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A Review: Calcium Carbonate ($CaCO_3$) Extract from Natural Ceramics for Thin Film Application

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Abstract: $CaCO_3$ is widely used as one of the main materials in bone tissue engineering. The biodegradable material used is thin films and has been widely recognized as a prospective approach to altering a biomaterial's surface properties. Ideal thin films must be able to imitate mechanical and biological properties besides supporting the growth of large tissue constructions. Different uses of procedures, tools, and processing requirements have led to the development of several layer-by-layer assembly techniques that are widely used in porous membranes, particles, and biological matters. Employing new ways of nature-based materials such as mineral products extracted from $CaCO_3$ has caused the increasing demands for natural materials that can be easily fulfilled by using cockle shells, eggshells, or fish scales as main sources due to their availability and low cost. $CaCO_3$ biomaterial derived from cockle shells is the preferable alternative due to environmental sustainability and the effective usage of mineralized seashell by-products. The thin film is expected to be incorporated at bone surfaces to control tissue-biomaterial interaction and have mechanical properties similar to soft biological tissues.

Keywords: calcium carbonate; tissue engineering; biomaterial; cockle shells.

1. Introduction

Tissue engineering not only focuses on the development of implants that are used to replace organs and tissues but also concentrates on the production and synthesis of active biological materials that help construct new tissues and retain the essential functions of living organisms. Due to the limitless supply and lack of disease transmission, engineered bone tissue is an alternative to the traditional use of bone grafts [1].

Early implants were made of non-biodegradable materials despite their outstanding mechanical qualities. Removing the implant necessitates another surgery, which is difficult and upsetting for the patient who is already in the recovery stage. In the realm of tissue engineering, autograft and allograft are the most often used bone graft procedures. Infection, discomfort, scarring, donor-site morbidity, and blood loss are only a few of the drawbacks that these procedures, despite their widespread use, must endure patients [2,3].

One of the main building blocks of bone is hydroxyapatite, known as HAp, an inorganic calcium phosphate mineral. It might be endowed with important qualities, including biocompatibility, biodegradability, and suitable mechanical characteristics. Materials degrade slowly over time and, therefore, are difficult to resorb quickly. Both synthetic and natural calcium-rich sources can be used to make synthetic Hap. Cow, fish, cuttlefish, and cockle shells are a few examples of such natural materials [4].

Biomaterials and biological systems communicate via surfaces. To make a biomaterial biocompatible, it is crucial to regulate its surface qualities to promote positive interactions with host tissues [5]. Popular biomaterial coatings such as organic thin films and coatings of polymers offer great flexibility in chemical groups that can be incorporated at the surface to control tissue-biomaterial interactions, as they have mechanical properties similar to soft tissues [6]. Polymer coatings and thin films have a wide range of potential applications in biomaterials, such as biocompatible coatings for implants, polymer thin films for tissue engineering, use in drug delivery systems, and gene therapy.

2. Biodegradable Materials in Tissue Engineering

Biodegradable materials are being sought as they can be used as an implant and do not require a second surgical operation for removal [7,8]. The materials must facilitate the process of bone tissue regeneration and reconstruction of bone tissues while offering mechanical support and degradation of non-toxic items that are inevitably extracted by the body [9]. Natural biodegradable biomaterials, including chitosan, collagen, elastin, hyaluronic acid, and gelatins, are being studied for use in bone, nerve, liver, and cardiac tissue engineering applications [10,11]. However, their uses are restricted due to the challenges inherent in manipulating the chemical and physical characteristics of natural biomaterials. Researchers are thus looking for synthetic biodegradable materials with easily modifiable physical and chemical features [12,13].

Thin films have usually been perceived as a promising approach for changing a biomaterial's surface properties. Such films have been produced using a wide variety of biodegradable substances, including synthetic and natural substances with a range of characteristics and architectures. Ideal thin films must be able to mimic soft tissue characteristics as well as mechanical and biological and sustain the expansion of massive tissue structures [14]. The components, procedures, and conditions of the thin film must be non-toxic and not affect cellular functions within the body. Different use of procedures and tools, including processing requirements, has led to the development of several layer-by-layer assembly techniques that are widely used for biological matters, particles, and porous membranes.

Examples of layer-by-layer assembly techniques include dewetting, dipping, centrifugation, roll-to-roll, creaming, calculated saturation, spinning, immobilization, spraying, high gravity, atomization, magnetic assembly, electrodeposition, electro-coupling, fluidized beds, fluidics, and filtration. The assembly methods determine the process properties and affect the film's physicochemical properties, such as wettability, reactivity, conductivity, and corrosion properties [14].

2.1. Usage of natural ceramics in bone tissue application.

Over the years, many studies have used approaches such as carbonation or solution to produce raw material of inorganic calcium carbonate ($CaCO_3$) [15,16]. Thus, scientists and researchers have found new ways of using materials dependent on nature, such as mineral products that extract $CaCO_3$ [17]. The new trend is highly preferable in terms of environmental preservation, and due to the cockle shell's nature, it can provide raw material at a reasonably low price and naturally consists of good purity of mineral components [18].

Seashells are said to have a mineral composition similar to corals, leading to the usage of cockle shells as alternative biomaterials for bone substitutes. Polymorphs contained in $CaCO_3$ are appropriate biomaterials since bone tissues can replace them. The cockle shell consists of about 96% $CaCO_3$, while other components include organic substances and oxides like Silicon Dioxide (SiO_2), Magnesium Oxide (MgO), and Sulfur dioxide (SO_3) [4,19].

The three-layered structure of a fresh eggshell is composed of a frothy cuticle layer on the outside, a spongy middle layer, and lamellar layers on the inside. The eggshell accounts for about 11% of the egg's overall weight [20,21]. $CaCO_3$ is an egg's main component and inorganic substance, making up around 94% of the eggshell's chemical composition. This makes it a crucial component for synthesizing Hap [22,23]. Others are organic matter, which makes up 4%, magnesium carbonate (1%), calcium phosphate (1%), and insoluble proteins [24].

Fish scales are also a few of the alternative sources that can be used to produce $CaCO_3$ for bone tissue applications. Fish scales, a by-product of fish processing, are biocomposites made of lipids, protein, pigment, connective tissues, and other elements. It consists of proteins such as keratin, collagen, and mucin, which range from 41% to 84% [25]. A high amount of calcium phosphate compound, such as Hap, ranges from 38% to 46%, was found in fish scales [26]. Elements like Calcium (Ca), Magnesium (Mg), Phosphorus (P), Sodium (Na), and Sulfur (S) are also available in limited proportions [27]. Fish scale removal has become crucial due to strict regulatory measures to reduce pollution, forcing seafood businesses to pick by-product restoration strategies [28].

All natural resources to produce $CaCO_3$ are environmentally sustainable and have promising potential to be used in biomaterial applications, as in Figure 1. It has been commonly stated that cockle shells contain high-quality, pure calcium carbonate aragonite polymorphs. Furthermore, it also has a mineral composition almost similar to bone with high calcium carbon (CaC) content, and it is free of heavy metals like arsenic and mercury, making it useful for biological applications [18].

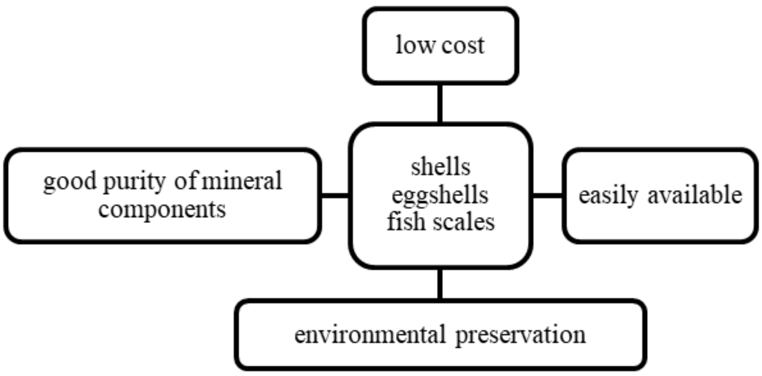

Figure 1. Environment sustainability from recycling natural resources (shells, eggshells, and fish scales).

Compared to other composite materials, shells are shown to have superior mechanical strength, including tensile strength, stiffness, and fracture toughness [29,30]. The complicated structures and interaction of biological macromolecules benefitted from the supremacy of molluscan shells. These external calcareous shells, microlaminated mineral and biopolymer composites, tend to have a large portion and scale, making them ideal for human biomedical applications [31]. Shells also show 3000 times greater strength than mineral crystals, besides present with exceptional nanoscale precision [32].

Thus, $CaCO_3$ biomaterial derived from cockle shells is the preferable alternative due to environmental sustainability and the effective usage of mineralized seashell by-products. Cockle shells, which also contain naturally good purity of mineral components and the source of raw material, can be obtained at low prices due to their abundance in nature [18,33].

2.2. Polymer in biomedical application.

Natural and synthetic natural materials are widely used in clinical applications. Materials such as ceramics, glass, metals, composites, and synthetic polymers are deemed useful in the medical field and are used due to their mechanical properties, as simplified in Table 1 [34,35].

Table 1. Polymer properties [34,36].

Material	Properties
Polymer • Natural • Synthetic	• High strength • Toughness • Ductile • Biocompatibility • Controllable degradation rate

The most popular biocompatible and biodegradable material is gelatin polymer, which contains approximately 85–92% of proteins, mineral salts, and water [37,38]. It is a type I molecular collagen derivative widely utilized in food, cosmetic, and medicinal applications [39-41]. It is often made when the collagen's triple helical structure is irreversibly hydrolyzed by enzymes and heat, resulting in random coils of collagen. Although less organized, gelatin's molecular structure is similar to that of collagen and thus can be used as a substitute to carry out comparable biomaterial roles for cellular growth in vitro [42,43]. The properties of gelatin are simplified as in Figure 2.

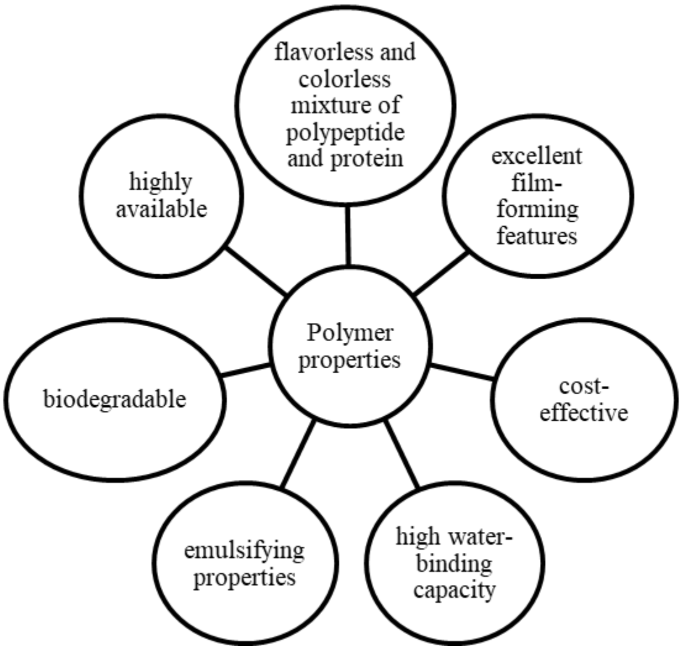

Figure 2. The properties of polymer [45].

Various materials, including pig skins, insects, fish, and cow bones, can be used to extract the gelatin. Studies on the gelatin biocompatibility gathered from these sources have demonstrated that gelatin generally does not cause antigenicity, toxicity, or other negative consequences in human cells [44]. The polymer used in this research is gelatin as the holder of $CaCO_3$ to form a degradable composite that can dissolve and should somehow fade away to allow an entirely natural bone tissue replacement.

3. Summary

The potential of $CaCO_3$ from cockle shells is expected to assist in forming new bone formation. This is because the content of $CaCO_3$ in cockle shells is high compared to other natural and waste resources such as eggshells. Besides, it is easy to handle and abundantly available on the coast and the rivers. The artificial thin film in this research is completed with the combination of gelatin as the bioceramics carrier of $CaCO_3$. The effective applications of bioceramics in this field for current materials are issued by the degree of bioresorption and poor mechanical strength. More progress is expected in combining $CaCO_3$ from cockle shells with gelatin.

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Conflicts of Interest

The funders had no role in the study's design, in the collection, analyses, or interpretation of data, in the writing of the manuscript, or in the decision to publish the results.

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