A Review: Calcium Carbonate ($CaCO_3$) extract from natural ceramics for thin film application

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Abstract: $CaCO_3$ are 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 being able to support 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 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 of natural materials that can be easily fulfil by using cockle shells, eggshells, or fish scales as main sources as well as due to their availability and low cost. The thin film in this research is expected to get incorporated at bone surfaces to control tissue-biomaterial interaction and have mechanical properties that are similar to the soft biological tissues. This paper review has 5 related sub-topics; 1. Introduction, 2. Biomaterial in Tissue Application, 3. Usage of Natural Ceramics in Bone Tissue Application, 4. Polymer in Biomedical Application and 5. Summary.

1 INTRODUCTION

Tissue engineering is not only focusing on the development of implants which are used to replace organs and tissues, but also concentrate on the production and synthesis of active biological materials that help to construct new tissues and retain the essential functions of living organisms. Due to the limitless supplies and no disease transmission, engineered bone tissue is clearly an alternative to the traditional use of bone grafts [1].

The early materials used to produce implants were non-biodegradable material even it has relatively good mechanical properties. Patients need to undergo another surgery to remove the implant, causing another painful and traumatic experience to the patient that still experiencing recovering phase. Allograft and autograft are the most common bone grafts treatments in tissue engineering field. Although these treatments are widely used, they are bound to limitation to the patients such as infection, pain, scarring, donor-site morbidity and blood loss [2].

The biological systems interact with biomaterials through their surfaces. The control of a biomaterial's surface properties is important such that it interacts well with host tissues in order to make the material biocompatible [3]. Popular biomaterials coatings such as organic thin films and coatings of polymers offer great flexibility in chemical groups that can be incorporated at surface to control tissue-biomaterial interactions, as they have mechanical properties similar of soft tissues [3]. There are many potential uses of polymer coatings and thin films in biomaterial applications such as biocompatible coatings for implants, polymer thin films for tissue engineering and usage for drug deliveries and gene therapy.

2 BIODEGRADABLE MATERIALS IN TISSUE APPLICATION

Biodegradable materials are being sought as they can be used as an implant and do not require a second surgical operation for removal [4]. Biodegradable 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 [5]. Studies for bone, nerve, liver and cardiac tissue engineering applications are focusing on the usage of natural biodegradable biomaterials such as chitosan, collagen, elastin, hyaluronic acid and gelatins. However, the difficulty in controlling the chemical and physical properties of the natural biomaterials has limits the applications. As a result, synthetic biodegradable materials are sought by researchers where the physical and chemical properties can be easily be modified [6].

Thin films have been generally acknowledged as a promising approach in the alteration of a biomaterial's surface properties. A wide range of biodegradable materials have been used to make such films, both from synthetic and natural materials with various properties and structures. Ideal thin films must be able to imitate the properties of soft tissues as well as the mechanical and biological properties besides being able to support the growth of large tissue constructions [7].

Components, procedures and conditions of thin film must be non-toxic and do not affect cellular functions within the body. Different use of procedures and tools including processing requirements have led to the development of several layer-by-layer assembly techniques that widely used for biological matters, particles and porous membranes. Examples include dewetting, dipping, centrifugation, roll-to-roll, creaming, calculated saturation, spinning, immobilization, spraying, high gravity, atomization, magnetic assembly, electro deposition, electro coupling, fluidized beds, fluidics and filtration as shown in Figure 1. The assembly methods not only determines the process properties, but also affecting the films physicochemical properties such as wettability, reactivity, conductivity and corrosion properties [7].

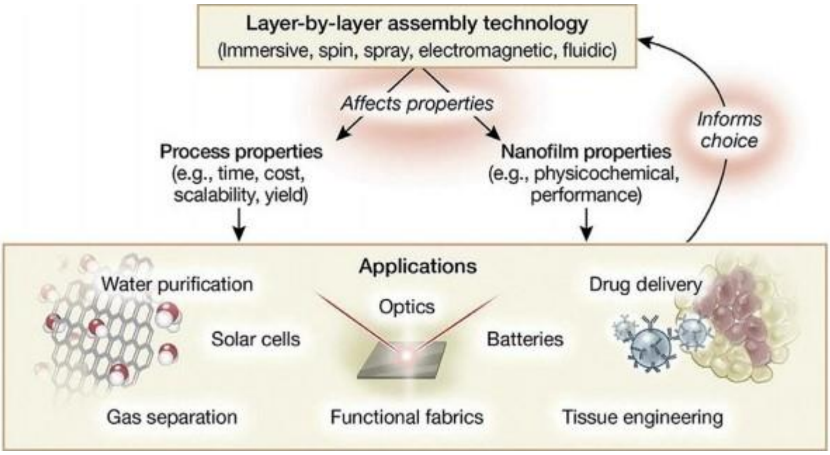

Fig. 1. An overview showing the assembly technology influences film and process properties as well as application area [7]

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 ($CaCO_3$) [8], [9]. Thus, scientists and researchers have found new ways of using materials dependent on nature, such as mineral products that extract $CaCO_3$ [10]. The new trend is highly preferable in term of environmental preservation and due to cockle shells nature; it can provide raw material in reasonable low price and highly consist of good purity of mineral component naturally [11].
The cockle shell consists of about 96% $CaCO_3$ whilst other components include organic substances and oxides like Silicon Dioxide (SiO_2), Magnesium Oxide (MgO) and Sulfur dioxide (SO_3) [12]. Seashells are said to have mineral composition that is similar to corals which leads to the usage of cockle shells as alternative biomaterials for bone substitute. Polymorphs contained in calcium carbonate are appropriate biomaterial since it can be replaced by bone tissues.

Fresh eggshell consists of a three-layered structure; the foamy cuticle layer on the outer surface resembles a ceramic; the middle layer is spongy; the inner layer consists of lamellar layers. 11% of the egg total weight is represented by the eggshell [13]. The major component and inorganic substance in an egg that makes up about 94% of eggshells chemical composition is $CaCO_3$ which makes it an essential material for hydroxyapatite production [14]. Others are organic matter which makes up 4%, magnesium carbonate (1%), and calcium phosphate (1%) as well as insoluble proteins [15].

Fish scales are also few of the alternative sources that can be used to produce $CaCO_3$ for bone tissue applications. Fish scales which are waste product by fish processing industries are biocomposites that composed of lipid, protein, pigment, connective tissues and various materials. It consists of proteins such as keratin, collagen and mucin, range from 41% to 84% [16]. Calcium phosphate compound such as hydroxyapatite and calcium carbonate can be found in fish scales in high amount. The amount of Hap in fish scales ranges from 38% to 46% with a small percentage of $CaCO_3$ content [17]. Elements like Calcium (Ca), Magnesium (Mg), Phosphorus (P), Sodium (Na) and Sulfur (S) are also available in limited proportions [18]. Strict regulatory measures to control pollution have pressured sea food producers to choose for by-product restoration initiatives, hence it has become important to get rid of fish scales [19].

All of natural resources to produce $CaCO_3$ are environmentally sustainable as in figure 2 and have promising potential to be use in biomaterial applications. Cockle shell has been widely reported to have good quality and pure calcium carbonate aragonite polymorph content. Furthermore, it also comprises almost similar mineral composition as bone with high calcium carbon (CaC) content and has no evidence of heavy metal element such as mercury (Hg) or arsenic (As) inside the shell product, which is indeed practical for biomedical uses [11].

Compared to other composite materials, Shells are shown to have superior mechanical strength which displayed include tensile strength, stiffness and fracture toughness [20]. The complicated structures and interaction of biological macromolecules was benefitted from the supremacy of molluscan shells. These external calcareous shells, which are microlaminated mineral and biopolymer composites, tend to have a large portion and scale that makes them ideal for human biomedical applications [21]. Shells also shown 3000 times greater strength than mineral crystal besides present with an exceptional nanoscale precision [22].

Thus, calcium carbonate biomaterial derived from cockle shells is the most preferable alternative due to environmental sustainability and the effective usage of mineralized seashell by-products. Cockle shells which also contains naturally good purity of mineral components and the source of raw material can be obtained at low prices due to its abundance in nature [11].

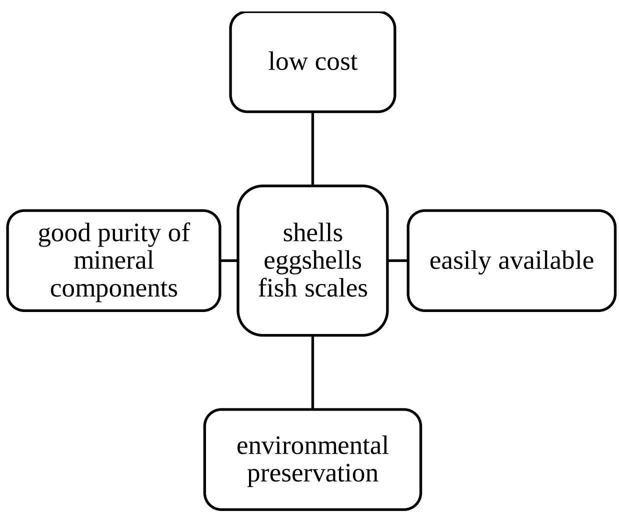

Fig. 2. Environment sustainability from recycling natural resources (shells, eggshells and fish scales)

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 [23], [24].

Table 1. polymer properties [23], [25]

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 [26]. It is a type I collagen molecular derivative and massively used in pharmaceutical, food and cosmetic applications [27]. It is generally produced by irreversible triple helical structure of collagen hydrolyzation through processes such as heat and enzymatic denaturation, producing random coiled domains. Thus, gelatin has molecular composition similar to collagen but less organization [28]. Because of this, gelatin has the capacity to replace and perform similar biomaterial functions as collagen for cellular development *in vitro*.

Gelatin can be extracted from various sources such as pig skins, insects, fishes and cattle bones. Studies conducted on the gelatin biocompatibility derived from these sources showed that gelatin, in general, does not induce antigenicity, toxicity and other harmful effects in human cells [29]. Polymer used in this research is gelatin as the holder of $CaCO_3$ to form a degradable composite that can dissolve and should in some way fade away to allow an entirely natural bone tissue replacement. The properties of gelatin are simplified as in Figure 3.

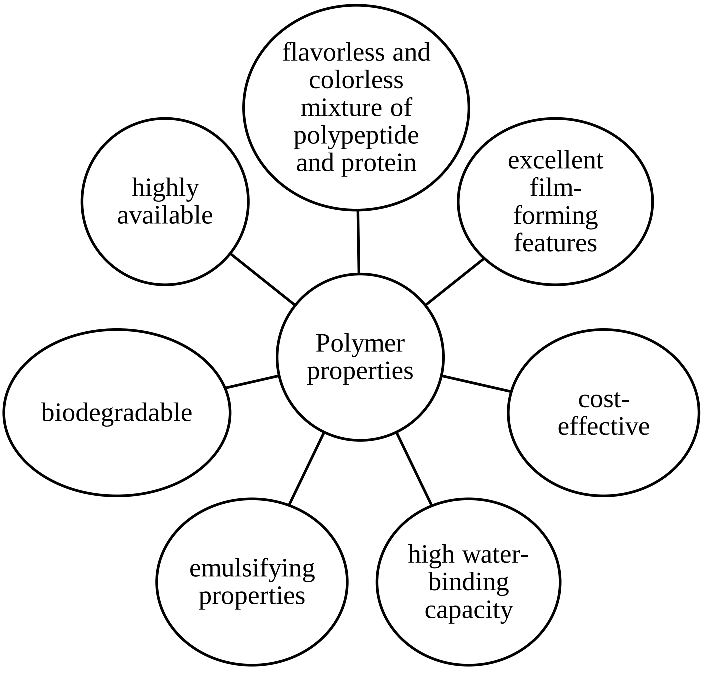

Fig. 3. The properties of polymer [30]

3 SUMMARY

The potential of $CaCO_3$ from cockle shells is expecting to assist the formation of 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 the poor mechanical strength. More progress is expected in the combination of $CaCO_3$ from cockle shells with gelatin.

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