Biomedical Applications of Poly(Propylene Carbonate)

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Poly(propylene carbonate) (PPC) is an emerging “carbon fixation” polymer that holds the potential to become a “biomaterial of choice” in healthcare owing to its good biocompatibility, tunable biodegradability and safe degradation products. Several physical, chemical and biological modifications of PPC have been achieved by introducing biocompatible polymers, inorganic ions or small molecules, which can endow PPC with better cytocompatibility and desirable biodegradability, and thus enable various applications. Indeed, a variety of PPC-based degradable materials have been used in medical applications including medical masks, surgical gowns, drug carriers, wound dressings, implants and scaffolds.

Keywords: poly(propylene carbonate) or PPC ; biomaterials ; biomedical application ; drug carriers ; implants ; wound dressings

1. Introduction

Polymers are now widely used as biomaterials in clinics and scientific research. Among them, synthetic polymers have become a major source of biomedical materials due to their outstanding mechanical properties, structural maneuverability and processability. They can be tailored and modified to meet the demand of various applications, such as artificial skin, implanted scaffolds and drug delivery systems and are thus regarded as very promising alternative biomaterials in healthcare [1][2].

Poly(propylene carbonate) (PPC) is an aliphatic polycarbonate with the advantages of low-cost, low-toxicity, environmental friendliness and biodegradability. PPC was first synthesized by Inous in a $ZnEt_2/H_2O$-catalyzed system through the copolymerization of CO_2 and propylene oxide (PO) [3]. The immobilization of CO_2 as a feedstock into PPC will not only reduce the usage of petrochemicals, but also mitigate the environmental problems caused by greenhouse gases. Such a “carbon fixation” function makes PPC an ideal polymer for the era of “carbon neutrality”.

Hence, various homogeneous and heterogeneous catalysts have been developed over recent decades to synthesize PPC with enhanced properties and productivity to achieve broader applications [4][5][6]. At present, PPC has been extensively used in food packaging [7][8], battery manufacturing [9][10], agricultural mulch films [11] and cushioning foams [12], etc. In addition, owing to its good biocompatibility and non-toxic degradation products, PPC also holds significant promise for biomedical applications, such as drug carriers [13][14], tissue engineering scaffolds [15][16] and medical dressings [17].

2. Biomedical Applications of Poly(Propylene Carbonate)

PPC holds significant potential for a wide range of medical applications. Indeed, PPC has been used in a variety of medical supplies including masks, surgical gowns, insulating pads and trash bags for medical disposal. In addition to these low-end applications, most of the recent research on PPC-based biomaterials is focused on drug carriers, medical dressings and implants (**Table 1**), especially for biomodified PPC. A brief overview of the advances in using PPC as drug carriers, medical dressings, implants and scaffolds is provided.

Table 1. Categorical overview of PPC-based materials for biomedical applications.

Suggested Application	Material	Preparation Method	Ref.
Drug carriers for cancer treatment	mPEG-PPC-mPEG/doxorubicin	Grafting copolymerization and drug loading by shear emulsification	[13]
	PEG-PPC-PEG/doxorubicin	Condensation and drug loading by nanoprecipitation	[18]
	mPEG-block-PPC-*g*-dodecanol/CH-3-8 polymeric nanoparticles	Grafting copolymerization and drug loading by coupling reaction	[19]
	mPEG-block-PPC-*g*-gemcitabine-*g*-dodecanol/miR-205 polymeric micelles	Grafting copolymerization and drug loading by coupling reaction	[20]
	PEG-block-PPC-*g*-tetraethylenepentamine/GDC-0449/let-7b micelles	Grafting copolymerization and drug loading by coupling reaction	[21]
	GE_{11} peptide-PEG-block-PPC-*g*-gemcitabine-*g*-dodecanol mixed micelles	Grafting copolymerization and drug loading by coupling reaction	[22]
Drug carriers for hepatic fibrosis treatment	mPEG-block-PPC-*g*-dodecanol-*g*-tetraethylenepentamine/miR-29b1/GDC-0449 micelles	Grafting copolymerization and drug loading by coupling reaction	[23]
	mPEG-block-PPC-*g*-dodecanol-*g*/MDB5 micelles	Grafting copolymerization and drug loading by coupling reaction	[24]
Drug carriers for type I diabetes treatment	mPEG-block-PPC-*g*-dodecanol-*g*-tetraethylenepentamine/sunitinib micelles	Grafting copolymerization and drug loading by coupling reaction	[25]
Drug carriers for spinal cord injury treatment	PPC/dibutyryl cyclic adenosine monophosphate/chondroitinase ABC microfibers	Electrospinning	[26]
Drug carriers for other treatments	PPC/PCL/metoprolol tartrate blends	Melt blending	[27]
	PPC/imidacloprid microspheres	Emulsification and solvent evaporation	[14]
	Poly(vinyl-cyclohexene carbonate)-*g*-PPC	Grafting copolymerization	[28]
	PPC-block-poly(4-vinylcatechol acetonide) copolymers	Grafting copolymerization	[29]
Wound dressings	Parallel-aligned PPC microfibers/chitosan nanofibers	Electrospinning and oxygen plasma treatment	[16]
	PPC nanofiber mats	Electrospinning, spin coating and UV treatment	[30]
Artificial skins	Curcumin-loaded PPC-*g*-chitosan nanofibers	Electrospinning and encapsulation	[31]
	Spermidine-functionalized PPC composite films	Spin coating	[32]
Bone repair scaffolds	Porous PPC-starch-bioglass scaffolds	Gas foaming	[15]
	PPC-starch composites	Melt blending	[33]
	Microporous PPC/laponite nanocomposites	Melt blending and surface treatment with sodium hydroxide	[34]
	PPC-starch-bioglass blends	Melt blending	[35]
	PPC multilayer membranes	Aminolysis and layer-by-layer assembly	[36]
	Porous PPC/poly(D-lactic acid)/β-tricalcium phosphate scaffolds	Salt leaching	[37]
Medical adhesives/glues	Poly(ethyl cyanoacrylate)/PPC/caffeic acid films	Polymerization in presence of PPC and solvent evaporation	[38]

Suggested Application	Material	Preparation Method	Ref.
Wearable electronic devices	Poly(methyl methacrylate)-PC-lithium perchlorate/multi-walled carbon nanotube/Mn_3O_4 micro-supercapacitors layer-by-layer-assembled films	Hydrothermal reaction, photolithography and layer-by-layer assembly	[39]

2.1. Drug Carriers

As listed in **Table 1**, a variety of PPC-based drug delivery systems have been developed, particularly with PEG. Amphiphilic block copolymers composed of PPC and PEG possess favorable thermo-responsiveness and can self-assemble into nanoscale micelles in aqueous solutions, which are promising candidates for drug encapsulation [13][18][19][20][21][22][23][24][25]. Mahato and co-workers synthesized a methoxy poly(ethylene glycol)-block-poly(2-methyl-2-carboxyl-propylene carbonate-graft-dodecanol) (mPEG-*b*-PCC-*g*-DC) nanoparticle [19]. This nanoparticle can effectively improve the prognosis of pancreatic cancer by overcoming chemotherapy resistance and reducing systemic toxicity. Meanwhile, drug carriers of PPC with other modifications have also been reported, which are normally prepared by electrospinning, melt blending and emulsification and solvent evaporation [14][26][27]. Li and co-workers fabricated PPC-loaded imidacloprid microspheres by emulsion solvent evaporation [14]. The microspheres can achieve a high drug loading of 45%, an entrapment efficiency of 78% and a sustained drug release at shear rate of 10,000 r/min. Furthermore, the targeted delivery of PPC-based drug carriers can also be made by incorporating targeting ligands through biological modification [22][40]. For example, Goutam Mondal and co-workers prepared an epidermal growth factor receptor (EGFR)-targeted gemcitabine (GEM)-conjugated polymeric mixed micelles GE11-PEG-PCD/mPEG-*b*-PCC-*g*-GEM-*g*-DC to treat pancreatic cancer. In mice, GE11-linked micelles can deliver GEM to EGFR-expressing pancreatic cancer cells, act on tumor blood vessels and show significant inhibition of pancreatic tumor growth [22].

2.2. Medical Dressings

The application of PPC as a wound dressing is unfortunately compromised by its hydrophobicity. Hence, modification of PPC by plasma treatment, UV irradiation and/or polymer grafting is normally used to make PPC-based medical dressings [16][30][31]. These biomodifications facilitate cell adhesion, proliferation and tissue regeneration while maintaining the essential properties of PPC, such as low toxicity and biodegradability. For example, Alexander Welle et al. prepared PPC nanofibers through electrospinning and subsequent UV irradiation [30]. The UV-irradiated nanofibers exhibited good adhesion and viability of L929 fibroblasts and primary rat hepatocytes, as well as collagen deposition, which show good potential for wound dressings. Peng et al. introduced freeze-dried chitosan nanofibers onto a PPC microfiber mat after oxygen plasma treatment [16]. The composite nanofibers (T-PPC/CS) were hydrophilic and showed superior cell morphology, attachment and proliferation, which makes them suitable for wound dressings. Guo et al. adopted electrospinning to encapsulate curcumin into chitosan-grafted PPC nanofibers [31]. The nanofibers (PPC-*g*-CS CUR) showed granulation and antioxidant effects in animals, which hold great promise for applications in wound repair.

2.3. Implants and Scaffolds

Among various biodegradable synthetic polymers, PPC is a promising candidate for clinical implants and scaffolds owing to its non-toxic degradation products. Again, various biomodifications have been utilized to prepare PPC-based implants and scaffolds. For example, Fariba Dehghani et al. fabricated a porous scaffold with excellent biocompatibility and benign degradation by-products through gas foaming of PPC blended with starch and bioglass particles [15]. The scaffold demonstrated outstanding cell proliferation and tissue infiltration in vitro and in vivo as well as ideal mechanical properties. Therefore, the scaffold is expected to provide good joint implants. Fang et al. prepared an elastic porous bone scaffold of PPC-poly(D-lactic acid)-β-tricalcium phosphate (PDT) via a non-solvent method [37]. This scaffold not only showed good cytocompatibility and low inflammatory response, but also functioned as an osteogenesis-inducer to promote bone repair in rabbits. Liu et al. modified PPC with biopolymers and spermidine to prepare PPC-based artificial skin [32], which showed excellent mechanical properties, swelling properties, cytocompatibility, and pro-healing properties. More importantly, the PPC-based artificial skin exhibited low immunogenicity owing to the modification of spermidine, which is manifested by reduced pro-inflammatory cytokines in rats and accelerated transition from the M1 macrophage-dominated phase to the M2 macrophage-dominated phase.

2.4. Other Biomedical Applications

In addition to the above applications of PPC-based biomaterials, PPC can also be used as a component in the formulation of medical glues for wound closing [38], bio-resistant coatings for antibacterial purposes [41], wearable electronic devices [39] and biomedical instruments [42] to detect various life indicators.

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