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Enhancing Polylactic Acid (PLA) with Green Nanofillers for Medical Applications: An Overview

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Abstract

Recently, many researchers have been attracted to green nanocomposites, whose raw materials come from biodegradable, as a concern for sustainability issues. Polylactic acid (PLA) is the most promising polymer material as it possesses biodegradability and excellent biocompatibility properties. However, PLA has a few drawbacks, such as poor flexibility, impact strength, and thermal stability, limiting its use in diverse applications. To counter these limitations, incorporating various green materials as nanofillers has been studied and reviewed. This review explores different types of eco-friendly nanofillers for the improvement of the chemical, physical, and mechanical properties of PLA nanocomposites and their potential usage in medical applications.

Keywords: Green filler; nanofillers; polylactic acid; biomedical

Introduction

Plastic was first developed in 1860, and the global plastic industry officially began in 1907. Since then, plastic consumption worldwide has surged dramatically, growing about 180 times from 1950 to 2018. The 1930s to the 1950s marked a transformative phase in medical device development, driven by the advent of plastics. Plastics during this time started to replace traditional materials like glass, metal, and rubber in the manufacturing of medical devices, signifying a notable shift in materials used in the healthcare industry [1]. This shift was driven by the unique properties of plastics, including their versatility, durability, and ability to be moulded into complex shapes.

Despite their utility, increasing awareness of the impact of plastic on the environment has spurred industries to seek more sustainable alternatives. Current recycling rates are low, with only 7% of plastic waste recycled annually, 8% incinerated, and the remainder sent to landfills [2]. This accumulation and persistence of waste have become a global issue, as unmanaged plastic waste threatens terrestrial and marine ecosystems. Studies indicate that approximately 700 marine species are affected by plastic debris [3]. Moreover, the abundance of plastic can also affect human health by degrading into fine particles that may lead to kidney disease, birth defects, cancer, and other health issues if absorbed by the human body.

In response to these challenges, there is a growing focus on biopolymers as sustainable alternatives to conventional plastics. The utilization of biodegradable polymers is gaining popularity, as evidenced by the growing number of publications focused on their manufacture, properties, and biomedical applications, according to data compiled by Kurowiak et al. [4] There has been an increasing trend in research related to "polymers for biomedical applications" from 2013 to 2023. Biopolymers offer superior biocompatibility and biodegradability, are derived from renewable sources and are capable of breaking down harmlessly under appropriate conditions. This review aims to assess the impact of different green nanofillers integrated into PLA-based materials. It will evaluate their properties, discuss current limitations, and identify avenues for enhancing their use in medical applications, contributing to the ongoing pursuit of environmentally friendly materials in healthcare.

PLA Polymer

Synthesis and properties of PLA

Polylactic acid (PLA) is a thermoplastic aliphatic polyester produced either from natural resources via fermentation [5][6] or through synthetic polymerization of lactic acid monomers [7][8]. The lactic acid monomers are derived from renewable starch-rich materials such as corn, tapioca and wheat. These produce various PLA polymers, such as poly-L-lactic acid (PLLA), poly-D-lactic acid (PDLA), and poly-D,L-lactic acid (PDLLA), each distinguished by its stereochemical configuration [9][8]. PLA is highly known for its distinctive properties, such as renewability, biocompatibility, processability, and energy efficiency. Its benefits include good mechanical strength, ease of composability, and using renewable monomers. As PLA is derived from biodegradable resources, its degradation results in non-polluting and non-toxic by-products [10], making it a sustainable alternative to traditional petrochemical plastics.

PLA is highly favoured across diverse applications, as illustrated in Figure 1, including packaging [11][12], construction [13], agriculture [14][15] automotive [9], electronics [16] and medical uses [17][18]. In medical applications, PLA is regarded as safe due to its gradual breakdown in the body into harmless lactic acid fragments. Its biocompatibility enhances its value in healthcare settings, where it is utilized in drug delivery systems, medical implants, and tissue scaffolds [19][20][21]. The popularity of PLA-based medical devices is on the rise, owing to their advantageous mechanical and physical properties, and their use is expected to continue growing in the future.

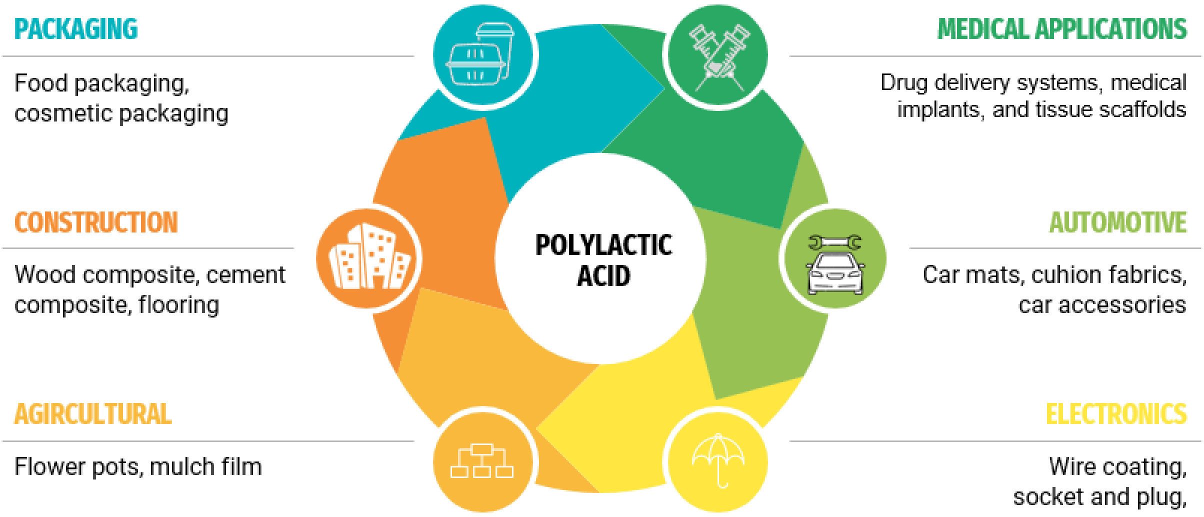

Figure 1 Overview of various application of PLA.

PLA in medical applications

The selection of materials for medical and healthcare applications is crucial. In recent years, the plastics industry has seen significant growth characterized by increased commercial acceptance, increased funding, expanded manufacturing capabilities, and intensified research and development efforts. The emergence of bioplastics has prominently driven this evolution. Bioplastics, including polycaprolactone (PCL), polylactic acid (PLA), polyglycolide (PGL), and their copolymers have become effective substitutes for traditional plastics in the medical sector [1][22]. These materials offer inherent advantages such as biodegradability, biocompatibility, and the ability to be customized to specific medical requirements. Their adoption signifies a shift towards more sustainable and environmentally friendly solutions in healthcare, in line with global initiatives to mitigate environmental impact while maintaining rigorous standards of patient care and safety.

PLA, for example, is a transparent, biocompatible, and biodegradable plastic that is easily processed. During fabrication, PLA exhibits behaviour similar to traditional petrochemical plastics, making it broadly applicable in biomedical settings [23][24]. Several essential properties are typically required for PLA to be considered suitable for medical devices.

Good biocompatibility

PLA, derived from renewable sources, is highly esteemed in medicine due to its exceptional biocompatibility, which ensures minimal immune responses and toxicity within biological systems. When employed in medical implants for humans and animals, PLA integrates with various tissues, undergoes gradual degradation, and metabolizes without leaving harmful residues. This predictable degradation profile makes PLA ideal for applications that need temporary structural reinforcement. or controlled release of therapeutic agents [25]. Importantly, PLA's degradation process produces non-toxic by-products that do not harm biological systems [26].

The research underscores PLA's ability to promote cell adhesion and proliferation, which is essential for tissue regeneration and effective integration of medical implants. Extensive in vitro and in vivo studies validate PLA's biocompatibility in living systems. In vitro investigations typically assess cell viability, proliferation, and morphology when exposed to PLA materials [27][28][29]. In vivo studies involve implanting PLA devices in animal models to evaluate tissue response, inflammatory reactions, and long-term degradation patterns.

Porosity is a key factor in the use of biomedical scaffolds. High-porosity scaffolds with larger void spaces facilitate efficient biofactor release, promoting nutrient exchange and enhancing cell attachment and proliferation [30][31]. Conversely, scaffolds with smaller pore sizes offer robust mechanical support and precise control over cell behaviour and differentiation, mimicking the natural extracellular matrix and supporting cellular activities effectively [32]. Effective selection of scaffold porosity balances biological functionality with mechanical requirements to optimize performance in biomedical applications.

Excellent mechanical properties

Polylactic acid (PLA) must demonstrate superior mechanical properties, including strength, stiffness, and toughness, to satisfy the stringent requirements of medical applications. In bone tissue engineering, achieving a flexural modulus that aligns with natural bone is critical, influenced by bone location, density, and physiological conditions. This alignment ensures that the implant offers sufficient mechanical support and seamlessly integrates with surrounding tissue, promoting successful healing and long-term functionality [33]. Mechanical properties are pivotal in supporting tissue regeneration processes. For PLA employed in load-bearing implants or surgical instruments, robust mechanical strength is essential to withstand physiological stresses from implantation through the regeneration phase, thereby preventing fractures or deformations [34]. Researchers have explored diverse scaffold designs for effective tissue substitution and mechanical support at defect sites. The performance of these hybrid scaffolds depends on various factors, including fabrication techniques, material composition, orientation of nanomaterials, and interactions within the polymer matrix [25][35][19][36][37]. The incorporation of different filler types significantly impacts PLA's mechanical behaviour. For example, cellulose-based fillers enhance PLA composites' crystallinity, thereby enhancing their stiffness and strength [38][39][36]. Similarly, clay-based fillers increase the flexural modulus, imparting greater stiffness due to their rigid structure [40][41][42].

Optimal degradation rate

PLA degradation in medical applications must occur at a controlled rate that aligns with healing processes or the expected lifespan of devices, typically achieving over 90% biodegradation within 12 weeks [43]. Hydrolysis significantly influences this process, primarily through ester bond cleavage in aqueous environments like bodily fluids. Water absorption initially causes molecular weight reduction and ester bond cleavage in PLA, with subsequent involvement of various cells such as macrophages and fibroblasts [25]. Enzymatic activity further contributes to tissue layer reduction surrounding PLA implants, ensuring predictable degradation and non-toxic by-products like lactic acid, crucial for temporary implants and drug delivery systems

Methods like blending, copolymerization, and surface modification effectively control PLA's degradation rate to meet specific needs. Understanding crystallinity's impact on degradation kinetics is key for customizing PLA for diverse applications. Recent studies using micro-injection moulding and calorimetric analysis have explored crystallinity changes during PLA hydrolysis, providing insights into degradation processes. Additives like calcium carbonate and β-tricalcium phosphate adjust 3D-printed scaffold degradation rates, aligning them with bone tissue growth rates [44].

The storage modulus is also critical for assessing PLA's thermal stability in biomedical and composite research, indicating stiffness and rigidity crucial for structural integrity under varying loads. Evaluating storage modulus across temperatures informs PLA's performance in physiological conditions, which is essential for biomedical and composite material applications.

Development of PLA nanocomposites with green filler

A significant amount of PLA biopolymers are extensively utilized in producing biocomposites, which involve blending with various reinforcement materials to improve the properties of the PLA matrix [45][46]. The demand for PLA-based composites in medical implants is increasing, prompting the emergence of various manufacturing techniques which each method offers unique advantages for advancing these innovative materials [20].

The development of PLA nanocomposites involves incorporating nano-scale particles (<100 nm) to improve interface interactions between matrix and filler, resulting in unique properties [12][47][48].

Emphasizing sustainability, there is a growing trend towards integrating green materials into PLA, sourced from renewable and environmentally friendly sources [49]. These materials, including nanoparticles from natural fibres like cellulose nanocrystals, nanoclays, and other bio-based sources, aim to boost mechanical and other properties while maintaining PLA's biocompatibility in medical applications [50]. Incorporating green nanofillers supports safety standards, reducing the risk of adverse or negative reactions or tissue rejection in medical implants [51][20]. This section explores various types of green nanofillers integrated into PLA composites and their impact on enhancing PLA's suitability for medical uses.

Natural nanofiber based-PLA composites

A natural nanofiber filler is derived from renewable sources, enhancing mechanical strength, toughness, and overall performance in composite materials. Notable examples include cellulosic and lignocellulosic biomass, which hold substantial potential to advance nanotechnology research significantly [52]. Nanocellulose, extracted from various natural sources of lignocellulosic biomass through suitable extraction techniques, represents a renewable biomaterial with unique properties well-suited for advanced material applications [37]. Cellulose is made up of numerous fibrils that bond together through hydrogen interactions, which contribute to its strength and rigidity [51]. As nanotechnology advances, researchers are increasingly exploring its extraction from various sources. The specific characteristics of nanocellulose—its size, shape, morphology and properties—are influenced by many factors, such as the primary source, treatment methods, and extraction procedures employed, underscoring its versatility in various advanced material applications [52]. Several studies have explored the utilization of nanocellulose to reinforce PLA, particularly for 3D printing applications in medical devices aimed at producing biodegradable implants and scaffolds. PLA/CNC composites, in particular, show promise for biomedical applications, especially in bone regeneration.

Mechanical properties

When incorporated into PLA, nanocellulose derived from natural fibres such as jute or hemp can improve the mechanical properties of PLA while preserving its biodegradability [53][54]. The result of mechanical performance based on various types of nanocellulose fillers in PLA-based composites is presented in Table 1. Luo et al. [19] produced porous scaffolds using cotton cellulose nanocrystal (CNC)/PLA nanocomposites through in situ polymerization followed by thermally induced phase separation. They examined these composites' mechanical behaviour and biocompatibility by adjusting the CNC content in the range of 0.2 to 1.0 wt. %. The compression modulus of the 0.8 wt. % CNC/PLA scaffolds exceeded that of the pure PLA scaffold by 368%. The compression modulus serves as a metric for assessing the stiffness and rigidity of a material when subjected to compression.

Gauss et al. [36] developed PLA biocomposites with grafted nanofibrillated cellulose (g-NCF) through an in-situ polymerization process and investigated these composites' mechanical and thermal behaviour. NCF in the 3 to 20% range were studied for grafted with PLA composite. Incorporating the g-CNF content up to 20 wt. % resulted in enhancements in tensile strength and Young's modulus, illustrating a positive correlation between nanofiller content and mechanical properties. Besides, this study found that the storage modulus of PLA/g-CNF composites that undergo heat treatment notably increased, indicating enhanced thermo-mechanical stability. Incorporating g-CNFs that developed crystalline regions within the composites contributed to higher storage modulus values, underscoring improved thermo-stability. The presence of nanofibers limited the movement of PLA chains, enhancing the composite's elastic properties and reducing viscosity. These results emphasize the effectiveness of g-CNF reinforcement and post-printing annealing in improving the performance of PLA composites for 3D printing applications.

The addition of 3 wt. % CNC extracted from *Ficus thonninggii* incorporated into the PLA scaffold showed a 30% enhancement in Young's modulus compared to neat PLA. Furthermore, the enhancement of elongation at break with up to 3% CNC loading indicates that incorporating CNC could potentially enhance the elastoplasticity of PLA by good interaction between fibre and PLA matrix [33]. The strengthened scaffold is essential for robust structural support in bone tissue engineering applications. Its improved mechanical strength enables it to withstand physiological loads better and mimic the properties of natural bone tissue. In 2021, Wang et al. [55] conducted a study on PLA films reinforced with cellulose nanofibrils (CNF) extracted from microcrystalline cellulose (MCC) through solution casting and melt compression. With the addition of 2.5 wt. % CNF improved tensile strength by 8.8% in the PLA/CNF biocomposite film. The irregular cross-section observed through SEM after tensile testing indicates that the PLA/CNF composite material possesses better tensile compared to pure PLA. The irregularities observed on the fracture surface indicate that the material absorbed more energy during fracture, demonstrating its increased ability to withstand higher forces before failing.

Based on the results, the inclusion of cellulose markedly improves the mechanical characteristics of the composite material. These findings underscore robust interfacial bonding and efficient load transfer between the matrix and reinforcement, which are crucial for bolstering tensile strength and durability. In summary, nanocellulose fillers show potential in augmenting the mechanical performance of PLA matrices, primarily due to their nanoscale dispersion and enhanced interaction with the PLA matrix. This research emphasizes that integrating CNC into the composite enhances its capacity to endure compressive forces without enduring permanent deformation, a critical factor in refining scaffold mechanical properties for future research and development efforts.

Table 1: Summary of findings on various nanocellulose fillers in PLA-based composites.

Nanocellulose Type	Filler Content (wt. %)	Glass Transition (°C)	Young modulus (GPa)	Tensile Strength (MPa)	Elongation at break (%)	Reference
Modified Nanofibrilated cellulose (CNF)	0	70	3.3	64	5.1	[36]
	3.0	71	4.5	71	2.1	
	10.0	71	5.4	72	1.6	
	20.0	-	6.6	65	1.1	
Cellulose nanocrystal (CNC) extracted from *Ficus thonningii.*	0	66	2.4	-	2.5	[33]
	1.0	57	2.7	-	3.0	
	3.0	56	3.0	-	3.5	
	5.0	57	2.0	-	2.0	
Cellulose nanofibrils (CNF) extracted from microcrystalline cellulose (MCC)	0	61	-	48	4.0	[55]
	1.0	60	-	48	3.0	
	2.5	59	-	52	2.5	
	5.0	59	-	47	2.1	
Nanocellulose esterified with lauryl chains	0	57	-	40	-	[56]
	1.0	58	-	45	-	
	3.0	58	-	26	-	
	5.0	58	-	27	-	
	10.0	58	-	21	-	
	20.0	62	-	18	-	

Biocompatibility

In medical applications, materials derived from composites for use in tissue engineering are essential as they provide temporary support and guidance for the development of new tissues [57]. These 3D porous biomaterials act as scaffolds for reconstructing tissue defects, promoting cell adhesion, growth, and the regeneration of extracellular matrix, nerves, muscles, and bones. Therefore, scaffold design requires careful consideration of properties like high porosity, interconnected pores, and biocompatibility [58]. Research has highlighted the potential of natural fibres, particularly nanocellulose, in enhancing biocompatibility within tissue engineering. Nanocellulose, including CNC, resembles the natural extracellular matrix, encouraging cell adhesion and growth while exhibiting outstanding biocompatibility [59]. The incorporation of CNC enhances cell attachment and proliferation, which is particularly beneficial for developing implantable scaffold materials in hard tissue engineering. The biocompatible and biodegradable nature of CNC further positions them as promising candidates in biomedical applications, including drug delivery systems, tissue engineering, and advanced nanocomposites, driving innovations in materials science and engineering [33][59].

Stepnova et al. [60] investigated a biocomposite film composed of PLLA functionalized with CNCs, demonstrating enhanced mineralization when exposed to Ca^{2+} or PO_4^{3-} solutions. Their findings indicate that the addition of functionalized CNCs significantly enhances the capture of calcium ions by the composite material, as evidenced by the increased intensity of the red colour stain observed on the surface film, as depicted in Figure 2. This indicates the potential for developing materials for bone tissue regeneration in the biomedical field. In vivo testing involved subcutaneously implanting both pure PLLA and its composites on the backs of rats, followed by a 4-week monitoring period. Histomorphometric analysis of the resected implants indicated that PLLA/f-CNC composite materials exhibited the lowest inflammatory responses compared to pure PLLA, evidenced by reduced levels of macrophages, lymphocytes, and fibroblasts. This suggests that the composite materials did not induce acute inflammation. Moreover, the thickness of the fibrous capsule around the composite materials was notably thinner than that around pure PLLA, highlighting superior tissue integration and biocompatibility of the composites. Incorporating hydrophilic materials such as cellulose optimizes the properties of biocomposite materials by enhancing interaction with the biological environment, thereby contributing to a lower inflammatory response.

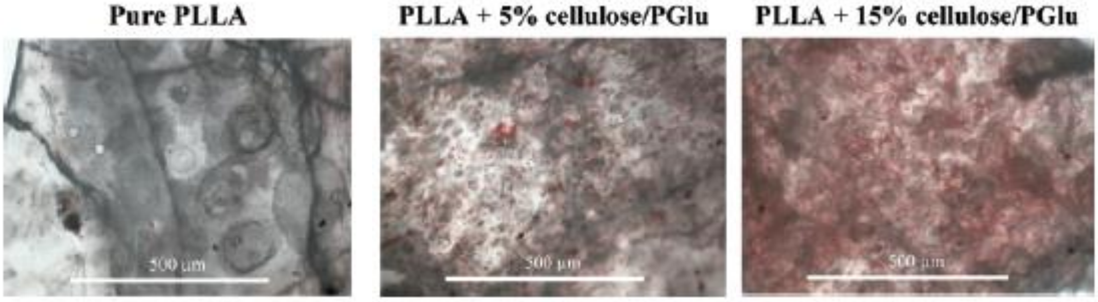

Figure 2 In vitro mineralization study of the (a) pure PLLA and (b) PLLA/f-CNC 5wt% (c) PLLA/f-CNC 15wt%. The calcium deposits were stained by alizarin red S assay. The intensity of the red colour is proportional to the amount of calcium ions on the surface of the films [60]

N'Gatta et al. [33] using CNC extracted from *Ficus thonninggii* to incorporate with PLA composite scaffolds. From contact angle analysis, incorporating CNC led to a reduction of about 17% in the scaffold's water contact angle, demonstrating enhanced wettability. This improvement is essential for facilitating cell adhesion and proliferation on the scaffold surface. Furthermore, scanning electron microscopy (SEM) analysis showed that the incorporation of 3% CNC into the composite scaffold resulted in an increase in interconnected pore size from (362 ± 19 µm) in neat PLA to (487 ± 17 µm) in CNC/PLA composites. This structural enhancement facilitates improved cell attachment, proliferation, and tissue regeneration processes within the scaffold.

In contrast, Radakisnin et al. [32] Incorporating CNF from *Pennisetum-purpureum* into PLA-based composite scaffolds reduced pore size with increasing CNF content. The porosity of these scaffolds decreased proportionally with higher CNF content, reaching a minimum of 76.89% in scaffolds containing 20 wt. % CNFs. This decrease indicated a denser CNF network arrangement, significantly impacting scaffold porosity. Field emission scanning electron microscopy (FESEM) analysis verified the scaffolds' advantageous features, such as interconnected pores, high surface area, and effective fluid retention capacity, which are crucial for supporting cell attachment and proliferation. The study highlights the role of CNF reinforcement in modifying scaffold pore structure in PLA/CNF composites, influencing cell behaviour within scaffold environments.

Mineral-based nanofiller-PLA nanocomposites

Natural nanofillers like clays, calcium carbonates, and silica are recognized as green fillers due to their natural origin and environmentally friendly characteristics. These fillers exhibit exceptional properties that are advantageous for diverse applications. They provide robust mechanical reinforcement, enhance thermal stability, improve barrier properties, and are cost-effective and eco-friendly. Moreover, they are compatible with various polymers, making them highly suitable for biomedical composite applications. Many researchers use this nanofiller as a reinforcement in PLA composites.

Mechanical Properties

Kumar et al. [40] reinforced PLA with environmentally friendly sepiolite nanoclay filler through melt blending techniques. At 1 wt. % loading of sepiolite, he observed a significant enhancement in the mechanical properties of the composites, with a notable 32% increase in tensile strength and a 10% increase in tensile modulus. These improvements are primarily attributed to the interactions that developed between the silanol groups of this nano clay and the polymer chains of PLA, which is similar to findings by Fukushima et al. [61]. The integration of sepiolite enhances the load-bearing capabilities and structural integrity of the composite materials while also influencing the flexural modulus by increasing material stiffness due to its rigid structure.

Using melt compounding, Krishnamachari et al. [41] produced PLA composites with organically modified nanoclay (Cloisite 30B). They observed enhancements in tensile strength Young's modulus with adding 1 wt. % of Cloisite 30B. An increment about 40% on tensile modulus was found with 8.0 wt. % of montmorillonite (MMT) clay content incorporated within PLLA composites conducted by Lee et al. [21]. Robledo-Ortíz et al. [62] investigated three different types of nanoclay-reinforced PLA composites. These nanocomposites were prepared via twin-screw extrusion using nanoclays ranging from 6 mm to 20 mm in particle size. The study demonstrated that each nanoclay type had unique effects on the properties of the PLA nanocomposites, including variations in strength, depending on the type and concentration of nanoclay employed. The observed enhancement in mechanical strength highlights the nanoclay's ability to effectively augment the PLA matrix's mechanical stability. This improvement is critical as it aligns the composite materials with the specific requirements of various biomedical applications.

In addition to clay, other eco-friendly mineral fillers, including calcium-based fillers, have also been explored for their role in PLA nanocomposites. Calcium-based materials are known for their superior biocompatibility and bioactivity due to their structural similarity to bone tissue [63]. In addition, they offer significant enhancements in mechanical properties and high biocompatibility, making them highly suitable for a range of biomedical applications [64][65]. Pundir et al. [66] employed the melt blending technique to create PLA-nanocalcium carbonate (nano$CaCO_3$) composites, utilizing calcium carbonate with an average particle size of 65 nm. They observed notable enhancements in mechanical properties, particularly tensile strength and elongation at break, attributed to the presence of nano$CaCO_3$ filler [66]. This filler improved the stiffness behaviour of the PLA nanocomposites, making them suitable for diverse applications. Transmission electron microscopy (TEM) images demonstrated that at a nano$CaCO_3$ content of 1 wt. %, the filler was homogenously dispersed throughout the PLA matrix, contributing to the enhanced mechanical properties. However, the filler content should be increased to 3 wt. % of nano$CaCO_3$ resulted in the agglomeration of filler particles within the nanocomposites, indicating a less uniform distribution. This uneven distribution adversely affected the mechanical strength and stiffness of the nanocomposites.

It is worth mentioning that optimizing the loading levels of fillers in polymers is crucial because it significantly impacts the mechanical performance of nanocomposites [41]. Critical factors include ensuring the uniform dispersion of the filler within the polymer matrix and enhancing the strength of the interface between the fillers and the matrix. These factors are essential for efficient stress distribution during mechanical loading. Various methods have been developed to address these challenges. For instance, the master batch technique, as explored by Oliver-Ortega et al. [42] has proven effective in enhancing the dispersion of bentonite nanoclay within PLA matrices. This method involves a two-step mixing process demonstrating notable improvements in Young's modulus and tensile strength. Higher filler loading increases interactions between fillers, leading to the formation of lump. This highlights the challenge of achieving homogeneous dispersion in PLA matrices and underscores its significant impact on the mechanical behaviour of the composites. Kumar et al. [67] investigated the incorporation of treated calcium carbonate (CC) into PLA, achieving a uniform dispersion of CC nanoparticles within the PLA matrix. This was demonstrated by the observed improvement in the nanocomposites' storage moduli and glass transition temperature, as evidenced by DMA analysis. Apart from that, Feven et al. [68] introduced modified nano-hydroxyapatite (mNHA) into PLA matrix showed that the mechanical behaviour of PLA-mNHA by 19.7% (modified with 3-aminopropyl triethoxysilane) and 10.6% (modified with sodium n-dodecyl sulfate). The tensile strength of these PLA-mNHA nanocomposites matches the strength needed for bones, underscoring their potential as suitable materials for load-bearing implants.

By precisely adjusting mechanical properties such as strength and durability, nanoclay-enhanced PLA composites show significant promise for utilization in medical devices and other medical applications. This advancement not only bolsters the structural integrity of the materials but also supports their functionality and long-term performance in biomedical contexts, contributing significantly to advancements in healthcare and treatments.

Biocompatibility

Mineral fillers are well-suited for medical applications because they are biodegradable and inert and can support tissue integration, demonstrating strong biocompatibility and capacity to modulate biochemical processes within the body. These characteristics are crucial for creating effective and safe medical devices and implants that integrate seamlessly with biological systems. Additionally, achieving good thermal stability allows these materials to withstand physiological temperatures without undergoing degradation or changes in mechanical properties, ensuring long-term performance and safety. In bone tissue engineering, optimal thermal characteristics are critical to minimize mismatch with surrounding tissues, supporting scaffold compatibility and tissue integration. Furthermore, precise thermal properties are essential for controlled drug delivery systems, regulating the release kinetics of bioactive molecules and enhancing the scaffold's effectiveness in promoting tissue regeneration and healing. Managing thermal behaviour is, therefore, pivotal in designing mineral-filled materials that meet the stringent requirements of biomedical applications. Krishnamachari noted that the thermal properties of PLA nanocomposites could be precisely adjusted by incorporating modified nano clay (Cleosite 30B), as indicated by shifts observed in the glass transition temperature (Tg) in the DSC results [41].

The addition of clay as a filler to reinforce the PLA matrix has shown promising biocompatibility. Connolly et al. [69] reported that PLA composites containing modified sodium-activated bentonite clays exhibited minimal toxicity in skin migration tests without notable reductions in cell viability or causing skin irritation observed in vitro. Gandolfi et al. [70] found that the incorporation of calcium silicate and dicalcium phosphate dihydrate into PLA porous scaffolds improved the biocompatibility of the composites, as evidenced by their non-toxic nature. These studies collectively suggest that migration levels from the nanocomposites were negligible, implying the potential safe use of these materials in cosmetic packaging and medical applications.

Kumar et al [40] observed a marginal increase in water absorption of PLA bionanocomposites reinforced with sepiolite nanoclay, approximately 17%, with the incorporation of 2 wt. % sepiolite nanoclay into neat PLA. This increase is due to the hydrophilic nature of both sepiolite and calcium carbonate fillers, which promote water absorption and impart hydrophilicity to the bionanocomposites. Similar results were found by Pundir et al. [66] when incorporating environmentally friendly nanocalcium carbonate fillers into PLA composites, demonstrating a substantial increase in water absorption of up to 1500% at comparable weight percentages. The addition of hydroxyapatite (HAP) particles into the PLLA matrix has been shown to enhance cell adhesion and proliferation, indicating that PLLA/HAP nanocomposites hold significant promise for bone repair and tissue engineering applications [64].

Nanoclay holds promise for significantly enhancing scaffold strength and bioactivity. Ongoing efforts to advance PLA/nanoclay scaffolds focus on modifying them to better suit bone tissue engineering applications. In vitro assessments revealed that integrating nanoclay into PLA scaffolds notably enhanced the biocompatibility of the materials [71]. Another innovative approach in tissue engineering involves integrating bioactive molecules with controlled release patterns. Grigora et al. [72] found that the uncoated PLA/MMT nanocomposite scaffolds exhibit inherent biocompatibility, promoting favourable cell growth within their porous structure. However, further applying Strontium bioglass (SrBG) coating enhances their suitability for bone tissue engineering applications. This enhancement supports cell proliferation and facilitates osteogenic differentiation. Other green materials, such as chitosan, have also been explored. Torrez-Hernandez et al. [73] created PLA composites with chitosan as a filler, showcasing improvements that enhance cell proliferation, adhesion, and metabolic activity on the composite surfaces.

Conclusion

In designing PLA-based biomedical devices, it is crucial to understand the key properties of PLA-based biomaterials, including mechanical performance, biodegradability and biocompatibility. Recent advancements in nanotechnology have introduced new opportunities for creating advanced nanocomposites with improved degradation and mechanical characteristics. Green nanofillers, in particular, offer significant potential for enhancing the structure and properties of PLA matrices while also supporting sustainability and environmental benefits. This review has examined how incorporating green nanofillers into PLA matrices can optimize degradation rates, biocompatibility, and mechanical properties. The ongoing research highlights the promising potential of PLA-based nanocomposites for next-generation biomedical applications. Nevertheless, further advancements are needed to address existing challenges before these materials can be adapted for large-scale production and practical use.

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