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REVIEW

Polyhydroxyalkanoates: Current applications in the medical field

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Abstract **Polyhydroxyalkanoates (PHAs) are a class of biopolyesters that are synthesized intracellularly by microorganisms, mainly by different genera of eubacteria. These biopolymers have diverse physical and chemical properties that also classify them as biodegradable in nature and make them compatible to living systems. In the last two decades or so, PHAs have emerged as potential useful materials in the medical field for different applications owing to their unique properties. The lower acidity and bioactivity of PHAs confer them with minimal risk compared to other biopolymers such as poly-lactic acid (PLA) and poly-glycolic acid (PGA). Therefore, the versatility of PHAs in terms of their non-toxic degradation products, biocompatibility, desired surface modifications, wide range of physical and chemical properties, cellular growth support, and attachment without carcinogenic effects have enabled their use as in vivo implants such as sutures, adhesion barriers, and valves to guide tissue repair and in regeneration devices such as cardiovascular patches, articular cartilage repair scaffolds, bone graft substitutes, and nerve guides. Here, we briefly describe some of the most recent innovative research involving the use of PHAs in medical applications. Microbial production of PHAs also provides the opportunity to develop PHAs with more unique monomer compositions economically through metabolic engineering approaches. At present, it is generally established that the PHA monomer composition and surface modifications influence cell responses.PHA synthesis by bacteria does not require the use of a catalyst (used in the synthesis of other polymers), which further promotes the biocompatibility of PHA-derived polymers.**

Keywords Biopolymers, polyhydroxyalkanoates, biocompatibility, medical implantations

Background

Polyhydroxyalkanoates (PHAs) are biopolyesters that are synthesized by many genera of eubacteria under unfavorable conditions (Doi et al., 1995). These biopolymers have diverse physical and chemical properties that allow them to be naturally biodegradable and compatible to living systems (Wu et al., 2009). Depending on the cultivation strategy, nature of bacterial strains, and type of polymerase genes present, the composition of these biopolymers can be varied at the monomer level (Chuah et al., 2013). Furthermore, PHAs can be classified into short-chain-length (scl) PHAs with (C4-C5) and medium-chain-length (mcl) PHAs with (C6–C14), according to the variation in the side chain length due to the number of carbon atoms, and may further be grouped a shomo-polymers (either scl-PHAs or mcl-PHAs) or copolymers (a mixture of different monomers of scl-PHA and/or mcl-PHA monomers). In view of the high production costs of PHAs as compared to conventional plastics, the global production and use of these biopolymers as bulk packaging material is not expected in the upcoming decades. However, growing interest in the production of PHAs from a wide range of raw materials is equally supported owing to their diverse physical properties (Laycock et al., 2013; Kai and Loh, 2014). Although various strategies for the production of PHAs from bacteria have been developed, the ability of modification of certain functional groups to PHAs, such as -OH, -COOH, epoxy, and halogens, would certainly be useful to be able to specifically tune their mechanical and thermal properties.

In PHA-accumulating bacteria, these inclusions naturally serve as carbon and energy storage materials and help the bacteria to survive under starvation conditions. If the products containing these PHAs then enter the environment, they are broken down completely into carbon dioxide and water,

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which is significant given the importance of these two molecules as the raw materials for photosynthesis. Hence, PHAs can more appropriately fit into the carbon cycle as compared to petroleum-based plastics.

Nanoparticles of an organic nature have been explored for applications in many fields, as they can be used as covering materials for various medically important drugs and their surfaces can be altered to target sites without a loss in permanence in living or nonliving cells (Bao et al., 2013). Therefore, PHAs have found numerous applications in the biomedical field due to their versatile physical and chemical properties.PHA has an advantage over other bioplastics such a spoly-glycolic acid (PGA), poly-lactic acid (PLA), and poly (dl-lactide-co-glycolide) (PLGA), since its monomers 3-hydroxybutyric acid (3HB) or 4-hydroxybutyric acid (4HB) are less acidic than the α-hydroxy acids of PGA, PLA, and PLGA, and are eventually eradicated from the human body in less than one hour; indeed, they can be naturally detected in almost all parts of the body as a degradation product (Hocking and Marchessault, 1994). The breakdown of PHA inside human cells varies from tissue to tissue and also depends on the dispensation methodology used to make its various profiles such as PHA nanofibers, thin films, or scaffolds (Brigham and Sinskey, 2012). Development of advanced methodologies used to fabricate the surface and properties of PHAs would certainly open new horizons for their applications in many more medical fields in the upcoming decades. Figure 1 shows a schematic of the development of PHAs with substantial applications in the medical field. Here, we briefly describe some of the pioneering work involving the use of PHAs in these applications.

Essential features of a biomaterial

Biodegradability

The first property that makes PHAs compatible to living cells is their biodegradability. Some studies have examined the biodegradation of P(3HB), P(3HB-co-3HV), P(3HB-co-3HHx), and others. Lipases and other hydrolytic enzymes have been reported to degrade P(3HB-co-4HB) into its oligomers of oligo hydroxy acids, and the conformation of 4HB makes it especially more prone to in vivo enzymatic degradation (Wu et al., 2009). Production of 5-hydroxyvalerate (5HV) and 6-hydroxyhexanoate (6HHx) has also been demonstrated to occur as a result of the enzymatic breakdown of PHA (Mukai et al., 1993). The biodegradation of P(3HB) has been very well examined in various cell lines with a target for use as biomaterials with various geometries, including variably wide P(3HB) films and plates (Freier et al., 2002; Gogolewski et al., 1993; Kunze et al., 2006; Qu et al., 2006), tubes (Borkenhagen et al., 1998; Gogolewski et al., 1993; Hazari et al., 1999a; Hazari et al., 1999b), thread-like filaments (Miller and Williams, 1987; Shishatskaya et al., 2005), and microspheres (Saito et al., 1991). In contrast to other bioplastics like PGA and PLGA, P(3HB) has shown little resistance to *in vitro* degradation as well as to biodegradation in living mammalian cells. P(3HB) implantation was studied in the mandibular region of rats and in the condyles of rabbits, and was found to degrade within six months in both cases (Kostopoulos and Karring 1994; Luklinska and Bonfield, 1997). Moreover, P(3HB-co-3HV) and P(3HB-co-3HHx) implants were found to be completely resorbed after three months in the subcutaneous region of rabbits (Jones et al., 2000; Philip et al., 2007). Thus, the biodegradable nature of PHAs ensures that their use as biomaterials would not be questioned given their apparent persistence after implantation, allowing them to achieve the target objective.

Cytotoxicity

In addition, the effects of these monomeric units of PHAs on the overall shape, physiology, growth, and cytotoxicity of target and surrounding cells have been investigated. It has been demonstrated that various monomers of 3HB, 3HB-co-4HB, 3HB-co-3HHx, and 3HHx did not affect murine fibroblast L929 cells if present at a concentration of less than 20 mg/L. However, when the concentration doubled,t hese monomers retarded cellular growth and caused subsequent apoptosis, whereas the cytotoxicity of the oligomers decreased inversely with the length of the side chain (Sun et al., 2007). Nevertheless, the cytotoxicity could be considered to be negligible given that the oligomers never crossed the threshold concentration of 20 mg/L; moreover, healthy human blood always contains a 3HB level of 3 – 10 mg/100 mL (Pawan and Semple, 1983). Some monomers such as 4HB are also present in different organs, muscle tissues, as well as in the brain. In fact, 4HB has been used in a daily intravenous dose for long-term sedation and anesthesia at 20–40 g for nearly half a century (Nelson et al., 1981; Entholzner et al., 1995). Considering that the properties of PHAs can be varied by creating blends and composites with some additives (organic or inorganic) to diversify their applications (Kim et al., 2005), such modifications can also be used to customize the degradation rate of the polymer as well. Both material addition, such as PLA, gelatin, or maleic anhydride (Wang et al., 2005; Li et al., 2008; Zhao et al., 2012), and non-material treatments such as ultraviolet treatment (Shangguan et al., 2006) have been reported to speed up the breakdown of PHA.

Recently, Basnett et al. (2013) demonstrated that a new combination of a P(3HO)/P(3HB) composite showed more potential in terms of increased biocompatibility and reduced cytotoxicity over the homopolymer P(3HO) to human microvascular endothelial cells (HMEC-1). This advantage was mainly attributed to the high thermodynamics, strength of the composite, and relatively accelerated breakdown rate of PHA, which was suggested to lead to the development of new biodegradable stents (Basnett et al., 2013). Clearly, PHA

monomers (3HB, 4HB, and 3HV) have proven to be less dangerous when compared to commonly used scaffolding polymers (i.e., PLA and PGA) due to their lower acidity and reduced bioactivity (Taylor et al., 1994). It has been suggested that a terpolymer P(3HB-co-3HP-co-5HV) and a longer 5HV-containing polymer should exhibit even lower toxicity to living cells (Chuah et al., 2013). Similarly, P(3HB-co-3HHx), with higher tensile strength and flexibility than P(3HB) and P (3HBV) (Doi et al., 1995), showed good hemocompatibility (Wu et al., 2009) and a high affinity to a variety of cells (Yang et al., 2002), which makes it even more advantageous for medical sutures applications. Some modifications to the physical properties of PHA, by linking it to some other functional groups, might be useful to construct nearly non-toxic PHA scaffolds. Based on these findings, it may be concluded that the cytotoxicity of PHAs can be reduced to a minimal level or that complete non-cytotoxicity could be achieved in medical implantations if an appropriate combination of monomers is targeted toward certain types of animal cells.

Biocompatibility

In addition to their non-toxic degradation products and biocompatibility, the abilities of PHAs to support cell adhesion and growth are essential for their commercialization (Basnett et al., 2013), although these abilities are also abetted by plasticizer addition, surface alteration (as a result of treatments with acids, alkalis, lipases and/or ligands attachments, ammonia plasma), and implantation of non-contaminated PHAs (Zhao et al., 2002; Qu et al., 2005; Shen et al., 2009; Chen et al., 2013). P(3HB-co-3HHx)/P(3HB) scaffolds have proven to be strong growth promoters for the chondrocytes of rabbits (Zhao et al., 2003; Valappil et al., 2006). In a recent study conducted on mesenchymal stem cells (MSCs), P(3HB-co-3HHx) was found to promote and retain the chondrogenesis phenotype of MSCs as well as to sustain the chondrocyte-specific secretion of extracellular matrix (ECM) (Yan et al., 2011). Moreover, the effects of P (3HB) have been tested in many cell types such as osteoblasts, fibroblasts, and chondrocytes, showing excellent biocompatibility with no side effects (Köse et al., 2003). Furthermore, unmodified mcl-PHA has been recently shown to have reasonably biocompatible behavior with human mesenchymal stromal cells (Naveen et al., 2015). Although these modification treatments increase the potential applications of PHAs, it is also important to reduce the molecular weights of the materials that are used to alter the mechanical properties of the PHAs.

Non-carcinogenicity

Currently, the most crucial aspect of the use of PHAs in medical application is their non-carcinogenic behavior, as they have shown improvements in cell growth either *in vitro* or following *in vivo* implantation. One study using osteosarcoma UMR-108 cells showed that PHAs [P(3HB), P (3HBV), P(3HB-co-3HHx), P(3HB-co-4HB), and P(3HBV-co-3HHx)] did not affect the cancerous proliferation in primary osteoblasts (Peng et al., 2011). *In vitro* experiments with films of P(3HB-co-3HV) targeting human retinal pigment epithelial cells showed healthy cell proliferation under a controlled growth rate without any unusual cell spreading (Tezcaner et al., 2003). The role of PHAs on cell proliferation and biocompatibility has been established in various studies; however, there is still no clear evidence that they are completely non-carcinogenic for all cell lines (Zink et al., 2004). In any possible cancer cell induction process, it

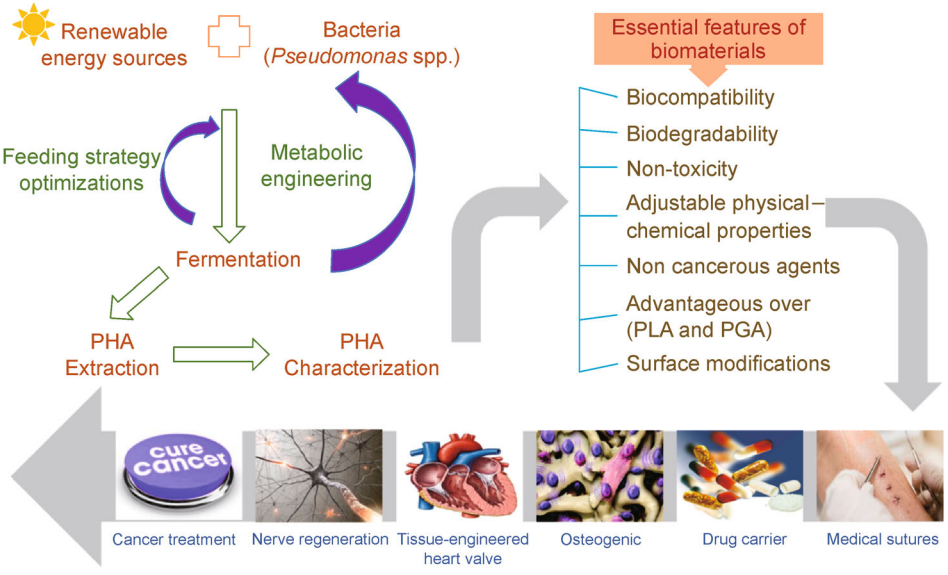

Figure 1 Schematic representation for the development of medical implants using renewable energy sources in bacterial fermentations. Other bacteria such as *Ralstonia eutropha* and recombinant *Escherichia coli* can also produce large quantities of PHA.

is important to consider the potential changes to nuclear shape and DNA damage caused by PHA implantations. Any disturbance in normal cell cycle regulation by these materials is more likely to result in carcinogenesis.

Owing to their resourceful properties that are essential for any first-choice biomaterial, PHAs have found numerous *in vivo* and *in vitro* applications, with experiments conducted in nearly all types of cells lines. Many implants such as medical sutures, adhesion barriers, and valves used to guide tissue repair, as well as regeneration devices such as cardiovascular patches, articular cartilage repair scaffolds, bone graft substitutes, and nerve guides have been functionalized with various forms of PHAs (Chen and Wu, 2005; Wu et al., 2009).

Applications of PHAs as biomaterials

Osteogenic and chondrogenic effects

As biomaterials can initiate a change in cellular behavior (Pelham and Wang, 1997), different PHAs with specific surface features can result in respective cellular retaliation. This cellular response was demonstrated when the planar and grooved P(3HB-co-3HHx) films exhibited chondrogenic and osteogenic initiation, respectively, on bone marrow-derived mesenchymal stem cells (BMSCs) (Wang et al., 2011; Li et al., 2015). In fact, the presence of these materials made a significant contribution to increasing or decreasing the expression of some specific gene markers responsible for variations in cellular response. These findings demonstrated that surface modification can be a major factor for promoting a desired signaling transduction process for various tissue substitutes. Cells respond to a certain engineered surface by sensing the material through some integrin clusters and focal adhesion formation (Geiger et al., 2009). Thus, cell proliferation-inducing materials, especially PHAs, can be used as ECM (McBeath et al., 2004; Gardel and Schwarz, 2010). Furthermore, a combination of a PHA binding protein with an mcl-PHA could also be an effective strategy to enhance the proliferation of these cell lines. Nevertheless, more work is required to determine the expression of integrins on the engineered surfaces of PHAs in order to describe the respective cellular behaviors (e.g., shape, attachment, motility, variations, and growth patterns).

Tissue-engineered heart valve

PHA tissue engineering (scaffolds of soft or hard tissues) has an edge over other methods in terms of the tailor-made flexible properties with a wide range of combinations and building blocks through diverse fabrication methodologies. Sodian and colleagues took advantage of this ability of PHA to implant a complete trileaflet tissue-engineered heart valve using seeded autologous cells with polymer P(3HHx-co-3HO) in a lamb, which worked effectively for three months without any thrombus development and only slight stenosis (Sodian et al., 2000; Levine et al., 2015). When PGA was used to blend with P(3HHx-co-3HO), non-progressive heart valve regurgitation was observed at six months after material implantation (Stock et al., 2006). Otherwise, a P(3HB-co-3HHx) surface modified with fibronectin coating and/or ammonia plasma treatment to human umbilical vein endothelial cells (HUVECs) and smooth muscle cells from the rabbit aorta (RaSMCs) resulted in enhanced growth by forming a confluent monolayer (Qu et al., 2005). The controlled growth coupled with functionalized heart tissue should be rated equally when designing aPHA biomaterial and its surface modifications.

PHAs as medical sutures

Sterile fibers such as medical sutures (absorbable or non-absorbable) are used for ligation, hemostasis, tissue fixation, and wound healing (He et al., 2013). After implantation, absorbable sutures lose their tensile strength within two months (Bennett, 1988) and degrade into non-toxic products. The most desired characteristics required of absorbable sutures include an even superficial texture, convenience to tie and grip, biocompatibility, resistance to bacterial growth, great tensile power, ability to be sterilized easily, and eventual absorbance and disappearance (Moy et al., 1992; Hon et al., 2009). These properties were exhibited by the P(3HBV)/PLA and P(3HB-co-3HHx) strands, which showed excellent features for their use as biomedical sutures, although better tensile strength and elasticity was observed in the case of P (3HB-co-3HHx) as compared to the excellent biocompatibility of P(3HBV)/PLA (He et al., 2013).

In another study, a copolymer, P(3HB-co-3HHx), improved osteoblasts attachment, propagation, and differentiation compared with the homopolymer P(3HB) (Wang et al., 2004; Li et al., 2005). In fact, P(3HB-co-3HHx)also promoted the chondrogenesis of human BMSCs (Yan et al., 2011). A terpolymer, P(3HB-co-4HB-co-3HHx), has shown even more promise for MSC differentiation as compared to the copolymer P(3HB-co-3HHx) (Wei et al., 2009). Scaffolds of P(3HB-co-3HHx) blended with collagen were successfully utilized to grow MSCs (Lomas et al., 2013). In a more recent study, expression of many different integrins was revealed when P(3HBV-co-3HHx) showed a great impact on promoting apoptosis of osteoblasts. These osteoblasts were targeted by different PHA films[P(3HB), P(3HBV), P(3HB-co-3HHx), and P(3HBV-co-3HHx)] to support attachment and proliferation. Interestingly, the P(3HBV-co-3HHx) films showed a lower degree of attachment, delayed cell division, and greater apoptosis (Wang et al., 2013). It may be deduced that these are the properties of PHA biofilms that play a key role in the cellular response. Apart from the initial success in the tissue engineering of osteoblasts, more work is required in the field of cartilage tissue engineering with PHAs. To achieve the desired chemical and physical properties,

electrospinning may be used to process and evaluate biomedical PHAs[P(3HB), P(3HB-co-4HB), P(3HB-co-3HV), and P(3HB-co-3HHx)]. Ricotti et al. (2012)demonstrated that electrospun P(3HB) scaffoldings reduced cell growth but stimulated the differentiation of the skeletal myotube development capability of myoblastic cell lines (C2C12 and H9c2 cells) (Ricotti et al., 2012). Volova et al. (2013) explored different aspects of the electrospinning of PHA fibers with different formulations that affect the physical-mechanical properties, and also suggested the various alterations possible to obtain tailor-made properties of these fibers. They produced PHA scaffolds by electrospinning and reported that they never affected the proliferation, sustainability, and attachment of NIH 3T3 mouse fibroblast cells, suggesting their potential use in tissue engineering (Volova et al., 2013). Indeed, these variations revealed the bio-physical-mechanical parameters of PHAs that were influenced by the presence of monomer fractions and fiber orientation.

PHAs as drugs carriers

Owing to their wide range of properties, PHAs have also been successfully used as drug carrier systems. For example, PHA polymers releasing 3HB monomers can also increase the calcium levels inside cells, thus protecting the mitochondria, suggesting that these biopolymers might be suitable drugs for bone and nervous system diseases. An mcl-PHA containing 3HD (R10) was depolymerized to obtain purified R10 monomers to be conjugated with a D-peptide (DP18) and its various derivatives. These conjugates improved the anti-cancer activities of the peptides and presented a definite synergy between the conjugated peptide (R10DP18L) and some cancer chemotherapy drugs. The anti-cancer activity was more prevalent in R10DP18L as compared to peptides combined with decanoic acid (C10DP18L) (O'Connor et al., 2013). Investigation of the mechanism revealed that alignment of hydroxyl monomers is more important for the anti-proliferation effect of a PHA/peptide conjugate. In addition, some recent studies have also highlighted the use of PHAs as nanoparticles for targeted drug delivery (Shrivastav et al., 2013). The future of PHAs will most certainly be associated with their applications as drug carriers for various microbial-caused diseases in general, and specifically for cancer therapy and tumor treatment-related drug delivery agents. However, the proper formulation of the microsphere/microcapsule/nanoparticles of PHA-containing desired drugs remains an aspect of important concern to ensure that the properties of the drug and/or PHA are not affected and that the releasing speed of the drug is close to its target.

Nerve regeneration

Recent advances of tissue engineering have brought hope to patients with brain damage for the repair and regeneration of damaged neurons, thanks to the identification of certain neural stem cells (NSCs) and neural progenitor cells (NPCs) in the central nervous system, which was once considered an impossible task. P(3HB), P(3HBV), P(3HB-co-4HB), and P (3HB-co-3HHx) have shown promising results for enhanced neural survival, promotion of greater axon-dendrite segregation, and for NSC growth, proliferation, and viability (Novikov et al., 2002, 2008; Xu et al., 2010; Yu et al., 2009; Chen and Tong, 2012). It can be inferred that for neural regeneration/repair, unique surface characteristics combined with desirable bio-functions should comprise the most suitable strategy (Lu et al., 2013), and the use of different PHA blends in this strategy might provide a solution to the problem (Lizarraga-Valderrama et al., 2015). The treatment of P(3HB-co-3HHx) films with alkali (NaOH) have demonstrated a significant increase in the hydrophilicity of these biomaterials that enhanced the attachment of NSCs/NPCs in the presence of low quantities of serum (Lu et al., 2014). More work is required to promote nerve regeneration with *in vivo* studies considering the sensitivity of the target material and the biocompatibility of the biomaterial used. A thin, flexible, and porous PHA biomaterial with suitable superficial characteristics and neuro-inductive and neuro-conductive ability would be an ideal choice for nerve regeneration.

Infection-resistant biomaterial

Biomaterial-affiliated bacterial infections are emerging as a serious threat in clinical practice, and those related to antibiotic-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* are of major concern. Biomaterials associated with an inflammatory response can be monitored with the use of various tools such as the hydro-indocyanine green dye method, reactive oxygen species imaging, and, more recently, near-infrared fluorescence imaging probes (Dinjaski et al., 2014). Antimicrobial polymers have appeared as potential compounds to replace the use of conventional drugs for antimicrobial mechanisms with reduced potential for resistance development (Kuroda and Caputo, 2013). Many macromolecules with a positive charge have been employed as biocidal polymers that could combat the target cells with a net negative charge. Recently, Dinjaski et al. (2014) reported a functionalized form of bacterial PHAs with antibacterial properties against such infections. Interestingly, the PHAs containing a thioester group in the side chains showed more promise as compared to P(3HO) and PET both inside and outside of living mammalian cells. It has also been established that the bacterial attachment to biomaterials depends on the type of monomers present and the purity of the substance (Mauclaire et al., 2010). The antimicrobial activity of PHACOS can be enhanced by incorporating more antimicrobial thioester ligands into the PHA main chain. The incorporation of other active groups might be very helpful to induce antibacterial activities against bacterial species other than *S. aureus.* Although the definite mechanism for the

antibacterial activity of PHACOS is still under debate, it may be attributed to the fact that PHACOS is specific for certain bacterial strains. Altering the thioester composition and molecular weight of the polymer increases the likelihood of conferring antimicrobial activity to these PHA biomaterials against more microorganisms. The presence of some metals in the PHA monomer composition might be of certain use in combating invading disease-causing agents because of their antimicrobial activities.

Prospects and challenges

Comparatively, little work is currently being carried out to investigate the potential of PHAs as biomedical materials. These studies are benefitting from the fact that the PHA polymer presents a great variety of characteristics in terms of its biodegradability, elasticity, non-toxicity, biocompatibility, surface modification capabilities, ability to function as nanoparticles, and possibility for tailor-made physical-chemical properties. All PHAs produced to date are of bacterial origin, which is a very costly process; hence, they are actively being exploited in research and development purposes. The microbial production of PHA also favors the possibility to obtain PHAs with some more unique monomer compositions in a more economical manner through metabolic engineering approaches. Identification of some novel strains of bacteria with the ability to accumulate unique types of PHA monomers possessing further versatile properties might be helpful in this regard. At present, it can be established that the PHA purity, monomer composition, and surface modifications all influence cell responses. These biodegradable polymers certainly deserve a stand-out position, as countless clinical procedures involving these polymers as medical implants are carried out on a daily basis worldwide. However, the human body's immune response to the implanted materials definitely needs to be addressed more precisely, and the use of animal models for testing these implants has helped enormously for this purpose. Finally, we can conclude that there are more glimpses of obtaining ideal bio-implants in the next few years than previously thought possible (based on the views and expectations in the previous century), as we have seen massive advancements in the production of more non-toxic, biocompatible, and versatile PHAs in the past decade.

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Compliance with ethics guidelines

The authors declare no conflict of interest.

Authors' contribution

Both authors conceived of the work and agreed on the manuscript contents. The literature review and main manuscript writing were performed by Iftikhar Ali.

List of Abbreviations

PHA = Polyhydroxyalkanoate
PLA = Poly-lactic acid
PGA = Poly-glycolic acid
PLGA = Poly(dl-lactide-co-glycolide)
Scl-PHA = Short-chain-length PHA
Mcl-PHA = Medium-chain-length PHA
P(3HB) = Poly(3hydroxybutyrate)
P(3HO) = Poly(3hydroxyoctanoate)
P(3HB-co-3HV) = Poly(3hydroxybutyrate-co-3hydroxyvalerate)
P(3HB-co-3HHx) = Poly(3hydroxybutyrate-co-3hydroxyhexanoate)
P(3HB-co-4HB) = Poly(3hydroxybutyrate-co-4hydroxybutyrate)
P(3HHx-co-3HO) = Poly(3hydroxyhexanoate-co-3hydroxyoctanoate)
P(3HB-co-3HP-co-5HV) = Poly(3hydroxybutyrate-co-3hydroxy-pentanoate-co-5hydroxyvalerate)
P(3HB-co-4HB-co-3HHx) = Poly(3hydroxybutyrate-co-4hydroxy-butyrate-co-3hydroxyhexanoate)
3HB = 3-Hydroxybutyrate
4HB = 4-Hydroxybutyrate
5HV = 5-Hydroxyvalerate
3HHx = 3-Hydroxyhexanoate
6HHx = 6-Hydroxyhexanoate
3HD = 3-Hydroxydecanoate
3HB-co-4HB = 3-Hydroxybutyrate-co-4hydroxybutyrate
3HB-co-3HHx = 3-Hydroxybutyrate-co-3hydroxyhexanoate
PHACOS = Poly(3hydroxy-acetyllthioalkanoate-co-3hydroxyalkanoate)

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