Review Article

Current Uses of Poly(lactic-co-glycolic acid) in the Dental Field: A Comprehensive Review

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Poly(lactic-co-glycolic acid) or PLGA is a biodegradable polymer used in a wide range of medical applications. Specifically PLGA materials are also developed for the dental field in the form of scaffolds, films, membranes, microparticles, or nanoparticles. PLGA membranes have been studied with promising results, either alone or combined with other materials in bone healing procedures. PLGA scaffolds have been used to regenerate damaged tissues together with stem cell-based therapy. There is solid evidence that the development of PLGA microparticles and nanoparticles may be beneficial to a wide range of dental fields such as endodontic therapy, dental caries, dental surgery, dental implants, or periodontology. The aim of the current paper was to review the recent advances in PLGA materials and their potential uses in the dental field.

1. Introduction

Poly(lactic-co-glycolic acid) or PLGA is one of the most successfully used synthetic biodegradable polymers in the medical field being approved by the US Food and Drugs Administration and European Medicine Agency [1]. Biocompatibility, biodegradability, flexibility, and minimal side effects are the main advantages when using this polymer for biomedical applications. Main synthesis [2] and degradation mechanisms are described in Figure 1. The present work describes in detail current PLGA uses in the dental field and the relation between different dental fields such as endodontics, periodontology, dental caries, dental surgery, or dental implants and various PLGA materials: membranes, scaffolds, films, and nano- or microparticles.

2. PLGA in Dentistry

PLGA materials prove to be effective in a wide variety of dental applications, as it is shown in Figure 2. They are used in a multitude of ways, from developing screws for bone fixation [3–5], treating periodontal pathogens [6], and producing buccal mucosa [7] or in direct pulp-capping procedures [8, 9]. PLGA can be used in periodontal treatment, for better local administration of antibiotics and to decrease the systemic side effects of general antibiotic delivery [10], in the form of PLGA implants [6], disks [10], and dental films [11]. Also, gel composite fabrics of PLGA can be used in bone regeneration [12], as high degradable PLGA and SiO(2)-CaO gel nonwoven fabrics that were exposed to simulated body fluid for 1 week led to a deposition of a layer of apatite crystals on

FIGURE 1: PLGA, poly(lactic-co-glycolic acid), synthesis and degradation. The main reaction used to obtain PLGA is ring opening polymerization and polycondensation of lactic and glycolic acids. Most important mechanisms of PLGA degradation involve hydrolysis, oxidation, and enzymatic degradation.

FIGURE 2: Most common PLGA materials and their applications in the dental field.

their surface [12]. Granular composite of gatifloxacin-loaded PLGA and b-tricalcium phosphate is local delivery means in the treatment of osteomyelitis, as the composite managed to slowly deliver gatifloxacin and showed sufficient bacterial activity in vitro against *Streptococcus milleri* and *Bacteroides fragilis*, microorganisms responsible for osteomyelitis. Also, after only 4-week implantation GFLX-loaded PLGA and β TCP managed to significantly reduce the inflammation and support the osteoconduction and vascularization of the treated sites in rabbit mandible [13]. Moreover, sterilized

PLGA scaffold is a promising material for producing tissue-engineered buccal mucosa [7]. Additionally, PLGA composites with bioceramics can be used in direct pulp capping [9, 14] either by incorporating growth factors into PLGA microparticles [14] or by direct pulp capping with PLGA composites of mechanically exposed teeth [9]. However no hard tissue was observed in direct pulp capping with PLGA and pulp necrosis was evident due to the low adhesion of PLGA to the pulp despite the biocompatibility shown in cellular test [8]. So, PLGA composites with bioceramics

TABLE 1: PLGA membranes in animal and human studies.

Type of PLGA membranes	Clinical application	Species	Study
PGA/PLA membrane + deproteinized bovine bone	Guided bone regeneration of bony defects	Humans	[25]
PGA/PLA membranes	Periodontology (class II furcation)	Humans	[26]
PGA/PLA membranes + hydroxyapatite	Periodontology (class II furcation)	Humans	[26]
PLGA membranes	Bony defects distal to mandibular second molars	Humans	[17]
PLGA membranes	Guided bone regeneration around dental implants	Humans	[27]
PLGA membranes	Bone regeneration	Dogs	[16]
PLGA membrane + atelocollagen gel + rhBMP-2 (recombinant human bone morphogenetic protein-2)	Mandibular transsections	Rabbits	[20]
PLGA membrane + atelocollagen gel + rhBMP-2 (recombinant human bone morphogenetic protein-2)	Mandibular defects	Rabbits	[21]
PLGA-grafted hyaluronic acid bilayer films	Guided bone regeneration	Rats	[22]
Poly(lactic acid-co-glycolic acid-co- ϵ -caprolactone) membrane	Bone healing	Dogs	[23]
PLGA membranes	Bone healing	Rabbits	[18]
PLGA/SiO ₂ PLGA/TiO ₂ membranes	Bone healing	Rabbits	[24]

remain a better option than PLGA alone in pulp capping, with better tissue response as compared to calcium hydroxide [8, 9]. The promising results of the PLGA materials suggest the need for further studies mainly in the domain of delivery of substances to the dental tissues or concerning the pulp-capping abilities exhibited by the PLGA composites.

3. PLGA Membranes

A variety of polymeric bioresorbable membranes are used in bone regeneration techniques because they permit single-step procedures, thus reducing patient discomfort and costs and potential surgical complications [15]. Greater bone regeneration is also achieved when a membrane is applied in periodontal therapy [16]. Considering this, PLGA membranes have been studied with promising results [17, 18], either alone or, more recently, combined with other materials. Table 1 indicates the variety of animal and human studies concerning PLGA membranes in dentistry.

PLGA membranes were studied for periodontal regeneration. Scaling and root planning procedures followed by placing PLGA membranes resulted in significant clinical attachment and bone gain in defects distal to the mandibular second molars [17, 19], while recently a bioactive and resorbable PLGA membrane has been used in calvarial defects for improving bone healing in rabbits [18]. Adding various active substances to PLGA membranes led to increased results. Thus PLGA membrane which coated an atelocollagen gel including rhBMP-2 was used for reconstruction of mandible transsections [20] and defects [21] and the histological analyses suggest that the PLGA membrane was gradually absorbed and replaced by fibrous connective or bone tissue [21]. Moreover, PLGA-grafted hyaluronic acid bilayer films have

been successfully tested for guided bone regeneration in rats [22] leading to 63.1% covering of the bone defect area, with no negative effects [22]. Hyaluronic acid-PLGA was synthesized in the form of 150 nm nanoparticles and afterwards incorporated in a HA-PLGA bilayer blend film of 33 micron, which was fully degraded and absorbed completely in 12 weeks [22]. Also combined macroporous bioresorbable membranes for bone healing were manufactured from a combination of poly(lactic acid-co-glycolic acid-co- ϵ -caprolactone) (PLGC) [23]. In a 6-month study on canine mandible were used different PLGC membranes alone or reinforced with titanium, and all showed more bone than the controls, even if the membranes were used alone or together with autologous bone [23]. Recent studies used PLGA membranes treated with oxygen plasma and with SiO₂ nanoparticles that succeeded to promote 59% bone neoformation much more than PLGA membranes alone, in a recent experiment on rabbits skull [24].

Other studies focused on the in vivo behavior of different membranes such as collagen, polylactide/polyglycolide copolymer, and citric acid copolymer. Results show no statistical differences between these membranes [16]. Also, the PGA/PLA polyglycolic/poly(lactic acid) copolymer membrane led to relatively similar results compared with the application of collagen membranes [25]. Moreover, no statistically significant differences were observed when connective tissue grafts were used instead of the PLGA membranes [26], suggesting that better results were obtained when hydroxyapatite was added to the polymer membrane [26]. A recent study on 40 patients concluded that the PLGA membrane was able to successfully assess bone regeneration, but the control showed better results at maintaining horizontal thickness of regenerated bone and revealed less soft tissue complications

TABLE 2: Applications of PLGA scaffolds in dentistry.

Type of PLGA scaffold	Additional substances	Application	Study
PLGA	BMP-2 (bone morphogenetic protein-2)	Bone regeneration around dental implants	[41]
PLGA	PEG1 (prostaglandin E1)	Alveolar ridge preservation/augmentation	[44]
PLGA	Simvastatin	Bone formation in extraction sockets	[42]
PLGA-gelatin sponge	rhBMP-2 (recombinant human bone morphogenetic protein-2)	Alveolar ridge augmentation	[46]
PLGA/calcium phosphate cement		Bone ingrowth	[52]
PLGA + autogenous bone graft		Bone regeneration around implants	[40]
PLGA/low crystalline apatite		Bone regeneration	[53]
PLGA/calcium phosphates		Maintaining alveolar bone height/augmenting alveolar bone height through standard sinus lift approaches	[28]
PLGA + beta-tricalcium phosphate		Bone and cementum regeneration	[55]
PLGA/CaP (calcium phosphate)		Periodontal regeneration of class II furcation defects	[50]
PLGA + bone allograft	rhBMP-2 (osteoinductive protein)	Alveolar ridge augmentation	[43]
PLGA	Simvastatin and SDF-1 α (stromal cell derived factor-1 α)	Bone regeneration	[45]
PLGA/ β -tricalcium phosphate	Fibroblast growth factor-2	Bone augmentation	[54]

[27]. Overall, the process of adding bone promoting factors or other materials to the PLGA membranes seems to improve the results [20–22, 24] in bone tissue regeneration.

4. PLGA Scaffolds

PLGA scaffolds are currently used as standalone biomaterials, cell carriers, or drug delivery devices [28]. Research in medicine benefits from the development of the PLGA scaffolds founding many potential applications in fields like cardiac tissue regeneration [29], wound healing [30], guided bone regeneration of bone tissue [31, 32], delivery of growth factors and genes [33], and culture of stem cells [34, 35]. Over the last years, many efforts in bone tissue engineering have been dedicated to the development of biodegradable scaffolds with both excellent biocompatibility and mechanical properties mimicking those of natural bone tissues [36, 37]. PLGA scaffolds have been used to regenerate damaged tissues, for example, in bone formation [38] or in regenerative dentistry, together with stem cell-based therapy [39]. Table 2 shows studies concerning the applications of PLGA scaffolds in bone healing and regeneration. Bone formation was obtained with PLGA carriers incorporated with autogenous bone graft [40] or different bone promoting substances such as bone morphogenetic protein-2 BMP-2 [41] or simvastatin [42]. Alveolar ridge augmentation, much needed in dental implant therapy, could also profit due to the PLGA materials [43], as atrophic sites were reconstructed using bioresorbable PLGA,

bone allograft, and an osteoinductive protein such as rhBMP-2 [43]. Sockets were significantly greater in rats treated after extraction with PLGA/PEG1, after only 4 weeks of implantation [44]. Also PLGA scaffolds loaded with simvastatin and SDF-1 α promoted bone regeneration significantly more than controls in mouse calvarial defects [45]. Moreover, the addition of recombinant human bone morphogenetic proteins to the PLGA-gelatin sponge scaffolds showed significantly greater bone formation with no immune or other adverse reactions in alveolar ridge augmentation in dogs [46].

Composite PLGA/CaP scaffolds have also been applied in bone regeneration procedures (alone or in combination with osteoblast cells [28, 47–52]). PLGA/CaP (calcium phosphate) bilayered biomaterial was employed with greater periodontal regeneration in class II furcation defects in dogs than traditional flexible membranes, showing greater bone volumetric values, trabecular number, and trabecular thickness [50]. Besides PLGA/CaP, other composites such as PLGA/apatite scaffolds [53] and PLGA/ β -tricalcium phosphate scaffolds [54] have showed to be bioeffective in bone formation [53, 54]. Significantly greater cementum and bone were formed in dogs periodontal defects after receiving treatment with rhGDF-5 coated onto beta-tricalcium phosphate (beta-TCP) particles and immersed in a bioresorbable poly(lactic-co-glycolic acid) (PLGA) composite [55]. Moreover PLGA scaffolds alone or in combination with cells were used in maxillary sinus augmentation [56]. Bone regeneration was obtained by seeding on a PLGA scaffold bone marrow mesenchymal stem cells [57] or dental pulp

TABLE 3: Applications of PLGA scaffolds in regenerative dentistry.

Type of PLGA scaffolds	Cells seeded on scaffolds	Application	Study
PLGA + calcium phosphate	Bone marrow derived cells	Bone formation	[116]
PLGA	Osteoblast cells	Maxillary sinus augmentation	[56]
PLGA	Bone marrow stem cells	Bone regeneration	[57]
PLGA + calcium phosphate	Bone marrow stem cells	Bone regeneration	[47]
PLGA + nanohydroxyapatite	Tooth bud cells	Cell proliferation and differentiation	[60]
PLGA/hydroxyapatite	Dental pulp stem cells	Osteoblastic differentiation	[59]
PLGA/hydroxyapatite	Dedifferentiated fat cells	Bony defects closure	[61]
PLGA nanofibers	Dental pulp stem cells	Bone regeneration	[58]
PLGA	Adipose-derived stromal cells	Regeneration of bone, periodontal ligament and cementum	[66]
PLGA	Dental pulp stem cells	Dentine/pulp-like tissue	[64]
PLGA	Dental pulp stem cells	Dentine-like structure	[63]
PLGA + tricalcium phosphate	Tooth bud cells	Dentin-like and pulp-like tissues	[65]
PLGA + CCN3 (nephroblastoma overexpressed)	Dental pulp stem cells	Dentinogenesis	[62]

stem cells [58]. Moreover PLGA/hydroxyapatite scaffolds have proven to promote cell proliferation and differentiation of stem cells [59, 60]. Also bone was regenerated using a PLGA/hydroxyapatite scaffold seeded with dedifferentiated fat cells [61] or PLGA calcium phosphate scaffold with bone marrow stem cells [47]. The addition of bone marrow stem cells to the PLGA calcium phosphate scaffolds showed 20 times more bone formation than scaffolds alone [47].

Polymer materials have been used as scaffolds to guide the dental stem cells with the goal to create tooth-like structures. PLGA materials have been used in dentin regeneration [62] or to produce dentin-like structures [63]. Researchers were able to seed and grow dental pulp stem cells on PLGA scaffolds, and those scaffolds were transplanted in rabbits and appeared to produce osteodentine-like structures as well as tubular bilayered structures of vertically aligned parallel tubules resembling tubular-like dentine [64]. Furthermore, PLGA/tricalcium phosphate with tooth bud cells gave rise to dentin-like and pulp-like tissues [65]. Swine dental pulp stem cells were seeded on PLGA scaffolds and were implanted in rat canals of extracted teeth, which were placed into fresh postextraction sockets of mini pigs [65]. After 10 weeks of implantation the histological analysis showed newly formed organic matrix consistently deposited on the canal walls and the presence of a continuous layer of polarized or nonpolarized cells showing columnar or spindles shaped morphology [65]. Also, stromal cells from the adipose tissue on a PLGA scaffold regenerated bone, periodontal ligament, and cementum layers [66]. Table 3 indicates the main applications of PLGA scaffolds in regenerative dentistry.

Although they show promising results in a variety of applications, the biocompatibility of the PLGA scaffolds is under debate. The degradation products of PLGA (lactic and glycolic acid) can decrease the pH in the surrounding tissues, causing inflammation or foreign body reactions in vivo [67]. Also, the acidic degradation products have the potential to

inhibit apatite crystals formation [68], leading to presumably deficient osteointegration. The hydrophobic proprieties of the bioresorbable polyesters negatively influence their cell adhesion [69]. Moreover, in an attempt to reduce the inflammation and improve the biocompatibility of PLGA different particles have been incorporated with promising results into the PLGA materials: titanium nanoparticles [70], tripolyphosphate nanoparticles [71], demineralized bone particles [67], and nanoapatite particles [72]. Also the PLGA scaffolds were functionalized with fibronectin [69] and the PLGA fibers were coated with apatite layer [73]. Another problem is the fact that salivary born aerobic and anaerobic microorganism adhered significantly more to PLGA compared to other polymeric (PLLA and PLLA-TCP) scaffolds. *E. faecalis* (a bacteria present in recurrent endodontic infections) and *P. gingivalis* (a periodontitis related pathogen) showed the highest adhesion to the PLGA scaffold, rising concerns about possible implant-associated infections [74].

5. PLGA Microparticles

The concept of using polymer-based sustained-release delivery systems to maintain therapeutic drug concentrations for longer periods of time is accepted for decades [75]. Microparticles and nanoparticles are preferred over other methods as a result of their flexibility in preparation and use [76]. Several medical applications of PLGA microparticles include gene delivery [77], anticancer therapy [78], and vaccines [79]. PLGA microparticles have been successfully studied in a wide range of dental fields, such as endodontic therapy [80], dental caries vaccination [81], regenerative dentistry [14], dental surgery [82, 83], or periodontology [84]. Also Table 4 summarizes the main applications of the PLGA microparticles in dentistry.

TABLE 4: Applications of PLGA microparticles in dentistry.

Field	PLGA microparticles	Loaded with	Study
Endodontic therapy	PLGA microparticles with added zein	Amoxicillin	[80]
Dental caries vaccination	PLGA microparticles coated with chitosan	Recombinant <i>Streptococcus mutans</i> glucan-binding protein D	[81]
Dental regeneration (tertiary dentin)	PLGA microparticles in a PLGA/calcium phosphate cement	Growth factors	[14]
Haemostatic device	PLGA microparticles	Thrombin	[85]
	PLGAmicroparticles	Hydroxyapatite ofloxacin	[88]
periodontal treatment	PLGA microparticles	Chlorhexidine	[87]
	PDLLA-PLGA microparticles	Growth and differentiation factors	[89]
	PLGA and poly(epsilon-caprolactone)	Doxycycline	[84]
Bone regeneration	PLGA microparticles	Simvastatin	[91]
	PLGA microparticles	Alendronate sodium	[97]
	PLGA microparticles	Dexamethasone	[94]
	PLGA microparticles in collagen membrane	Dexamethasone	[93]
Implant therapy	PLGA microparticles in PLGA membrane	VEGF (vascular endothelial growth factor)	[92]
	PLGA microparticles	Insulin	[82, 83]
	PLGA microparticles	Basic fibroblast factor	[96]
	PLGA microparticles	Fluvastatin	[98]
	PLGA microparticles	rhBMP-2 (recombinant human bone morphogenetic protein-2)	[99]

In endodontics PLGA and zein microspheres were able to deliver amoxicillin at significant levels in the root canal [80] and overcame the concentrations levels needed for an appropriate endodontic disinfection [80]. Amoxicillin was elected because it is effective against *Enterococcus faecalis*, a microorganism responsible for endodontic failure and most resistant to root canal preparation and intracanal dressings [80]. Moreover, PLGA microspheres incorporated with recombinant *Streptococcus mutans* glucan-binding protein D (rGbpD) may give rise to a future dental vaccine [81] as a study on immunized rats treated with chitosan-coated PLGA microspheres shows. Growth factors incorporated in PLGA microspheres induce the formation of tertiary dentin [14], while thrombin-loaded poly(D,L-lactide-co-glycolide) microspheres formed a new biodegradable haemostatic device [85]. Periodontology can also profit from the controlled delivery proprieties of PLGA microparticles. A wide variety of substances have been incorporated into the PLGA carriers and slowly released locally for periodontal treatment and regeneration: tetracycline [86], doxycycline [84], or chlorhexidine [87]. PLGA microspheres incorporated with hydroxyapatite and ofloxacin were fabricated to be used as a local drug delivery system for periodontitis treatment and showed good results against *S. aureus* and *E. coli* [88], while PDLLA-PLGA microparticles filled with growth and differentiation factors were able to accelerate osteogenesis, bone maturation, fibers

realignment, and cementogenesis of the periodontal apparatus, in rats maxillae [89]. Bone regeneration is the dental field where most of the studies concerning PLGA microparticles concentrate on. Intracellular delivery of estrogen (a sex steroid that increases bone formation) using cationic PLGA microparticles significantly upregulates osteogenic differentiation of human bone marrow mesenchymal stromal cells by improving the osteogenic differentiation markers ALP and Cbfa-1 expressions after 1 and 2 weeks [90]. PLGA microspheres containing simvastatin [91], growth factors [92], or dexamethasone [93, 94] significantly enhanced bone formation. Also PLGA microparticles loaded with growth factors [95, 96] were used for better osteointegration of titanium implants, while biphosphonate PLGA microspheres can be used in the future to treat alveolar bone resorption [97]. Injectable PLGA microspheres containing fluvastatin were developed to enhance osteogenesis around titanium implants in the rat tibia and after a single injection the PLGA microspheres with fluvastatin safely stimulated bone formation around titanium implants and increased the mechanical properties of bone [98]. The biomechanical retention of implants was improved after adding PLGA microparticles loaded with insulin, as an animal study on type I diabetic rats concluded [82]. Moreover, PLGA microparticles were used for better osseointegration of titanium implants, also in type II diabetic rats [95], as insulin-like growth factor I was slowly

TABLE 5: Applications of PLGA nanoparticles in dental medicine.

Type of PLGA nanoparticles	Loaded with	Dental field	Study
PLGA nanoparticles	Minocycline	Periodontal infections	[101]
Dental implants coated with PLGA nanoparticles	Basic fibroblast growth factor	Implantology	[112]
PLGA nanoparticles	Methylene-blue photosensitizer	Endodontic infections	[108]
PLGA nanoparticles	Methylene-blue photosensitizer	Periodontology (reduction of dental plaque biofilms)	[109]
PLGA nanoparticles heparin-conjugated	BMP-2 (bone morphogenetic protein-2)	Bone regeneration (osteogenic differentiation of bone marrow stem cells)	[110]
PLGA nanoparticles	Simvastatin	Bone regeneration (enhanced osteogenesis of bone marrow mesenchymal stem cells)	[111]

released for 30–40 days by PLGA microparticles and led to bone deposition around the interface of titanium implants [95]. A scaffold incorporated with PLGA microparticles loaded with a bone morphogenetic protein (rhBMP-2) was more effective to induce implant osseointegration than the same scaffold with the protein directly encapsulated without the PLGA microparticles [99]. Microparticles usage also raised several practical problems. Thus when the particles were studied in implant therapy procedures, some authors reported loss of PLGA drugs during implant placement. Different approaches, such as inserting blood mixed with PLGA microspheres into the implant hole [82, 95] or adding the blood mixed with PLGA on the titanium implants [96], showed significant loss of PLGA microparticles, because of the mechanical friction.

The multitude of dental applications in which PLGA particles can be used is encouraging. The promising results in the bone regeneration field and periodontology may need further studies and clinical trials. Overall, microparticles of polylactic-polyglycolic acids seem to be a promising controlled delivery device in dental treatment.

6. PLGA Nanoparticles

Microparticles and nanoparticles are mainly designed as targeted drug delivery systems with the aim of minimizing the side effects associated with the use of the free drugs. Various terms have been used to describe the nanoparticles: nanocarriers, nanovehicles, nanosystem, nanodisc, nanoworm, nanorod, nanotube, drug-polymer conjugates, drug-protein conjugates, liposomes, polymer micelles, dendrimers, and drug nanocrystals [100]. Nanoparticles provide a wide range of advantages such as smaller particle size which facilitates the penetration into the cells, higher entrapment efficiency for increased drug release, lower minimum inhibitory concentration, and minimum bacterial concentrations meaning that a better antibacterial activity is achieved with a smaller amount of drug [101]. In the medical field PLGA nanoparticles were developed as gene carriers [102] and also they have been extensively studied as vaccine

delivery systems [103–105] or in the anticancer therapy [106, 107]. Targeted PLGA nanoparticles but not microparticles specifically deliver antigen to human dendritic cells [104].

Nanoparticles of PLGA can be used in a wide variety of applications in dental medicine, as shown in Table 5. Minocycline-loaded PLGA nanoparticles showed better antibacterial activity than the use of free minocycline [101] and can provide a potential carrier system for the transport of antibiotics to periodontal tissues. The inhibition zone of minocycline-loaded nanoparticles (9.2 mm) was greater than that of free minocycline (3.5 mm) against *Aggregatibacter actinomycetemcomitans*, the most important pathogen in periodontal infections [101]. Moreover, methylene-blue loaded PLGA nanoparticles showed a greater photodynamic effect than would free MB and exhibited approximately one order of magnitude killing of *E. faecalis* biofilm species (a microorganism found in endodontic failures) in experimentally infected root canals of human extracted teeth [108]. Also methylene-blue loaded PLGA nanoparticles exhibited a greater photodynamic effect than free MB in suspensions of human dental plaque bacteria as well as in biofilms collected from 14 patients with chronic periodontitis [109]. So, PLGA nanoparticles loaded with methylene-blue photosensitizer could be used in endodontic infections [108] as well as in the reduction of human dental plaque bacteria found in patients with chronic periodontitis [109]. Additionally, PLGA nanoparticles add significant improvements to bone regeneration techniques, delivering growth and differentiation factors with promising results. The delivery of PLGA nanoparticles loaded with bone morphogenetic protein-2 to bone marrow mesenchymal stem cells induced far more extensive bone formation in vivo than either implantation of the nanoparticles loaded with BMP-2 alone or osteogenically differentiated stem cells [110]. Also, PLGA nanoparticles containing simvastatin were used to enhance osteogenesis of bone marrow mesenchymal stem cells, which can be further used in bone regeneration [111]. Nanoparticles of PLGA with growth factor have also been used with success in implant therapy, stimulating the bone formation adjacent to the surface of a dental implant inserted in bone

[110]. The histomorphometric analysis showed a 44% mean bone-to-implant contact percentage, after only 12 weeks of implantation in rabbit tibiae [112]. Results obtained in these studies are promising, but further experiments are needed to test the effects of applying nanoparticles of PLGA in dental treatments.

7. PLGA Limitations

In conclusion, to date, PLGA membranes have controversial results when used alone in bone regeneration therapy [16, 25–27]. Some authors suggested that PLGA has limited benefic effects in bone [113] and periodontal [114] regeneration. Moreover, oral microorganisms (such as *S. mutans*, *E. faecalis*, *P. nigrescens*, *P. gingivalis*, *S. sanguis*, and *C. albicans*) seem to have a good adherence to the PLGA scaffolds in vitro and this could result in bacterial-related infections in vivo [115]. Research should be intensified and extended in order to overcome the practical problems encountered in the manipulation of the PLGA microparticles [82]. And we must also consider the insufficient data concerning PLGA nanoparticles in the dental field.

8. Conclusions

Due to their biocompatibility, PLGA materials have been successfully studied in almost all dental fields, from endodontics to periodontology and implantology. The promising results of the in vitro and in vivo experiments suggest that further studies concerning PLGA applications should be undertaken in dental research.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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