Al-Khwarizmi Engineering Journal

Al-Khwarizmi Engineering Journal
ISSN (printed): 1818 – 1171, ISSN (online): 2312 – 0789
Vol. 22, No. 2, June, (2026), pp. 32- 53

Review of Current Trends, Materials and Challenges in 3D Printing for Biomedical Applications Using Polylactic Acid

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(Received 22 July 2025; Revised 24 November 2025; Accepted 13 April 2026; Published 1 July 2026)
https://doi.org/10.22153/kej.2026.04.002

Abstract

Polylactic acid (PLA) is a widely used biomaterial in additive manufacturing (AM) because of its biodegradable and biocompatible nature and availability. Hence, this study focuses on the importance of PLA in biomedical applications such as personalised medicine, tissue engineering, drug delivery and customised implants and explores the possibility of PLA-based biomedical products. Different AM technologies, such as fused deposition modelling, stereolithography, and selective laser sintering, and their possible uses with PLA are presented. Apart from pure PLA, the use of composite materials based on PLA is important, as these materials can improve mechanical and biological properties, which are highly desirable for various clinical applications. Several critical issues, such as material properties, resolution, regulatory affairs, biodegradability and sustainability, are examined and discussed. In addition, the potential of PLA-based 3D printing technologies, including multimaterial 3D printing and bioprinting for biomedical applications, is explored.

Keywords: *Polylactic acid; 3D printing; Biomedical applications; PLA-based composites; Tissue engineering; Fused deposition modelling; Bioprinting; Drug delivery; Personalised medicine*

1. Introduction

The use of 3D printing technologies in biomedical applications has transformed the production of medical devices, implants and prostheses. Polylactic acid (PLA) is an optimal material for biomedical 3D printing because of its high biocompatibility, biodegradability and ease of manipulation. PLA is a biodegradable thermoplastic derived from renewable resources such as maise starch and sugarcane. This renders it an advantageous option for environmental sustainability and a potential material for medical applications [1].

PLA is amongst the common materials used in the biomedical sector because of its biodegradability and can be fabricated by several additive manufacturing (AM) techniques, such as fused deposition modelling (FDM), stereolithography (SLA) and selective laser sintering (SLS). This research is based on PLA applications in tissue engineering, drug delivery, prosthetics and implants. The main purpose of this review is to examine the challenges and advancements of 3D printing of PLA for biomedical applications, opportunities and barriers and to determine how these barriers can be addressed so that 3D printing technology can be effectively and efficiently used in clinical practice.

This systematic review adheres to PRISMA guidelines and seeks to synthesise research regarding the use of PLA-based 3D printing technologies in biomedical applications. A thorough search was performed using the Scopus, PubMed, Web of Science and ScienceDirect databases for articles published from January 2022 to May 2025. The search terms included ‘polylactic acid’, ‘PLA’, ‘3D printing’, ‘biomedical applications’, ‘implants’ and ‘tissue engineering’. Only original research articles from peer-reviewed Q1/Q2 journals were included; review articles were excluded unless they presented original comparative data or technical standards. A total of 143 articles were initially retrieved; after full-text screening, 46 studies met the inclusion criteria.

The suitability of the selected articles was assessed according to the experimental design, sample size, materials and method for the preparation and testing of 3D-printed PLA scaffolds. The necessary data for materials, printing methods, mechanical and biological properties, in vitro and in vivo behaviour and clinical performance were collected, and a consensus was reached in case of disagreement. On the basis of the primary data reported in the literature and a comprehensive review of the results achieved in different clinical fields, this study discusses the biomedical applications of PLA.

2. PLA-based 3D Printing Technologies for Biomedical Uses

Many methods are used to 3D print PLA in biomedical research. The advantages and disadvantages of these methods vary depending on the characteristics of the biomaterials and the purpose of their application.

2.1. Fused Deposition Modelling (FDM)

FDM is a widely used AM technology. The FDM 3D printing process offers an affordable, versatile and simple manufacturing method. FDM 3D printing lays down droplets of thermoplastics from a nozzle along the x- and y-axes, building a 3D object in layers and allowing for the creation of a large number of different complex structures and features. FDM technology is used in the medical field, space industry, automotive industry and education sector [2–6]. The capacity for rapid prototyping and product customisation has established the FDM as a fundamental technology in the advancement of contemporary manufacturing [2], [4], [5], [7].

FDMs belong to a class of AM technologies that are based on polymers, typically thermoplastics, such as PLA, acrylonitrile butadiene styrene (ABS) and polyether ether ketone. Despite the advantages associated with PLA, such as its biodegradable nature and eco-friendliness, the mechanical strength of the polymer is inadequate. Hence, the polymer material should be modified by the incorporation of filler material [4], [6], [8], [9]. Prior to recent advancements in material science, 3D printing technology was limited to a relatively small range of common plastics and polymers, ceramics and metals. With recent advancements in materials science, a wide range of new materials can be 3D printed, including polymer composites, fibre-reinforced polymers and recycled resins. Furthermore, with the ability to 3D print with these new materials, users find that their printed parts are stiffer, have improved thermal and electrical properties and are far more durable [3–5], [9]. When nanoparticles are mixed with short or long fibres, the performance and value of FDM products can be greatly improved [4], [9].

Some forums debate the best 3D-printing materials to construct ‘bioplugs’ or ‘pacemaker seed plugs’ for a project to plant wildflowers over a pacemaker. Recommendations include the utilisation of polycaprolactone (PCL) or PLA, but FDM materials still need to be improved when used as dental implants or soft tissue scaffolds. The sustainability or biodegradability of bioplastic materials, such as PLA, is precisely the reason they are used on short-term disposable devices such as syringes, swabs and medical examination gloves. However, these materials are somewhat weak, which makes them entirely unsuitable for load-bearing applications such as dental implants [10].

Influence of process parameters on the mechanical and physical properties of FDM-printed samples. The purpose of this study was to investigate the influence of process parameters (extrusion temperature, layer thickness, print speed and infill density) on the mechanical and physical properties of specimens printed by FDM [3], [5], [8]. The parameters mentioned above should be optimised to achieve the desired properties, shorten the production time and reduce costs [3], [5], [8]. The rheology of the filament materials during 3D printing is critical because it ensures a consistent and continuous extrusion process, controls the deposition behaviour and ultimately impacts the interlayer adhesion between the layers [5]. Controlling the rheology of soft materials at different time scales and correlating them to the physical properties of the final printed structure has unlocked a plethora of novel functions and enabled 4D printing, where an object can change its shape or functionality in time [6], [18].

FDM is a popular 3D printing technology because of the variety of applications it supports. FDM 3D printing is typically used for rapid prototyping manufacturing of end-user parts and products that go to market medical devices such as orthotics and prosthetics components, syringes and other medical devices such as automotive parts and components and aerospace parts and components [2–6], [8]. This technology was extremely important during the COVID-19 pandemic because it allowed the rapid production of items such as face mask supports and swab holders [6]. Auxetic structures, which have a negative Poisson's ratio and better mechanical properties, show how FDM can be used to create new, useful products with unique microstructures [11]. FDM is a common way to 3D print in biomedical settings.

In FDM, a heated nozzle extrudes a thermoplastic filament, such as PLA, layer by layer to construct solid objects. FDM is cost effective, user friendly and suitable for the production of prostheses, orthotics and customised implants. The primary advantage of FDM is its cost-effectiveness, enabling the production of medical devices on a small scale [12].

FDM, whilst advantageous, encounters multiple limitations. The mechanical properties of FDM-printed components frequently do not match those of parts created through conventional manufacturing techniques, mainly because of challenges such as inadequate interlayer adhesion and the presence of voids [3], [4], [9], [11]. The availability of materials and the intrinsic properties of thermoplastics may limit the spectrum of viable applications [3], [8]. Another challenge is ensuring high precision and surface quality, especially for complex shapes and loaded components [3], [5], [11].

Practical research on FDM focuses on new materials, increasing the sustainability of the FDM process and the integration of FDM with other AM technologies [2], [4], [5]. Actual research on FDM focuses on new materials, increasing the sustainability of the FDM process and the integration of FDM with other AM technologies [4], [5], [9]. 4D printing is a term that has been tossed around the 3D printing community fairly often lately. When FDM is used as a process to create what are known as smart materials, plastic can change shape in response to external stimuli [6], [13]. Scientometric analysis reveals an increasing trend in the output of research and global collaboration, with the research being more applicable to practice [7].

FDM is amongst the leading AM technologies. Advancements in materials and process optimisation and the exploration of new application fields have promoted the development of FDM technology. Whilst FDM has not yet reached its full potential concerning the mechanical properties and performance of materials and is therefore not yet defect-free, the ongoing development of FDM technology can create new application fields for this process.

2.2. Stereolithography (SLA)

In this study, stereolithography (SLA) AM technologies were employed to prepare a photosensitive resin material that can be selectively cured by a laser or light source. The SLA system used in this study is composed of two types: point scanning and digital micromirror devices (DMDs). The point-scanning method uses a focused light beam to draw the desired pattern on the resin by tracing it layer by layer, whereas the DMD method uses a 2D light pattern projected onto the resin surface. The factors that affect the mechanical properties of the printed samples are the layer thickness, print direction, curing time, curing temperature and laser power. The mechanical properties of the samples, such as hardness, tensile strength, flexural strength and surface roughness, were investigated in relation to various parameters [14–16].

SLA uses a UV laser to polymerise each layer of liquid photopolymer resin. SLA is used to create complex medical devices, such as dental implants and surgical guides, given the high resolution and surface finish that can be achieved [17]. The SLA resins derived from the PLA are highly accurate and are used to create medical models and custom implants with high accuracy.

The SLA material showed high precision. Although SLA technology has many advantages, the main drawback of this technology is that expensive 3D SLA printers and photopolymer materials are needed. Therefore, this technology is generally not recommended for the production of large-scale objects [18]. In contrast to other photopolymers, PLA-based resins for SLA 3D printing are not as widely available.

New computational models to optimise parameters Some of the variables that require experimental adjustment are being studied using recent models that aim to improve print speed whilst keeping the final printed part quality intact. The models suggest that a higher scan speed corresponds to a shallower penetration depth of the cured layer, whilst optimising the concentration of the photo-initiator achieves the maximum penetration depth. In addition, printing parts with resins with lower viscosity and higher surface tension results in rapid recoating rates and, hence, high print speed and part quality [15], [16].

SLA is a technique used for 3D printing using photopolymer resin. Most of the photopolymer resins used in SLA 3D printing have been developed to meet mechanical requirements for optical, medical or general applications. However, other types of polymers, such as polymer composites, hydrogels and nanocomposites, can be used for 3D printing. When graphene oxide (GO) is added to ceramic powders, the mechanical performance of the printed parts can be significantly improved; therefore, the possibility for the application of 3D printing increases. GO nanocomposites increase tensile strength and shear strength, whereas SLA-printed ceramic composites exhibit ductile behaviour appropriate for custom prostheses [19–21]. Hydrogels produced via SLA are significant in bioengineering, facilitating the development of tissue scaffolds, lab-on-a-chip devices and models that closely resemble native tissues and are characterised by high shape fidelity and consistent mechanical properties [14].

SLA is great for biomedical uses, such as tissue scaffolds, drug-eluting devices and personalised implants, because of its high resolution and accuracy. SLA ensures custom dosage forms in the pharmaceutical industry, moving away from the traditional ‘one dose fits all’ strategy and towards patient-centred treatment [14], [22], [23]. SLA is widely used in prototyping and manufacturing in the aerospace, automotive and electronics industries because it allows parts with complex shapes and smooth surfaces. This process is being used to produce advanced optical parts, such as clear resin lenses for high-power LED packages. These lenses are more flexible and work better than traditional moulding methods [15], [19], [24].

Despite their benefits, SLA-printed parts often need to be postprocessed after printing to ensure that they are strong and accurate. UV curing strengthens the structure of materials and helps them to stick together better, but it can also result in materials that are brittle, with edge chipping as they are being machined. Adjusting the postprocessing parameters is crucial for obtaining the desired material properties [25]. The main issues are still related to the production sector and to the regulatory framework: materials, process repeatability and scalability. These problems can be solved by increasing the performance of SLA technologies [15], [22]. Genetic algorithms and artificial neural networks are used to increase the yield and performance of AM processes and to develop new composite materials. However, the applications of SLA technology in the Industry 4.0 context are beginning to be highlighted, from the production of single pieces to cost reduction for short series and recycling [15].

SLA is a flexible and accurate AM technology and therefore is largely applicable. However, material and process developments, together with simulation modelling, are still allowing researchers to improve this technology, and several challenges need to be solved, particularly related to postprocessing and scaling-up. In any case, this technology is expected to be one of the fundamentals of the future of digital manufacturing and custom production.

2.3. Selective Laser Sintering (SLS)

SLS is amongst the most widely used AM technologies. In SLS, a laser is used to selectively sinter (fused together) the powdered material (primarily the use of polymers) according to the CAD 3D model defined for the object to be manufactured. The laser fuses together the powdered material, such as PLA, layer by layer. The SLS process enables the production of strong and long-lasting parts with a high level of surface detail and accuracy, which can be applied to orthopaedic devices, prostheses and bone implants [10]. SLS is an AM process that produces strong parts with complex geometries and allows for the use of a wide range of materials, including PLA. In the SLS, the solid parts are created without any need for support material during the process. This is slightly different from other AM techniques. The SLS process creates parts with mechanical properties close to those of injection-moulded parts whilst allowing designers to select materials that suit their design needs. The SLS process is widely used in various industries, including aerospace, automotive, construction and medical devices. SLS has been traditionally working with polyamide powders, but researchers can now expand the material range of SLS to a wide variety of polymers and polymer composites, which enables the production of SLS parts with improved mechanical properties and with electric conductivity and multifunctionality. Compared with other types of composites, electrically conductive polymer composites (ECPCs) fabricated by SLS show better performance, particularly in terms of strain and self-sensing properties. SLS allows the formation of segregated filler networks at the boundary of the powder particles between adjacent laser-melted tracks, which contributes to the increase in the conductivity of the ECPCs [26], [27]. You can recycle unused powders. In addition, large quantities of 3D can be printed at once without the need for support, which makes SLS technology even more appealing for industrial applications [26].

This study promotes a novel method for manufacturing drugs, i.e. in situ laser sintering, including SLS. The technology proposed in this study allows for the production of custom formulations with customised release profiles in a significantly shorter amount of time. When laser parameters (laser power, frequency and velocity) and powder blend composition are controlled, complex drug products, including bilayer tablets and customised oral drug products, can be produced. The proposed technology also allows for a much faster transition from an off-the-shelf product to a personalised product, which has the potential to greatly improve patient outcomes and adherence to their medications [28–30]. SLS allows researchers to 3D print items from remote locations and to open up new and innovative supply chains. This opens up a world of possibilities, including improving the quality of life by enabling researchers to produce parts and products when and where they are needed [28].

The influence of the process parameters on the SLS-fabricated samples and the application process parameters, such as the laser intensity, part orientation, build position and powder properties, strongly affect the internal structure and properties of the SLS-fabricated samples. Samples fabricated with higher laser intensity have higher density, hardness and stability. However, slower drug release is observed in pharmaceutical applications [29], [30]. All these characteristics (orientation, thickness and position) may influence some characteristics, such as geometry, and thus indirectly affect the overall accuracy of the final component in terms of dimension and surface finish. [31], [32]. These machine settings need to be adjusted periodically to ensure that the quality and performance of the parts being produced do not decrease.

SLS technology allows for designs that have never been possible before, including nonassembled parts and multifunctional components. With the use of SLS 3D printing technology, fully functional nylon prosthetic components that include integrated joints and springs can be 3D printed and are immediately ready for use without any post-assembly [33]. The novelty of this project is the investigation of the potential of SLS 3D printing as a smart material fabrication technique. In this context, the main objectives of the proposed research are to develop self-healing and recyclable thermoset networks and flexible elastomer composites for sensor applications. The ambition of this project is to open up new perspectives and possibilities of SLS 3D printing technology, which go well beyond the current conventional AM use cases [27], [34].

Although SLS has several benefits, it also has several drawbacks. The range of processable polymers is limited, and structural features such as porosity and surface characteristics can significantly affect the mechanical behaviour of the final product [32], [35]. All the process parameters must be controlled, and a suitable material must be selected to ensure accurate shape and uniform mechanical properties of the component [31], [32]. Formulating a drug product that delivers the active pharmaceutical ingredient (API) in the exact right amount to the exact right location in the body at the exact right time in the exact right form is extremely challenging. The API must be delivered at the exact right concentration to produce the desired therapeutic response, and it must be delivered in the exact right amount at the exact right time to maintain that therapeutic response. The API must be delivered in a form that is not only therapeutically effective but also safe for the patient [28–30].

SLS is a 3D printing technology that is used in many applications in the industrial and pharmaceutical sectors to develop products. The main focus of this research is on increasing the number of materials that can be used with SLS, optimising the parameter settings and developing multifunctional parts that are exactly what the customer desires. SLS is still driving design and manufacturing innovation, despite its challenges, which include the lack of materials available and the complexity of controlling the SLS process.

3. Materials Used in 3D Printing for Biomedical Purposes with PLA

Mixing other materials into PLA makes the material stiffer and more useful and can even ensure that the material is bioactive. In biomedicine, composite materials can be tailored to overcome the limitations of PLA.

3.1. PLA composites with hydroxyapatite

In this study, a PLA composite material was prepared by incorporating hydroxyapatite (HA) to study its potential biomedical applications, particularly in the field of bone tissue engineering. Composite materials are often used for bone tissue engineering because of the properties of HA, which aid in the growth of bone. The HA subcomponent in the PLA/HA composite has high osteoconductive properties [10]. The mechanical properties of the PLA/HA blend improved. This blend is envisaged for the preparation of bone scaffolds and orthopaedic implants. The composite material is targeted towards the design of a scaffold that closely resembles the native bone to promote bone regeneration. The blended material utilises the biodegradability and processability of PLA along with the bioactivity and osteoconductive properties of HA.

Adding HA to the PLA matrix makes the composites much stronger and more durable. Studies have shown that the best amount of HA increases the hardness and tensile, compressive and flexural strength, allowing these composites to be suited for use in load-bearing applications. PLA/HA composites with 30 wt% HA had a tensile strength of 62 MPa and a compressive strength of 61 MPa. These composites also had high cell survival, which suggests that they could be used in biomedical settings [36].

The application of HA nanowhiskers and high-shear dispersion techniques increased the tensile strength of the composite by 48% and increased its elastic modulus by 84% relative to that of pure PLA whilst increasing cell viability. Excessive HA content or inadequate dispersion may cause agglomeration, which adversely affects mechanical performance and reliability [38], [39].

The surface properties of a material, such as stiffness, topography and adhesion, influence initial cell adhesion and subsequent differentiation. In this study, the effects of altered surface properties of PLA/HA on the initial adhesion and osteogenic differentiation of human mesenchymal stem cells were investigated. The addition of HA to the PLA scaffolds resulted in a significantly altered surface topography and led to a uniform distribution of stem cells and enhanced differentiation. These results suggest that HA added to bioresorbable PLA scaffolds promotes initial cell adhesion [40]. Nanomechanical mapping demonstrated that the HA-modified PLA scaffolds had a Gaussian distribution of elastic modulus and adhesion force values, which supported enhanced cell behaviour, including the attachment and deposition of minerals. Cross-linking with GLYMO increased the surface roughness and mechanical properties and enhanced cell viability [41].

The addition of HA generally increased the thermal stability of the composite scaffolds. TG and DSC analyses revealed that HA significantly increased the glass transition temperature of the composite scaffolds and thus suppressed the hydrolysis degradation of the PLA matrix, maintaining the mechanical strength during biotissue regeneration [36], [41], [42]. HA serves to neutralise the acidic products of PLA hydrolysis, thereby reducing the degree of local acidification surrounding the scaffold and creating a more osteogenic environment [42], [43].

The effects of various fabrication procedures on the structure and properties of PLA/HA were investigated. The fabricated samples were prepared using three distinct fabrication procedures, namely, 3D printing, solution blow spinning and injection moulding. These fabrication procedures are conducted to tailor the structure of the PLA/HA composites, such as the porosity and fibre structure, to obtain a high porosity and uniform fibre diameter. In scaffold applications, high porosity and uniform fibre diameter are required for adequate nutrient diffusion and cell infiltration [43], [44]. Control of HA distribution and dispersion is crucial for obtaining consistent mechanical performance. Reliable composites were obtained at relatively low loading levels of HA (4–5 wt%) [38], [39].

The in vitro biocompatibility and cytotoxicity of the PLA/HA composites were examined by cell adhesion experiments and MTT tests, respectively. The results showed that the PLA/HA composites had good biocompatibility and were noncytotoxic [36], [43], [45]. These composites facilitate osteogenic differentiation of human mesenchymal stem cells in the absence of common osteogenic media, indicating an intrinsic osteoconductive property [40], [43]. HA was used as a bioactive molecule to stimulate the growth of cells and to enhance mineralisation and bone-like tissue formation.

Although great progress has been made in this area, the dispersion of HA in the polymer matrix, interfacial bonding, stability of the PLA/HA composites and related challenges still need to be solved. Therefore, surface modification of HA particles and optimisation of preparation conditions should be further studied to improve the application value of PLA/HA composites [41], [46]. More investigations are needed to determine the desired polymer properties and processing techniques for the application of polymer composites in the field of regenerative medicine. The materials should satisfy the mechanical, biophysical and bioresorption requirements needed for the body to treat various diseases. Compared with individual polymers, polymer blends, namely, PLA/HA composites, are the main biomaterials used in bone tissue engineering owing to their enhanced mechanical, biological and biophysical characteristics. Hence, materials and process developments can open up more applications in the field of regenerative medicine.

3.2. PLA blends with PCL

PLA is a biodegradable polymer widely studied in the literature. Its applications are vast, ranging from biodegradability, biocompatibility and compostability to mechanical properties similar to those of titanium. Although PLA has numerous advantages, it has several major drawbacks, such as brittleness and low thermal stability, along with slow crystallisation of the polymer. Hence, blending PLA with PCL, a flexible biodegradable polyester, helps overcome the disadvantages of PLA. Therefore, the biodegradability of the scaffold prepared from the blends of PLA/PCL is expected to be highly applicable for soft tissue engineering, as the blends increase the flexibility of PLA and accelerate the biodegradability of the polymer. Furthermore, scaffolds made of PCL are helpful for cartilage repair and vascular tissue engineering, where blends of PLA and PCL are generally immiscible. Various compatibilisation techniques can be adopted to increase the miscibility of the blends.

The structure and properties of PLA/PCL blends are closely related to the composition and processing conditions. The addition of PCL to PLA significantly changed the plastic behaviour and mechanical properties. For example, when the PCL content was only 10 wt%, the PCL particles were attributed to only particle debonding, and there was no obvious increase in the elongation at break.

Debonding and void growth were observed at 20 wt%, and the shear yield dominated and considerably increased in terms of elongation at break and energy absorption at 40 wt% [47]. Enhanced compatibility by the addition of compatibilisers or crosslinking agents such as benzoyl peroxide (BPO) improved the yield tensile strength, elongation at break, foamability and cell structure of the material. The immiscibility of the PLA and PCL phases is a significant challenge. Numerous strategies have been proposed to enhance compatibility.

1. Recently, the researchers of this study reported that reactive compatibilisation via the addition of chain extenders such as Joncryl decreased the sizes of PCL droplets and significantly improved the toughness of the nanocomposites but at the cost of the modulus [48].
2. The adhesion of foam to the substrates was greatly improved by in situ crosslinking because of the BPO-induced reactions in the PU system, whilst the mechanical properties and stability of the foam structure improved [49].
3. The compatibility and blending of the polyurethane-based compatibilisation of PCL diol with isocyanates in the presence of PLA led to the in situ formation of PLA-co-PCLU copolymers. The as-obtained PLA-co-PCLU copolymer showed significantly enhanced compatibility with PCL, leading to increased blend homogeneity and reduced spherulites [50].
4. Improvement in the mechanical and other properties of bioplastic polymers modified and filled with bioplastics, including biotougheners. The use of highly branched PCL-grafted cellulose considerably increased the tensile toughness of the bioplastics and, at the same time, markedly reduced their migration into foodstuff [51].

PCL has an important effect on the thermal stability of PLA/poly(3-hydroxybutyrate) (PHB)/PCL ternary blends and has good compatibility with PLA/PHB blends; the addition of PCL to PLA/PHB increased the onset temperature of degradation of the blends [52]. The effect of blending PCL with PLA has been investigated with particular reference to the structure and gas barrier properties of the blends. The blends showed increased crystallinity together with improved barrier properties. Compared with those of the neat amorphous polymer, the water vapor and oxygen permeability of the blends decreased [53]. Natural extracts, including green tea, increase antioxidant activity and barrier performance [53].

Biocompatible blends of PLA and PCL have been widely explored in the biomedical field, especially for tissue engineering and biomedical devices. This study explored the effect of PLA/PCL blends on the behaviour of 3D-printed structures that were used to develop biocompatible scaffolds for tissue engineering. Experimental analysis revealed that compared with the neat PLA scaffold, the 3D-printed scaffold fabricated from a blend of PLA/PCL with 20 wt% PCL showed enhanced mechanical and thermal properties [54]. This study presents a novel approach involving the use of antimicrobial nanoparticles in ternary blends that support high cell viability. These blends are thus suitable for the fabrication of different medical devices, such as ureteral stents. This study was published in the Journal of Biomedical Materials Research Part B (Applied Biomaterials). Superbug infections in ureteral stents occur frequently because of inadequate drainage, biofilm retention and antimicrobial resistance [52]. Biocompatible films of PLA/PCL blends with natural antioxidants were prepared, and their mechanical, barrier and biodegradation properties were evaluated as active food packaging materials. Compared with control films, films composed of PLA/PCL blends with natural antioxidants presented higher mechanical strength, barrier properties and biodegradation resistance [53]. This research addresses the preparation of a new material for biomedicine by mixing PLA and PCL with plant extracts or nanoparticles of antimicrobial agents to replace the use of bioactive polymers. The mixtures of the two biodegradable polymers blended with the extract of Cucurbita moschata (zevel) possess greater antibacterial activity and less cytotoxicity than the individual materials [55]. Blends containing metallic nanoparticles exhibit high cell viability and promote cell proliferation [55].

Biodegradability is considered one of the most important criteria in modern material design. Although PLA is amongst the most attractive biodegradable materials because of its attractive mechanical performance, eco-friendliness and high-value biodegradability, it still has several drawbacks, such as brittleness and a low melting temperature. A variety of biopolymers, such as other aliphatic polyesters, have been blended with PLA to overcome these disadvantages. The properties of the PLA/PCL blends were distinct and significantly dependent on the blend composition, the type of compatibilisation method adopted and the presence of reinforcements/fillers. In some cases, recent compatibilisation methods, namely, reactive blending and biotougheners, have yielded significantly improved mechanical, thermal and biological behaviour. These findings indicate that PLA/PCL blends could be utilised in biomedical, packaging and structural applications [47–51], [53], [54].

3.3. PLA resins biocompatible for bioprinting

PLA is the most widely used polymer in bioprinting because of its biocompatibility. Biocompatibility allows the material to be directly in contact with living cells and tissues. Therefore, the use of PLA bioinks enables the fabrication of 3D cellular scaffolds that can be used for the fabrication of engineered constructs that can potentially be used for the repair or replacement of damaged tissues and organs and, as such, to restore lost physiological functions. Moreover, the mixing of PLA with other biological components, such as collagen and gelatine, improved the adhesion and bioactivity of the final constructed bioengineered constructs. As a result, the overall bioactivity and cell growth of the bioink-printed structures are enhanced [56]. The 'Polymers' has published an article called 'Biocompatibility of Bio-Polylactic Acid for 3D Printing'. The authors reported that compared with other 3D-printed materials such as acrylate methacrylate resins, ABS and PC-Blend, PLA does not trigger the rapid production of intracellular reactive oxygen species in microalgae culture, which results in low cytotoxicity and high biocompatibility [57]. Previously, the laboratory of researchers in this study successfully grew cells on PLA scaffolds and confirmed that the cells could adhere, grow and differentiate. The purpose of this study was to explore the culture and osteogenic differentiation of human bone marrow-derived mesenchymal stromal cells on the surface of metal-PLA composite scaffolds. The experimental results proved that the cells cultured on the surface of the metal-PLA composite scaffolds exhibited a high degree of osteogenic differentiation [58]. Mouse embryonic fibroblasts grown on PLA-grafted polymers on glass substrates exhibited a cell viability of > 90%, confirming the cytocompatibility of the PLA material [59].

A variety of mechanical properties, ranging from very hard and brittle to very soft and flexible, can be achieved with PLA resins by adding fillers or additives or blending with other polymers. Optimising the formulation of acrylate PLA grafted with PVAc and reactive diluents allows materials with 3D-printed tailored tensile properties to be elongated and achieve a broad range of hard and elastomeric applications [59]. Mesoporous bioactive glass (MBG)-filled PLA composite scaffolds with improved compressive modulus and yield strength were prepared and validated to successfully mimic the hierarchical structure and mechanical properties of bone [60]. Metal-filled PLA composites, including steel-filled PLA, exhibit enhanced mechanical properties and porosity, thereby facilitating their application in load-bearing biomedical contexts [58].

PLA resins are compatible with multiple 3D bioprinting techniques, such as fused filament fabrication, digital light processing (DLP) and pneumatic-based extrusion. The adaptability of PLA to various printing platforms facilitates the development of intricate, high-resolution and biomimetic structures. The 3D MOSAIC platform employs PLA micromesh substrates to facilitate the bioprinting of hydrogels, allowing the creation of heterogeneous, multimaterial constructs with complex architectures [61]. PLA/MBG composite bioinks have been successfully used in pneumatic-based bioprinting to produce scaffolds with macroporous structures (500–700 μm) that help bone cells grow [60].

Recent progress has focused on developing highly applicable PLA resins by adding bioactive or stimuli-responsive parts. For volumetric bioprinting, hybrid materials are used to combine PLA with plasmonic nanoparticles or decellularised extracellular matrix. These materials promote dynamic, stimuli-responsive 3D in vitro models [61]. Hybrid systems improve the usefulness of PLA-based resins by improving scaffold simulation and altering the circumstances of real tissues.

Apatite-forming biocomposites composed of PLA have been investigated for application in bone tissue engineering in recent years, which can not only accelerate the mineralisation process of tissues but also shorten the time of apatite formation and promote the expression of relevant genes [58], [60]. PLA has been used in a wide array of applications, ranging from soft tissue engineering to soft robotics and biodegradable durable commodity plastics [59], [63]. Bioprinting has become a hotspot in the field of biomaterials research. Bioprinting based on biomaterials is expected to replace traditional surgical repair. Amongst them, PLA is a material with great development prospects for bioprinting because of its easy moulding, biodegradability, nontoxicity, good mechanical properties, strong polar forces and high crystal density.

One of the most commonly used polymers for bioprinting is PLA, which is biocompatible, has a wide range of mechanical properties and is easily printable. Researchers are working on developing additives and composites to improve and broaden the use of PLA to enhance its properties and expand its potential uses. One of the most promising new materials for biomedical applications is tissue engineering scaffolds.

4. Uses of PLA-Based 3D Printing in Medicine

4.1. Engineering of Tissues

Personalised medicine and the emergence of new drug delivery systems represent amongst the most exciting innovations in contemporary medicine, representing a new paradigm in which all medical procedures and decisions are tailored to the specific needs of each individual patient. One of the main challenges for personalised medicine is that current drug delivery systems are far from meeting the requirements for a truly individualised therapeutic approach and have a limited ability to personalise the design of drug delivery systems for the majority of therapeutic routes, from simple oral administration to more complex transdermal, site-specific or implantable administration routes. One strategy that is enabling a more rational design of new drug delivery systems is the use of polymers based on the PLA family obtained by AM, commonly known as 3D printing, which has evolved rapidly in recent years, allowing for the development of complex, efficient and customisable drug delivery systems for all therapeutic routes. Material and design innovations, in addition to advancements in 3D printing technologies, suggest a promising future for 3D printing-based drug delivery systems, which can contribute to the personalisation of medicines, turning the personalisation of drug delivery systems into a fundamental aspect of personalised medicine [62]. In situ 3D printing with PLA material can generate multiscale and biomimic tissues or organs that mimic the native anatomy, microstructure and physiological functions of the original living tissues. Bioprinting is a relatively new technology that is being rapidly developed in the field of healthcare and medicine to address the ever-increasing demand for tissue engineering and organ transplantation [65], [66].

Improving scaffolds requires PLAs to be mixed with other polymers and bioactive ingredients. Recent studies have investigated the development of composite scaffolds that include PLA and polyhydroxyalkanoate, PHB, HA, cellulose nanocrystals (CNCs) and MBG. Biocomposites containing bioactive glass particles were produced, and their mechanical properties were investigated. The results showed that compared with control samples, composites have better mechanical, bioactivity and biocompatibility properties. These properties are of particular interest for tissue engineering, where materials with the required properties for the growth of cells and the repair of damaged tissues are needed [60], [67–69]. The synthesised PLA/MBG (i.e. magnetron-sputtered bioactive glass) scaffolds can rapidly form apatite crystals, possess a higher compressive modulus and more closely resemble bone. These findings indicate that cells in the body can be encouraged to become bone cells [60]. Although both experimental groups exhibited improved wettability and physical properties (i.e. especially for samples produced from the second-generation PLA/CNC composite, which showed increased toughness) compared with their precursors, biocompatibility with bone cells significantly improved [69].

Using the FDM technique and photo-crosslinking, 3D-printed bioscaffolds can be tailored with a specific internal structure, which is highly desired. The experimental results show that scaffolds with the desired architecture, porosity and fibre thickness can be easily constructed. Using algorithm-aided design along with the unique 'oozing effect' phenomenon that is associated with the FDM process, highly porous structures constructed using PLA with numerous microfibers were achieved. The unique porous architecture of the scaffolds closely mimics the ECM and facilitates the adhesion and proliferation of osteoblasts, thereby enhancing the biocompatibility of the 3D-printed scaffolds [70].

Photo-crosslinking-based 3D printing methods such as DLP and SLA allow for a higher spatial resolution of the engineered structure and design at the microscale. This reaction results in the ability to modulate the physical characteristics of the scaffold to a greater degree and to a degree that more closely matches the requirements of tissue engineering [46].

3D-printed scaffolds have become a popular choice for tissue engineering involving the use of PLA as a biomaterial for the construction of various types of tissues, including bone, cartilage, neural, cardiac, vascular and skin. PLA composites were used for bone tissue engineering by incorporating bioactive materials such as HA, MBG and magnetic particles to improve the bioactivity of the scaffolds to promote mineralisation, cell attachment and proliferation. The incorporation of exosomes in these composites was also reported to promote osteogenic differentiation. This makes the bone regeneration process growth factor-free [60], [67], [71]. PLA has been extensively used in drug-eluting scaffolds for controlled drug release, medical devices, prosthetics, orthotics and even surgical instruments. This volume is a collection of recent advancements in the biomedical applications of PLA [66].

In vitro and in vivo studies have demonstrated that PLA-based scaffolds promote cell viability, proliferation and differentiation. The customised pore sizes and surface characteristics enhance tissue ingrowth and vascularisation [60], [65], [69]. Designing the structure and composition of the scaffold allows tissue engineering scaffolds to be fabricated with a desired property suitable for patient-specific implantation, facilitating optimal tissue growth. The exosome-loaded magnetic PLA constructs presented in this study represent a novel approach to improve in vivo biomaterial integration and modulate osteogenesis, and research in this field is progressing rapidly [71].

Despite the progress achieved, obstacles still need to be overcome to further improve the expected increase in degradation rates, mechanical properties and bioactivity for different tissue engineering applications. Future work will focus on improving the design of multifunctional composite materials, on the optimisation of 3D printing techniques to achieve high precision and scalability and on the transfer of bioabsorbable scaffolds developed in the laboratory to the clinical field [46], [65], [72]. Overcoming these challenges can ensure that PLA-based 3D printing remains a relevant technology for regenerative medicine and personalised healthcare.

3D printing with PLA has become widely used in tissue engineering to create smart, biocompatible scaffolds that can be tailored to specific clinical needs. The field of tissue engineering has benefited significantly from recent progress in materials science and 3D printing technology, and the use of PLA-based bioconstructs is expected to translate into better health care.

4.2. Systems for Delivering Drugs

PLA-based 3D-printed drug delivery devices allow one to control exactly when and where medicines are released. When materials breakdown, the devices also breakdown once they are used; ideally, materials should not be removed as often [17]. Pharmaceutical companies have recently come to realise the potential of 3D printing technology to develop tailored drug delivery systems using PLA using 3D printing technologies such as FDM and photopolymerisation, thereby achieving highly complex and more effective drug delivery systems. Bioabsorbable PLA polymers are widely recognised for being safe and highly biocompatible. Therefore, 3D printing using PLA can aid in the design of complex and innovative drug delivery systems that are highly individualised. These can be highly effective in terms of the desired therapeutic outcome [73–79].

This work investigates the applicability of 3D printing with a PLA bioplastic to produce implantable drug release devices that are capable of site-specific and controlled drug release. Using reservoir-type drug delivery systems produced from mixtures of PLA and PCL membranes, antibiotics were successfully released over a period of 25 days. The drug release profile was tailored by adjusting the membrane composition, film thickness and device dimensions. The bioactivity and biocompatibility of the devices were confirmed for up to 60 days in vivo [80]. Dolutegravir-infused PLA filaments have been printed in 3D into long-lasting implants for HIV treatment. These implants release the medicine for up to 47 days and are biocompatible with human cells [81].

PLA is widely used in the 3D printing of oral dosage forms, such as pills, polypills, caplets and orodispersible films. These systems can be altered so that drugs can be released in a controlled or targeted way. The thickness of the compartments and the interior structure are two design factors that determine how quickly drugs are released. PLA works well with other polymers, such as PVA and PCL, which makes it possible to produce multimaterial tablets with complicated release profiles. This approach is especially helpful for treating illnesses of the central nervous system (CNS), where obtaining the right dose is extremely important [73], [78], [82].

Microneedles manufactured from PLA using FDM are less intrusive at delivering drugs through the skin. Microneedles are biocompatible and biodegradable. Their shape and mechanical qualities can be improved using the appropriate 3D printing settings and postprocessing treatments. PLA/PCL blends are used to ensure that PLAs are less brittle and that MNs are appropriate for use in skin penetration [76], [78]. 3D printing can be used to prepare tablets of PLA and pH-responsive polymers such as Eudragit® FS100, which can be used to deliver drugs directly to the colon.

These systems incorporate drug-loaded hydrogels within PLA-based shells, facilitating targeted release in the colon and advancing personalised medicine via customisable dosages and drug combinations [81].

PLA-based 3D-printed systems facilitate precise control of drug release kinetics by manipulating design parameters, including membrane composition, implant size and compartmentalisation. Phase diagram modelling facilitates the rational design of PLA-based amorphous solid dispersions (ASDs) by predicting the stability and release behaviour of APIs within PLA matrices [74], [80–82]. Personalised medication devices can be 3D printed on demand for any required drug release profile, dosage or combination therapy. New software and 3D printing technologies enable the design and production of customised complex drug products, which can enhance patient adherence to their medication regimen and the overall therapeutic outcome [73], [77–79].

PLA can be blended with other thermoplastic polymers, such as PCL, PVA, ABS and HIPS, to enhance mechanical properties, 3D printing behaviour and drug release behaviour. In addition, adding plasticisers and using phase diagram modelling can help improve the stability of drugs in drug delivery systems prepared from PLA [73], [74], [76].

Despite the tremendous progress, scaling up the 3D printing process and ensuring the reproducibility and consistency of 3D-printed samples and other challenges need to be addressed in the future. Furthermore, the optimisation of the properties of 3D-printed materials, the widening of the scope of drugs that can be produced by 3D printing and the optimisation of drug release from 3D-printed drug delivery systems are needed. The future of 3D printing of drugs using PLA as a biopolymer could be related to personalised medicine, where drugs can be produced that improve drug efficacy and enhance drug compliance and patient therapy, which would greatly benefit public health [73], [74], [77–79].

3D printing using polymers from the PLA family has promoted the development of personalisable, complex and highly efficient drug delivery systems for the administration of drugs by different routes, such as oral, implantable, transdermal or site-specific routes. Future advancements in materials, designs and 3D printing technologies can ensure the long-term success of personalisable drug delivery systems in the context of personalised medicine.

4.3. Customised Implants and Prosthetics

Recently, a variety of 3D-printed drug release systems have been developed by researchers using a wide variety of polymers. The majority of these systems were prepared from biodegradable materials such as PLA [17]. A biodegradable drug release system decomposes and releases drugs at the desired time and location in the body, after which the drugs are degraded, thereby eliminating the need for surgical removal. Thus, the use of PLA-based drug release systems for revolutionising 3D-printed drug delivery systems is extremely important. These drug release systems can have complex geometries, and their customised designs have greatly enhanced the performance of drug delivery systems. Recently, PLA has attracted much interest in the biomedical engineering field. The reason is that PLA is bioresorbable, which means that it can easily decompose at body temperature. Because of this unique property, PLA is used in a variety of 3D printing technologies, including FDM and photopolymerisation [73–79].

The 3D-printed implantable drug delivery system using 3D-printed bioplastics in this study shows that 3D prints composed of a bioplastic material, such as PLA, can be used for designing and developing implantable drug delivery systems capable of releasing APIs for a long time. In this study, reservoir-type implants were 3D printed using biodegradable PLA as a solid core material and PCL membrane material. The release of drugs from the membrane part of the device was demonstrated, and the release profiles could be adjusted by changing the type, thickness and size of the membrane. Hence, implants with long-term antibacterial activity and good biocompatibility have been developed [80]. 3D-Printed Long-Acting HIV Therapy For the first time, researchers have used 3D printing to produce an innovative HIV long-acting therapy in the form of a polymer implant that releases a potent HIV-suppressing drug for up to 47 days. The new implant is biocompatible at the tissue level and can be administered as part of patient standard care. The drug (i.e. dolutegravir) is currently given orally twice a day. Researchers have 3D printed polymer scaffolds using PLA pellets. They loaded the scaffold with the drug in the form of a micropellet and demonstrated controlled drug release in a laboratory environment for up to 47 days [81].

PLA is a type of polymer that can be used for the 3D printing of oral solid dosage forms such as tablets, polypills, caplets and films (e.g. orodispersible films). They can be formulated for controlled release or targeted release. The thickness of the formulation and the internal structure may affect the release profile of the drug. The formulations can be formulated as multicomponent systems by blending PLA with other polymers, such as PVA and PCL. Multimaterial systems may be required to achieve complex release profiles, especially for CNS drugs where precise dosing is needed [73], [78], [82].

Microneedles developed from PLA using FDM are a way to deliver drugs via skin that is not highly invasive. Microneedles are safe for humans and animal species and breakdown naturally. Their shape and mechanical properties can be improved by using 3D printing settings and postprocessing treatments. PLA/PCL blends are used to ensure that the PLAs are less brittle and that the microneedles are suitable for skin penetration [76], [78]. 3D-printed direct-release tablets developed from mixtures of drugs in combination with polymers, such as PLA and pH-responsive polymers (i.e. Eudragit® FS100), for drug delivery to the colon are feasible materials.

The main purpose of this project is the development of a new drug delivery system composed of a drug-loaded hydrogel core surrounded by PLA shells, which releases the active component in the colon. The use of hydrogels in combination with 3D-printed polymer matrices (e.g. PLA) allows the realisation of a drug delivery system customised for specific applications through the achievement of versatile, adaptive and controlled release of the target drug [81].

PLA-based 3D-printed systems can release drugs in a tailored manner according to the required pharmacological profile by controlling the porosity and soluble polymer content during the extrusion and printing process. Membrane design parameters such as membrane chemistry, device dimensions and design configuration can be optimised for the intended therapeutic application. Phase diagram modelling can be used to predict the composition of ASDs on the basis of a PLA platform and thus impact API stability and drug release in PLA-based drug delivery systems [74], [80–82]. The on-demand production of customised drug delivery systems by applying 3D printing technology holds great promise for advancing patient care. Furthermore, by tailoring individual formulations for specific therapeutic needs, such as targeted drug release, exact required doses or combination therapies, customised drug delivery systems can improve the therapeutic effectiveness of drugs and enhance the patient experience. Advancements in software and 3D printing technology also provide the necessary tools to realise the full potential of complex customised drug delivery systems, thereby enhancing patient adherence to drug therapy [73], [77–79].

The material can be blended with other thermoplastic polymers, such as PCL, PVA, ABS and HIPS, to achieve the required mechanical properties, printing characteristics and drug release profiles. The inclusion of plasticisers and the utilisation of phase diagram modelling improve the stability and efficacy of PLA-based drug delivery systems [73], [74], [76].

Despite significant progress, challenges remain in enhancing production capacity, ensuring reproducibility and navigating regulatory processes. Current research aims to improve the characteristics of materials, add more printable drugs to the list and create new ways to release drugs. PLA-based 3D printing for medication delivery provides new possibilities for better personalisation, effectiveness and patient compliance in therapy [73], [74], [77–79].

PLA-based 3D printing has changed the way drugs are delivered by promoting customised and effective systems for oral, implantable, transdermal and targeted uses. Improvements in materials, design and printing technologies promote the use of these systems in personalised medicine.

4.4. Planning and Simulating Surgery

Surgeons use the PLA to construct models of the body that help them see and plan complicated surgeries. These models are especially useful for surgeries that require highly accurate bone regeneration and organ transplantation [83].

3D printing, especially when using PLA and its composites, has changed how surgeries are planned and simulated by rapidly building complex anatomical models that are unique to each patient. 3D printing a model of the patient's skull allows surgeons to gain a clear understanding of the malformation and to practice the surgery on the 3D-printed model, which gives them a higher level of accuracy and confidence during the actual surgery. 3D printing in surgery is now a common practice across a wide range of specialties, including oral and maxillofacial, orthopaedic, spinal, vascular and liver specialties; compared with the current standard of 2D imaging and traditional surgical planning, the advantages are more apparent for the 3D approach [84–91].

Title: Biodegradable polylactic acid and its composites Abstract PLA, as a biocompatible and biodegradable polymer material, has many characteristics, such as being easy to prepare or low cost. With the development of research in the biomedical field, many PLA composite materials have been prepared by adding various reinforced materials into the PLA matrix, and the filled materials, including zirconium oxide, have radiopacity and mechanical properties similar to those of human bone. This makes them useful for anthropomorphic simulators in medical and dentistry training [87]. Adding plasticisers and ceramic fillers to PLA makes it easier to print and enhances its physical qualities. This makes it easier to use in realistic surgical models [74], [87].

PLA-based 3D printing is widely used in oral and maxillofacial surgery to construct anatomical models, surgical guides and implants that fit perfectly.

These models enable accurate preoperative planning, enhance surgical outcomes and decrease operating duration. The incorporation of point-of-care 3D printing facilitates in-house manufacturing, promoting swift prototyping and direct engagement of surgeons in the design of devices [84], [86]. This technology facilitates trauma management, orthognathic surgery and joint replacement, with evidence demonstrating positive clinical outcomes and enhanced workflow efficiency [84], [86].

3D-printed PLA models are being utilised in orthopaedic trauma surgery for the planning of complex articular fracture repairs, the simulation of surgical approaches and the fabrication of patient-specific instruments. The models provide an exact representation of the bone structure; therefore, they are helpful in virtual and actual planning [91]. These materials act as good navigation tools in surgery [91]. PLA 3D-printed models helped in the better management of the disease; therefore, the surgery was more precise. In spinal surgery, 3D-printed spinal drill guides and anatomical models developed from PLA or other similar polymers are used to assist in accurate pedicle screw placement and to decrease surgical time. These models are extremely useful for the simulation of complex tasks, and surgeons use in-house 3D printing of the models to improve their workflow [93]. Simulation-based training and planning using 3D-printed PLA models is gradually becoming increasingly common in vascular and liver surgeries. The models derived from the 3D images of the patient's liver enable surgeons to obtain real-life surgical practice, thereby increasing the confidence of the surgeons and reducing the surgical time and the amount of contrast used [88], [90]. Patient-specific soft models in liver surgery provide accurate and cost-effective preoperative planning and realistic simulations [90].

3D-printed models developed from PLA possess many pedagogical values, including better tactile feelings and more accurate anatomical presentations than imaging or virtual reality. Furthermore, these models are useful for clinical practitioners to practice surgical skills on a safe model before a real operation and therefore enhance their operational skills [85], [89]. PLA-based composites that mimic the properties of tissue greatly enhance the realism and hence effectiveness of medical simulators [87], [90].

3D bioprinting of biomimetic soft tissue analogues is a highly relevant and rapidly evolving field with vast potential but is also encountering many hurdles, such as mimicking the elasticity and toughness of native tissue whilst simultaneously providing printable materials with appropriate mechanical properties to create complex structures that can accurately mimic the intricate features of native anatomy [85], [87]. Studies concerning costs are needed to clarify and prove the validity of the methodologies used [86], [88]. The researchers of this study are currently developing the next generation of PLA composite materials to enable real-time imaging and to explore opportunities in other surgical specialties [74], [85], [87].

The 3D printing of AM using PLA biomaterials is an increasingly relevant resource in surgical planning and preparation. Accurate, customised 3D models can be produced at a relatively low cost, enhancing preoperative planning and intraoperative precision and aiding in education. Further advancements in biomaterials and process improvements to AM are likely to facilitate greater adoption in surgical workflows.

5. Problems and Limitations

PLA is amongst the common 3D printing materials used in the biomedical field. Although it has been extensively studied, several drawbacks still exist. For example, PLA does not have enough mechanical strength for load-bearing implantable biomedical devices such as bone substitutes [93]. The degradation rate of PLA is unsuitable for some biological applications. Therefore, modified or composite materials are needed [1]. Regulatory issues with the approval of PLA-based medical devices are expected to persist and continue to be a significant issue for several years. This is due to strict safety and performance regulations in the medical industry [94].

Considerable knowledge is available on the use of PLA in 3D printing for biomedical applications. FDM, being a cost-effective method for rapid prototyping, is not ideal for the precision printing required for biomedical devices. This is generally less than the FDM 3D printing resolution for highly precise features that can be achieved with SLA and SLS 3D printing technologies. Refer to [10] and [18] for further information on the resolution and surface properties of 3D-printed devices, which is critical for medical-grade biomaterials used in dental and surgical applications. Furthermore, a significant amount of information is related to the mechanical limitations of neat PLA. According to a meta-analysis conducted in Refs. [1], [17] and [89], compared with the neat polymer itself, incorporating other materials with neat PLA improved the mechanical properties of the composites of PLA/HA and PLA/PCL. This is a trend note in the field of tissue engineering, where standalone biomaterials are being replaced with hybrid biomaterials that possess functionalities suited to the specific application needed.

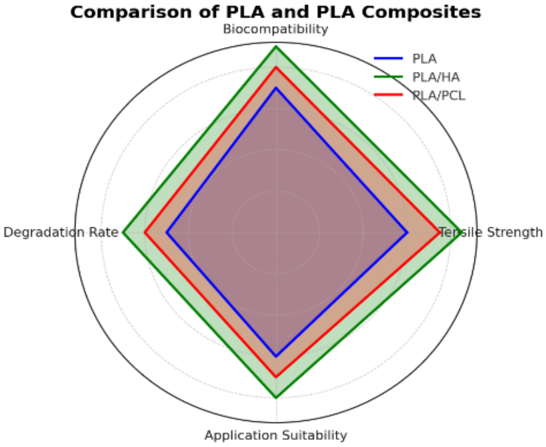

Fig. 1. Comparison of PLA and PLA composites using a radar chart

Materials regulation is a barrier to translation. Koch et al. (2022) reported that material with potential for use in bench and in vivo studies could not be approved as medical material because of a lack of long-term data and because of variability in composite formulation. Bioink standardisation is a common theme in bioprinting studies [95].

Research is essential to address issues related to performance, standards and long-term clinical trials for bioplastic materials. However, recent advancements still need further development, and the overall level of progress achieved in the bioplastic material industry is satisfactory. Although PLA is amongst the oldest bioplastic materials, it has often served as a reference material for many other materials and applications developed in recent years. Future biomedical applications of PLA and its derivatives are expected to involve blends and composites, and 3D printing might be required to achieve the necessary level of spatial resolution, mechanical performance and bioactivity.

In addition to the mechanical and regulatory concerns already mentioned, several emerging challenges could also impede the translation of PLA-based 3D printing in the biomedical field.

The use of 3D-printed PLA devices in clinics and hospitals is actually limited by a number of factors. Although the initial results obtained in preclinical studies look highly promising, the use of 3D-printed implantable devices in hospitals is actually blocked by a lack of standard clinical procedures and long-term clinical evidence. The work of the researchers of this study was published in the prestigious journal 'Advanced Healthcare Materials' by Martins et al.

The ethical and long-term safety of PLA biomaterials for medical applications is currently unknown. It is important to investigate the immune response of degradation products to biodegradable polymers, especially in long-term implantation, especially in human-sensitive groups. A recent in vivo study conducted was entitled 'Soft tissue reactions of different biodegradable polylactide implants,' [96].

Most studies using polymers, including PLA, are based on in vitro or short-term in vivo studies in animal models. Long-term multicentre clinical trials using PLA-based scaffolds in human patients are rare. This approach was also mentioned by Liu et al. in their article published in 'Materials Today, Bio' in 2025.

This review is novel in that it integrates advancements in material science, bioprinting technology and the associated translational challenges, which are not yet adequately covered in existing reviews, that focus mainly on laboratory-scale studies [46]. The practical challenges faced by hospitals and ethical issues are also addressed.

A notable research gap is as follows:

1. The standardisation of biocompatibility evaluation methods;
2. Systematic ethical assessments regarding the use of patient-derived materials in bioprinting;
3. Robust longitudinal studies are needed to validate safety and efficacy.

These are major challenges in the translation of PLA into a clinical commodity material for the safe, effective and ethically acceptable delivery of tissue-engineered products for personalised medicine.

6. Future Directions and Conclusions

This review focuses on PLA bioplastic material for 3D printing in the biomedical sector and refutes some of the existing limitations stated in the literature. It provides insight into the translation, ethics and research gaps in this area.

The use of 3D printing with PLA for biomedicine is interesting. Researchers are looking into using 3D-printed PLA for drug and antibiotic release directly to the site of the injury. This is achieved by encapsulating the medication in a lattice structure created from 3D-printed PLA. In this regard, this study reveals the effects of temperature on the structure and properties of 3D-printed PLA scaffolds.

advancing the mechanical properties of PLA by developing composites and enhancing its

Improving biocompatibility and developing new applications, particularly in the areas of tissue engineering and drug delivery, are important challenges for the future. In addition, new multimaterial and bioprinting technologies are expected to enable the production of future medical products that will be more sophisticated and tailored to the needs of the time and can be produced individually for each patient. A number of 3D printing technologies are suitable for biomedical applications of PLA. The choice of technology depends on the specific requirements of the particular medical application.

This project addresses the scientific questions concerning future research on PLA polymers by developing and performing standardised, long-term in vivo and clinical trials on PLA implants. The aims were as follows: define a uniform procedure for the use of 3D-printed medical products in hospitals, investigate the long-term biocompatibility and degradation of PLA materials in different patient groups, widen the bioethics agenda to include individualisation of bioprinted PLA products and combine material sciences expertise with medical and bioethics expertise.

Table 1,
Comparison of common 3D printing techniques for PLA-based biomedical applications

3D Printing Technique	Resolution	Cost	Application	Advantages	Disadvantages
Fused Deposition Modelling (FDM)	Medium	Low	Prosthetics, implants	Cost-effective, easy to use	Lower strength, limited precision
Stereolithography (SLA)	High	High	Dental implants, surgical guides	High precision, good surface quality	Expensive, limited material availability
Selective Laser Sintering (SLS)	Medium	High	Orthopaedic implants, bone scaffolds	High strength, complex geometries	Expensive, lower resolution

These are the major directions for the future development of PLA as a biocompatible material for translating laboratory discoveries into the clinic and suggesting a personal, ethically acceptable biomedical technology for modern healthcare.

One of the most popular bioplastics used in biomedical 3D printing is PLA. Owing to its economic advantages, mechanical properties and versatility, PLA has been widely applied in the medical field. As biomedical 3D printing technology is advancing, PLA 3D printing holds a significant place in the fields of personalised medicine, regenerative medicine and healthcare in the future.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgment

The authors gratefully acknowledge Universiti Teknikal Malaysia Melaka (UTeM), Malaysia, and Universitas Brawijaya, Indonesia, for their support and collaboration in this research.

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استعراض للاتجاهات الحالية والمواد والتحديات في مجال الطباعة ثلاثية الأبعاد للتطبيقات الطبية الحيوية باستخدام حمض البولي لاكتيك (PLA)

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المستخلص

يُعد حمض البولي لاكتيك (PLA) مادة شائعة الاستخدام في الطباعة ثلاثية الأبعاد. وقد عززت الطبيعة القابلة للتحلل الحيوي والمتوافقة حيوياً لـPLA ، إلى جانب ملاءمته للتصنيع الإضافي، من أهميته في القطاع الطبي الحيوي. يسلط هذا البحث الضوء على التطبيقات المتزايدة لـ PLA في الطب الشخصي وهندسة الأنسجة وتوصيل الأدوية والغرسات المخصصة. كما تناقش هذه الورقة البحثية تقنيات الطباعة ثلاثية الأبعاد المختلفة مثل النمذجة بالترسيب المنصهر (FDM)والطباعة المجسمة (SLA) والتلبيد الانتقائي بالليزر (SLS) وتوافقها مع PLA. كما تمت مناقشة خصائص المواد المركبة القائمة على PLA وإمكانياتها في تحسين الخصائص الميكانيكية والبيولوجية المطلوبة للتطبيقات الطبية الحيوية. بالإضافة إلى ذلك، تمت مناقشة خصائص المنتجات المطبوعة ثلاثية الأبعاد مثل خصائص المواد ودقة الطباعة والمتطلبات التنظيمية والأداء على المدى الطويل. وأخيرًا، تم توضيح النطاق المستقبلي لـ PLA في الطباعة ثلاثية الأبعاد من خلال تطبيقات الطباعة متعددة المواد والطباعة الحيوية.