# Biomedical Applications of Polycaprolactone (PCL) Composites: Structure, Properties, and Future Prospects

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**Abstract:** Polycaprolactone (PCL) is a semi-crystalline, biodegradable aliphatic polyester that has emerged as a versatile biomaterial for tissue engineering, drug delivery, and regenerative medicine applications due to its exceptional biocompatibility, controlled degradation kinetics (2-4 years *in vivo*), and FDA approval status for multiple medical devices. Despite these advantages, pure PCL exhibits significant limitations including low mechanical strength (16-24 MPa tensile strength), hydrophobic surface properties (water contact angle 80-90°), and minimal bioactivity, which restrict its clinical utility in load-bearing and cell-interactive applications. To address these shortcomings, researchers have developed PCL-based composite systems by incorporating bioactive ceramics (hydroxyapatite, β-tricalcium phosphate), natural polymers (collagen, chitosan, gelatin), synthetic polymers (PLA, PLGA), and nanomaterials (carbon nanotubes, graphene oxide) to create multifunctional biomaterials with enhanced properties. This comprehensive review analyzes PCL composite development over the past two decades, emphasizing fabrication techniques including electrospinning, 3D printing, solvent casting, and melt blending, which enable precise control over scaffold architecture and functionality. Comparative analysis with other biodegradable polymers (PGA, PLGA) reveals PCL's unique advantages in long-term applications, with studies demonstrating >90% cell viability, ~65% bone regeneration in animal models, and sustained drug release profiles extending 6-8 weeks. Recent innovations include smart, stimuli-responsive PCL systems for targeted therapy, gene delivery platforms, and bioprinting applications that have advanced from laboratory research to clinical trials, with several PCL-based products (Neurolac®, Osteoplug®) receiving regulatory approval. Current challenges include manufacturing scalability, long-term biocompatibility assessment, and complex regulatory pathways for multi-component systems. Future developments focus on integrating artificial intelligence for scaffold design, 4D printing technologies for dynamic structures, and multidisciplinary approaches combining materials science with precision medicine. This review demonstrates that PCL-based composites represent a transformative class of biomaterials with customizable properties that bridge fundamental research and clinical translation, positioning them at the forefront of next-generation biomedical technologies.

**Keywords:** Biodegradable composites; biomedical applications; drug delivery systems; Polycaprolactone, tissue engineering.

## 1. INTRODUCTION

In recent years, biodegradable polymers have become indispensable in biomedical research and clinical practice. Their ability to break down into harmless metabolites not only eliminates the need for secondary removal surgeries but also minimizes chronic inflammatory responses [1,2]. These advantages have led to their widespread adoption in drug delivery, regenerative medicine, and tissue engineering [3].

Among the different candidates, polycaprolactone (PCL) has attracted strong interest due to its rare combination of biocompatibility, flexibility, and a very slow degradation rate [4]. These features make it particularly useful in applications where prolonged stability is required, such as bone fixation devices, long-term scaffolds, and controlled drug release carriers. Additionally, PCL is highly adaptable to different fabrication techniques, including electrospinning and additive manufacturing, which enable the creation of complex architectures suited for patient-specific therapies [5].

Despite these benefits, PCL on its own presents shortcomings that limit its broader clinical utility. Its hydrophobic nature hinders early-stage cell attachment, while its relatively low strength restricts application in load-bearing conditions. Furthermore, being biologically inert, it provides minimal biochemical cues for tissue regeneration. To address these barriers, considerable research has focused on composite systems where PCL is blended or reinforced with bioactive ceramics, natural polymers, or nanomaterials. Such modifications enhance degradation behavior, improve surface interactions, and increase mechanical reliability [6,7]. Recent reports also highlight how advanced fabrication technologies have expanded the scope of PCL-based composites, offering more precise control over architecture and functionality [8,9].

## 2. POLYCAPROLACTONE (PCL): PROPERTIES AND BIOMEDICAL RELEVANCE

PCL is a semicrystalline aliphatic polyester synthesized via ring-opening polymerization of ε-caprolactone using catalysts like stannous octoate. Its linear structure contributes to its crystallinity and mechanical properties [10,11]. Polycaprolactone (PCL) exhibits a distinct set of physicochemical properties, including controlled biodegradability, moderate mechanical strength, thermal stability, and surface wettability, which collectively define its performance in biomedical and environmental applications.

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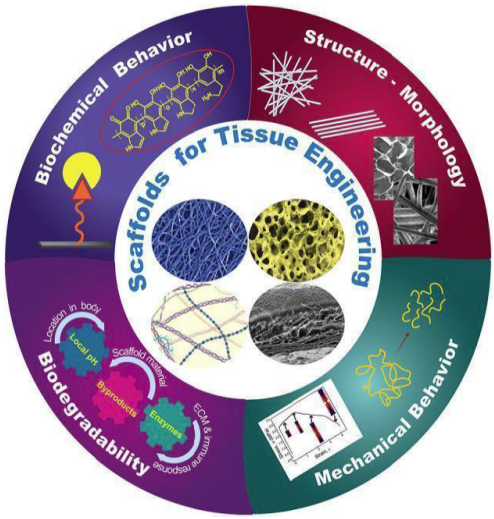


**Figure 1:** Elements of biomaterial scaffolds that are essential for inducing the behavior of cells.

## 2.1. Physicochemical Properties

### *2.1.1. Biodegradability*

PCL degrades slowly through hydrolysis of its ester linkages, suitable for long-term applications. It exhibits excellent biodegradability, making it highly suitable for biomedical and environmental applications. The rate of degradation can be tailored by modifying molecular weight or blending PCL with other polymers [4,12]. Due to its controlled degradation profile, PCL is widely used in long-term drug delivery systems, tissue engineering scaffolds, and bioresorbable implants [6].

### *2.1.2. Mechanical Strength*

PCL possesses moderate mechanical strength, which makes it suitable for soft and flexible biomedical applications. It has good elongation at break and ductility, allowing it to deform without cracking under stress [13]. However, its low tensile and compressive strength limit its use in load-bearing applications without reinforcement. The mechanical performance of PCL can be adjusted by controlling its molecular weight and crystallinity [14]. Despite its limitations, PCL's mechanical properties are adequate for applications like soft tissue engineering, wound dressings, and controlled drug delivery systems [15].

### *2.1.3. Thermal Stability*

PCL exhibits a low melting point (~60°C), allowing easy processing. It also demonstrates good thermal stability, with a melting temperature typically around 58-63 °C [16]. It maintains its structural integrity during common polymer processing methods such as extrusion, electrospinning, and 3D printing. PCL begins to thermally degrade at temperatures above 200 °C, making it suitable for applications requiring moderate heat resistance [17]. This thermal behavior supports its versatility in biomedical device fabrication and drug delivery systems [18].

### *2.1.4. Wettability and Water Contact Angle*

PCL exhibits relatively low wettability due to its hydrophobic surface, typically showing a water contact angle between 80° and 90° [19,20]. This moderate to high contact angle can limit initial cell adhesion and protein adsorption on its surface. To enhance its biomedical performance, surface treatments such as plasma modification or blending with hydrophilic polymers are often applied to reduce the contact angle. Improved wettability of PCL supports better cell attachment, proliferation, and overall biocompatibility in tissue engineering applications [21,22].

### *2.1.5. Comparative Analysis with Other Biodegradable Polymers*

To better understand PCL's position among biodegradable polymers used in biomedical applications, a comparative analysis with polyglycolic acid (PGA) and poly(lactic-co-glycolic acid) (PLGA) is essential. These three polymers represent the most widely utilized biodegradable materials in tissue engineering and drug delivery systems, each offering distinct advantages based on their molecular structure and degradation characteristics.

This comparative analysis demonstrates that while PGA offers rapid degradation and high mechanical strength, and PLGA provides tunable properties through copolymer ratios, PCL's extended degradation timeline and processing flexibility make it particularly suitable for long-term biomedical applications requiring sustained performance over months to years.

## 2.2. Biological Properties

### *2.2.1. Biocompatibility and Biostability*

PCL exhibits excellent cytocompatibility, with fibroblast and osteoblast cultures showing >90% cell viability after 7 days and enhanced proliferation on

**Table 1: Comparative Properties of Biodegradable Polymers: PCL, PGA, and PLGA**

| Property | PCL | PLA | PGA | PLGA |
|---|---|---|---|---|
| Molecular weight [g/mol] | 3,000-80,000 [10,11] | 10,000-300,000 [23,28] | 20,000-100,000 [23,24] | 10,000-200,000 [25,26] |
| Density [g/cm$^3$] | 1.07-1.15 [16] | 1.21-1.25 [23,28] | 1.50-1.70 [23,24] | 1.20-1.30 [25,26] |
| Tensile strength [MPa] | 16-24 [4, 13] | 50-70 [23,28] | 60-99 [23,24] | 40-55 (composition-dependent) [25,26] |
| Young's modulus [GPa] | 0.21-0.44 [4,13,14] | 2-3 [23,28] | 6-7 [23,24] | 1-2 [25,26] |
| Crystallinity [%] | ~69 [4,16] | 37-40 [23,28] | ~45-55 [23,24] | Amorphous to semi-crystalline (varies with ratio) [25,26] |
| Glass transition temperature [°C] | -65to -60 [4,17] | 55-65 [23,28] | 35-40 [23,24] | 45-55 [25,26] |
| Melting temperature [°C] | 56-65 [16,17] | 170-180 [23,28] | 225-230 [23,24] | No sharp melting point [25,26] |
| Decomposition temperature [°C] | ~350 [16,17] | ~250-280 [23,28] | ~260-280 [23,24] | ~200-250 [25,26] |

electrospun scaffolds [29,30]. *In vivo*, PCL–HA composites achieved ~65% bone regeneration in rat calvarial defects within 8 weeks [31]. Subcutaneous implantation studies reported structural stability for over 12 months with only mild local responses, while degradation products (6-hydroxycaproic acid) were safely metabolized via the citric acid cycle [32]. These outcomes confirm PCL's suitability for long-term biomedical applications such as bone regeneration, vascular grafts, and extended drug delivery.

#### *2.2.4. FDA Approval Status*

PCL holds FDA approval for use in various medical applications, including drug delivery devices, absorbable sutures, adhesion barriers, and aesthetic fillers like microsphere-based collagen stimulators. Its regulatory clearance spans both implantable and resorbable medical devices, underscoring its safety profile and compatibility with human tissues [33-36]. The FDA has incorporated PCL into its Material Safety Summaries, reflecting its long-term stability and biocompatibility when used in clinical settings. Publicly available safety assessments note minimal systemic reactions and primarily mild, device-specific, local responses-such as transient inflammation or seroma formation-aligned with other approved biomaterials [23,37].

## 3. LIMITATIONS OF PURE PCL IN BIOMEDICAL APPLICATIONS

Despite its widespread use in biomedical applications, pure polycaprolactone (PCL) possesses several limitations that restrict its effectiveness in certain clinical settings, given below.

### 3.1. Slow Degradation Rate

Pure PCL exhibits a significantly slow degradation rate under physiological conditions, often taking several months to years to fully resorb in the body. While this can be beneficial for long-term applications, it poses limitations in cases where rapid tissue regeneration or drug release is required. The prolonged presence of the material may lead to chronic inflammation or impede natural tissue remodeling in fast-healing tissues such as skin or muscle [38,39].

### 3.2. Hydrophobicity

PCL has a relatively high water contact angle, indicating its hydrophobic nature. This poor wettability limits its ability to support initial protein adsorption and cell adhesion, both of which are critical for effective tissue integration. The hydrophobic surface can hinder cellular proliferation and delay healing processes, especially in applications like wound healing or tissue scaffolds [40,41].

### 3.3. Mechanical Constraints

While PCL is flexible and ductile, it lacks sufficient mechanical strength for load-bearing applications such as bone or joint implants. Its low tensile and compressive strength restrict its use in high-stress environments without reinforcement. Additionally, pure PCL can deform under sustained mechanical load (creep), which compromises its long-term structural reliability in orthopedic and dental applications [4,42].

### 3.4. Limited Bioactivity

Pure PCL is biologically inert, meaning it does not actively interact with surrounding tissues to stimulate healing or regeneration. It lacks inherent cues for osteoconduction or angiogenesis, which are essential for applications such as bone regeneration or vascular grafts. This limited bioactivity necessitates the addition of bioactive fillers (e.g., hydroxyapatite, growth factors) to enhance its functionality [43,44].

### 3.5. Limited Antibacterial Properties

Polycaprolactone (PCL) by itself does not possess inherent antibacterial properties, which may limit its effectiveness in infection-prone biomedical applications. However, its polymer matrix can be easily modified to incorporate antibacterial agents such as silver nanoparticles, antibiotics, or natural extracts. These modifications help inhibit bacterial growth on implant surfaces, reducing the risk of post-surgical infections [45].

These limitations highlight the need for modifying or reinforcing PCL through blending, surface functionalization, or composite formation to expand its utility across a broader range of biomedical applications.

## 4. PCL-BASED COMPOSITES: NEED AND STRATEGIES

### 4.1. Why Blend or Reinforce PCL?

Blending or reinforcing PCL addresses its shortcomings by enhancing bioactivity, mechanical strength, and degradation behavior. Despite the benefits of PCL, its slow degradation rate, hydrophobicity and limited bioactivity remain significant barriers in clinical use [23,46]. Blending or copolymerizing PCL with other constituents alters the scaffold's functional properties. In this regard, different studies have combined distinct polymers, metals, and ceramics with PCL to increase its properties [47].

The glass transition temperature (Tg) of PCL is 213 K, while its melting temperature (Tm) is between 332 and 337 K [48]. It blends well with other polymers and has a low melting point, making it ideal for scaffolding and drug delivery systems. Although PCL has sufficient biocompatibility on its own, enhanced bioactivity is preferred for a few uses [49]. PCL can be made more bioactive by either copolymerization or the addition of bioactive fillers. The co-polymerization, kind of biopolymer link, monomer type, and adjacent groups all influence hydrolysis and consequently the rate of breakdown [55]. Copolymerization and blending have both been utilized to slow the degradation of polymeric scaffolds. According to research, integrating polymers and/or ceramics with PCL may help alter the rate of deterioration while keeping the functional qualities of the scaffold [50].

PCL has a hydrophobic tendency in general. Hydrophilicity and improved cellular compatibility are required for it to function as a scaffold. Multiple efforts have been made to alter the exterior PCL constructs by covering them with gelatin, proteoglycans, growth factors, fibrin, and fibronectin. PCL scaffolds with double protein coatings promote proliferation, colonization, and cell adhesion. However, because of the surface's ECM matrix rearrangement, the arginine-glycine-aspartic acid (RGD) coating showed smoother surfaces and early bone deposition onto scaffold surfaces [51,52].

### 4.2. Types of Reinforcements Used

Natural fibers such as collagen, chitosan, and cellulose, ceramic fillers like hydroxyapatite (HA) [53,54] and β-tricalcium phosphate (β-TCP) [55,56] are commonly used as reinforcements in PCL composites to enhance biocompatibility and mimic the extracellular matrix. Carbon-based materials, including graphene oxide [57] and carbon nanotubes [58], are used to enhance the mechanical strength and electrical conductivity of PCL composites. Synthetic polymers such as polylactic acid (PLA) [59] and polyglycolic acid (PGA) [23] are blended with PCL to tailor degradation rates and mechanical performance. Synthetic polymers like poly-lactic co-glycolic acid (PLGA) [60], polyglycolic acid (PGA), poly-L-lactic-acid (PLLA) [61], polylactic acid (PLA) [62], graphene [63], and gelatin (Ge) [64] are used to make blended composites, and ceramics such as hydroxyapatite (HA), β-tricalcium phosphate (β-TCP), zinc oxide (ZnO), titanium oxide ($TiO_2$), bioglassetc [65,66].

## 5. PROCESSING TECHNIQUES FOR PCL COMPOSITES

To make blended PCL composites, several technologies such as electrospinning, melt blending and extrusion, solvent casting, 3D printing, and melt electrospinning can be employed [67,68]. The fabrication method is determined by the type of scaffold, such as porous or fibrous. These techniques influence the final morphology, porosity, mechanical strength, and degradation behavior of the composites, which are crucial for biomedical applications. Solvent casting is often used for simple film formation, whereas melt blending is favored for thermoplastic formulations. Electrospinning and 3D printing provide high-resolution scaffolds tailored for tissue engineering and regenerative medicine [69].

### 5.1. Electrospinning

Electrospinning is a widely used technique to fabricate nanofibrous scaffolds from PCL composites for biomedical applications. It enables the production of fibers with high surface area and porosity, closely mimicking the structure of natural extracellular matrix [70,71]. By incorporating bioactive materials or other polymers into the PCL solution, electrospun composites can achieve enhanced mechanical

strength and biological functionality. This method allows for controlled fiber diameter and alignment, which are important for guiding cell behavior and tissue regeneration. As a result, electrospun PCL composites are extensively used in wound healing, tissue engineering, and drug delivery systems [72].

### 5.2. Solvent Casting

Solvent casting is a simple and effective method used to fabricate PCL composites into thin films or membranes for biomedical applications. In this technique, PCL and reinforcing agents or bioactive fillers are dissolved in a suitable solvent and cast onto a flat surface, followed by solvent evaporation. This process allows uniform dispersion of additives, improving the composite's mechanical, thermal, and biological properties [64,73]. Solvent casting is ideal for incorporating drugs, nanoparticles, or natural polymers to enhance biocompatibility and functionality. PCL composite films produced by this method are commonly used in wound dressings, drug delivery systems, and barrier membranes [74].

### 5.3. Melt blending and extrusion

Melt blending and extrusion are widely used thermal processing techniques for fabricating PCL composites with improved mechanical and functional properties. In this method, PCL and reinforcing materials such as ceramics, polymers, or nanoparticles are mixed at elevated temperatures without using solvents, making the process environmentally friendly [75,76]. The molten mixture is then extruded into desired shapes like filaments, rods, or sheets suitable for biomedical applications. This technique ensures good dispersion of fillers and allows for scalable production with controlled composition and geometry. Melt-blended PCL composites are commonly used in orthopedic implants, scaffolds, and 3D printing filaments [76].

Table **2** summarizes the effect of different compositions and fabrication techniques on the functional performance of PCL-based scaffolds, highlighting how material combinations and processing routes influence their mechanical properties, degradation behavior, and biomedical applications.

### 5.4. 3D Printing/Additive Manufacturing

3D printing, or additive manufacturing, is a versatile technique used to fabricate complex and customized structures from PCL composites for biomedical applications. It allows precise control over scaffold architecture, porosity, and geometry, which is crucial for tissue engineering. By incorporating bioactive fillers or reinforcing agents into PCL, the printed composites can exhibit enhanced mechanical strength and biological performance.

This method supports the creation of patient-specific implants and drug delivery devices with tailored degradation profiles. PCL composites processed through 3D printing are widely applied in bone regeneration, cartilage repair, and soft tissue engineering. SLA, SLS, FDM, and bioprinting are some of the additive manufacturing (AM) processes utilized to create PCL-based scaffolds.These methods are reviewed in Table **3**.

## 6. BIOMEDICAL APPLICATIONS OF PCL-BASED COMPOSITES

Polycaprolactone-based composites have emerged as versatile platforms for various biomedical applications due to their biodegradability, tunable degradation, and ability to be processed into functional scaffolds [4, 28]. The key application areas are outlined below.

### 6.1. Tissue Engineering

PCL-based scaffolds have shown promising outcomes in bone, cartilage, and skin regeneration due to their tunable mechanics and biodegradability [15,31,53,54]. In a rabbit calvarial defect model, PCL/HA composites achieved ~65% new bone formation within 8 weeks, significantly outperforming pure PCL (~35%) [31,53]. Electrospun PCL nanofibers seeded with chondrocytes demonstrated a twofold increase in glycosaminoglycan (GAG) production compared to PLA-based scaffolds, indicating superior cartilage matrix deposition [30,59,62]. For skin repair, porous PCL dressings accelerated wound closure by ~40% compared to untreated controls, with improved angiogenesis and collagen deposition [51,64,74]. Vascular graft studies further report endothelialization rates above 80% within 30 days, comparable to or better than PLGA conduits [61,77].

### 6.2. Drug Delivery Systems

PCL carriers enable sustained drug release through a biphasic profile: an initial burst (surface drug) followed by diffusion- and degradation-controlled release lasting weeks to months [6,32,46]. For instance, doxorubicin-loaded PCL nanoparticles released ~30% in 24 h and ~85% over 30 days, while gentamicin-loaded microspheres maintained activity for >6 weeks [6,45,60]. Hydrophobic drugs (e.g., paclitaxel) show high encapsulation (>80%) and slower release due to strong affinity with PCL [4,49], whereas hydrophilic agents require stabilizers to avoid rapid release [46,50]. These features make PCL particularly effective for long-term cancer therapy, wound care, and growth factor delivery [6,44,45].

**Table 2*:* Effect of composition and fabrication Methods on Functional Characteristics of PCL Scaffold**

| Composite & configuration | Fabrication process used | Effect on functional properties | Degradation | Application | Ref. |
|---|---|---|---|---|---|
| PCL/rhBMP-2/HA | Extrusion based 3D printing | Enhanced the angiogenesis, osteoblastic differentiation of stem cells, and new bone formation. | - | Dental reconstructive surgery | [31,53,54] |
| PCL/PLGA 0.1:0.9,0.5:0.5, 0.9:0.1 | 3D printing | High porosity in 50:50 scaffold with high mechanical properties supporting load bearing application. | | Scaffold for human periodontal ligament stem cells application | [46,60] |
| PCL/PGA/HA PGA (0 & 25%) HA (0,10,20%) | Solvent extraction, extrusion based 3D printing | Enhanced mechanical properties, increased hydrophilicity & cell adhesion. | Enhanced degradation | Bone tissue engineering and resorbable barrier membrane | [4,42,55] |
| PCL/Ge/nHA ((70:30):15) | Electrospinning | Increased ALP activity, proliferation, cell adhesion, and mineral deposit on scaffold. | Faster degradation of scaffold | Bone tissue engineering | [51,52,64] |
| PCL/CA & PCL/CA/LA | Electrospinning | Enhanced cell spreading and proliferation | - | Regenerative medicine and tissue engineering applications | [47,64] |
| PCL | Solvent casting & fused deposition modeling | Increased stiffness, crystallinity | 1%-7% degradation & degradation is non-toxic at molecular level | Long term (2yrs) use and bone generation | [38,39,74] |
| PCL/SrHA 0,10,15% | Electrospinning | | Degradation rate: PCL < PCL/SrHA 10 % wt< PCL/SrHA 15 % wt. | Tissue engineering | [53,54,77] |
| PCL/PLA 16:4,18:2,9:1 | Two photon polymerization | Higher content of PCL results in higher compressive modulus but gradual decrease in compressive strength as a result of progressive mass loss over time. | Degradation rate: 16:4<18:2<9:1 Slower degradation as compared to PLA | Regenerative medicine and tissue engineering applications | [59,62] |
| PCL/PLLA & PCL/PCLA 50:50 | Dual cylinder chamber molding | | PCL/PLLA degradation rate is intermediate and increases with PLLA content | Tissue-engineered vascular grafts | [61,77] |
| PCL/β TCP (E beam treated) 100:0,80:20,60:40, 40:60 | Dissolution and precipitation phases, Pre-E-Beam Surface Treatment | - | Accelerated degradation due to E beam treating | Subcutaneous implantation | [55,56,58] |
| PCL/β-TCP 80:20 | Extrusion based 3D printing | Controlled porosity, improved mechanical properties | Increased degradation rate 60% porous material showed mass loss of 40% at 48 hrs | Osteonecrosis of the femoral head | [53,55,76] |
| PCL/Gelatin 70:30 | Electrospinning | - | Degradation rate: PCL<PCL/Gelatin | Skin tissue engineering application | [51,64,74] |
| PCL/HA/ZnO (ZnO 1,3,6%) | Electrospinning | Increased ALP activity followed by mineralization | ZnO accelerates scaffold degradation | Mid- and long-term resorption for accelerated bone tissue regeneration | [65,66,78] |
| PCl/TiO2 | Microsphere sintering | Good cell differentiation leading to ECM mineralization | | Load-bearing bone tissue engineering applications | [63,77,79] |

**Table 2 (Continue)**

| Composite & configuration | Fabrication process used | Effect on functional properties | Degradation | Application | Ref. |
|---|---|---|---|---|---|
| PCL coated TCP/Bioglass | lost sponge foam method | Formation of apatite on scaffold's surface | Coated specimen showed higher degradation than the uncoated scaffolds | Bone/tissue engineering | [65,66,80] |
| PCL/PTMC (1:1,1:3,3:1) | Electrospinning | Increased macrophage-mediated foreign body reaction | Degradation speed increases along with PTMC | - | [50,81,82] |

**Table 3: 3D Printing Methods for PCL Based Composites**

| 3D printing process | Advantages | Limitations | Ref. |
|---|---|---|---|
| SLA | High resolution, high precision, manufacturing of complicated shapes | Difficult to produce a micron-sized scaffold,photo initiator-induced cytotoxicity, limited layer thickness, expensive | [83,84] |
| SLS | Controlled porosity and pore size | Non-load bearing scaffolds, expensive, involves high temperatures | [85,86] |
| FDM | Easy to use, economical, controlled functional properties | Restricted resolution, involves high temperatures | [44,69,87] |
| Binder jet printing | Compatible with a range of materials, economical & fast | Limited resolution and direction of injection, low cell density | [88-90] |

### 6.3. Wound Healing

Electrospun PCL dressings loaded with silver nanoparticles or antibiotics improve antibacterial protection and maintain moisture balance at the wound site [5,45,64]. Growth-factor-incorporated scaffolds enhance angiogenesis and accelerate tissue repair [53,72,74].

### 6.4. Dental and Orthopedic Applications

Guided bone regeneration membranes made from PCL prevent soft tissue ingrowth and support bone repair [31,53,54]. PCL reinforced with HA or β-TCP mimics natural bone mineral and improves osteointegration in dental implants [55,56,76].

### 6.5. Nerve Regeneration and Neural Interfaces

PCL conduits provide structural guidance for axonal regrowth across nerve gaps [50,61]. While incorporation of conductive materials (e.g., CNTs, graphene) enhances electrical stimulation for neural repair [58,59,63]. These composites are also being explored in bioelectronic neural interfaces for signal transmission [57,58,77].

### 6.6. Environmental and Packaging Applications

Beyond biomedicine, PCL has gained attention in sustainable packaging and environmental remediation [18,22,23]. Under industrial composting conditions, PCL films typically degrade within 6-12 months, while in soil or aquatic environments, complete mineralization may require 2-3 years, depending on crystallinity and thickness [4,16,38]. In comparison, PLA shows faster degradation in compost (~3-6 months) but slower breakdown in soil due to lower microbial activity [23,28,62].

Lifecycle assessment (LCA) studies further highlight PCL's advantages: production generates up to 30-40% lower $CO_2$ emissions than conventional polyethylene when bio-based raw materials are used [27,73]. Moreover, PCL blends with starch or PLA not only accelerate degradation but also reduce environmental footprint without compromising mechanical properties [59,62,64].

## 7. RECENT ADVANCES AND INNOVATIONS

Recent innovations in PCL-based composites focus on creating multifunctional materials for advanced biomedical technologies. Smart composites are engineered to respond to physiological cues like pH and temperature, enabling controlled and site-specific drug delivery [91,92]. For example, PCL blended with thermo-responsive polymers can trigger drug release in response to temperature changes, while pH-sensitive versions target acidic tumor environments [99]. Another key area is targeted therapy, where PCL surfaces are functionalized with biomolecules to deliver therapies directly to specific cells [92,93]. PCL scaffolds are also a frontier in gene delivery, providing localized and sustained release platforms for genetic

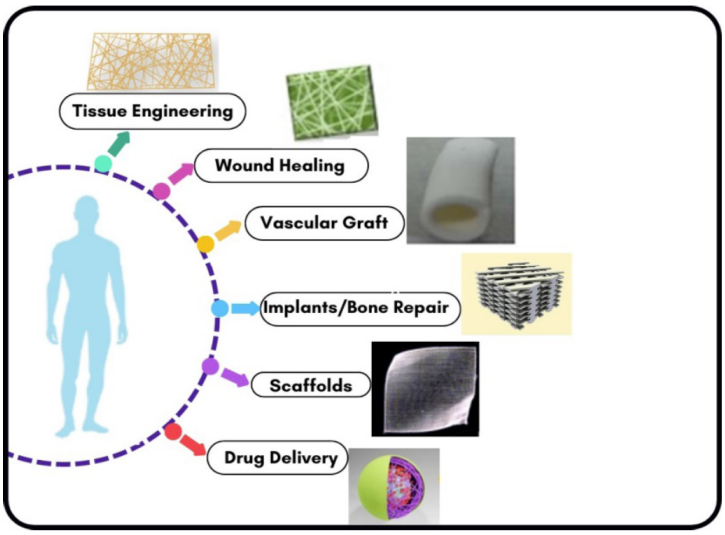


**Figure 2:** Biomedical applications of PCL composites.

materials like DNA, siRNA, and CRISPR/Cas9 components to promote tissue regeneration and treat diseases [93,94].

### 7.1. AI-Driven Scaffold Design and Machine Learning Applications

The integration of artificial intelligence (AI) and machine learning (ML) has become a transformative approach in PCL composite design. Predictive models use complex algorithms to optimize scaffold architecture and processing parameters, significantly reducing development time and costs [95]. AI-guided methods can predict a scaffold's mechanical properties and refine 3D printing parameters for improved uniformity [95,96]. Additionally, ML models can forecast a composite's performance, including degradation and drug release kinetics, before physical testing [96]. By analyzing vast datasets and scientific literature, these computational tools are accelerating knowledge discovery, making AI an indispensable part of next-generation PCL development [95,96].

### 7.2. Clinical Translation and Market Impact

In terms of clinical translation, PCL-based products have successfully bridged the gap from laboratory research to commercial application. Several bioresorbable medical devices, such as the Neurolac® nerve conduit and the Osteoplug® cranial implant, have gained regulatory approvals after demonstrating their safety and efficacy in clinical trials, including a randomized controlled trial (NCT01119144) that found a PCL/Tricalcium Phosphate implant to be a safe alternative to titanium [97]. This clinical success is a major catalyst for the PCL market, which is projected to grow from its 2022 valuation of approximately $950 million to over $1.1 billion by 2030 [97]. Driven by a robust compound annual growth rate (CAGR) of nearly 10%, the healthcare sector is a primary force in this expansion, confirming the strong market penetration and commercial viability of these advanced bioresorbable devices [97].

PCL's cost-effectiveness is a key factor in its commercial success. Compared to other biomedical polymers and traditional materials, its relatively low production cost makes it an attractive option. This economic advantage, combined with its favorable properties and the potential to reduce long-term healthcare costs by avoiding implant removal surgeries, positions PCL as a commercially viable and competitive material in the growing medical device market.

## 8. CHALLENGES AND FUTURE PERSPECTIVES

Despite the growing promise of PCL-based composites in biomedical applications, several key challenges must be addressed to enable their broader clinical translation and commercial success.

### 8.1. Scalability and Reproducibility

While laboratory-scale fabrication techniques allow for precise control over composition and structure, scaling up these processes often results in variability in material properties, porosity, and drug loading efficiency [98,99]. This inconsistency hampers large-scale production and limits the feasibility of standardized medical devices and implants. Advanced manufacturing protocols and robust quality control systems are therefore needed to ensure batch-to-batch reproducibility and compliance with medical standards [98]. To address these challenges, adherence to international standards is paramount. Organizations such as the International Organization for Standardization (ISO) and ASTM International have

established comprehensive guidelines that govern the biological evaluation, mechanical testing, and quality management systems for medical devices [100]. For example, standards within the ISO 10993 series ensure the biocompatibility of PCL by providing protocols for *in vitro* and *in vivo* testing, while specific ASTM standards, such as F2902, offer guidance for the assessment of absorbable polymeric implants [101]. By implementing these standards, manufacturers can establish robust quality control protocols that ensure batch-to-batch consistency in material properties and performance, thereby facilitating the transition from lab-scale prototypes to reliable, mass-produced medical devices [102].

### 8.2. Long-term Biocompatibility

Although PCL is generally well-tolerated and approved by regulatory agencies, the inclusion of additives, fillers, or surface modifications can alter its degradation profile and elicit unexpected immune responses over extended periods [44]. Comprehensive *in vivo* studies, including chronic implantation models, are essential to evaluate the safety and functionality of composite materials over their entire lifespan within the body.

### 8.3. Regulatory Issues

These issues also present considerable barriers to clinical translation. The multi-component nature of PCL-based composites often involving drugs, biologics, or nanoparticles places them in complex regulatory categories that vary between regions. The lack of standardized testing protocols and inconsistent classification systems can delay product approval and market entry [100,101]. There is a growing need for harmonized guidelines and collaborative efforts between researchers, industry stakeholders, and regulatory bodies to streamline the path from bench to bedside [102].

### 8.4. Integration with Digital Manufacturing

In the realm of manufacturing, the integration of PCL composites with digital fabrication technologies such as 3D and 4D printing represents a promising yet underexplored frontier [98,103]. These technologies allow for the creation of patient-specific implants and dynamic scaffolds that can change shape or function in response to environmental cues [103]. However, the development of PCL formulations that are both printable and retain desirable mechanical and biological properties is still in its infancy. Further research is needed to optimize composite inks, printing parameters, and post-processing methods to fully leverage these innovations.

### 8.5. Multidisciplinary collaborations for next-gen Applications

Finally, the advancement of next-generation biomedical applications will require strong multidisciplinary collaboration. The convergence of materials science, biology, engineering, data science, and clinical medicine is essential for the design of intelligent, biofunctional PCL-based systems [103]. For instance, integrating machine learning algorithms for scaffold design or combining PCL composites with gene-editing tools like CRISPR demands coordinated expertise across domains. Funding mechanisms, shared research platforms, and translational consortia will play a critical role in fostering these collaborations and accelerating innovation in the field.

### 8.6. Intellectual Property Landscape

In the medical device industry, the intellectual property (IP) landscape is critical for commercial success, and PCL-based technologies are no exception [102]. Patents are a fundamental tool, providing companies with exclusive rights to their innovations, which in turn secures their market position and attracts crucial investment for research and development. This is especially true for complex technologies like PCL composites and 3D-printed implants, where a strong IP portfolio is a valuable assets [44]. The IP landscape for PCL includes patents on new materials, specific device designs, and innovative manufacturing processes, all of which are essential for navigating regulatory hurdles and achieving global market entry [103].

## 9. CONCLUSION

### 9.1. Summary of Key Findings

This review has comprehensively explored the properties, fabrication strategies, and biomedical applications of Polycaprolactone (PCL)-based composites. PCL's unique combination of biocompatibility, biodegradability, mechanical flexibility, and FDA approval makes it a highly attractive base material for a wide range of biomedical uses. The incorporation of natural polymers, ceramics, and nanomaterials into PCL has enabled the development of multifunctional composites with enhanced biological performance, tailored degradation rates, and improved mechanical integrity. Applications in tissue engineering, drug delivery, wound healing, and dental and orthopedic devices demonstrate the versatility and impact of PCL composites across diverse medical domains. Furthermore, the emergence of smart, stimuli-responsive systems and gene-delivery scaffolds highlights the adaptability of PCL platforms to meet next-generation biomedical demands.

### 9.2. Importance of PCL Composites in Advancing Biomedical Technology

PCL-based composites represent a vital advancement in the design of bioengineered systems due to their ability to bridge material science and medical functionality. Their tunable properties allow for the creation of personalized, patient-specific devices, while their compatibility with advanced fabrication methods such as electrospinning and 3D printing positions them at the forefront of regenerative medicine. Additionally, the ease of chemical modification and capacity to host therapeutic agents make PCL composites ideal candidates for multifunctional biomedical platforms. These features collectively underscore the strategic role of PCL composites in driving innovation in tissue regeneration, targeted therapy, and bioresorbable medical devices.

### 9.3. Outlook on Future Development Paths

Looking ahead, the future of PCL-based composites lies in addressing current challenges while harnessing emerging technological frontiers. Focused efforts are needed to improve long-term biocompatibility, standardize large-scale manufacturing, and navigate complex regulatory frameworks. The integration of digital manufacturing techniques such as 4D printing and the incorporation of biosensors, gene-editing tools, and smart drug release systems offer promising avenues for next-generation applications. Moreover, fostering multidisciplinary collaboration across materials science, bioengineering, data science, and clinical practice will be essential for translating laboratory innovations into real-world clinical solutions. With continued research and strategic development, PCL composites are poised to play a transformative role in the evolution of biomedical technologies.

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## COMPETING INTEREST DECLARATION

The authors declare that they have no competing interests.

## AUTHOR CONTRIBUTIONS

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