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# Controlled Degradation in Bone Tissue Scaffolds: A Review of PCL-Enhanced PLA Composites with Naturally Derived Hydroxyapatite

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### ABSTRACT

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Bone tissue engineering demands scaffolds with degradation rates that precisely match natural bone regeneration, a challenge that has driven research into composite biomaterials. Traditional polymer-based scaffolds often exhibit sub-optimal degradation profiles, with polylactic acid (PLA) typically degrading too rapidly while creating potentially harmful acidic environments. This review examines how polycaprolactone (PCL) enhances PLA scaffolds in reinforcing naturally derived hydroxyapatite (HAp) from cockle shell to achieve tuneable degradation behaviour for bone tissue applications. Literature review of various PCL/PLA ratios indicates that compositions containing 30-50% PCL have been reported to provide favourable degradation profiles while maintaining adequate mechanical support throughout the regeneration process. Current research demonstrates that PCL-enhanced PLA/HAp composites exhibit more gradual degradation with improved mechanical property retention compared to single-polymer systems. However, significant gaps remain in understanding the complex interactions between HAp synthesis parameters and polymer degradation mechanics, as well as in establishing reliable correlations between in vitro and in vivo performance. Future research should focus on systematically investigating these relationships while developing advanced manufacturing techniques that precisely control spatial component distribution for optimized degradation profiles that match specific anatomical requirements.

## 1. Introduction

Bone disorders and injuries represent a significant global health burden, with an estimated 2.2 million bone grafting procedures performed annually worldwide [1]. While autologous bone grafts remain the gold standard for treatment, they are limited by donor site morbidity and restricted availability [2]. These limitations have driven the development of tissue-engineered alternatives, with bone scaffolds emerging as a promising approach to address the growing clinical need for bone replacement solutions.

The ideal bone scaffold must possess appropriate mechanical properties, biocompatibility, osteoconductivity, and critically, a degradation rate that matches the pace of new bone formation

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[3]. When degradation occurs too rapidly, mechanical support is lost before sufficient new bone has formed; conversely, overly slow degradation can impede tissue integration and remodeling [4]. This challenge of controlled degradation has become a central focus in bone tissue engineering research.

Biodegradable polymers, particularly polylactic acid (PLA), have been extensively investigated for bone scaffold applications due to their biocompatibility and tunable properties. However, PLA-based scaffolds often exhibit limitations in terms of degradation behavior, with relatively rapid hydrolytic degradation leading to accelerated mechanical failure and potential inflammatory responses due to acidic degradation products [5]. The incorporation of polycaprolactone (PCL), a biodegradable polyester with slower degradation kinetics—into PLA matrices has emerged as a promising strategy for creating composite systems with more controlled degradation profiles [6,7].

Hydroxyapatite (HAp,  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ), the primary inorganic component of natural bone, is frequently incorporated into polymer scaffolds to enhance osteoconductivity and mechanical properties. Naturally derived HAp from marine sources such as cockle shells has gained increasing attention due to its sustainability, cost-effectiveness, and potential for superior biocompatibility [8]. Cockle shells, abundantly available as food industry waste in coastal regions, contain high-purity calcium carbonate (95-98%) that can be converted to HAp through appropriate synthesis methods [9].

This review aims to comprehensively examine the current state of knowledge regarding controlled degradation in bone tissue scaffolds, with specific focus on PCL-enhanced PLA composites incorporating naturally derived HAp. The paper systematically analyzes the synthesis methods for biogenic HAp from marine sources, particularly cockle shells, and how synthesis parameters influence HAp characteristics. It further explores the fabrication techniques for PCL/PLA/HAp composite scaffolds and their impact on structural and mechanical properties, along with the degradation mechanisms in these composite systems, with emphasis on how PCL modulates the degradation behavior of PLA/HAp scaffolds [10]. Additionally, this review investigates the relationship between material composition, processing conditions, and resultant degradation profiles, ultimately identifying current research gaps and future directions for optimizing degradation control in bone tissue scaffolds.

## **2. Bone Tissue Engineering: Principles and Requirements**

### ***2.1 Structure and Composition of Natural Bone Tissue***

Bone is a complex, hierarchically structured tissue that serves multiple critical functions in the body, including mechanical support, protection of vital organs, mineral homeostasis, and hematopoiesis [11]. Understanding the intricate composition and structure of natural bone is essential for developing effective bone tissue engineering strategies.

At the macroscopic level, bone exists in two primary forms: cortical (compact) bone and cancellous (trabecular) bone. Cortical bone, which constitutes approximately 80% of the skeletal mass, is characterized by its dense, organized structure with low porosity (5-10%) and high mechanical strength (compressive strength of 100-230 MPa) [12]. In contrast, cancellous bone exhibits a highly porous (50-90%), sponge-like architecture with interconnected trabeculae, providing a significantly larger surface area for metabolic activities while maintaining lower mechanical strength (compressive strength of 2-12 MPa) [4].

At the compositional level, bone consists of approximately 65% inorganic components, 25% organic matrix, and 10% water by weight [13]. The inorganic phase is primarily composed of hydroxyapatite (HAp) nanocrystals ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ), which provide rigidity and compressive strength. These HAp crystals are not stoichiometrically pure but contain various ionic substitutions

(e.g., carbonate, magnesium, sodium) that influence their biological and mechanical properties [14]. The organic phase consists predominantly of type I collagen (90%), with the remaining 10% comprising non-collagenous proteins, proteoglycans, and glycoproteins that contribute to bone's biological functions and viscoelastic properties.

The hierarchical organization of bone spans multiple length scales, from the nanoscale arrangement of collagen fibrils and HAp crystals to the macroscale architecture of osteons in cortical bone and trabeculae in cancellous bone. This hierarchical structure enables bones to achieve its remarkable combination of strength and toughness while maintaining relatively low density [10]. Furthermore, bone is a dynamic tissue that undergoes continuous remodeling through the coordinated activities of osteoblasts (bone-forming cells), osteoclasts (bone-resorbing cells), and osteocytes (mature bone cells embedded within the mineralized matrix), allowing for adaptation to mechanical loads and repair of microdamage.

## 2.2 Essential Requirements for Effective Bone Tissue Scaffolds

The complex nature of bone tissue presents significant challenges for the development of effective bone scaffolds. An ideal bone scaffold should possess several key characteristics to successfully support bone regeneration.

### 2.2.1 Mechanical properties

Mechanical compatibility with the surrounding bone tissue is crucial for scaffold functionality. The scaffold should provide sufficient mechanical support to withstand physiological loads while avoiding stress shielding effects that can lead to bone resorption [15]. The mechanical requirements vary depending on the specific application site, with load-bearing regions (e.g., femur, tibia) demanding higher strength compared to non-load-bearing areas. Generally, compressive strength of 2-12 MPa for cancellous bone replacement and 100-230 MPa for cortical bone replacement, with an elastic modulus in the range of 0.05-0.5 GPa and 15-20 GPa, respectively, are considered appropriate [16].

Additionally, the scaffold should exhibit appropriate fatigue resistance and fracture toughness to withstand cyclic loading. The mechanical properties should ideally evolve over time as the scaffold degrades and new bone forms, maintaining structural integrity throughout the regeneration process. Table 1 simplified the mechanical properties comparison among different location and type of bone in musculoskeletal system of human body. From the table, it can be seen that the natural bone exhibits complex mechanical behaviour, with cortical bone showing compressive strength of 100 – 230 MPa and Young's modulus of 7 – 30 GPa (Gonzalez-Sanchez et al., 2024; Ingole et al., 2021). Current synthetic scaffolds often struggle to match these properties while maintaining adequate porosity for cell infiltration and vascularization (Wilson & Brown, 2023).

Table 1. Mechanical Properties Comparison

| Material                | Compressive Strength<br>(MPa) | Young's Modulus<br>(GPa) | Reference                     |
|-------------------------|-------------------------------|--------------------------|-------------------------------|
| Natural cortical bone   | 100 – 230                     | 7 – 30                   | Gonzalez-Sanchez et al., 2024 |
| Natural cancellous bone | 2 – 12                        | 0.05 – 0.5               | Oftadeh et al., 2015          |
| PCL scaffold            | 2 – 4                         | 0.4 – 0.6                | Domingos et al., 2017         |

|                                |          |           |                             |
|--------------------------------|----------|-----------|-----------------------------|
| PLA scaffold                   | 40 – 120 | 1.2 – 3.0 | Serra et al., 2013          |
| HAp scaffold                   | 30 – 100 | 70 – 120  | Mondal et al., 2016         |
| PCL/HAp composite<br>(10% HAp) | 5 – 15   | 0.5 – 0.8 | Rezaei &<br>Mohammadi, 2018 |
| PCL/HAp composite<br>(30% HAp) | 15 – 30  | 0.8 – 1.5 | Wong et al., 2023           |
| PLA/HAp composite<br>(20% HAp) | 50 – 90  | 2.5 – 4.5 | Shahabi et al., 2020        |
| PCL/PLA/HAp<br>composite       | 35 – 75  | 1.5 – 3.0 | Wang et al., 2021           |
| Calcium phosphate<br>cement    | 10 – 100 | 0.5 – 15  | Zhang et al., 2014          |
| Bioactive glass                | 40 – 60  | 30 – 50   | Fu et al., 2011             |

### *2.2.2 Biocompatibility*

Biocompatibility encompasses the scaffold's ability to support normal cellular activity without eliciting undesirable local or systemic effects [17]. This includes absence of cytotoxicity, immunogenicity, and carcinogenicity; support of cell adhesion, proliferation, and differentiation; appropriate interaction with the host immune system; and generation of non-toxic degradation products that can be metabolized or excreted safely. The scaffold's surface chemistry and topography play crucial roles in determining cell-material interactions, influencing protein adsorption, cell attachment, and subsequent cellular responses [18].

### *2.2.3 Biodegradability*

Controlled biodegradability is a critical requirement for bone scaffolds, as they are intended to serve as temporary templates rather than permanent implants. The ideal scaffold should degrade at a rate that matches the pace of new bone formation, gradually transferring load-bearing responsibilities to the regenerating tissue [19]. This synchronized degradation-regeneration process is challenging to achieve due to variations in bone healing rates among different patients and anatomical sites.

The degradation mechanism should produce biocompatible breakdown products and avoid sudden mechanical failure or adverse local tissue responses due to pH changes or particulate accumulation. Furthermore, the degradation process should not compromise the scaffold's mechanical integrity prematurely [20].

### *2.2.4 Porosity and Architecture*

The scaffold's architectural features significantly influence its biological and mechanical performance. Key considerations include several important aspects. An overall porosity of 60-90% is generally considered optimal for bone regeneration, balancing mechanical strength with mass transport requirements [21]. Regarding pore size, macropores (100-350  $\mu\text{m}$ ) facilitate cell migration, vascularization, and new bone ingrowth, while micropores (<20  $\mu\text{m}$ ) enhance protein adsorption and cell attachment through increased surface area [22]. Pore interconnectivity is essential for cell migration, nutrient/waste transport, and vascularization throughout the scaffold volume. Additionally, micro- and nano-scale surface features influence protein adsorption, cell attachment,

and cellular differentiation. The scaffold architecture should ideally mimic the hierarchical structure of natural bone, incorporating features across multiple length scales to recapitulate both the biological and mechanical aspects of the native tissue [14].

### *2.2.5 Biological Activity*

Beyond serving as a passive structural template, an ideal bone scaffold should actively promote osteogenesis through several biological mechanisms. Osteoconductivity refers to the ability to support bone cell attachment, migration, and growth along the scaffold surface. Osteoinductivity describes the capacity to stimulate undifferentiated progenitor cells to differentiate into bone-forming osteoblasts. Osteogenicity involves the presence of bone-forming cells within the scaffold (typically achieved through cell seeding rather than material properties). These biological properties can be enhanced through the incorporation of bioactive components such as growth factors, cell-binding motifs, or ions (e.g.,  $\text{Sr}^{2+}$ ,  $\text{Mg}^{2+}$ ,  $\text{Zn}^{2+}$ ) that stimulate osteoblast activity or angiogenesis [23].

## *2.3 Current Approaches and Limitations in Bone Tissue Engineering*

Current approaches to bone tissue engineering employ various strategies to address the complex requirements outlined above, each with specific advantages and limitations.

### *2.3.1 Material-Based Approaches*

#### *2.3.1.1 Polymer-Based Scaffolds*

Biodegradable polymers, including natural (e.g., collagen, chitosan, alginate) and synthetic varieties (e.g., PLA, PCL, PLGA), offer tunable degradation rates and processing versatility. However, they typically lack sufficient mechanical strength for load-bearing applications and possess limited bioactivity [24].

#### *2.3.1.2 Ceramic-Based Scaffolds*

Bioceramics such as HAp and  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) demonstrate excellent biocompatibility and osteoconductivity but are often brittle and difficult to process into complex architectures. Their degradation rates can be challenging to control, particularly for HAp, which exhibits very slow resorption in vivo [25].

#### *2.3.1.3 Composite Scaffolds*

Composite approaches combining polymers and ceramics aim to harness the advantages of both material classes. Polymer/ceramic composites can achieve improved mechanical properties compared to polymers alone, along with enhanced bioactivity. However, achieving homogeneous distribution of the ceramic phase within the polymer matrix and optimizing the interface between components remain significant challenges [26].

Despite significant advancements, several limitations persist in current bone tissue engineering approaches. Degradation rate mismatch remains a significant challenge, as achieving synchronized degradation with new bone formation is difficult, with many scaffolds degrading either too rapidly or too slowly relative to the bone regeneration process [4,18]. Maintaining adequate mechanical

support throughout the degradation process is problematic, with many scaffolds experiencing premature strength loss. Insufficient vascularization in larger constructs leads to necrotic core formation and limited regeneration in the scaffold interior [16]. Scalability and manufacturing challenges arise when translating laboratory-scale fabrication techniques to clinically relevant dimensions while maintaining precise control over scaffold architecture [14]. Additionally, effectively incorporating bioactive components while preserving their activity during processing and sterilization presents significant hurdles in biological activity optimization.

## *2.4 Clinical Perspectives and Challenges*

From a clinical perspective, several additional considerations impact the successful translation of bone tissue engineering approaches. Bone healing capacity varies significantly among patients based on age, health status, and genetic factors, with elderly patients, those with compromised vascular supply, or conditions such as osteoporosis or diabetes often exhibit impaired bone regeneration potential, necessitating enhanced scaffold performance [11]. Different anatomical locations present unique challenges regarding mechanical loading, vascular supply, and tissue interfaces; for instance, craniofacial applications may prioritize aesthetic outcomes and complex geometries, while load-bearing long bone applications demand superior mechanical performance [27,28]. The translation of novel bone scaffolds to clinical use faces regulatory hurdles related to manufacturing consistency, sterilization effects, shelf life, and clinical validation, with the complexity of composite systems incorporate multiple components further complicating the regulatory pathway [29]. Additionally, the economic viability of advanced bone tissue engineering approaches compared to conventional treatments influences their clinical adoption, making sustainable and cost-effective material sourcing, such as utilizing naturally derived HAp from waste materials like cockle shells, a promising direction for addressing these economic considerations [9].

## **3. Material Components**

### *3.1 Ceramic Materials*

Hydroxyapatite (HAp,  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ) is the principal inorganic constituent of natural bone, comprising approximately 65-70% of bone tissue by weight [29]. Naturally derived HAp from sources such as cockle shells offers significant advantages over synthetic HAp, including closer resemblance to biological apatite, enhanced bioactivity, and sustainability benefits [30]. Cockle shells contain high-purity calcium carbonate (95-98%) in aragonite form, which can be converted to HAp through various synthesis methods. This waste-to-biomaterial approach addresses environmental concerns while creating value-added products for medical applications. Figure 1 shows the schematic illustration of the wet precipitation method for synthesizing HAp from cockle shells, showing key processing steps and parameters that influence the characteristics of the resulting HAp particles.

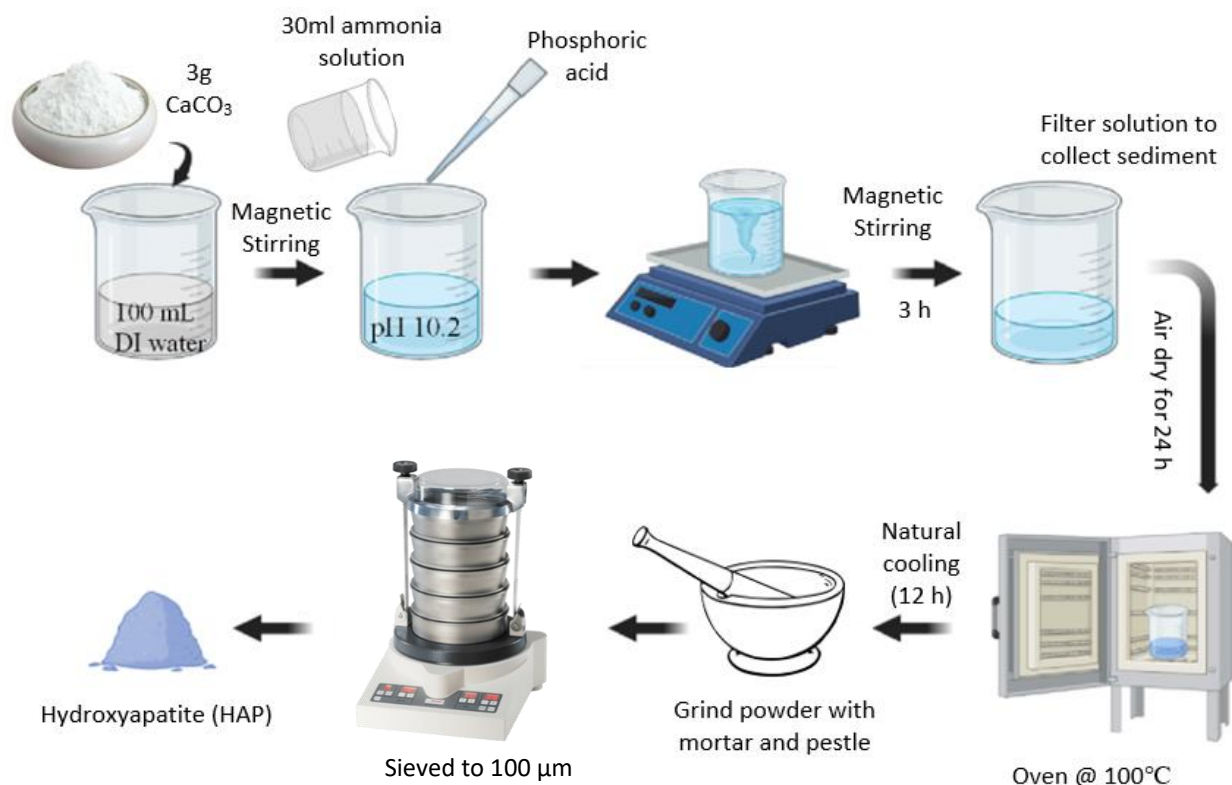


**Fig. 1.** Schematic illustration of the wet precipitation method for synthesizing hydroxyapatite from cockle shells

The wet precipitation method represents the most common approach for converting cockle shells to HAP, offering good control over particle characteristics through key parameters: temperature (60-80°C), pH (9-11), and aging time (24-48 hours). These parameters significantly influence HAP crystallinity, particle size, and morphology, which subsequently affect degradation behaviour when incorporated into polymer composites. Cockle shell-derived HAP typically exhibits nano-scale dimensions (20-100 nm) with moderate crystallinity, providing good surface area for cell interactions while enabling controlled degradation in polymer matrices.

### 3.2 Polylactic Acid (PLA)

Polylactic acid (PLA) is a biodegradable aliphatic polyester derived from renewable resources that has been widely employed in bone tissue engineering due to its biocompatibility and relatively good mechanical properties. PLA exists in different forms depending on lactic acid stereochemistry, with semi-crystalline PLLA exhibiting higher mechanical strength (tensile strength 50-70 MPa, Young's modulus 3-4 GPa) and slower degradation [6]. Degradation occurs primarily through hydrolytic cleavage of ester bonds, influenced by stereochemistry, molecular weight, crystallinity, and environmental factors like pH and temperature.

Despite its advantages, PLA exhibits several limitations for bone scaffold applications [31]. Its relatively high stiffness and brittleness can cause mechanical mismatch with natural bone, particularly in areas subject to cyclic loading. PLA's degradation profile often misaligns with bone regeneration timelines, and its acidic degradation products can create local inflammatory environments if not effectively buffered. Furthermore, PLA shows limited bioactivity regarding cell

attachment and osteogenic differentiation, necessitating modification with bioactive components for enhanced biological performance in bone applications.

### **3.3 Polycaprolactone (PCL)**

Polycaprolactone (PCL) is a semi-crystalline aliphatic polyester characterized by slower degradation, excellent processability, and greater mechanical flexibility compared to PLA. PCL exhibits significantly different properties, including lower stiffness (Young's modulus 0.2-0.4 GPa), higher elongation at break (300-800%), lower glass transition temperature (-60°C), and lower melting point (60°C). These characteristics make PCL valuable for applications requiring flexibility and fatigue resistance, complementing PLA's higher stiffness but more brittle nature.

PCL's integration into PLA matrices offers an effective strategy for modulating scaffold degradation through several mechanisms. Its hydrophobicity reduces water uptake, potentially slowing PLA hydrolysis, while its flexibility helps maintain structural integrity during degradation, preventing catastrophic mechanical failure as PLA degrades. PCL's significantly slower degradation (2-4 years versus 1-2 years for PLA) provides continued support as PLA resorbs, allowing more gradual load transfer to regenerating tissue. The PCL/PLA ratio represents a critical parameter for controlling degradation, with higher PCL content generally resulting in more gradual degradation profiles and improved mechanical stability, though potentially reducing initial scaffold stiffness.

## **4. Fabrication Techniques for Composite Scaffolds**

### **4.1 Conventional Methods**

Conventional fabrication techniques for PCL/PLA/HAP composite scaffolds include solvent casting/particulate leaching, which offers simplicity and good porosity control but limited pore interconnectivity; and freeze-drying, which creates highly porous structures with interconnected pores but often compromised mechanical properties. Melt blending approaches utilize the thermoplastic nature of both PLA and PCL, avoiding organic solvents while presenting challenges in HAP distribution and potential polymer degradation during high-temperature processing. These conventional methods provide accessible routes for composite scaffold fabrication but offer limited control over internal architecture and often struggle with achieving homogeneous HAP distribution.

### **4.2 Advanced Fabrication Techniques**

Advanced fabrication technologies like additive manufacturing (3D printing) enable precisely controlled scaffold architecture based on computer designs, allowing for patient-specific scaffold production and functionally graded structures. Electrospinning produces fibrous structures that mimic extracellular matrixes with high surface area-to-volume ratios favorable for cell attachment, though challenges include relatively low mechanical strength and difficulties in creating thick three-dimensional structures. These advanced techniques offer improved control over scaffold architecture compared to conventional methods but require careful optimization of processing parameters to maintain the properties of each component, particularly the bioactivity of naturally derived HAP and the degradation characteristics of the polymer blend.

### **4.3 Processing-Structure-Property Relationships**

The fabrication technique significantly influences composite scaffold properties through its effect on HAp distribution, polymer-HAp interface quality, and phase separation between PCL and PLA. Solution-based methods typically achieve more homogeneous HAp distribution and better polymer mixing compared to melt processing, which often results in particle agglomeration and phase separation. These structural characteristics directly affect mechanical properties and degradation behavior, with homogeneous structures generally exhibiting more predictable and controlled degradation profiles. The challenge in optimizing PCL/PLA/HAp composite scaffolds lies in selecting processing techniques that achieve desired structural features while preserving the individual properties of each component that contribute to controlled degradation behavior.

## **5. Degradation Behavior**

### ***5.1 Degradation Mechanisms***

PCL/PLA/HAp composite scaffolds undergo complex degradation involving multiple mechanisms. PLA typically experiences bulk hydrolytic degradation over 12-24 months, while PCL undergoes slower, more surface-oriented degradation spanning 24-48 months [5,6]. Naturally derived HAp introduces additional complexity by affecting water uptake patterns, buffering acidic degradation products from PLA, and gradually dissolving in physiological environments [20]. The interface between HAp particles and polymer matrix often serves as the initial degradation site, with preferential water accumulation accelerating local hydrolysis [20]. This interplay creates a dynamic degradation environment that evolves as the relative composition changes during the degradation process.

### ***5.2 PCL as a Degradation Modulator***

PCL effectively modulates degradation in PLA/HAp scaffolds by maintaining structural integrity after PLA has substantially degraded, providing continued mechanical support during intermediate and later regeneration stages. Its hydrophobic nature reduces overall water uptake, potentially slowing PLA hydrolysis, while its elastomeric properties help maintain structural cohesion as degradation proceeds. The PCL/PLA ratio critically influences degradation behaviour, with higher PCL content generally resulting in more gradual degradation profiles. Studies suggest PCL contents of 30-50% often provide favourable degradation characteristics for bone applications, though optimal ratios depend on specific anatomical requirements and patient factors [17,24].

### ***5.3 Effect of HAp Characteristics on Degradation***

Key characteristics of naturally derived HAp significantly impact composite scaffold degradation. Nano-scale HAp (20-100 nm) typically provides more effective buffering of acidic degradation products compared to micro-scale particles due to higher surface area. Lower crystallinity HAp, common in naturally derived sources, exhibits faster dissolution that can better match polymer degradation and tissue regeneration rates [10]. Synthesis parameters directly influence these properties—higher temperatures (70-80°C) yield more crystalline, stable HAp; higher pH values (10-11) produce more stoichiometric HAp with improved stability; and extended aging periods (36-48 hours) result in more stable crystalline structures [31]. Optimizing these parameters allows tailoring HAp characteristics to achieve desired composite degradation profiles.

## **5.4 In Vitro and In Vivo Degradation Studies**

In vitro degradation studies typically assess mass loss, molecular weight reduction, mechanical property evolution, pH changes, and morphological transformations in physiological solutions. Results show PCL-enhanced PLA/HAp composites generally exhibit more gradual degradation with less pronounced initial burst degradation than PLA/HAp systems [24]. In vivo studies, though limited, demonstrate more rapid initial degradation compared to in vitro conditions due to enzymatic activity and dynamic fluid exchange, but maintain the relative pattern among different compositions. Naturally derived HAp generally elicits favourable biological responses including reduced inflammation compared to polymer-only scaffolds. The imperfect correlation between in vitro and in vivo results highlights the need for more sophisticated models and extended studies to better predict long-term degradation behaviour under physiological conditions.

## **6. Research Gaps and Future Directions**

### **6.1 Current Limitations and Challenges**

For manuscript publication several critical gaps remain in understanding PCL-enhanced PLA composites with naturally derived HAp. Knowledge of interactions between cockle shell-derived HAp and polymer matrices during degradation is limited, particularly regarding how specific HAp characteristics influence degradation mechanisms [18]. The relationship between HAp synthesis parameters and final scaffold properties requires systematic investigation, as does the HAp-polymer interface that significantly affects mechanical and degradation behavior. Methodological challenges include lack of standardized degradation protocols, scarcity of long-term in vivo studies, poor correlation between in vitro and in vivo results, and difficulties in scaling up fabrication while maintaining consistent properties—especially for composites with naturally-derived components subject to batch variations.

### **6.2 Emerging Trends and Future Research Directions**

Promising approaches to address current limitations include surface functionalization of naturally derived HAp to enhance polymer interfaces, development of gradient or multiphasic scaffolds for region-specific degradation optimization, and advanced manufacturing techniques to achieve hierarchical biomimetic structures [14,30]. Computational modeling is increasingly valuable for predicting degradation behavior before physical fabrication, while stimuli-responsive elements could enable "smart" scaffolds with adaptive degradation profiles [22]. Priority research should focus on systematically investigating relationships between HAp synthesis parameters (temperature, pH, aging time) and composite performance, optimizing polymer ratios for specific anatomical applications, developing functionalized naturally derived HAp that enhances biological activity while maintaining controlled degradation, and creating manufacturing approaches that precisely control spatial component distribution. Integration with advanced tissue engineering strategies, such as pre-vascularization or stem cell incorporation, represents a promising direction for addressing complex bone regeneration requirements while maintaining controlled degradation profiles.

## **7. Conclusions**

This review has examined the controlled degradation behavior of PCL-enhanced PLA composite scaffolds incorporating naturally derived hydroxyapatite, with particular focus on cockle shell-derived

HAp as a sustainable biomaterial source. The integration of these three components offers a promising approach for optimizing degradation rates in bone tissue engineering, with naturally derived HAp providing bioactivity and sustainability advantages while PCL modulates degradation kinetics by maintaining structural support as the faster-degrading PLA component is resorbed. Despite significant advances, important research gaps remain regarding HAp synthesis optimization, component interface characterization, and correlation between laboratory and clinical performance. Addressing these challenges will contribute to developing next-generation scaffolds with precisely controlled degradation profiles that match natural bone regeneration processes while supporting sustainability goals through waste material utilization in high-value biomedical applications.

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