Food and Scientific Reports
e-ISSN 2582-5437
foodandscientificreports.com

Popular Article

Production of *Polyhydroxyalkanoates* Using Marine Algae and Their Biomedical Applications

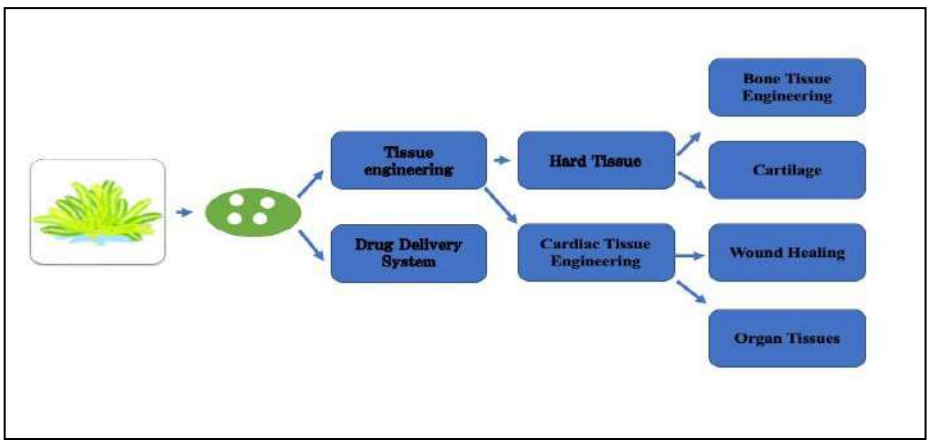
Akhila S. Viswan, Sreelakshmi K. R.✉, Mohan C.O., and Bindu J.

ICAR-Central Institute of Fisheries Technology, Matsyapuri. P.O, Willigdon Island, Cochin, Kerala, India

✉ Corresponding author: sreecift@gmail.com

ABSTRACT

Polyhydroxyalkonates (PHAs) are biopolymers that are produced by microorganisms under nutrient limiting conditions. These biopolymers can replace petrochemical plastics as they are fully biodegradable. An alternative source of organisms for production of PHA is marine algae. Both prokaryotic and eukaryotic algae can be used for this. The extraction from marine algae involves digestion of algal cells using sodium hypochlorite and dissolution of polymer in chloroform. The PHA is biocompatible, biodegradable, non-toxic and have plasticizing and encapsulation capacity. These properties make PHA one among the best polymer candidate for biomedical applications.



Keywords: Polyhydroxyalkanoates, micro algae, biocompatibility, biomedical applications

Cite this article:
Viswan, AS., Sreelakshmi KR, Mohan C.O., and Bindu J. (2023) *Tupistra clarkei*: Production of *Polyhydroxyalkanoates* Using Marine Algae and Their Biomedical Applications. *Food and Scientific Reports*, 4(8): 13-19.

Submitted: 26 July 2023
Accepted: 6 August 2023

Introduction

One of the major problems faced by the marine environment is the increasing load of non-biodegradable plastic wastes produced using petrochemicals. PHA was used as an alternative for these non-degradable plastics in order to reduce the marine pollution (Roja et al., 2019). Polyhydroxyalkonates (PHAs) are biopolymers produced by microorganisms under nutrient limiting conditions such as lack of nitrogen and abundance of carbon content. Almost 300 different species of gram negative and gram positive bacteria and a large group of archae are capable of producing PHA from carbon source (Ke et al., 2016). Microorganisms such as *Esterichia coli, Alcaligenes latus, Cupriavidus necator, Bacillus sp., Azotobacter sp*. etc. can produce the biopolymer PHA. PHAs are stored as intracellular granules in the microorganisms (Blunt et al., 2018). Two types of PHA, short chain polyhydroxyalkonate (scl-PHA), which is crystalline in nature and medium chain polyhydroxyalkonates (mcl-PHA), which is amorphous in nature are there. Lemoigne was the first person to report the presence of poly 3-hydroxybutyrate (PHB) in microorganisms in 1926 (Anderson et al., 1990).

A bioplastic is considered as fully biodegradable only when they satisfy the following five characteristics such as marine biodegradability, soil biodegradability, industrial compostability, home compostability and anaerobic digestibility. PHA is one of such bioplastic that satisfies all these five characteristics. Even though PHAs are biodegradable and biocompatible, the cost of production is much more comparable to other polymers. The cost of PHA is almost 15 times higher than other ordinary synthetic polymers. This can be reduced by the use of varied substrates (food waste and agriculture waste) and different cultures (Kim, 2000; Reddy et al., 2003) for PHA production.

PHA production using microalgae

Microalgae which include prokaryotic cyanobacteria and eukaryotic algae use water, carbon dioxide and inorganic salts to convert radiant energy into different products contained in biomass. These are photoautotrophic microorganisms with zero net CO_2 emission. Although there are only 40000 species of algae and cyanobacteria are published, values above 70000 were estimated on a conservative base (Sánchez-Bayo et al., 2020).

Algae can be used as a substitute renewable resource for biopolymer production due to its high growth rate, photosynthetic capacity and carbon dioxide fixation (Noreen et al., 2016). The PHA production by algae can be either directly from their biomass or from their secondary metabolites. PHB, the major class of polyhydroxyalkonates, produced from algal sources have biodegradability, biocompatibility, non-toxicity and plasticizing capacity. This can be used in various fields including medical, food packaging, agricultural etc. (Roja et al., 2019). Some of the eukaryotic microalgal strains used for the PHA production are *Chlorella vulgaris, C alothria fusa and Chlamydomonas reinhardtii*.

Cyanobacteria show species specific PHA production. Most of them produce PHB under different nutrient limiting conditions There are certain advantages for cyanobacteria over bacteria. *Synechococcus sp*. MA19 produces PHB in a limited amount of phosphate and an excess of reducing equivalents. *Spirulina platensis* and *Nostoc muscorum* also produce PHB under similar condition. *Synechocystis sp.* PCC 6803 accumulates PHB under nutrient limiting environment up to 14% (Jyothi, 2018). The dry cell weight of PHA produced by cyanobacteria is low compared to bacteria

(Didem et al., 2017). The recombinant cyanobacteria can also be used for improved production of PHA under nutrient limiting conditions and mixotrophic cultivation.

Table 1: PHA production by different algal species (Roja et al., 2019)

Algal species	PHA content (%)
Synechococcus subsalsus	16
Spirulina sp. LEB-18	12
Synechocystis PCC6803	4.1- 26
Synechococcus MA19	55
Arthrospira subsalsa	14.7
Phormidium sp.	14.8
Nostoc muscorum	8.7- 22
Oscillatoria jasorvensis	15.7
Calothrix scytonemicola	25.2
Anabaena sp.	2.3
Aulosira fertilissima	10
Calothrix sp.	6.4
Scytonema sp.	7.4

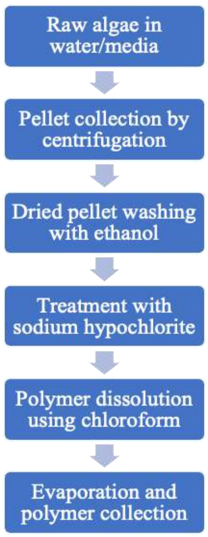


Figure 1: Extraction of PHA from Cyanobacteria (Garcia et al., 2020)

Biomedical applications of PHA

Non-toxicity, biodegradability and biocompatibility are the characteristic properties that make PHA more convenient for medical applications such as an anticancer agent and bio-control agent (Subhasree and Vipin., 2017). PHB is used for the production of thread like filaments, tubes, films and microspheres because of its capability to degrade in the living cells of mammal (Sabbir et al., 2021). Because of the biodegradability nature PHAs are used for drug delivery systems. Encapsulation properties and bioavailability are other factors which enhance the use of PHA in biomedical application. Moreover anything else, the natural origin of PHA makes it dominant in the biomedical field (Alejandra., 2019). The superior mechanical properties of PHA make it ideal candidate for use in tissue engineering. Molecular mass, environmental conditions, crystallinity are factors that determine the degradability of PHA. Mixing the PHA with other appropriate organic or inorganic materials is needed to get the indented rate of biodegradability and mechanical strength.

Table 2: Applications of different types of PHAs (Butt et al., 2018)

PHA	APPLICATION	IMPROVED CHARACTERISTIC
PHB + bacterial cellulose	Scaffolds for tendons and artificial ligaments	• Increase biodegradability, biocompatibility • Increase hydrophobicity, roughness
PHB + hydroxyapatite	Bone defects	• Improve mechanical properties and strength
PHB scaffolds + collagen I	Osteogenic differentiation	
PHBV	Injured spinal chord	• Repair the injured spinal chord
PHBHHX	Bone tissue engineering	• Culture in time period of just 20 days
PhaP + RGD protein + PHBHHX scaffold	Bone tissue engineering	• Spreading of bone marrow mesenchymal cells • Cell proliferation • Chondrogenic differentiation
P3HB4HB	Artificial blood vessel	• Adjustable strength and elasticity • Activate elastin formation
PHBV, PHB, P(3HB-co-4HB), P(3HB), P(4HB), P(3HB-co-15 mol% 3HV)	Fabricating tissues	• Helps maintain the pore size and shape • Increase biocompatibility • Enhance mechanical properties
PHBVHHx, PHA nanofibres	Liver tissue engineering	• Improve biodegradability • Improve mechanical properties • Improve neural stem cell adhesion
Poly (3-HB-3HHx))	Achilles tendon injury	
P(3-HO), PHB	Cartilage repairing	• Improve melting temperature • Improve flexibility • Improve strength of scaffold
PEG + PHB	Bone tissue engineering	• Improve biodegradability & biocompatibility
PHA	Heart tissue	• Compatible • Reproducible & degradable

P (3HB-co-4HB)	Tri-leaflet heart valve	• Thermoplastic property
P (4HB)	Autologous cardiovascular tissues	• No blood leakage
PGA + P(3H)-co-3HHX)	Pulmonary valve leaflet	• Good mechanical properties • No thrombus formation • High vascular cell growth
PHB	Schwarm cell	• Enhance the survival • Proliferation • Attachment
P(3HB-3HV), PHB	Microspheres for progesterone	• Biodegradable
P(3HB-co-3HV), P(3HB)	Drug delivering agents	• Biodegradable
P(3HB-4HB), PHBV, PHB	Chronic osteomyelitis therapy	• Biodegradable
PHB	Anticancer agent	• Faster drug release
mcl-PHA	Drug delivery system	• Low crystallinity • Low melting point
PHB microspheres	Staphylococcal Enterotoxin B vaccination	

Conclusion

The production of bioplastics using micro algae will ensure eco-friendly production of good quality plastics compared to petroleum based plastics. The issue with this technology is the yield of PHA from marine algae during industrial production. Further studies are to be concentrated in order to improve the production to appropriate quantities so as to ensure its use for biomedical applications.

References

Alejandra Rodriguez-Contreras. (2019). Recent Advances in the Use of Polyhydroxyalkonates in Biomedicine. *Bioengineering*, 6(3), 82.

Anderson, A. J, Dawes, E. A. (1990). Occurance, metabolism, metabolic role and industrial use of bacterial polyhydroxyalkonate. *Microbiologicsl Reviews*. 1990, 54, 450-472

Butt, F. I., Muhammad, N., Hamid, A., Moniruzzaman, M., Sharif, F. (2018). Recent progress in the utilization of biosynthesized polyhydroxyalkanoates for biomedical applications–review. *International journal of biological macromolecules*, *120*, 1294-1305.

Didem Özçimen , Benan İnan, Ogün Morkoç and Aybüke Efe. (2017). A Review on Algal Biopolymers. *Journal of Chemical Engineering Research Updates*, 4, 7-14.

García, G., Sosa-Hernández, J. E., Rodas-Zuluaga, L. I., Castillo-Zacarías, C., Iqbal, H., & Parra-Saldívar, R. (2020). Accumulation of PHA in the microalgae Scenedesmus sp. under nutrient-deficient conditions. *Polymers*, *13*(1), 131.

Jyothi Kaparapu. (2018). Polyhydroxyalkanoate (PHA) Production by Genetically Engineered Microalgae: A Review. *Journal on New Biological Reports*, JNBR 7(2) 68 – 73.

K. Roja, D. Ruben Sudhakar, Susaimanickam Anto, Thangavel Mathimani. (2019). Extraction and characterization of polyhydroxyalkanoates from marine green alga and cyanobacteria. *Biocatalysis and Agricultural Biotechnology*, S1878-8181(19)31125-9.

Kim B. S. (2000) Production of Poly (3-hydroxybutyrate) from Inexpensive Substrates. *Enzyme Microbial Technoogy,l* 27:774-777.

Noreen A. , Zia K. M., Zuber M., Ali M., Mujahid M. (2016) A critical review of algal biomass: A versatile platform of bio-base Polyesters from renewable resources. *International Journal of Biological Macromolecules,* 86: 937-949.

Reddy C. S. K., Ghai R., Kalia R. V. C. (2003) Polyhydroxyalkonates: An overview; *Bioresource Technology,* 87: 137-146.

Sabbir Ansari, Neha Sami, Durdana Yasin, Nazia Ahmad, Tasneem Fatma (2021) Biomedical Applications of Environmental Friendly Poly-hydroxyalkanoates. *International Journal of Biological Macromolecules*, 183, 549–563.

Sánchez-Bayo, A., Morales, V., Rodríguez, R., Vicente, G., Bautista, L. F. (2020). Cultivation of microalgae and cyanobacteria: Effect of operating conditions on growth and biomass composition. *Molecules*, *25*(12), 2834.

Subhasree Ray, Vipin Chandra Kalia. (2017). Biomedical Applications of Polyhydroxyalkanoates; *Indian Journal of Microbiology*, 57(3):261–269.

Warren Blunt, David B. Levin and Nazim Cicek. (2018). Bioreactor Operating Strategies for Improved Polyhydroxyalkanoate (PHA) Productivity; *Polymers,* 10, 119

Y. Ke, X.Y. Zhang, S. Ramakrishna, L.M. He, G. Wu. (2016). Reactive blends based on Polyhydroxyalkonates: Preparation and biomedical application. *Material Science and Engineering C,* S0928-4931(16)30297-1.

Miss. Akhila S. Viswan

- Completed MSc. Food science and technology with project experience in Fish processing

Dr. Sreelakshmi K.R.

- Presently working as Scientist in fish processing at Central Institute of Fisheries Technology, Cochin, Kerala. Her major areas of interest includes fish product development and packaging, development of nano sensors and biodegradable polymers.