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Performance comparison of PLA- and PLGA-coated porous bioceramic scaffolds: mechanical, biodegradability, bioactivity, delivery and biocompatibility assessments

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Abstract

Bioceramics, particularly calcium phosphates, bioactive glasses, and crystalline silicates, are a principal group of biomaterials employed for the regeneration of damaged tissues and therapeutic delivery. The development of ceramic tissue engineering scaffolds with an appropriate combination of mechanical and biological properties is still one of the key challenges in this field. In this regard, the deposition of polymeric coatings on the scaffolds is a simple and effective approach to reinforce their functions. Among different polymers, the influences of biodegradable aliphatic polyester coatings, especially polylactic acid (PLA) and poly(lactic-co-glycolic acid) (PLGA), over the performance of the scaffolds have been investigated in numerous research. This review paper provides a comprehensive comparison of PLA- and PLGA-coated bioceramic scaffolds which are mainly employed in bone tissue engineering. It is concluded that both the polymers enhance the mechanical behaviors of the scaffolds, but control their biodegradability, bioactivity, and delivery kinetics, where PLA acts almost more influentially than PLGA in comparison. However, the response of

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biocompatibility to this surface treatment is condition-dependent and requires case-by-case experiments to be determined accurately.

Keywords: Hard tissue engineering; Osteogenesis; Angiogenesis; Drug Delivery

Table of Content

1. Introduction

Aliphatic polyesters are considered as prominent representatives of synthetic biodegradable polymers which are broadly utilized in medical purposes, especially in delivery and tissue regeneration, mostly owing to their biodegradable and biocompatible nature [1, 2]. Among them, polylactic acid (PLA) and poly(lactic-co-glycolic acid) (PLGA), derived from natural monomers of lactide and glycolide, have attracted much attention from both scientific and technological viewpoints. Table 1 briefly compares the synthesis methods, structure, properties, and prevalent biomedical applications of these polymers.

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Table 1. Overview of PLA and PLGA characteristics

Polymer	Synthesis method	Structure	Properties	Applications
PLA	1. Ring-opening polymerization 2. Condensation polymerization	Linear (Amorphous, semi-crystalline, and crystalline)	Hydrophobic, biocompatible, adjustable biodegradability	Anchors, screws, plates, pins, rods, mesh, drug carriers, and coating on scaffolds
PLGA	Ring-opening copolymerization	Linear (Amorphous, semi-crystalline, and crystalline)	Hydrophobic and hydrophilic (depending on the ratio of monomers), biocompatible, adjustable biodegradability	Grafts, implants, sealant films, pins, sutures, drug carriers, and coating on scaffolds

PLA is a hydrophobic and biodegradable aliphatic polyester with a linear structure produced via either ring-opening or condensation polymerization of lactic acid (LA) (Figure 1a). It can be manufactured in a widespread range of structures and thereby properties, due to the chiral nature of LA with two asymmetric centers, forming three different conformations of D, L , and D,L isomers. High L-level monomers can be employed to fabricate crystalline PLA, although higher D-type monomers (>15%) give rise to amorphous polymers. Highly-pure L- and D-lactides make semi-crystalline polymers, including poly(L-lactide) (PLLA) and poly(D-lactide) (PDLA), respectively, whereas D,L-lactide forms the amorphous structure called poly (D,L-lactide) (PDLLA). Depending on the distribution of the aforementioned isomers within the structure, PLA can be synthesized in different molecular weights varying from a few

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thousands to several millions, thermal, mechanical, and biological characteristics. This polymer is degraded in the physiological environment due to the hydrolysis of the ester-bond backbone, leading to the formation of non-toxic compounds (LA, CO_2, and water) which are easily excreted or metabolized [3, 4]. Its biodegradation takes place both on the surface and bulk of the structure via water diffusion into the polymer structure. It is worth mentioning that the polymer absorption rate can be adjusted via changing its molecular weight, morphology, and enantiomeric purity. In particular, PLLA is mostly preferable when improved mechanical properties and a low degradation rate are needed [5, 6]. Due to desirable biocompatibility and mechanical behaviors, PLA and its isomers have attracted significant attention to produce medical implants like anchors, rods, plates, screws, pins, mesh, and drug delivery systems [4]. The gradual degradation and high strength make them suitable for supportive structures and load-bearing constructs since they gradually transfer the load to the adjacent tissue while the damaged part is healing.

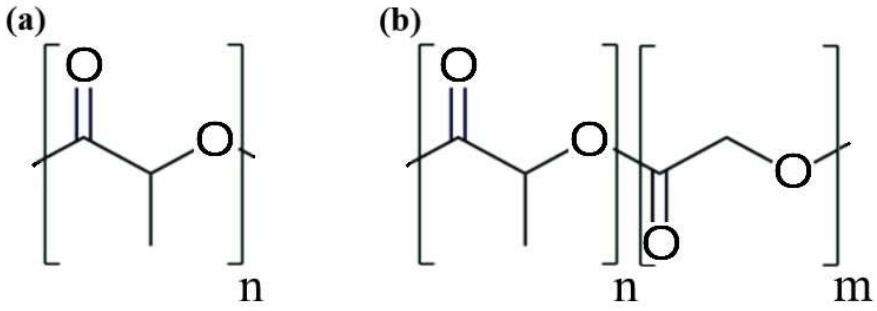

Figure 1. The structure of (a) PLA and (b) PLGA.

PLGA is another attractive aliphatic polyester produced through the polymerization of its monomers, i.e. lactic and glycolic acids, with a linear structure (Figure 1b). Depending on the ratio of the constituent monomers, different forms of PLGA with amorphous, semi-

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crystalline, and crystalline structures can be produced. The degradation of PLGA takes place via the hydrolysis of ester bonds into nontoxic products [7]. By changing the ratio of the two co-monomers, this polymer can show an extensive range of degradability; the more glycolic acid exists in the copolymer, the more hydrophilicity and degradability are obtained. This tunable degradation behavior aligning with excellent biocompatibility introduces PLGA as a promising candidate in biomedical applications like implants, sutures, grafts, sealant films, pins, and micro and nano drug carriers [8, 9].

In spite of all the remarkable above-mentioned characteristics, there are drawbacks in regard to using pure PLA and PLGA scaffolds in tissue engineering and drug delivery. On the one hand, owing to their hydrophobicity leading to a slow bioresorption, these polymers are not preferable for short-term applications. On the other hand, utilizing them for tissue regeneration applications is hindered by their low osteoconductivity and inadequate mechanical behaviors as load-bearing scaffolds [6, 10]. Therefore, PLA and PLGA are often used along with other materials, especially ceramics, as coating layers because of the appropriate complementary characteristics they show with ceramic substances. In this regard, the dip-coating technique in which the substrate is soaked into a solution of the polymer has been given much notice as the most common encapsulation method. In order to alter the quality of encapsulation, vacuum and/or centrifuging should be exerted after immersion [11, 12]. Various coatings have been focused on as a modification method to alter the properties of scaffolds in a good number of reviews. For instance, Philippart et al. [13] reviewed the impact of various polymer coatings on the mechanical behavior of bioactive inorganic scaffolds. Furthermore, Yunos et al. [14] looked over the microstructure and biofunction of bioceramic scaffolds coated with different polymers. However, to our knowledge, no dedicated review

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papers have been to date published on the impact difference of PLA and PLGA coatings on the performance of bioceramic tissue engineering scaffolds. Accordingly, the main emphasis of the current review paper is this comparison in terms of biodegradability, bioactivity, delivery, biocompatibility, and mechanical behaviors.

2. PLA and PLGA coatings on bioceramic scaffolds

Tissue engineering scaffolds have been extensively researched with the aim of developing platforms that offer the most suitable outcome in damaged tissue regeneration. Several criteria independent of the type of tissue should be considered in characterizing an ideal scaffold, such as mechanical competence, biodegradability, bioactivity, the ability to deliver therapeutic loads, and biocompatibility [15-18]. The mechanical performance of scaffolds has to match that of the targeted tissue and be sufficient to support loads that the new tissue will finally bear. A crucial factor in temporary scaffolds is that they should be degraded slowly over a duration, making spaces for new growing tissues and avoiding the necessity of a second surgery to remove the scaffold. Regarding their biodegradability, the degradation rate should be close to the tissue growth rate and the released products should be nontoxic. Also, when scaffolds come to make a stable long-term bonding to the living tissue, bioactivity should be also taken notice of. For scaffolds employed as the carrier of therapeutic agents, the capability for the controlled delivery of growth factors, drugs, and genes to the targeted site is also critical. Biocompatibility is the most fundamental property meaning that scaffolds should provide cells with a suitable environment to adhere, migrate, differentiate, and proliferate without inducing long-term inflammatory reactions.

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Among different materials that have been researched to construct tissue engineering scaffolds, bioceramics have been highly regarded because they generally exhibit better tissue responses and generate no foreign body reactions compared with metals and polymers. Moreover, ceramics are mostly bioresorbable, and their ionic dissolution products can be processed through body metabolisms or even exploited to promote the physiological behavior of cells and serve a desired therapeutic effect [19, 20]. By virtue of outstanding biocompatibility, biodegradability, osteoconductivity, and osteoinductivity, bioceramics and specifically calcium phosphates, silicates, and bioactive glasses have been abundantly applied in clinical applications. An overview of common bioceramic scaffolds in the literature and their requirements are shown in Figure 2.

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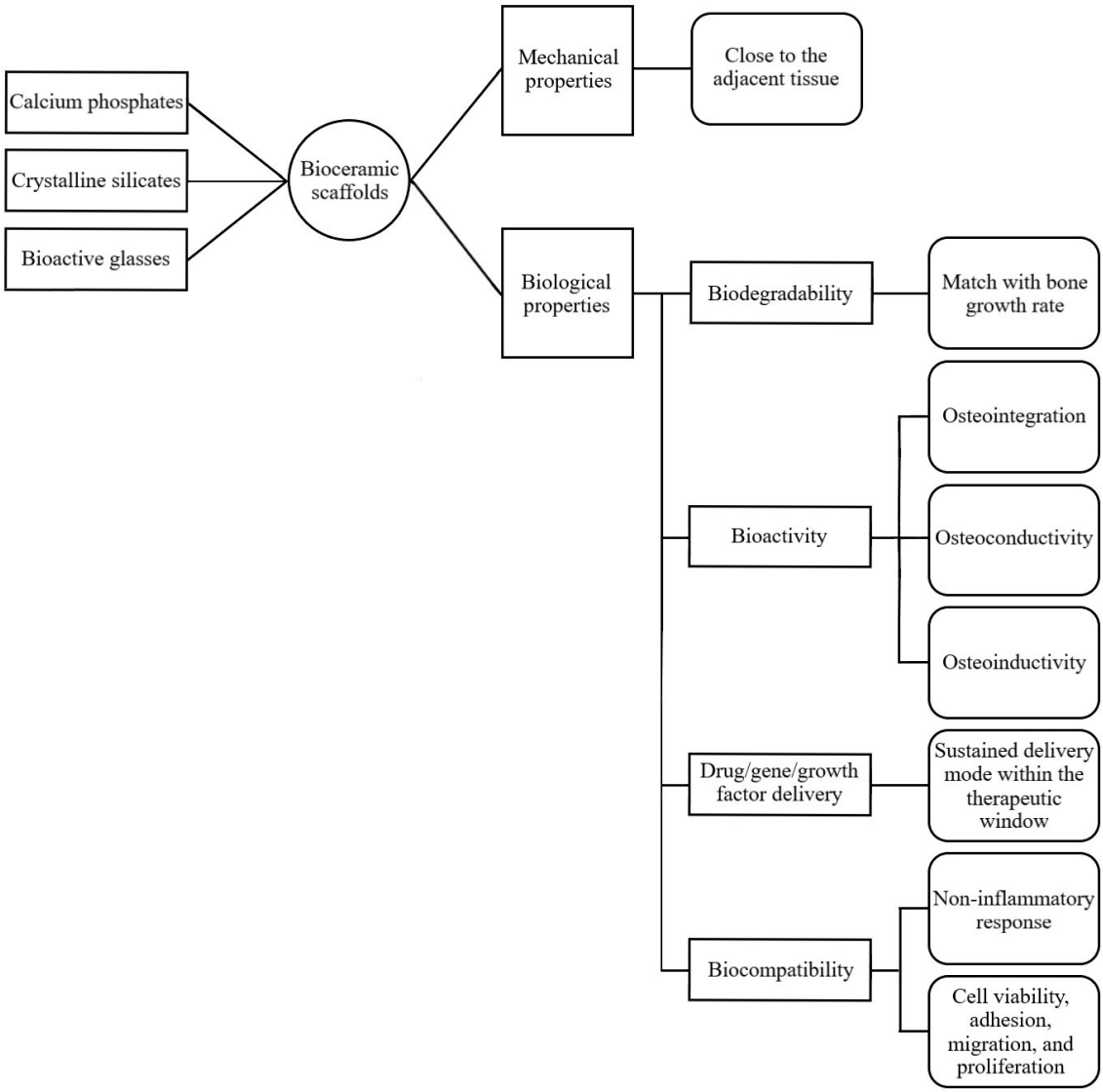

Figure 2. Most investigated bioceramic scaffolds and their requirements for tissue reconstruction.

2.1. Calcium phosphate scaffolds

Calcium phosphates (apatites), including tricalcium phosphate (TCP) and hydroxyapatite (HA), have a key contribution to the progress of scaffolds for hard tissue reconstruction. But their weaknesses, such as low strength, have prompted many studies to reinforce their

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biofunctionality. In this regard, the impact of PLA and PLGA coatings on calcium phosphate scaffolds has been investigated extensively, as summarized in Table 2.

Table 2. Overview of studies conducted on the effect of PLA and PLGA coatings on the biofunctionality of apatite scaffolds

Coating polymer	Bioceramic	Effect of coating on properties	Reference
PLA	HA	Fortifying mechanical performance, limiting degradation, hindering biomineralization, no harmful effect on biocompatibility	[21]
	HA	Improving compressive strength and Young's modulus	[22]
	HA	Preventing burst drug release	[23]
	β-TCP	Remarkable enhancement in compressive strength, affecting cell adhesion and migration adversely	[24]
PLGA	HA	Making scaffolds tougher and stronger, retarding the fast biosorption, no notable change in biocompatibility	[21]
	HA/TCP	Reinforcing compressive strength and toughness, adequate cell viability	[25]
	β-TCP	Positive impact on compressive strength, bending strength, and toughness, desirable cells attachment and spreading	[11]
	β-TCP	Ameliorating compressive strength and toughness, reaching a sustained delivery mode, minor influence on biocompatibility	[26]
	HA/TCP/ZrO_2	Achieving stable mechanical behaviors, impeding the significant weight loss of scaffolds, controlling initial burst drug release, providing a suitable substrate for cells proliferation and growth	[27]

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HA-PLA pairs: PLA-coated HA scaffolds have been evaluated mainly from mechanical viewpoints. With this in mind, it has been shown that PLA-coated samples enjoy much more compressive strength, Young's modulus, and bending strength in comparison to those bare. This is assigned to the diffusion of the polymer solution into interior parts, filling micro-defects, and thickening struts. Besides, with the increase in the PLA amount, mechanical characteristics go up further as the coating layer gets thicker [21, 22]. Regarding the degradation behavior, owing to the hydrophobicity of the polymer, the coated HA is degraded slowly, which limits the mineral deposition adversely [21]. From the delivery perspective, PLA-coated doxorubicin-loaded HA scaffolds have been assessed, demonstrating that the coating controls the drug elution notably with an effective and sustained release profile. The increase in the polymer concentration causes more suppression in the initial burst release [23]. In addition, based on observations, the PLA coating itself shows no deterioration effect on the cellular activities of HA scaffolds [21].

HA-PLGA pairs: Concerning the properties of PLGA-coated HA scaffolds, it has been found that the polymer coating makes struts tougher and stronger, displaying a positive impact on maintaining mechanical stability. Furthermore, the coating retards the fast degradation of HA samples to a great extent. It should also be noted that PLGA and HA have adequate biocompatibility when they come in contact with living cells [21, 25].

TCP-PLA pairs: The influence of PLA infiltration on TCP scaffolds has been looked over as well. It has been confirmed that the coating forms a thin cover on the internal surface of the samples without blocking macropores, inducing a conspicuous improvement in compressive strength. Despite the mechanical advancement, PLA is a hydrophobic polymer hampering the cell adhesion and migration through the whole coated construct [24].

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TCP-PLGA pairs: PLGA coatings have been also applied on TCP scaffolds. This polymer penetrates into crack-like defects and reduces the pore sizes, which promotes the compressive strength, toughness, and of bending strength the samples. Moreover, by enhancing the PLGA level, more parts of the scaffolds are covered and struts are thicker, further ameliorating the mechanical characteristics. Additionally, the coating layer lowers exposure to the physiological medium and consequently hinders the significant weight loss of the scaffolds [11, 26, 27]. In PLGA-coated TCP delivery systems, a stable delivery is achieved as the polymer acts as a barrier against burst elution. The release rate depends on the PLGA concentration in the coating, where the lower PLGA content produces a higher delivery rate [26, 27]. Results reveal that cells are able to attach firmly and spread over the coated samples with no abnormality [11, 26, 27].

Concluding remarks: PLA and the PLGA coatings can make notable enhancements in the mechanical performance of calcium phosphate-based scaffolds, ascribed to the decrease of defects, the reinforcement of struts after infiltration, and the ductile characteristics of the polymer coatings. Based on the results, it can be asserted that PLA is more influential in fortifying the calcium phosphate scaffolds mechanically. Furthermore, acting as a physical barrier against the ceramic degradation and the penetration of the medium inside the scaffolds, these polymers impede the fast bioresorption of calcium phosphates. However, given the amorphous structure of PLGA, water molecules can diffuse easily into the construct, indicating that the degradability of PLGA-coated scaffolds is rather more than that of those coated with PLA. Therefore, PLA is a preferable candidate for upholding mechanical stability alongside degradation for a longer time. Accordingly, the slow degradation of PLA gives rise to more control on the release rate of pharmaceutical compounds from the carriers compared to PLGA.

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The bioactivity of the scaffolds coated with PLA and/or PLGA has not been evaluated. But it is expected that both polymers, given their hydrophobic nature, restrict the ceramic dissolution and the deposition of essential ions required for apatite formation in the first step of bioactivity. Similarly, with respect to biocompatibility, it can be stated that although the polymers are biocompatible, they do not promote surface properties essential for cell interactions. Based on the literature, no clear comparison is possible to be made between the biocompatibility of PLA- and PLGA-coated scaffolds as estimating this property is very dependent on the utilization conditions of the scaffolds.

2.2. Crystalline silicate scaffolds

Silicates have been proved to instigate vascularization and osteogenic differentiation thanks to beneficial ions (i.e., Si, Ca, and Mg) released during degradation, making them hopeful biomaterials in bone regeneration scaffolds. Nevertheless, their inferior mechanical properties restrict their clinical applications. In this regard, silicate-based scaffolds coated with PLA or PLGA have been given attention (Table 3). It is noticeable that the biodegradation of silicates inspiring the alkalosis effect buffers the acidic degradation of the polyesters and as a consequence prevents the creation of a harmful environment for cells [28].

Table 3. Overview of studies conducted on the effect of PLA and PLGA coatings on the biofunctionality of crystalline silicate scaffolds

Coating polymer	Bioceramic	Effect of coating on properties	Reference
PLA	$CaSiO_3$	Effective improvements in mechanical characteristics, no positive influence on biocompatibility	[29]

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PLGA	$CaSiO_3$	Reaching better mechanical behaviors, preventing fast degradation, not hampering bioactivity but lessening its kinetics, desirable delivery behavior, maintaining adequate biocompatibility	[30]
	$CaSiO_3$	Suppressing rapid bioresorption, not debilitating bioactivity but decreasing its kinetics, supporting cellular activities	[31]
	Bredigite ($MgCa_7Si_4O_{16}$)	Enhancing mechanical performance, hindering fast degradation, sufficient biocompatibility	[32]
	Bredigite	Inhibiting fast biosorption, altering drug delivery behavior, creating appropriate surfaces for living cells	[12]
	Bredigite	Giving required strength, restricting the degradation rate, disabling apatite precipitation, no harmful effect on biocompatibility	[33]
	Bredigite	Causing sustained and prolonged drug delivery	[32]
	Bredigite, diopside ($MgCaSi_2O_6$), and akermanite ($MgCa_2Si_2O_7$)	Controlling degradation, reducing initial burst drug release, promoting cells viability and biocompatibility	[28]

Silicate-PLA pairs: The biological and biomechanical performance of PLA-coated silicate scaffolds have been investigated. It has been deduced that the polymer fills micropores and seals defects, enhancing the compressive strength effectively. Moreover, the ductile characteristic of the polymer is deniable in toughening the construct. Regarding the biocompatibility of the scaffolds, it has been found that seeded cells are not well-attached to the coating layer and do not spread desirably as a result of the hydrophobic nature of PLA [29].

Silicate-PLGA pairs: Many experiments have been conducted to determine the impact of PLGA coatings on the function of silicates. As turned out, the encapsulated samples enjoy better mechanical properties than uncoated ones due to the blockage of pre-existing pores,

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which are also enhanced further as the concentration of the polymer goes up [30, 32, 33]. Moreover, the coating layer acts as a physical barrier and controls the rate of silicate bioresorption [12, 28, 30-33]. Along with the degradation of the polymer, some parts of the underneath substrate come in contact with the physiological medium, providing nucleation sites for apatite deposition. It is also noticed that bioactivity is not suppressed considerably due to the reduction of pH upon the polymer degradation. But the bioactivity kinetics is influenced adversely since the coating limits the dissolution and deposition of essential ions crucial for apatite precipitation [30, 31, 33]. In silicates loaded with pharmaceutical agents, PLGA-capsulated carriers offer a stable delivery mode for a long time since the coating inhibits the rapid drug elution [12, 28, 30, 32]. Concerning the biocompatibility of the coated silicate scaffolds, it has been figured out that PLGA creates a suitable surface for cell adhesion and proliferation. By increasing the thickness of the coating, biocompatibility is also reinforced [12, 28, 30-33].

Concluding remarks: PLA and PLGA coatings make substantial improvements in the mechanical integrity of scaffolds by penetrating into small defects and preventing the propagation of cracks from such flaws. As only one research has analyzed PLA-coated scaffolds, distinguishing the preferable polymer mechanically is not precise. With regard to biodegradation, bioactivity, and the ability for targeted delivery, scaffolds coated with PLGA have been well studied. Accordingly, it has been approved that PLGA tunes biodegradation and buffers the local physiological environment alkalized due to the silicate decomposition. Although the construct dissolution rate is declined because of the applied PLGA coatings, it does not change the whole bioactivity inauspiciously. This polymer layer also provides a stable and prolonged drug release within the therapeutic window. On top of that, PLGA maintains the

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adequate interconnectivity of pores within the construct and provides beneficial surface features required for, first, proper cellular activities and second, sufficient supply and exchange of nutrients and gases to cells and metabolic waste products out of the scaffolds. The same biodegradation and bioactivity behaviors are expectable for PLA-coated scaffolds. However, PLA is more resistant to water than PLGA; hence, it causes more reduction in the degradation rate and bioactivity kinetics of scaffolds. Besides, PLA coatings can show a high potential in controlling and restricting drug release from silicate carriers, leading to a sustained delivery, even more than PLGA coatings due to slower degradation. In addition, no article has claimed that PLA coatings affect the biocompatibility of the scaffolds advantageously. But it is acceptable that the polymer does not promote any foreign body responses owing to its biocompatible nature. Therefore, comparing PLA- and PLGA-coated scaffolds in term of biocompatibility is not practical.

2.3. Bioactive glass scaffolds

Bioactive glasses have been commonly utilized as scaffolding biomaterials for hard tissue repair and regeneration. They are characterized by their ability to foster cell growth and bond to hard and soft tissues. Degradation products of bioactive glasses can activate osteogenic genes and stimulate angiogenesis. Their bonding capability with surrounding tissues is attributed to the development of hydroxyapatite or amorphous apatite on their surface when they undergo degradation in the physiological environment. In addition, their degradation rate is tunable by changing their chemical composition. A restrictive factor in the utilization of glass scaffolds is their deficient strength in load-bearing applications [13]. With the main aim of

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improving bioactive glass scaffolds biologically and biomechanically, PLA and PLGA coatings have been frequently applied on them (Table 4).

Table 4. Overview of studies conducted on the effect of PLA and PLGA coatings on the biofunctionality of bioactive glass scaffolds

Coating polymer	Bioceramic	Effect of coating on properties	Reference
PLA	Bioactive glass (0106)	Reinforcing mechanical stability, not weakening bioactivity but delaying its transformation	[34]
	Bioactive glass (45S5)	Conspicuous advances in mechanical characteristics	[35]
	Bioactive glass (45S5)	Maintaining mechanical performance even after immersion in SBF, decreasing bioactivity kinetics without any deterioration effect on bioactivity	[36]
PLGA	Bioactive glass (58S)	Stable mechanical behaviors, supporting cell migration, attachment, and proliferation	[37]

Glass-PLA pairs: PLA coatings on bioactive glass scaffolds have been often assessed from mechanical and bioactivity viewpoints. It has been confirmed that the coating fills microcracks and micropores of struts and lessens the pore size, triggering outstanding advances in the bending and compressive strengths. The polymer fibrils causing crack bridging are also the main factor in toughening the structure [34-36]. Moreover, it has been found that this polymer can maintain the mechanical stability of Bioglass 45S5 during soaking in the simulated body fluid (SBF). This results from two contributing factors; first, the deteriorating transition of $Na_2Ca_2Si_3O_9$ to amorphous apatite and second, the constructive development of a

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nanocomposite PLA and hydroxyapatite film on the struts during degradation [36]. It is well-stablished that the coating delays the transformation kinetics of the struts to amorphous apatite during soaking in the medium. By soaking the coated specimens in SBF, the degradation of the polymer occurs, which dictates that the bioactive materials beneath the coating layer become exposed to the biological medium over time, forming a carbonate hydroxyapatite (HCAp) layer on the substrate [34, 36].

Glass-PLGA pairs: Researches conducted on PLGA-coated bioactive glass scaffolds have focused on biocompatibility and mechanical aspects. The applied coating increases the struts thickness, improving the compressive strength conspicuously. Additionally, the encapsulated samples still have macropores across which cells migrate accompanied by covering cracks and defects in interior regions, prompting the overall mechanical performance. This also conveys that the coated scaffolds preserve cell migration, attachment, and proliferation [37].

Concluding remarks: PLA and PLGA coatings provoke valuable impacts on the mechanical characteristics of bioactive glasses via minimizing structural defects and thickening the struts. The crack bridging effect of the polymer fibrils also has a consequential role in modifying the construct ductility. Published researches have only explored the bioactivity of the scaffolds coated with PLA, declaring that the polymer slows down the rate of the apatite formation without any inhibiting influence on the whole bioactivity. Since PLGA is not as strong as PLA in hydrophobicity, the bioactivity kinetics in scaffolds coated with PLGA would be supposedly more than those coated with PLA. More importantly, no destructive induction by means of both polymers on biocompatibility is anticipated. Having said that, because of the

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limited data on PLGA-coated bioactive glass scaffolds, comparing the exact effects of PLA and PLGA coatings is not really doable.

3. Conclusions and future research directions

PLA and PLGA coatings have the potential to yield diverse functional properties to ceramic scaffolds feasibly, in particular mechanical behaviors. Both polymers are influential not only in ameliorating mechanical characteristics but also in adjusting the scaffolds biodegradation kinetics. Additionally, introducing these coatings on carriers loaded with therapeutic agents is helpful in reaching a sustained delivery mode. In spite of these favorable outcomes, due to the hydrophobicity of both the polymers, they generally hamper the apatite formation and whole bioactivity kinetics. Although both the polymers do not encourage cell attachment remarkably, they do not lead to the inflammatory body response thanks to their biocompatible nature. But evaluating the effects of PLA and PLGA coatings on biocompatibility is tightly dependent on various parameters, such as the intrinsic biodegradability and possible therapeutic impregnation of the scaffold.

Comparatively, the polymers confer varied improvements owing to their different characteristics. The current review has comprehensively differentiated PLA and PLGA coatings deposited on bioceramic tissue engineering scaffolds, separated from other affecting factors like the scaffold manufacturing process. It should be albeit mentioned that differences among ceramic-polymer pairs studied in the previous sections would not be completely detectable due to the inhomogeneity in the number of research conducted on each pair. However, regardless of the type of the ceramic substrate, the foremost comparison in the properties of scaffolds coated with PLA and PLGA is presented as follows:

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(a) PLA-coated scaffolds generally offer a higher mechanical performance, even during degradation.

(b) PLA certainly is a superior candidate in retarding the rapid bioresorption of bioceramics.

(c) PLA is more successful in restricting the initial burst release of therapeutic compounds, adjusting the carrier release kinetics, and reaching prolonged delivery.

(d) Although both the polymers have undesirable effects on the bioactivity kinetics, it is supposed that PLGA-coated scaffolds enjoy better bioactivity overall.

(e) Both the coatings do not encourage biocompatibility significantly; nevertheless, the preferred polymer is deeply contingent on other crucial factors, for example whether the scaffold is loaded with any therapeutic agents or not.

Despite a great number of researches conducted on PLA- and PLGA-coated bioceramic scaffolds, several challenges still remain to be straightened out, consisting of realizing long-term degradation processes of scaffolds in detail to figure out the exact effects of different dissolution products and their release kinetics on the cell response, especially *in vivo*. Furthermore, as reviewed in this paper, both the polymers do not promote the biocompatibility of scaffolds prominently, which necessitates further studies on modification approaches on polymer coatings to induce positive surface features that enhance cell attachment and following cellular behaviors exposed to the scaffolds.

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