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Biopolymers; Definition, Classification and Applications

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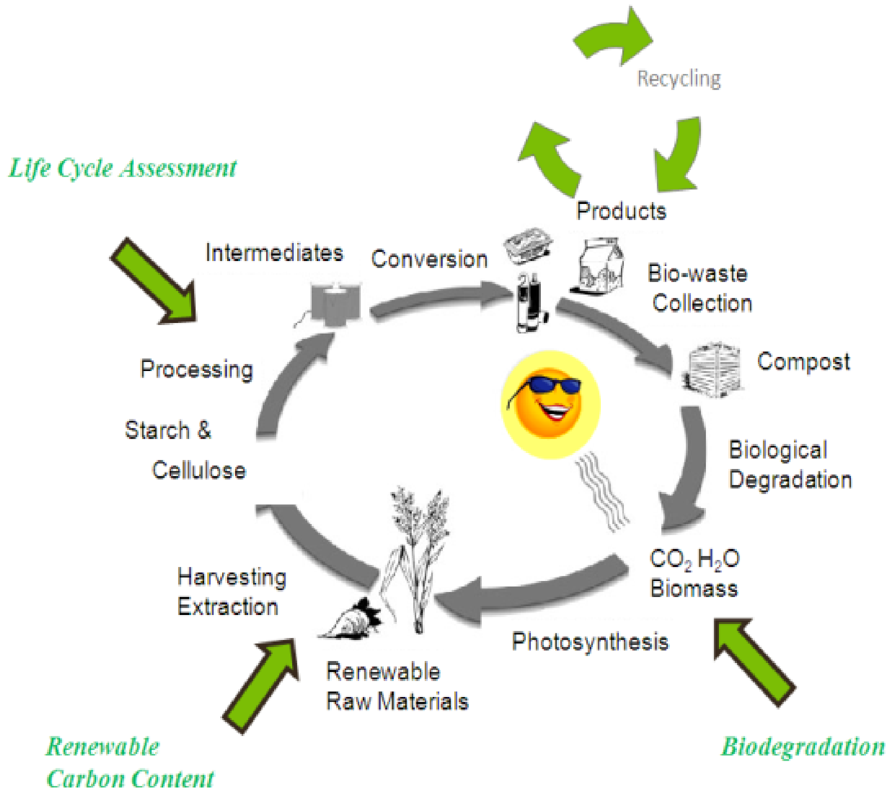
Graphical abstract



DURING recent years significant advances have been made in using and development of biodegradable polymeric materials for life applications. Degradable polymeric biomaterials are preferred because these materials have specific physical, chemical, biological, biomechanical and degradation properties. Wide ranges of natural or synthetic biopolymers capable of undergoing degradation hydrolytically or enzymatically are being investigated for many applications. This review aimed to provide an overview for the importance of biomaterials, produced or degraded naturally, classification and applications.

Keywords: Natural Polymers, Biodegradable materials, Classification, Applications.

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Definition

Recently, concerted efforts to protect the environment not only by using natural renewable materials environmentally friendly, but also using materials that decompose naturally in the environment was done and increasing rapidly (Fig. 1).

One of these materials is biopolymers, a kind of polymers, that produced by living organisms such as alginate and carrageenan which produced naturally occurring anionic polysaccharide isolated from the seaweeds (Fig. 2) [1], chitosan found in insects and crustaceans shells of certain other organisms, including many fungi, algae, and yeast [2]. Monomeric units of Biopolymers are sugars, amino acids, and nucleotides. Cellulose, starch and chitin, proteins and peptides, DNA and RNA are all examples of biopolymers.

Biopolymers and their derivatives are varied, plentiful and important for life. They exhibit the characteristics of a wonderful and increasingly important for various applications. For example, these biomaterials can be divided into proteins and poly (amino acids), poly- di- and monosaccharides such as cellulose, starch, fructose and glucose [3].

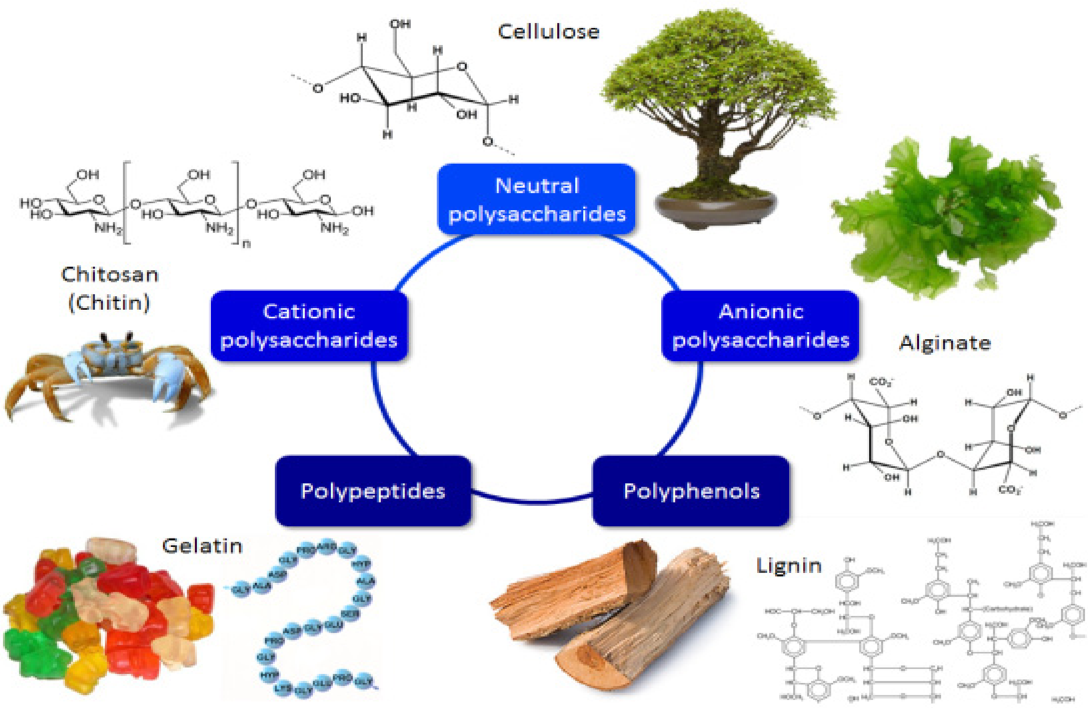

Fig. 1. Natural renewable biomaterials.

Fig. 2. Biopolymers in nature.

Biodegradable Natural polymers

To select a biomaterial for tissue engineering is the most critical step in scaffolds development. The main requirement should include biocompatible, non-toxic, providing favorable cellular interactions and tissue development, besides, the properties of mechanical strength, tensile strength etc. is also needed of synthetic polymer[4] Biodegradable should be requested and also should support the reconstruction of a new tissue without inflammation. According to the chemical structure of a vast variety of polymers as living organisms synthesized, they can be classified into major classes: (i) polysaccharides, (ii) proteins, and (iii) polyesters. Also basing on the advances in biotechnology, natural polymers can be obtained by the fermentation of microorganisms [5] or *in vitro* production by enzymatic processes [6].

Based material classification

Biomaterials can be classified depending on based material; in this case they are classified into four main types of Biopolymers.

Sugar based Biopolymers

Biopolymers based on sugar can be produced by blowing, vacuum forming injection, and extrusion. Lactic acid polymers (Polyactides) are created from milk sugar (lactose) which is extracted from maize, potatoes, wheat and sugar beet. Polyactides, manufactured by methods like vacuum forming, blowing and injection molding, are resistant to water [7].

Starch based Biopolymers

Biopolymers based on starch acts as natural polymer and can be obtained from vegetables like wheat, tapioca, potatoes and maize.

The material is stored in tissues of plants as carbohydrates. It is composed of glucose and can be obtained by melting starch. This polymer is not present in animal tissues. Dextrans, produced by starch hydrolysis, which is a group of low-molecular-weight carbohydrates, enzymatically synthesized by immobilized *Enterococcus faecalis* Esawy dextransucrase onto biopolymer carriers [8, 9].

Cellulose based Biopolymers

Biopolymers based on cellulose are used for packing cigarettes, CDs and confectionary. This polymer is composed of glucose and is the primary obtained from natural resources, plant cellular walls, like cotton, wood, wheat and corn [10].

Biopolymers based on Synthetic materials

Biopolymers based on Synthetic compounds also used for making biodegradable polymers such as aliphatic aromatic copolyesters are obtained from petroleum. They are compostable and bio-degradable completely though they are manufactured from synthetic components [10].

Biodegradable synthetic polymer

Polyglycolide Acid (PGA)

It is a highly crystalline polymer (45–55% crystallinity). It also exhibits a high tensile modulus with a very low solubility in organic solvents [11]. The currently most commonly used in synthetic biodegradable polymer are considered to be poly (glycolic acid) and poly (lactic acid) (Fig. 1-3). Polyglycolide was initially investigated for developing resorbable sutures because of its excellent fiber forming ability. Polyglycolides are broken down into glycine or converted into carbon dioxide and water via the citric acid cycle [12].

Polylactide Acid (PLA)

Similar to polyglycolide, it is also a crystalline polymer (37% crystallinity) (Fig. 3,2). It has a glass transition temperature of 60–65°C and a melting temperature of approximately 175°C [13]. Poly (L-lactide) is a slow-degrading polymer compared to polyglycolide. L-lactide (LPLA) homopolymer is a semicrystalline polymer with high tensile strength exhibitition, low elongation, and have a high modulus consequently that make them suitable in orthopedic fixation and sutures that have wild applications like load-bearing.

Poly (lactide-co-glycolide)

In adapting the property of PGA in wide application, copolymer of PGA with the more hydrophobic poly (lactic acid) (PLA) (Fig. 3) were investigated more intensive in Maurus PB`s team review [12]. Compared to homopolymers, the intermediate co-polymers were found to be less stable [14]. Different ratios of poly (lactide-co-glycolides) have been commercially developed and are being investigated for a wide range of biomedical applications [15].

Polycaprolacton

A semicrystalline polymer with high solubility of polycaprolactone and low melting point (59-64°C) can stimulate its biomaterial application research (Fig. 3,4) [16]. Due to the short half-life, there is a problem with delivery of bioactive agent, therefore, a proper transport of the bioactive agents like drug; enzyme etc. a vehicle is needed [17]. Starch-poly-epsilon-caprolactone microparticles then were developed in some applications such as drug delivery and tissue engineering applications. In addition, an emulsion solvent extraction/evaporation technique was prepared in these microparticles [18].

Poly dioxanone

Poly dioxanone (PDS) is a colorless, non-toxic and semicrystalline polymer (Fig. 3-5). It was the choice material for commercially developed monofilament suture in the 1980s which with a glass transition temperature of -10 to 0°C together with approximately 55% crystallinity [19]. PDS may be broke down into glycoxylate or converted into glycine and subsequently into carbon dioxide and water similar to polyglycolides [12].

Polyurethane

Polyurethanes are generally prepared by the polycondensation reaction of diisocyanates with alcohols and/amines (Fig. 3-6) [20]. Mainly usage for cardiovascular diseases like pacemakers and vascular grafts, bio-stable polyurethanes and poly (ether urethanes) are investigated for the future view in medical implanting extensively. Flexibility and mechanical strength are the reason why the polyurethane is the biocompatible used in a wide range of medical devices [21, 22]. Also for the biocompatibility, polyurethane can attach to membrane and don't stimulate immune reactions easily. A semipermeable membrane is also developed by Knauth team who work in artificial skin for premature neonates [23].

Polyhydroxybutyrate (PHB), polyhydroxyvalerate (PHV) and copolymers

Both PHB and PHB-PHV can be processed into different shapes and structures i.e. films, sheets, spheres and fibers. In addition, both PHB and PHB-PHV are also found to be soluble in the wide range of solvents (Fig. 3-7). Polymers like polyhydroxybutyrate (PHB), polyhydroxyvalerate (PHV), and copolymers with short biodegradation time are derived from microorganism's fermentation [24]. PHB has high potential in gas barrier and could degrade to D-3 hydroxybutyric acid *in vivo* together with a low toxicity. Not only controlled drug release, sutures, and artificial skin was adapted but also has been investigated as a material for bone pins and plates development [25]. Bioactive ceramics are also added to make them become potential biopolymer, these bioactive ceramics are hydroxyapatite (HA) and tricalcium phosphate (TCP) that could better enhances the ability of the composites to induce the formation of bone-like apatite on their surfaces [26].

Polyanhydried

As a possible substitute for polyesters in textile application polyanhydrides were explored and due to its pronounced hydrolytic instability it is still a failor [27]. Owing to this problem, an exploration with polyanhydride as degradable implant material was carried out by Domb`s team (Fig. 3-8) [28]. In addition to the benefit of polyanhydride, it can also possess an excellent biocompatibility *in vivo* [29]. Poly[(carboxyphenoxy propane)-(sebacic acid)] (PCPP-SA) is considered as the most extensively investigated polyanhydride. To compress molding or microencapsulation, drug loaded device has been best prepared and used to deliver the bis-chloroerhylnitrosourea (BCNU) to the brain which can treat brain cancer. Another potential vehicle for gentamicine to treat osteomyelitis was found by a co-polymer of 1:1 sebacic acid and erucic acid dimer [30]. Compare drug delivery and clinical trial, various polymers are available for localized drug delivery but more efficient polymer for drug delivery was shown by polyanhydride [31].

Poly (ortho esters)

Poly (ortho esters) is a degradable polymer which has become into developing in recent number of years (Fig. 3-9) [32]. Poly (ortho esters)`s erosion in aqueous environments is very slow because it has hydrophobic properties. The surface erosion mechanism is not the only unique feature of poly (ortho esters) but also with the rate of degradation for these polymers, pH sensitivity, and flexibility in the glass transition temperatures which can be controlled by using varying levels of chain diols [33].

Biopolymers Types

Two different criteria underline the definition of a "biopolymer" (or "bio plastic"): (1) the source of the raw materials and (2) polymer biodegradation.

Biopolymers made from renewable raw materials (bio-based), and being biodegradable.

These polymers can be produced by either biological systems (microorganisms, animals, and plants) or synthesized chemically from biological starting materials (e.g., corn, sugar, starch, etc.) Biodegradable bio-based biopolymers include (1) synthetic polymers from renewable resources such as poly (lactic acid) (PLA); (2) biopolymers produced by microorganisms, such as PHAs; (3) natural occurring biopolymers, such as starch or proteins— natural polymers are by definition those which are biosynthesized by various routes in the biosphere. The most used bio-based biodegradable polymers are starch and PHAs [34].

Biopolymers made from renewable raw materials (bio-based), and not being biodegradable.

These biopolymers can be produced from biomass or renewable resources and are non-biodegradable. Non-biodegradable bio-based biopolymers include (1) renewable resource's synthetic polymers such as specific polyamides from castor oil (polyamide 11), specific polyesters based on bio propanediol, bio polyethylene (bio-LDPE, bio-HDPE), bio polypropylene (bio-PP), or bio poly (vinyl chloride) (bio-PVC) based on bioethanol (e.g., from sugarcane), etc.; (2) natural occurring biopolymers such as natural rubber or amber [35].

Biopolymers made from fossil fuels, and being biodegradable.

These biopolymers are produced from fossil fuel, such as synthetic aliphatic polyesters made from crude oil or natural gas, and are certified biodegradable and compostable. PCL, poly (butylene succinate) (PBS), and certain "aliphatic–aromatic" copolyesters are at least partly fossil fuel-based polymers, but they can be degraded by microorganisms [35].

Shapes

Biopolymers have been classified by the shape into many types. These types such as disk, beads; thin films (membrane) and nanoparticles as follow:-

5.1. Disk

Gel disks are widely used in the literature. Researchers usually use the casting method, e.g. a Petri dish, to make a single film of gel and then cut it into disks using cork borers. Elnashar *et al.,* 2005 [36], invented a new equipment to make many uniform films in one step and with high accuracy using the equipment "Parallel Plates" as shown in Fig. 4.

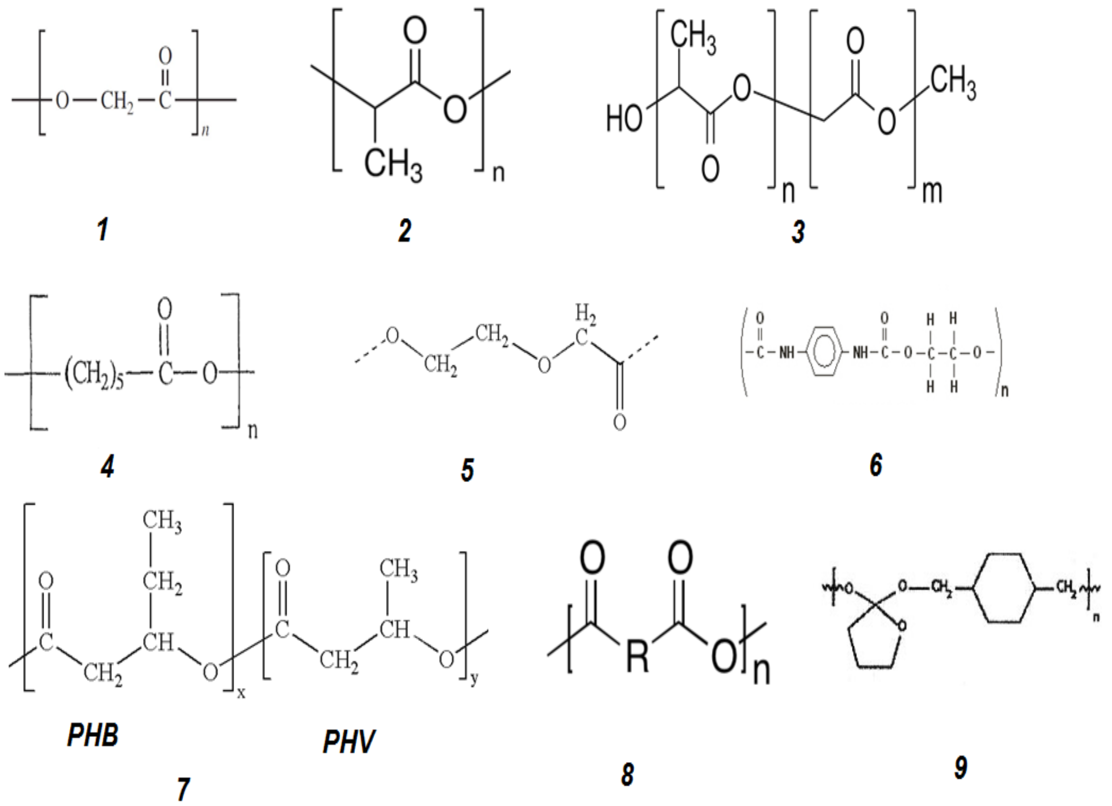

Fig. 3. Biodegradable synthetic polymers; 1: Polyglycolide Acid; 2: Polylactide Acid; 3: Poly (lactide-co-glycolide); 4: Polycaprolacton; 5: Poly dioxanone; 6: Polyurethane; 7: Polyhydroxybutyrate, polyhydroxyvalerate; 8: Polyanhydried; 9: Poly(ortho esters).

Fig. 4. Parallel plates equipment for making uniform gel disks.

Beads

Gel beads are mostly used in industries as they have the largest surface area and can be formed by many techniques such as the interphase technique, ionic gelation methods, dripping method and the Innotech Encapsulator [37]. The Innotech Encapsulator as shown in Fig. 5 has the advantage of high bead production (50 – 3000 beads per second depending on bead size and encapsulation-product mixture viscosity), which is suitable for the scaling up production on the industrial scale [38].

Fig. 5. Inotech Encapsulator IE-50 R.

Membrane

Polymeric membrane can be done by dissolving the polymer material in its solvent and then casting, washing and dryness as in Fig. 6. Sakurai`s research team give observation on the domain structure and show the conclusion that the intracellular concentration of calcium ions, a second messenger in the transmission of biological signals or an enzyme cofactor in the coagulation system, get the influences from polymeric materials [39]. It also reported in the study where the membrane from nonthrombogenicity of a PEUU can be improved remarkably by surface-grafting of polyoxyethylene chains [40].

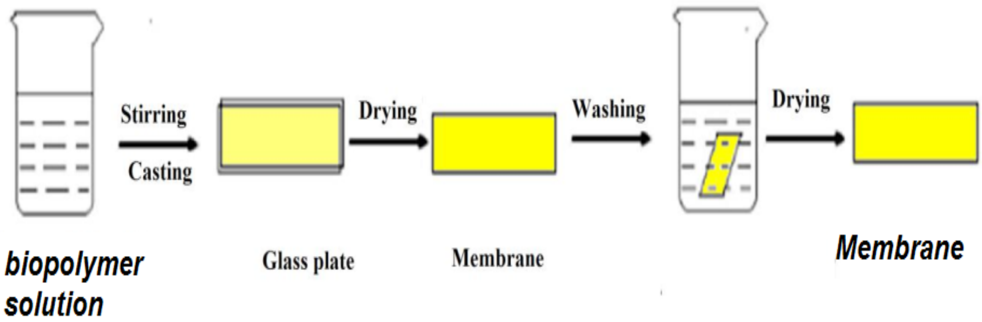

Fig. 6. Membrane preparation method.

Nanoparticles

Nanoparticles are defined as sub-micron solid particles, which can be used for nano-encapsulation of bioactive compounds [41]. Nanoparticles, nano-spheres or nano-capsules can be obtained depending on the method of preparation. Nano-capsules are vesicular systems in which the bioactive compounds are confined to a cavity consisting of an inner liquid core surrounded by a polymeric membrane while Nano-spheres are matrix systems in which the bioactive compounds are physically and uniformly dispersed [41], biodegradable polymeric nanoparticles can be produced from proteins (such as, gelatin and milk proteins), polysaccharides (such as chitosan, sodium alginate and starch) [42, 43], and synthetic polymers (such as poly (D, Llactide), poly (lactic acid) PLA [44], poly (D, L-glycolide), PLG, poly (lactide-co-glycolide), PLGA, and poly (cyanoacrylate) PCA) [45].

Recently, different methods have been adopted for preparation of nanoparticles from natural macromolecules (like chitosan, sodium alginate, gelatin, etc). Konecsni and Nickerson 2012 prepared chitosan nanoparticles containing rutein by using ionic gelation method [46].

Applications

Because of the great importance of these biomaterials, it has many important uses that overlap in various important applications in our life [47, 48].

Industrial applications

Biopolymers used in industry to save money and time especially in immobilization techniques [49], for example penicillin G Acylase was immobilized onto poly vinyl chloride to produce 6- amino peicillinc acid which is the back bone in b- lactam antibiotic industry [50]. Alginate, carrageenan and carboxy methyle cellulose was used to encapsulate date palme extract [51] and levan immobilization [52].

Acceleration of endothelialization

Herring`s team synthesized a cell-hybridization-type artificial vascular tissue successfully [53]. But the survival of collected cells is very difficult in seeding autogolal vascular endothelial cells to fibrin layer formed on a polymer membrane by preclotting (seeded graft). Avoiding the problem with this difficulty, cultured graft was proposed, in which endothelial cells are adhered and grown up in advance on the surface of porous membrane to cover it completely with a layer of endothelium [54, 55] but a steady supply of living cells and an immune response comes as the second problems.

Polymer membranes is strongly desired and to obtain cell-hybridization materials without encountering these problems this is because of the living cells can be easily adhere and proliferate upon implanting in a living body, the design and synthesis of polymer membranes is also strongly needed where biopolymer has a good future.

Chitin in wound healing dressing is used from its ability for N-acetylglucosamine which can not only accelerate the rate of tissue repair but also prevent the formation of scars and contraction of the skin [56, 57]. Using as a powder form, however, chitosan and chitin are now being incorporated in films, membranes, gels and woven or non- woven dressings [58].

Conjugation of reagent suppressing platelet activation

Platelets on the material`s surface get influence from adhesion and activation works in thrombus formation. Reagents suppress platelet activation, adrenalin-shielding reagent, drugs participating in the prostaglandin metabolic system can affect the cyclic nucleotide production, and those participating in the Ca^{2+} regulating mechanism are considered. Polymer membranes immobilize platelet tranquilizers to yield highly nonthrombogenic materials. Ebert *et al.*; [59] report that PGI2-immobilized polystyrene beads has a great inhibition effect on platelet in both adhesion and activation and their team also pointed out that adhesion and activation of platelets are suppressed on heparin-immobilized materials too [60, 61].

In cosmetic aspect

The non-toxic and environmentally friendly nature of the PLPs`s advantange contribute to the invention of cosmetic use. The patent from Dimotakis group claims that the solubility of the PLPs in both aqueous and non-aqueous polar solvents provide versatility where amenable formulate into any type of cosmetic composition for the invention and use of keratinous tissue. And the patent also stimulate that the PLP has the capability in absorbing light outside the visible range and emit light with a good quantum yield. With substantially the same intensity where the light is absorbed, they successfully invent the function of UV-protectant effect and skin enlighting or colorizing effect according to the use of photoluminescent polymers that polymers having grafted thereon or incorporated into the amino acid or an amino acid derivative`s backbone or skeleton [62].

Food packing material with safety

Nano materials for polymer modification bring a breakthrough in recent years. The advantage of natural or synthetic polymer with food packaging materials, mechanical strength, flexibility, heat resistance, barrier properties, and other properties have been effectively improved [63]. In food packaging, there are starch nano composite materials from which starch / montmorillonite nano composite film, cellulose nano composite materials, protein nano composite materials and poly lactic acid nano composite materials were prepared. As a food packaging material, it can also improve the antimicrobial effect of packaging, mechanical strength, flexibility, heat resistance and barrier properties, etc. Many countries in Europe and the United States give research through the animal *in vivo* and *in vitro* experiments then demonstrated that nanoparticles have a certain degree of toxicity in animal organs, respiratory and cardiovascular systems which will cause certain damage [64,65]. As a result of this conclusion, the sixth meeting of the official nano materials in EU was held in the Belgian capital Brussels on November 16, 2008 with the aim at "registration, evaluation, authorization and restriction of chemicals" and regulated that industrial raw materials was included in the scope of regulation [66].

Medical industry

As the first biodegradable sutures was approved in the 1960s [13]. Polymers have vertical uses in medical industry from the preparation of polycaprolactone and glycolic acid. Multy purpose of products basing on glycolic acid, lactic acid and other materials, including poly (dioxanone), poly(trimethylene carbonate) copolymers, and poly(-caprolactone) homopolymers and copolymers have been wildly used as medical devices. Accompanied with approved devices, plenty of researches have further study on polyanhydrides, polyorthoesters, polyphosphazenes, and other biodegradable polymers. Clinical use with the major class of synthetic biodegradable polymers with products was also remained like polyglycolides, polylactides and their copolymers [67].

An obvious advantage of nature origin based polymers lies in biological macromolecules. The releasing of soluble degradation product could leads to an actual mass loss of the implant where phagocytosis by macrophages and histocytes, intracellular degradation and finally, metabolic elimination through the citric acid (Krebs) cycle to carbon dioxide and water, which are expelled from the body via respiration and urine. The implantation site, the enzyme availability and their action mode comes from the degradation. Natural polymers prevent the chronic inflammation or immunological reactions and toxicity`s possibility where implants or drug delivery system was detected with synthetic polymers [68].

As cellulose, starches, natural rubber and DNA are biodegradable and bioresorbable to support the reconstruction of a new tissue without inflammation are included in the widely variety of polymers [69].

Fibrinolytic enzymes for immobilization to polymer membranes are chosen from urokinase, streptokinase, fibrinolysine, and brynolase. The enzymes immobilized on membranes have been used clinically [70].

Some examples for the binary immobilization of antithrombogenic reagents were also provided by some research such as the immobilization of prostaglandin-heparin complex [71] and the urokinase-heparin coimmobilization [72]. According to some articles reported with polytetrafluoroethylene membrane coated with heparin--collagen complex, an early thrombus formation is inhibited by the action of heparin and a longterm endothelialization is accelerated by collagen [73].

Clinical uses

Orthopedics

A quantity number of biopolymers are being used in orthopaedics in substitute of metallic component from long time ago.

Cardiovascular Systems

A great success in heart disease has been proved by biodegradable implants where metallic implant sometimes creates problems. Good results have been shown by biodegradable implants showed better results than metallic ones. Synthetic polymer implants can`t grow and attach with cardiac cells, and in congenital heart diseases they do not give accurate results because of their in-viability. In the replacement of a surgical defect in the right ventricular outflow tract in the heart copolymer of biodegradable poly urethane is generally used [74]. Biodegradable polymers act a good way as a guided tissue regeneration membrane (GTR) etc. in dental problems like filling the cavities. The exclusion of epithelial cells allows the supporting, slower-growing tissue including connective and ligament cells to proliferate [75].

In sutures and ophthalmic

Suture is a complicated designed and manufactured medical product meet a demand between physical and chemical in a big range which are divided into natural and synthetic wildly.

Biodegradable polymeric nano-particles have been attracted a great interest by many research groups not only in food but pharmaceutical fields as well due to the big usage with favorable properties like good biocompatibility, structure variations, easy design and preparation and interesting bio-mimetic characters. Particularly in the field of smart bioactive carriers, polymer nanoparticles can deliver bioactive compounds into the intended site of action directly [76]. Besides, there are varieties of functional biopolymers and specialized equipment that can be chosen in polymeric nanoparticles` producing [77]. In addition, natural nano-carriers like cyclodextrins and caseins have emerged as an attractive option for controlled bioactive systems according to their resemblances with the extracellular matrix in the human body and various other favorable physicochemical properties [78].

Conclusion

This review detailed definition, classification, types and some important applications of biomaterials used in different applications in our life. From the biomaterials unique properties, these materials are perfect candidates for different bio-related applications.

Conflict of interest

There is no conflict of interest

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البوليمرات الحيوية :التعريف، التصنيف والتطبيقات

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خلال السنوات الأخيرة الماضية تم إحراز تقدم كبير في استخدام وتطوير المواد البوليمرية القابلة للتحلل الحيوي في مختلف التطبيقات الحيوية. يفضل استخدام المواد الحيوية البوليمرية القابلة للتحلل لأن هذه المواد لها خصائص فيزيائية وكيميائية وبيولوجية وبيولوجية ميكانيكية وكذلك قدرتها على التحلل. ويجري استخدام العديد من البوليمرات الحيوية الطبيعية أو الاصطناعية القادرة على التحلل المائي أو الإنزيمي في العديد من التطبيقات الصناعية المختلفة. تهدف هذه الدراسة إلى تقديم نظرة عامة لأهمية المواد الحيوية المنتجة أو المتحللة بشكل طبيعي ، كذلك التصنيف والتطبيقات لهذه المواد الحيوية.