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REVIEW ARTICLE-MECHANICAL ENGINEERING

Recent Advances in Metal Particle Reinforced Polylactic Acid Biocomposites via Additive Manufacturing for Biomedical Applications

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Abstract
Polylactic acid (PLA) has attracted significant attention in biomedical applications due to its biodegradability, biocompatibility, and ease of processing; however, its poor mechanical properties, low toughness, and limited suitability for load-bearing applications significantly restrict its broader clinical use. The primary challenges hindering the development of high-performance PLA-based biocomposites are insufficient interfacial bonding between the polymer matrix and metal reinforcements, non-homogeneous dispersion of metallic phases, and unpredictable degradation behaviors within physiological environments. This study comprehensively explores the advancements in PLA based metal-reinforced biocomposites manufactured through additive manufacturing techniques, specifically focusing on enhanced mechanical properties and biocompatibility. The integration of metallic reinforcements, including titanium, stainless steel, magnesium, and silver, into PLA matrices significantly improves tensile strength, durability, and overall mechanical performance. Material Extrusion (ME) technology emerges as a pivotal manufacturing method, enabling the fabrication of complex, customized geometries essential for biomedical applications. The research systematically evaluates the optimization of metal reinforcement ratios and their effects on the viscosity, moldability, mechanical robustness, and biocompatibility characteristics of the resulting biocomposites. The study reveals that while certain metals enhance mechanical properties, others contribute antimicrobial properties and improved bioactivity, making these composites particularly suitable for tissue engineering applications. However, challenges persist in achieving uniform metal distribution, ensuring adequate metal-polymer interfacial adhesion, and controlling biodegradation rates. This review bridges existing literature gaps by providing a holistic perspective on how PLA-based metal-reinforced biocomposites can meet both mechanical and biological requirements, advancing their potential applications in the biomedical field, particularly for personalized implants and scaffolds in tissue engineering.

Keywords Metal-reinforced biocomposites · Fused deposition modeling · Biomedical applications · Tissue engineering · Biodegradability

1 Introduction

Polylactic acid (PLA) is a biodegradable and biocompatible polymer that has gained significant attention across various industries, including packaging, textiles, and biomedical applications due to its sustainable and versatile properties [1]. Derived from renewable resources such as corn starch and sugarcane, PLA offers numerous advantages, including low toxicity, ease of processing, and the ability to degrade into environmentally benign byproducts under composting conditions [2]. These attributes position PLA as a leading candidate for applications ranging from disposable consumer goods to high-value biomedical devices, including sutures, stents, and scaffolds for tissue engineering [3].

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In the medical field, PLA's biocompatibility and biodegradability are particularly advantageous. Its ability to degrade within the human body into non-toxic lactic acid byproducts has enabled its widespread adoption in drug delivery systems, temporary implants, and tissue regeneration [4]. However, despite these benefits, the mechanical limitations of PLA such as brittleness, low impact resistance, and insufficient thermal stability significantly hinder its applicability in high-performance and load-bearing applications. For instance, PLA exhibits a tensile strength of around 50–70 MPa, a compressive strength of approximately 60–70 MPa, and an elastic modulus of about 3.5–4 GPa [5]. While these properties are comparable to the lower range of human cortical bone, which has a tensile strength of approximately 50–150 MPa, a compressive strength of around 100–200 MPa, and an elastic modulus ranging from 7 to 30 GPa, PLA's mechanical properties fall short of the requirements for high-stress or weight-bearing environments without reinforcement [6].

To address these challenges, various strategies have been explored, including the development of PLA-based composites reinforced with materials such as natural or synthetic fibers, metals, and ceramics [7–11]. These reinforcements may enhance the strength, stiffness, and thermal stability of PLA, making it more suitable for demanding applications.

Advancements in additive manufacturing (AM) technologies have revolutionized the fabrication of PLA-based biocomposites. AM, commonly known as 3D printing, enables the production of complex, customized geometries from computer-aided design (CAD) models, eliminating the need for expensive molds and reducing production lead times. This is particularly beneficial for biomedical applications where personalized designs are essential for optimizing patient outcomes [12].

Among the various AM techniques, Material Extrusion (ME), such as Fused Deposition Modeling (FDM), has emerged as a popular method for fabricating PLA-based biocomposites. FDM utilizes thermoplastic filaments like PLA to create structures layer by layer, allowing for the incorporation of reinforcements that improve mechanical and thermal properties [13, 14]. While components produced through ME may exhibit lower mechanical strength compared to those manufactured via traditional methods like injection molding, ongoing research focuses on optimizing process parameters, such as nozzle temperature, print speed, and layer height, to enhance the performance of 3D-printed components [7, 15].

Despite these advancements, challenges persist in achieving the desired material properties, process repeatability, and integration of AM with existing manufacturing systems. Variations in machine calibration, environmental conditions, and material properties can affect the consistency of printed components [16–18]. Moreover, the limited mechanical strength and dimensional accuracy of some AM-printed parts highlight the need for further innovations in material formulations and process optimization. The integration of dual-nozzle systems and hybrid materials in AM holds promise for overcoming these limitations. By combining PLA with other thermoplastic polymers or reinforcing agents, researchers can develop composites that leverage the advantages of each material, resulting in improved mechanical and thermal properties [19].

In recent years, research on metal-reinforced PLA biocomposites for biomedical applications has gained significant momentum. Several studies have demonstrated that incorporating metallic or functional nanomaterials into PLA matrices can substantially enhance both mechanical strength and biological functionality, making them promising candidates for load-bearing and bioactive implants. For example, surface modification of magnesium-based implants has been shown to improve corrosion resistance and biocompatibility [20]. Graphene-based hydrogel-PLA scaffolds are being explored for applications in neural tissue engineering due to their electrical conductivity and cell-supportive architecture [21]. Moreover, the design of immuno-modulatory composite scaffolds capable of mimicking immune-osteogenic signaling pathways has emerged as a novel strategy to enhance tissue integration and regeneration [22]. Recent reviews have further highlighted advances in additive manufacturing techniques and the development of nanoengineered antimicrobial materials, underscoring the growing interest in multifunctional PLA-based systems for biomedical use [23, 24].

This review systematically examines the enhancement of PLA's mechanical properties and biocompatibility, particularly in the context of metal-reinforced PLA biocomposites. Its primary objectives include:

- *Enhanced Mechanical Strength* This review explores how the integration of metal particles into PLA matrices can significantly improve the mechanical strength, durability, and overall performance of PLA biocomposites. Previous studies have shown that metal-reinforced PLA biocomposites possess superior tensile strength compared to pure PLA, making them promising for applications requiring high mechanical performance, such as biomedical implants and load-bearing structures [18].
- *Optimized Biocompatibility* Understanding the impact of metal reinforcement on PLA's biocompatibility is essential for medical applications, where materials must be safe for long-term use in the human body [25]. This work investigates the potential synergistic effects of metal particles on PLA's biological performance, aiming to provide critical insights into how these composites can be tailored to meet the stringent biocompatibility requirements for medical use [26].

- *Effectiveness of Material Extrusion Technology* The review also evaluates ME technology's role in producing complex structures of metal-reinforced PLA biocomposites [13, 14]. ME offers a pathway to fabricate custom-designed components, but challenges remain in ensuring the materials meet the specific mechanical and thermal properties required for medical applications [19]. This study explores how optimization of ME parameters can enhance the fabrication of these advanced biocomposites

Despite the existing research indicating that metal-reinforced PLA composites exhibit improved tensile strength and durability, comprehensive reviews that assess the advancements in this area remain sparse. In particular, the discourse surrounding the application of PLA composites in medical implants is limited, especially regarding how metal reinforcements can enhance biodegradability and biocompatibility [26]. This review aims to bridge this gap by evaluating the synergistic effects of metal reinforcement on PLA, with a focus on biomedicine and tissue engineering applications. By investigating these interactions, the review seeks to provide a holistic perspective on how these biocomposites can meet both mechanical and biological demands, advancing their use in medical applications.

To guide the reader through the structure of this review, Fig. 1 presents a schematic overview of the manuscript's organization. This hierarchical outline reflects the logical progression of the content, beginning with the fundamental properties of PLA, moving through additive manufacturing methods and metal reinforcements, and culminating in biomedical applications, structural challenges, critical discussion, and conclusions. This structure is designed to support a comprehensive understanding of how metal-reinforced PLA biocomposites are being developed and optimized for high-performance biomedical use.

2 Material Properties of PLA

2.1 Chemical Structure and Production

PLA is a versatile thermoplastic polyester synthesized primarily from lactic acid, which is derived from renewable resources like corn starch, sugarcane, and various other biomass materials. The polymer's backbone is composed of linear aliphatic polyester units, where each lactic acid unit is interconnected through ester bonds [27].

The production methods for PLA typically involve (i) condensation polymerization and (ii) ring-opening polymerization of lactic acid (Fig. 2). Each method significantly influences the polymer's molecular weight and mechanical properties, thereby dictating its applicability across specific applications [28].

Direct condensation polymerization involves the polymerization of lactic acid monomers, releasing water as a byproduct. The straightforward nature of this method often results in a lower molecular weight ($< 50{,}000$ g.mol^{-1}) due to the challenge of completely removing the byproduct, which can limit the mechanical strength of the polymer. Advanced catalytic systems and dehydration processes are integral to overcoming these limitations, enhancing the polymer's molecular weight and material strength [29].

Ring-opening polymerization is preferred for industrial applications due to its efficiency in producing higher molecular weight PLA. Ring-opening polymerization involves the polymerization of lactide (a cyclic dimer of lactic acid) in the presence of catalysts such as tin(II) octoate, Zn(II), and $Sn(Oct)_2$. The polymer's properties vary with the stereochemistry of the lactide monomer, giving rise to different forms such as poly-L-lactic acid (PLLA), poly-D-lactic acid (PDLA), and racemic PLA (PDLLA) [30].

PLA's structure allows for diverse configurations, influencing its crystallinity and optical purity. Typically, PLA with more than 90% L-lactic acid content tends to form a semi-crystalline structure, while lower percentages result in amorphous forms [31–33]. Both PLLA and PDLA manifest similar thermal properties, with melting temperatures around 170–180 °C and glass transition temperatures approximately 55–60 °C [31]. The molecular weight of PLA can vary significantly, from 35,500 to 150,000 g/mol, depending on the synthesis method employed. This variation is critical as lower molecular weight PLA tends to crystallize faster and achieve higher crystallinity levels [34].

Commercial PLA grades predominantly use an L-lactic acid-rich mixture, reflective of the output from bacterial fermentation processes that favor L-lactic acid production [35]. The irregularity of PLA's molecular chains and the formation of inter- or intramolecular hydrogen bonds impede the chains' mobility, affecting the diffusion rate into the lattice and the regular arrangement during melt cooling. This leads to PLA's modest heat resistance, with a heat deflection temperature ranging only between 55 and 65 °C [36].

The tailorable nature of PLA's molecular weight, crystallinity, and degradation rate through synthesis adjustments and stereochemistry modifications enables its use in a wide array of applications. Continued advancements in catalyst development and polymerization techniques aim to reduce production costs and further enhance the material's mechanical properties and biodegradability. The physical properties of PLA, including specific gravity, molecular weight, melt flow index, and melting temperature, are presented in Table 1.

The variations in stereochemical composition permit the production of both amorphous and crystalline forms of PLA, highlighting the adaptability of this biopolymer to meet specific application requirements.

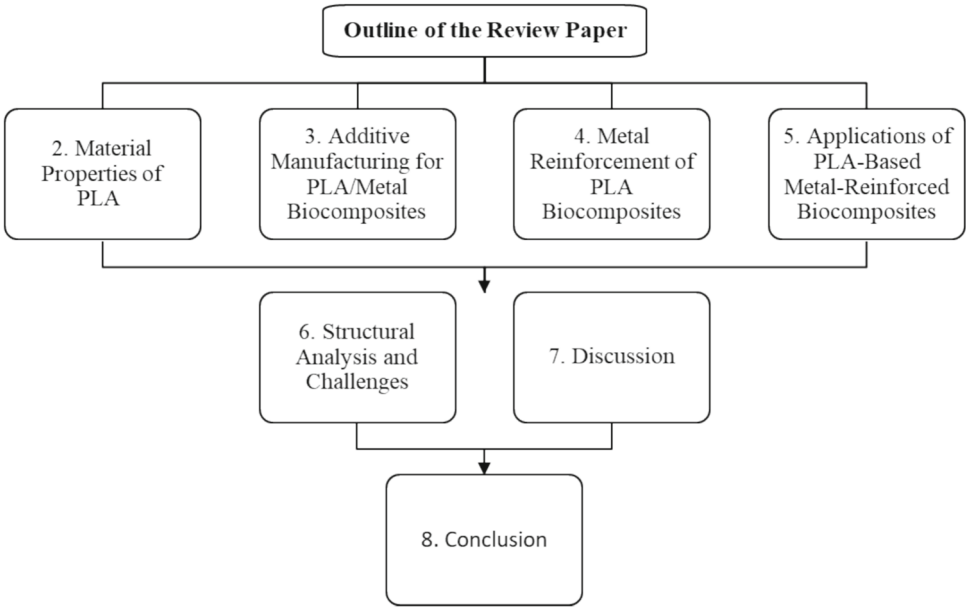


Fig. 1 Schematic overview of the review paper structure, illustrating the hierarchical organization of major sections

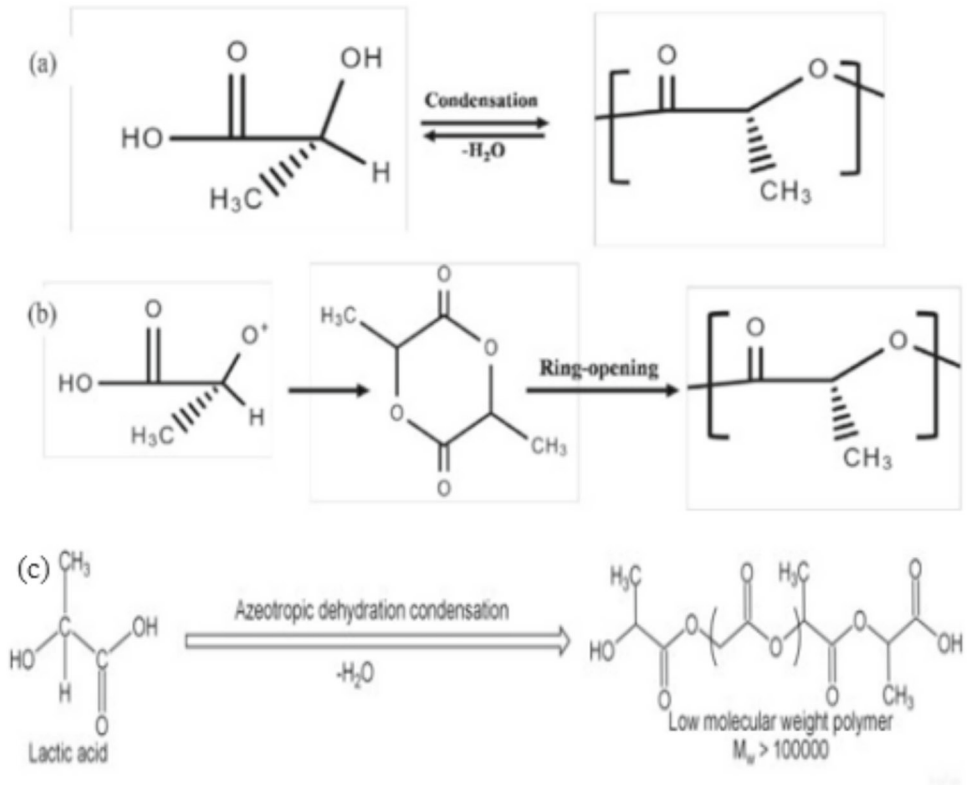


Fig. 2 The structure of **a** PLA, **b**, Ring-opening polymerization **c** Direct condensation polymerization [30]

2.2 Mechanical Properties

PLA offers moderate tensile strength and flexural strength, which are critical for applications requiring rigidity and load-bearing capacity [38]. As shown in Fig. 3, PLA offers numerous advantages, including an energy-efficient production process that generates minimal greenhouse gas emissions, making it a highly sustainable material [39]. PLA's key attributes, such as biodegradability, widespread availability, antibacterial activity, and favorable mechanical and thermal properties, make it an appealing choice for developing sustainable products, particularly in biomedical and

Table 1 Physical properties of PLA, including specific gravity, molecular weight, melt flow index, and melting temperature [37]

Physical Property	Range
Specific Gravity	1.0–1.5
Molecular Weight	Approximately 1.6×10^5 Daltons
Melt Flow Index	4–22 g/10 min
Melting Temperature	140–210 °C

packaging applications [40]. However, PLA, while offering several advantages, has certain limitations that affect its suitability for various applications [41].

Additionally, PLA exhibits poor barrier properties, making it less suitable for applications requiring moisture or gas resistance. This lower glass transition temperature impacts its performance in heat-resistant applications, highlighting areas where PLA may not be the optimal choice due to its inherent properties (Table 2) [2].

Such drawbacks restrict its performance in high-demand applications, particularly those requiring enhanced mechanical durability or thermal resistance. Ongoing research focuses on improving PLA's performance by incorporating reinforcements like metal particles. However, PLA still faces challenges in engineering applications, such as low impact strength, limited ductility, low elongation at break, poor thermal resistance, slow crystallization rate, brittleness, and susceptibility to moisture [41, 44].

PLA exists in different structural forms that significantly impact its mechanical performance. The degree of crystallinity in PLA is largely determined by its stereochemical composition, particularly the ratio of L-lactide to D-lactide monomers. Poly-L-lactic acid (PLLA), which contains primarily L-isomers, can achieve high crystallinity (up to 35%), while Poly-D-lactic acid (PDLA) containing primarily D-isomers can also form crystalline structures. In contrast, Poly-DL-lactic acid (PDLLA), which contains a racemic mixture of D and L isomers, typically results in an amorphous structure. The D-content percentage in PLA is a critical parameter affecting crystallization behavior; as D-content increases, the crystallization rate decreases, resulting in more amorphous structures [45].

The mechanical properties of PLA vary significantly between crystalline and amorphous forms. Crystalline PLA (PLLA) generally exhibits higher tensile strength (45–70 MPa) and Young's modulus (3.0–3.8 GPa) compared to amorphous PLA (PDLLA), which typically shows tensile strength of 25–40 MPa and Young's modulus of 1.9–2.4 GPa. However, crystalline PLA tends to be more brittle with elongation at break of only 2–6%, while amorphous PLA offers slightly better elongation at 5–8%. Researchers found that highly crystallized PLA samples sometimes showed a gradual decrease in tensile strength from 29.4 MPa (amorphous) to 25.8 MPa (crystalline), though this finding varies across different molecular weights and processing conditions. Similar trends are observed in flexural properties, with crystalline PLA exhibiting higher flexural strength (80–100 MPa) and flexural modulus (3.5–4.2 GPa) compared to amorphous PLA's flexural strength of 50–70 MPa and flexural modulus of 2.5–3.2 GPa [46].

Several factors influence PLA's crystallinity and consequently its mechanical properties. Molecular weight plays a significant role, with higher molecular weight PLA tending to decrease overall crystallinity due to longer polymer chains, while simultaneously increasing tensile strength through greater chain entanglement and increasing shear viscosity. Thermal history during processing also significantly impacts crystallinity—slow cooling promotes crystal formation and growth, annealing at temperatures between glass transition temperature (Tg) and melting temperature (Tm) enhances crystallinity, and the crystallization temperature affects spherulite size and morphology [47]. Research shows that PLA crystallized at different temperatures (100–130 °C) develops different spherulite structures, with many small nuclei forming at lower temperatures (100–110 °C) and

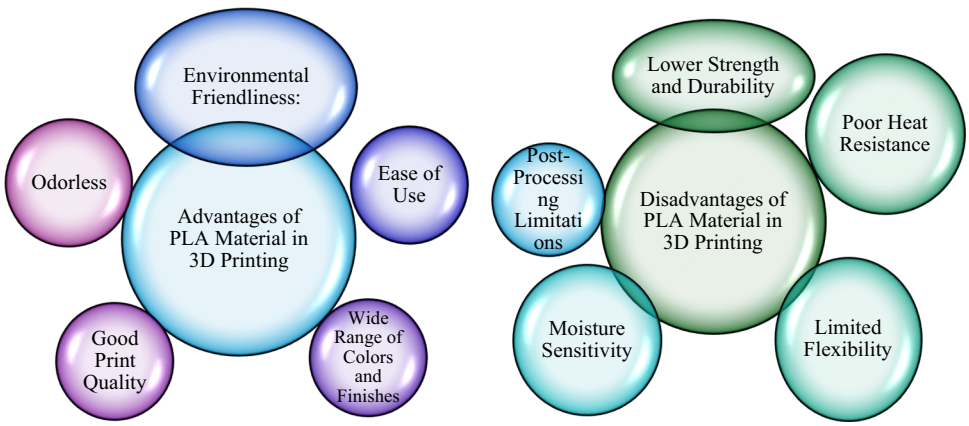


Fig. 3 Advantages and limitations of PLA in biomedical and engineering applications

Table 2 Mechanical Properties of PLA [42, 43]

	YM (GPa)	UTS (MPa)	BS (MPa)	EF (%)	Toughness (kJ/m^2)	Barrier Properties /cm^3·mm/m^2·day·atm)	Thermal Stability (°C)	Glass Transition Temp (°C)
PLA	3.2	49	70	2.5	2.5–6	10–20	50–65	55–60

YM = Young's Modulus, UTS = Ultimate Tensile Strength, BS = Bending Strength, EF = Elongation to Failure

fewer, larger spherulites developing at higher temperatures. Additionally, various additives can alter the crystallization behavior of PLA, with nucleating agents accelerating crystallization rates, plasticizers (such as citrate ester, PEG, sorbitol) improving crystallinity while reducing brittleness, and reinforcing fibers acting as nucleation sites for crystal growth [48].

The different forms of PLA offer distinct advantages for various applications. Crystalline PLA (PLLA) provides higher stiffness (Young's modulus up to 3.8 GPa), superior heat deflection temperature, better barrier properties against gases, enhanced chemical resistance, and reduced creep under sustained loading. These properties make crystalline PLA better suited for load-bearing applications such as orthopedic fixation devices and structural components, hot-fill packaging, and applications requiring dimensional stability at elevated temperatures. In contrast, amorphous PLA (PDLLA) offers improved ductility and impact resistance, better transparency, more consistent shrinkage during processing, more uniform mechanical properties, and a faster biodegradation rate. These characteristics make amorphous PLA preferable for applications requiring transparency, complex geometries, controlled drug delivery systems, and applications where processing consistency is critical [49].

Recent studies suggest that incorporating nanoclay particles into PLA can further enhance its properties. The hydrogen bonding between PLA's carbonyl groups and the ammonium groups in clay allows for a more effective mixing of the two materials. Moreover, natural fibers, cellulose, and nanocellulose have been shown to improve PLA's mechanical and thermal properties, making PLA-based biocomposites suitable for a wider range of applications [50].

2.3 Biocompatibility and Degradation

Composite materials offer notable advantages over traditional bulk materials, primarily owing to their enhanced properties, particularly in terms of the strength-to-weight ratio [51–53]. Traditional composites are frequently fabricated using synthetic polymers derived from petroleum-based sources, which lack biodegradability and pose environmental challenges. These materials contribute to pollution during decomposition, while the depletion of oil reserves exacerbates sustainability concerns. In contrast, PLA-based biocomposites present a promising, eco-friendly alternative to non-biodegradable and unsustainable composites processes. As a result, conventional petroleum-based composites pose environmental challenges. Moreover, the accelerated depletion of oil reserves presents a substantial predicament, as these resources are currently in danger of being completely exhausted due to their excessive utilization. Biocomposites derived from—PLA offer a highly auspicious alternative for replacing non-biodegradable and unsustainable composites [54]. Biocomposites utilize renewable biopolymers like PLA or starch as the matrix material and incorporate natural fibers for reinforcement. Common natural fibers used in biocomposites include sisal, hemp, wheat straw, coconut, and flax [55, 56].

Composite materials have experienced widespread use in diverse industries, including aviation, automotive, sports, furniture, medical equipment, and food packaging. This growing demand underscores the vast potential of biocomposites in industrial and commercial applications, offering a more sustainable solution compared to traditional composites [43].

3 Additive Manufacturing for PLA/Metal Biocomposites

Additive manufacturing (AM) technologies offer transformative approaches for developing composite materials, especially for integrating metal reinforcements into PLA. This section explores the pivotal AM techniques that transform raw materials into complex, functional products tailored for biomedical applications.

3.1 Overview of Additive Manufacturing Methods

AM, more commonly known as 3D printing, represents a revolutionary shift in the way materials and products are designed and manufactured. This technology layers materials to form objects from 3D model data, usually layer upon layer, as opposed to subtractive manufacturing methodologies [57, 58]. AM is distinguished by its ability to streamline complex designs, reduce lead times, and lower material waste, making it a cornerstone of sustainable manufacturing practices [59]. In the domain of material science, AM is particularly

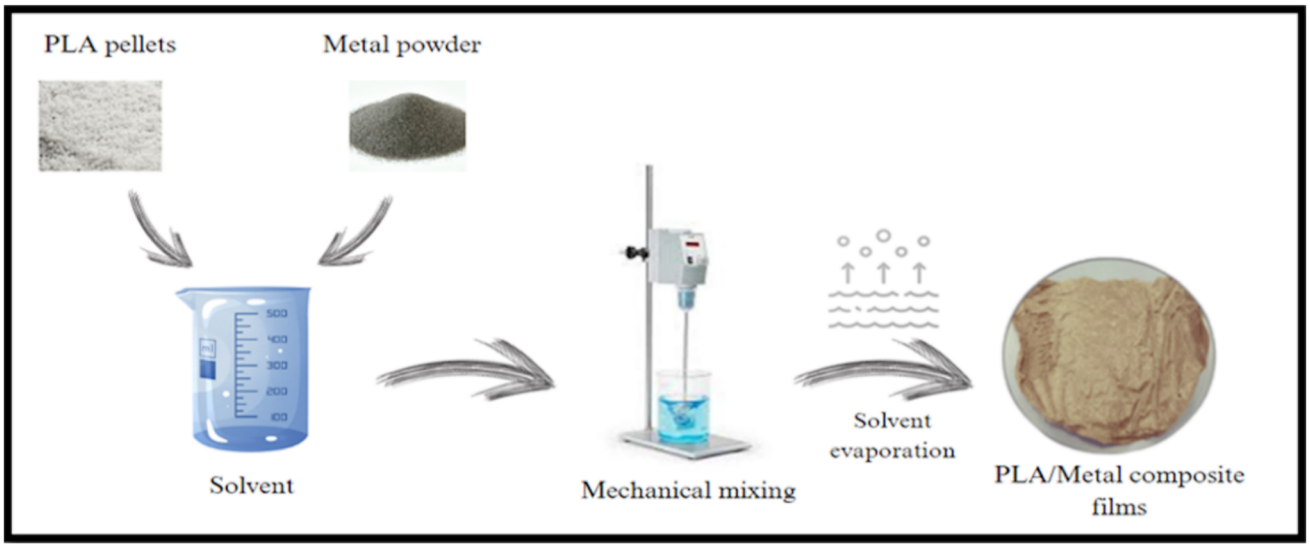


Fig. 4 Composite film preparation via solvent film casting

effective in enhancing the properties of PLA biocomposites by integrating metal reinforcements.

The fabrication of PLA-based metal-reinforced biocomposites via additive manufacturing typically involves two key stages; (i) composite filament preparation, and (ii) 3D printing using extrusion-based or powder-based techniques.

a. Composite Filament Preparation via*Melt Extrusion (ME)* Before 3D printing, PLA and metal powders (e.g., Ti, Cu, Mg, Fe, Ag) must be homogeneously blended and processed into printable filament form (Fig. 4). This is commonly achieved using melt extrusion, where polymer granules and metal powders are fed into a heated extruder, mixed under controlled shear and temperature, and then extruded into filament strands (Fig. 5) [60]. The desktop 3D printer employs a composite filament that has been fabricated to the requisite form and dimensions for the purpose of generating porous scaffolds (Fig. 6).

ME enables uniform dispersion of metal particles within the polymer matrix, which is critical for achieving consistent mechanical and biological performance. The process is also scalable and cost-effective, making it suitable for both laboratory-scale and industrial-scale filament production. Furthermore, ME allows for the incorporation of a wide range of metal filler concentrations, providing flexibility in tailoring the composite's properties for specific biomedical applications [61]. However, one primary challenge is the risk of metal particle agglomeration during mixing, which can lead to heterogeneous material properties. Additionally, the presence of metal powders increases the likelihood of nozzle clogging during subsequent 3D printing, potentially disrupting the fabrication process [62]. Maintaining uniform extrusion also demands strict control over processing parameters such as feed rate and temperature, which can be difficult to stabilize, especially when transitioning between different filler contents or polymer grades [63].

b. 3D Printing via*Fused Deposition Modeling (FDM)* Once composite filaments are produced, Fused Deposition Modeling (FDM), also known as Fused Filament Fabrication (FFF), due to its rapid prototyping capabilities and high design flexibility. In this technique, the filament is heated just above its melting point and deposited layer-by-layer through a nozzle to form 3D structures.

It is particularly advantageous for producing customized biomedical devices, where patient-specific geometries and quick turnaround times are critical [64]. Additionally, FDM is a cost-effective technique that minimizes material waste, making it suitable for iterative design and testing in both research and clinical settings [65]. Despite these advantages, the technique also presents several challenges. One of the primary concerns is the limited interlayer adhesion inherent to the layer-by-layer deposition process, which can reduce the mechanical strength and reliability of the final product [66]. Moreover, printed components often exhibit surface roughness, necessitating post-processing treatments to achieve the smoothness required for biomedical applications. The incorporation of metal particles into PLA filaments can further complicate the process by hindering extrusion flow, leading to inconsistent material deposition and potential print defects.

c. Powder-Based Fabrication via*Selective Laser Sintering (SLS)* SLS is a laser-based powder bed fusion technique capable of fabricating PLA/metal biocomposites from fine powders without the need for filament extrusion [67]. A high-power laser selectively sinters powder particles layer-by-layer based on a digital model. This method supports higher resolution and density, as well as complex internal

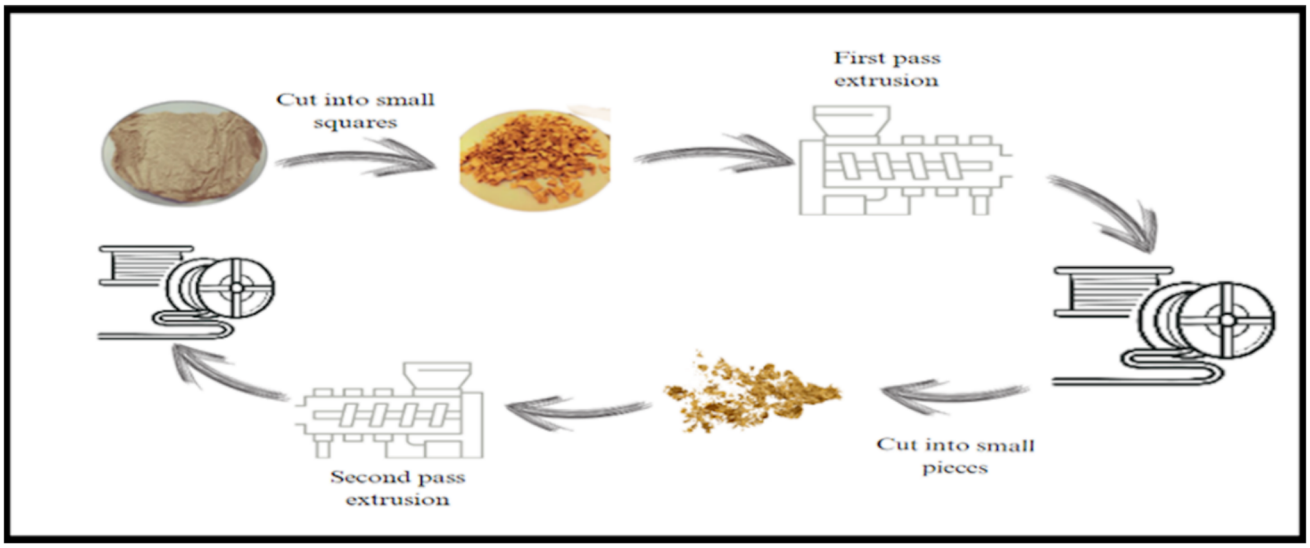


Fig. 5 Composite filament preparation

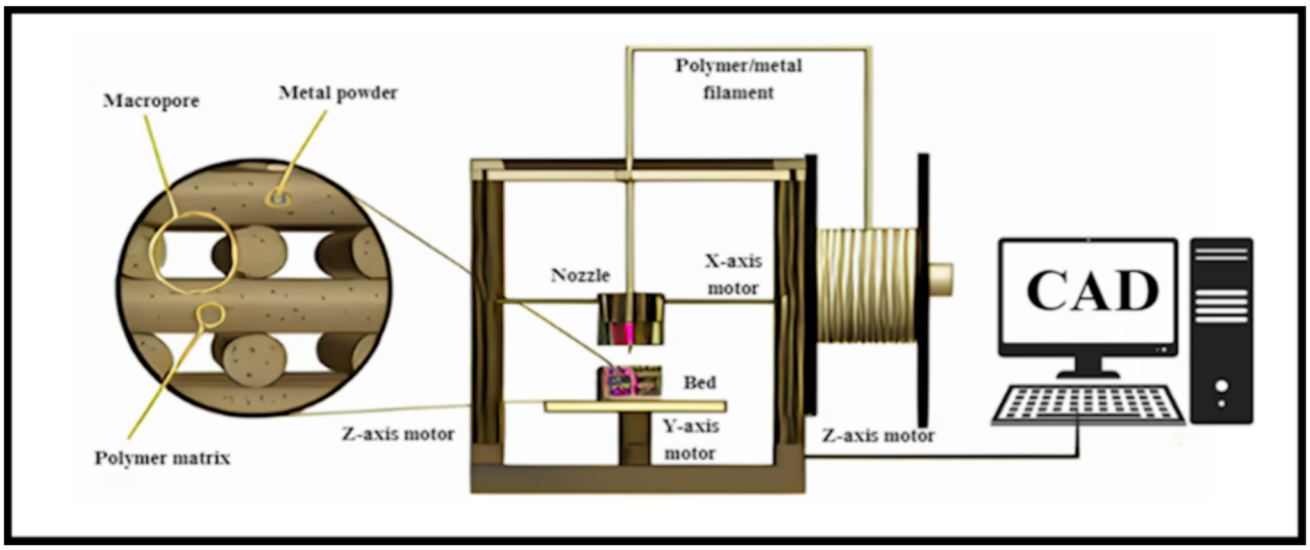


Fig. 6 Illustration depicting the ME method used to fabricate polymer/metal 3D porous scaffolds

geometries not achievable via FDM. SLS is particularly valuable for functional applications requiring high dimensional accuracy, mechanical integrity, and conductive networks, such as bone-mimicking implants or antibacterial scaffolds.

SLS presents a significant benefit for PLA/metal composites by enabling the fabrication of intricate geometries without requiring support structures, since the unsintered powder acts as a support during the printing process. This technique produces parts with excellent mechanical properties, with sintered components having close to 100% density and mechanical properties comparable to injection-molded parts [68]. SLS can create parts with intricate internal features and moving components that would be impossible with other manufacturing methods. The method has demonstrated significant effectiveness in producing electrically conductive polymer composites with outstanding functional performance, primarily due to the development of a segregated filler network at the boundaries of the powder particles. However, these advantages come at a cost. SLS systems require expensive hardware and have higher operational costs compared to more accessible techniques like FDM or ME. The process also involves more complex parameter control, including laser power, scan speed, and bed temperature, which must be carefully optimized to avoid defects such as warping or incomplete sintering. Moreover, the commercial availability of PLA-based powder blends compatible with SLS remains limited, which restricts widespread adoption for biomedical applications. Despite these challenges, SLS remains a

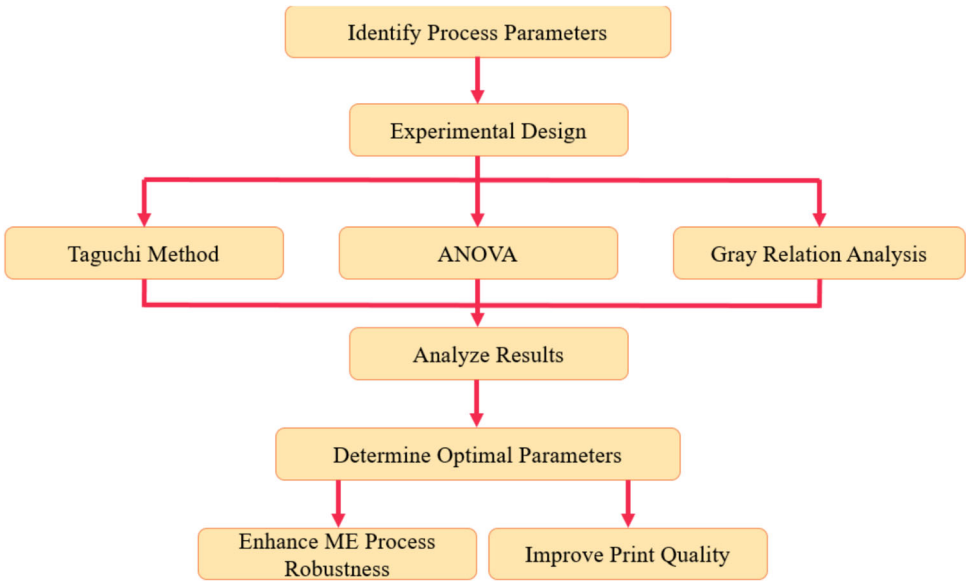


Fig. 7 ME Optimization Strategy Flow Diagram

promising technique for fabricating high-performance biocomposites with intricate architectures [69].

In this review, we have focused on additive manufacturing techniques relevant to thermoplastic-based PLA/metal biocomposites, such as FDM, and ME. Although Stereolithography (SLA) and Digital Light Processing (DLP) are powerful techniques for producing high-resolution parts, they are primarily designed for photopolymer resin systems and are not inherently compatible with the thermoplastic and particulate-based feedstocks used in PLA/metal composite fabrication. Therefore, SLA and DLP were excluded from this review to maintain relevance to fused filament and powder-based fabrication routes, which are more appropriate for metal-reinforced PLA systems.

3.2 The Optimization of ME Processes

Figure 7 illustrates a systematic optimization strategy for the ME process, which plays a critical role in determining the structural integrity and functional performance of printed components. The optimization process begins with defining the overall strategy and identifying key process parameters, such as extruder temperature, print speed, and layer height, that directly affect print quality and mechanical behavior.

An experimental design is subsequently developed to evaluate how these parameters affect product quality. Key analytical techniques such as the Taguchi Method, Analysis of Variance (ANOVA), and Gray Relation Analysis (GRA) are commonly employed to interpret the resulting experimental data (Table 3). These methodologies facilitate multi-factor optimization, allowing researchers to uncover parameter interactions and accurately quantify variability in outcomes under different process settings.

The Taguchi method systematically identifies optimal parameter settings by employing orthogonal arrays and the signal-to-noise (S/N) ratio. The S/N ratio quantifies deviations from desired performance targets under variable conditions, thus enabling the selection of robust parameter combinations. This method not only enhances printed object performance but also ensures consistent quality despite environmental fluctuations and inherent material variability. By analyzing results from orthogonal arrays, researchers identify key parameters and their optimal configurations, ensuring maximum structural integrity and functional reliability.

ANOVA is utilized to statistically evaluate the influence of individual and interacting parameters, such as nozzle temperature, filament diameter, print speed, and cooling rate, on final properties, including mechanical strength, dimensional accuracy, and surface finish. By systematically varying these parameters across defined ranges, ANOVA decomposes total data variability into contributions from each factor, clearly indicating which parameters significantly impact print quality. For instance, ANOVA can discern whether changes in layer height or extruder temperature more substantially affect mechanical properties, guiding precise parameter adjustments.

Moreover, modern multi-objective optimization approaches like GRA complement these techniques. GRA evaluates the relationships between multiple performance characteristics and process parameters, even when data are incomplete or uncertain. By consolidating multiple responses into a single gray relational grade, GRA simplifies complex multi-objective scenarios, making it especially

Table 3 ME Optimization Method/ techniques or tools

	Investigators									
	Torres et al [70]	Liu et al [71]	Fernandes et al. [72]	Huu et al. [73]	Zaman et al. [74]	Attoye et al. [75]	Cho et al. [76]	Rajpurohit et al. [77]	Qattawi et al. [78]	Beniak et al. [79]
Taguchi method	✓	✓			✓		✓			
Regression analysis	✓									
ANOVA	✓	✓	✓	✓	✓		✓	✓		✓
Gray relation analysis		✓								
Fractional factorial design										
Face-centered CCD (FCCCD)				✓						
OFAT Method and FEM						✓			✓	
S/N ratio		✓			✓		✓			

valuable for biomedical applications where material properties—such as mechanical strength and biodegradation rates which must be carefully balanced.

By analyzing the S/N ratio, ME practitioners can identify parameter settings that not only achieve the desired outcomes (e.g., tensile strength, surface finish) but also ensure that the process is less sensitive to external fluctuations. For instance, optimizing the nozzle temperature and print speed to maximize the S/N ratio would mean that the selected parameters yield consistent quality prints with minimal defects, regardless of minor fluctuations in environmental conditions or material inconsistencies.

Additional statistical tools like Fractional Factorial Design and Face-Centered Central Composite Design (FCCCD) enrich the optimization process by providing more nuanced exploration of parameter interactions. Fractional Factorial Design efficiently reduces the number of required experimental runs while maintaining comprehensive insights into key interactions. FCCCD, as a form of response surface methodology, is particularly suited to optimize parameters in complex multi-factor scenarios involving nonlinear relationships, commonly encountered in ME processes.

3.3 Effects of Printing Parameters on Mechanical Properties of PLA/Metal Biocomposites

In the field of material extrusion for PLA/metal biocomposites, printing parameters such as temperature, speed, layer height, and infill density critically influence mechanical properties, including porosity, adhesion, and interlayer bonding [80]. Here we discussed their effects on adhesion, mechanical properties. To better illustrate the relationship between key ME process parameters and mechanical performance outcomes, Figs. 8, 9 and 10 provide a comparative analysis of tensile strength as a function of nozzle temperature, layer height, and raster angle.

3.3.1 Temperature

The flowability of PLA is highly temperature-dependent, influencing the encapsulation of metal particles and the interfacial adhesion between materials. A higher nozzle temperature enhances the flow of PLA, leading to better encapsulation of metal particles and improved mechanical properties, as seen in PLA/Cu composites [86]. Furthermore, maintaining an optimal bed temperature is essential in minimizing warping and ensuring strong layer adhesion, which is critical for maintaining the integrity and dimension accuracy of printed parts [87]. Excessively high temperatures, however, can lead to thermal degradation, impacting material properties adversely.

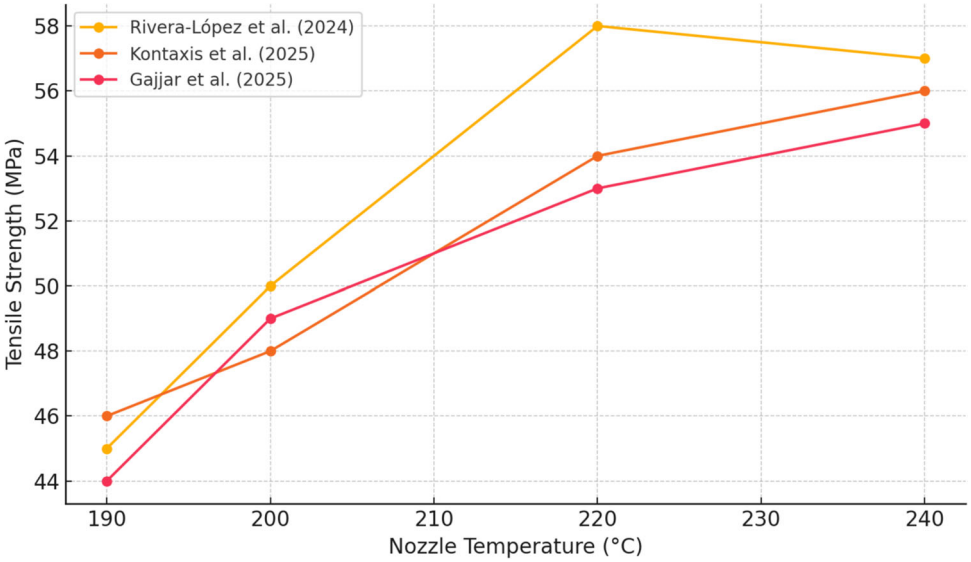


Fig. 8 Nozzle Temperature vs Tensile Strength [81–83]

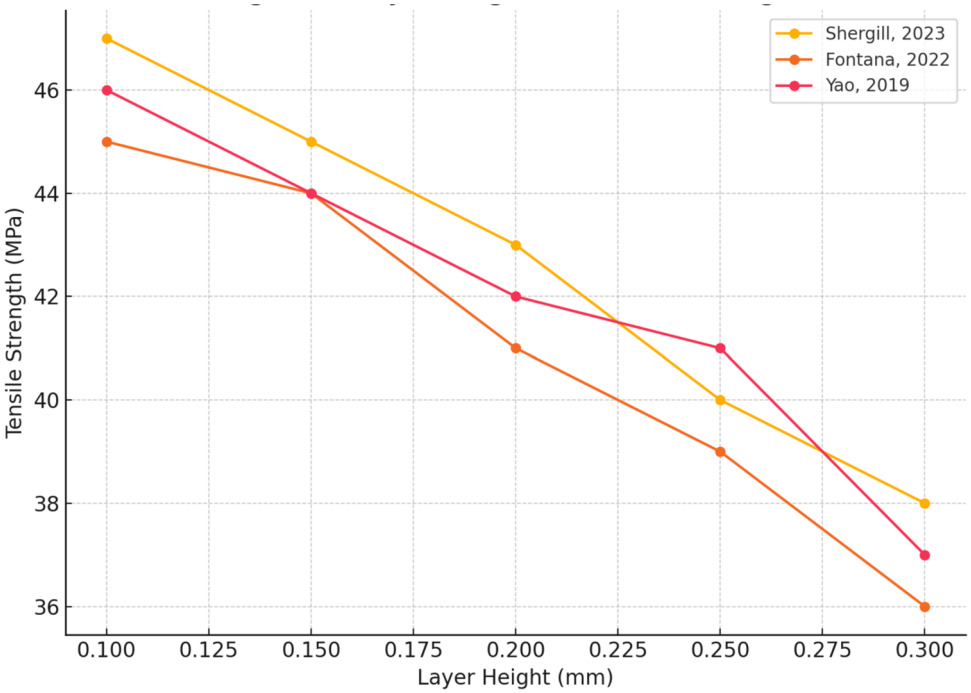


Fig. 9 Layer Height vs Tensile Strength [42, 84, 85]

3.3.1.1 Printing Speed Printing speed directly impacts the cooling rate and ultimately affects layer adhesion and mechanical strength. Slower speeds allow for better interlayer bonding due to reduced cooling rates, enhancing mechanical integrity. Nonetheless, overly slow speeds can cause material degradation through excessive heat exposure. An optimal balance is necessary to achieve structural stability without compromising material integrity [88].

3.3.1.2 Layer Height Layer height is a determinant of the surface finish, resolution, and internal structure of the printed material. Reducing layer height tends to improve mechanical properties by increasing interlayer adhesion and minimizing voids within the structure. This improved bonding is crucial for the even distribution of metal particles within the polymer matrix, enhancing both the tensile strength and overall mechanical performance. However, smaller layer heights extend print duration, necessitating a balance between time efficiency and part quality [10].

3.3.1.3 Infill Density and Pattern Infill density and pattern significantly impact the mechanical strength, weight, and stress distribution of the printed composite. Higher infill densities generally yield stronger structures, albeit with

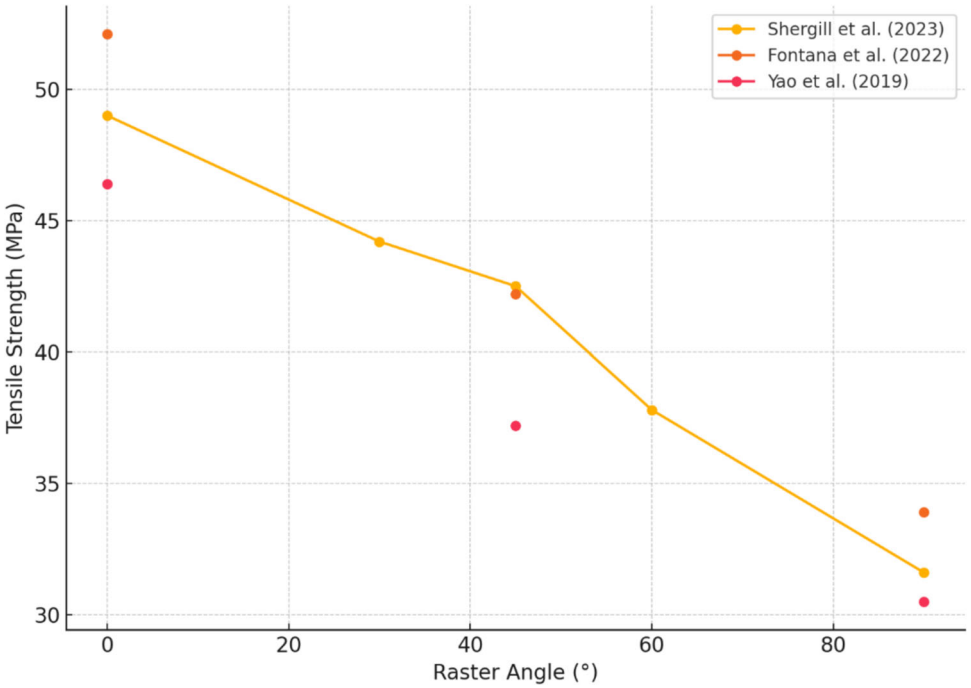


Fig. 10 Raster Angle vs Tensile Strength [42, 84, 85]

increased material usage and weight. Infill patterns, such as grid or honeycomb, can optimize load distribution, thus improving mechanical properties. Proper selection of infill parameters is vital for balancing strength, material usage, and functional performance [89].

The combined effects of these parameters must be considered to achieve optimal mechanical properties. For instance, higher nozzle temperatures combined with slower printing speeds can enhance interlayer adhesion but may require adjustments in layer height and infill density to prevent overheating and material degradation. Balamurugan et al. highlighted the importance of optimizing multiple parameters simultaneously to achieve the best mechanical performance in PLA/metal composites [86].

Optimizing printing parameters is crucial for enhancing the mechanical properties of PLA/metal composites produced via ME. By carefully adjusting temperature, speed, layer height, and infill density, researchers can significantly improve the performance and reliability of the printed parts [90]. Future research should focus on developing comprehensive guidelines for parameter optimization to facilitate the widespread adoption of PLA/metal composites in various applications. The ME process parameters used as input for optimization are presented in Table 4.

4 Metal Reinforcement of PLA Biocomposites

To enhance inherent weaknesses of biomedical PLA such as brittleness, relatively low mechanical strength, and suboptimal thermal resistance, the integration of metal reinforcements such as titanium, copper, magnesium, and silver into PLA composites has emerged as a pivotal innovation. Metal reinforcements involve embedding metal particles or fibres into the PLA matrix.

To provide a comprehensive and coherent analysis of metal-reinforced PLA biocomposites, this section is organized into three subsections. Section 4.1 presents the intrinsic properties of commonly used metal reinforcements, focusing on parameters such as tensile strength, corrosion behavior, density, and biocompatibility. Section 4.2 explores the mechanisms by which these metals enhance the mechanical, antimicrobial, and biodegradable characteristics of PLA-based composites. Finally, Sect. 4.3 reviews recent case studies involving additive manufacturing techniques, highlighting how different metallic reinforcements have been experimentally integrated into PLA matrices, along with their processing conditions, composite structures, and biomedical performance outcomes.

4.1 Properties of Metal Reinforcements

Selecting appropriate metal reinforcements significantly influences the mechanical and biological performance of PLA-based biocomposites. Here, the intrinsic quantitative properties including mechanical characteristics, corrosion

Table 4 The ME process parameters are utilized as input for optimization

	Investigators										
	Torres et al [70]	Liu et al [71]	Fernandes et al. [72]	Yılan et al [91]	Huu et al. [73]	Zaman et al. [74]	Attoye et al. [75]	Cho et al. [76]	Rajpurohit et al. [77]	Qattawi et al. [78]	Beniak et al. [79]
Layer thickness	✓	✓	✓		✓	✓		✓	✓	✓	✓
Post-processing (heat treating) time	✓										
Infill density	✓		✓			✓		✓		✓	
Raster width		✓							✓		
Air gap		✓									
Raster angle (raster orientation)		✓	✓		✓				✓		
Build orientation		✓			✓		✓			✓	
Extruder temperature			✓							✓	✓
Number of contours/Shells						✓					
Printing speed							✓			✓	
Nozzle Temperature							✓				
Infill pattern						✓				✓	

rates, densities, and biocompatibility profiles of commonly used metallic reinforcements are summarized: titanium (Ti), copper (Cu), 316L stainless steel, magnesium (Mg), iron (Fe), and silver (Ag) [92].

4.1.1 Titanium (Ti)

Titanium and its alloys, particularly Ti-6Al-4 V, are among the most widely preferred metallic materials for long-term biomedical implants due to their exceptional biocompatibility, non-toxicity, and high osseointegration capacity [93]. One of the key reasons for their clinical success is their excellent corrosion resistance in physiological environments, attributed to the spontaneous formation of a stable and inert titanium dioxide (TiO_2) surface layer [94]. This oxide film significantly limits ion release, thereby reducing the risk of adverse effects such as thrombosis and inflammation. Furthermore, titanium exhibits a relatively low density (~ 4.5 g/cm^3) compared to other structural metals such as stainless steel, offering significant advantages in weight-sensitive applications like orthopedic and dental implants [95].

From a mechanical standpoint, the hardness of titanium (614–736 MPa) is comparable to that of cortical bone, while its tensile strength (~ 900–1100 MPa) and yield strength (~ 830–900 MPa) provide superior load-bearing capability [96]. The elastic modulus of titanium alloys, typically ranging from 50 to 120 GPa, however, is considerably higher than that of natural bone (4–30 GPa). This mismatch may lead to stress shielding, a phenomenon where the implant bears the majority of the mechanical load, causing surrounding bone tissue to resorb due to insufficient physiological stimulation [97]. Over time, this can compromise implant stability.

Moreover, titanium alloys are prone to generating wear debris during long-term implantation, especially under fretting and micromotion conditions [98]. These wear particles can elicit inflammatory responses and contribute to periprosthetic bone loss, negatively affecting implant longevity. To mitigate such limitations, surface modification techniques such as plasma nitriding and physical vapor deposition (PVD) coatings have been investigated to reduce ion release, improve wear resistance, and enhance biological performance. Despite their many advantages, the primary drawbacks of titanium-based materials include their relatively high production costs and processing difficulties, particularly in additive manufacturing contexts [99].

4.1.2 Copper (Cu)

Cu, following zinc and iron, is the third most abundant essential trace element in the human body. It plays a vital role in numerous physiological processes, including the functioning of enzymatic systems, the synthesis of connective tissues, and bone development [100]. Copper deficiency has been associated with skeletal abnormalities such as occipital angle syndrome and an increased risk of cardiovascular diseases, emphasizing its importance in maintaining musculoskeletal and systemic health [101].

From a materials science perspective, copper exhibits moderate mechanical properties, with a tensile strength ranging from ~ 200 to 400 MPa, yield strength of ~ 70–350 MPa, and high ductility (elongation of 20–60%) [102]. Its relatively high density (~ 8.96 g/cm^3), however, may limit its use in applications where weight is a critical factor. More notably, copper is renowned for its potent antibacterial activity, mediated by the sustained release of $Cu2^+$ ions, which disrupt bacterial membranes and inhibit microbial replication [103]. In addition to its antimicrobial effects, copper contributes to angiogenesis by upregulating vascular endothelial growth factor (VEGF), thereby promoting vascularization and tissue regeneration—an especially advantageous trait for wound healing and bone repair.

Despite these benefits, copper's clinical use as a bulk implant material is limited due to its potential cytotoxicity at concentrations exceeding 1–5 μg/mL, and its susceptibility to corrosion in physiological environments. These factors can lead to uncontrolled ion release, oxidative stress, and inflammatory responses [104]. Therefore, copper is most effectively utilized as a reinforcing or coating agent in biodegradable polymer matrices such as PLA.

4.1.3 316L Stainless Steel

316L stainless steel is one of the most commonly used materials in biomedical engineering due to its excellent mechanical and chemical properties [105]. It exhibits high tensile strength (~ 480–620 MPa), yield strength (~ 170–310 MPa), and remarkable ductility (~ 30–50% elongation), which makes it particularly suitable for load-bearing applications such as orthopedic implants and fixation devices [106]. Its chromium-rich passive oxide layer offers outstanding corrosion resistance in physiological environments, resulting in extremely low corrosion rates (~ 0.0001–0.001 mm/year) [107]. Furthermore, the low carbon content in the 316L variant enhances resistance to intergranular corrosion, improving long-term performance and reliability in vivo. Additional benefits include good machinability and weldability, allowing for ease of fabrication using CNC machining, laser cutting, and welding techniques. Compared to alternatives such as titanium, 316L stainless steel is also more cost-effective, making it an attractive option for producing affordable medical devices. It also demonstrates excellent thermal stability, allowing for repeated sterilization cycles under high-temperature conditions, including autoclaving.

Despite these advantages, 316L stainless steel presents several limitations that restrict its application in certain biomedical contexts. Its relatively high density (~ 7.9 g/cm^3)

is a disadvantage in weight-sensitive applications, such as craniofacial or pediatric implants, where lighter materials are preferred [108]. More importantly, 316L is not biodegradable, making it unsuitable for temporary or resorbable implants that are expected to degrade over time. Although the alloy contains a significant amount of nickel (10–14%), the ion release from 316L stainless steel is extremely limited due to the formation of a stable passive oxide layer on its surface. As a result, allergic or inflammatory responses are rare and generally occur only in highly sensitive individuals. Moreover, the material's inert surface limits its osteointegration capacity, often necessitating additional surface modifications to enhance bone cell adhesion and tissue integration [109]. Over prolonged use under dynamic loading conditions, 316L may also exhibit fatigue-induced microcracks or wear. Finally, in acidic or inflammatory environments, the release of trace metallic ions such as Ni, Cr, and Fe—although minimal—can increase cytotoxic risks in extreme cases.

4.1.4 Magnesium (Mg)

Magnesium (Mg) alloys have emerged as promising candidates for temporary biomedical implants due to their unique combination of biodegradability, biocompatibility, and mechanical compatibility with bone [110]. One of the most significant advantages of Mg-based materials is their ability to gradually degrade in physiological environments, eliminating the need for secondary surgeries to remove the implant after tissue healing. This property makes them particularly attractive for applications such as surgical fixation devices, orthopedic bone plates, screws, and scaffolds in tissue engineering.

Mechanically, magnesium alloys offer tensile strengths in the range of 150–350 MPa and elongation values between 3 and 15%, which are sufficient for many non-load-bearing and moderately loaded biomedical applications [111]. Their low density (~ 1.74 g/cm^3), approximately one-quarter that of stainless steel and comparable to cortical bone, further enhances their suitability for lightweight implant systems, reducing stress-shielding effects and improving patient comfort.

However, one of the primary challenges associated with Mg alloys is their high physiological corrosion rate (0.5–5 mm/year) [110]. While beneficial for temporary implant resorption, this rapid degradation can lead to premature loss of mechanical integrity and uncontrolled hydrogen gas evolution, which may result in localized inflammation, tissue swelling, or gas pocket formation around the implant site. Therefore, controlling the corrosion behavior is critical, often requiring surface coatings, alloying with elements such as P, F, Zn or Ca, or other modification strategies to achieve a balance between degradation rate and biological safety [112].

From a crystallographic perspective, Mg alloys exhibit strong anisotropic behavior due to their hexagonal close-packed (HCP) structure, which limits their plastic deformation at room temperature [113]. Deformation primarily occurs via < a > basal slip and mechanical twinning, while non-basal slip systems remain inactive due to their high critical resolved shear stress. This results in low ductility and limited formability, particularly under ambient conditions. These intrinsic microstructural characteristics must be considered during both manufacturing and in vivo performance evaluations.

In summary, while magnesium alloys offer significant advantages in terms of bioresorbability and bone-mimicking density, their successful implementation in biomedical applications relies on precise control of their degradation behavior, enhanced corrosion resistance, and careful mechanical design to prevent premature failure during the healing process.

4.1.5 Silver (Ag)

Silver (Ag) has long been recognized for its potent antimicrobial properties and has been widely utilized in biomedical applications such as wound dressings, implant coatings, surgical sutures, and drug delivery systems [114]. It is generally accepted that silver exerts its antibacterial effect primarily through the release of Ag^+ ions, which can increase bacterial cell membrane permeability, disrupt DNA replication, interfere with metabolic pathways, and ultimately lead to cell death [114]. These effects have been observed at ion concentrations ranging from low μg/mL levels to tens of ppm, depending on factors such as bacterial strain, ion release rate, and the specific material system [115].

Despite its broad-spectrum efficacy, silver is not suitable for use as a bulk implant material. Its high density (~ 10.49 g/cm^3) and relatively low tensile strength (~ 170 MPa) limit its mechanical applicability, particularly in load-bearing implants. [116]. More critically, uncontrolled Ag^+ ion release from bulk materials poses a risk of cytotoxicity, as excessive concentrations can lead to oxidative stress, cellular damage, and inflammatory responses. In addition, silver's high cost and lack of biodegradability further constrain its use in long-term or resorbable implant systems.

To address these limitations, silver is more commonly employed in nanostructured forms (typically 1–100 nm) or as a surface coating on biodegradable polymeric or metallic substrates [117]. In such configurations, silver enables controlled and localized antimicrobial action, often achieving high antibacterial efficiency at significantly lower ion concentrations—thereby reducing cytotoxic risk. However, this efficacy is strongly dependent on material design, ion release

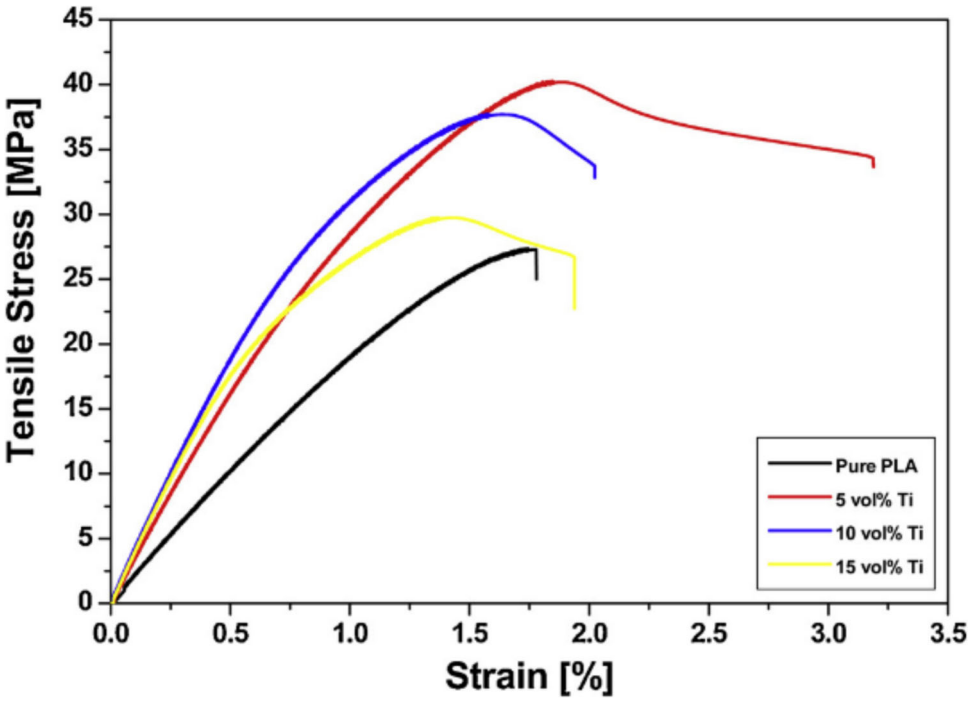


Fig. 11 Tensile stress–strain curves for neat PLA and PLA reinforced with 5%, 10%, and 15% Ti. Increasing Ti content improves stiffness and strength, with the highest enhancement observed at 15% Ti, where the elastic modulus doubled compared to neat PLA [121]

kinetics, and surface characteristics. Therefore, precise control over silver release profiles remains essential in the design of Ag-based biomedical materials.

4.2 Mechanisms of Metal Reinforcements in PLA Biocomposites

4.2.1 Enhanced Mechanical Properties

Integrating metals such as titanium, magnesium, and stainless steel into PLA significantly improves its mechanical properties, increasing tensile and compressive strength, elastic modulus, and overall durability [90, 118, 119]. These improvements make PLA composites particularly suitable for critical load-bearing biomedical applications such as bone grafts and orthopedic implants.

Titanium (Ti), in particular, has been extensively studied for its ability to enhance both the strength and ductility of PLA [120]. For example, Lee et al. incorporated 5%, 10%, and 15% Ti into PLA and reported a two-fold increase in elastic modulus from 2 GPa (neat PLA) to 4 GPa at 15% Ti (Fig. 11). Moreover, the ultimate tensile strength (UTS) increased from approximately 28 MPa (pure PLA) to 40 MPa at 5% Ti. The compressive yield modulus also showed a significant increase, rising from around 3.5 GPa to about 7 GPa at 10% Ti, while the ultimate compressive strength improved from around 13 to 30 MPa. These findings demonstrate that the mechanical performance of PLA/Metal composites can be tailored for specific biomedical applications through careful adjustment of filler content [121].

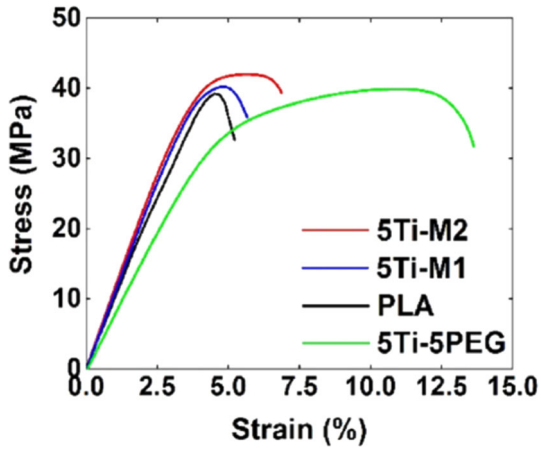


Fig. 12 Tensile stress–strain curves for neat PLA and PLA reinforced with 5% Titanium produced with two different methods (M1 and M2), and PLA reinforced with 5% Ti and PEG [122]

However, experimental enhancements do not always align with theoretical predictions derived from the rule of mixtures. For instance, Mohammed et al. observed only a modest increase (approximately 2%) in UTS after adding Ti powders to PLA, significantly below theoretical predictions (Fig. 12). This discrepancy can be attributed to factors such as particle size, shape, agglomeration, and non-uniform distribution within the PLA matrix. These microstructural issues can significantly impair stress transfer at the interface, thereby limiting the mechanical benefits of reinforcement [122].

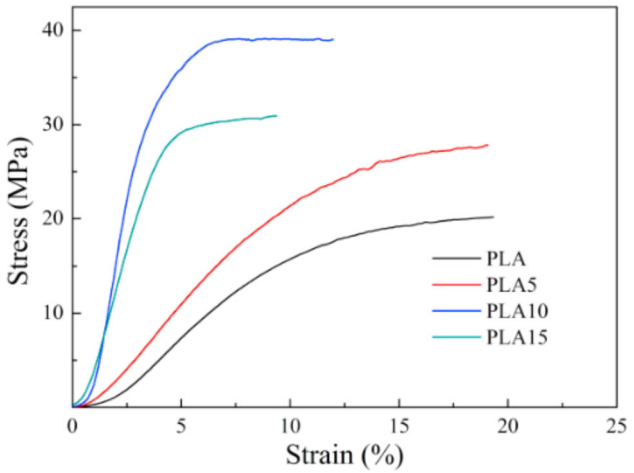


Fig. 13 Compression stress–strain curves for neat PLA and PLA composites with 5%, 10%, and 15% stainless steel. Maximum mechanical enhancement was achieved at 10%, beyond which increased void content compromised stiffness [123]

The incorporation of stainless steel fillers into PLA has been shown to significantly enhance its mechanical properties. Jiang et al. investigated PLA composites reinforced with 5%, 10%, and 15% stainless steel by volume (Fig. 13). Their results demonstrated that adding 10% stainless steel increased the elastic modulus by up to six times and nearly doubled the ultimate compressive strength compared to neat PLA. However, a further increase to 15% filler content led to a reduction in stiffness, primarily attributed to increased void formation and poor interfacial bonding. These findings highlight the importance of optimizing filler content to balance mechanical reinforcement with structural integrity [123].

Incorporating silver into PLA provides notable mechanical and microstructural benefits alongside its well-known antimicrobial properties. Silver nanoparticles refine the PLA microstructure at a molecular level, leading to denser polymer chain arrangements and improved tensile strength and wear resistance. Such enhancements make PLA-Ag composites particularly durable under prolonged mechanical stress and abrasive conditions.

According to Clyne and Hull (2019), the incorporation of metallic fillers such as titanium, stainless steel or magnesium into PLA scaffolds improves not only the elastic modulus and strength of the structure but also the bonding integrity at strut junctions [124]. In pure PLA scaffolds, post-yield deformation often involves interfacial slip at the nodes between misaligned struts, caused by shape distortion resulting from thermal shrinkage during cooling. These weakly bonded regions may accumulate residual shear stress and serve as initiation sites for cracking. In contrast, metal-based reinforcements have been shown to suppress thermal contraction, resulting in stronger and more stable node connections [125].

Moreover, whether used in the form of fibers or powders, stainless steel serves as an internal load-bearing framework that distributes stress more uniformly throughout the PLA matrix. This reinforcement improves the composite's structural reliability and reduces the risk of mechanical failure, particularly under dynamic or multi-directional loading conditions. Additionally, any voids formed at the intersections are typically compacted during compression testing, thus exerting minimal impact on the overall compressive strength.

4.2.2 Antimicrobial Effects

The integration of metals such as silver and copper into PLA composites bestows them with potent antimicrobial properties, crucial for reducing infection risks in medical applications [126]. These metals act at the microbial level to inhibit the growth and proliferation of bacteria on the surfaces of implants and other medical devices, thereby significantly enhancing patient safety and improving recovery outcomes.

Silver nanoparticles are renowned for their broad-spectrum antimicrobial and fungicidal activity and is particularly effective against a wide array of microorganisms [127]. The antibacterial mechanism of silver is primarily attributed to its ability to release Ag^+ ions through oxidation. This oxidation process occurs readily when zero-valent silver (Ag^0) comes into contact with oxygen or water molecules, facilitating the transformation to Ag^+ [128].

The antibacterial mechanism of silver is mainly due to its capacity to release Ag^+ ions via the oxidation process, which occurs rapidly when zero-valent silver (Ag^0) interacts with oxygen or water molecules, resulting in the conversion to Ag^+. Silver ions demonstrate a pronounced attraction for biomolecules containing sulfur and phosphorus, which are prevalent on bacterial membranes. Silver ions exhibit a strong affinity for sulfur and phosphorus-containing biomolecules, which are abundant on bacterial membranes. This interaction can lead to structural damage in membrane proteins and disruption of cellular function, ultimately compromising bacterial viability. Moreover, Ag^+ ions are also believed to bind to phosphate groups within DNA molecules, interfering with replication processes and inhibiting key enzymatic activities essential for cell survival. The effectiveness of silver ions extends to preventing the formation of biofilms, which are often responsible for chronic infections associated with implants [129].

Recent studies have demonstrated the effectiveness of silver nanoparticles incorporated into PLA-based systems. For instance, Demchenko et al. developed PLA-PEI nanocomposites, in which silver nanoparticles were formed via in situ thermochemical reduction of Ag^+ ions at 160 °C. These materials exhibited strong antibacterial activity against *S. aureus* and *E. coli* after 24-h incubation at 37 °C, with clearly defined

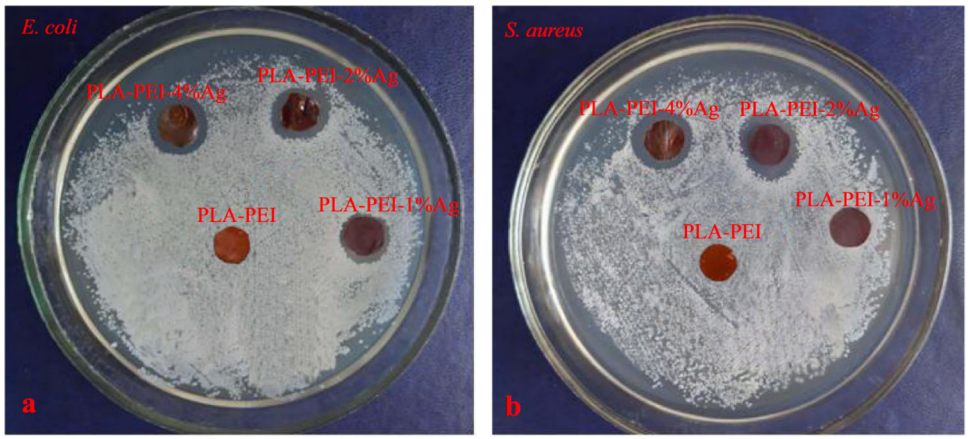


Fig. 14 Antibacterial performance of PLA-PEI nanocomposites containing 0%, 1%, 2%, and 4% silver nanoparticles against *E. coli* (**a**) and *S. aureus* (**b**). For E. coli, clear inhibition zones can be observed surrounding the samples with 1% and 2% Ag content, while the 2% Ag formulation displays the largest zone of growth suppression. No inhibitory effect is visible around the PLA-PEI control samples, indicating the essential role of silver in the antibacterial activity [128]

inhibition zones observed around the film edges. The antimicrobial effect was found to be most pronounced at 2% Ag content (14 mm for *S. aureus* and 14.5 mm for *E. coli*), while further increases to 4% did not yield additional benefits (Fig. 14). In contrast, control samples without silver showed no bacterial inhibition, confirming the essential role of Ag nanoparticles in microbial suppression [128].

Copper is another metal with notable antimicrobial efficacy and stands out as a cost-effective alternative to silver [130]. It has been reported to exhibit lower toxicity than many other heavy metals, including silver, while also offering higher cytocompatibility [131]. Although its biocidal activity is slightly lower—requiring approximately 10 mg of $Cu2^{+}$ per kilogram of water to eliminate 10^{6} *Saccharomyces cerevisiae* cells—it remains a compelling candidate for antibacterial applications [132]. Similar to silver, copper ions exert potent antimicrobial effects across a broad spectrum of bacterial pathogens, including those frequently found in clinical environments. Copper disrupts bacterial membranes and interferes with essential metabolic pathways, leading to rapid cell death [133]. This mechanism makes copper-infused PLA composites particularly attractive for applications requiring continuous antimicrobial protection, such as wound dressings, catheters, and other invasive medical devices [134]. Furthermore, copper's ability to quickly neutralize bacteria may help reduce the development of antibiotic resistance—an increasingly urgent issue in modern healthcare.

A comparative evaluation of the antibacterial behavior of PLA composites reinforced with copper, bronze, and silver was performed using viability assays against *Escherichia coli* (gram-negative, rod-shaped) and *Staphylococcus aureus* (gram-positive, cocci-shaped) (Fig. 15). After 4 h of incubation, the number of viable bacteria adhering to the scaffold surfaces was quantified via absorbance measurements and normalized to neat PLA.Viability results, normalized to neat PLA, showed that untreated PLA-Br (bronze-filled PLA) exhibited the most effective bactericidal performance, followed by PLA-Cu and PLA-Ag. Upon surface treatment with acetic acid, PLA-Cu demonstrated the most pronounced reduction in *E. coli* viability among all samples, while PLA-Br remained the most effective against *S. aureus*. These improvements are attributed to both the intrinsic contact-killing ability of the metal fillers and the microstructural surface modifications induced by acid etching, which expose embedded metal particles and enhance surface interaction with bacterial membranes [135].

This makes copper-infused PLA composites ideal for applications where frequent exposure to pathogenic bacteria is a concern, such as in wound care products, catheters, and other invasive medical tools Copper's ability to rapidly kill bacteria also helps in reducing the likelihood of antibiotic resistance, a growing concern in clinical settings.

The antimicrobial properties of these metal-reinforced PLA composites support their widespread use in medical scenarios where sterility is critical. For instance, surgical tools and orthopedic implants made from silver or copper-infused PLA can significantly reduce the risk of post-operative infections, promoting quicker healing and reducing the overall treatment cost [136]. Moreover, these composites are particularly valuable in applications involving prolonged exposure to potential contaminants, such as in wound dressings and external fixators, where ongoing antimicrobial protection is essential [137].

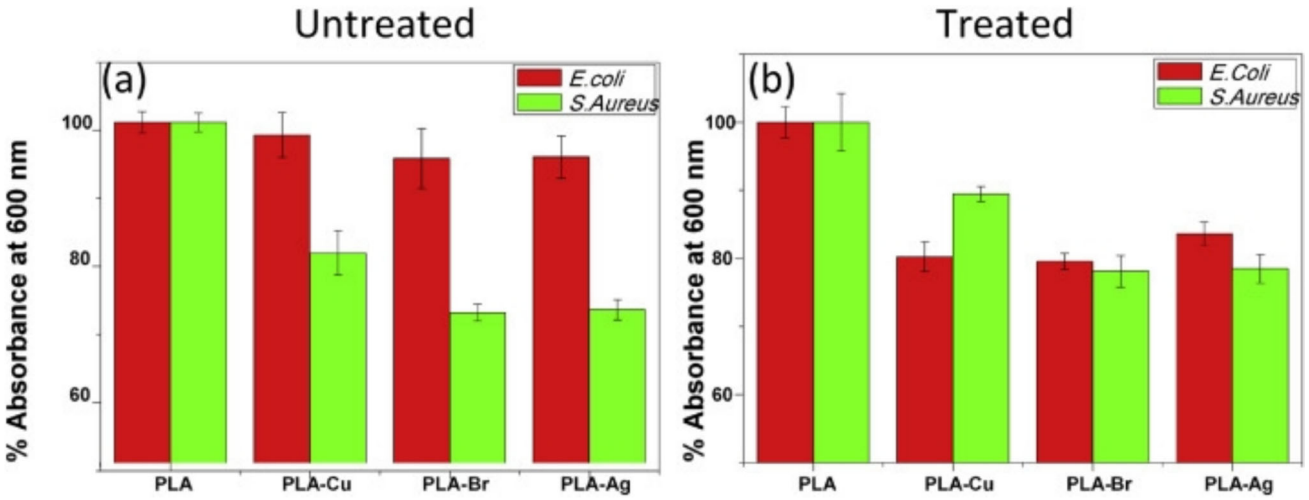


Fig. 15 Relative antibacterial activity of untreated (**a**) and acetic acid-treated **b** PLA composites against Escherichia coli and Staphylococcus aureus, based on % absorbance at 600 nm after 4 h of incubation. Lower absorbance values indicate higher antibacterial performance [135]

4.2.3 Biodegradation of PLA Biocomposites

PLA is a biodegradable polymer that undergoes hydrolytic degradation through the cleavage of its ester bonds, primarily in aqueous physiological environments. This characteristic makes PLA particularly attractive for biomedical applications such as temporary implants, where the material can safely degrade over time, eliminating the need for secondary surgical removal. However, in clinical scenarios, the rate and uniformity of degradation must be precisely controlled to match tissue healing dynamics. The incorporation of metallic reinforcements into PLA matrices can significantly alter the degradation kinetics [138].

Metal additives such as magnesium are known for their biodegradable properties, which can be leveraged to precisely control the degradation rate of PLA composites [139]. Magnesium has a corrosion rate that aligns well with the healing processes of human tissues, making it an ideal choice for temporary biomedical implants such as screws, plates, or scaffolds in tissue engineering [140]. Nevertheless, magnesium's inherent rapid corrosion and hydrogen gas generation in physiological environments can lead to localized tissue swelling and impaired tissue–implant interface, presenting challenges to clinical use without additional surface modifications or coatings. Incorporation of magnesium particles into PLA composites addresses these issues by providing controlled degradation and significantly reducing adverse effects like swelling. Consequently, PLA-Mg composites degrade gradually, synchronized with tissue regeneration, thus eliminating the necessity for implant removal surgery after healing [141].

The biodegradation process in metal-reinforced PLA composites is primarily influenced by the dissolution rate of the embedded metallic fillers. As these metal particles dissolve, they accelerate PLA hydrolysis by exposing more of the polymer surface to bodily fluids, a process further catalyzed by acidic degradation by-products of PLA itself [89]. In a study by Cifuentes et al., PLA was reinforced with 10 wt% magnesium particles of two distinct morphologies: spherical and irregular. Biodegradation tests were conducted in phosphate-buffered saline (PBS) and distilled water over a period of 28 days. The results indicated that composites containing spherical Mg particles exhibited a lower degradation rate, with approximately 3% weight loss, compared to those with irregularly shaped particles, which reached a 12% weight loss. The higher degradation rate in the latter group was attributed to the formation of microcracks and increased surface area, which facilitated fluid penetration and accelerated matrix degradation [142].

The degradation behavior of PLA composites is not solely determined by material composition, but also significantly influenced by environmental factors such as pH, temperature, and enzymatic activity. Metal-reinforced PLA composites can be engineered to respond to these physiological cues, enabling tailored degradation profiles that suit specific clinical environments [143]. Zhao et al. investigated the degradation behavior of PLA composites reinforced with 2% and 5% magnesium in simulated body fluid (SBF) at 37 °C. As shown in Fig. 16a, the addition of Mg particles resulted in a gradual increase in the pH of the surrounding medium, indicating a neutralizing effect on the acidic by-products typically generated during PLA degradation. This buffering capacity of magnesium contributes to a more stable degradation environment, potentially minimizing inflammation and improving biocompatibility. Additionally, all samples exhibited weight gain over time due to the deposition of calcium phosphate on the composite surfaces (Fig. 16b). Notably, the extent of calcium phosphate formation was positively correlated

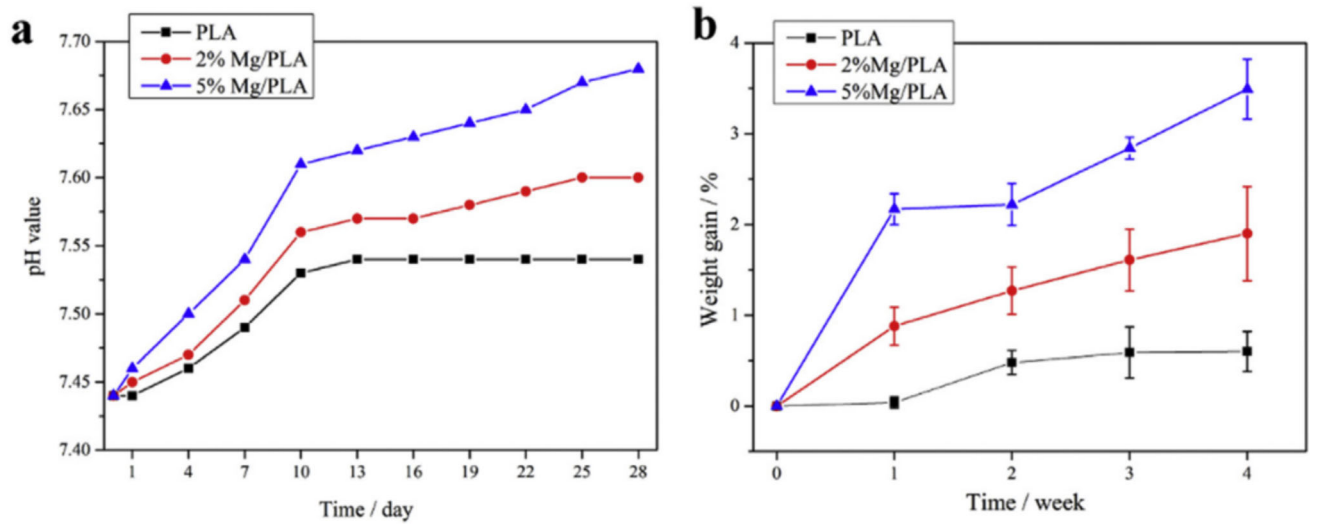


Fig. 16 **a** pH evolution over 28 days and **b** weight gain (%) over 4 weeks for PLA, 2% Mg/PLA, and 5% Mg/PLA composites in simulated body fluid at 37 °C. Increasing Mg content resulted in higher pH values and greater calcium phosphate deposition, indicating improved degradation control and mineralization [144]

with magnesium content, suggesting that higher Mg levels enhance bioactivity and mineralization potential—both of which are desirable for applications in bone tissue engineering [144].

4.2.4 Biocompatibility and Bioactivity

Biocompatibility refers to a material's ability not only to coexist safely with surrounding biological tissues but also to actively support biological processes such as healing, integration, and tissue regeneration [145]. Metal-reinforced PLA composites have been increasingly researched and utilized due to their unique combination of bioactivity and biocompatibility, which are enhanced by the incorporation of specific metals such as titanium, silver, and copper [146].

Magnesium, for instance, has demonstrated notable benefits in bone regeneration due to its ability to enhance osteoblast activity, the cells primarily responsible for bone formation. Mg ions released into the physiological environment promote osteoblast adhesion, proliferation, and differentiation, and encourage mineralization of the extracellular matrix, thus significantly contributing to bone strength and regeneration [86, 147]. Similarly, titanium is widely recognized for its excellent biocompatibility and osteoconductive properties. When integrated into PLA matrices, titanium provides robust mechanical support and promotes the attachment and proliferation of bone cells, essential for successful implant integration (osseointegration). Furthermore, titanium's inherent bioinertness minimizes adverse immune reactions, making it highly suitable for long-term implantation scenarios [148].

Silver incorporation is primarily beneficial for its antimicrobial capabilities, significantly reducing the risk of implant-related infections, a common complication in biomedical applications. Moreover, silver ions can positively influence fibroblast behavior, facilitating improved connective tissue formation and wound healing processes. Copper, on the other hand, is renowned for its angiogenic effects, essential for delivering nutrients and oxygen to regenerating tissues. Copper ions enhance angiogenesis through the upregulation of vascular endothelial growth factors (VEGFs), thereby supporting rapid and robust tissue regeneration [149]. Additionally, zinc is recognized for promoting osteogenic differentiation and supporting bone mineralization. Zn-reinforced PLA composites thus possess enhanced osteoinductive capabilities, guiding progenitor cells to mature along the osteoblastic lineage, which is highly beneficial for bone tissue engineering applications [150].

However, integrating metallic fillers into PLA is not without challenges. A primary concern is controlling metal ion release, as excessive ions can potentially induce cytotoxicity or trigger undesired immune reactions [151]. Ensuring that degradation by-products remain non-toxic and biocompatible is critical to maintaining implant safety and efficacy [152]. To mitigate these risks, current strategies focus on carefully optimizing metal content, applying advanced coatings or encapsulation techniques to regulate ion release, and performing thorough biological assessments to validate material stability and compatibility under physiological conditions [153].

Table 5 Comparative properties of metal-reinforced PLA biocomposites summarized from recent studies

Metal Type	Metal Content (wt%)	Particle Size (μm / nm)	Mechanical Test Type	Comparison Basis	Key Improvement
Ti	5 (Ti), 5,10 (PEG)	40 μm	Tensile & Compression	PLA vs PLA/Ti/PEG	Ductility improved significantly without strength loss. Contact angle decreased by 25°, printability maintained, surface roughness optimized, and cell viability improved [122]
Ti	0, 5, 10, 15 and 20	325 mesh	Tensile, Compression, Impact	PLA vs PLA/Ti	Mechanical strength enhanced up to 10 vol% Ti; impact resistance > pure PLA; improved in vitro biocompatibility (cell adhesion, proliferation, differentiation) [154]
Cu	–	30 μm	Tear, Tensile, Hardness, Flexural, Water Absorption	PLA vs HFDM Cu/PLA vs Cu-infused PLA	Strategically embedded Cu mesh via HFDM improved strength and integrity; bonding effectiveness confirmed by microstructure analysis [155]
Cu	14	20–30 μm	Compression, Flexural	PLA/Cu (at varying FDM parameters)	Higher nozzle and bed temperature enhanced compressive and flexural strength of 14 wt% Cu/PLA [156]
316L	5,10 and 15	between 20 μm and 50 μm	Compression	PLA vs PLA/316L	↑ Compressive strength & modulus (at 10–15 vol%), ↓ thermal expansion coefficient, surface roughness controlled, similar degradation rate [123]

Table 5 (continued)

Metal Type	Metal Content (wt%)	Particle Size (μm / nm)	Mechanical Test Type	Comparison Basis	Key Improvement
316L	40 μm	50–150 μm	Tensile test (joint strength)	PLA/316L joint vs. pure PLA	Mechanical interlocking governs PLA–316L joining; surface roughness and cavity shape crucial; optimal design (Cylindrical 1) reached 96% strength of pure PLA with low scatter; temp. alignment critical
Mg	1, 3, 5, 7 wt% (opt. 3%)	avg. ~ 50 μm	Tensile, Compression	PLA vs PLA/Mg (varying %Mg)	3% Mg showed ↑ tensile strength (~ 48 MPa vs 36 MPa PLA), ↑ modulus, better thermal stability; excess Mg led to agglomeration and poor interface [157]
Mg	5,10,30,50	less than 50 μm	Nanoindentation (Hardness, Young's modulus),	PLA vs PLA/Mg	Young's modulus increased by up to 2.9 GPa (vs 4.9 ± 0.1 GPa in neat PLA) Hardness increased by 60 MPa Good particle dispersion, no agglomeration Enhanced printability and thermal stability Strong Mg/PLA interface (especially with PEI) [158]
Ag	4	5 × 90 μm (Flakes)	Tensile, Compression	PLA vs PLA/Ag nanocomposites with varying Ag contents	Ag offered best trade-off with improved antibacterial activity and acceptable mechanical behavior [159]

4.3 Case Studies of Metal Reinforcements via Additive Manufacturing

The recent research on PLA/metal particle composites and their effect on mechanical and morphological properties is critically investigated here. We evaluate Ti, Cu, 316L stainless steel, Mg, and Ag particles in combination with PLA matrices. To quantitatively illustrate the differences in mechanical and biological behavior of PLA biocomposites reinforced with various metals, the key properties of these materials are summarized in Table 5. The comparison includes tensile strength, ductility, biodegradation rate, and biocompatibility features, providing a clear and concise overview of each reinforcement type's biomedical potential.

These comparisons indicate that titanium and stainless steel reinforced PLA composites offer superior mechanical strength and ductility, making them well-suited for load-bearing applications. Magnesium and silver present notable bioactive properties, beneficial for promoting osteogenesis and antimicrobial functionality, respectively, though careful

management of degradation rates and concentration is necessary.

Following this comparative analysis, individual subsections explore in greater depth the material behavior, processing considerations, and biomedical implications of each metal reinforcement system.

4.3.1 PLA/Ti Biocomposites

Lee et al. investigated the effect of titanium (Ti) reinforcement at 5%, 10%, and 15% volume fractions in PLA-based composite scaffolds, focusing on both mechanical and osteogenic performance. As Ti content increased, a notable decline in the crystallization temperature and degree of crystallinity was observed, suggesting a disruption in the structural regularity of the PLA matrix. In contrast, the glass transition temperature (Tg) and melting temperature (Tm) rose with higher Ti content, indicating enhanced thermal stability of the composites [154].

While neat PLA exhibited superior tensile, compressive, and impact strengths compared to its Ti-reinforced counterparts, the incorporation of Ti significantly improved the in vitro biocompatibility of the material. As shown in Fig. 17, tensile stress–strain curves (a) reveal a moderate enhancement in mechanical behavior with increasing Ti content. More strikingly, cell proliferation assays (b) demonstrated a significant increase in cell viability across all PLA/Ti composites over a 7-day period, compared to pure PLA. Furthermore, alkaline phosphatase (ALP) activity (c)—an established marker of osteogenic differentiation—was markedly elevated with increasing Ti content, underscoring the osteoinductive potential of these composites.

Asadollahi et al. explored the incorporation of polyethylene glycol (PEG) into polylactic acid (PLA) through two distinct processes, specifically the dissolving method. PEG was introduced at two different concentrations: 5% and 10%. The results indicated that using PEG in combination with the introduction of titanium via the Direct Composite Molding (DCM) method markedly enhanced the ductility of the composites while preserving their inherent strength. Moreover, the contact angle of PEG decreased by 25 °C, attributed to the increased hydrophilicity and altered surface roughness due to the presence of titanium particles. These enhancements were achieved without compromising the overall quality of the printed materials. Additionally, the surface roughness of the scaffolds was optimized, further enhancing their functional properties. Notably, scaffolds containing both Ti and PEG demonstrated significant improvements in cell adhesion and a reduction in cytotoxicity compared to scaffolds composed solely of PLA [122].

4.3.2 PLA/Cu Biocomposites

In their research, Yang et al. found that PLA-Cu filaments demonstrated superior mechanical properties such as bending, tensile, and shear strengths compared to PLA filaments containing 40% Cu powder. This enhancement underscores the potential of copper to significantly reinforce PLA structures, making them more suitable for applications requiring higher mechanical resilience [160].

Butt et al. explored the innovative Hybrid Material Extrusion (HME) technique, which involves integrating metal meshes into the PLA matrix. This process begins with the printing of a tension rod followed by the application of a wire mesh over it, and concludes with the addition of a 3D-printed layer on top. This method significantly increases the composite's resistance to tearing, fracture loads, and bending strengths. Notably, PLA-Cu HME materials exhibit only minor streaks and small cracks, showing improved structural integrity compared to pure PLA, which displayed distinct fractures at force application points [155].

Huu et al. employed the Face-Centered Central Composite Design (FCCCD) methodology to optimize the 3D printing parameters for achieving the highest compression strength in PLA-Cu composites. They identified optimal parameters as a 90° construction direction, 0.2-layer thickness, and 30° scanning angle. They observed that reducing layer thickness while increasing the number of layers enhanced the heat distribution, leading to better diffusion between fibers and, consequently, higher compressive strength [73].

Balamurugan et al. assessed how variations in nozzle type, bed temperature, and layer thickness influence the mechanical properties of PLA-Cu composites. Increases in nozzle and bed temperatures were found to significantly affect the characteristics of the composites, suggesting the need for careful thermal management during the printing process [156].

Pavan et al. investigated the wear characteristics of PLA-Cu composites using a pin-on-disk method within the Material Extrusion system. Employing Gray Relational Analysis, they optimized the friction strength and wear rate by varying load, track diameter, and speed. Their findings highlighted that the load exerted during testing had a substantial impact, affecting about 76% of the overall quality of the samples [161].

Balamurugan et al. also developed novel composite filaments by incorporating copper particles into PLA for medicinal applications. The filaments were tested under various operational settings to assess their density and mechanical properties. The results demonstrated that friction force and wear rate significantly influence the structural integrity and performance of the printed objects, with considerable contributions from machining speed and track diameter [156].

Alberts et al. discovered that adding copper to PLA increased particle emission rates and reduced particle sizes

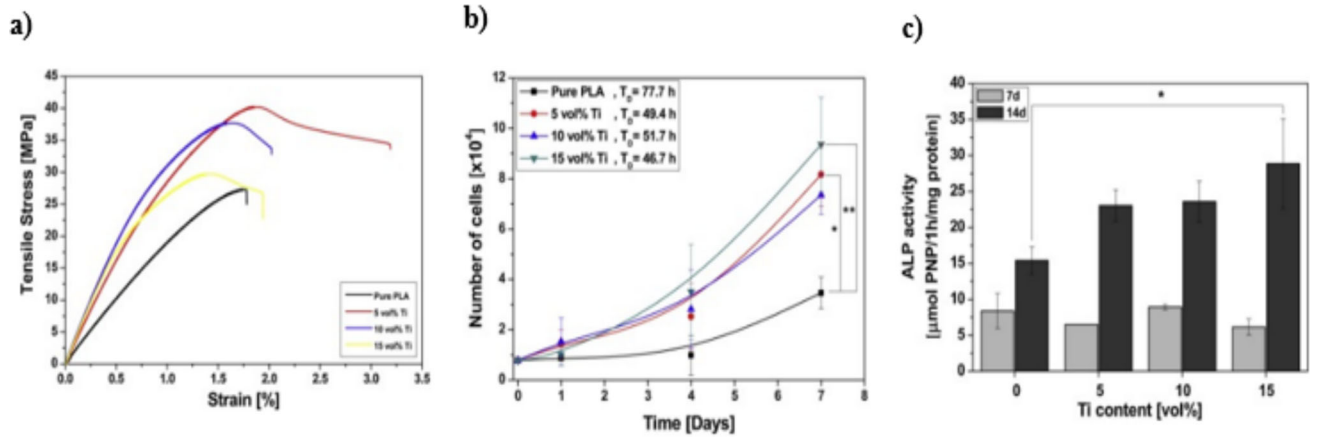


Fig. 17 Tensile behavior, cell proliferation, and ALP activity of PLA/Ti composites with 5%, 10%, and 15% Ti. Mechanical strength and osteogenic potential increase with Ti content, confirming improved bioactivity and biocompatibility [154]

during the printing process. SEM–EDS analysis revealed no detectable metallic elements in the emissions from filaments containing both tungsten and copper, suggesting effective encapsulation or binding of metals within the PLA matrix [162].

Sadeghian et al. conducted an investigation into the impact of copper additions on the fracture resistance of 3D-printed PLA. Using semi-circular bending samples under mixed-mode loading, they studied the microfracture mechanisms using Scanning Electron Microscopy (SEM). The study found that copper additions significantly enhanced the fracture resistance of PLA when printed in various orientations, highlighting the beneficial role of copper in improving the structural durability of 3D-printed objects [163].

4.3.3 PLA/Stainless Steel Biocomposites

Researchers demonstrated that varying the stainless steel content between 10 and 60% allowed precise tuning of physical and thermal properties [164]. Initial increases in steel content reduced the repose and collapse angles, indicating improved particle packing and flowability, while further increases eventually reversed this trend. Moreover, a reduced flat-plate angle and lower compressibility were observed at optimized stainless steel concentrations, suggesting enhanced structural rigidity and packing density. Thermal analyses confirmed that higher stainless steel contents increased the composite's melting temperature and improved thermal stability, making these materials suitable for sterilization processes and applications involving exposure to elevated temperatures.

Jiang et al. investigated the surface morphology and internal microstructure of PLA composites reinforced with varying amounts of stainless steel (5–15 wt%) using scanning electron microscopy (SEM). SEM observations revealed minor cracks in composites containing 5% stainless steel, likely due to filament friction or thermal stresses during cooling. Stainless steel particles were clearly identifiable and well dispersed within the PLA matrix at lower concentrations. However, increasing filler content to 10% and 15% led to noticeable agglomeration, void formation, and interlayer gaps, potentially compromising structural integrity (Fig. 18). The ME process, however, induced thermal expansion, which can lead to residual stresses, particularly at the junctures of scaffold struts. These stresses are critical as they might initiate crack formation under load. Despite this, the composites showed reduced shrinkage upon cooling, which is indicative of improved interlayer bonding and overall structural integrity of the printed scaffolds [123].

Complementing experimental efforts, Drakoulas et al. performed numerical simulations on PLA scaffolds containing 5% stainless steel, consisting of four-layered struts with uniform, isometric pores. Their results underscored the scaffold's potential for load-bearing tissue engineering applications, emphasizing the critical role pore geometry plays in nutrient diffusion and cellular migration [165].

4.3.4 PLA/Mg Biocomposites

Recent research has focused extensively on enhancing the properties of PLA by integrating magnesium particles, aiming to create advanced biomaterials suitable for biomedical applications. Antoniac et al. [166] developed an innovative anterior cruciate ligament (ACL) model using PLA reinforced with magnesium and vitamin E. This composite demonstrated remarkable biocompatibility and osteoconductivity, ensuring structural integrity and durability of implant screws during additive manufacturing processes.

Addressing the challenge of enhancing filament strength, another study explored reinforcing PLA filaments with magnesium particles to create porous scaffolds via fused filament fabrication [167]. It was determined that the inclusion of

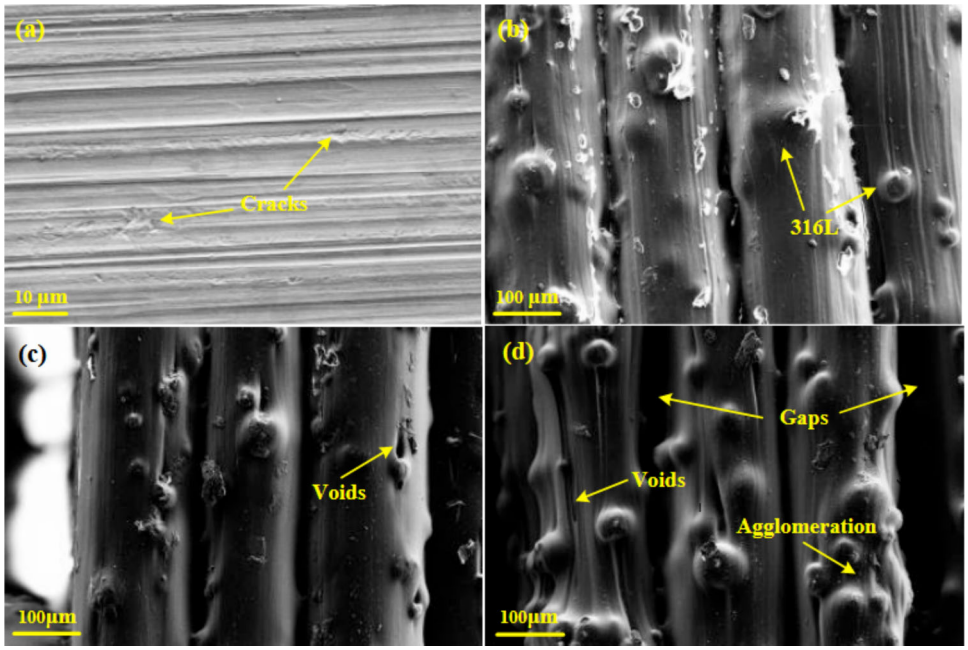


Fig. 18 SEM images of surface **a** PLA and 5% stainless steel, **b** PLA and 5% Stainless steel content scaffold, **c** PLA and 10% Stainless steel content scaffold, **d** PLA and 15% Stainless steel content scaffold [123]

a polyethylene glycol (PEG) plasticizer was necessary for successful printing when Mg content exceeded 4%. The resulting composite filaments containing PEG could reliably produce precise, porous scaffolds with minimal structural defects.

Ferrández et al. [158] focused on the PLA/Mg interface development, manufacturing new composites through extrusion processing. Their study showed that adding matrix fillers improved the extrusion process significantly, facilitating the fabrication of personalized components using 3D printing technologies. Complementing this, Ali et al. reviewed recent progress in polymer/Mg composites, discussing advanced 3D printing methods, manufacturing processes, and the associated challenges of biomedical implementation [157].

Exploring PLA/Mg composites for orthopedic implants, Zhao et al. [144] demonstrated that integrating Mg particles effectively neutralized acidic by-products from PLA degradation and promoted apatite formation. Crucially, these composites showed no cytotoxic effects toward osteoblastic cells and successfully encouraged the formation of mineralized, bone-like nodules, enhancing bioactivity and osteogenesis.

In another significant study, Bakhshi et al. [168] used material extrusion (ME) processes to fabricate porous PLA-Mg scaffolds with high precision. Incorporating up to 8 wt% Mg significantly improved mechanical strength and biodegradation rates. Among tested variants, the scaffold containing 6 wt% Mg exhibited superior cellular performance, outperforming pure PLA scaffolds in both mechanical and biological evaluations.

Kalva et al. [169] investigated WE43 magnesium alloy integration into PLA filaments, demonstrating excellent printability with commercially available ME-based 3D printers at 5% and 10% Mg content. These composites, particularly promising for bone implants, confirmed their potential as viable biomaterials with suitable mechanical and biological characteristics.

Leonés et al. [89] successfully produced PLA-Mg composite filaments with varying Mg microparticle contents (1.2–15 wt%). Their results confirmed that filament diameters were compatible with standard 1.75 mm 3D printers, suggesting strong potential for various biomedical applications through accessible additive manufacturing approaches.

Finally, Zeynivandnejad et al. [170] studied the mechanical behavior of PLA-Mg composites produced through extrusion and subsequent 3D printing. Dog-bone-shaped samples printed with different infill orientations revealed that mechanical properties depended strongly on print orientation. Specifically, 0° oriented samples reached the highest ultimate tensile strength (UTS) of 43 MPa, while 90° oriented samples displayed the lowest strength at 26 MPa. Despite this orientation dependence, the incorporation of Mg particles generally resulted in reduced mechanical performance compared to pure PLA specimens.

Collectively, these studies underscore the versatility and potential of PLA/Mg composites in biomedical additive manufacturing, highlighting opportunities for precise control over mechanical properties, degradation profiles, and biological interactions for tailored clinical applications.

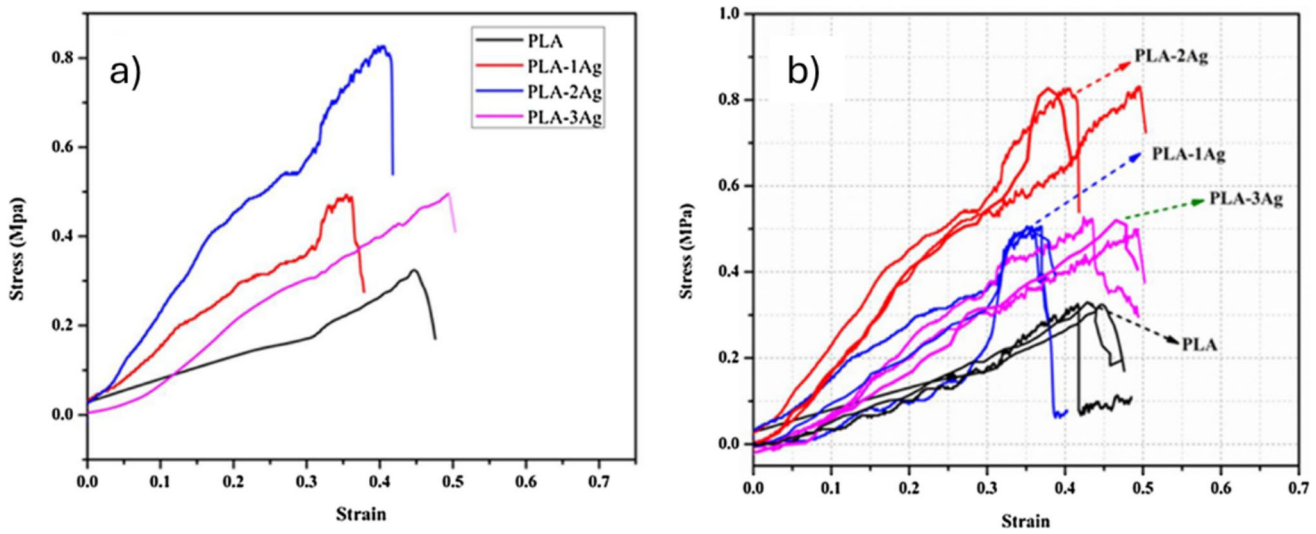


Fig. 19 Mechanical behavior of PLA/Ag nanocomposites with varying silver content. Stress–strain curves showing enhanced mechanical strength with increasing Ag nanoparticle content, especially at 2 wt% loading [80]

4.3.5 PLA/Ag Biocomposites

Post-processing techniques have been effectively applied to enhance the performance of 3D-printed PLA composites containing silver particles. In one study, antibacterial scaffolds composed of PLA reinforced with silver and copper were treated with acetic acid to induce surface porosity and improve functionality. This surface modification led to significant improvements in both biological and antibacterial performance, with antibacterial efficacy increasing by approximately 20–25% and bioactivity by 10–18%. These findings suggest a synergistic effect between metal reinforcement and post-processing treatments, highlighting the potential of combined strategies to optimize scaffold performance in biomedical applications [159].

Silver nanoparticles were incorporated into PLA at varying concentrations (1–3 wt%) to investigate their effect on mechanical performance (Fig. 19). Tensile testing revealed a significant increase in ultimate tensile strength (UTS) with the addition of 2 wt% Ag, reaching approximately 0.8 MPa compared to 0.32 MPa for neat PLA. However, further increasing the silver content to 3 wt% resulted in a reduction of UTS to around 0.5 MPa. This decline is likely due to nanoparticle agglomeration at higher concentrations, which can act as stress concentrators and impair stress transfer within the matrix [80].

5 Applications of PLA-Based Metal-Reinforced Biocomposites

The integration of metallic particles such as silver, magnesium, titanium, and stainless steel into PLA matrices has opened new avenues in biomedical applications, where both mechanical robustness and biological performance are critical. These advanced biocomposites offer tailored biodegradation rates, enhanced tensile strength, antimicrobial activity, and improved osteointegration, making them suitable for a wide range of clinical uses. This section discusses key application areas including tissue engineering, dental and orthopedic implants, and cardiovascular scaffolds. Figures 20, 21, 22, and 23 provide representative illustrations of these applications: PLA-Mg scaffolds promoting cell proliferation and adhesion (Fig. 20), scaffold-based tissue engineering (Fig. 21), epithelial tissue regeneration strategies using scaffold-based techniques (Fig. 22), and porous orthopedic screws enabling bone integration (Fig. 23).

5.1 Tissue Engineering

PLA plays a pivotal role in the fields of tissue engineering and regenerative medicine, particularly in bone grafting techniques aimed at enhancing hard tissue regeneration. The current methods in bone grafting include autografts, where bone is transplanted from one part of the patient's body to another, allografts, which utilize bone from a donor, and synthetic grafts that incorporate materials like PLA to mimic the properties of bone and promote integration [171]. Although these methods prioritize integrating PLA into existing bone structures, studies have revealed that PLA can promote the growth of new bone tissue and blood vessels [172]. Research has shown that PLA scaffolds can effectively support osteogenesis and vascularization, making them suitable for applications in bone tissue engineering [173]. For instance, Liu et al. demonstrated that mineralized collagen bone grafts modified with PLA exhibited enhanced

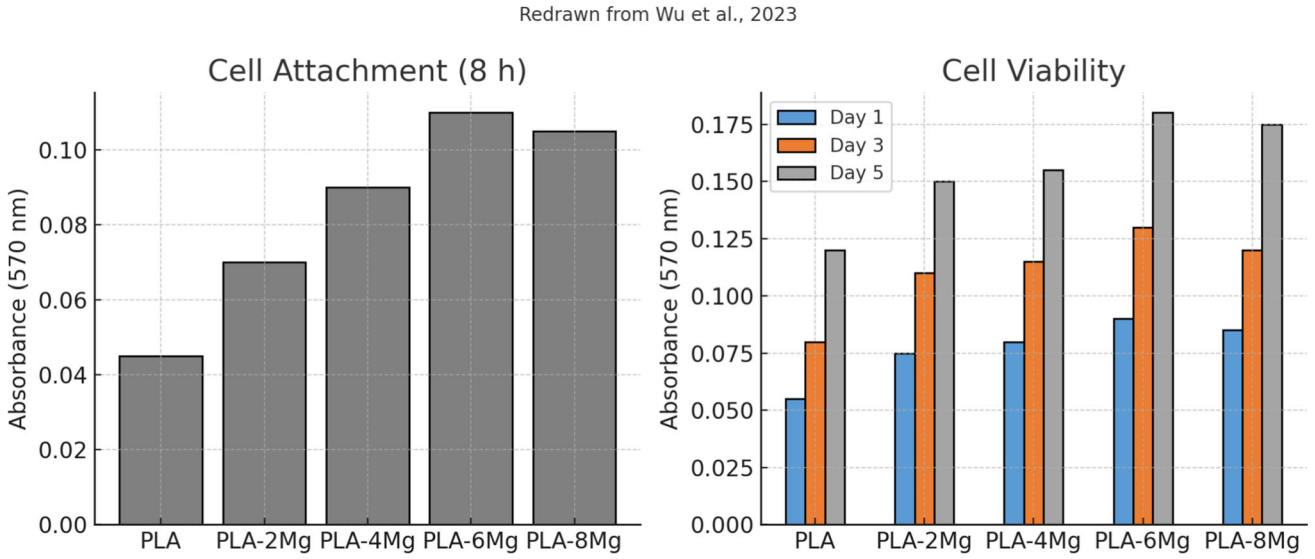


Fig. 20 **a** Cell attachment (8 h) and **b** cell viability (1, 3, 5 days) of L929 cells on PLA and PLA-Mg composite scaffolds, as measured by Alamar blue assay [178]

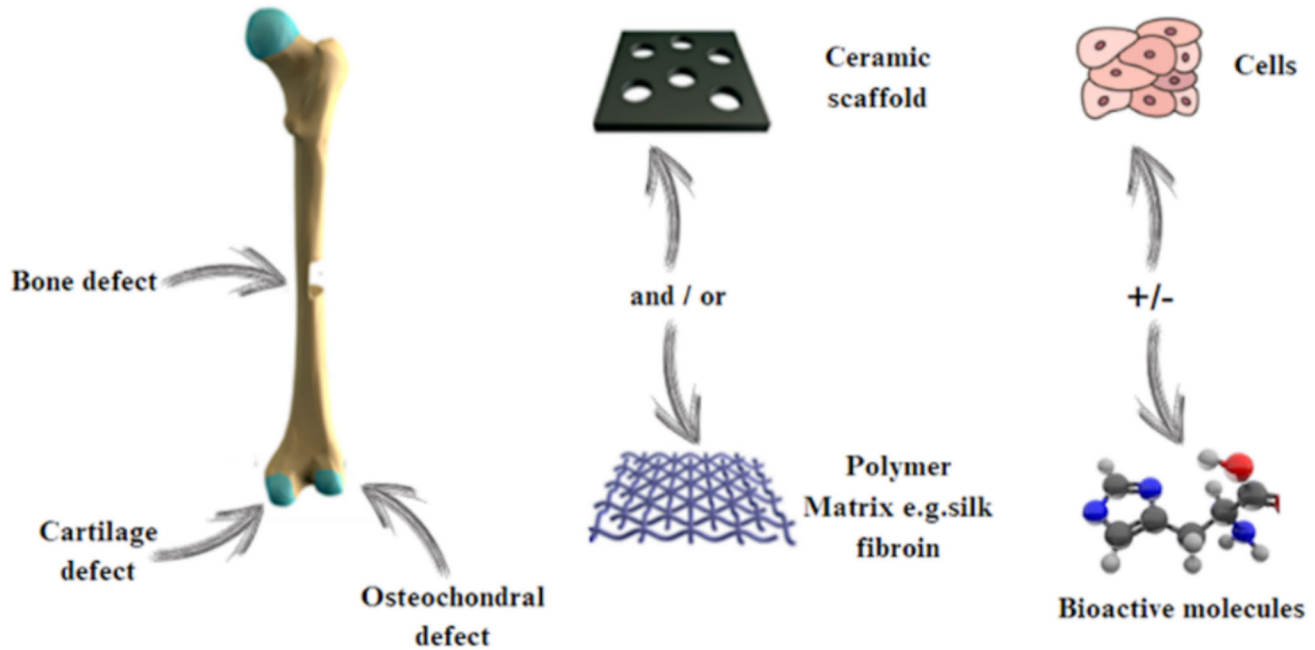


Fig. 21 Schematic representation of scaffold-based tissue engineering: Integration of bone, cartilage, and osteochondral defects with ceramic scaffolds or polymer matrices (e.g., silk fibroin) combined with cells and bioactive molecules for enhanced tissue regeneration

osteogenic properties in vivo, indicating the potential of PLA to facilitate new bone formation [174]. Furthermore, the use of 3D-printed PLA scaffolds has been shown to promote bone-like matrix deposition in vitro, underscoring PLA's effectiveness in regenerative applications [175].

Despite its promising applications, the physiological properties of PLA may exhibit limitations, such as degradation rates and biological responses, that must be addressed before implantation to ensure optimal outcomes in regenerative therapies. For instance, while PLA is widely used in bone tissue engineering due to its biocompatibility and biodegradability, studies have indicated that its degradation rate can be too rapid in certain physiological environments, potentially leading to inadequate mechanical support during the critical healing phase [171]. Additionally, the acidic byproducts generated during PLA degradation can adversely affect local

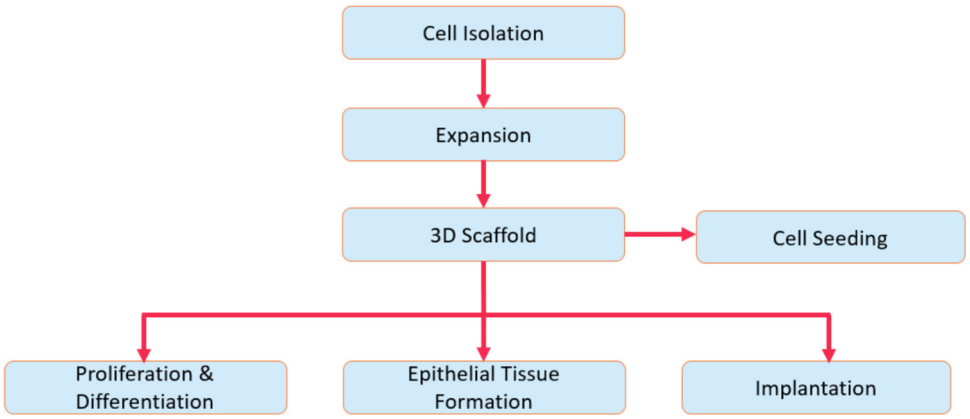


Fig. 22 Schematic overview of the epithelial tissue engineering process, highlighting scaffold-based strategies for epithelial regeneration, including key stages such as cell expansion, seeding, and implantation

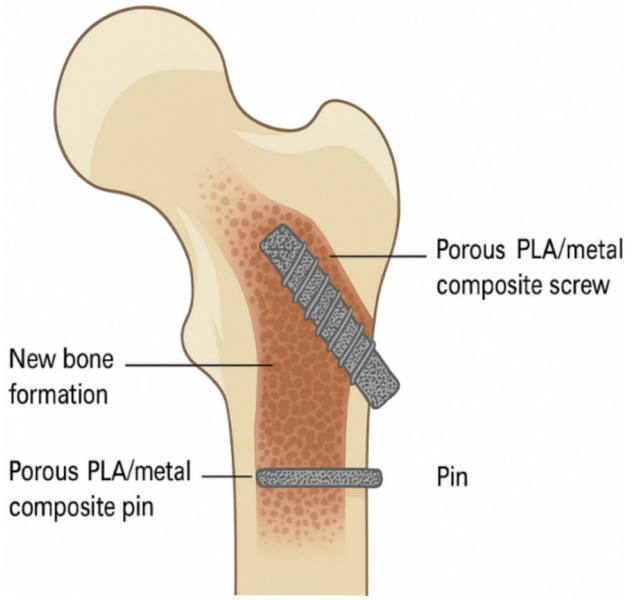


Fig. 23 Schematic illustration of a porous PLA/metal composite orthopedic screw and pin integrated into bone tissue, showing scaffold porosity and the formation of new bone around the implant

tissue environments, potentially hindering the overall regenerative process [176].

The compatibility of scaffold materials with their biological environment is essential, as these materials must resist immune rejection and avoid releasing cytotoxic by-products that could hinder tissue regeneration [177]. Figure 20 illustrates the biological performance of PLA-Mg composite scaffolds, focusing on early-stage cell attachment and cell viability using L929 fibroblast cells. As shown in Fig. 20a, increasing magnesium content from 0 to 6% results in a marked improvement in cell attachment after 8 h, indicating that Mg incorporation enhances initial cell adhesion, a critical factor for subsequent tissue integration. Notably, PLA-6 Mg exhibits the highest absorbance at 570 nm, suggesting the most favorable surface characteristics for cell anchoring. Figure 20b presents cell viability over a period of 1, 3, and 5 days. All composite groups outperform pure PLA in promoting cell proliferation, with PLA-6 Mg again demonstrating superior performance on Day 5. These results collectively suggest that moderate levels of magnesium reinforcement improve both early cellular responses and sustained viability, making PLA-Mg composites promising candidates for bioactive scaffold development in tissue engineering applications.

The challenges associated with PLA-based bone replacement methods have prompted extensive research aimed at optimizing the properties of PLA for regenerative therapies. When high-molecular-weight hyaluronic acid particles are combined with polylactic acid (PLA), they have been shown to enhance the osteogenic potential of PLA scaffolds, thereby promoting improved integration and functionality in bone tissue engineering applications [179].

Research has demonstrated that the incorporation of hyaluronic acid into PLA scaffolds enhances cell adhesion and facilitates the proliferation and differentiation of osteoblasts, which are crucial for effective bone regeneration [180].

Additionally, various interactions between hyaluronic acid and PLA have been reported. For instance, Russias et al. [181] examined how the addition of hyaluronic acid to PLA impact the physical characteristics of PLA under high-speed flow. This approach resulted in a uniform dispersion of HA throughout the surface of the PLA. The findings indicated an increase in the surface roughness of PLA/hyaluronic acid composites, accompanied by a decrease in the water contact angle. These modifications lead to advantageous outcomes by enhancing protein adsorption and promoting cell adhesion to the substance. Enhanced wettability results in the benefits and also promotes the growth and specialization of pre-osteoblast cells. Consequently, this viable manufacturing technique reduces osteoclastic-induced degradation while enhancing osteoblastic activity, both of which are beneficial for bone growth.

5.2 Tissue Engineering with Bone and Glass Materials

Tissue engineering utilizes scaffolds made from polylactic acid (PLA) and calcium phosphate glass to enhance bone tissue regeneration. Calcium phosphate glass is a versatile material with a chemical composition that closely resembles bone, enabling precise control over its degradation rate and compatibility with living tissues. This makes it an effective choice for bone tissue engineering applications. The PLA/calcium phosphate glass scaffolds can be produced using various methods, including foaming, where glass particles are incorporated into a PLA matrix, resulting in a uniform composite [172]. The incorporation of calcium phosphate glass into PLA scaffolds has been shown to improve osteoconductivity and promote bone regeneration, making these composites particularly suitable for applications in bone repair and regeneration [182].The foaming method used for scaffold fabrication enhances the mechanical properties of the composite and facilitates the development of a porous structure that is essential for nutrient flow and cell infiltration, further supporting tissue regeneration [183]. This combination of PLA and calcium phosphate glass represents a promising approach in the field of bone tissue engineering, addressing the critical need for materials that can effectively integrate with biological tissues while providing the necessary mechanical support [184]. Additionally, PLA/calcium phosphate glass composites provide the necessary mechanical strength and exhibit suitable cellular-material interactions. This combination of properties ensures that the composites not only withstand mechanical loads effectively but also support cellular adhesion and proliferation, making them ideal candidates for applications in bone tissue engineering and regenerative medicine (Fig. 21) [185].

The PLA/calcium phosphate composite scaffold demonstrated excellent biocompatibility and enhanced angiogenesis and nutrient retention. The composites facilitated osteoblast infiltration and growth, with a 4% increase in porosity from 93 to 97%. The glass-reinforced composite showed improved characteristics compared to the PLA control, with a strength of 120 MPa, a 61% increase, and a tensile strength of 20.2 MPa, compared to 17.5 MPa for the PLA control [186].

5.3 Engineering of Epithelial and Cardiovascular Tissues

PLA is being utilized in tissue engineering for the regeneration of epithelial cells within scaffolds. Blends of polyglycolic acid (PGA) and PLA have gained significant interest for their potential applications in treating short bowel syndrome, a condition characterized by a reduction in the lengths of the jejunum and ileum by an average of 33%, leading to malnutrition [187].

Figure 22 provides a schematic representation of the epithelial tissue engineering process. It outlines key stages such as cell isolation, expansion, scaffold fabrication, and cell seeding, followed by downstream events including cell proliferation, differentiation, epithelial tissue formation, and eventual implantation. Advanced methodologies such as organoids, spheroids, microengineered 3D scaffolds, and organ-on-a-chip systems are also integrated into this framework to better mimic the physiological architecture and function of native tissues.

Experimental stents can be used to produce PLA coating on PGA sheets. In studies involving animal models with cardiovascular illness, 28 out of 61 scaffolds induced the generation of type I collagen, indicating effective integration. Organoid units, consisting of mesenchymal cells enveloped by an epithelium, were observed, with the composition comprising the nuclei of stromal cells. Out of 61 scaffolds, the study found that 47 of them had notable cyst sizes, and collagen was present on 26 of these scaffolds. The authors inferred a potential correlation between the presence of type I collagen and its immunogenicity and permeability [188, 189]. The findings suggest that the integration of PLA and PGA in scaffold design can significantly influence cellular responses and tissue regeneration outcomes. The presence of type I collagen is particularly important, as it plays a crucial role in the healing process and is a marker of successful tissue integration. Moreover, the study highlights the importance of scaffold composition and structure in promoting favorable biological responses, which are essential for the development of effective tissue engineering strategies [190].

The electrophysiological studies revealed that the mucosal cells growing on the scaffold exhibited active ion transport and had a similar strength in their epithelial barrier. The histological assessment, revealed the existence of crypts and an appropriate epithelial morphology, indicating that PGA/PLA scaffolds have the potential for the growth and durability of epithelial cells within the intestinal epithelium. Therefore, the PGA/PLA composite scaffolds demonstrate significant potential in promoting the growth and long-term survival of epithelial cells [191].

5.4 Dental Applications

PLA has attracted attention for dental applications due to its structural compliance and biocompatibility, particularly in promoting osseointegration—the fusion of dental implants with oral hard tissues. Although not widely used in dental implantology, drug-loaded PLA implants have shown promising results in enhancing healing and tissue integration [192, 193].

Incorporating bioactive substances into PLA scaffolds can improve osteoconductivity and support bone tissue regeneration, crucial for successful dental implants PLA's favorable biocompatibility and customizability make it a promising candidate for further exploration in dental implantology [194]. Additionally, composite materials containing PLA can promote bone regeneration [193].

In addition to implants, PLA also serves in dental resins used for diverse restoration procedures. The assessment of these restoration materials focuses on their mechanical properties, stability, and aesthetic appeal. Resins can have enhanced mechanical properties when used with scaffolds made of PLA composites. Ranjbar et al. [195] conducted a study on PLA/Al_2O_3 nano scaffolds, which were synthesized by cross-linking the polymer with Al_2O_3. Their research demonstrated that these PLA/Al_2O_3 nano scaffolds exhibited improved mechanical properties, including flexural strength, modulus, and compressive strength, compared to conventional resins. This aligns with findings from Attoye et al., who reported that PLA, when used in Fused Deposition Modeling (FDM), generally shows superior mechanical properties compared to ABS, particularly when printed in the Y-axis orientation, which optimizes the mechanical performance of the fabricated parts.

In addition to its standalone applications, PLA has been effectively blended with other polymers to address post-surgical complications. Studies have shown that poly(lactic-co-glycolic acid) (PLGA) membranes significantly enhance oral bone healing in rat models and have been utilized to protect calvarial cells in rabbits, thereby facilitating bone regeneration in damaged regions [196]. The integration of PLGA with PLA not only augments the mechanical properties of the scaffolds but also improves their biocompatibility, rendering them highly suitable for diverse applications in tissue engineering and regenerative medicine [197]. Furthermore, PLA's drug delivery capabilities have been utilized for therapeutic applications in dentistry, such as facilitating the sustained release of antibiotics during endodontic operations [198].

5.5 Orthopedic Applications

PLA presents prospective benefits for the development of biodegradable orthopedic devices. PLA was initially employed in absorbable suture devices, which were patented in 1973. Since then, PLA has been used in other applications, including absorbable fracture repair plates [199]. Its polymer-based composition minimizes the artifact generation by enhancing superior imaging quality due to its radiolucent features. Furthermore, PLA copolymers can be modified by incorporating other materials, such as chitosan, to tailor their degradation rates [200]. PLA/chitosan copolymers provide enhanced material resilience and an extended degradation period. Studies indicate that PLA can exhibit a degradation period of approximately 8–12 weeks in vivo, making it a promising material for internal bone repair. This timeframe suggests that PLA may effectively reduce infection risk and promote stable integration when used in such applications. The combination of PLA with chitosan not only improves the mechanical properties of the scaffolds but also enhances their biocompatibility, making them ideal candidates for applications in bone tissue engineering. The favorable outcomes observed in these studies underscore the potential of PLA/chitosan copolymers in promoting effective healing and integration with surrounding tissues [176].

PLA-based orthopedic implants possess osteogenic or anabolic properties [201]. These implants can promote cell proliferation through including bioactive compounds. Recent studies have further demonstrated the potential of metal-reinforced PLA biocomposites in biomedical applications. For example, Wang et al. engineered bioactive interfaces for PLA-based scaffolds, significantly improving bone regeneration [202]. Huang et al. (2021) reported enhanced biocompatibility and osteogenesis with magnesium oxide-PLA composites [203]. Similarly, Zhao et al. (2024) demonstrated that silver-doped PLA nanocomposites exhibit both strong antibacterial activity and osteogenic effects, supporting their multifunctional use in tissue engineering [204].

Biodegradable fixation devices represent a promising alternative to conventional metallic implants, particularly in reducing the long-term risks of osteopenia and implant-related complications. A key advantage of PLA-based materials is their biodegradability, which eliminates the need for secondary surgical removal and supports gradual stress transfer from the degrading implant to the regenerating bone, aligning with the principles of mechanobiology [123]. The incorporation of porous PLA/metal composite screws and pins further enhances osteointegration by combining the mechanical reinforcement of metallic particles with the bioactivity and resorbability of the PLA matrix. As schematically illustrated in Fig. 23, such composite implants support new bone formation and provide temporary structural stability while being gradually resorbed and replaced by native tissue.

PLA orthopedic implants have shown significant success in animal models. For example, the integration of proteolipid and phosphatidylinositol 3,4-diphosphate has enhanced bone formation in rats and dogs [201]. PLA-based sutures and fixation bars have also been used to repair mandibular fractures in canines. Resorbable, self-reinforced, fibrillated PLA fixation rods have reduced rabbit osteotomies. L-PLA, with a tensile strength of 11.4–82.7 MPa and flexural strength of 45–145 MPa, is considered a suitable biomaterial for orthopedic implants due to its mechanical durability and hydrophobic properties. PLA and its copolymer-based porous scaffolds serve as cell transporters, storing nutrients

and facilitating the removal of cellular waste. Additionally, they promote cellular entrance by creating a permeable framework [154].

However, a significant challenge with PLA orthopedic scaffolds is the insufficient presence of epitope on their surfaces for cell adhesion. Modifications are necessary to enhance the affinity of PLA surfaces for targeted cell or protein binding, and increasing surface bioactivity within the pores is critical. Although PLA has numerous benefits, it can pose difficulties in orthopedic applications due to low fatigue strength, deformation under constant stress, inadequate adhesion, and potentially limited compatibility with the human body in some instances. The brittleness of PLA is attributed to its gradual crystallization process, and its low reactivity can impede cell penetration and necessitate the use of autografts to observe the scaffolds. The autograft procedure can lead to discomfort at the donor site, bleeding, necrosis, extended healing durations, and increased infection risk, making these procedures complex and challenging [200].

6 Structural Analysis and Challenges

The integration of metal reinforcements into PLA presents several challenges, including achieving uniform dispersion of metal particles within the polymer matrix, ensuring strong interfacial adhesion between the metal and polymer phases, and preventing particle agglomeration. Recent advances in additive manufacturing techniques, processing parameters, and surface modification strategies have played a key role in addressing these issues, enabling the development of high-quality, reliable metal-reinforced PLA composites for biomedical applications.

6.1 Interfacial Adhesion and Surface Treatments

The mechanical properties of PLA/metal composites are critically dependent on the interfacial adhesion between the PLA matrix and metal particles [205]. Research has demonstrated that enhancing interfacial compatibility through methods such as chemical grafting and the use of compatibilizers can significantly improve the tensile strength and flexural properties of these composites. Notably, the incorporation of maleic anhydride-grafted PLA has been shown to enhance interfacial adhesion, thereby improving mechanical performance [205, 206]. The differences in interfacial adhesion between untreated and surface-treated metal particles in a PLA matrix are illustrated schematically (Fig. 24).

The evaluation of these composites typically involves mechanical testing, including tensile and flexural strength assessments, to gauge the effectiveness of interfacial bonding. For instance, Jiang et al. found that PLA composites reinforced with treated sisal fibers exhibited enhanced tensile strength due to improved interfacial compatibility [207]. Similarly, Du et al. reported that styrene-assisted maleic anhydride grafted PLA as a compatibilizer significantly enhanced the mechanical properties of PLA composites [208].

Additionally, the performance of PLA/metal composites can be assessed through dynamic mechanical analysis (DMA) and thermal analysis, offering insights into the viscoelastic properties and thermal stability of the materials. Studies indicate that improved interfacial adhesion facilitates better stress transfer between the PLA matrix and metal particles, leading to superior overall performance [209].

6.2 Enhancing Metal Particle Performance Throough Surface Treatments

The adhesion between metal and polymer matrices is often weak due to the inherent differences in their surface properties, which can lead to reduced mechanical strength and durability of the composite [179, 210]. Surface treatments, including chemical modifications and plasma treatments, can significantly improve the bonding characteristics by creating reactive sites that facilitate stronger interactions at the interface, thus enhancing the mechanical properties of the composites [211, 212]. Moreover, the incorporation of metal particles into PLA composites can lead to improved thermal and electrical conductivity, but this is contingent upon effective surface treatment to ensure uniform dispersion and strong interfacial bonding [213].

Figure 25 illustrates how surface coatings such as polydopamine or silane can enhance the dispersion of metal particles in PLA composites. These treatments improve interfacial compatibility, leading to uniform particle distribution within the matrix. This not only strengthens mechanical performance but also improves cellular responses—critical for biomedical applications where consistent bioactivity and structural integrity are required.

Coupling agents, such as maleic anhydride and isocyanates, can significantly enhance the compatibility between the hydrophobic PLA and the hydrophilic metal surfaces, leading to improved stress transfer at the interface. For instance, the incorporation of a coupling agent has been shown to increase the tensile strength of PLA composites, although specific values such as an increase from 60 to 85 MPa require further validation as they are not directly supported by the cited references [214] This increase can be attributed to the formation of chemical bonds between the coupling agent and both the PLA matrix and the metal particles, which effectively reduces the likelihood of interfacial debonding during mechanical loading [215]. Quantitatively, studies have indicated that the addition of coupling agents can reduce internal defects within the composite, such as voids

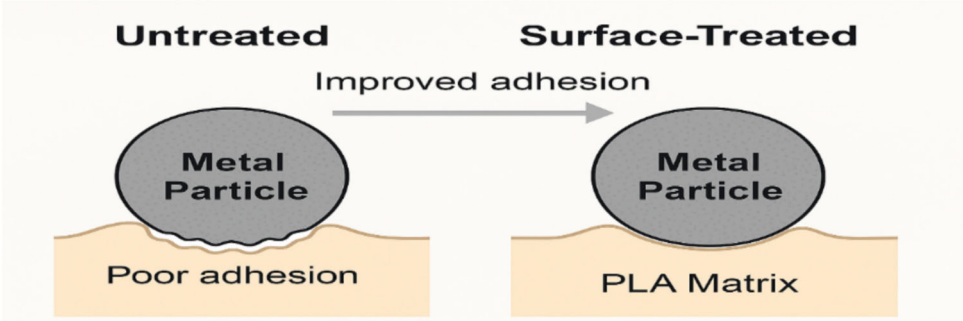


Fig. 24 Schematic illustration of interfacial adhesion between the PLA matrix and metal particles: untreated particles exhibit poor adhesion, while surface-treated particles show improved adhesion

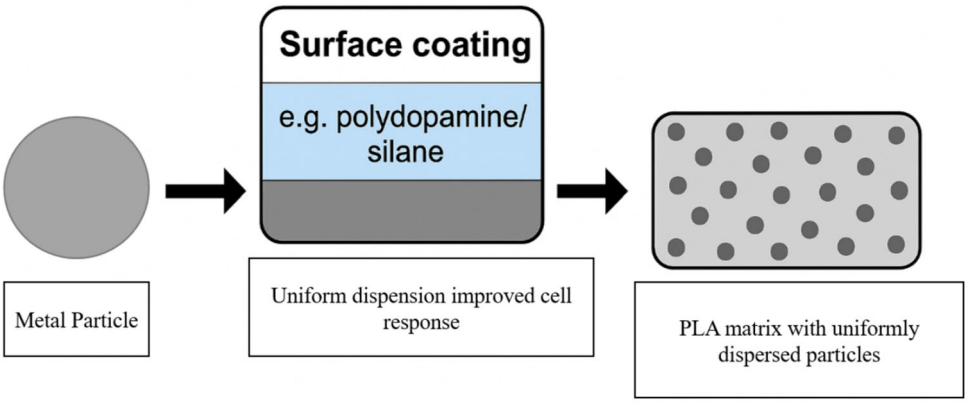


Fig. 25 Schematic illustration of surface coating of metal particles (e.g., polydopamine or silane) to achieve uniform dispersion within the PLA matrix and enhance cell response

and cracks, which are often responsible for stress concentrations that weaken the material [216]. For example, while the KH-550 coupling agent has been reported to enhance the interface adhesive strength, the specific claims regarding its effects on internal defects and mechanical properties need to be substantiated with appropriate references. Furthermore, the use of coupling agents can also modify the thermal properties of the composites, although the specific effects on the glass transition temperature (Tg) of PLA blends require further evidence [217]. Overall, the strategic application of coupling agents is essential for optimizing the performance of PLA-based composites, particularly those containing metal particles, by enhancing interfacial adhesion and mechanical integrity. The incorporation of compatibilizers, such as polylactide-graft-glycidyl methacrylate (PLA-g-GMA), has been shown to significantly improve interfacial adhesion, resulting in a tensile strength increase compared to neat PLA, though specific percentages such as 33% need to be verified with relevant studies [218]. This enhancement is primarily due to the formation of chemical bonds between the compatibilizer and the metal surface, which mitigates issues related to particle agglomeration and enhances the dispersion of metal particles within the PLA matrix. Furthermore, improved interfacial adhesion not only increases mechanical strength but also enhances other properties such as gas barrier performance, making treated PLA-based composites suitable for a wide range of applications, including packaging and biomedical devices. By employing coupling agents, such as PLA-grafted maleic anhydride, the interfacial adhesion can be significantly improved, as these agents facilitate chemical bonding between the PLA and the metal surfaces [219]. Additionally, surface treatments can improve the dispersion of metal particles within the PLA matrix, reducing agglomeration and ensuring a more uniform distribution, which is crucial for achieving the desired functional properties in applications ranging from biomedical devices to structural components.

The incorporation of coupling agents is another effective strategy to enhance interfacial adhesion. Coupling agents act as a bridge between the PLA matrix and metal particles, facilitating better bonding and stress transfer. Silane coupling agents, for example, have been used to modify the surface of metal particles, leading to improved dispersion and adhesion within the PLA matrix. This approach not only enhances the mechanical strength of the composite but also improves its overall durability and performance [220].

6.3 Strategies for Optimizing Printing Parameters

Parameters such as nozzle temperature, bed temperature, and layer thickness play a significant role in determining the quality of the printed composite. Figure 26 provides an overview of the key printing parameters and optimization

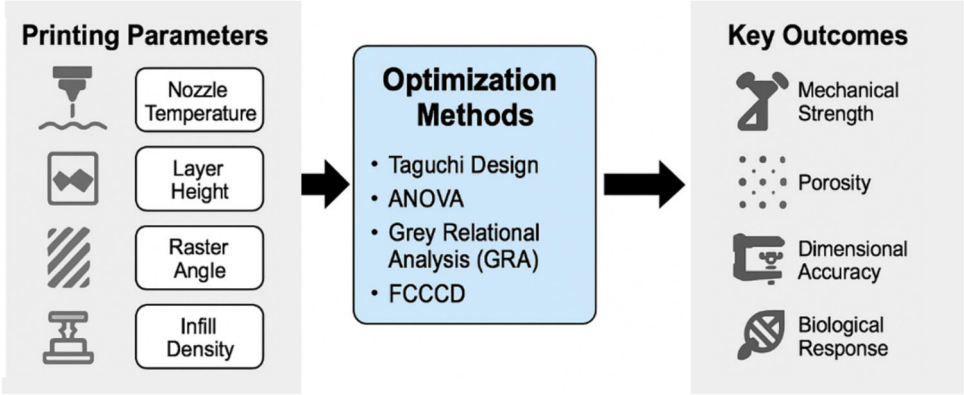


Fig. 26 Main printing parameters and optimization strategies used to tailor the structural and functional properties of PLA/metal biocomposites produced via additive manufacturing

techniques, such as Taguchi Design, ANOVA, Grey Relational Analysis (GRA), and FCCCD that are commonly used to tailor mechanical strength, porosity, dimensional accuracy, and biological performance.

Balamurugan et al. investigated the effects of these parameters on PLA/Cu composites and found that higher nozzle and bed temperatures improved the bonding between the PLA matrix and Cu particles, resulting in enhanced mechanical properties [221]. Specifically, the study demonstrated that optimal temperature settings facilitate better interfacial adhesion, which is crucial for the overall performance of the composite material. Similarly, adjusting the layer thickness can influence the degree of interlayer adhesion, which is vital for the structural integrity of the printed composite. Research has shown that thinner layers tend to enhance interlayer bonding, thereby improving the mechanical strength of the final product [222]. Conversely, thicker layers may lead to poor adhesion between layers, resulting in reduced mechanical performance and increased susceptibility to failure under load [223]. Moreover, the evaluation of mechanical properties is essential to understand the impact of these parameters on the performance of PLA/Cu composites. For instance, tensile strength and compressive strength tests are commonly employed to assess the mechanical integrity of the printed materials. Studies have indicated that the incorporation of coupling agents can further enhance these properties by improving interfacial adhesion between the PLA matrix and metal particles [224]. In summary, the careful optimization of printing parameters, including nozzle temperature, bed temperature, and layer thickness, is crucial for achieving high-quality PLA/Cu composites. The interplay between these factors significantly influences the mechanical properties and overall performance of the printed materials, making it essential for applications in various fields, particularly in biomedical engineering.

6.4 Mechanical Properties of Porous Scaffolds

These scaffolds feature intricate pore geometries and a network of interconnected pores. Utilizing PLA and 316L stainless steel, ME-printed scaffolds were produced, showcasing pore dimensions ranging between 700 to 1020 μm and strut thicknesses spanning from 610 to 1000 μm. The investigation revealed that incorporating 316L particles into the PLA matrix at a 15% volume fraction led to a reduction in the average pore size from 880 to 800 μm, while the average strut width increased from 720 to 840 μm. [123]. The SEM imagery, as seen in Fig. 27a, highlights the even distribution of 316L powder within the PLA matrix struts. In contrast, the PLA/Ti scaffold, depicted in Fig. 27b, exhibited a controlled pore architecture with a porosity of 47% and an average pore diameter of 787 μm when titanium was used. Figure 27c and d display the cryogenically fractured surfaces of PLA/Cu and PLA/bronze composite scaffolds, respectively, both featuring a 50% porosity and 400 μm pore diameter, with spherical metal filler particles evident. The PLA/Fe scaffolds demonstrated an average pore width of 820 μm and a strut width of 844 μm, with a uniform distribution of iron powder throughout the PLA. However, the integration of iron powder occasionally impeded the PLA matrix flow during the printing process, potentially leading to voids within layers, as indicated by red arrows in Fig. 27a and e. Figure 27f illustrates the interconnected porosity and evenly dispersed magnesium powder particles within the PLA/Mg composite scaffolds. Moreover, PCL/Mg composite scaffolds, shown in Fig. 27g, exhibited satisfactory printability and resolution, with a porosity of 66% and a pore size of 480 μm, as detailed in Fig. 27i. The incorporation of magnesium fillers into the PCL matrix, as shown in Fig. 27h, was found to enhance the surface roughness of the scaffolds.

However, the PLA/Mg composite scaffolds' interconnected porosity structure and well-dispersed Mg powder particles may cause a decrease in mechanical strength compared to pure PLA scaffolds. Additionally, the increased

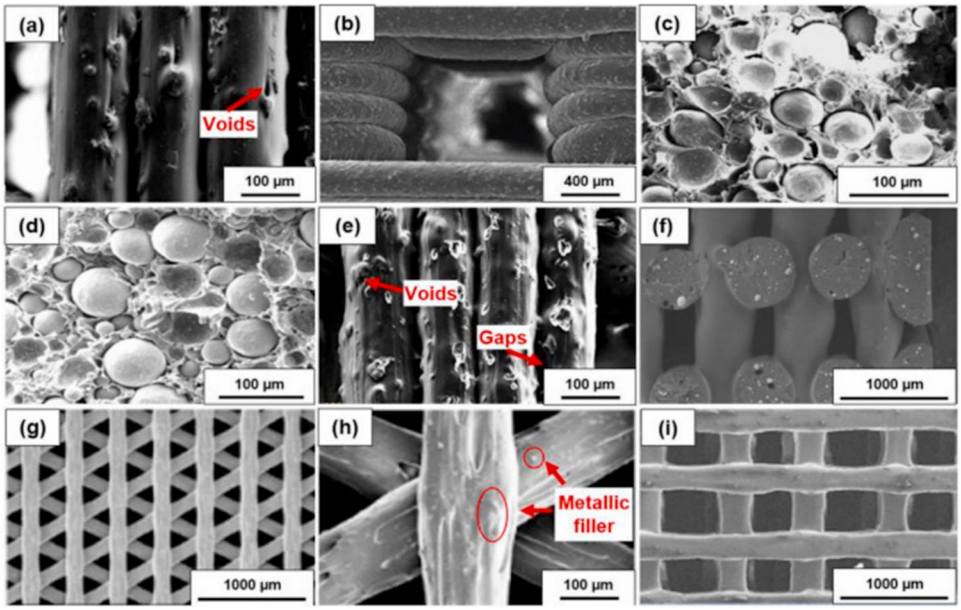


Fig. 27 SEM images of different polymer/metal composite 3D porous scaffolds, showing their shape and how the particles are spread out **a** PLA/10 vol% 316L stainless steel [123], **b** PLA /15 vol% Ti [154], **c** Cross-section of PLA/24 vol% Cu [159], **d** Cross-section of PLA/30 vol% bronze [135], **e** PLA/10 vol% Fe [225], **f** PLA/7 vol% Mg, **g, h** PCL/6.8 vol% Mg and **i** PCL/6.1 vol% Mg [158]

surface roughness of the PCL/Mg composite scaffolds could lead to a higher risk of bacterial adhesion and colonization.

This increase in surface roughness can be attributed to the presence of the Mg fillers, which create a more textured surface compared to the PCL matrix alone. The interconnected porous structure and increased surface roughness of the PCL/Mg composite scaffolds suggest that they may have enhanced cell adhesion and proliferation capabilities, making them potentially suitable for tissue engineering applications.

7 Discussion

7.1 Critical Analysis

In this section, we critically evaluate the current state of research on PLA/metal biocomposites, identifying key advancements, challenges, and gaps in the literature.

7.1.1 Advancements in Mechanical Properties

Numerous studies, including those by Liu et al. (2019) and Ambone et al. (2020), have demonstrated that the integration of metal particles into PLA significantly enhances its mechanical properties. These studies report improvements in tensile strength, durability, and overall mechanical performance. However, the extent of these improvements varies depending on the type and concentration of metal particles used. While titanium and silver have shown promising results, other metals such as magnesium and copper also warrant further investigation.

7.1.2 Biocompatibility Concerns

The biocompatibility of PLA/metal biocomposites is a critical factor for biomedical applications. Previous research, such as that by Rajeshkumar et al. [2], has highlighted the potential of PLA composites in medical implants due to their biodegradability and biocompatibility. However, the addition of metal particles introduces new variables that can affect biocompatibility. Our review indicates that while some metals, like silver, have antimicrobial properties that can be beneficial, others may pose cytotoxicity risks. Comprehensive in vivo studies are necessary to fully understand the long-term biocompatibility of these composites.

7.1.3 Manufacturing Challenges

ME technology has been widely used for producing PLA/metal biocomposites. Studies by Mustapha and Metwalli (2021) and Çevik and Kam (2020) have shown that ME is effective for fabricating complex structures with enhanced mechanical properties. However, the layer-by-layer construction inherent to ME can result in a rough surface finish, which may not be suitable for all biomedical applications. Additionally, the mechanical properties of ME-produced parts are highly sensitive to printing parameters such as temperature, speed, and layer height. Variations in these parameters can lead to inconsistencies in the final product, potentially affecting the reproducibility of the results.

7.1.4 Context-Dependent Biocompatibility

Biocompatibility is not a static property but is highly context-dependent, varying with the specific biomedical application and the biological environment in which the material is used. Several factors influence the biocompatibility of PLA/metal biocomposites:

1. *Type of Metal Reinforcement* Different metals have varying effects on biocompatibility. For instance, silver has well-documented antimicrobial properties, which can be beneficial in preventing infections. However, it can also pose cytotoxicity risks at higher concentrations. Titanium, on the other hand, is known for its excellent biocompatibility and is widely used in medical implants.
2. *Surface Properties* The surface roughness and chemistry of the biocomposite can significantly influence cell adhesion, proliferation, and differentiation. A rough surface may promote better cell attachment but could also lead to increased bacterial colonization.
3. *Degradation Products* The biocompatibility of PLA/metal biocomposites is also affected by the degradation products released over time. PLA degrades into lactic acid, which is generally biocompatible. However, the degradation products of the metal particles need to be carefully evaluated for any potential cytotoxic effects.
4. *Biological Environment* The specific biological environment, such as the type of tissue or fluid in contact with the biocomposite, can also affect its biocompatibility. For example, materials that are biocompatible in bone tissue may not perform as well in soft tissues.
5. *Mechanical Stress* The mechanical environment, including the type and magnitude of stress applied to the biocomposite, can influence its biocompatibility. Materials that perform well under static conditions may fail under dynamic loading.

7.1.5 Regulatory Considerations

Regulatory considerations are critical for the successful translation of PLA/metal biocomposites from research to clinical applications. Several regulatory factors must be addressed:

1. *Regulatory Approval* Biomedical materials must undergo rigorous testing and obtain approval from regulatory bodies such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA). This process includes preclinical studies, clinical trials, and post-market surveillance to ensure the safety and efficacy of the materials.
2. *Standards and Guidelines* Compliance with international standards and guidelines, such as ISO 10993 for biological evaluation of medical devices, is essential. These standards provide a framework for assessing the biocompatibility, toxicity, and overall safety of biomedical materials.
3. *Quality Control* Consistent quality control measures must be implemented during the manufacturing process to ensure that the final product meets regulatory requirements. This includes monitoring the purity of raw materials, controlling the manufacturing environment, and conducting thorough testing of the final product.
4. *Documentation and Reporting* Comprehensive documentation and reporting are required throughout the regulatory approval process. This includes detailed records of preclinical and clinical studies, manufacturing processes, and quality control measures.

7.2 Ethical Considerations

Ethical considerations, such as informed consent and patient safety, must be prioritized in all stages of research and development. Regulatory bodies often require ethical approval from institutional review boards (IRBs) or ethics committees before clinical trials can commence.

7.3 Gaps and Future Directions

Despite the promising advancements, several gaps remain in the current research:

1. *Optimization of Metal Reinforcement Ratios* The optimal ratios of metal reinforcement for different applications are not well-established. Future research should focus on systematically studying the effects of varying metal concentrations on the mechanical properties and biocompatibility of PLA composites.
2. In Vivo*Testing* Most studies have been limited to in vitro conditions. Comprehensive in vivo studies are essential to evaluate the long-term biocompatibility and performance of metal-reinforced PLA composites in biological environments.
3. *Broader Range of Metals* While titanium and silver have been extensively studied, other metals or combinations of metals might yield different results. Future studies should investigate a wider range of metal reinforcements to identify the most effective formulations.
4. *Surface Finish Improvements* Additional post-processing steps may be required to achieve the desired surface quality for biomedical applications. Research into advanced post-processing techniques could help overcome this challenge.

5. *Environmental Impact*: Given the growing emphasis on sustainability, future research should also consider the environmental impact of producing and disposing of metal-reinforced PLA composites. Life cycle assessments could provide valuable insights into their overall sustainability.

8 Conclusion

This review highlights the growing interest in PLA-based metal-reinforced biocomposites manufactured via additive techniques for biomedical applications. While these composites offer promising improvements in mechanical strength and functional performance, their widespread use remains limited due to unresolved challenges in biocompatibility, process optimization, and material consistency. One of the key research priorities identified is the precise optimization of metal reinforcement ratios, which directly affect the printability, mechanical robustness, and biological response of the final constructs. Despite a growing number of studies exploring various reinforcement strategies, the literature remains fragmented—particularly lacking comprehensive evaluations that integrate mechanical, physical, and biological performance. The incorporation of metals such as titanium, stainless steel, and silver into PLA matrices presents a novel and fertile research direction, especially when considered alongside antimicrobial or bioactive functionalities. The review underscores the need for more systematic investigations into the interfacial behavior of metal-polymer systems, degradation kinetics, and long-term performance under physiological conditions. By synthesizing current knowledge and identifying key research gaps, this study aims to guide future work towards the development of safe, reliable, and high-performance biocomposites tailored for load-bearing and tissue-regenerative applications.

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Declarations

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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