Potential of Starch Nanocomposites for Biomedical Applications

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Abstract. In recent years, the development of biodegradable materials from renewable sources based on polymeric biomaterials have grown rapidly due to increase environmental concerns and the shortage of petroleum sources. In this regard, naturally renewable polymers such as starch has shown great potential as environmental friendly materials. Besides, the unique properties of starch such as biodegradable and non-toxic, biocompatible and solubility make them useful for a various biomedical applications. Regardless of their unique properties, starch materials are known to have limitations in term of poor processability, low mechanical properties, poor long term stability and high water sensitivity. In order to overcome these limitations, the incorporation of nano size fillers into starch materials (nanocomposites) has been introduced. This review aims to give an overview about structure and characteristics of starch, modification of starch by nanocomposites and their potential for biomedical applications.

1. Introduction
Synthetic polymeric materials have been extensively used in every field of human activity. However, the concern related with their usage are potential pollution due to non-degradable properties, no renewability and high costs \cite{1, 2}. Thus, intense research towards development of new environmental friendly materials based on biopolymers has been conducted. Natural biopolymers are produced by living organisms such as animals, plants, algae and microorganism. Among of these natural polymers, the most abundant polysaccharides known as starch has received considerable attention as biodegradable materials.

The unique physiochemical and functional characteristics of starch, vary from different plant sources like maize, wheat, cassava and potato. Starch has been famously used in food, pharmaceutical and biomedical applications because of its biocompatibility, total degradability without toxic residues, low cost, wide availability, renewability and has thermoplastic behavior \cite{3–5}. In addition, starch has already known to have great potential in biomedical fields including tissue engineering scaffolds, bone cements, drug delivery systems and stent \cite{6–9}.

Starch feasible to process into thermoplastic materials through the use of various industrial techniques, in which similar to those commonly used for synthetic thermoplastic such as injection
molding, extrusion, and thermo molding to produce porous or dense materials [10]. Nonetheless, thermoplastic starch (TPS) products are water sensitive and would lead to poorer mechanical and physical properties, due to their hydrophilic nature. In order to improve the mechanical properties and water resistance, starch can be altered by several methods such as blending with synthetic or natural polymers to form composite materials. Recently, special attention has been focused on the use of nano sized fillers into starch matrix to form nanocomposites. The application of nanocomposites could yield significant enhanced mechanical properties of starch based materials as compared to conventional micro composites. This is because the mutual effect between filler at nanometer size permits them to form molecular bridges in polymer matrix.

In this paper, a review on the research progress for the development of nanocomposites based on starch will be presented. The review focus on the influences of the incorporation of starch, layered silicate, and hydroxyapatite nanofillers on the properties of the composites.

2. Structural and Properties of Starch
Starch is a polymeric carbohydrate, which stored in plant tissues as insoluble semicrystalline granules that vary in shape, size and structure, relying on the sources. Native starch is composed primarily of two homopolymers (glucans), which are amylose (a linear polymer) and amylopectin (a highly branched polymer) as shown in (figure 1), as well as minor components such as lipids and proteins. The structure of the starch granule depends on the distribution of the amylose and amylopectin, while the ratios between amylose and amylopectin varies depending on the starch source because of differences in geographic origin and culture conditions. Table 1 shows the amylose and amylopectin content of starches from different plant sources.

![Chemical structures of a) amylose and b) amylopectin](image)

Figure 1. Chemical structures of a) amylose and b) amylopectin [11].

Amylose is a linear structure primarily based on α-D (1, 4) repeating units with a molecular weight of $10^5 - 10^6$ and can have a degree of polymerisation (DP) as high as 600. The large number of hydroxyl groups in the structure have proven hydrophilic properties of the polymer, resulting a material with high affinity for moisture. On the other hand, amylopectin is highly multiple branched polymer consists of short α-1, 4 chains linked by α-1, 6 bond containing 10 – 60 glucose units and side chains with 15 – 45 glucose units. The molecular weight of amylopectin ranging from $10^7 – 10^9$ [12].
Starch consists three types of crystallinity, which are the A type primarily from cereal starches like maize, wheat and rice; while the B type are from tubers like potato, cassava and sagoo; and lastly the C type contain both the polymorphic A and B type crystallinity patterns, which typically found in bean and other root starches.

Starch properties, such as water absorption, gelatinization and pasting, retrogradation, and susceptibility to enzymatic attack, are depend on the amylose/amylopectin content and granule size [13]. Furthermore, the functional properties of starches are also influence by other factors like chemical modification, system composition, pH, and ionic strength of the media.

Table 1. Amylose and amylopectin content of starch from different sources [14].

| Type of starch    | Amylose (%) | Amylopectin (%) |
|-------------------|-------------|-----------------|
| Amylo maize       | 48-77       | 23-52           |
| Banana            | 17-24       | 76-83           |
| Corn              | 17-25       | 75-83           |
| High-amylose corn | 55-70       | 30-45           |
| Potato            | 17-24       | 76-83           |
| Rice              | 15-35       | 65-85           |
| Sorghum           | 25          | 75              |
| Cassava           | 19-22       | 28-81           |
| Wheat             | 20-25       | 75-80           |
| Waxy              | <1          | >99             |
| Yam               | 9-15        | 85-91           |

3. Starch for Biomedical Applications
The unique physiochemical and functional characteristics of natural starches such as good biocompatibility, biodegradability, non-toxic and degradation as requirement make them useful for a wide range of biomedical applications [15]. Several starch based biodegradable polymers have been widely studied over the last few years, particularly in bone tissue engineering, drug delivery systems and hydrogels.

As an example, studies investigated by Boesel et al. [16] showed that starch based biodegradable bone cements are able to provide a temporary structural support and disappear gradually thereafter, thus allow the ingrowth of new bone for complete healing process. In addition, starch based biodegradable polymers for bone tissue engineering scaffold have been reported. According to Gomes et al. [17], an ideal scaffolds must be design using a biomaterial which possess sufficient degradation rate in which compatible with the formation of new tissue. Thus, the selection of starch for scaffold application is applicable. Other potential attraction of starch based biodegradable polymers are reported in drug delivery systems. Drug delivery systems using biodegradable starch is advantageous in deliverability process without need for surgical removal [11].

The successful of the above studies indicates that starch has potential as biomaterials to apply in medical field. Nevertheless, current starch based biodegradable polymers have obviously inferior mechanical properties, thus restraining the capability to be used in the large number of biomedical applications. Consequently, a development of nanocomposites starch material has been introduced to eliminate the limitations of biodegradable starch alone.

4. Starch Based Nanocomposites
As previously mentioned, most of native starches are limited in their direct application due to its inferior mechanical properties, poor long term stability and high water sensitivity [18]. Thus, in order
to overcome these limitations, the integration of various nanofillers like particles, fibres and layers into starch matrix to form nanocomposites have received considerable attention. The integration of nanofiller size has greatly influences the final properties of the nanocomposites as compared to conventional micro composites. This is because the mutual effect between filler at nanometer size permits them to form molecular bridges in starch matrix [19], hence resulting an enhancement in nanocomposites properties, such as mechanical properties, thermal stability, moisture resistance, oxygen barrier property and biodegradation rate. Additionally, nanocomposites offer an extensive advantages over conventional composites, as their use of relatively small amounts of fillers (less than 15%) able to achieve desired properties without adding excessive weight and can help improve optical transparency of the composite, since the nanofillers are much smaller than the light wavelength and do not scatter light [20].

Nevertheless, the properties of the nanocomposites material, rely not only on the properties of its constituents, but also on the interfacial bonding between matrix and the filler. Good dispersion of the nanofillers within the starch matrix will cause the strong interface adhesion and thus allowing the formation of a rigid molecular network which can enhance diverse properties of the nanocomposites. Furthermore, there are some aspects that influence the enhancement of starch matrix characteristics, which are plasticizer/additive use during processing, starch source, natural starch modification, existence of other polymer and nano reinforcement aspect ratio [21].

4.1. Starch/Layer Silicate

Development of biopolymer including starch reinforcing nanoparticles such as layer silicate has been one of the newest innovative steps in the nanocomposites. The addition of low percentage layer silicate into starch matrix has proven to be a favourable option in enhancing mechanical and barrier properties of the biopolymer. There are four possible dispersion state of layer silicate in starch matrix which are, phase separated, intercalated, exfoliated and disordered intercalated (partially exfoliated) [22]. Montmorillonite (MMT) is the most widely studied type of layer silicate in starch based nanocomposite because it is environmental friendly, availability at lower cost and processability [23].

Several studies have reported that starch nanocomposite reinforced layer silicate are commonly show an improvement in properties, particularly in tensile strength, Young’s modulus, thermal stability, moisture resistance, oxygen barrier property and biodegradation rate. The potential application of these materials was further investigated by Ardakani et al. [1] using solution casting method to prepare nanocomposite films from potato, corn, wheat, MMT, CMMT (modified by citric acid), 30B-MMT and glycerol. The addition of potato starch, CMMT and glycerol was found to improve mechanical properties of the films at optimum conditions. Another research conducted by Muller et al. [24], reported bionanocomposite films prepared by extrusion method using cassava starch, bentonite clay and glycerol. The nanocomposite films presented an outstanding improvements in mechanical properties and reduced the water vapour permeability when compared with native starch films. Gao et al. [25] studied starch/clay nanocomposites using various clay materials with different hydrophilicities by the film blowing method. The properties of the starch nanoclay film were significantly influenced by the hydrophilicity of the clay, in which medium range hydrophilicity favoured the nanocomposites formation. Furthermore, investigation by Avella et al. [26] showed a good increase in modulus and tensile strength for starch-nanocomposites prepared from MMT and potato starch.

The success of the above studies indicates that layer silicate show potential in improving the mechanical and barrier properties of starch-based biomaterials as well as exhibited other desired functions in various applications.

4.2. Starch/hydroxyapatite

Various embodiments of the present nanotechnology include starch/hydroxyapatite (HA) nanocomposites. HA has been used widely in biomedical applications, particularly for contact with bone tissue due to resemblance properties to mineral bone. HA could be found in natural or synthetic
form and it possesses favourable properties such as, biocompatible and osteoconductive (cell regeneration process) [24, 25]. Owing to these properties, HA able to promote fast cell regeneration without intermediate connective tissues.

A number of studies [26–29] have been proven that HA promotes faster cell regeneration without intermediate connective tissue, and it is currently used in clinical applications. However, HA is challenging to shape due to its brittleness and lack of flexibility. Similarly, starch materials have some problems associated with mechanical properties. Thus, combination of hydroxyapatite with starch materials may offer the solution for the brittleness issue. Sadjadi et al. [31] claimed that the polar nature of starch encourage a good adhesion between starch and hydroxyapatite. From the research conducted by Sadjadi, the presence of starch has significant effect on the final morphology of HA due to the interaction of OH- groups from starch and Ca$^{2+}$ from HA. In another study, Ayza et.al [12] suggested that the starch acted as the pore generator in membranes and other porous ceramics. This porous criteria is crucial in bone tissue engineering as porous architecture directly related to the scaffolds mechanical strength, cell migration, and this would ensure bone oxygenation and angiogenesis. Additionally, nano sized HA may have other special properties due to small size and huge specific surface area. Recent research suggested that, nano sized HA has reported significant increase in osteoblast adhesion as compared to micro sized ceramic materials [31, 32].

5. Conclusions

Based on the review, starch biomaterial was found to be one of the most promising candidates for various industry applications. The excellent biocompatibility, total degradability without toxic residues, low cost, wide availability and renewability properties of starch would open many applications in biomedical fields, such as bone tissue engineering and drug delivery systems. In addition, starch biomaterials can be process into thermoplastic materials through the use of various industrial techniques, in which similar to those widely used for synthetic thermoplastic. Recently, special attention has been given on nanotechnology by reinforce nano sized fillers into starch matrix to develop novel nanocomposite materials. The application of nanocomposites could significantly enhanced the properties of starch based materials, which would be strongly required for biomedical applications.

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