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Polyhydroxyalkanoates, the Biopolymers of Microbial Origin- A Review

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Abstract

Because petroleum-based plastics are not biodegradable, as well as the energy they require in their production, the rising plastic substantially contributes to the depletion of the environment. In contrast to synthetic plastics, polyhydroxyalkanoates (PHAs) are sustainable and eco-friendly bioplastics. A variety of microorganisms, such as fungi, bacteria, and algae, can be used to entirely synthesize PHAs. Enhanced biodegradability, biocompatibility, as well as other mechano-chemical properties are some of the promising properties of value-added biopolymers. It was also shown that PHA polymers have different properties depending on their chemical composition (units of monomer) and substrates. As an alternative to petroleum-based polymers, PHAs have great promise and need further study to determine how to economically produce and utilize them. Various applications of microbially synthesized PHAs are described in the review. Several microbial groups have also been shown to synthesize these biopolymers by genetic regulation. Also revealed in this review are the potential biomedical, environmental, and industrial applications of this biopolymer.

Keywords: Polyhydroxyalkanoates, Biopolymers, Microbes, Bioplastics

Introduction

Plastics have become one of the most commonly utilized materials on the planet. Plastics have undeniably become an integral part of modern society, that enables it to function, from uses in construction, biomedical industries, and disposable packaging to maintaining food quality, and much more. In 2018, 359 million metric tons of petroleum-based plastics were produced worldwide, a serious environmental threat (Othman *et al.*, 2021). The market size of PHA was estimated to be 73.6 million USD and is expected to grow to 93.5 million by 2022 (Varghese *et al*., 2022). Each of these plastics has a variety of uses in everyday life. Polymers of this type are not biodegradable, which is their main disadvantage (Qin *et al*., 2021). Thus, to make petrochemical plastics more environmentally friendly, several studies have been conducted. Various value-added biopolymers are polyesteramide, polyethylene, polyhydroxyalkanoates (PHAs) **Figure 1**, polycaprolactone (PCL), polylactic acid (PLA), etc (Varjani *et al*., 2021). In contrast to petroleum-derived plastics, bioplastics, also known as PHAs, are made of renewable resources, such as proteins, vegetable oil, and starch. These biopolymers provide a sustainable alternative to petroleum-based plastics than can conserve fossil fuels and reduce CO_2 emissions, making them an important component of sustainable development (Nofar *et al*., 2019).

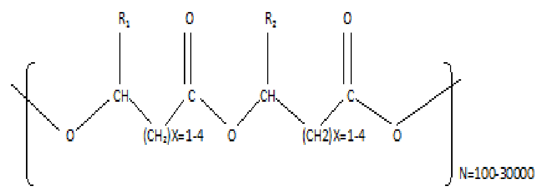

Figure 1. Polyhydroxyalkanoates structure (R_1 and R_2 are alkyl groups-C) (Ranganadhareddy, 2022)

The production of these biopolymers at a large scale, however, poses significant challenges. As well as a high energy requirement, one of the challenges in the PHA production process is the price of the carbon sources utilized by the microorganisms (Ranganadha *et al.*, 2019). Waste organic resources, waste from agriculture, wastewater, plant oils, fats from animals, and waste cooking oils have all been utilized in the process (Guleria *et al.*, 2022). PHA can also be extracted and purified using advanced energy-efficient and environmentally friendly technologies (Ranganadha *et al.*, 2021). In addition to polyhydroxybutyrate, there are various poly (3-hydroxybutyrate)/ polyhydroxybutyrate derivatives (Ranganadhareddy, 2022). The first monomer components were identified in monomeric form in poly- (3-hydroxybutyrate)/ polyhydroxybutyrate. About 150 monomers make up different PHAs (Sharma *et al.*, 2021). Polymeric PHAs have properties similar to petroleum-based polymers along with strong tensile strengths and high melting temperatures. Their properties like biocompatibility, biodegradability, and piezoelectricity make PHAs attractive biopolymers in biomedical applications (Ranganadha, 2022). Using microbially synthesized PHAs as models, this review aims to understand the diversity and properties of these compounds. Additionally, these value-added polymers have been described regardingtheir biosynthesis and genetics. PHAs are also discussed in detail in terms of their environmental, industrial, and biomedical applications. Sustainable and eco-friendly alternatives to petroleum-based

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plastics are a family of biocompatible and biodegradable polyesters called microbial PHAs. PHAs can be produced from microbial sources, according to various reports. Although the present article describes PHA biosynthesis from microbial sources and these biopolymers' properties, production on a commercial scale, methods of extraction as well as their applications, it does not explain their synthesis. To synthesize eco-friendly biopolymers, it is necessary to understand extraction procedures and screen for efficient microbes that produce PHA.

Classification

Various microorganisms can synthesize polyhydroxyalkanoates (PHAs), which are eco-adoptable polyesters of hydroxyalkanoate (HA). They are commonly stored in the cytoplasm as insoluble inclusion bodies, ranging from 0.2 to 0.5 um in diameter (Obruca *et al.,* 2021). Cells synthesize PHAs when adverse conditions prevail, such as low oxygen levels or a lack of nutrients, such as phosphorus and nitrogen (Ranganadha & Chandrasekhar, 2021). However, the presence of a carbon source is one prerequisite for the biosynthesis of PHAs (Choi *et al.,* 2020). As a result of this, microorganisms producing PHAs can tolerate and store these polymeric materials' osmotolerance in high concentrations (Nandakumar *et al.,* 2021). The materialistic properties of PHAs resemble those of synthetic plastics in stark contrast to biopolymers, such as polyethylene terephthalates (PET) or polylactic acid (PLA). PHAs have been extensively studied as they are the most potential biopolymers due to their properties (Talan *et al.,* 2021).

Compared to chemical means, it is easier to produce PHAs with higher molecular weight through biomedical means, spite the possibility to synthesize PHAs through both chemical and biological approaches (Costa *et al.,* 2019). Different microbial groups have different metabolic pathways for the production of PHA (Adriana *et al*., 2020; Röhr *et al*., 2020). These biopolymers can be produced by both exponential and stationary phases of microbial growth. PHAs are produced in the exponential phase under favorable, balanced conditions whereas, the synthesis and accumulation of PHAs occur in the stationary phase as a result of limitations in nutrients such as phosphorus, excess carbon, nitrogen, and oxygen. Cells of microbes store excess nutrients in the form of PHAs, and when favorable growth conditions arise, they are released. In addition, a carbon source is essential to the production of microbial PHA (Reddy *et al.*, 2019).

Biosynthetic Pathway of Polyhydroxyalkanoate

Through the Calvin Benson cycle, atmospheric CO_2 is converted into PHA, which is converted to Acetyl-CoA through glycolysis. Acetyl-CoA is converted into the most prevalent PHA, PHB by three enzymatic reactions (Ranganadha, 2022). Two Acetyl-CoA molecules are combined into Acetoacetyl-CoA by the first enzyme, Pham. PhaBis the second enzyme thathelps in the formation of hydroxybutyric-CoA by the reduction of Acetoacetyl-CoA. Finally, a growing PHB molecule is added with hydroxybutyric-CoA fatty acid monomer via an ester bond by PhaEC (Krieger & Kececioglu, 2022; Ranganadhareddy, 2022) as shown in **Figure 2**.

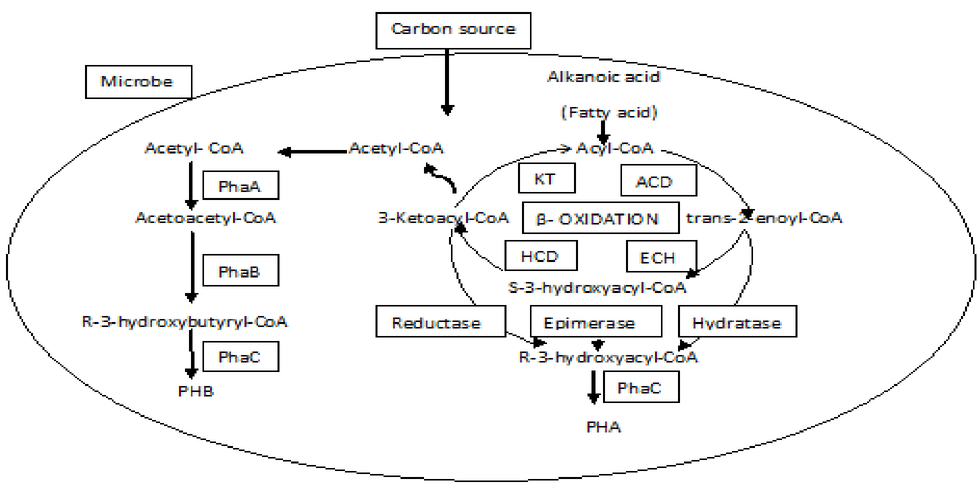

Figure 2. Biosynthetic pathway of Polyhydroxybutyrate in microbes (Ranganadha, 2022)

PHA Properties

Depending on their chemical composition as well as the chain length (copolyesters or homopolyesters), PHAs have different properties, being thermoplastic polymers synthesized naturally by microorganisms (Cywar *et al.,* 2022). Under aerobic conditions naturally, these polymers produced carbon dioxide and water when degraded by various microbes (Mishra *et al.,* 2018). On the other hand, carbon dioxide and methane were released as a result of anaerobic degradation. Complete biodegradability, high processability, biocompatibility, structural diversity, and non-toxicity are the general characteristics of PHAs (Mahmoudpour *et al*., 2018). Certain materialistic properties such as aroma barrier and moisture resistance properties can be retained by the artificial modification of PHB through the addition of monomers such as polypropylene (PP) (Nofar *et al*., 2019). Polyesters are used for tissue engineering in the case of scaffolds, biological materials in reusable suturing, cardiovascular devices, and substitutes for bone implants have been approved by the Food and Drug Administration (FDA) based on these properties. Additionally, to regulate medication release, PHAs are used for dressings as nano and microspheres and devices for drug carriers. It has also been reported that these polymers are used as a coating and packaging material. The usage of these polyesters for tissue engineering as scaffolds, biomaterials in reusable sutures, cardiovascular devices, and substitutes for bone implants has been approved by the Food and Drug Administration (FDA) based on these properties (Muneer *et al.,* 2020). Additionally, to control the release of drugs, PHAs are used for dressings as nano- and micro- spheres and devices for drug carriers. It has also been reported that these polymers are used as a coating and packaging material (Ranganadhareddy *et al.,* 2022).

The polymers derived from biopolymer PHA have various properties similar to polymers produced from petroleum by-products like polypropylene, like high melting point (175 ˚C) and high tensile strength 930-35Mpa) (Xu *et al*., 2019). As PHAs are partially crystalline, the polymer amorphous phase is observed by using the glass transition temperature (Tg). Although, the crystalline phase's thermal properties are described using melting temperature (Tm) (Ranganadha *et al.,* 2020). The temperature at which the polymers of PHA melt and the number of carbon atoms contained in the side chain are directly proportional to each other. In contrast, the side chain's length is inversely proportional to the glass transitional temperature. Furthermore, an increase of 24 ˚C in the Tm (45˚C- 69˚C) could be observed when the number of carbon atoms increased from C4 TO C7 in the side chain (3HA). On the contrary, Tg was seen to decrease with an increase in the side chain of carbon atoms (from 1 to 7) (Oliveira *et al.,* 2020).

Due to their low Tg value compared to MCL-PHAs, SC—PHAs are more crystalline and brittle. For example, with a Tg of 4 ˚C and a Tm of 180 ˚C, the SCL-PHA P (3HB) is very brittle, stiff, and crystalline (Ansari *et al*., 2021). Contrary to this, the melting temperature range for MCL-PHAs is 42 ˚C to 75 ˚C, with a Tg ranging between 25 ˚C and 65ºC (Zhang *et al.,* 2021). Compared to SCL-PHAs, MCL-PHAs are less crystalline because of their irregular side groups. These irregular side groups obstruct the compact packaging inside the polymers. The crystalline structure and the Tg result in the elastomeric properties of these kinds of polymers. Out of all the biopolymers synthesized by microorganisms, properties similar to thermoplastic elastomers are seen only in MCL-PHAs (Muneer *et al.,* 2021). However, the elastomeric properties are shown inside a small temperature range due to their low Tm. The thermoplastic polymers become easy to mold as they are fluid at a temperature greater than their Tm which makes them completely powdered. Furthermore, it was observed that the Tg of the MCL-PHAs decreased when the length of the side chain increased (Larrañaga & Lizundia, 2019)

Additionally, a decrease in the Tg of MCL-PHAs was seen when the average side chain length increased. This characteristic was observed as a result of the increasing polymer chain mobility. The thermal properties of the PHAs were determined by the substrate used for the synthesis of the PHAs. For example, MCL-PHAs demonstrated a Tg of 43.7 ˚C. These MCL-PHAs were produced using coconut oil as substrate by P. putida. When the PHAs were synthesized using the same strain with linseed oil as substrate, a Tg of 61.7 ˚C was observed, which is 18 ˚C less (Larrañaga & Lizundia, 2019).

There is a variation in the mechanical properties too, based on the length of the polymer chain. Among MCL-PHAs and SCL-PHAs, the properties like tensile strength and elongation at bred show a significant variation (Oliveira *et al.,* 2020). Higher flexibility and elasticity are demonstrated by MCL-PHAs while SCL-PHAs are highly crystalline and more brittle. Even so, these properties are not small for all PHAs, with some exceptions present. For example, Young's modulus of 3.5 GPa and tensile strength of 40 MPa. Likewise, elongation at break for P(3HB) and P(4HB) was seen to be 1000% and 3% respectively (Meng & Chen, 2017). The location of the R-groups in the side chains is a key distinction between these two polymers. The mechanical properties and 3D polymeric structure of these polymers are altered by the R-group position (Zhang *et al.,* 2018).

Additionally, the blending of other polymers and co-monomers in various ratios with the biopolymers for different industrial applications and biomedical applications improves the flexibility of the PHA (Amina *et al*., 2018; Zheng et al., 2019). For instance, P (3HB-co-3HHx) copolymer has mechanical properties like flexibility, hardness, and rigidity, which differ greatly from those of P (3HB) (Ranganadhareddy *et al.,* 2018). These properties are dependent heavily on the units 3HHx. A copolymer containing a 5.9% mol fraction of 3HHx exhibited the highest flexibility (163% elongation at break). Likewise, Young's modulus (631.3 MPa) and the maximum result for tensile strength (25.7 MPa) were attained when 2.5% was the mol fraction of 3Hx units in the copolymer (Behera *et al*., 2022). To analyze the mechanical properties, scaffolds and biopolymeric films were produced by the usage of mixtures of P (3HB) and P (3HB-co-3HHx) in another study (Ansari, 2019). An increase from 40 to 60% in the ratio of P (3HB-co-3HHx) in the blend resulted in a slight decrease in tensile strength, and the flexibility remarkably increased (to 106% from 15%). The scaffolds containing 60% of P (3HB-co-3HHx) supported the rapid proliferation of chondrocytes on the surface and escalated growth. Therefore, it can be inferred that the PHA biopolymer effect in industrial as well as biomedical applications can be significantly enhanced by the suitable blending of PHAs.

Applications of PHA

Industrial Applications

Different monomer compositions are used to industrially produce the polymersto meet various requirements for their wide use in the industrial sectors. A US-based company, Metabolix, manufactures P (3HBco-3HB) and its copolymer BIOPOL®. Many different types of applications can be performed with this including shampoo bottles, packaging, disposable cups, disposable razors, etc (Alexandrovich *et al.,* 2018).

Biomedical Implants

Human implants containing PHAs have become commonplace, including screws, staples, sutures, stents, bone plates, nerve guides, articular cartilage repair devices, and adhesion barriers. A potential biomedical application for the PHA is that it is biodegradable, biocompatible, stimulates bone formation, and promotes wound healing, among many other properties. It has mechanical properties like tensile strength and elasticity modulus which are similar to the mechanical properties of the bone. Currently, only some PHAs are sufficiently manufactured that can be used as materials for implants. The composition of these implant materials can alter their degradability and mechanical properties. There have been reports that SCL and MCL-PHA members (PHBVHHx, PHBHHx, P3HB4HB, PHBV, and PHB) could be used for biomedical implants (Akhtartavan *et al.,* 2019; Ho *et al*., 2022). It has been known that tissue regeneration and cell proliferation can be enhanced by these biopolymers. Another advantage of the PHA-based implants is that even during their degradation, the pH does not change where they are implanted. This allows the host immune system to tolerate them.

Tissue Engineering

The main objective of tissue engineering is the promotion of the growth of new tissues using biomaterials, cells, and different signaling molecules for the restoration of damaged tissues. It involves maintaining, restoring, and improving various tissues of the body like skin tissue, periodontal tissue, heart valve tissue, nerve tissue, vascular tissue or bone, and cartilage tissue (Wu *et al.,* 2022). The regeneration of muscle, blood vessels, skin, and repair of nerves and cartilages have also been performed by PHAs.

Therapeutic Carrier

The use of these polymers as drug carriers was the first pharmaceutical application of PHAs. A drug delivery system that consisted of a polymeric matrix was used to deliver the therapeutics to the target site in a controlled manner. Additionally, the bioavailability of the drugs can be increased by these polymers. These polymers can escape the immune system without causing any therapeutic toxicity or other immune responses (Masood *et al*., 2015).

Conclusion and Future Perspectives

In the last few years, Polyhydroxyalkanoates have emerged as a potential substitute for synthetic plastics. In scientific research and commercial applications, these biopolymers have gained widespread interest. Microorganisms such as fungi, bacteria, and microalgae have been utilized to achieve the commercial production of these value-added biopolymers. The substrate and types of PHAs determine the production and extraction of microbially produced PHAs, respectively. Extracting and purifying these biopolymers can be performed by various methods, and each method has a specific effect on the purity of the resulting PHA. As biopolymers, these materials can be used in a variety of environmental, agriculture, and biomedical applications due to their biodegradability and biocompatibility. These biopolymers are manufactured by various industries with a wide range of applications, for example, thermoplastic materials, packaging and coatings, food supplements for animals, injection moldings, drug carriers, and anti-fouling agents. These biopolymers can be used as a replacement for plastics, thus reducing the amount of pollution emitted by petroleum-derived plastics.

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References

Adriana, M., Lidia, D., Federica, R., Stefania, S., Raffaele, D. P., & Luigi, S. (2020). Effectiveness of colistin with rifampicin and meropenem against colistin-resistant Acinetobacter baumannii strains:an in vitro study. *Pharmacophore, 11*(2), 1-6.

Akhtartavan, S., Karimi, M., Karimian, K., Azarpira, N., Khatami, M., & Heli, H. (2019). Evaluation of a self-nanoemulsifying docetaxel delivery system. *Biomedicine & Pharmacotherapy, 109,* 2427-2433. doi:10.1016/j.biopha.2018.11.110

Alexandrovich, S. O., Yurievna, V. S., Olegovich, P. I., Yurievna, K. N., Ilyinichna, V. L., & Pavlovna, Y. T. (2018). Provision of Microbiological Safety in the Food Industry based on Special Technological Supporting Solutions. *International Journal of Pharmaceutical Research & Allied Sciences, 7*(1), 103-113.

Amina, T., Abess, B., & Yassine, N. (2018). Phenolic content, HPLC analysis and Antioxidant activity extract from *Tamarix Articulata*. *Journal of Advanced Pharmacy Education and Research, 8*(4), 1-8.

Ansari, M. (2019). Bone tissue regeneration: biology, strategies and interface studies. *Progress in Biomaterials 8*(4), 223-237. doi:10.1007/s40204-019-00125-z

Ansari, S., Sami, N., Yasin, D., Ahmad, N., & Fatma, T. (2021). Biomedical applications of environmentally friendly polyhydroxyalkanoates. *International Journal of Biological Macromolecules, 183,* 549-563. doi:10.1016/j.ijbiomac.2021.04.171

Behera, S., Priyadarshanee, M., Vandana, & Das, S. (2022). Polyhydroxyalkanoates, the bioplastics of microbial origin: Properties, biochemical synthesis, and their applications. *Chemosphere, 294,* 133723. doi:10.1016/j.chemosphere.2022.133723

Choi, S. Y., Rhie, M. N., Kim, H. T., Joo, J. C., Cho, I. J., Son, J., Jo, S. Y., Sohn, Y. J., Baritugo, K. A., Pyo, J., et al. (2020). Metabolic engineering for the synthesis of polyesters: A 100-year journey from polyhydroxyalkanoates to non-natural microbial polyesters. *Metabolic Engineering, 58,* 47-81. doi:10.1016/j.ymben.2019.05.009

Costa, S. S., Miranda, A. L., de Morais, M. G., Costa, J. A. V., & Druzian, J. I. (2019). Microalgae as a source of polyhydroxyalkanoates (PHAs)-A review. *International Journal of Biological Macromolecules, 131,* 536-547. doi:10.1016/j.ijbiomac.2019.03.099

Cywar, R. M., Rorrer, N. A., Hoyt, C. B., Beckham, G. T., & Chen, E. Y. X. (2022). Bio-based polymers with performance-advantaged properties. *Nature Reviews Materials, 7,* 83-103. doi:10.1038/s41578-021-00363-3

Guleria, S., Singh, H., Sharma, V., Bhardwaj, N., Arya, S. K., Puri, S., & Khatri, M. (2022). Polyhydroxyalkanoates production from domestic waste feedstock: A sustainable approach towards bio-economy. *Journal of Cleaner Production, 340,* 130661. doi:10.1016/j.jclepro.2022.130661

Ho, W. E., Sun, L., Goh, H. J., Tint, M. T., Sun, L., & Leow, M. K. S. (2022). Brown adipose tissue influences adiponectin and thyroid hormone changes during Graves' disease therapy. *Adipocyte, 11*(1), 389-400. doi:10.1080/21623945.2022.2104509

Krieger, S., & Kececioglu, J. (2022). Heuristic shortest hyperpaths in cell signaling hypergraphs. *Algorithms in Molecular Biology, 17*, 12. doi:10.1186/s13015-022-00217-9

Larrañaga, A., & Lizundia, E. (2019). A review on the Thermo mechanical properties and biodegradation behavior of polyesters. *European Polymer Journal, 121,* 109296. doi:10.1016/j.eurpolymj.2019.109296

Mahmoudpour, M., Dolatabadi, J. E. N., Torbati, M., & Rad, H. A. (2019). Nanomaterials-based surface plasmon resonance signal enhancement for detection of environmental pollution. *Biosensors and Bioelectronics, 127,* 72-84. doi:10.1016/ j.bios.2018.12.023

Masood, F., Yasin, T., Hameed, A., (2015). Polyhydroxyalkanoates–what are the uses? Current challenges and perspectives. *Critical Reviews in Biotechnology, 35*(4), 514-521. doi:10.3109/07388551.2014.913548

Meng, D. C., & Chen, G. Q., (2017). Synthetic biology of polyhydroxyalkanoates (PHA). *Synthetic Biology–Metabolic Engineering,* 147-174. doi:10.1007/10_2017_3

Mishra, R. K., Sabu, A., & Tiwari, S. K. (2018). Materials chemistry and the futurist eco-friendly applications of nanocellulose: Status and prospect. *Journal of Saudi Chemical Society, 22*(8), 949-978. doi:10.1016/j.jscs.2018.02.005

Muneer, F., Nadeem, H., Arif, A., & Zaheer, W. (2021). Bioplastics from Biopolymers: An Eco-Friendly and Sustainable Solution of Plastic Pollution. *Polymer Science Series C, 63,* 47-63. doi:10.1134/S1811238221010057

Muneer, F., Rasul, I., Azeem, F., Siddique, M. H., Zubair, M., Nadeem, H. (2020). Microbial Polyhydroxyalkanoates (PHAs): Efficient Replacement of Synthetic Polymers. *Journal of Polymers and the Environment, 28,* 2301-2323. doi:10.1007/s10924-020-01772-1

Nandakumar, A., Chuah, J. A., & Sudesh, K. (2021). Bioplastics: A boon or bane. *Renewable and Sustainable Energy Reviews, 147,* 111237. doi:10.1016/j.rser.2021.111237

Nofar, M., Sacligil, D., Carreau, P. J., Kamal, M. R., & Heuzey, M. C. (2019). Poly (lactic acid) blends Processing, properties, and applications. *International Journal of Biological Macromolecules, 125,* 307-360. doi:10.1016/j.ijbiomac.2018.12.002

Obruca, S., Sedlacek, P., & Koller, M. (2021). The underexplored role of diverse stress factors in microbial biopolymer synthesis. *Bioresource Technology, 326,* 124767. doi:10.1016/j.biortech.2021.124767

Oliveira, G. H. D., Zaiat, M., Rodrigues, J. A. D., Rmsay, J. A., & Ramsay, B. A. (2020). Towards the Production of MCL-PHA with Enriched Dominant Monomer Content: Process Development for the Sugarcane Biorefinery Context. *Journal of Polymer Science and Environment, 28,* 844-853. doi:10.1007/s10924-019-01637-2

Othman, A. R., Hasan, H. A., Muhamad, M. H. Ismail., N. I., & Abdullah, S. R. S. (2021). Microbial degradation of microplastics by enzymatic processes: a review. *Environmental Chemistry Letters, 19,* 3057-3073. doi:10.1007/s10311-021-01197-9

Qin, M., Chen, C., Song, B., Shen, M., Cao, W., Yang, H., Zeng, G., & Gong, J. (2021). A review of biodegradable plastics to biodegradable microplastics: Another ecological threat to soil environments. *Journal of Cleaner Production, 312,* 127816. doi:10.1016/j.jclepro.2021.127816

Ranganadha, A. R. (2022). Microalgae as a source of biopolymer- A Comprehensive Review. *Journal of Biochemical Technology, 13*(2), 40-45. doi:10.51847/dTb7rBmjNO

Ranganadha, A. R., & Chandrasekhar, Ch. (2021). Production of polyhydroxybutyrate from the marine source- A Review. *Indian Journal of Ecology, 48*(6), 1829-1836.

Ranganadha, A. R., Sravani, K., Sanjana, N., & Chandrasekhar, Ch. (2021). Production of biopolymer from bacteria – A Review. *Environmental and Earth Sciences Research Journal, 8*(2), 91-96. doi:10.18280/eesrj.080205

Ranganadha, R. A., Krupanidhi, S., Venkateswarulu, T. C., Bharath, K. R., Sudhakar, P., & Vidyaprabhakar, K. (2019). Molecular characterization of a biopolymer-producing bacterium isolated from the sewage sample. *Current Trends in Biotechnology and Pharmacy, 13*(3), 325-335.

Ranganadha, R. A., Vidyaprabhakar, K., Venkateswarulu, T. C., Krupanidhi, S., Nazneen Bobby, Md., Abraham, P. K., Sudhakar, P., & Vijetha, P. (2020). Statistical optimization of Polyhydroxtbutyratye (PHB) production by novel Acinetobacternosocomialis RR20 strain using Response Surface Methodology. *Current Trends in Biotechnology and Pharmacy, 14*(1), 62-69.

Ranganadhareddy, A. (2022). A Review on Production of Polyhydroxyalkanoates in Microorganisms. *Journal of Biochemical Technology, 13*(1), 1-6. doi:10.51847/Uo3EEbmgID

Ranganadhareddy, A., Venkateswarulu, T. C., Sudhakar, P., Krupanidhi, S., & Vidyaprabhakar, K. (2018). Optimization of process parameters for Polyhydroxybutyrate production from isolated *Acinetobacter nosocomial RR20* through submerged fermentation. *Current Trends in Biotechnology and Pharmacy, 12*(2), 16-25.

Ranganadhareddy, A., Vijetha, P., & Chandrasekhar, C. (2022). Bioplastic production from microalgae and their applications- A critical review. *Journal of Biochemical Technology, 13*(2), 13-18. doi:10.51847/H3pUzozErq

Reddy, A. R., Peele, K. A., Krupanidhi, S., Prabhakar, K. V., & Venkateswarulu, T. C. (2019). Production of Polyhydroxtbutyratye from Acinetobacternosocomialis RR20 strain using modified mineral salt medium: a statistical approach. *International Journal of Environment Science and Technology, 16*(10), 6447-6452. doi:10.1007/s13762-018-2102-3

Röhr, D., Boon, B. D. C., Schuler, M., Kremer, K., Hoozemans, J. J. M., Bouwman, F. H., El-Mashtoly, S. F., Nabers, A., Frederik, G., Rozemuller, A J. M., et al. (2020). Label-free vibrational imaging of different Aβ plaque types in Alzheimer's disease reveals sequential events in plaque development. *Acta Neuropatholgica Communications, 8,* 222. doi:10.1186/s40478-020-01091-5

Sharma, V., Sehgal, R., & Gupta, R., (2021). Polyhydroxyalkanoate (PHA): properties and modifications. *Polymer, 212,* 123161. doi:10.1016/j. polymer.2020.123161

Talan, A., Pokhrel, S., Tyagi, R. D., & Drogui, P. (2022). Biorefinery strategies for microbial bioplastics production: Sustainable pathway towards Circular Bioeconomy. *Bioresource Technology Reports, 17,* 100875. doi:10.1016/j.biteb.2021.100875

Varghese, S., Dhanraj, N. D., Rebello, S., Sindhu, R., Binod, P., Pandey, A., Jisha, M. S., & Awasthi, M. K. (2022). Leads and hurdles to sustainable microbial bioplastic production. *Chemosphere, 305,*135390, doi:10.1016/ j.chemosphere. 2022.135390

Varjani, S., Shah, A. V., Vyas, S., & Srivastava, V. K. (2021). Processes and prospects on valorizing solid waste for the production of valuable products employing bio-routes: A systematic review. *Chemosphere, 282,* 130954. doi:10.1016/j.chemosphere.2021.130954

Wu, N., Tu, Y., Fan, G., Ding, J., Luo, J., Wang, W., Zhang, C., Yuan, C., Zhang, H., Chen, P., et al. (2022). Enhanced photodynamic therapy/photothermaltherapy for nasopharyngeal carcinoma via a tumor microenvironment-responsive self-oxygenated drug delivery system. *Asian Journal of Pharmaceutical Sciences, 17*(2), 253-267. doi:10.1016/j.ajps.2022.01.002

Xu, Z., Wang, Y., Wu, D., & Ananth, K. P., Bai, J. (2019). The process and performance comparison of polyamide 12 manufactured by multi-jet fusion and selective laser sintering. *Journal of Manufacturing Processes, 47*, 419-426. doi:10.1016/j.jmapro.2019.07.014

Zhang, J., Shishatskaya, E. I., Volova, T. G., da Silva, L. F., & Chen, G. Q. (2018). Polyhydroxyalkanoates (PHA) for therapeutic applications. *Materials Science & Engineering: C, 86*, 144-150. doi:10.1016/j.msec.2017.12.035

Zhang, Q., Song, M., Xu, Y., Wang, W., Wang, Z., & Zhang, L. (2021). Bio-based polyesters: Recent progress and prospects. *Progress in Polymer Science, 120,* 101430. doi:10.1016/j.progpolymsci.2021.101430

Zheng, Y., Chen, J. C., Ma, Y. M., & Chen, G. Q. (2020). Engineering biosynthesis of polyhydroxyalkanoates (PHA) for diversity and cost reduction. *Metabolic Engineering, 58*, 82-93. doi:10.1016/j.ymben.2019