3390/pharmaceutics13111946>
- DeStefano V, Khan S, Tabada A (2020) Applications of PLA in modern medicine. *Eng Regen* 1:76–87. <https://doi.org/10.1016/j.engreg.2020.08.002>
- Diment LE, Thompson MS, Bergmann JHM (2017) Clinical efficacy and effectiveness of 3D printing: a systematic review. *BMJ Open*. <https://doi.org/10.1136/bmjopen-2017-016891>
- do Reis SRR, Helal-Neto E, da Silva de Barros AO, Pinto SR, Portilho FL, de Oliveira Siqueira LB, Alencar LMR, Dahoumane SA, Alexis F, Ricci-Junior E, Santos-Oliveira R (2021) Dual encapsulated dacarbazine and zinc phthalocyanine polymeric nanoparticle for photodynamic therapy of melanoma. *Pharma Res* 38(2):335–346. <https://doi.org/10.1007/s11095-021-02999-w>
- Domínguez-Robles J, Martin NK, Fong ML, Stewart SA, Irwin NJ, Rial-Hermida MI, Donnelly RF, Larrañeta E (2019) Antioxidant pla composites containing lignin for 3D printing applications: a potential material for healthcare applications. *Pharmaceutics* 11(4):5–7. <https://doi.org/10.3390/pharmaceutics11040165>
- Dong J, Li M, Zhou L-L, Lee S-Y, Mei C, Xu X, Wu Q (2017) The influence of grafted cellulose nanofibers and post-extrusion annealing treatment on selected properties of poly(lactic acid) filaments for 3D printing. *J Polym Sci Part B: Polym Phys* 55(11):847–855. <https://doi.org/10.1002/polb.24333>
- Dong W, Zhou M, Li Y, Zhai S, Jin K, Fan Z, Zhao H, Zou W, Cai Z (2020) Low-salt dyeing of cotton fabric grafted with pH-responsive cationic polymer of polyelectrolyte 2-(N, N-dimethylamino)ethyl methacrylate. *Colloids Surf A* 594:124573. <https://doi.org/10.1016/j.colsurfa.2020.124573>
- Dong A, Wu H, Liu R, Wang Q, Fan X, Dong Z (2021) Horseradish peroxidase-mediated functional hydrophobization of jute fabrics to enhance mechanical properties of jute/thermoplastic composites. *Polym Eng Sci* 61(3):731–741. <https://doi.org/10.1002/pen.25612>
- Du H, Liu W, Zhang M, Si C, Zhang X, Li B (2019) Cellulose nanocrystals and cellulose nanofibrils based hydrogels for biomedical applications. *Carbohydr Polym* 209:130–144. <https://doi.org/10.1016/j.carbpol.2019.01.020>
- Dufresne A (2017) 1. Cellulose and potential reinforcement. In: *Nanocellulose: from nature to high performance tailored materials*. De Gruyter, pp 1–46. <https://doi.org/10.1515/9783110480412-002>
- Dydak K, Junka A, Dydak A, Brożyna M, Paleczny J, Fijałkowski K, Kubiela G, Aniołek O, Bartoszewicz M (2021) In vitro efficacy of bacterial cellulose dressings chemisorbed with antiseptics against biofilm formed by pathogens isolated from chronic wounds. *Int J Mol Sci*. <https://doi.org/10.3390/ijms22083996>
- Echeverría C, Muñoz-Bonilla A, Cuervo-Rodríguez R, López D, Fernández-García M (2019) Antibacterial PLA fibers containing thiazolium groups as wound dressing materials. *ACS Appl Bio Mater* 2(11):4714–4719. <https://doi.org/10.1021/acsabm.9b00923>
- Edwards JV, Prevost NT, Yager D, Mackin R, Santiago M, Chang S, Condon B, Dacorta J (2022) Ascorbic acid as an adjuvant to unbleached cotton promotes antimicrobial activity in spunlace nonwovens. *Int J Mol Sci* 23(7):10. <https://doi.org/10.3390/ijms23073598>
- Elliott JR (1957) The development of cotton wool as a wound dressing. *Med Hist* 1(4):362–366. <https://doi.org/10.1017/S002572730002161X>
- Elsababy M, Song Y, Eissa NG, Khan S, Hamad MA, Wooley KL (2021) Morphologic design of sugar-based polymer nanoparticles for delivery of antidiabetic peptides. *J Control Release* 334:1–10. <https://doi.org/10.1016/j.jconrel.2021.04.006>
- Estupiñán Ó, Niza E, Bravo I, Rey V, Tornín J, Gallego B, Clemente-Casares P, Moris F, Ocaña A, Blanco-Lorenzo V, Rodríguez-Santamaría M, Vallina-Álvarez A, González MV, Rodríguez A, Hermida-Merino D, Alonso-Moreno C, Rodríguez R (2021) Mithramycin delivery systems to develop effective therapies in sarcomas. *J Nanobiotechnol* 19(1):1–21. <https://doi.org/10.1186/s12951-021-01008-x>
- Fadakar Sarkandi A, Montazer M, Harifi T, Mahmoudi Rad M (2021) Innovative preparation of bacterial cellulose/silver nanocomposite hydrogels: In situ green synthesis, characterization, and antibacterial properties. *J Appl Polym Sci* 138(6):1–12. <https://doi.org/10.1002/app.49824>
- Fan T, Daniels R (2021) Preparation and characterization of electrospun polylactic acid (PLA) fiber loaded with birch bark triterpene extract for wound dressing. *AAPS PharmSciTech* 22(6):205. <https://doi.org/10.1208/s12249-021-02081-z>
- Fang Y, Zhu X, Wang N, Zhang X, Yang D, Nie J, Ma G (2019) Biodegradable core-shell electrospun nanofibers based on PLA and γ -PGA for wound healing. *Eur Polym J* 116:30–37. <https://doi.org/10.1016/j.eurpolymj.2019.03.050>
- Fatehi P, Abbasi M (2020) Medicinal plants used in wound dressings made of electrospun nanofibers. *J Tissue Eng Regen Med* 14(11):1527–1548. <https://doi.org/10.1002/term.3119>
- Ferrari M, Cirisano F, Carmen Morán M (2019) Mammalian cell behavior on hydrophobic substrates: influence of surface properties. *Colloids Interfaces* 3(2):10. <https://doi.org/10.3390/colloids3020048>
- Fogh K, Nielsen J (2015) Clinical utility of foam dressings in wound management: a review. *Chronic Wound Care Manag Res* 2:31. <https://doi.org/10.2147/CWCMR.S50832>
- Foong CY, Hamzah MSA, Razak SIA, Saidin S, Nayan NHM (2018) Influence of poly(lactic acid) layer on the physical and antibacterial properties of dry bacterial cellulose sheet for potential acute wound healing materials. *Fibers Polym* 19(2):263–271. <https://doi.org/10.1007/s12221-018-7850-7>

- Francesco A, Petkova P, Tzanov T (2018) Hydrogel dressings for advanced wound management. *Curr Med Chem* 25(41):5782–5797. <https://doi.org/10.2174/0929867324666170920161246>
- Freitas Jr RA (1999) Nanomedicine, volume I: basic capabilities. In: *Nanomedicine: vol I*. <http://www.nanomedicine.com/NMI.htm>
- French AD (2014) Idealized powder diffraction patterns for cellulose polymorphs. *Cellulose* 21(2):885–896. <https://doi.org/10.1007/s10570-013-0030-4>
- French AD (2017) Glucose, not cellobiose, is the repeating unit of cellulose and why that is important. *Cellulose* 24(11):4605–4609. <https://doi.org/10.1007/s10570-017-1450-3>
- French AD (2020) Increment in evolution of cellulose crystallinity analysis. *Cellulose* 27(10):5445–5448. <https://doi.org/10.1007/s10570-020-03172-z>
- Gassan J, Chate A, Błędzki AK (2001) Calculation of elastic properties of natural fibers. *J Mater Sci* 36:3715–3720. <https://doi.org/10.1023/A:1017969615925>
- Gębarowski T, Wiatrak B, Janeczka M, Żuk M, Pistor P, Gąsiorowski K (2020) Were our ancestors right in using flax dressings? Research on the properties of flax fibre and its usefulness in wound healing. *Oxid Med Cell Longev*. <https://doi.org/10.1155/2020/1682317>
- Ghamkhari A, Abbaspour-Ravasjani S, Talebi M, Hamishehkar H, Hamblin MR (2021) Development of a graphene oxide-poly lactide nanocomposite as a Smart Drug Delivery System. *Int J Biol Macromol* 169:521–531. <https://doi.org/10.1016/j.ijbiomac.2020.12.084>
- Ghorbanizamani F, Moulahoum H, Bayir E, Zihnioglu F, Timur S (2021) Glutathione encapsulation in core-shell drug nanocarriers (polymersomes and niosomes) prevents advanced glycation end-products toxicities. *Int J Pept Res Ther* 27(4):2809–2821. <https://doi.org/10.1007/s10989-021-10291-z>
- Giram PS (2021) Evaluation of biocompatibility of synthesized low molecular weight PLGA copolymers using zinc L-proline through green route for biomedical application. 1–14. <https://doi.org/10.1002/pat.5452>
- Giri BR, Poudel S, Kim DW (2021) Cellulose and its derivatives for application in 3D printing of pharmaceuticals. *J Pharm Investig*. <https://doi.org/10.1007/s40005-020-00498-5>
- Gomaa SF, Madkour TM, Moghannem S, El-Sherbiny IM (2017) New polylactic acid/ cellulose acetate-based antimicrobial interactive single dose nanofibrous wound dressing mats. *Int J Biol Macromol*. <https://doi.org/10.1016/j.ijbiomac.2017.07.145>
- Gorlachova M, Mahltig B (2021) 3D-printing on textiles—an investigation on adhesion properties of the produced composite materials. *J Polym Res* 28(6):1–10. <https://doi.org/10.1007/s10965-021-02567-1>
- Graça MFP, de Melo-Diogo D, Correia IJ, Moreira AF (2021) Electrospun asymmetric membranes as promising wound dressings: a review. *Pharmaceutics* 13(2):183. <https://doi.org/10.3390/pharmaceutics13020183>
- Grgac SF, Tarbuk A, Dekanic T, Sujka W, Draczynski Z (2020) The chitosan implementation into cotton and polyester/cotton blend fabrics. *Materials* 13(7):1–19. <https://doi.org/10.3390/ma13071616>
- Guan YY, Zeng SQ, Qin Y, Mu Y, Liu H (2021) Vitamin E-tocopheryl polyethylene glycol succinate decorated drug delivery system with synergistic antitumor effects to reverse drug resistance and immunosuppression. *Colloids Surf A Physicochem Eng Asp*. <https://doi.org/10.1016/j.colsurfa.2021.127387>
- Gullo M, Sola A, Zanichelli G, Montorsi M, Messori M, Giudici P (2017) Increased production of bacterial cellulose as starting point for scaled-up applications. *Appl Microbiol Biotechnol* 101(22):8115–8127. <https://doi.org/10.1007/s00253-017-8539-3>
- Güney Akkurt M, Gülsöy M (2022) Polylactide nanoparticles encapsulating indocyanine green for photothermal therapy of prostate cancer cells. *Photodiagn Photodyn Ther*. <https://doi.org/10.1016/j.pdpdt.2021.102693>
- Guo R, Li K, Tian B, Wang C, Chen X, Jiang X, He H, Hong W (2021a) Elaboration on the architecture of pH-sensitive surface charge-adaptive micelles with enhanced penetration and bactericidal activity in biofilms. *J Nanobiotechnol* 19(1):1–18. <https://doi.org/10.1186/s12951-021-00980-8>
- Guo X, Jin H, Lo PC (2021b) Encapsulating an acid-Activatable phthalocyanine-doxorubicin conjugate and the hypoxia-sensitive tirapazamine in polymeric micelles for multimodal cancer therapy. *Biomater Sci* 9(14):4936–4951. <https://doi.org/10.1039/d1bm00443c>
- Guo Z, Bai Y, Zhang Z, Mei H, Li J, Pu Y, Zhao N, Gao W, Wu F, He B, Xie J (2021c) Thermosensitive polymer hydrogel as a physical shield on colonic mucosa for colitis treatment. *J Mater Chem B* 9(18):3874–3884. <https://doi.org/10.1039/d1tb00499a>
- Gupta AP, Kumar V (2007) New emerging trends in synthetic biodegradable polymers—polylactide: a critique. *Eur Polym J* 43(10):4053–4074. <https://doi.org/10.1016/j.eurpolymj.2007.06.045>
- Hajikhani M, Emam-Djomeh Z, Askari G (2021a) Fabrication and characterization of mucoadhesive bioplastic patch via coaxial polylactic acid (PLA) based electrospun nanofibers with antimicrobial and wound healing application. *Int J Biol Macromol* 172:143–153. <https://doi.org/10.1016/j.ijbiomac.2021.01.051>
- Hajikhani M, Emam Djomeh Z, Askari G (2021b) Lycopene loaded polylactic acid (PLA) and PLA/copolymer electrospun nanofibers, synthesis, characterization, and control release. *J Food Process Preserv* 45(1):e15055. <https://doi.org/10.1111/jfpp.15055>
- Han H, Liu C, Zhu J, Li FX, Wang XL, Yu JY, Qin XH, Wu DQ (2020) Contact/release coordinated antibacterial cotton fabrics coated with n-halalamin and cationic antibacterial agent for durable bacteria-killing application. *Int J Mol Sci* 21(18):1–14. <https://doi.org/10.3390/ijms21186531>
- He J, Hu X, Cao J, Zhang Y, Xiao J, Peng L, Chen D, Xiong C, Zhang L (2021) Chitosan-coated hydroxyapatite and drug-loaded poly(trimethylene carbonate)/polylactic acid scaffold for enhancing bone regeneration. *Carbohydr Polym* 253:117198. <https://doi.org/10.1016/j.carbpol.2020.117198>
- Hendrick E, Frey M (2014) Increasing surface hydrophilicity in poly(lactic acid) electrospun fibers by addition of

- Pla-B-Peg co-polymers. *J Eng Fibers Fabr* 9(2):153–164. <https://doi.org/10.1177/155892501400900219>
- Hermann A, Hill S, Metz A, Heck J, Hoffmann A, Hartmann L, Herres-Pawlis S (2020) Next generation of zinc bisguanidine polymerization catalysts towards highly crystalline, biodegradable polyesters. *Angew Chem* 59(48):21778–21784. <https://doi.org/10.1002/anie.202008473>
- Higazy IM, Mahmoud AA, Ghorab MM, Ammar HO (2021) Development and evaluation of polyvinyl alcohol stabilized polylactide-co-caprolactone-based nanoparticles for brain delivery. *J Drug Deliv Sci Technol*. <https://doi.org/10.1016/j.jddst.2020.102274>
- Hindi SSZ (2016) The interconvertibility of cellulose's allomorphs. *BioCrystal J* 1(11):1–12. <https://doi.org/10.15680/IJRSET.2017.0601125>
- Hirai A, Tsuji M, Horii F (1997) Culture conditions producing structure entities composed of Cellulose I and II in bacterial cellulose. *Cellulose* 4(3):239–245. <https://doi.org/10.1023/A:1018439907396>
- Ho MH, Claudia JC, Tai WC, Huang KY, Lai CH, Chang CH, Chang YC, Wu YC, Kuo MYP, Chang PC (2021) The treatment response of barrier membrane with amoxicillin-loaded nanofibers in experimental periodontitis. *J Periodontol* 92(6):886–895. <https://doi.org/10.1002/JPER.20-0256>
- Hosny KM, Alkhalidi HM, Alharbi WS, Md S, Sindi AM, Ali SA, Bakhaidar RB, Almeahady AM, Alfayez E, Kurakula M (2022) Recent trends in assessment of cellulose derivatives in designing novel and nanoparticulate-based drug delivery systems for improvement of oral health. *Polymers*. <https://doi.org/10.3390/polym14010092>
- Hrib J, Sirc J, Hobzova R, Hampejsova Z, Bosakova Z, Munzarova M, Michalek J (2015) Nanofibers for drug delivery - Incorporation and release of model molecules, influence of molecular weight and polymer structure. *Beilstein J Nanotechnol* 6(1):1939–1945. <https://doi.org/10.3762/bjnano.6.198>
- Hu Y, Liu H, Zhou X, Pan H, Wu X, Abidi N, Zhu Y, Wang J (2019) Surface engineering of spongy bacterial cellulose via constructing crossed groove/column micropattern by low-energy CO₂ laser photolithography toward scar-free wound healing. *Mater Sci Eng C* 99(1):333–343. <https://doi.org/10.1016/j.msec.2019.01.116>
- Hu JK, Suh HW, Qureshi M, Lewis JM, Yaqoob S, Moscato ZM, Griff S, Lee AK, Yin ES, Mark Saltzman W, Girardi M (2021) Nonsurgical treatment of skin cancer with local delivery of bioadhesive nanoparticles. *Proc Natl Acad Sci USA* 118(7):1–8. <https://doi.org/10.1073/pnas.2020575118>
- Huang CY, Lin SY, Hsu TA, Hsieh HP, Huang MH (2021a) Colloidal assemblies composed of polymeric micellar/emulsified systems integrate cancer therapy combining a tumor-associated antigen vaccine and chemotherapeutic regimens. *Nanomaterials*. <https://doi.org/10.3390/nano11071844>
- Huang T, Dongfang K, Ek M (2021b) Hydrophobization of cellulose oxalate using oleic acid in a catalyst-free esterification suitable for preparing reinforcement in polymeric composites. *Carbohydr Polym* 257:117615. <https://doi.org/10.1016/j.carbpol.2021.117615>
- Huang X, Huang D, Zhu T, Yu X, Xu K, Li H, Qu H, Zhou Z, Cheng K, Wen W, Ye Z (2021c) Sustained zinc release in cooperation with CaP scaffold promoted bone regeneration via directing stem cell fate and triggering a pro-healing immune stimuli. *J Nanobiotechnol* 19(1):1–20. <https://doi.org/10.1186/s12951-021-00956-8>
- Huang Y, Jin Y, Wang B, Tian H, Weng Y, Sun K, Men S (2022) Preparation and characterization of compatibilized and toughened polylactic acid/cellulose acetate films by long-chain hyperbranched polymers. *J Appl Polym Sci* 139(19):52097. <https://doi.org/10.1002/app.52097>
- Ifuku S, Tsuji M, Morimoto M, Saimoto H, Yano H (2009) Synthesis of silver nanoparticles templated by TEMPO-mediated oxidized bacterial cellulose nanofibers. *Biomacromolecules* 10(9):2714–2717. <https://doi.org/10.1021/bm9006979>
- Inai R, Kotaki M, Ramakrishna S (2005) Structure and properties of electrospun PLLA single nanofibres. *Nanotechnology* 16(2):208–213. <https://doi.org/10.1088/0957-4484/16/2/005>
- Ishizaki T, Saito N, Takai O (2010) Correlation of cell adhesive behaviors on superhydrophobic, superhydrophilic, and micropatterned superhydrophobic/superhydrophilic surfaces to their surface chemistry. *Langmuir* 26(11):8147–8154. <https://doi.org/10.1021/la904447c>
- Jain A, Kunduru KR, Basu A, Mizrahi B, Domb AJ, Khan W (2016) Injectable formulations of poly(lactic acid) and its copolymers in clinical use. *Adv Drug Deliv Rev* 107:213–227. <https://doi.org/10.1016/j.addr.2016.07.002>
- Jirawitchalart S, Mitaim S, Chen CY, Patikarnmonthon N (2022) Cotton cellulose-derived hydrogel and electrospun fiber as alternative material for wound dressing application. *Int J Biomater*. <https://doi.org/10.1155/2022/2502658>
- Kamber NE, Jeong W, Waymouth RM, Pratt RC, Lohmeijer BGG, Hedrick JL (2007) Organocatalytic ring-opening polymerization. *Chem Rev* 107(12):5813–5840. <https://doi.org/10.1021/cr068415b>
- Kamel S, Khattab TA (2020) Recent advances in cellulose-based biosensors for medical diagnosis. *Biosensors* 10(6):1–26. <https://doi.org/10.3390/BIOS10060067>
- Kammann T, Hoff J, Yildirim I, Shkodra B, Müller T, Weber C, Gräler MH, Maus UA, Paton JC, Singer M, Traeger A, Schubert US, Bauer M, Press AT (2021) Intracellularly released cholesterol from polymer-based delivery systems alters cellular responses to pneumolysin and promotes cell survival. *Metabolites* 11(12):1–14. <https://doi.org/10.3390/metabo11120821>
- Kanikireddy V, Varaprasad K, Jayaramudu T, Karthikeyan C, Sadiku R (2020) Carboxymethyl cellulose-based materials for infection control and wound healing: a review. *Int J Biol Macromol* 164:963–975. <https://doi.org/10.1016/j.ijbiomac.2020.07.160>
- Kanmaz D, Aylin Karahan Toprakci H, Olmez H, Toprakci O (2018) Electrospun polylactic acid based nanofibers for biomedical applications. *Mater Sci Res India* 15(3):224–240. <https://doi.org/10.13005/msri/150304>
- Kesavan SK, Selvaraj D, Perumal S, Arunachalaksi A, Ganesan N, Chinnaiyan SK, Balaraman M (2022) Fabrication of hybrid povidone-iodine impregnated

- collagen-hydroxypropyl methylcellulose composite scaffolds for wound-healing application. *J Drug Deliv Sci Technol* 70:103247. <https://doi.org/10.1016/j.jddst.2022.103247>
- Khamrai M, Banerjee SL, Kundu PP (2017) Modified bacterial cellulose based self-healable polyelectrolyte film for wound dressing application. *Carbohydr Polym* 174:580–590. <https://doi.org/10.1016/j.carbpol.2017.06.094>
- Khattak S, Qin X-T, Wahid F, Huang L-H, Xie Y-Y, Jia S-R, Zhong C (2020) Permeation of silver sulfadiazine into TEMPO-oxidized bacterial cellulose as an antibacterial agent. *Front Bioeng Biotechnol* 8:616467. <https://doi.org/10.3389/fbioe.2020.616467>
- Kim DY, Ju HJ, Kim JH, Choi S, Kim MS (2021) Injectable: In situ forming hydrogel gene depot to improve the therapeutic effect of STAT3 shRNA. *Biomater Sci* 9(12):4459–4472. <https://doi.org/10.1039/d1bm00624j>
- Kittinaovarat S, Hengprapakron N, Janvikul W (2012) Comparative multifunctional properties of partially carboxymethylated cotton gauze treated by the exhaustion or pad-dry-cure methods. *Carbohydr Polym* 87(1):16–23. <https://doi.org/10.1016/j.carbpol.2011.08.072>
- Klemm DO, Philipp B, Heinze T, Heinze U, Wagenknecht W (1999) Comprehensive cellulose chemistry. Volume 1. Fundamentals and analytical methods. *J Am Chem Soc* 121(37):8677–8677. <https://doi.org/10.1021/ja9857514>
- Kodal M, Topuk ZD, Ozkoc G (2015) Dual effect of chemical modification and polymer pre-coating of flax fibers on the properties of short flax fiber/poly(lactic acid) composites. *J Appl Polym Sci*. <https://doi.org/10.1002/app.42564>
- Korica M, Peršin Z, Fras Zemljič L, Mihajlovski K, Dojčinović B, Trifunović S, Vesel A, Nikolić T, Kostić MM (2021) Chitosan nanoparticles functionalized viscose fabrics as potentially durable antibacterial medical textiles. *Materials* 14(13):3762. <https://doi.org/10.3390/ma14133762>
- Kost B, Gonciarz W, Krupa A, Socka M, Rogala M, Biela T, Brzeziński M (2021) pH-tunable nanoparticles composed of copolymers of lactide and allyl-glycidyl ether with various functionalities for the efficient delivery of anti-cancer drugs. *Colloids Surf B* 204:111801. <https://doi.org/10.1016/j.colsurfb.2021.111801>
- Kowalski A, Duda A, Penczek S (2000) Kinetics and mechanism of cyclic esters polymerization initiated with tin(II) octoate. 3. Polymerization of L,L-dilactide. *Macromolecules* 33(20):7359–7370. <https://doi.org/10.1021/ma000125o>
- Kruse M, Greuel M, Kreimendahl F, Schneiders T, Bauer B, Gries T, Jockenhoevel S (2018) Electro-spun PLA-PEG-yarns for tissue engineering applications. *Biomed Tech* 63(3):231–243. <https://doi.org/10.1515/bmt-2017-0232>
- Kudryavtseva VL, Zhuravlev, MV, Tverdokhlebov SI (2017) Surface modification of polylactic acid films by atmospheric pressure plasma treatment. *AIP Conference Proceedings*, 1882. <https://doi.org/10.1063/1.5001616>
- Kumari A, Yadav SK, Yadav SC (2010) Biodegradable polymeric nanoparticles based drug delivery systems. *Colloids Surf B* 75(1):1–18. <https://doi.org/10.1016/j.colsurfb.2009.09.001>
- Lafia-Araga RA, Sabo R, Nabinejad O, Matuana L, Stark N (2021) Influence of lactic acid surface modification of cellulose nanofibrils on the properties of cellulose nanofibril films and cellulose nanofibril-poly(lactic acid) composites. *Biomolecules* 11(9):1346. <https://doi.org/10.3390/biom11091346>
- Lao J, Deng W (2021) Research progress of absorbable oxidized regenerated cellulose hemostatic materials. *Anesth Clin Res* 12(8):1–2. <https://doi.org/10.35248/2155-6148.21.12.1017>
- Lazarini SC, Yamada C, Barud HS, Trovatti E, Corbi PP, Lustrri WR (2018) Influence of chemical and physical conditions in selection of *Gluconacetobacter hansenii* ATCC 23769 strains with high capacity to produce bacterial cellulose for application as sustained antimicrobial drug-release supports. *J Appl Microbiol* 125(3):777–791. <https://doi.org/10.1111/jam.13916>
- Lee SH, Yeo SY (2016) Improvement of hydrophilicity of polylactic acid (PLA) fabrics by means of a proteolytic enzyme from *Bacillus licheniformis*. *Fibers Polym* 17(8):1154–1161. <https://doi.org/10.1007/s12221-016-5923-z>
- Lee K-Y, Bharadia P, Blaker JJ, Bismarck A (2012) Fabrication of oxidized bacterial cellulose by nitrogen dioxide in chloroform/cyclohexane as a highly loaded drug carrier for sustained release of cisplatin. *Compos A Appl Sci Manuf* 43(11):2065–2074. <https://doi.org/10.1016/j.compositesa.2012.06.013>
- Lee HJ, Kim IS, Kim SH (2019). Pretreatment of microfibrillated cellulose on polylactide composites. <https://doi.org/10.1007/s13233-020-8016-1>
- Lee JH, Park SH, Kim SH (2020) Surface alkylation of cellulose nanocrystals to enhance their compatibility with polylactide. *Polymers* 12(1):1–16. <https://doi.org/10.3390/polym12010178>
- Li Z, Tan BH, Lin T, He C (2016) Recent advances in stereocomplexation of enantiomeric PLA-based copolymers and applications. *Prog Polym Sci* 62:22–72. <https://doi.org/10.1016/j.progpolymsci.2016.05.003>
- Li Y, Tian Y, Zheng W, Feng Y, Huang R, Shao J, Tang R, Wang P, Jia Y, Zhang J, Zheng W, Yang G, Jiang X (2017) Composites of bacterial cellulose and small molecule-decorated gold nanoparticles for treating gram-negative bacteria-infected wounds. *Small* 13(27):1–10. <https://doi.org/10.1002/sml.201700130>
- Li G, Zhao M, Xu F, Yang B, Li X, Meng X, Teng L, Sun F, Li Y (2020) Synthesis and biological application of polylactic acid. *Molecules*. <https://doi.org/10.3390/molecules25215023>
- Li F, Yu X, Huang Z, Liu D (2021a) Interfacial improvements in cellulose nanofibers reinforced polylactide bionanocomposites prepared by in situ reactive extrusion. *Polym Adv Technol* 32(6):2352–2366. <https://doi.org/10.1002/pat.5264>
- Li Yi, Yang HY, Lee DS (2021b) Advances in biodegradable and injectable hydrogels for biomedical applications. *J Control Release* 330:151–160. <https://doi.org/10.1016/j.jconrel.2020.12.008>
- Li Z, Gao J, Xiang Z, Zhang H, Wang Y, Zhang X (2021c) A pH-responsive polymer linked with immunomodulatory drugs: synthesis, characteristics and in vitro biocompatibility. *J Appl Toxicol* 41(5):724–735. <https://doi.org/10.1002/jat.4042>

- Liang W, Lu Q, Yu F, Zhang J, Xiao C, Dou X, Zhou Y, Mo X, Li J, Lang M (2021) A multifunctional green antibacterial rapid hemostasis composite wound dressing for wound healing. *Biomater Sci* 9(21):7124–7133. <https://doi.org/10.1039/D1BM01185E>
- Liu S, Wang X, Zhang Z, Zhang Y, Zhou G, Huang Y, Xie Z, Jing X (2015) Use of asymmetric multilayer polylactide nanofiber mats in controlled release of drugs and prevention of liver cancer recurrence after surgery in mice. *Nanomed Nanotechnol Biol Med* 11(5):1047–1056. <https://doi.org/10.1016/j.nano.2015.03.001>
- Liu M, Duan X-P, Li Y-M, Yang D-P, Long Y-Z (2017) Electrospun nanofibers for wound healing. *Mater Sci Eng C Mater Biol Appl* 76:1413–1423. <https://doi.org/10.1016/j.msec.2017.03.034>
- Liu S, Liu M, Wu G, Zhang X, Yu J, Zhang Y, Wang P, Yin X (2019) Enhanced surface hydrophilicity of polylactic acid sutures treated by lipase and chitosan. *Text Res J* 89(16):3291–3302. <https://doi.org/10.1177/0040517518811936>
- Liu H, Liu K, Han X, Xie H, Si C, Liu W, Bae Y-S (2020) Cellulose nanofibrils-based hydrogels for biomedical applications: progresses and challenges. *Curr Med Chem* 27(28):4622–4646. <https://doi.org/10.2174/0929867327666200303102859>
- Lourenço BN, Marchioli G, Song W, Reis RL, van Blitterswijk CA, Karperien M, van Apeldoorn A, Mano JF (2012) Wettability influences cell behavior on superhydrophobic surfaces with different topographies. *Biointerphases* 7(1–4):1–11. <https://doi.org/10.1007/s13758-012-0046-6>
- Luan Y, Wu J, Zhan M, Zhang J, Zhang J, He J (2013) “One pot” homogeneous synthesis of thermoplastic cellulose acetate-graft-poly(l-lactide) copolymers from unmodified cellulose. *Cellulose* 20(1):327–337. <https://doi.org/10.1007/s10570-012-9818-x>
- Lumbreras-Aguayo A, Meléndez-Ortiz HI, Puente-Urbina B, Alvarado-Canché C, Ledezma A, Romero-García J, Betancourt-Galindo R (2019a) Poly(methacrylic acid)-modified medical cotton gauzes with antimicrobial and drug delivery properties for their use as wound dressings. *Carbohydr Polym* 205:203–210. <https://doi.org/10.1016/j.carbpol.2018.10.015>
- Lumbreras-Aguayo A, Meléndez-Ortiz HI, Puente-Urbina B, Alvarado-Canché C, Ledezma A, Romero-García J, Betancourt-Galindo R (2019b) Poly(methacrylic acid)-modified medical cotton gauzes with antimicrobial and drug delivery properties for their use as wound dressings. *Carbohydr Polym* 205:203–210. <https://doi.org/10.1016/j.carbpol.2018.10.015>
- Ma Y, Qian S, Hu L, Qian J, Fontanillo Lopez CA, Xu L (2019) Mechanical, thermal, and morphological properties of PLA biocomposites toughened with silylated bamboo cellulose nanowhiskers. *Polym Compos* 40(8):3012–3019. <https://doi.org/10.1002/pc.25144>
- Ma G, Du X, Zhu J, Xu F, Yu H, Li J (2021) Multi-functionalized dendrimers for targeted co-delivery of sorafenib and paclitaxel in liver cancers. *J Drug Deliv Sci Technol*. <https://doi.org/10.1016/j.jddst.2021.102493>
- Maleki H, Azimi B, Ismaeilimoghadam S, Danti S (2022) Poly(lactic acid)-based electrospun fibrous structures for biomedical applications. *Appl Sci*. <https://doi.org/10.3390/app12063192>
- Menclová K, Svoboda P, Hadač J, Doležel R, Ryska M, Mandys V, Pohnán R (2021a) Regenerative abilities of a nanofiber wound dressing based on polylactide. *Rozhledy v Chirurgii: Měsíčník Československé Chirurgické Společnosti* 100(9):435–439. <https://doi.org/10.33699/PIS.2021.100.9.435-439>
- Menclová K, Svoboda P, Hadač J, Juhás Š, Juhásová J, Pejchal J, Mandys V, Eminger K, Ryska M (2021b) Nanofiber wound dressing materials—a comparative study of wound healing on a porcine model. *Mil Med*. <https://doi.org/10.1093/milmed/usab155>
- Mendes BB, Conniot J, Avital A, Yao D, Jiang X, Zhou X, Sharf-Pauker N, Xiao Y, Adir O, Liang H, Shi J, Schroeder A, Conde J (2022) Nanodelivery of nucleic acids. *Nat Rev Methods Prim*. <https://doi.org/10.1038/s43586-022-00104-y>
- Mezzasalma L, Dove AP, Coulembier O (2017) Organocatalytic ring-opening polymerization of L-lactide in bulk: a long standing challenge. *Eur Polym J* 95(March):628–634. <https://doi.org/10.1016/j.eurpolymj.2017.05.013>
- Miao C, Hamad WY (2016) In-situ polymerized cellulose nanocrystals (CNC)—poly(L-lactide) (PLLA) nanomaterials and applications in nanocomposite processing. *Carbohydr Polym* 153:549–558. <https://doi.org/10.1016/j.carbpol.2016.08.012>
- Michalski A, Brzezinski M, Lapienis G, Biela T (2019) Star-shaped and branched polylactides: synthesis, characterization, and properties. *Prog Polym Sci*. <https://doi.org/10.1016/j.progpolymsci.2018.10.004>
- Mohd Ghazali AE, Pickering KL (2021) The effect of fibre surface treatment and coupling agents to improve the performance of natural fibres in PLA composites. *J Polym Eng* 41(10):842–853. <https://doi.org/10.1515/polyeng-2021-0120>
- Mohebian Z, Tajmohammadi I, Yavari Maroufi L, Ramezani S, Ghorbani M (2022) A novel aloe vera-loaded ethylcellulose/hydroxypropyl methylcellulose nanofibrous mat designed for wound healing application. *J Polym Environ* 30(3):867–877. <https://doi.org/10.1007/s10924-021-02240-0>
- Mohiti-Asli M, Lobo EG (2016) Nanofibrous smart bandages for wound care. In: *Wound healing biomaterials*. Elsevier, pp 483–499. <https://doi.org/10.1016/B978-1-78242-456-7.00023-4>
- Mohsenimehr S, Khani MR, Fani N, Baghaban Eslaminejad MR, Shokri B, Ghassami A (2020) Surface modification of PLA scaffold using radio frequency (RF) nitrogen plasma in tissue engineering application. *Surf Topogr Metrol Prop* 8(1):015012. <https://doi.org/10.1088/2051-672X/ab7c30>
- Molapour Rashedi S, Khajavi R, Rashidi A, Rahimi MK, Bahador A (2021) Nanocomposite-coated sterile cotton gauze based on polylactic acid and nanoparticles (zinc oxide and copper oxide) and tranexamic acid drug with the aim of wound dressing. *Regener Eng Transl Med* 7(2):200–217. <https://doi.org/10.1007/s40883-021-00203-4>
- Montaser AS, Rehan M, El-Senousy WM, Zaghoul S (2020) Designing strategy for coating cotton gauze fabrics and its application in wound healing. *Carbohydr Polym*

- 244:116479. <https://doi.org/10.1016/j.carbpol.2020.116479>
- Moritz S, Wiegand C, Wesarg F, Hessler N, Müller FA, Kralisch D, Hipler UC, Fischer D (2014) Active wound dressings based on bacterial nanocellulose as drug delivery system for octenidine. *Int J Pharm* 471(1–2):45–55. <https://doi.org/10.1016/j.ijpharm.2014.04.062>
- Murphy CA, Collins MN (2018) Microcrystalline cellulose reinforced poly(lactic acid) biocomposite filaments for 3D printing. *Polym Compos* 39(4):1311–1320. <https://doi.org/10.1002/pc.24069>
- Należcz-Jawecki G, Grabińska-Sota E, Narkiewicz P (2003) The toxicity of cationic surfactants in four bioassays. *Ecotoxicol Environ Saf* 54(1):87–91. [https://doi.org/10.1016/S0147-6513\(02\)00025-8](https://doi.org/10.1016/S0147-6513(02)00025-8)
- Naomi R, Idrus RBH, Fauzi MB (2020) Plant-vs. Bacterial-derived cellulose for wound healing: a review. *Int J Environ Res Public Health* 17(18):1–25. <https://doi.org/10.3390/ijerph17186803>
- Naseem R, Tzivelekis C, German MJ, Gentile P, Ferreira AM, Dalgarno K (2021) Strategies for enhancing polyester-based materials for bone fixation applications. *Molecules*. <https://doi.org/10.3390/molecules26040992>
- Ng H-M, Sin LT, Bee S-T, Tee T-T, Rahmat AR (2017) Review of nanocellulose polymer composite characteristics and challenges. *Polym-Plast Technol Eng* 56(7):687–731. <https://doi.org/10.1080/03602559.2016.1233277>
- Nicoli Aldini N, Fini M, Giardino R (2008) From hippocrates to tissue engineering: surgical strategies in wound treatment. *World Surg* 32(9):2114–2121. <https://doi.org/10.1007/s00268-008-9662-1>
- Nischwitz SP, Popp D, Shubitidze D, Luze H, Zrim R, Klemm K, Rapp M, Haller HL, Feisst M, Kamolz LP (2021) The successful use of polylactide wound dressings for chronic lower leg wounds: A retrospective analysis. *Int Wound J* 2021:1180–1187. <https://doi.org/10.1111/iwj.13713>
- Niza E, Ocaña A, Castro-Osma JA, Bravo I, Alonso-Moreno C (2021) Polyester polymeric nanoparticles as platforms in the development of novel nanomedicines for cancer treatment. *Cancers*. <https://doi.org/10.3390/cancers13143387>
- Noh YK, Dos Santos Da Costa A, Park YS, Du P, Kim IH, Park K (2019) Fabrication of bacterial cellulose-collagen composite scaffolds and their osteogenic effect on human mesenchymal stem cells. *Carbohydr Polym* 219:210–218. <https://doi.org/10.1016/j.carbpol.2019.05.039>
- Nowak A, Ossowicz-rupniewska P, Rakoczy R, Konopacki M, Perużyńska M, Drożdżik M, Makuch E, Duchnik W, Kucharski Ł, Wenelska K, Klimowicz A (2021) Bacterial cellulose membrane containing epilobium angustifolium l. Extract as a promising material for the topical delivery of antioxidants to the skin. *Int J Mol Sci* 22(12):1–21. <https://doi.org/10.3390/ijms22126269>
- Oh JK (2011) Polylactide (PLA)-based amphiphilic block copolymers: synthesis, self-assembly, and biomedical applications. *Soft Matter* 7(11):5096–5108. <https://doi.org/10.1039/c0sm01539c>
- Olonisakin K, Li R, Zhang X, Xiao F, Gao J, Yang W (2021) Effect of TDI-assisted hydrophobic surface modification of microcrystalline cellulose on the tensile fracture of MCC/PLA composite, and estimation of the degree of substitution by linear regression. <https://doi.org/10.1021/acs.langmuir.0c03130>
- Ossowicz-rupniewska P, Rakoczy R, Nowak A, Konopacki M, Klebeko J, Świątek E, Janus E, Duchnik W, Wenelska K, Kucharski Ł, Klimowicz A (2021) Transdermal delivery systems for ibuprofen and ibuprofen modified with amino acids alkyl esters based on bacterial cellulose. *Int J Mol Sci* 22(12):1–18. <https://doi.org/10.3390/ijms22126252>
- Pal N, Banerjee S, Roy P, Pal K (2019) Melt-blending of unmodified and modified cellulose nanocrystals with reduced graphene oxide into PLA matrix for biomedical application. *Polym Adv Technol* 30(12):3049–3060. <https://doi.org/10.1002/pat.4736>
- Parize DDS, de Oliveira JE, Williams T, Wood D, Avena-Bustillos RJ, Klamczynski AP, Glenn GM, Marconcini JM, Mattoso LHC (2017) Solution blow spun nanocomposites of poly(lactic acid)/cellulose nanocrystals from Eucalyptus kraft pulp. *Carbohydr Polym* 174:923–932. <https://doi.org/10.1016/j.carbpol.2017.07.019>
- Pawar RP, Tekale SU, Shisodia SU, Totre JT, Domb AJ (2014) Biomedical applications of poly(lactic acid). *Rec Patents Regener Med* 4(1):40–51. <https://doi.org/10.2174/2210296504666140402235024>
- Peltzer M, Pei A, Zhou Q, Berglund L, Jiménez A (2014) Surface modification of cellulose nanocrystals by grafting with poly(lactic acid). *Polym Int* 63(6):1056–1062. <https://doi.org/10.1002/pi.4610>
- Periyasamy AP (2016) Effect of PVAmHCl pre-treatment on the properties of modal fabric dyed with reactive dyes: an approach for salt free dyeing. *J Text Sci Eng* 6(4):2. <https://doi.org/10.4172/2165-8064.1000262>
- Picheth GF, Pirich CL, Sierakowski MR, Woehl MA, Sakakibara CN, de Souza CF, Martin AA, da Silva R, de Freitas RA (2017) Bacterial cellulose in biomedical applications: a review. *Int J Biol Macromol* 104:97–106. <https://doi.org/10.1016/j.ijbiomac.2017.05.171>
- Pigareva VA, Alekhina YA, Grozdova ID, Zhu X, Spiridonov VV, Sybachin AV (2021) Magneto-sensitive and enzymatic hydrolysis-resistant systems for the targeted delivery of paclitaxel based on polylactide micelles with an external polyethylene oxide corona. *Polym Int*. <https://doi.org/10.1002/pi.6306>
- Portela R, Leal CR, Almeida PL, Sobral RG (2019) Bacterial cellulose: a versatile biopolymer for wound dressing applications. *Microb Biotechnol* 12(4):586–610. <https://doi.org/10.1111/1751-7915.13392>
- Prabhu RH, Patravale VB, Joshi MD (2015) Polymeric nanoparticles for targeted treatment in oncology: Current insights. *Int J Nanomed* 10:1001–1018. <https://doi.org/10.2147/IJN.S56932>
- Qi Y, Ma HL, Du ZH, Yang B, Wu J, Wang R, Zhang XQ (2019) Hydrophilic and antibacterial modification of poly(lactic acid) films by γ -ray irradiation. *ACS Omega* 4(25):21439–21445. <https://doi.org/10.1021/acsomega.9b03132>
- Qiu Y, Qiu L, Cui J, Wei Q (2016) Bacterial cellulose and bacterial cellulose-vaccarin membranes for wound healing. *Mater Sci Eng C* 59:303–309. <https://doi.org/10.1016/j.msec.2015.10.016>
- Radwan NH, Nasr M, Ishak RAH, Awad GAS (2021) Moxifloxacin-loaded in situ synthesized Bioceramic/

- Poly(L-lactide-co- ϵ -caprolactone) composite scaffolds for treatment of osteomyelitis and orthopedic regeneration. *Int J Pharm.* <https://doi.org/10.1016/j.ijpharm.2021.120662>
- Ramot Y, Haim-Zada M, Domb AJ, Nyska A (2016) Biocompatibility and safety of PLA and its copolymers. *Adv Drug Deliv Rev* 107:153–162. <https://doi.org/10.1016/j.addr.2016.03.012>
- Raquez JM, Habibi Y, Murariu M, Dubois P (2013) Polylactide (PLA)-based nanocomposites. *Prog Polym Sci* 38(10–11):1504–1542. <https://doi.org/10.1016/j.progpolymsci.2013.05.014>
- Rathinamoorthy R (2022) Recent trends in the development of smart bacterial cellulose wound dressings. *Indian J Fibre Text Res* 47(1):30–44. <https://doi.org/10.56042/ijfr.v47i1.64914>
- Redondo FL, Giaroli MC, Villar MA, de Freitas AGO, Ciolino AE, Ninago MD (2020) Direct 3D printing of poly(lactic acid) on cotton fibers: characterization of materials and study of adhesion properties of the resulting composites. *Macromol Symp* 394(1):1–7. <https://doi.org/10.1002/masy.201900190>
- Rehan M, Zaghoul S, Mahmoud FA, Montaser AS, Hebeish A (2017) Design of multi-functional cotton gauze with antimicrobial and drug delivery properties. *Mater Sci Eng C* 80:29–37. <https://doi.org/10.1016/j.msec.2017.05.093>
- Revin VV, Dolganov AV, Liyaskina EV, Nazarova NB, Balandina AV, Devyataeva AA, Revin VD (2021) Characterizing bacterial cellulose produced by *Komagataeibacter sucrofermentans* h-110 on molasses medium and obtaining a biocomposite based on it for the adsorption of fluoride. *Polymers.* <https://doi.org/10.3390/polym13091422>
- RoyChoudhury AK (2017) Acid–alkali finish. *Principles Text Finish* 2017:79–108. <https://doi.org/10.1016/b978-0-08-100646-7.00005-9>
- Rusdi RAA, Halim NA, Norizan MN, Abidin ZHZ, Abdullah N, Ros FC, Ahmad N, Azmi AFM (2022) Pre-treatment effect on the structure of bacterial cellulose from *Nata de Coco* (*Acetobacter xylinum*). *Polimery/polymers* 67(3):110–118. <https://doi.org/10.14314/polimery.2022.3.3>
- Rutala WA, Weber DJ (2015) Disinfection, sterilization, and control of hospital waste. In *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. Elsevier, pp 3294–3309.e4. <https://doi.org/10.1016/B978-1-4557-4801-3.00301-5>
- Rytlewski P, Mróz W, Żenkiewicz M, Czwartos J, Budner B (2012) Laser induced surface modification of polylactide. *J Mater Process Technol* 212(8):1700–1704. <https://doi.org/10.1016/j.jmatprotec.2012.03.019>
- Safdari F, Carreau PJ, Heuzey MC, Kamal MR (2017) Effects of poly (ethylene glycol) on the morphology and properties of biocomposites based on polylactide and cellulose nanofibers. *Cellulose.* <https://doi.org/10.1007/s10570-017-1327-5>
- Said MM, Rehan M, El-Sheikh SM, Zahran MK, Abdel-Aziz MS, Bechelany M, Barhoum A (2021) Multifunctional hydroxyapatite/silver nanoparticles/cotton gauze for antimicrobial and biomedical applications. *Nanomaterials* 11(2):1–25. <https://doi.org/10.3390/nano11020429>
- Salahuddin N, Gaber M, Elneanaey S, Snowdon MR, Abdelwahab MA (2021) Co-delivery of norfloxacin and tenoxicam in Ag-TiO₂/poly(lactic acid) nanohybrid. *Int J Biol Macromol* 180:771–781. <https://doi.org/10.1016/j.ijbio mac.2021.03.033>
- Salisbury A, Mullin M, Foulkes L, Chen R, Percival SL (2022) Controlled-release iodine foam dressings demonstrate broad-spectrum biofilm management in several in vitro models. *Int Wound J* 19(7):1717–1728. <https://doi.org/10.1111/iwj.13773>
- Samain X, Langlois V, Renard E, Lorang G (2011) Grafting biodegradable polyesters onto cellulose. *J Appl Polym Sci* 121(2):1183–1192. <https://doi.org/10.1002/app.33659>
- Sebai A, Ruśkowski P, Bijak V, Gadomska-Gajadhr A, Kruk A, Synoradzki L (2018) Direct synthesis of polylactide (PLA)-chlorphenesin prodrug and optimization thereof with the aid of DOE. *Org Process Res Dev* 22(1):21–26. <https://doi.org/10.1021/acs.oprd.7b00266>
- Senapati S, Upadhyaya A, Dhruw S, Giri D, Maiti P (2021) Controlled DNA delivery using poly(lactide) nanoparticles and understanding the binding interactions. *J Phys Chem B* 125(35):10009–10017. <https://doi.org/10.1021/acs.jpcc.1c06520>
- Sharifi M, Bahrami SH, Nejad NH, Milan PB (2020) Electrospun PCL and PLA hybrid nanofibrous scaffolds containing *Nigella sativa* herbal extract for effective wound healing. *J Appl Polym Sci* 137(46):49528. <https://doi.org/10.1002/app.49528>
- Sharma R, Sayed U (2016) Surface modification of cellulosic fabric. *Int J Adv Chem Eng Biol Sci* 3(1):90–96. <https://doi.org/10.15242/IJACEBS.ER0416009>
- Shen W, Zhang G, Li YL, Fan G (2018) Effects of the glycerophosphate-poly(lactide) copolymer formation on electrospun fibers. *Appl Surf Sci* 443:236–243. <https://doi.org/10.1016/j.apsusc.2018.02.199>
- Shojaeiarani J, Bajwa DS, Hartman K (2019) Esterified cellulose nanocrystals as reinforcement in poly(lactic acid) nanocomposites. *Cellulose* 26(4):2349–2362. <https://doi.org/10.1007/s10570-018-02237-4>
- Shu W, Wang Y, Zhang X, Li C, Le H, Chang F (2021) Functional hydrogel dressings for treatment of burn wounds. *Front Bioeng Biotechnol* 9:788461. <https://doi.org/10.3389/fbioe.2021.788461>
- Sibarani J, Sirait SH, Widihati IAG, Manurung M (2021) Positively charged nanomicelles in water of amphiphilic copolymer chitosan-g-poly(lactide) as drug carrier of photoporphyrin IX for photodynamic therapy. *J Appl Polym Sci* 138(30):1–9. <https://doi.org/10.1002/app.50729>
- Sinha Ray S (2012) Polylactide-based bionanocomposites: a promising class of hybrid materials. *Acc Chem Res* 45(10):1710–1720. <https://doi.org/10.1021/ar3000376>
- Sipos P, Györy, H., Hagymási, K, Ondrejka P, Blázovics A (2004) Special wound healing methods used in ancient egypt and the mythological background. *World J Surg* 28(2):211–216. <https://doi.org/10.1007/s00268-003-7073-x>
- Slomkowski S, Penczek S, Duda A (2014) Poly(lactides)—an overview. *Polym Adv Technol* 25(5):436–447. <https://doi.org/10.1002/pat.3281>

- Song X-y, Wang M, Weng Y, Huang Z (2017) Effect of bamboo flour grafted lactide on the interfacial compatibility of polylactic acid/bamboo flour composites. *Polymers* 9(12):323. <https://doi.org/10.3390/polym9080323>
- Song X, Fang C, Li Y, Wang P (2022) Characterization of mechanical properties of jute/PLA composites containing nano SiO₂ modified by coupling agents. *Cellulose* 29(2):835–848. <https://doi.org/10.1007/s10570-021-04300-z>
- Spinella S, Re GL, Liu B, Dorgan J, Habibi, Y, Raquez J, Dubois P, Gross RA (2015) Modification of cellulose nanocrystals with lactic acid for direct melt blending with PLA. 070019. <https://doi.org/10.1063/1.4918454>
- Stoica AE, Chircov C, Grumezescu AM (2020a) Nanomaterials for wound dressings: an up-to-date overview. *Molecules*. <https://doi.org/10.3390/molecules25112699>
- Stoica AE, Chircov C, Grumezescu AM (2020b) Nanomaterials for wound dressings: an up-to-date overview. *Molecules* (basel, Switzerland). <https://doi.org/10.3390/molecules25112699>
- Stoleru E, Dumitriu RP, Munteanu BS, Zaharescu T, Tănase EE, Mitelut A, Ailiesei GL, Vasile C (2016) Novel procedure to enhance PLA surface properties by chitosan irreversible immobilization. *Appl Surf Sci* 367:407–417. <https://doi.org/10.1016/j.apsusc.2016.01.200>
- Sun H, Yan L, Zhang R, Lovell JF, Wu Y, Cheng C (2021a) A sulfobetaine zwitterionic polymer-drug conjugate for multivalent paclitaxel and gemcitabine co-delivery. *Biomater Sci* 9(14):5000–5010. <https://doi.org/10.1039/d1bm00393c>
- Sun S, Du X, Fu M, Khan AR, Ji J, Liu W, Zhai G (2021b) Galactosamine-modified PEG-PLA/TPGS micelles for the oral delivery of curcumin. *Int J Pharm*. <https://doi.org/10.1016/j.ijpharm.2021.120227>
- Sun Z, Wang X, Liu J, Wang Z, Wang W, Kong D, Leng X (2021c) ICG/l-arginine encapsulated PLGA nanoparticle-thermosensitive hydrogel hybrid delivery system for cascade cancer photodynamic-NO therapy with promoted collagen depletion in tumor tissues. *Mol Pharm* 18(3):928–939. <https://doi.org/10.1021/acs.molpharmaceut.0c00937>
- Suzuki A, Nagata F, Inagaki M, Kato K (2018) Surface modification of PLA nanofibers for coating with calcium phosphate. *Trans Mater Res Soc Japan* 43(5):271–274. <https://doi.org/10.14723/tmrjs.43.271>
- Szarlej P, Carayon I, Gnatowski P, Glinka M, Mroczynska M, Brillowska-Dabrowska A, Kucińska-Lipka J (2021) Composite polyurethane-poly(lactide) (Pur/pla) flexible filaments for 3d fused filament fabrication (fff) of antibacterial wound dressings for skin regeneration. *Materials*. <https://doi.org/10.3390/ma14206054>
- Takahashi M, Takenaka H (1987) Transition from cellulose i family to cellulose ii family. *Polym J* 19(7):855–861. <https://doi.org/10.1295/polymj.19.855>
- Tang Q, Lim T, Shen LY, Zheng G, Wei XJ, Zhang CQ, Zhu ZZ (2021) Well-dispersed platelet lysate entrapped nanoparticles incorporate with injectable PDLLA-PEG-PDLLA triblock for preferable cartilage engineering application. *Biomaterials* 268(1):120605. <https://doi.org/10.1016/j.biomaterials.2020.120605>
- Tanzi MC, Verderio P, Lampugnani MG, Resnati M, Dejana E, Sturani E (1994) Cytotoxicity of some catalysts commonly used in the synthesis of copolymers for biomedical use. *J Mater Sci Mater Med* 5(6–7):393–396. <https://doi.org/10.1007/BF00058971>
- Tarbuk A, Grancaric AM, Leskovac M (2014a) Novel cotton cellulose by cationisation during the mercerisation process-part 1: Chemical and morphological changes. *Cellulose* 21(3):2167–2179. <https://doi.org/10.1007/s10570-014-0245-z>
- Tarbuk A, Grancaric AM, Leskovac M (2014b) Novel cotton cellulose by cationization during mercerization-part 2: The interface phenomena. *Cellulose* 21(3):2089–2099. <https://doi.org/10.1007/s10570-014-0194-6>
- Teodoro KBR, Sanfelice RC, Migliorini FL, Pavinatto A, Facure MHM, Correa DS (2021) A review on the role and performance of cellulose nanomaterials in sensors. *ACS Sensors* 6(7):2473–2496. <https://doi.org/10.1021/acssensors.1c00473>
- Tham CY, Abdul Hamid ZA, Ahmad Z, Ismail H (2014) Surface modification of poly (lactic acid) (PLA) via alkaline hydrolysis degradation. *Adv Mater Res* 970:324–327. <https://doi.org/10.4028/www.scientific.net/AMR.970.324>
- Thomas S (2008) Hydrocolloid dressings in the management of acute wounds: a review of the literature. *Int Wound J* 5(5):602–613. <https://doi.org/10.1111/j.1742-481X.2008.00541.x>
- Thomas S, Uzun M (2019) Testing dressings and wound management materials. In: *Advanced textiles for wound care*, 2nd edn. Elsevier Ltd, pp 23–54. <https://doi.org/10.1016/b978-0-08-102192-7.00002-3>
- Toncheva A, Spasova M, Paneva D, Manolova N, Rashkov I (2014) Polylactide (PLA)-based electrospun fibrous materials containing ionic drugs as wound dressing materials: a review. *Int J Polym Mater Polym Biomater* 63(13):657–671. <https://doi.org/10.1080/00914037.2013.854240>
- Toncheva A, Mincheva R, Kancheva M, Manolova N, Rashkov I, Dubois P, Markova N (2016) Antibacterial PLA/PEG electrospun fibers: comparative study between grafting and blending PEG. *Eur Polym J* 75:223–233. <https://doi.org/10.1016/j.eurpolymj.2015.12.019>
- Torgbo S, Sukyai P (2018) Bacterial cellulose-based scaffold materials for bone tissue engineering. *Appl Mater Today* 11:34–49. <https://doi.org/10.1016/j.apmt.2018.01.004>
- Tsegay F, Elsherif M, Butt H (2022) Smart 3D printed hydrogel skin wound bandages: a review. *Polymers*. <https://doi.org/10.3390/polym14051012>
- Tsuji H (2005) Poly(lactide) stereocomplexes: Formation, structure, properties, degradation, and applications. *Macromol Biosci* 5(7):569–597. <https://doi.org/10.1002/mabi.200500062>
- Tsuji H (2016) Poly(lactic acid) stereocomplexes: a decade of progress. *Adv Drug Deliv Rev* 107:97–135. <https://doi.org/10.1016/j.addr.2016.04.017>
- Tudoroiu EE, Dinu-Pîrvu CE, Kaya MGA, Popa L, Anuța V, Prisada RM, Ghica MV (2021) An overview of cellulose derivatives-based dressings for wound-healing management. *Pharmaceuticals*. <https://doi.org/10.3390/ph14121215>

- Tyler B, Gullotti D, Mangraviti A, Utsuki T, Brem H (2016) Poly(lactic acid) (PLA) controlled delivery carriers for biomedical applications. *Adv Drug Deliv Rev* 107:163–175. <https://doi.org/10.1016/j.addr.2016.06.018>
- Umar Aslam Khan M, Haider S, Haider A, Izwan Abd Razak S, Rafiq Abdul Kadir M, Shah SA, Javed A, Shakir I, Al-Zahrani AA (2021) Development of porous, antibacterial and biocompatible GO/n-HAp/bacterial cellulose/ β -glucan biocomposite scaffold for bone tissue engineering. *Arab J Chem* 14(2):102924. <https://doi.org/10.1016/j.arabjc.2020.102924>
- Urbańczyk GW (1985) *Nauka o włóknie*. Wydawnictwa Naukowo-Techniczne
- Urbaniak-Domagala W, Krucinska I, Wrzosek H, Komisarzczyk A, Chrzanoska O (2016) Plasma modification of polylactide nonwovens for dressing and sanitary applications. *Text Res J* 86(1):72–85. <https://doi.org/10.1177/0040517515581586>
- Vincent Edwards J, Graves E, Prevost N, Condon B, Yager D, Dacorta J, Bopp A (2020) Development of a nonwoven hemostatic dressing based on unbleached cotton: a de novo design approach. *Pharmaceutics* 12(7):1–19. <https://doi.org/10.3390/pharmaceutics12070609>
- Volokhova AS, Waugh JB, Arrington KJ, Matson JB (2019) Effects of graft polymer compatibilizers in blends of cellulose triacetate and poly(lactic acid). *Polym Int* 68(7):1263–1270. <https://doi.org/10.1002/pi.5820>
- Wąchała R, Ramięga T, Pyć R, Antczak T (2011) Otrzymywanie włókien nanocelulozy. *Biotechnol Food Sci* 76(2):87–100
- Wada M, Okano T, Sugiyama J (2001) Allomorphs of native crystalline cellulose I evaluated by two equatorial d-spacings. *J Wood Sci* 47(2):124–128. <https://doi.org/10.1007/BF00780560>
- Wada M, Heux L, Sugiyama J (2004) Polymorphism of cellulose I family: reinvestigation of cellulose IVI. *Biomacromolecules* 5(4):1385–1391. <https://doi.org/10.1021/bm0345357>
- Walker M, Hobot JA, Newman GR, Bowler PG (2003) Scanning electron microscopic examination of bacterial immobilisation in a carboxymethyl cellulose (AQUACEL®) and alginate dressings. *Biomaterials* 24(5):883–890. [https://doi.org/10.1016/S0142-9612\(02\)00414-3](https://doi.org/10.1016/S0142-9612(02)00414-3)
- Wan Y, Qu X, Lu J, Zhu C, Wan L, Yang J, Bei J, Wang S (2004) Characterization of surface property of poly(lactide-co-glycolide) after oxygen plasma treatment. *Biomaterials* 25(19):4777–4783. <https://doi.org/10.1016/j.biomaterials.2003.11.051>
- Wang S, Cui W, Bei J (2005) Bulk and surface modifications of polylactide. *Anal Bioanal Chem* 381(3):547–556. <https://doi.org/10.1007/s00216-004-2771-2>
- Wang Q, Sun J, Yao Q, Ji C, Liu J, Zhu Q (2018) 3D printing with cellulose materials. *Cellulose* 25(8):4275–4301. <https://doi.org/10.1007/s10570-018-1888-y>
- Wang J, Tavakoli J, Tang Y (2019a) Bacterial cellulose production, properties and applications with different culture methods—a review. *Carbohydr Polym* 219(February):63–76. <https://doi.org/10.1016/j.carbpol.2019.05.008>
- Wang Y, Shi L, Wu H, Li Q, Hu W, Zhang Z, Huang L, Zhang J, Chen D, Deng S, Tan S, Jiang Z (2019b) Graphene oxide-IPDI-Ag/ZnO@hydroxypropyl cellulose nanocomposite films for biological wound-dressing applications. *ACS Omega* 4(13):15373–15381. <https://doi.org/10.1021/acsomega.9b01291>
- Wang X, Cheng R, Zhong Z (2021) Facile fabrication of robust, hyaluronic acid-surfaced and disulfide-crosslinked PLGA nanoparticles for tumor-targeted and reduction-triggered release of docetaxel. *Acta Biomater* 125:280–289. <https://doi.org/10.1016/j.actbio.2021.02.044>
- Wang Z, Sun C, Wu H, Xie J, Zhang T, Li Y, Xu X, Wang P, Wang C (2022) Cascade targeting codelivery of ingenol-3-angelate and doxorubicin for enhancing cancer chemotherapeutic effects through synergistic effects in prostate cancer. *Materials Today Bio* 13:1–10. <https://doi.org/10.1016/j.mtbio.2021.100189>
- Wen X, Zheng Y, Wu J, Wang LN, Yuan Z, Peng J, Meng H (2015) Immobilization of collagen peptide on dialdehyde bacterial cellulose nanofibers via covalent bonds for tissue engineering and regeneration. *Int J Nanomed* 10:4623–4637. <https://doi.org/10.2147/IJN.S84452>
- Wijaya CJ, Ismadji S, Apamarta HW, Gunawan S (2020) Hydrophobic modification of cellulose nanocrystals from bamboo shoots using rarasaponins. *ACS Omega*. <https://doi.org/10.1021/acsomega.0c02425>
- Wilkins RH (1964) Neurosurgical classic—XVII. *Journal of Neurosurgery*, 21(3), 240–244.
- Williams C (1999) An investigation of the benefits of Aquacel Hydrofibre wound dressing. *Br J Nurs* 8(10):676–678. <https://doi.org/10.12968/bjon.1999.8.10.6607>
- Wilson BK, Sinko PJ, Prud'Homme RK (2021) Encapsulation and controlled release of a camptothecin prodrug from nanocarriers and microgels: tuning release rate with nanocarrier excipient composition. *Mol Pharm* 18(3):1093–1101. <https://doi.org/10.1021/acs.molpharmaceut.0c01012>
- Wu H, Silva C, Yu Y, Dong A, Wang Q, Fan X, Wang P, Yuan J, Cavaco-Paulo A (2017) Hydrophobic functionalization of jute fabrics by enzymatic-assisted grafting of vinyl copolymers. *New J Chem* 41(10):3773–3780. <https://doi.org/10.1039/c7nj00613f>
- Wu C-N, Fuh S-C, Lin S-P, Lin Y-Y, Chen H-Y, Liu J-M, Cheng K-C (2018) TEMPO-oxidized bacterial cellulose pellicle with silver nanoparticles for wound dressing. *Biomacromolecules* 19(2):544–554. <https://doi.org/10.1021/acs.biomac.7b01660>
- Wu S, Bian C, Li X, Chen M, Yang J, Jin Y, Shen Y, Cheng L (2021) Controlled release of triamcinolone from an episcleral micro film delivery system for open-globe eye injuries and proliferative vitreoretinopathy. *J Control Release* 333:76–90. <https://doi.org/10.1016/j.jconrel.2021.03.023>
- Wu Y, Wang Y, Wang F, Huang Y, He J (2022) Preparation of 3D printed polylactic acid/bacterial cellulose composite scaffold for tissue engineering applications. *Polymers* 14(21):4756. <https://doi.org/10.3390/polym14214756>
- Wu H-J, Ni R, Shi Y, Hu Y, Shen Z, Pang Q, Zhu Y (2023) The promising hydrogel candidates for preclinically treating diabetic foot ulcer: a systematic review and meta-analysis. *Adv Wound Care* 12(1):28–37. <https://doi.org/10.1089/wound.2021.0162>
- Xiao C, Zhang G, Liang W, Wang Z, Lu Q, Shi W, Zhou Y, Guan Y, Lang M (2022) Preparation of green cellulose

- diacetate-based antibacterial wound dressings for wound healing. *Front Mater Sci* 16(2):220599. <https://doi.org/10.1007/s11706-022-0599-3>
- Xu QingBo, Xie L, Diao H, Li F, Zhang Y, Fu F, Liu X (2017) Antibacterial cotton fabric with enhanced durability prepared using silver nanoparticles and carboxymethyl chitosan. *Carbohydr Polym* 177:187–193. <https://doi.org/10.1016/j.carbpol.2017.08.129>
- Xu Q, Duan P, Zhang Y, Fu F, Liu X (2018a) Double protect copper nanoparticles loaded on L-cysteine modified cotton fabric with durable antibacterial properties. *Fibers Polym* 19(11):2324–2334. <https://doi.org/10.1007/s12221-018-8621-1>
- Xu QingBo, Ke X, Shen L, Ge N, Zhang Y, Fu F, Liu X (2018b) Surface modification by carboxymethyl chitosan via pad-dry-cure method for binding Ag NPs onto cotton fabric. *Int J Biol Macromol* 111:796–803. <https://doi.org/10.1016/j.ijbiomac.2018.01.091>
- Xu QingBo, Zheng W, Duan P, Chen J, Zhang Y, Fu F, Diao H, Liu X (2019) One-pot fabrication of durable antibacterial cotton fabric coated with silver nanoparticles via carboxymethyl chitosan as a binder and stabilizer. *Carbohydr Polym* 204:42–49. <https://doi.org/10.1016/j.carbpol.2018.09.089>
- Xu J, Li K, Liu M, Gu X, Li P, Fan Y (2021) Studies on preparation and formation mechanism of poly(lactide-co-glycolide) microrods via one-step electrospray and an application for drug delivery system. *Eur Polym J*. <https://doi.org/10.1016/j.eurpolymj.2021.110372>
- Yang Y, Qiu X, Sun Y, Wang Y, Wang J, Li Y, Liu C (2018) Development of bioabsorbable polylactide membrane with controllable hydrophilicity for adjustment of cell behaviours. *R Soc Open Sci*. <https://doi.org/10.1098/rsos.170868>
- Yang Z, Li X, Si J, Cui Z, Peng K (2019) Morphological, mechanical and thermal properties of poly(lactic acid) (PLA)/cellulose nanofibrils (CNF) composites nanofiber for tissue engineering. *J Wuhan Univ Technol Mater Sci Ed* 34(1):207–215. <https://doi.org/10.1007/s11595-019-2037-7>
- Yanti NA, Ahmad SW, Muhiddin NH, Ramadhan LOAN, Suriana, Walhidayah T (2021) Characterization of bacterial cellulose produced by acetobacter xylinum strain lkn6 using sago liquid waste as nutrient source. *Pak J Biol Sci* 24(3):335–344. <https://doi.org/10.3923/pjbs.2021.335.344>
- Yao J, Liu J, Zhi H, Tao H, Xie X, Shi Q (2021) Surface-modified polylactic acid nanospheres with chitosan for antibacterial activity of 1, 2-benzisothiazolin-3-one. *Carbohydr Polym*. <https://doi.org/10.1016/j.carbpol.2021.118406>
- Yin Y, Lucia LA, Pal L, Jiang X, Hubbe MA (2020) Lipase-catalyzed laurate esterification of cellulose nanocrystals and their use as reinforcement in PLA composites. *Cellulose*. <https://doi.org/10.1007/s10570-020-03225-3>
- Yu H, Li Y, Pan Y, Wang H, Wang W, Ren X, Yuan H, Lv Z, Zuo Y, Liu Z, Lin W, Yao Q (2023) Multifunctional porous poly (L-lactic acid) nanofiber membranes with enhanced anti-inflammation, angiogenesis and antibacterial properties for diabetic wound healing. *J Nanobiotechnol* 21(1):110. <https://doi.org/10.1186/s12951-023-01847-w>
- Zajdel A, Wilczok A, Jelonek K, Kaps A, Musiał-Kulik M, Kasperczyk J (2021) Cytotoxic effect of targeted biodegradable epothilone B and rapamycin co-loaded nanocarriers on breast cancer cells. *J Biomed Mater Res Part A* 109(9):1693–1700. <https://doi.org/10.1002/jbm.a.37164>
- Zhang Y, Li X, Yang Y, Lan A, He X, Yu M (2014) In situ graft copolymerization of ϵ -lactide onto cellulose and the direct melt spinning. *RSC Adv* 4(65):34584–34590. <https://doi.org/10.1039/C4RA02727B>
- Zhang C, Cui F, Zeng G, Jiang M, Yang Z, Yu Z, Zhu M, Shen L (2015) Quaternary ammonium compounds (QACs): a review on occurrence, fate and toxicity in the environment. *Sci Total Environ* 518–519:352–362. <https://doi.org/10.1016/j.scitotenv.2015.03.007>
- Zhang L, Yin H, Lei X, Lau JNY, Yuan M, Wang X, Zhang F, Zhou F, Qi S, Shu B, Wu J (2019) A systematic review and meta-analysis of clinical effectiveness and safety of hydrogel dressings in the management of skin wounds. *Front Bioeng Biotechnol* 7:342. <https://doi.org/10.3389/fbioe.2019.00342>
- Zhang C, Wan L, Gu H, Hu Q, Ding Y, Ying S (2021a) Preparation and properties of foamed cellulose acetate/polylactic acid blends. *Polym Eng Sci* 61(12):3069–3081. <https://doi.org/10.1002/pen.25819>
- Zhang X, Guan G, Wang Z, Lv L, Chávez-Madero C, Chen M, Yan Z, Yan S, Wang L, Li Q (2021b) Drug release evaluation of Paclitaxel/Poly-L-Lactic acid nanoparticles based on a microfluidic chip. *Biomed Microdevices*. <https://doi.org/10.1007/s10544-021-00596-7>
- Zhang Y, Yu J, Zhang H, Li Y, Wang L (2022) Nanofibrous dressing: potential alternative for fighting against antibiotic-resistance wound infections. *J Appl Polym Sci* 139(20):52178. <https://doi.org/10.1002/app.52178>
- Zheng W, Chen C, Zhang X, Wen X, Xiao Y, Li L, Xu Q, Fu F, Diao H, Liu X (2021) Layer-by-layer coating of carboxymethyl chitosan-gelatin-alginate on cotton gauze for hemostasis and wound healing. *Surf Coat Technol* 406:126644. <https://doi.org/10.1016/j.surfcoat.2020.126644>
- Zhong C (2020) Industrial-scale production and applications of bacterial cellulose. *Front Bioeng Biotechnol* 8:1–19. <https://doi.org/10.3389/fbioe.2020.605374>
- Zhou L, Ke K, Yang MB, Yang W (2021) Recent progress on chemical modification of cellulose for high mechanical-performance Poly(lactic acid)/Cellulose composite: a review. *Compos Commun* 23:100548. <https://doi.org/10.1016/j.coco.2020.100548>
- Zhu X, Zhong T, Huang R, Wan A (2015) Preparation of hydrophilic poly(lactic acid) tissue engineering scaffold via (PLA)-(PLA-b-PEG)-(PEG) solution casting and thermal-induced surface structural transformation. *J Biomater Sci Polym Ed* 26(17):1286–1296. <https://doi.org/10.1080/09205063.2015.1088125>

- Zhu Q, Chang K, Qi L, Li X, Gao W, Gao Q (2021) Surface modification of poly(L-lactic acid) through stereocomplexation with enantiomeric poly(D-lactic acid) and its copolymer. *Polymers*. <https://doi.org/10.3390/polym13111757>
- Zięba M, Włodarczyk J, Gupta A, Pastusiak M, Chaber P, Janeczek H, Musioł M, Sikorska W, Kaczmarczyk B, Radecka I, Kowalczyk M, Savickas A, Savickiene N, Adamus G (2021) Bioresorbable electrospun mats of poly(D,L)-lactide/poly[(R,S)-3-hydroxybutyrate] blends for potential use in the treatment of difficult-to-heal skin wounds. *Eur Polym J* 147:110334. <https://doi.org/10.1016/j.eurpolymj.2021.110334>
- Zmejkoski D, Spasojević D, Orlovska I, Kozyrovska N, Soković M, Glamočlija J, Dmitrović S, Matović B, Tasić N, Maksimović V, Sosnin M, Radotić K (2018) Bacterial cellulose-lignin composite hydrogel as a promising agent in chronic wound healing. *Int J Biol Macromol* 118:494–503. <https://doi.org/10.1016/j.ijbiomac.2018.06.067>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.