Keep track of your impact, and get tips for increasing your reach.

Log in to your account

See what others are doing in your discipline.

Join a Community

Kind regards,

Your Author Marketing Team

For all your customer support needs please visit our support portal. or contact Author Support, authorsupport@springernature.com

Sign up to get notified when your work is cited

Unsubscribe

Storage

Reply

Forward

ScienceDirect

The Microbe

Volume 9, December 2025, 100582

Microbial production of poly (3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) as a sustainable alternative to petroleum-based plastics: Advances, challenges, and prospects

S.P. Shibin [a b], Jayesh Puthumana [a], Isaac Sarojini Bright Singh [a], Roy M. Thomas [b], G. Madhu [b]

Show more

https://doi.org/10.1016/j.microb.2025.100582

Get rights and content

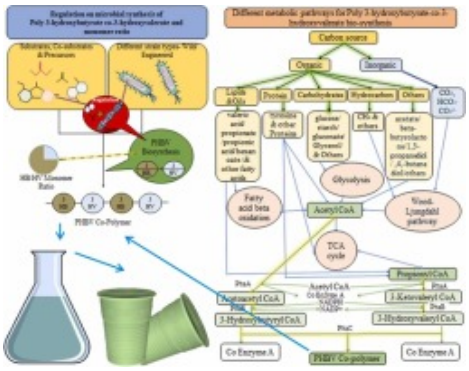
Highlights

- PHBV is a promising biodegradable alternative to petroleum-based plastics with excellent mechanical and thermal properties.
- Microbial fermentation enables efficient PHBV production, but costs and yields limit commercial scalability.
- Advances in metabolic engineering, fermentation strategies, and low-cost feedstocks are improving production efficiency.
- Industry–academia collaborations are crucial for overcoming challenges and driving PHBV commercialization.
- PHBV shows strong potential for sustainable applications in packaging, agriculture, and medicine.

Abstract

The depletion of fossil fuel reserves in the coming decades highlights the urgent need for sustainable alternatives to petroleum-based plastics. Among biodegradable biopolymers, poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV), a member of polyhydroxyalkanoates (PHAs), has gained significant attention due to its eco-friendly nature and desirable material properties. PHBV exhibits superior mechanical strength, thermal stability, and biodegradability, making it a viable candidate for applications in agriculture, medicine, and food packaging. Microbial fermentation enables the production of both PHB and PHBV with similar efficiency, depending on substrate availability. However, commercial scalability remains a challenge due to high production costs, limited feedstock availability, and suboptimal yields. Advances in fermentation strategies, metabolic engineering, and the utilisation of cost-effective carbon sources are actively being explored to enhance PHBV production efficiency. Additionally, industry-academia collaborations and open innovation play a crucial role in overcoming existing limitations, driving technological breakthroughs, and facilitating the commercialisation of PHBV. This review provides an updated perspective on the latest advancements, challenges, and prospects of microbial PHBV production, highlighting its potential as a sustainable alternative to conventional plastics.

Graphical Abstract



Download: Download high-res image (213KB)

Download: Download full-size image

Previous Next

Keywords

Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV); Biodegradable plastics; Microbial fermentation; Sustainable biopolymers; Metabolic engineering

1. Introduction

The increasing use of fossil fuels in both domestic and industrial sectors has significantly contributed to climate change (Kim et al., 2022, Sohn et al., 2022). Fossil fuel reserves are projected to be depleted within a few decades; oil by 2052, natural gas by 2060, and coal by 2090 (Kuo, 2019). This may lead to an urgent and unavoidable need for sustainable alternatives to petroleum-based

plastics. Polyhydroxyalkanoates (PHAs), particularly the polyhydroxybutyrate (PHB) group, have emerged as promising biopolymers that can serve as eco-friendly substitutes for many conventional plastics available (Jain and Tiwari, A., 2010, Naser et al., 2021). These biodegradable biopolymers, produced by various bacterial strains, exhibit favourable properties, making them suitable for diverse applications in agriculture, medicine, and food packaging (Acharjee et al., 2023, McAdam et al., 2020). PHAs offer a viable solution to plastic pollution and its detrimental effects on ecosystems, as they are non-toxic, biocompatible, and biodegradable into environmentally harmless compounds (Sharma et al., 2022, Acharjee et al., 2023). While considering the rising environmental awareness and the eventual depletion of petroleum resources, PHAs represent a promising pathway toward sustainable plastic production (Bernard, 2014, Divya, 2013).

Among PHAs, poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV), or P(3HB-co-3HV), has gained particular attention due to its enhanced flexibility, thermal stability, and improved mechanical properties over PHB alone (Anitha and Srivastava, 2021, Jo et al., 2024, Divya, 2013, Keskin et al., 2017, Policastro et al., 2021, García-Chumillas et al., 2024). However, despite their advantages, PHAs-including PHBV- face significant barriers to their large-scale commercialisation. High production costs, low yields, and complex processing techniques hinder their widespread adoption (McAdam et al., 2020).

The recent research on PHAs, particularly PHBV, is generally focusing on optimising production conditions, improving material characteristics, and exploring their applications across biological, industrial, and environmental sectors (Anitha and Srivastava, 2021, Jo et al., 2024). This review provides an updated perspective on the latest advancements and challenges associated with PHBV production and also highlights their potential as sustainable alternatives to petroleum-based plastics.

2. Microbial pathways and strain selection for PHBV synthesis

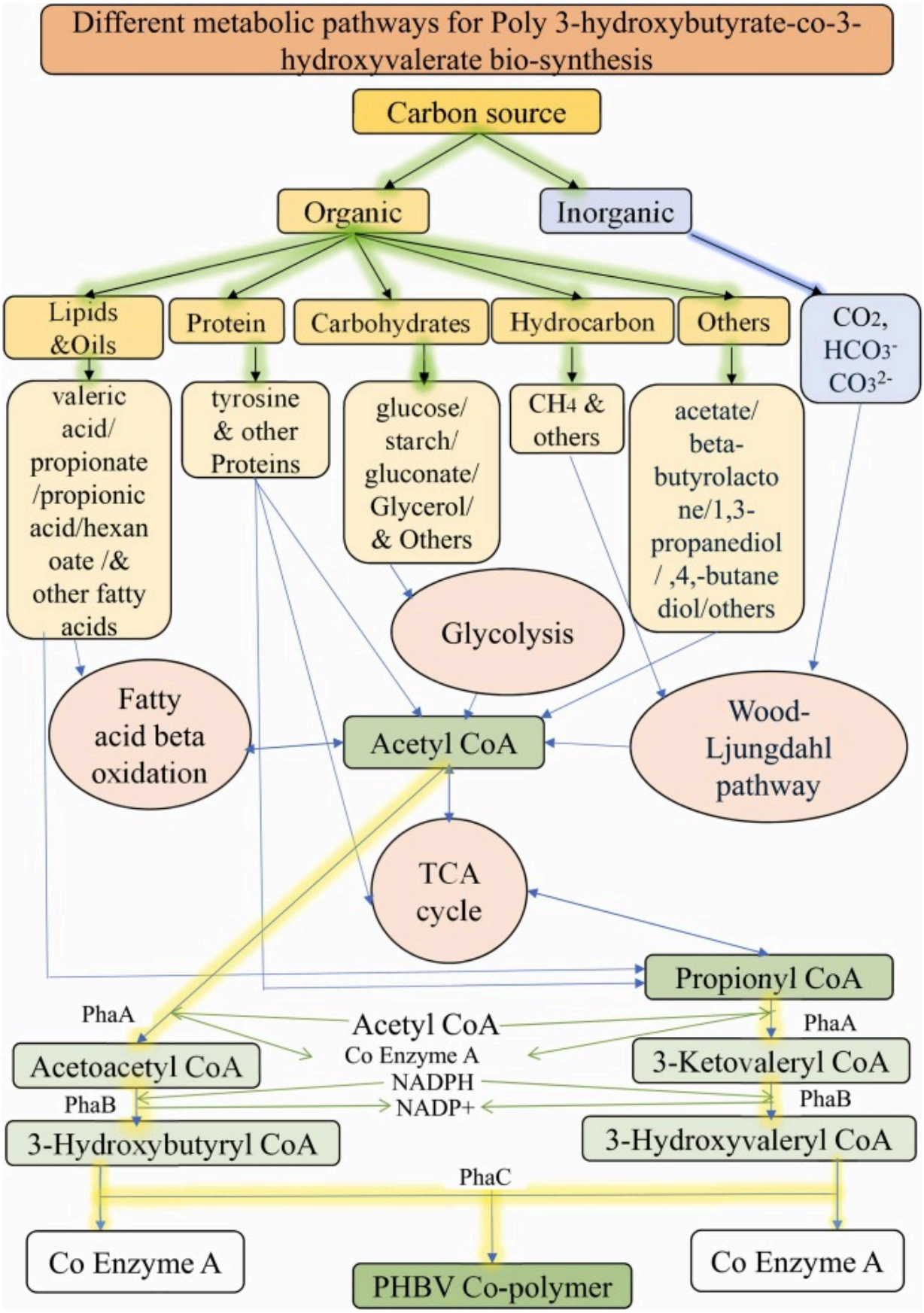
Microbial metabolism is highly interconnected with multiple pathways that influence both cell growth and product formation. Enhancement of cell biomass and PHBV accumulation requires a clear understanding of gene regulation, enzymatic activity and metabolic routes together with optimised fermentation conditions (Longo et al. 2024). Microbial cells activate distinct metabolic pathways depending on the available carbon source. These pathways govern PHBV accumulation in the cytoplasm. The choice of microorganism and the quality of the carbon substrate strongly determine the type of PHAs that are synthesised. In copolymers such as PHBV, the carbon source also regulates the monomer ratio. Even in a single species, pathway selection can differ depending on the physiological, biochemical and genetic state of the strain.

For instance, *Haloferax mediterranei* possesses two essential genes, *phaB1* and *phaB2*, that encode acetoacetyl-CoA reductases required for PHBV precursor synthesis (Feng et al. 2010). This organism uses four distinct propionyl-CoA biosynthetic routes: citramalate/2-oxobutyrate, aspartate/2-oxobutyrate, methylmalonyl-CoA and the recently identified 3-hydroxypropionate pathway (Han et al. 2013). During growth on glucose, *H. mediterranei* produces propionyl-CoA mainly through the citramalate/2-oxobutyrate pathway with 53% flux and the 3-hydroxypropionate pathway with 30.6% flux (Han et al. 2013). Propionyl-CoA carboxylase (PCC) has also been identified as a key enzyme in this organism since it catalyses propionyl-CoA carboxylation (Hou et al. 2015). In

contrast, *Rhodococcus ruber* 3HV monomer synthesis proceeds through pyruvate carboxylation followed by tricarboxylic acid (TCA) cycle reactions that generate succinate as a precursor of propionyl-CoA. A critical enzyme in this pathway is methylmalonyl-CoA transcarboxylase, which supports oxaloacetate recycling for efficient carbon flux. About 12 % of the carbon flux toward 3HV synthesis follows an alternative route that involves direct pyruvate carboxylation and reverse TCA cycle reactions leading to succinyl-CoA (Anderson et al. 1995).

2.1. Sequential stages of PHBV biosynthesis in microorganisms

PHBV biosynthesis can be divided into two stages (Fig. 1).



Download: Download high-res image (889KB)

Download: Download full-size image

Fig. 1. Different metabolic pathways for Poly 3-hydroxybutyrate-co-3-hydroxyvalerate bio-synthesis form different carbon sources.

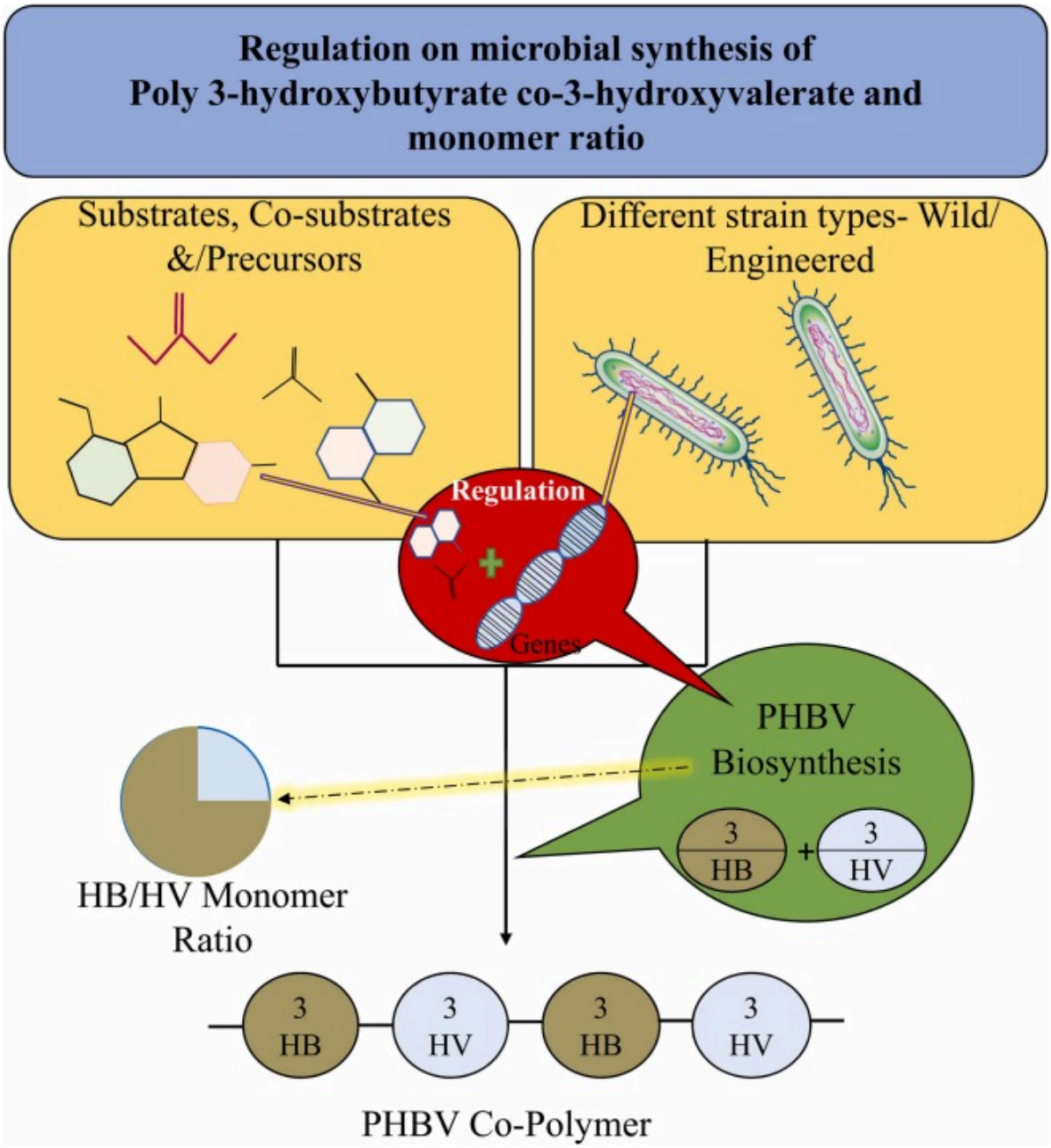
2.1.1. Stage 1: Precursor formation

Organic substrates such as carbohydrates, proteins, lipids and hydrocarbons and inorganic substrates such as CO_2 are converted into acetyl-CoA and propionyl-CoA. These conversions take place through interconnected metabolic routes including glycolysis, fatty acid β-oxidation and the Wood–Ljungdahl pathway. Propionyl-CoA can be produced directly from catabolism of carbon substrates or indirectly from acetyl-CoA through the TCA cycle. The relative proportion of acetyl-CoA and propionyl-CoA determines the HB/HV monomer ratio.

2.1.2. Stage 2: Polymer assembly

Two molecules of acetyl-CoA condense to form acetoacetyl-CoA through the action of *PhaA*. Acetoacetyl-CoA is reduced to 3-hydroxybutyryl-CoA by *PhaB*. In parallel, one acetyl-CoA and one propionyl-CoA combine to yield 3-ketovaleryl-CoA catalysed by *PhaA*. This intermediate is converted to 3-hydroxyvaleryl-CoA by *PhaB*. Finally, *PhaC* catalyses the polymerization of 3-hydroxybutyryl-CoA and 3-hydroxyvaleryl-CoA to produce PHBV.

The core pathway of PHBV biosynthesis is well described, but the efficiency of production and the ratio of monomers differ widely among microbial strains and growth conditions (Fig. 2). These variations result from genetic differences, regulatory controls and enzyme activities. Table 1 summarises the major genes and enzymes involved in PHBV biosynthesis in different microorganisms.



Download: Download high-res image (523KB)

Download: Download full-size image

Fig. 2. Regulation on microbial synthesis of Poly 3-hydroxybutyrate co-3-hydroxyvalerate and monomer ratio.

Table 1. Enzymes involved in the metabolic pathway towards PHBV production.

Pathways	Gene	Enzyme name	Enzyme action	Reference
PHBV Production from the precursor molecules, Acetyl CoA and Propionyl CoA (Common pathway)	*PhaA*	β-ketothiolase	Condensation of two molecules of acetyl-CoA to form one molecule of acetoacetyl-CoA condensation of one molecule each of Acetyl CoA and Propionyl CoA to form one molecule of 3-Ketovaleryl CoA	(Miscevic et al., 2020)

Pathways	Gene	Enzyme name	Enzyme action	Reference
	BktBαβ:	PHA-specific beta-ketothiolase – alpha and beta subunits	Condensation of two molecules of acetyl-CoA to form one molecule of acetoacetyl-CoA condensation of one molecule each of Acetyl CoA and Propionyl CoA to form one molecule of 3-Ketovaleryl CoA	(Miscevic et al., 2020)
	PhaB	NADPH-dependent acetoacetyl-CoA reductase	Acetoacetyl-CoA is then reduced by *PhaB* to (R)−3-hydroxybutyryl-CoA	(Miscevic et al., 2020)
	Hbd	Beta-hydroxybutyryl-CoA dehydrogenase	Acetoacetyl-CoA is then reduced by PhaB to (R)−3-hydroxybutyryl-CoA	(Miscevic et al., 2020)
	PhaC	PHA synthase	Polymerizes the (R)−3-hydroxybutyryl-CoA & (R)−3-hydroxyvalaryl CoA into the PHBV polymer.	(Miscevic et al., 2020)
	Buk	Butyrate kinase	Involves in polymerization of (R)−3-hydroxybutyryl-CoA & (R)−3-hydroxyvalaryl CoA into the PHBV polymer	(Miscevic et al., 2020)
	Ptb	Phosphotransbutyrylase	Involves in polymerization of (R)−3-hydroxybutyryl-CoA & (R)−3-hydroxyvalaryl CoA into the PHBV polymer	(Miscevic et al., 2020)
	TesB	Acyl-CoA thioesterase II	Involves in polymerization of (R)−3-hydroxybutyryl-CoA & (R)−3-hydroxyvalaryl CoA into the PHBV polymer	(Miscevic et al., 2020)
	Pct	Acetate/propionate CoA-transferase	Involves in polymerization of (R)−3-hydroxybutyryl-CoA & (R)−3-hydroxyvalaryl CoA into the PHBV polymer	(Miscevic et al., 2020)
	AACS	Acetoacetyl-CoA-synthetase	Acetyl-CoA + malonyl-CoA ⇌ acetoacetyl-CoA + CoA + CO_2.	(Bergstrom, 2023)
	PhaZ	PHA depolymerase	Breaks down PHA	(de Eugenio et al., 2007)
	HBDH	Hydroxybutyrate dehydrogenase	Conversion of (R)−3-hydroxybutyrate to acetoacetate	(Machado and da Silva, 2023)

Pathways	Gene	Enzyme name	Enzyme action	Reference
	PhbP	Phasin	Formation and size of polyhydroxybutyrate (PHB) granules and can also influence the activity of the PHB synthase enzyme.	(Mezzina and Pettinari, 2016)
	PhaR		Negative regulator of *PhaP*	(Jang et al., 2017)
PHBV precursors production form fatty acids and regulation	*Fab A*		Conversion of acyl CoA to 3ketoacyl CoA	(Paduvari and Somashekara, 2025)
	Fab B		Conversion of 3ketoacyl CoA to (S)3hydroxyketoacyl CoA	(Paduvari and Somashekara, 2025)
	Fab G	β-ketoacyl-ACP reductase	Conversion of 3ketoacyl CoA to (R)3hydroxyketoacyl CoA	(Paduvari and Somashekara, 2025)
	Fab H	Beta-ketoacyl-ACP synthase III	Fatty acid synthesis	(Zhang and Cronan, 1998)
	Fab F	β-ketoacyl-ACP synthase II	Fatty acid synthesis	(Zhang and Cronan, 1998)
	PhaJ		Conversion of 2,3trans-enoylCoA to (R)3hydroxyketoacyl CoA	(Paduvari and Somashekara, 2025)
	PhaG		Conversion of (R)3hydroxyketoacyl ACP to (R)3hydroxyfatty acid	(Paduvari and Somashekara, 2025)
PHBV precursors production from carbohydrate	*PDH*	Pyruvate dehydrogenase complex	Pyruvate is converted to acetyl-CoA	(Nielsen, 2014)
	ALD	Aldehyde dehydrogenase	Acetaldehyde can be converted to acetate	(Nielsen, 2014)

Pathways	Gene	Enzyme name	Enzyme action	Reference
	ACS	Acetyl-CoA synthetase	Acetate is converted to acetyl-CoA	(Nielsen, 2014)
	ADH	Alcohol dehydrogenase	Acetaldehyde can be converted to ethanol	(Nielsen, 2014)
	PDC	Pyruvate decarboxylase	Pyruvate can be converted to acetaldehyde	(Nielsen, 2014)
	CIT	Citrate synthase	Acetyl-CoA is oxidized in the TCA cycle	(Nielsen, 2014)
	MLS	Malate synthase	Acetyl-CoA of the cytosol can also enter the glyoxylate cycle (GYC)	(Nielsen, 2014)
	PCC	Propionyl CoA carboxylase	Methyl malonyl CoA is formed from propionyl	(Hofherr et al., 2009)
	Mut	Methyl malonyl CoA mutase	Succinyl CoA is formed from Methyl malonyl CoA	(Hofherr et al., 2009)
	YgfH	Propionyl-CoA: succinate-CoA transferase	Propionyl-CoA to propionate	(Luo et al., 2016)
	PCT	Propionate CoA-transferase	Propionate to propionyl-CoA	(Luo et al., 2016)
	PACD	Propionyl-CoA dehydrogenase	Propionyl-CoA to acryloyl CoA	(Luo et al., 2016)
	Chn A	Cyclohexanol dehydrogenase	Cyclohexanol breakdown	(Choi et al., 2005)
	ChnB	Cyclohexanone monooxygenases	Catayses cyclohexanone	(Sheng et al., 2001)
	ChnC	6-hexanolide hydrolase	Breaks down the biodegradable polymer poly(ε-caprolactone) (PCL)	(Tsuji et al., 2005)
	ChnD	6-Hydrohexanone dehydrogenase	6-hydroxyhexanoate to 6-oxohexanoate, using NAD+ as an electron acceptor	(Woo et al., 2024)
	prpC1 and prpC2	2-methylcitrate synthase (MCS)	To utilize propionate as a carbon source	(Claes et al., 2002)
	PrpC	2-methylcitrate synthase	Condensation of propionyl-CoA with oxaloacetate to form 2-methylcitrate	(Zheng et al., 2020)

Pathways	Gene	Enzyme name	Enzyme action	Reference
	PrpD	2-methylcitrate dehydratase	Isomerization event via dehydration to synthesize 2-methyl-cis-aconitate	(Zheng et al., 2020)
	AcnC	Aconitase C	Catabolism of propionate	(Blank et al., 2002)
	PrpB	2-methylisocitrate lyase (2-MIC lyase)	Catalyses the cleavage of (2 R,3S)−2-methylisocitrate into pyruvate and succinate	(Grimek et al., 2003)
	CitB	Citrate synthase	Oxaloacetate to citrate	(Zheng et al., 2020)
	Sdh	Succinate dehydrogenase	Succinate to fumarate and vice versa	(Zheng et al., 2020)
	FumC	Fumarase	Malate to fumarate and vice versa	(Zheng et al., 2020)
	Mdh	Malate dehydrogenase	Oxaloacetate to malate and vice versa	(Zheng et al., 2020) (Huang et al., 2023)
	Sucl	Succinyl-CoA ligase (succinyl-CoA synthetase)	Succinyl-CoA to Succinate And vice versa	(Zheng et al., 2020) (Huang et al., 2023)
	Mcs	2-methylcitrate synthase	Propionyl CoA is converted to 2-methylcitrate	(Huang et al., 2023)
PHBV precursors production from protein/Amino acid	*tdcB*	Threonine dehydratase	Converts L-threonine into α-ketobutyrate and ammonia	(Masani et al., 2009)

2.2. Engineering of microbial pathways for PHBV production

Microorganisms employ diverse metabolic routes for PHBV biosynthesis and utilise a wide range of carbon sources. Each strain harbours multiple interconnected sub-pathways in addition to the core PHBV pathway. These competing routes often divert carbon flux and reduce the efficiency of PHBV accumulation. Metabolic engineering has therefore emerged as a powerful strategy to optimise PHBV biosynthesis by streamlining precursor supply and redirecting substrate flow toward polymer production (Policastro et al. 2021). Engineered strains can be designed as “customised factories” capable of producing PHBV with the desired 3HV content by eliminating competing pathways and enhancing flux through desired nodes. A variety of metabolic engineering strategies have been explored to date (Table 2).

Table 2. Different metabolic engineering strategies used for the pathway modification.

Strategy used	Strain & substrate used	Observation	Reference
Overexpression of phosphotransacetylase/acetate kinase pathway (Pathway modifications)	*E. coli* JM109; Acetate & propionate;	Produced 1.09 g/L PHBV with a 3-HV monomer content of 10.37 mol%.	(Chen et al., 2018)
Overexpression of transhydrogenase and acetoacetyl-CoA reductase genes	*R.rubrum;* fructose,	Yielding up to 13 mol% 3HV	(Heinrich et al., 2015)
	R. rubrum; syngas (CO_2 and CO)	Increased 3HV production to 56 mol%	(Heinrich et al., 2015)
Co-expression of a gene prpE & operon phaBCA from *Acinetobacter* sp. RA3849	*S. enterica* serovar *typhimurium* JE4199; Glycerol & propionic acid	41.4 % of CDW as PHBV. 30.6 mol% as HV content (customise the HV CONTENT)	(Aldor et al., 2002)
	S. enterica serovar *typhimurium* TR6583; Glycerol & propionic acid;	32.2 % of CDW as PHBV. 5.6 mol% as HV content. (Customise the HV CONTENT)	(Aldor et al., 2002)
	S. enterica serovar *typhimurium* TR6583; Glycerol & propionic acid	24.1 % of CDW as PHBV. 21.7 mol% as HV content (Customise the HV CONTENT)	(Aldor et al., 2002)
Overexpressing the PHBV genes by genetic recombination	*A. hydrophila* 4AK4; acetate & propionate	3.79 g/L CDW, containing 15.02 wt% P(3HB-co−4.23 mol% 3HV)	(Shi et al., 2020)
Chromosomal expression through CRISPR/Cas9 method	*H. bluephagenesis*; glucose	6.3 g/L CDW, 65 % PHBV in CDW and 25 mol% 3HV in PHBV (27 % and 12 % increase in CDW and PHBV content, respectively)	(Chen et al., 2019)
genetic engineering by inserting the genes for PHBV biosynthesis in *Alcaligenes latus*	Recombinant *E. coli* XL1-Blue(pJC4); Glucose & propionic acid;	CDW is 120.3 g/L with 42.5 % of CDW as PHBV content	(Choi and Lee, 1999)
	Recombinant *E. coli* XL1-Blue(pJC4); Acetic acid and oleic acid	PHBV is 158 g/L with 10.6 mol% HV content & CDW is 203.1 g/L	(Choi and Lee, 1999)
	Recombinant *E.coli* XL1-Blue(pJC4); Acetic acid & propionic acid;	PHBV is 88.1 g/L with 15.3 mol% of HV content & CDW as 141.9 g/L	(Choi and Lee, 1999)

Strategy used	Strain & substrate used	Observation	Reference
Knockout of genes, namely *prpC1* and *prpC2*	*C. necator; Glucose*	Maximum PHBV is 94.4 g/L 3HV ratios of 0.4–29.5 mol%	(Zhang et al., 2015)
phaCAB cluster is introduced into the genome of the strain	*C. glutamicum* strain WM001; glucose, corn steep liquor	15.0 g/L PHBV with a high percentage of 3-hydroxyvalerate	(Ma et al., 2018)

One approach involves pathway modification. In *Escherichia coli* JM109, overexpression of the phosphotransacetylase/acetate kinase pathway increased PHBV production to 1.09 g/L with a 3HV content of 10.37 mol% (Chen et al. 2018). A second strategy is the overexpression of specific genes. In *Rhodospirillum rubrum*, overexpression of transhydrogenase and acetoacetyl-CoA reductase enabled PHBV synthesis from fructose, with yields up to 13 mol% 3HV. The same strain could also use syngas (CO_2 and CO) as a substrate for PHBV production (Heinrich et al. 2015). A third method relies on co-expression of genes or operons. Aldor et al. (2002) demonstrated that introducing foreign biosynthetic operons into *Salmonella enterica* serovars allowed fine-tuning of the 3HV mol% in the polymer. More recent studies have employed chromosomal integration using CRISPR/Cas9. In *Halomonas bluephagenesis*, this strategy achieved 6.3 g/L cell dry weight (CDW), with 65 % PHBV content in CDW and 25 mol% 3HV (Chen et al. 2019). Other approaches combine gene overexpression with heterologous gene insertion. For example, *Aeromonas hydrophila* 4AK4 overexpressing PHBV biosynthetic genes produced 3.79 g/L CDW with 15.02 wt% PHBV containing 4.23 mol% 3HV (Shi et al. 2020). Recombinant *E. coli* XL1-Blue (pJC4) carrying foreign PHBV genes achieved 120.3 g/L CDW with 42.5 % PHBV content (Choi and Lee, 1999). Gene knockout can also enhance PHBV accumulation. In engineered *Cupriavidus necator*, deletion of *prpC1* and *prpC2* genes resulted in PHBV titers of 94.4 g/L with adjustable 3HV ratios ranging from 0.4 to 29.5 mol% (Zhang et al. 2015). Finally, gene cluster insertion has been used to create new PHBV producers. In *Corynebacterium glutamicum*, introduction of the *phaCAB* operon enabled production of 15.0 g/L PHBV in fermenters (Ma et al. 2018). Together, these strategies highlight the potential of metabolic engineering to significantly enhance PHBV productivity and customise polymer composition for industrial applications.

2.3. Wild-type and engineered microbial strains for PHBV production

The choice of microbial strain for PHBV production depends on the intended application, desired monomer composition, and the economic feasibility of the process. Both wild-type and engineered strains have been explored extensively (Table 3). Among wild-type microbes, *H. mediterranei* is considered a strong candidate due to its ability to grow in high-salinity environments, which reduces the need for sterile cultivation (Longo et al. 2024). This strain has been employed from flask-scale (Bhattacharyya et al., 2012, Priya et al., 2022) up to pilot-scale production (300 L) (Koller, 2015). The highest reported yield reached 77.8 g/L PHBV with 55.6 mol% 3HV content (Huang et al. 2006). *C. necator* is another widely studied strain. It has been cultivated from shake flasks (Sangkharak et al. 2021a; Novackova et al., 2019a) to fermenters (Du and Yu 2002a; Volova et al., 2021), with a maximum yield of 48 g/L PHBV in a 3 L bioreactor (Garcia-Gonzalez and De Wever,

2018). Other promising wild-type candidates include *Salinivibrio* sp. TGB10 (Tao et al. 2021) and *Photobacterium* sp. TLY01, which produced 27.36 and 16.28 g/L PHBV, respectively, at the fermenter scale (Tian et al. 2022).

Table 3. Different microbial strains used for the PHBV production on various scales.

Strain Used	Biomass Conc., PHBV conc. & 3-HV Content	Scale of production	Reference
C. necator H16 CCM 3726 (wild)	3HV Content ranges 0–20.6 % PHBV content ranges 0–55.4 % CDW	Flask	(Novackova et al., 2019)
C. necator TISTR 1095 (wild)	CDW is 7.5 g/L and PHBV 3.8 g/L with 20 mol% HV content)	Flask	(Sangkharak et al., 2021)
C. necator DSM 545 (wild)	CDW is 11.3 g/L and P(HBV is 10.0 g/ L	Flask	(Ingram and Winterburn, 2022)
C.necator H16 (wild)	PHBV is 6.8 g/L with 7 mol% of 3HV	Flask	(Lee et al., 2008)
C. necator (wild)	1.47 g/L is the PHBV content	Flask	(Chang et al., 2025)
C. necator (MTCC−1954) (wild)	1.44 g/L is the PHBV content	Flask	(Kerketta and Vasanth, 2019)
C.necator H16 (wild)	PHBV content is 69–90 % of CDW & 3HV Content is 27–41 mol%	Flask	(Ng et al., 2011)
C. necator TF 93 (wild)	1.1 g/L PHBV with 30 mol% HV content	1 L fermenter	(Ganzeveld et al., 1999)
C. necator DSM 545 (wild)	65 g/L CDW and 48 g/L PHBV with a 3HV content of 27 mol%	3-L bioreactor	(Garcia-Gonzalez and De Wever, 2018)
C. necator (wild)	CDW is 22.7 g/L and PHBV content is 72.6 % (w/ w). 2.8 mol% is the HV content	2 L fermenter	(Du and Yu, 2002)
C. necator, strain DSM 545 (wild)	PHBV content is 24.7 g L^{-1}	7 L Reactor level	(Ghysels et al., 2018)
C. necator, B5786 (wild)	1 mol% HV content in PHBV. CDW is approximately17 g/L with its 70–75 % as PHBV Content	10 L Bioreactor	(Volova et al., 2001)
C. necator DSM 7237 (wild)	23.4 g/ L of PHBV, which is 66.4 % (w/w) of CDW, with 31 mol% HV content	1 L bioreactor	(Kachrimanidou et al., 2014)
Cupriavidus sp. USMAA1020 (wild)	CDW is 13.3 g/L, and PHBV concentration is 10.23 g/L	Shake flask	(Huong et al., 2017)

Strain Used	Biomass Conc., PHBV conc. & 3-HV Content	Scale of production	Reference
C. necator TF 93 (wild)	1.1 g/L PHBV with 30 mol% HV content	1 L fermenter	(Ganzeveld et al., 1999)
C. malaysiensis USMAA2–4$_{ABH16}$ (wild)	0.41—0.52 g/g PHBV yield and 72—89 wt% PHBV; 12 mol% of 3HV content	6 L fermenter	(Wong et al., 2022)
C.malaysiensis sp. USMAA2–4; (wild)	9.8 g/L RCDW and 8.7 g/L PHBV conc. Productivity of the copolymer is 0.160 g/L/h	3.6 L bioreactor	(Shantini et al., 2021)
Alcaligenes eutrophus NCIMB 12080; (wild)	Cdw is 5.4 g/L & 27.3 % of CDW is PHBV	7 L fermenter	(Park and Damodaran, 1994)
B. megaterium NCIM 5472 (wild)	PHBV content of 86.6 % of CDW and PHBV yield of 3.64 g/L; 3HV mol% is 16.6	Flask	(Suhazsini et al., 2020)
B. thuringensis . (wild)	CDW is 2.75 ± 0.13 g/L	Flask	(Ciesielski et al., 2021)
Methylocystis sp. WRRC1. (wild)	PHBV is 78 % of CDW with 58 mol% HV Content	2 L fermenter	(Cal et al., 2016)
Methylobacterium extorquens G10 (wild)	CDM Ranges 15–52 g/L, PHBV content ranges 30–40 % of CDW, HV content ranges 0–50 %	Lab fermenter	(Ezhov et al., 2013)
H.mediterranei DSM 1411 (wild)	75.4 wt.-% volumetric productivity of 0.12 g/L.h with 10 % HV content	Bioreactor 10 L	(Hermann-Krauss et al., 2013)
H.mediterrane (wild)	Accumulated 50 wt.-% of CDW as PHBV with specific productivity q_p: 9.1 mg/g.h	10 L bioreactor	(Koller et al., 2007)
H. mediterranei (wild)	CDW of 3.19 g/L with 56.70 % as PHBV. 18.55 mol% 3HV content	Flask as well as bioreactor	(Priya et al., 2022)
H. mediterranei (wild)	PHBV yield is 0.2 g/L and PHBV content is 43 % PHA/cell dry mass with 6.5 mol% of 3HV content	Flask	(Alsafadi and Al-Mashaqbeh, 2017)
H. mediterranei DSM1411 (wild)	Initial CDW of 12.8 g /L and PHBV content of 3.20 g /L is scaled up to 18 g/L CDW with 4.5 g/L PHBV content. 18 mol% of 3 HV content	2 L Fermenter	(Alsafadi et al., 2020)
H. mediterranei (wild)	HV content was 12.36 mol % (utilizing 25 % pre-treated vinasse) and 14.09 mol % (utilizing 50 % pre-treated vinasse). & 70 % of CDW as PHBV (19.7 g/L)	Shake flask	(Bhattacharyya et al., 2012)
H. mediterranei (wild)	71 % of CDW as PHBV, that is 16.42 g/L	Flask	(Bhattacharyya et al., 2014)

Strain Used	Biomass Conc., PHBV conc. & 3-HV Content	Scale of production	Reference
H. mediterranei DSM1411 (wild)	7.2 g/L PHBV (10 mol% 3 HV)	300 L (Pilot scale)	(Koller, 2015)
H. mediterranei ATCC 33500 (wild)	20.0 g/L PHBV (10.4 mol% 3 HV) 50.8 % (w/w) of CDW	6.0 L fermenter	(Chen et al., 2006)
H. mediterranei ES1 (wild)	5.1 g/L PHBV & CDW is 12.3 g/L at 15 mm valerate. While using 17 mm valerate HV content is increased to 60.3 mol% but PHBV is reduced to 0.2 g/L	Shake flask to 7 L Fermenter as well shake flask	(Han et al., 2015)
H. mediterranei (ATCC 33500) (wild)	77.8 g/L PHBV with 55.6 mol% 3 HV CDW: 140 g/L	5 L Fermenter	(Huang et al., 2006)
H. mediterranei (ATCC 33500) (wild)	24.2 g/L PHBV with 38.7 mol% 3 HV CDW: 62.6 g/L	5 L Fermenter	”
H. mediterranei (ATCC 33500) (wild)	52.7 g/L PHBV with 40.2 mol% 3 HV CDW: 131 g/L	5 L Fermenter	”
H. mediterranei (ATCC 33500) (wild)	23 g/L PHBV with 27 mol% 3 HV CDW: 85.8 g/L	5 L Fermenter	”
H. borinquense strain E3 (wild)	CDW is 4.6 g/L; PHBV concentration of 1.52 g/L with 19.65 mol% 3HV unit	1 L flask	(Salgaonkar et al., 2019)
Halomonas. Hydrothermalis CCM 7104 (wild)	CDW is 2.34 g/L with 68.83 % PHBV. 50.15 mol% HV content	Flask	(Pernicova et al., 2019)
H.hydrothermalis CCM 7104 (wild)	CDW is 2.75 g/L with 47.17 % PHBV& 7.16 mol% HV content	Flask	(Pernicova et al., 2019)
H. hydrothermalis CCM 7104 (wild)	CDW is 2.19 g/L with 69.86 % PHBV content & 8.44 mol% of HV content	Flask	(Pernicova et al., 2019)
H. neptunia (wild)	CDW is 0.54 g/L with 23.66 % PHBV content & 29.5 mol% of HV content	Flask	(Pernicova et al., 2019)
H. neptunia (wild)	CDW is 1.23 g/L with 15.85 % PHBV content & 26.07 mol% of HV content	Flask	(Pernicova et al., 2019)
Photobacterium sp. TLY01	PHBV content is 16.28 g/L	Flask to Bioreactor	(Tian et al., 2022)
Photobacterium sp. TLY01 (wild)	PHBV content is 4.01 g/L	Flask to Bioreactor	Tian et al., 2022)
Hydrogenophaga pseudoflava (wild)	40 wt.-% PHBV, q_p: 12.5 mg/g.h	10 L bioreactor	(Koller et al., 2007)

Strain Used	Biomass Conc., PHBV conc. & 3-HV Content	Scale of production	Reference
Pseudomonas hydrogenovora (wild)	12 wt.-% PHBV, q_p: 2.9 mg/g.h	Data not available	Koller et al., 2007)
P.mendocina PSU (wild)	43.6 wt% of CDW as PHBV with 8.6 HV mol% @.3 % sodium propionate. CDW is 2.5–4 g/L	Lab level	(Martla et al., 2018)
Salinivibrio sp. M318 (wild)	CDW is 11.6 g/L with 52.4 % as PHBV. 24.7 mol% as HV content	Flask, bioreactor	(Van Thuoc et al., 2019)
Salinivibrio sp. TGB10 (wild)	CDW of 33.45 g/L and PHBV titer of 27.36 g/L were obtained	Flask, bioreactor	(Tao et al., 2021)
Salinivibrio sp. M318 (wild)	CDW is 10.8 g/L with 48.3 % as PHBV. 17 mol% as HV content	Flask, bioreactor	(Van Thuoc et al., 2019)
Salinivibrio sp. M318 (wild)	CDW is 11.2 g/L with 53 % as PHBV. 13.3 mol% as HV content	Flask, bioreactor	(Van Thuoc et al., 2019)
B.glumae MA13 (wild)	CDW 1.9 g/L and 25.20 % of CDW as PHBV. 30.15 mol% as HV (Flask level)	Shake flask	(Coutinho de Paula et al., 2019)
B.glumae MA13 (wild)	PHBV content of 9.5 g/L from14.7 g/L of CDW. Volumetric productivity is 0.22 g/ (L h) & 21.8 mol% of 3HV content (Fermenter level)	10 L bioreactor	(Coutinho de Paula et al., 2019)
B.glumae MA13 (wild)	CDW is 3.16 g/L and 34.02 % of CDW as PHBV. 0.24 mol% of HV content	Shake flask	(Coutinho de Paula et al., 2019)
Comamonas sp EB 172 (wild)	CDW of 10 g/L with its 73 % as PHBV content at limited oxygen (0 %) conc.	2–7 L fermenters	(Mumtaz et al., 2009)
C. taiwanensis (wild)	10–85 mol% of 3-HV fraction; 42–67 % CDM as PHBV	Data not available	Sheu et al., 2009)
Vibrio alginolyticus (wild)	1.44 g/L PHBV with a 3HV content of 24.42 mol% @ 4 g/L propionate conc.	Flask	(Li et al., 2021)
Rhodobacter sphaeroides U7 (wild)	PHBV content is 2.66 g/L	Not available	Kemavongse et al., 2008)
Activated sludge (wild)	The average PHBV cell content was 0.26 ± 0.08 gPHA $gVSS^{-1}$	1.25–200 L fermenter	(Arcos-Hernandez et al., 2013)
Mixed cultures (wild)	HV fraction ranging from 15 % to 39 %	2 L fermenter	(Albuquerque et al., 2011)
C. necator (engineered)	Maximum PHBV is 94.4 g/L 3HV ratios of 0.4–29.5 mol%	Shake flask to 7.5 L Fermenter	(Zhang et al., 2015)

Strain Used	Biomass Conc., PHBV conc. & 3-HV Content	Scale of production	Reference
Escherichia coli XL1-Blue (Pjc4) (engineered)	CDW is 120.3 g/L with 42.5 % of CDW as PHBV content	6.6-liter jar fermenter	(Choi and Lee, 1999)
E. coli XL1-Blue (Pjc4) (engineered)	PHBV is 158 g/L with 10.6 mol% HV content & CDW is 203.1 g/L	6.6-liter jar fermenter	(Choi and Lee, 1999)
E. coli XL1-Blue (Pjc4) (engineered)	PHBV is 88.1 g/L with 15.3 mol% of HV content & CDW as 141.9 g/L	6.6-liter jar fermenter	(Choi and Lee, 1999)
E. coli (engineered)	3-HV up to 3.71 g/L with a yield of 24.1 %	Lab scale 220 ml	(Miscevic et al., 2020b)
E. coli JM109 (engineered)	Produced 1.09 g/L PHBV with a 3-HV monomer content of 10.37 mol%.	Flask	(Chen et al., 2018)
A. hydrophila 4AK4 (Engineered)	3.79 g/L CDW, containing 15.02 wt% P(3HB-co–4.23 mol% 3HV)	Flask	(Shi et al., 2020)
S. enterica serovar *typhimurium* TR6583 (engineered)	40.7 % of CDW as PHBV. 14.2 mol% as HV content	Shake flask	(Aldor et al., 2002)
S. enterica serovar *typhimurium* JE4199 (engineered)	41.4 % of CDW as PHBV. 30.6 mol% as HV content	Shake flask	(Aldor et al., 2002)
S. enterica serovar *typhimurium* TR6583 (engineered)	32.2 % of CDW as PHBV. 5.6 mol% as HV content	Shake flask	(Aldor et al., 2002)
S. enterica serovar *typhimurium* TR6583 (engineered)	24.1 % of CDW as PHBV. 21.7 mol% as HV content	Shake flask	(Aldor et al., 2002)
R. rubrum (engineered)	Increased 3HV production to 56 mol%	Flask	(Heinrich et al., 2015)
C. glutamicum strain WM001 (engineered)	15.0 g/L PHBV with maximum 3HV fraction of 72.5 mol%	Shake flask, 3 L fermenter	(Ma et al., 2018)

Other strains such as *Burkholderia glumae* (9.5 g/L), *Comamonas* sp. EB172 (7.3 g/L) (Coutinho de Paula et al., 2019, Tabassum Mumtaz et al., 2009), *Halogeometricum borinquense* (Salgaonkar et al. 2019), *Rhodobacter sphaeroides* U7 (Kemavongse et al. 2008), and *Caldimonas taiwanensis* (Sheu et al. 2009) have also been reported. Marine bacteria such as *Cobetia* sp. can accumulate PHBV using carbon substrates like glucose, fructose, glycerol, and gluconic acid (Matsumoto et al. 2022). Photosynthetic microorganisms, including cyanobacteria and purple non-sulfur bacteria, can synthesise PHB when cultivated with agro-industrial effluents (Padovani et al. 2016). In addition,

mixed microbial cultures of wild-type strains have been employed for PHBV production (Albuquerque et al., 2011, Arcos-Hernandez et al., 2013).

Although wild strains are valuable, they often do not meet the requirements for large-scale, cost-effective PHBV production. In such cases, engineered strains offer significant advantages. Among these, *E. coli* remains the most successful production host. Recombinant *E. coli* XL1-Blue (pJC4) achieved up to 158 g/L PHBV with variable 3HV composition in laboratory-scale fermenters (Choi and Lee, 1999). Engineered *C. necator* also demonstrated high productivity, yielding 94.4 g/L PHBV with 3HV contents ranging from 0.4 to 29.5 mol% in a 7.5 L fermenter (Zhang et al. 2015). Other engineered strains used for PHBV production include *A. hydrophila* (Shi et al. 2020), *S. enterica* serovar *typhimurium* (Aldor et al. 2002), *R. rubrum* (Heinrich et al. 2015), and *C. glutamicum* (Ma et al. 2018). Together, these studies highlight both the versatility of wild-type strains and the enhanced performance of engineered microbes, underscoring the potential for scaling up PHBV production across diverse biological platforms.

3. Alternative carbon sources and novel approaches for customised PHBV production

3.1. Alternative carbon sources

The choice of carbon source plays a crucial role in the commercial production of PHBV, as it directly influences both production efficiency and the HB/HV monomer composition (Fig. 2). Numerous substrates have been evaluated to date (Table 4). For instance, the combination of acetic acid and oleic acid has yielded the highest reported PHBV content of 123.5 g/L in a 6.6 L fermenter, while acetic acid with propionic acid resulted in 88.1 g/L under the same conditions (Choi and Lee, 1999). When used individually, acetic acid supported PHBV production of 48 g/L (Garcia-Gonzalez and De Wever, 2018), and glucose gave 51 g/L (Choi and Lee, 1999). However, the high cost of these substrates limits their industrial applicability.

Table 4. Different carbon substrates used for the PHBV production on various scales.

Carbon sources & co-substrates/Precursors	**Strain used**	**Biomass & PHBV formed with HV incorporation mol%**	**Scale of production**	**Reference**
CO_2 with Valeric acid	*C. necator*, DSM545	PHBV content of 24.7 g/L	7 L Reactor	(Ghysels et al., 2018)
CO_2 & Valeric acid	*C. necator*	1.47 g/L of PHBV content	Flask	(Chang et al., 2025)
CO_2 & Hydrogen	*C. necator*, B5786	1 % HV content in PHBV	10 L Reactor	(Volova et al., 2001)
Methane & Valerate/ Pentanol	*Methylocystis* sp. WRRC1.	PHBV is 78 % CDW WITH 58 % HV Content	2 L fermenter	(Cal et al., 2016)

Carbon sources & co-substrates/Precursors	Strain used	Biomass & PHBV formed with HV incorporation mol%	Scale of production	Reference
Methanol & Pentanol	*Methylobacterium extorquens* G10	CDW= 15–52 g/L PHBV content= 30–40 % HV content 0–45 %	Lab fermenter	(Ezhov et al., 2013)
Pentanol & Ethanol	*Alcaligenes eutrophus* NCIMB 12080	CDW is 5.4 g/L & 27.3 % of CDW is PHBV	7 L fermenter	(Park and Damodaran, 1994)
Fructose & Levulinic acid	*C. necator* H16 CCM 3726	3HV Content= 0–20.6 % PHBV content = 0–55.4 % of CDW	Flask	(Novackova et al., 2019)
Glucose	*H. mediterranei* (ATCC 33500)	23 g/LPHBV with 27 mol% 3 HV content. CDW: 85.8 g/L	5 L Fermenter	(Huang et al., 2006)
Glucose & Propionic acid	Recombinant *E.coli* XL1-Blue(pJC4)	CDW: 120.3 g/L with 42.5 %PHBV content	6.6 L Fermenter	(Choi and Lee, 1999)
Glucose & Propionate	*Salinivibrio* sp. TGB10	CDW of 33.45 g/L and PHBV titer of 27.36 g/L were obtained	Flask as well as bioreactor level	(Tao et al., 2021)
Glucose and Valerate	*H. mediterranei* ES1	5.1 g/LPHBV with 50 mol% 3 HV content CDW: 12.3 g/L	7 L Fermenter as well shake flask	(Han et al., 2015)
Glycerol	*E.* coli (engineered)	3-HV up to 3.71 g l^{-1} with a yield of 24.1 %	Lab scale 220 ml	(Miscevic et al., 2020)
Glycerol (crude)	*H. mediterranei*	75.4 wt.-% PHBV with volumetric productivity of 0.12 g/L.h and 10 % HV content	Bioreactor 10 L	(Hermann-Krauss et al., 2013)
Crude glycerol, Sunflower meal hydrolysates and Levulinic acid	*C.necator* DSM 7237	23.4 g/ L PHBV, which is 66.4 % (w/w) of CDW with 31 mol% HV	1 L bioraector	(Kachrimanidou et al., 2014)
Glycerol & Propionic acid	Recombinant *S. enterica* serovar *typhimurium* JE4199	PHBV content of 41.4 % CDW with HV content of 30.6 mol%	Not available	(Aldor et al., 2002)
Glycerol & Propionic acid	Recombinant *S. enterica* serovar *typhimurium* TR6583	PHBV is 40.7 % of CDW & HV content is 14.2 mol%	Not available	”
Glycerol & Propionic acid	”	PHBV content of 32.2 % CDW with HV content of 5.6 mol%	Not available	”

Carbon sources & co-substrates/Precursors	Strain used	Biomass & PHBV formed with HV incorporation mol%	Scale of production	Reference
Glycerol & Propionic acid	”	PHBV content of 24.1 % CDW with HV content of 21.7 mol%	Not available	”
Glycerol & Propionic acid	*B.glumae* MA13	CDW is 1.9 g/L. PHBV content is 25.20 % CDW with 30.15 mol% HV	Shake flask	(Coutinho de Paula et al., 2019)
Glycerol & Propionic acid	”	PHBV is 9.5 g/L from CDW of 14.7 g/L. Volumetric productivity is 0.22 g/ (L h) & 21.8 mol% of 3HV content	10 L bioreactor	(Coutinho de Paula et al., 2019)
Crude glycerol & Hexanoic acid	”	CDM is 3.16 g/L PHBV is 34.02 % of CDW. 0.24 mol% HV content (Flask level)	Shake flask	(Coutinho de Paula et al., 2019)
Glycerol & Propionate	*Vibrio* alginolyticus	1.44 g/L PHBV with a 3HV content of 24.42 mol% @ 4 g/L propionate concentration	Flask	(Li et al., 2021)
Maduca indica	*C. necator* MTCC−1954	PHBV is 1.44 g/L	Flask level	(Kerketta and Vasanth, 2019)
Spent coffee & Groundnut oil	*C. necator* DSM 545	Highest total biomass (11.3 ± 0.2 g/L and PHBV content is 10.0 g/L	Flask	(Ingram and Winterburn, 2022
Spruce fir trees	*B. thuringensis.*	CDW was higher with wood juice from Douglas firs is 2.75 ± 0.13 g/L	Flask	(Ciesielski et al., 2021)
Extruded rice bran and Extruded corn starch (1:8)	*H. mediterranei* (ATCC 33500)	77.8 g/L PHBV & 55.6 mol% 3 HV. CDW is 140 g/L	5 L FERMENTER	(Huang et al., 2006)
Extruded corn-starch	*H. mediterranei* (ATCC 33500)	24.2 g/L PHBV (38.7 mol% 3 HV) CDW: 62.6 g/L	5 L FERMENTER	(Huang et al., 2006)
Extruded wheat bran and Extruded corn starch (1:2)	*H. mediterranei* (ATCC 33500)	52.7 g/LPHBV (40.2 mol% 3 HV) CDW: 131 g/L	5 L FERMENTER	(Huang et al., 2006)
Enzymatic extruded starch	*H. mediterranei* ATCC 33500	20.0 g/L PHBV (10.4 mol% 3 HV)	6.0 L fermenter	(Chen et al., 2006)
Clarified fermented molasses	*Mixed cultures*	HV fraction ranging from 15 % to 39 %	2 L ferementer	(Albuquerque et al., 2011)

Carbon sources & co-substrates/Precursors	Strain used	Biomass & PHBV formed with HV incorporation mol%	Scale of production	Reference
Gluconate/ VFAs/food starches: Valerate	*C. taiwanensis*	10–85 mol% of 3-HV fraction; 42–67 % CDW as PHBV (very small quantity up to 3 g of cell dry wet)	Not available	(Sheu et al., 2009)
Fatty acid (oleic acid) & 1-pentanol	*Cupriavidus* sp. USMAA1020	CDW (13.3 g/L) and PHA concentration (10.23 g/L)	Shake flask	(Huong et al., 2017)
Oleic acid and 1-pentanol	*C.malaysiensis* sp. USMAA2–4	9.8 g/L RCDW and 8.7 g/L PHBV conc. Productivity of the copolymer is 0.160 g/L/h	3.6 L bioreactor	(Shantini et al., 2021)
Palm oil mill effluent	*Comamonas sp* EB 172	CDW 10 g/L with 73 %PHBV content at limited oxygen (0 %)	2–7 L fermenters	(Mumtaz et al., 2009)
Palm olein & 1-pentanol	*C. malaysiensis* USMAA2–4$_{ABH16}$	0.41—0.52 g/g P(3HB-co–3HV) yield and 72—89 wt% PHBV; 12 mol% 3HV	6 L fermenter	(Wong et al., 2022)
Soyabean oil and valerate	*Photobacterium* sp. TLY01	PHBV vol reached 16.28 g/L	Flask to Bioreactor	(Tian et al., 2022)
Plant oil & Valerate/propionate	*C. necator* H16	concentration of PHA (6.8 g L^{-1}) containing 7 mol% of 3HV	Flask	(Lee et al., 2008)
Jatropha oil & Valerate/Propionate	*C.necator* H16	PHBV content: 69–90 %CDW 3HV Content: 27–41 %	Flask	(Ng et al., 2011)
Waste cooking oil, Corn starch, and Valerate;	*Photobacterium* sp. TLY01	PHBV titter reached 4.01 g/L	Flask to Bioreactor	(Tian et al., 2022)
Waste cooking oil	*C. necator* TISTR 1095	CDW 7.5 g/L and PHBV 3.8 g/L with 0.063 g/L.h of PHBV productivity & 20 mol% HV content	Flask	(Sangkharak et al., 2021a)
Waste frying oil & valerate	*Halomonas. hydrothermalis* CCM 7104	CDW is 2.34 g/L. PHBV content is 68.83 % of CDW. 3-HV content is 50.15 mol%.	Flask	(Pernicova et al., 2019)
Waste frying oil & Propionate;	*H. hydrothermalis* CCM 7104	CDW 2.75 g/L. PHBV content is 47.17 % of CDW. 3-HV content is 7.16 mol%.	Flask	(Pernicova et al., 2019)
Waste frying oil&n-propanol	*H. hydrothermalis* CCM 7104	CDW is 2.19 g/L. PHBV content is 69.86 % of CDW. 3-	Flask	(Pernicova et al., 2019)

Carbon sources & co-substrates/Precursors	Strain used	Biomass & PHBV formed with HV incorporation mol%	Scale of production	Reference
		HV content is 8.44 mol%.		
Waste frying oil & Propionate;	*H. neptunia*	CDW is 0.54 g/L. PHBV content is 23.66 % of CDW. 3-HV content is 29.5 mol%.	Flask	(Pernicova et al., 2019)
Waste frying oil & n-propanol;	*H. neptunia*	CDW is 1.23 g/L. PHBV content is 15.85 % of CDW. 3-HV content is 26.07 mol%.	Flask	(Pernicova et al., 2019)
Waste fish oil, Glycerol and Sodium valerate	*Salinivibrio* sp. M318	CDW is 11.6 g/L. PHBV content is 52.4 % of CDW. 3-HV content is 24.7 mol%.	Flask as well as bioreactor level	(Van Thuoc et al., 2019)
Waste fish oil, glycerol and sodium propionate	*Salinivibrio* sp. M318	CDW is 10.8 g/L. PHBV content is 48.3 % of CDW. HV % 17	Flask as well as bioreactor level	(Van Thuoc et al., 2019)
Waste fish oil, Glycerol and Sodium heptanoate	*Salinivibrio* sp. M318	CDW is 11.2 g/L. PHBV content is 53 % of CDW. HV % 13.3	Flask as well as bioreactor level	(Van Thuoc et al., 2019)
Food waste hydolysate & Levulinic acid	*H. mediterranei*	CDW of 3.19 ± 0.66 g/L. maximum yield of 56.70 % PHBV with 18.55 mol% 3HV content	Flask as well as bioreactor level	(Priya et al., 2022)
Date waste	*H. mediterranei* DSM1411	18 g/L CDW having 4.5 g/L PHBV with 18 mol% of 3 HV	2 L Fermenter	(Alsafadi et al., 2020)
Digested food wastes	*C. necator*	CDW and PHBV content reached up to 22.7 g/L and 72.6 % (w/ w), respectively with 2.8 mol% HV monomer unit	2 L fermenter	(Du and Yu, 2002)
Organic Waste (trade and industry waste, and fruit and vegetable waste)	*C. necator* TF 93	1.1 g/L PHBV with 30 % HV content	1 L fermenter	(Ganzeveld et al., 1999)
Waste water from biodiesel industry	*P. mendocina* PSU	43.6 wt% PHBV with 8.6 HV mol% CDW: 2.5–4 g/L	Lab level	(Martla et al., 2018)
Rice based ethanol stillage	*H.mediterranei*	71 ± 2 % of CDW PHBV accumulation with 16.42 ± 0.02 g/L PHA production.	Flask	(Bhattacharyya et al., 2014)

Carbon sources & co-substrates/Precursors	Strain used	Biomass & PHBV formed with HV incorporation mol%	Scale of production	Reference
Casava waste	*H.borinquense* strain E3	CDW is 4.6 g/L with maximum PHBV concentration of 1.52 g/L & 19.65 mol% of 3HV unit	Flask	(Salgaonkar et al., 2019)
Olive mill waste water	*H. mediterranei*	PHBV yield is 0.2 g/L and PHBV content is 43 % PHBV/cell dry mass) with 6.5 mol% 3–3HV content	Flask	(Alsafadi and Al-Mashaqbeh, 2017)
Hydrolyzed whey permeate	*H. mediterranei* DSM1411	7.2 g/L PHBV (10 mol% 3 HV)	300 L piolt scale	(Koller, 2015)
Whey lactose	*H.mediterrane*	accumulated 50 wt.-% of PHBV, specific productivity q_p: 9.1 mg/g.h	10 L bioreactor	(Koller et al., 2007)
Whey lactose	*H.pseudoflava*	40 wt.-% PHBV, q_p: 12.5 mg /g.h	10 L bioreactor	(Koller et al., 2007)
Whey lactose	*Pseudomonas hydrogenovora*	12 wt.-% PHBV, q_p: 2.9 mg/g.h	10 L fermenter	Koller et al., 2007)
Cheese whey & Propionic acid	*B. megaterium* NCIM 5472	PHBV content of 86.6 % and the PHBV yield of 3.64 g/L	Not available	(Suhazsini et al., 2020)
Acetate & Propionate	*E. coli* JM109 (Engineered)	produced 1.09 g/L PHBV with a 3-HV content of 10.37 mol%	Flask	(Chen et al., 2018)
Acetate & Valeric acid	*Rhodobacter sphaeroides* U7	PHBV content is 2.66 g/L	Not available	Kemavongse et al., 2008)
Acetate & Propionate	*A.hydrophila* 4AK4;	3.79 g/L CDW, containing 15.02 wt% P(3HB-co−4.23 mol% 3HV)	Flask	(Shi et al., 2020)
Acetic acid	*C. necator* DSM 545	65 g/L CDW and 48 g/L PHBV concentration with a 3HV fraction of 27 mol%	3 L Bioraector	(Garcia-Gonzalez and De Wever, 2018)
Acetic acid and oleic acid	Recombinant *E. coli* XL1-Blue(pJC4)	PHBV conc. (78.2 % of CDW) is 158 g/L with 10.6 mol% 3-HV content	6.6 L Fermenter	(Choi and Lee, 1999)
Acetic acid & Propionic acid	”	PHBV conc. (CDW 141.9 g/L) is 88.1 g/L with 15.3 mol% 3-HV	Fermenter 6.6 L	”

Carbon sources & co-substrates/Precursors	Strain used	Biomass & PHBV formed with HV incorporation mol%	Scale of production	Reference
Vinasse	*H. mediterranei*	The 3-HV contents are 12.36 mol % (utilising 25 % pre-treated vinasse) and 14.09 mol % (utilising 50 % pre-treated vinasse). & 70 % of CDW as PHBV (19.7 g/L)	Shake flask	(Bhattacharyya et al., 2012)

Because substrate cost is a major factor in commercial viability, recent research has focused on identifying inexpensive and renewable feedstocks. A major challenge remains the discovery of low-cost carbon sources that can enhance both the economic and environmental sustainability of PHBV production. Promising alternatives include CO_2, agro-industrial residues, organic wastes, and other industrial by-products. For example, *C. necator* produced 24.7 g/L PHBV from CO_2 in a 7 L fermenter (Ghysels et al., 2018), while crude glycerol yielded 23.4 g/L (Kachrimanidou et al., 2014). Methanol (30–40 % of CDW) (Ezhov et al., 2013a), ethanol and pentanol (1.4 g/L) (Park and Damodaran, 1994) have also been explored as carbon sources.

Agro-industrial wastes are particularly attractive due to their abundance and low cost. Examples include molasses such as date molasses (4.5 g/L) (Alsafadi et al., 2020), whey (7.2 g/L) (Koller, 2015), lignocellulosic substrates like spruce fir (Ciesielski et al., 2021), and waste oils. Waste cooking oil has supported 3.8 g/L PHBV (Sangkharak et al., 2021a), while waste frying oil and waste fish oil yielded PHBV contents of 68.8 % and 52.4 % CDW, respectively (Pernicova et al., 2019, Van Thuoc et al., 2019). Other examples include wastewater (43.6 wt% PHBV) (Martla et al., 2018), *Madhuca indica* residues (1.44 g/L), and spent coffee grounds (10 g/L) (Ingram and Winterburn, 2022).

Organic wastes such as fruit and vegetable residues (1.1 g/L) (Ganzeveld et al., 1999), rice-based ethanol stillage (16.4 g/L) (Bhattacharyya et al., 2014), and digested food waste (16 g/L) (Du and Yu, 2002) have also been applied successfully. Similarly, hydrolyzed whey permeate (7.2 g/L) (Koller, 2015), cheese whey (3.6 g/L) (Suhazsini et al., 2020), cassava waste (1.5 g/L) (Salgaonkar et al., 2019), vinasse (19.7 g/L) (Bhattacharyya et al., 2012), and extruded starches (20–52.7 g/L) (Huang et al., 2006, Chen et al., 2006) have shown promise. Oils such as soybean (16.3 g/L) (Tian et al., 2022), groundnut (10 g/L), jatropha (69–90 % CDW) (Ng et al., 2011), and palm oil mill effluent (7.3 g/L) (Mumtaz et al., 2009) further expand the spectrum of cost-effective substrates.

Even higher PHB contents have been achieved with certain waste substrates (Table 5). Wheat hydrolysate yielded 162.8 g/L PHB (Xu et al., 2010), waste rapeseed oil gave 105 g/L (Obruca et al., 2010), kenaf biomass 4.8 g/L (Saratale et al., 2019), and macroalgal biomass 2.2 g/L (Ghosh et al., 2019). Such examples highlight the vast potential of inexpensive substrates for PHBV production. Since the properties of PHBV depend on the 3HV fraction, tailoring the monomer composition to specific applications is a key challenge. One effective strategy is the use of volatile fatty acids (VFAs). Even-carbon VFAs typically yield copolymers with > 90 mol% 3HB, while odd-carbon VFAs result in > 87 mol% 3HV (Ferre-Guell and Winterburn, 2018).

Table 5. Different carbon substrates used for the PHB production on various scales.

Different Carbon source	Strain used	Conc. of biomass as well as PHB formed	Scale of production (working vol)	Reference
Waste rapeseed oil	*C.necator* H16	CDW is 138 g/L with PHB content of 105 g/L	Bioreactor 1.2 L	(Obruca et al., 2010)
Rapeseed oil	*C. necator*	1.2 g/L PHB content	Flask	(Verlinden et al., 2011)
Kenaf biomass	*C. necator*	CDW is 9.2 g/L and PHB content is 4.81 gL^{-1}	Flask	(Saratale et al., 2019)
Macroalgal biomass	*H.mediterranei* strain	CDW is 3.8 g/L, and PHB content is 2.2 g/L	40.40 L	(Ghosh et al., 2019)
Deoiled algae biomass	Mixed culture	PHB content is 0.43 ± 0.2 g g^{-1} CDW	Flask	(Naresh Kumar et al., 2020)
	C. necator CCGUG 52,238	CDW is 15 g/L and PHB content is 12 g/L	5 L fermenter	(Farah et al., 2011)
Beer brewery wastewater and maltose	*C. necator* (DSMZ 454)	CDW is 7. g/L and PHB content is 3 g/L	Flask	(Amini et al., 2020)
Cassava starch	*Bacillus megaterium*	CDW is 4.97 g/L, and PHB content is 1.476 gL^{-1}	Flask	(Krueger et al., 2012)
Cassava starch	*Cupriavidus* sp. *KKU38*	CDW is 5.97 g/L, and PHB content is 5.97 g/L	Flask	(Poomipuk et al., 2014)
Wheat hydrolysate	*Wautersia eutropha*	CDW is 175.05 g/L and PHB content is 162.8 g/L	1.5 L bioreactor	(Xu et al., 2010)
Calophyllum inophyllum oil	*C.necator*	PHB content is 10.6 g/L	2 L fermenter	(Arumugam et al., 2018)
Waste glycerol	*C. necator* DSM 545	CDW is 68.8 g/L and PHB content is 38 % (26.14 g/L)	1.5 L fermenter	(Cavalheiro et al., 2009)
Paddy straw	*C. necator*	CDW is 19.2 g/L and PHB content is 7.21 g/L	1 L flask	(Sandhya et al., 2013)
Pineapple and sugarcane waste	*B. safensis* EBT1	CDW is 8.5 g/L and PHB content is 5.9 g/L	2.5 L fermenter	(Sakthiselvan and Madhumathi, 2018)

3.2. Novel customisation approaches

Novel customisation approaches (Table 6) include co-substrate feeding, precursor addition, and mixed-substrate systems. For instance, in *C. necator*, co-feeding levulinic acid and sodium propionate enhanced both productivity and 3HV incorporation (Berezina and Yada, 2016). A combination of levulinic acid, sodium propionate, and pentanol further increased 3HV content (Berezina, 2012). Lignocellulosic hydrolysates with acetate also improved yields (Yin et al., 2020). In continuous mode, the addition of levulinic acid to crude glycerol and sunflower meal hydrolysates yielded 23.4 g/L PHBV with 31 mol% 3HV in *C. necator* DSM 7237 (Kachrimanidou et al., 2014).

Table 6. Novel approaches for customised PHBV production.

Noval strategy used	**Optimised conditions including strain, substrates and other parameters**	**Outcome reported**	**Scale of production**	**Reference**
co-substrates addition (batch)	*B.glumae* MA13; Crude glycerol & hexanoic acid	CDW is 3.16 g/L and 34.02 % of CDW as PHBV. 0.24 mol% HV	Sshake flask	(Coutinho de Paula et al., 2019)
	C. necator; levulinic acid and sodium propionate	3-HV content in PHBV was enhanced, and productivity increased	Lab level	(Berezina and Yada, 2016)
	C. necator; pentanol; levulinic acid, sodium propionate	increased 3-HV content in PHBV	Lab level	(Berezina, 2012)
	H. mediterranei ES1; Glucose and valerate	5.1 g/L PHBV & 12.3 g/L CDW	Shake flask to 7 L Fermenter	(Han et al., 2015)
	Bacillus megaterium NCIM 5472; Cheese whey & propionic acid	PHBV content of 86.6 % of CDW and PHBV yield of 3.64 g/L	Flask	(Suhazsini et al., 2020)
	C.necator H16; Plant oil & valerate/propionate	PHBV is 6.8 g/L with 7 mol% of 3HV	Flask	(Lee et al., 2008)
	C.necator H16; Jatropha oil, valerate/propionate	PHBV content is 69–90 % of CDW & 3HV Content is 27–41 mol%	Flask	(Ng et al., 2011)
	mixed microbial culture (MMC) (*Acidovorax* was dominant); lignocellulosic hydrolysates and acetate	2.308 g/L PHBV content	Lab level fermenter	(Yin et al., 2020)
co-substrates addition (Continuous)	C. necator DSM 7237; Crude glycerol, sunflower meal hydrolysates and Levulinic acid;	23.4 g/ L of PHBV, which is 66.4 % (w/w) of CDW, with 31 mol% HV content	1 L bioreactor	(Kachrimanidou et al., 2014)

Noval strategy used	Optimised conditions including strain, substrates and other parameters	Outcome reported	Scale of production	Reference
Precursor, co-substrates addition	*S. enterica* serovar Typhimurium JE4199 Glycerol & propionic acid; adjusting the arabinose or cyanocobalamin (precursor of coenzyme B_{12})	41.4 % of CDW as PHBV. 30.6 mol% as HV content	Flask level	(Aldor et al., 2002)
	S. enterica serovar Typhimurium TR6583; Glycerol & propionic acid; Adjusting the arabinose or cyanocobalamin (precursor of coenzyme B_{12}) concentration in the medium.	32.2 % of CDW as PHBV. 5.6 mol% as HV content	Flask level	(Aldor et al., 2002)
	S. enterica serovar *typhimurium* TR6583; Glycerol & propionic acid; adjusting the arabinose or cyanocobalamin (precursor of coenzyme B_{12}) concentration in the medium.	24.1 % of CDW as PHBV. 21.7 mol% as HV content	Flask level	(Aldor et al., 2002)

Precursor supplementation has also been used to modulate 3HV content. In engineered *S.enterica*, varying arabinose or cyanocobalamin concentrations controlled HV composition when glycerol was used as the substrate (Aldor et al., 2002). Similarly, propionate feeding in *Vibrio alginolyticus* allowed 3HV customisation (Li et al., 2021). Supplementation with valine and threonine facilitated α-ketobutyrate accumulation, subsequently converted to propionyl-CoA and incorporated into PHBV (Eschenlauer et al., 1996).

Although pure organic compounds like acetate and glucose can enhance yields, their costs remain high. More economical approaches include blending municipal wastewater with carbon-enriched industrial effluents (Yuan et al., 2015). Importantly, several wild-type bacteria can naturally produce the HV component from unrelated carbon sources such as crude glycerol (Hermann-Krauss et al., 2013), whey sugars (Koller et al., 2007, 2015; Suhazsini et al., 2020), fruit and vegetable residues (Ganzeveld et al., 1999), or olive mill wastewater (Alsafadi and Al-Mashaqbeh, 2017). This eliminates the need for costly precursor addition while enabling cost-effective HV incorporation (Policastro et al., 2021).

4. Optimisation of bioprocesses and scale-up considerations

Over the past few decades, several strategies have been developed to optimize PHBV production (Table 7). A major focus has been on refining growth conditions by adjusting temperature, agitation, aeration, nutrient feeding, and the carbon-to-nitrogen (C:N) ratio. Such interventions have significantly improved yields in multiple microbial systems. For example, in *Bacillus flexus* MTCC 12841,optimized parameters led to 9.73 g/L PHBV (59 % increase) with a biomass yield of 15.7 g/L (126 % improvement) compared to shake-flask experiments, accompanied by high carbon utilization efficiencies (Yp/s = 0.32 g/g and Yx/s = 0.51 g/g) (Wagle et al., 2019). Similarly, in *C.*

necator, an initial pH of **7.5 and temperature of 30°C**, with agitation at 600 rpm and aeration at 1 VVM, resulted in maximum PHBV production of 16.48 g/L in fermenter (Du and Yu, 2002).

Table 7. Different approaches reported so far for optimisation of bioprocesses.

Optimisation & scale-up strategy used	**Optimised conditions including strain, substrates and other parameters**	**Outcome reported**	**Scale of production**	**Reference**
Media and physical parameter optimisation	*Comamonas* sp EB 172; Palm oil mill effluent;	CDW of 10 g/L with its 73 % as PHBV content is reached from 5.9 g/LCDW. PHBV Conc. is increased by 42 % CDW 10 g/L with 73 %PHBV content at limited oxygen (0 %). Cell mass was greatly reduced to 42 % at normal (30–100 %) dissolved oxygen. Nitrogen limitation also gives the optimised result	2–7 L fermenters	(Mumtaz et al., 2009)
Media and physical parameter optimisation of temperature, agitation, aeration, nutrient feeding, and C: N ratio	*Bacillus flexus* MTCC 12841	Achieved a PHBV conc of 9.73 g/L —an increase of 59 %—with a biomass yield of 15.7 g/L, representing a 126 % improvement over optimized shake flask experiments	6.6 L fermenter	(Wagle et al., 2019)
One-parameter optimisation of C/N	Mixed microbial culture (MMC) (*Acidovorax* was dominant); lignocellulosic hydrolysates and acetate	1.91-fold increase in the yield of PHBV was achieved with a limited nitrogen medium (C/N = 33 was increased from 20) with 2.308 g/L PHBV content	Lab-level fermenter	(Yin et al., 2020)
One-parameter optimisation by controlling precursor level	*P. mendocina* PSU; Waste water from biodiesel industry	43.6 wt% of CDW as PHBV with 8.6 HV mol% @.3 % sodium propionate. CDW is 2.5–4 g/L	Lab level	(Martla et al., 2018)
One-parameter optimisation by controlling precursor level	*H. mediterranei* ES1	5.1 g/L PHBV & CDW is 12.3 g/L at 15 mm valerate. While using 17 mm valerate HV content is increased to 60.3 mol% but PHBV is reduced to 0.2 g/L	Shake flask to 7 L Fermenter as well shake flask	(Han et al., 2015)

Optimisation & scale-up strategy used	Optimised conditions including strain, substrates and other parameters	Outcome reported	Scale of production	Reference
Optimisation by two-level factorial designs	*Cupriavidus* sp. USMAA2–4, oleic acid and 1-pentanol	Screen variables affecting the growth and production.	Flask level	(Shantini et al., 2012)
Statistical Optimisation (Response surface methodology (RSM) using a 2^n factorial Central Composite Design (CCD))	*Rhodobacter sphaeroides* U7; acetate & valeric acid	PHBV production increased 3.86-folds (from 0.69 to 2.66 g/l) (PHA content increased 1.5-folds)	Flask level	(Kemavongse et al., 2008)
Statistical Optimisation using Plackett- Burman design (PBD) and response surface methodology (RSM)	*Bacillus megaterium* NCIM 5472; cheese whey permeate & propionic acid	PHBV content of 86.6 % of CDW and PHBV yield of 3.64 g/L;	Flask level	(Suhazsini et al., 2020)
Statistical optimisation using central composite design in RSM	*C. malaysiensis* sp. USMAA2–4; oleic acid and 1-pentanol remained the same before and after optimisation	9.8 g/L RCDW with 250 % increment and 8.7 g/L PHBV conc with 223 % increment were obtained. iQp increased from 0.037 g/L/h to 0.160 g/L/h	3.6 L bioreactor	(Shantini et al., 2021)
Dynamic optimisation to predict optimal feeding patterns for carbon and nitrogen in fed-batch bioreactors	*C. necator;* levulinic acid and sodium propionate	100 % productivity enhancement, at 3.9 mg/L/hour, for the production of PHBV with 80 % 3-HV	3 L shaking flasks	(Berezina and Yada, 2016)
Repeated-batch cultivation	*C. necator* TISTR 1095; Waste cooking oil	1.3-Fold increase in biomass. CDW is 7.5 g/L and PHBV 3.8 g/L & 20 mol% HV content.	Shake flask to 5 L fermenter.	(Sangkharak et al., 2021)
Overexpressing the PHBV genes by genetic recombination	*A.hydrophila* 4AK4; acetate & propionate	3.79 g/L CDW, containing 15.02 wt% P(3HB-co–4.23 mol% 3HV)	Flask level	(Shi et al., 2020)
Chromosomal expression through	*H.bluephagenesis*; glucose	6.3 g/L CDW, 65 % PHBV in CDW and 25 mol% 3HV in PHBV (27 %	Flask level	(Chen et al., 2019)

Optimisation & scale-up strategy used	Optimised conditions including strain, substrates and other parameters	Outcome reported	Scale of production	Reference
the CRISPR/Cas9 method		and 12 % increase in CDW and PHBV content, respectively)		

Nutrient optimisation has also proven effective. Increasing the C:N ratio from 20 to 33 enhanced PHBV yield 1.91-fold, achieving 2.3 g/L in *Acidovorax* (Yin et al., 2020). In *Comamonas* sp. EB 172, optimisation of nitrogen levels and aeration increased PHBV concentration by 42 %, yielding 10 g/L CDW with 73 % PHBV (Mumtaz et al., 2009). In *H. mediterranei* ES1, valerate optimisation resulted in 5.1 g/L PHBV with a CDW of 12.3 g/L (Han et al., 2015). Likewise, in *Pseudomonas mendocina* PSU, sodium propionate optimisation yielded 43.6 wt% PHBV with 8.6 mol% HV (Martla et al., 2018).

Statistical optimisation techniques have further streamlined process refinement. In *R. sphaeroides* U7, the use of a factorial Central Composite Design (CCD) in Response Surface Methodology (RSM) increased PHBV yield 3.86-fold from 0.69 g/L (Kemavongse et al., 2008). In *B. megaterium* NCIM 5472, Plackett-Burman Design (PBD) and RSM increased PHBV production to 3.64 g/L (Suhazsini et al., 2020). In *Cupriavidus* sp. USMAA2–4, RSM optimisation achieved 65 % PHBV content with 10.2 g/L CDW, reducing 1-pentanol usage by 33 % while improving yields (Shantini et al., 2012). A later study using CCD reported 8.7 g/L PHBV with a 223 % improvement compared to unoptimized conditions (Shantini et al., 2021). Dynamic optimisation approaches have also been applied. In *C.necator*, Berezina and Yada (2016) demonstrated a dual feeding strategy using levulinic acid and sodium propionate that doubled both yield and productivity. Repeated-batch cultivation in *C. necator* TISTR 1095 achieved a 1.3-fold increase in biomass and 3.8 g/L PHBV with 20 mol% HV content (Sangkharak et al., 2021).

Genetic engineering has provided additional opportunities for optimisation. In *A. hydrophila* 4AK4, overexpression of PHBV biosynthetic genes yielded 3.79 g/L biomass containing 15.02 wt% P(3HB-co-4.23 mol% 3HV) at flask level (Shi et al., 2020). Using CRISPR/Cas9 for chromosomal expression in *H. bluephagenesis*, optimised cultures achieved 6.3 g/L CDW with 65 % PHBV content and 25 mol% 3HV, corresponding to 27 % and 12 % improvements in CDW and PHBV yield, respectively (Chen et al., 2019).

Despite successful lab-scale optimisation, scale-up remains a major challenge as pilot- or industrial-scale processes often fail to replicate laboratory results. To address this, researchers have explored cost-effective substrates, pretreatment methods, nutrient limitations, feeding strategies, and metabolic engineering (Zhang et al., 2022). Table 8 summarises recent scale-up strategies.

Table 8. Different approaches reported so far for the scale-up of production.

Scale-up strategy adopted	Conditions, including strain, substrates and other parameters	Out come	Scale of production	Reference
Use of genetic engineering tools, as well as fed batch culturing	Recombinant *E.coli* XL1-Blue(pJC4); Acetic acid and oleic acid	PHBV is 158 g/L with 10.6 mol% HV content & CDW is 203.1 g/L	6.6-liter jar fermenter	(Choi and Lee, 1999)
	Recombinant *E.coli* XL1-Blue(pJC4); Acetic acid & propionic acid;	PHBV is 88.1 g/L with 15.3 mol% of HV content &CDW as 141.9 g/L	6.6-liter jar fermenter	(Choi and Lee, 1999)
Use of genetic engineering tools, as well as fed batch culturing with a pH-stat feeding mechanism	Recombinant *E. coli* XL1 Blue(pJC4); Glucose & propionic acid	CDW is 120.3 g/L with 42.5 % of CDW as PHBV content	6.6-liter jar fermenter	(Choi and Lee, 1999)
Fed batch culturing with pH-stat feeding	*Comamonas* sp EB 172; Palm oil mill effluent;	CDW of 10 g/L with its 73 % as PHBV content is reached	2–7 L fermenters	(Mumtaz et al., 2009)
Co-substrate addition and fed batch culturing	*Photobacterium* sp. TLY01; Soyabean oil and valerate;	PHBV content is 16.28 g/L	Flask to Bioreactor	(Tian et al., 2022)
	Photobacterium sp. TLY01; waste cooking oil, corn starch, and valerate;	PHBV content is 4.01 g/L	Flask to Bioreactor	Tian et al., 2022)
	Salinivibrio sp. M318; Waste fish oil, glycerol and sodium valerate	CDW is 11.6 g/L with 52.4 % as PHBV. 24.7 mol% as HV content	Flask as well as bioreactor level	(Van Thuoc et al., 2019) ,
	Salinivibrio sp. M318; Waste fish oil, glycerol and sodium propionate; batch to fed batch.	CDW is 10.8 g/L with 48.3 % as PHBV. 17 mol% as HV content	Flask as well as bioreactor level	’
	Salinivibrio sp. M318; Waste fish oil, glycerol and sodium heptanoate; batch to fed batch.	CDW is 11.2 g/L with 53 % as PHBV. 13.3 mol% as HV content	Flask as well as the bioreactor level	
Fed batch cultivation with pulse feeding of Co-substrate	*H. mediterranei*; Food waste hydolysate & Levulinic acid;	CDW of 3.19 g/L with 56.70 % as PHBV. 18.55 mol% 3HV content	Flask as well as the bioreactor level	(Priya et al., 2022)

Scale-up strategy adopted	Conditions, including strain, substrates and other parameters	Out come	Scale of production	Reference
Fed-batch culturing with a pH stat control mechanism, as well as providing additional oxygen	*C. necator* DSM 545; Acetic acid	65 g/L CDW and 48 g/L PHBV with a 3HV content of 27 mol%	3-L bioreactor	(Garcia-Gonzalez and De Wever, 2018)
Fed batch culturing	*H. mediterranei* DSM1411; date waste;	CDW of 12.8 g/L and PHBV content of 3.20 g /L, and is scaled up to 18 g/L CDW with 4.5 g/L PHBV content. 18 mol% of 3 HV content	2 L Fermenter	(Alsafadi et al., 2020)
	C. glutamicum strain WM001 (engineered); Glucose & corn steep liquor	15.0 g/L PHBV with maximum 3HV fraction of 72.5 mol%	Sahek flask as well as 3 L fermenter	(Ma et al., 2018)
	Salinivibrio sp. TGB10;	1.45 g/L PHBV in flask cultures for 24 hr cultivation. But a CDW of 33.45 g/L and a PHBV titer of 27.36 g/L were obtained after 108 h of fed-batch cultivation	Shake flask to 5 L fermenter	(Tao et al., 2021)
	B. glumae MA13; glycerol & propionic acid	CDW 1.9 g/L and 25.20 % of CDW as PHBV with 30.15 mol% as HV content in the flask level is increased to a PHBV content of 9.5 g/L from 14.7 g/L of CDW.	Shake flask and 10 L bioreactor	(Coutinho de Paula et al., 2019)
Repeated fed-batch culturing with pH stat control mechanism	*H. mediterranei* (ATCC 33500); Extruded rice bran and extruded corn starch	77.8 g/LPHBV (55.6 mol% 3 HV) CDW: 140 g/L	5 L fermenter	Huang et al., 2006)
	H. mediterranei (ATCC 33500); extruded corn-starch	24.2 g/L PHBV (38.7 mol% 3 HV) CDW: 62.6 g/L	5 L fermenter	
	H. mediterranei (ATCC 33500); extruded	52.7 g/L PHBV (40.2 mol% 3 HV) CDW: 131 g/L	5 L fermenter	

Scale-up strategy adopted	Conditions, including strain, substrates and other parameters	Out come	Scale of production	Reference
	wheat bran and extruded corn starch			
	H. mediterranei (ATCC 33500); Glucose	23 g/L PHBV (27 mol% 3 HV) CDW: 85.8 g/L	5 L fermenter	
	H. mediterranei ATCC 33500; Enzymatic extruded starch; starch/yeast extract	20.0 g/L PHBV (10.4 mol% 3 HV) 50.8 % (w/w) of CDW	6.0 L fer	(Chen et al., 2006)
Batch culturing	*H.borinquense* strain E3; casava waste	CDW is 4.6 g/L; PHBV concentration of 1.52 g/L with 19.65 mol% 3HV unit	1 L flask	(Salgaonkar et al., 2019)
Repeated-batch cultivation	*C.necator* TISTR 1095; Waste cooking oil	1.3-Fold increase in biomass. CDW is 7.5 g/L and PHBV 3.8 g/L with 0.063 g/L.h of PHBV productivity & 20 mol% HV content.	Shake flask to 5 L fermenter.	(Sangkharak et al., 2021)
Continuous feeding of one substrate and fed batch culturing with pulse and pH-stat feeding of co co-substrate	*C. necator*, strain DSM 545; CO2 and valeric acid	PHBV content is 24.7 g L^{-1}	7 L Reactor level	(Ghysels et al., 2018)

Fed-batch cultivation is widely employed for scale-up. For example, in *H. mediterranei* DSM1411, *C. glutamicum*, and *B. glumae* MA13, PHBV yields of 4.5 g/L (18 mol% HV), 15.0 g/L (72.5 mol% HV), and 0.48 g/L (30.15 mol% HV), respectively, were achieved (Alsafadi et al., 2020, Ma et al., 2018, Coutinho de Paula et al., 2019). In *Salinivibrio* sp. TGB10, fed-batch culture increased polymer yield from 1.45 g/L (flask) to 27.36 g/L (fermenter) (Tao et al., 2021). In *Comamonas* sp. EB 172, fed-batch pH-stat feeding yielded 7.3 g/L PHBV (Mumtaz et al., 2009). Batch cultivation of *H. borinquense* strain E3 yielded 1.52 g/L PHBV with 19.65 mol% 3HV (Salgaonkar et al., 2019).

Repeated-batch cultivation has also been effective. In *C. necator* TISTR 1095, scaling from shake-flask to 5 L fermenter improved biomass 1.3-fold (Sangkharak et al., 2021a). In *H. mediterranei*, repeated fed-batch cultivation under controlled pH achieved 77.8 g/L PHBV (Huang et al., 2006, Chen et al., 2006). Similarly, combined continuous and pulse feeding in *C. necator* produced 24.7 g/L PHBV (Ghysels et al., 2018), while pulse feeding with co-substrates in *H. mediterranei* yielded 3.19 g/L CDW containing 56.7 % PHBV and 18.55 mol% HV (Priya et al., 2022).

Co-substrate addition combined with fed-batch strategies has also shown success in *Photobacterium* sp. TLY01 and *Salinivibrio* sp. M318 (Tian et al., 2022, Van Thuoc et al., 2019). Recombinant *E. coli* XL1-Blue (pJC4) has demonstrated the highest reported PHBV yield, producing 158 g/L with 10.6 mol% HV in a fed-batch fermenter using acetic acid and oleic acid (Choi and Lee, 1999).

Overall, advances in process optimisation, statistical modelling, dynamic feeding, and genetic engineering have markedly improved PHBV yields at the laboratory scale. However, scale-up continues to present major challenges, with process inconsistencies and cost limitations hindering industrial adoption. Integrating robust bioprocess control with metabolic engineering and the use of low-cost substrates will be essential for bridging the gap between lab success and commercial viability.

5. Material properties and versatile applications of PHBV

PHBV shows better mechanical and thermal properties than PHB and is therefore suitable for a wider range of uses (Jo et al., 2024). These properties are strongly influenced by the 3HV content. Suppl. Tables 1 & 2 list different PHBV copolymers with increasing 3HV and the corresponding mechanical, molecular and thermal properties. As the 3HV level increases, Young's modulus and tensile strength gradually decrease while elongation at break and elasticity increase. Crystallinity also decreases and usually falls between 50 % and 60 % (McAdam et al., 2020). This trend makes PHBV more ductile and elastic yet less crystalline than PHB, which is supported by other studies (Ferre-Guell and Winterburn, 2018, Abbasi et al., 2022).

Thermal properties also vary with 3HV content. Higher 3HV lowers the melting temperature (Tm) and glass transition temperature (Tg) while crystallisation temperature (Tc) rises. Thermal decomposition temperature (Td) shows little change. The recovery method and impurity level also affect mechanical strength since high impurity generally reduces ductility. Thermal analysis and microscopy can help to tailor the microstructure of PHBV films and improve their flexibility (Doineau et al., 2023).

Despite these advantages, PHBV has some limitations, such as lower strength and restricted thermal stability when compared with petroleum-based polymers (Rivera-Briso and Serrano-Aroca, 2018). To overcome these drawbacks, researchers have applied several strategies, such as chemical modification and blending with other polymers. Blending has proved very effective. PHBV combined with P(3/4HB) shows higher ductility and slower crystallisation. PHBV mixed with poly[(R)-3-hydroxybutyrate]-alt-poly(ethylene oxide) achieves break strain values of up to 394 % with 15 wt% HE (Li et al., 2009). PHBV blended with PHBH displays better thermoformability, while the incorporation of natural rubber latex increases toughness and reduces voids (Feijoo et al., 2022, Kuntanoo et al., 2015). Such advances expand the possible applications of PHBV and strengthen its position as an industrially useful biopolymer.

PHBV is renewable, biocompatible and biodegradable. These features make it especially attractive for biomedical and environmental applications. In tissue engineering and drug delivery, PHBV supports controlled release and improved cellular interactions (Rodríguez-Cendal et al., 2023). For packaging, PHBV is highly valued due to its strong gas barrier performance. Oxygen permeability is 1 to 7×10^{-17} $mol\,m^{-1}.s^{-1}.Pa^{-1}$. Carbon dioxide permeability 3 to 9×10^{-17} $mol\,m^{-1}.s^{-1}.Pa^{-1}$. Water

vapour permeability is 0.002 to 0.0004 $\times 10^{-10}$ mol$m^{-1}.s^{-1}.Pa^{-1}$ (Berthet et al., 2016). These values make PHBV competitive with synthetic plastics such as polypropylene and polyethylene, which also offer good strength, portability and insulation (Sharma et al., 2022).

Beyond packaging, PHBV has wide application in biofuels, fine chemicals, implantable biomaterials, bioplastics and pharmaceuticals (Chen, 2009). Its broad utility underlines the potential of PHBV as a sustainable and eco-friendly replacement for petroleum-based plastics.

6. Extraction solvents for food packaging and biomedical use

PHBV is a promising material for food packaging and biomedical applications as it maintains safety, efficiency and polymer integrity. The choice of extraction method strongly influences these attributes. Solvent extraction is the most widely used approach due to its effectiveness and scalability. The main categories of solvents include green or non-halogenated options, halogenated solvents, and other organic alternatives.

6.1. Green or non-halogenated solvents

Green solvents such as ethyl acetate, dimethyl carbonate (DMC), and acetone provide high efficiency with better safety compared to halogenated counterparts (Jin et al., 2023). In a comparative study, ethyl acetate achieved excellent recovery and purity levels in the high-90 % range with the added advantage of recyclability (Gahlawat and Soni, 2019). A large solvent-screening study with 35 candidates showed acetone and DMC yielding 91–95 % recovery with comparable purity (Vermeer et al., 2022). Acetone can also be used with water as an antisolvent, which improves safety and ease of operation. Other options include 1,3-dioxolane, which achieves yields of ~99 % with high purity, though its flammability is a drawback (Wongmoon and Napathorn, 2022). Butyl acetate showed moderate yields, and isoamyl alcohol was unsuitable (Gahlawat and Soni, 2019). Ethyl acetate remains the most effective and consistent performer, outperforming structurally similar solvents like butyl acetate (Riedel et al., 2013).

6.2. Halogenated solvents

Chloroform, methylene chloride, and 1,2-dichloroethane are widely used halogenated solvents that provide high purity but are limited by toxicity, volatility, environmental concerns, and high cost (Bhattacharyya et al., 2012). Despite these drawbacks, chloroform is still commonly used in laboratory-scale PHBV extraction due to its strong dissolution capacity. It has been applied in electrospun film preparation, copolymer purification, and nanoparticle formulations (Melendez-Rodriguez et al., 2018, Leimann et al., 2013, Abbasi et al., 2022). However, halogenated solvents are not suitable for food or biomedical-grade manufacturing.

6.3. Other non-halogenated solvents and organic acids

Additional solvents reported for PHA extraction include methyl ethyl ketone (MEK), methyl isobutyl ketone (MIBK), ethanol, lactic acid esters, γ-butyrolactone (GBL), tetrahydrofuran (THF), and cyclic carbonates (Riedel et al., 2013). For solvent-casting applications such as biopackaging films, formic acid and acetic acid can dissolve PHBV and its blends with tannins, allowing homogeneous film formation at mild temperatures around 60 °C (Ferri et al., 2023).

7. Economic viability

The large-scale commercialisation of PHBV remains constrained mainly by its high production cost (Rivera-Briso and Serrano-Aroca, 2018). Current research, therefore, focuses on reducing costs and broadening applications to position PHBV as a leading biodegradable polymer of the future (Akaraonye et al., 2010). Advances in fermentation strategies, metabolic engineering, and the use of low-cost substrates show considerable promise in this regard (Akaraonye et al., 2010). Several approaches are now being explored to make PHBV production economically sustainable (Table 9).

Table 9. Strategies can be adopted for commercially viable PHBV production.

Strategies	Conditions	Outcome	Reference
Use of wild strains with no need for precursor	*H. mediterranei*	Total dry cell biomass of 140 g/L with 77.8 g/L PHBV (55.6 mol% 3 HV) is achieved in 5 L fermenter	(Huang et al., 2006)
	Comamonas sp EB 172	7.3 g/L PHBV	(Mumtaz et al., 2009).
	C. necator TISTR 1095,	3.8 g/L PHBV	(Sangkharak et al., 2021)
Use of cheap substrates like agricultural, industrial, municipal and domestic /commercial food wastes	Crude glycerol,	23.4 g/ L PHBV with 31 mol% HV	(Kachrimanidou et al., 2014)
	H. mediterranei; extruded rice bran and extruded corn starch (1:8 ratio); 5 L fermenter	77.8 g/L PHBV (55.6 mol% 3 HV)	(Huang et al., 2006).
	Palm oil mill effluent	7.3 g/L PHBV	(Mumtaz et al., 2009)
	Soybean oil	16.28 g/L PHBV	(Tian et al., 2022).
	Wheat hydrolysate in Wautersia *eutropha*	PHB content of 162.8 g/L is reported at bioreactor level	(Xu et al., 2010).
	Waste rapeseed oil	PHB content of 105 g/L is produced (PHB content of 105 g/L).	(Obruca et al., 2010)
	Paddy straw	PHB content is 7.21 g/L	(Sandhya et al., 2013),
	Kitchen waste	PHB content is 12 g/L	(Farah et al., 2011)

Strategies	Conditions	Outcome	Reference
	Macroalgal biomass	PHB content is 2.2 g/L	(Ghosh et al., 2019)
	Kenaf biomass	PHB content is 4.81 g/L	(Saratale et al., 2019)
Microbial strain with high productivity, high microbial growth & low growth time	During 78 h of cultivation of *M. organophilum*	99 g/L PHBVwith a 3HV fraction of 11.0 mol%. Productivity, qp is 1.269 g/L/h (Fed batch)	(Kim et al., 1999)
	118 h fermentation using *C. necator* DSM 545,	48 g/L PHBV concentration with a 3HV fraction of 27 mol% is obtained. qp is 0.413 g/L/h (fed batch)	(Garcia-Gonzalez and De Wever, 2018)
Use of engineered strains with optimised production pathways by metabolic engineering	*E. coli* XL1-Blue (Pjc4)	PHBV content of 158 g/L	(Choi and Lee, 1999)
	C.glutamicum strain WM001	15.0 g/L PHBV	(Ma et al., 2018).
	R. rubrum	Increased 3HV production to 56 mol%	*(*Heinrich et al., 2015*)*
	A. hydrophila 4AK4	3.79 g/L CDW, containing 15.02 wt% P(3HB-co−4.23 mol% 3HV)	(Shi et al., 2020)
	S. enterica serovar Typhimurium	40.7 % of CDW as PHBV. 14.2 mol% as HV content	(Aldor et al., 2002)
Process optimization	One parameter optimisation	A 1.91-fold increase in the yield of PHBV was achieved	(Yin et al., 2020*)*
	Optimisation by two-level factorial designs	Screen variables affecting the growth and production	(Shantini et al., 2012)
	Optimisation using PBD and RSM	PHBV yield of 3.64 g/L	(Suhazsini et al., 2020)
	Statistical Dynamic Optimisation	100 % productivity enhancement	(Berezina and Yada, 2016)
Different culturing techniques: batch, fed batch and continuous	continuous feeding of CO_2 in 7 L reactor	24.7 g/L PHBV is obtained	(Ghysels et al., 2018)
	Fed batch.	PHBV content is 16.28 g/L	(Tian et al., 2022)
	batch	PHBV content is 1.52 g/L	(Salgaonkar et al., 2019)

Strategies	Conditions	Outcome	Reference
Proper scale-up and bioreactor design through computational fluid dynamics	FLUENT	Gas holdup, liquid velocity vectors, shear stress, and volumetric oxygen transfer coefficient were investigated	(Mavaddat et al., 2014)
	COMSOL Multiphysics®	CFD allows for determining the compatibility of the gas velocity with biomass growth. The reactor geometry influences the biomass yield	(De Crescenzo et al., 2023)
Customisation of HV content in PHBV for different applications	In co-substrate feeding, along with crude glycerol, hexanoic acid is added	CDW is 3.16 g/L and 34.02 % of CDW as PHBV. 0.24 mol% HV	(Coutinho de Paula et al., 2019)
	In co-substrate feeding, propionic acid with cheese whey	PHBV content of 86.6 % of CDW and PHBV yield of 3.64 g/L	(Suhazsini et al., 2020)
	In co-substrate feeding, valerate/propionate with Plant oil is used	PHBV is 6.8 g/L with 7 mol% of 3HV	(Lee et al., 2008a).
	In the precursor feeding method, arabinose or cyanocobalamin is added as a precursor of coenzyme B_{12} in *S. enterica* serovar Typhimurium	41.4 % of CDW as PHBV with 30.6 mol% as HV content is obtained	(Aldor et al., 2002).
	In the dual feeding method, along with pentanol, levulinic acid and sodium propionate	Increased 3-HV content in PHBV	(Berezina, 2012).

7.1. Low-cost substrates without precursor addition

The price of raw materials is a major contributor to overall cost. Conventional carbon sources and precursor molecules are often expensive. Using inexpensive substrates from agricultural, industrial, municipal, and food waste streams can substantially reduce costs. For instance, crude glycerol produced 23.4 g/L PHBV with 31 mol% HV (Kachrimanidou et al., 2014). Extruded rice bran and corn starch in a 1:8 ratio yielded 77.8 g/L PHBV (55.6 mol% HV) in *H. mediterranei* using a 5 L fermenter (Huang et al., 2006). Palm oil mill effluent and soybean oil have also supported PHBV production of 7.3 g/L and 16.28 g/L, respectively (Tabassum Mumtaz et al., 2009, Tian et al., 2022). Beyond PHBV, several waste-derived substrates have achieved high PHB titres, including wheat hydrolysate (162.8

g/L) (Xu et al., 2010), waste rapeseed oil (105 g/L) (Obruca et al., 2010), paddy straw (7.21 g/L) (Sandhya et al., 2013), kitchen waste (12 g/L) (Farah et al., 2011), macroalgal biomass (2.2 g/L) (Ghosh et al., 2019), and kenaf biomass (4.81 g/L) (Saratale et al., 2019). Selecting wild strains that produce PHBV without precursor supplementation can further reduce costs. For example, *H. mediterranei* achieved 77.8 g/L PHBV (55.6 mol% HV) with a total biomass of 140 g/L in a 5 L fermenter (Huang et al., 2006).

7.2. High-productivity strains and metabolic engineering

Strains with high productivity, rapid growth, and short cultivation times are crucial for economic viability. Productivities of 1.269 g/L/h in *M. organophilum* (Kim et al., 1999) and 0.413 g/L/h in *C. necator* DSM 545 (Garcia-Gonzalez and De Wever, 2018) have been reported. Metabolic engineering has also improved yields significantly, including 158 g/L PHBV in E. coli XL1-Blue (Choi and Lee, 1999) and 15 g/L PHBV in *C. glutamicum* strain WM001 (Ma et al., 2018). Engineered strains such as *R. rubrum* (Heinrich et al., 2015), *A.hydrophila* 4AK4 (Shi et al., 2020), and *S. enterica* serovar *typhimurium* (Aldor et al., 2002) demonstrate the potential of pathway optimisation for boosting productivity.

7.3. Process optimisation and scale-up

Process optimisation techniques such as one-variable-at-a-time approaches (Yin et al., 2020), factorial design (Shantini et al., 2012), Plackett–Burman design with response surface methodology (Suhazsini et al., 2020), and dynamic optimisation (Berezina and Yada, 2016) have been used to reduce costs. The choice of cultivation mode also matters. Continuous feeding of CO_2 yielded 24.7 g/L PHBV in a 7 L reactor (Ghysels et al., 2018). Fed-batch systems achieved 16.28 g/L (Tian et al., 2022), while batch cultivation gave 1.52 g/L (Salgaonkar et al., 2019). Repeated-batch and repeated-fed-batch methods have also shown cost benefits (Huang et al., 2006; Sangkharak et al., 2021). However, outcomes optimised at lab scale often fail to translate directly to industrial settings. Scale-up requires careful bioreactor design, supported by computational fluid dynamics (CFD) to predict gas holdup, shear stress, and oxygen transfer rates (Mavaddat et al., 2014, De Crescenzo et al., 2023).

7.4. Customisation strategies

Tailoring PHBV with desired HV content for specific applications is another cost-reduction pathway. Feeding strategies such as co-substrate, precursor, and dual feeding are effective. Examples include crude glycerol with hexanoic acid (Coutinho de Paula et al., 2019), propionic acid with cheese whey (Suhazsini et al., 2020), and valerate or propionate with plant oil (Lee et al., 2008). Precursor feeding with arabinose or cyanocobalamin produced 41.4 % CDW as PHBV with 30.6 mol% HV in *S. enterica* (Aldor et al., 2002). Dual feeding with pentanol, levulinic acid, and sodium propionate allowed further customisation of HV levels (Berezina, 2012).

7.5. Recommendations for cost reduction

Key strategies for improving economic viability include reusing waste streams from downstream processing, integrating upstream and downstream operations, and transitioning from batch to continuous downstream processes. Decentralising production facilities near abundant feedstock sources can reduce transport costs and improve efficiency. Real-time monitoring of fermentation

parameters can minimise waste and improve overall control. Cross-sector collaboration, such as sourcing industrial by-products as feedstock, further enhances the economic sustainability of PHBV production.

8. Environmental impact assessment via lifecycle assessment

Life Cycle Assessment (LCA) studies highlight the environmental advantages of PHBV over many synthetic polymers. A recent LCA on scaling PHBV pellet production from pilot to industrial levels showed a marked reduction in environmental burdens, particularly in energy and nutrient use. Further improvements are possible through effluent recycling and optimised electricity consumption (Nhu et al., 2024). Substrate choice also plays a decisive role. For example, sugarcane-derived PHBV exhibits superior energy efficiency and global warming potential compared to corn-based production (Guo et al., 2013).

In terms of greenhouse gas emissions, PHB produced from lignocellulosic waste substrates releases about 345 kg CO_2-eq per kg, which is approximately 33 % lower than the 512 kg CO_2-eq per kg reported for PLA (Senila et al., 2024). End-of-life management adds another sustainability dimension. Mechanical recycling of short-life PHBV products has been identified as the most favourable scenario from a circularity perspective, as it offsets virgin material use and provides environmental credits (Nhu et al., 2024a). However, concerns remain about its real-world biodegradability. While laboratory tests often show significant mass loss or BOD reduction, field studies suggest that PHBV may not degrade efficiently in ambient marine or freshwater environments within practical timeframes (Doi et al., 1992).

Compared to conventional chemical synthesis routes, which rely heavily on non-renewable resources and contribute to environmental degradation, PHAs such as PHBV offer a more sustainable alternative (Naser et al., 2021). Importantly, the environmental footprint of PHBV can be kept minimal when raw materials are sourced sustainably (Singh Saharan et al., 2014). Consequently, there is growing interest in using inexpensive and abundant feedstocks such as agricultural residues and industrial waste streams, which not only reduce production costs but also align with circular economy principles (Singh Saharan et al., 2014).

9. Regulatory and application-specific considerations

Regulatory approval is central to PHBV adoption in food and biomedical applications. The European Food Safety Authority (EFSA) sets specific migration limits for oligomers under 1000 Da (≤ 5 mg/kg food) and for crotonic acid, a major PHBV degradation product (≤ 0.05 mg/kg food). Studies show that PHBV complies with both limits (Dedieu et al., 2023, Silano et al., 2019). In the United States, PHBV is classified under 21 CFR 177.1810 (“Resins and polymeric coatings”) for food contact applications. Although no numeric thresholds are defined, compliance is ensured through safety data and testing consistent with FDA regulations (Plastictoday; Pmarketresearch). Within the EU framework, however, current food contact materials (FCM) legislation—Regulation (EC) No 1935/2004 and (EU) No 10/2011—does not yet authorise mixed microbial cultures for FCM use. Consequently, PHBV production largely relies on pure wild-type or engineered strains rather than microbial consortia.

Processing conditions present another regulatory concern. Thermomechanical degradation during extrusion or moulding can release crotonic acid, raising food safety issues under EU law. These challenges can be mitigated with suitable plasticisers and optimised processing parameters (Dedieu et al., 2023, Schmidt et al., 2024). In terms of packaging performance, PHBV films generally remain within EU migration limits of 10 mg/dm² across various food simulants (water, acid, fatty). Exceptions arise under harsh ethanol conditions (95 %), which can impair stability (CORDIS, 2013). Even then, crotonic acid migration remains below the EFSA limit, with maximum reported levels of 0.042 mg/kg after four recycling cycles (Dedieu et al., 2023). Mechanical recycling is feasible at controlled conditions (e.g., 160 °C for 6 h), though residual contaminants restrict safe recycled PHBV content to ~21 % (Dedieu et al., 2022).

Biodegradation pathways further shape regulatory considerations. PHBV breaks down aerobically and anaerobically via microbial enzymes, releasing CO_2 and water (Cerruti da Costa et al., 2025). Yet, degradation in natural aquatic environments often proceeds much more slowly than in laboratory tests (Doi et al., 1992). For biomedical applications, toxicological studies strongly support PHBV's safety. In vitro assays show non-toxic behaviour and enhanced proliferation of mouse fibroblasts, human dermal fibroblasts, and osteosarcoma (Saos-2) cells on PHBV matrices (Napathorn, 2014). In skin tissue engineering, electrospun PHBV nanofibers promote keratinocyte adhesion and differentiation without triggering inflammation (Napathorn, 2014). Antibacterial composites of PHBV with silica nanoparticles demonstrate biocompatibility with L929 fibroblasts, antibacterial activity against *S. aureus* and *E. coli*, and soil biodegradability over 30 days (Ojha and Das, 2020).

Downstream processing remains critical for both food and biomedical applications. Laboratory-scale PHBV extraction often relies on halogenated solvents such as chloroform, valued for yielding high-purity polymers. However, their carcinogenic and toxic properties exclude them from regulatory approval in food and medical contexts (15th Report on Carcinogens, n.d, Gupta et al., 2024; ASTDR). Greener alternatives such as ethyl acetate, dimethyl carbonate, and acetone are now favoured, offering safer extraction routes without compromising polymer quality (Jin et al., 2023).

10. Market share/penetration of PHBV and other biodegradable plastics

The global biodegradable plastics market is currently dominated by starch-based blends, which account for nearly 50 % of total market share, followed by polylactic acid (PLA) at approximately 32 % in 2024. PLA has found widespread applications in food packaging, disposable tableware, and medical implants due to its biocompatibility and ease of processing (EmergenResearch, 2024). Polybutylene adipate terephthalate (PBAT) is another major player, holding around 33 % of the biodegradable packaging segment in 2025 and representing approximately 45 % of PBAT consumption in the packaging sector (Future Market Insights, 2025; Datahorizzon, 2025).

PHAs, including PHBV, remain at an early stage of commercialisation. High production costs and limited industrial-scale manufacturing capacity have so far constrained their market penetration. Currently, only 15–20 manufacturers worldwide produce PHAs for commercial use, and most applications remain niche or research-driven (GlobeNewsWire, 2023).

Despite these challenges, PHBV offers significant advantages over other bioplastics, including superior biodegradability, tunable mechanical properties, and suitability for biomedical and food-contact applications. Ongoing advances in fermentation technologies, metabolic engineering, low-cost substrate utilisation, and process optimisation are expected to reduce production costs and improve yields. As these technologies mature, PHBV has the potential to compete with PLA and PBAT in high-value markets such as packaging, medical devices, and speciality films, positioning it as a promising biodegradable alternative for the future.

11. Conclusion

The competitiveness of PHBV as a sustainable alternative to petroleum-based plastics continues to improve, driven by ongoing research aimed at enhancing its material properties, including barrier performance (Acharjee et al., 2023). Despite its promising features, the wider commercial adoption of PHBV is limited by factors such as low microbial yields, high feedstock costs, technological complexities, and expensive downstream recovery processes (Sudesh et al., 2000, Gao et al., 2022). Successful scale-up of microbial PHBV production depends on optimising cost-effective feedstocks, minimising yield losses, and improving overall process efficiency.

Unlike chemical synthesis, which can exacerbate environmental degradation and increase reliance on nonrenewable resources, microbial biosynthesis provides a sustainable pathway, though it poses technical challenges. Addressing these challenges requires strategic solutions such as the use of non-food biomass, development of low-cost and energy-efficient downstream processes, CFD-based scale-up strategies, and metabolic and genetic optimisation of microbial strains.

Bridging the gap between laboratory success and industrial-scale production demands strong collaboration between academia and industry. Open innovation platforms can facilitate knowledge exchange, accelerate technological breakthroughs, and promote the development of commercially viable, sustainable bioplastics. With continued interdisciplinary efforts, PHBV has the potential to emerge as a truly sustainable and competitive alternative to petroleum-based plastics, supporting the transition towards a greener and more circular economy.

CRediT authorship contribution statement

Roy M Thomas: Writing – review & editing, Supervision, Conceptualization. **G Madhu:** Writing – review & editing, Supervision, Conceptualization. **SP Shibin:** Writing – original draft. **Jayesh Puthumana:** Writing – review & editing, Conceptualization. **IS Bright Singh:** Writing – review & editing, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Download: Download Word document (28KB)

Supplementary material

Recommended articles

Data availability

No data was used for the research described in the article.

References

15th Report on Carcinogens, n.d 15th Report on Carcinogens. (n.d.). https://doi.org/10.22427/NTP-OTHER-1003 ↗.

Google Scholar ↗

Abbasi et al., 2022 M. Abbasi, D. Pokhrel, E.R. Coats, N.M. Guho, A.G. McDonald

Effect of 3-Hydroxyvalerate content on thermal, mechanical, and rheological properties of Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) biopolymers produced from fermented dairy manure

Polymers, 14 (19) (2022), p. 4140, 10.3390/polym14194140 ↗

View in Scopus ↗ Google Scholar ↗

Acharjee et al., 2023 S.A. Acharjee, P. Bharali, B. Gogoi, V. Sorhie, B. Walling, Alemtoshi

PHA-Based bioplastic: a potential alternative to address microplastic pollution

Water Air. Soil Pollut. (2023), p. 234, 10.1007/s11270-022-06029-2 ↗

Google Scholar ↗

Akaraonye et al., 2010 E. Akaraonye, T. Keshavarz, I. Roy

Production of polyhydroxyalkanoates: the future Green materials of choice

J. Chem. Technol. Biotechnol., 85 (2010), pp. 732-743, 10.1002/jctb.2392 ↗

View in Scopus ↗ Google Scholar ↗

Albuquerque et al., 2011 M.G.E. Albuquerque, V. Martino, E. Pollet, L. Avérous, M.A.M. Reis

Mixed culture polyhydroxyalkanoate (PHA) production from volatile fatty acid (VFA)-rich streams: effect of substrate composition and feeding regime on PHA productivity, composition and properties

J. Biotechnol., 151 (1) (2011), pp. 66-76, 10.1016/j.jbiotec.2010.10.070 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Aldor et al., 2002 I.S. Aldor, S.-W. Kim, K.L.J. Prather, J.D. Keasling

Metabolic engineering of a novel Propionate-Independent pathway for the production of Poly(3-Hydroxybutyrate- *co* -3-Hydroxyvalerate) in recombinant *salmonella enterica* serovar typhimurium

Appl. Environ. Microbiol., 68 (8) (2002), pp. 3848-3854, 10.1128/AEM.68.8.3848-3854.2002 ↗

View in Scopus ↗ Google Scholar ↗

Alsafadi and Al-Mashaqbeh, 2017 D. Alsafadi, O. Al-Mashaqbeh
A one-stage cultivation process for the production of poly-3-(hydroxybutyrate-co-hydroxyvalerate) from olive mill wastewater by *haloferax mediterranei*
N. Biotechnol., 34 (2017), pp. 47-53, 10.1016/j.nbt.2016.05.003 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Alsafadi et al., 2020 D. Alsafadi, M.I. Ibrahim, K.A. Alamry, M.A. Hussein, A. Mansour
Utilizing the crop waste of date palm fruit to biosynthesize polyhydroxyalkanoate bioplastics with favorable properties
Sci. Total Environ., 737 (2020), Article 139716, 10.1016/j.scitotenv.2020.139716 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Amini et al., 2020 M. Amini, H. Yousefi-Massumabad, H. Younesi, H. Abyar, N. Bahramifar
Production of the polyhydroxyalkanoate biopolymer by cupriavidus necator using beer brewery wastewater containing maltose as a primary carbon source
J. Environ. Chem. Eng., 8 (1) (2020), Article 103588, 10.1016/j.jece.2019.103588 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Anderson et al., 1995 A.J. Anderson, D.R. Williams, E.A. Dawes, D.F. Ewing
Biosynthesis of poly(3-hydroxybutyvate-co-3-hydroxyvalerate) in *rhodococcus ruber*
Can. J. Microbiol, 41 (13) (1995), p. 4, 10.1139/m95-162 ↗
Google Scholar ↗

Anitha and Srivastava, 2021 N.N.N. Anitha, R.K. Srivastava
Microbial synthesis of polyhydroxyalkanoates (PHAs) and their applications
Environ. Agric. Microbiol. Adv. Appl. (2021), pp. 151-181, 10.1002/9781119525899.ch7 ↗
View in Scopus ↗ Google Scholar ↗

Arcos-Hernandez et al., 2013 M.V. Arcos-Hernandez, S. Pratt, B. Laycock, P. Johansson, A. Werker, P.A. Lant
Waste activated sludge as biomass for production of Commercial-Grade polyhydroxyalkanoate (PHA)
Waste Biomass.. Valoriz., 4 (1) (2013), pp. 117-127, 10.1007/s12649-012-9165-z ↗
View in Scopus ↗ Google Scholar ↗

Arumugam et al., 2018 A. Arumugam, S.G. Senthamizhan, V. Ponnusami, S. Sudalai
Production and optimization of polyhydroxyalkanoates from non-edible *calophyllum inophyllum* oil using *cupriavidus necator*
Int. J. Biol. Macromol., 112 (2018), pp. 598-607, 10.1016/j.ijbiomac.2018.02.012 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

ASTDR, 2023 ASTDR, 2023. https://www.atsdr.cdc.gov/toxfaqs/tfacts38.pdf.
Google Scholar ↗

Berezina, 2012 N. Berezina
Enhancing the 3-hydroxyvalerate component in bioplastic PHBV production by *cupriavidus necator*

Biotechnol. J., 7 (2012), pp. 304-309, 10.1002/biot.201100191 ↗

View in Scopus ↗ Google Scholar ↗

Berezina and Yada, 2016 N. Berezina, B. Yada

Improvement of the poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) production by dual feeding with levulinic acid and sodium propionate in *cupriavidus necator*

N. Biotechnol., 33 (1) (2016), pp. 231-236, 10.1016/j.nbt.2015.06.002 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Bergstrom, 2023 J.D. Bergstrom

The lipogenic enzyme acetoacetyl-CoA synthetase and ketone body utilization for denovo lipid synthesis, a review

J. Lipid Res., 64 (8) (2023), Article 100407, 10.1016/j.jlr.2023.100407 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Bernard, 2014 M. Bernard

Industrial potential of polyhydroxyalkanoate bioplastic: a brief review

USURJ Univ. Sask. Undergrad. Res. J., 1 (2014), 10.32396/usurj.v1i1.55 ↗

Google Scholar ↗

Berthet et al., 2016 M. Berthet, H. Angellier-Coussy, V. Guillard, N. Gontard

Vegetal fiber-based biocomposites: Which stakes for food packaging applications?

J. Appl. Polym. Sci., 133 (2) (2016), 10.1002/app.42528 ↗

Google Scholar ↗

Bhattacharyya et al., 2012 A. Bhattacharyya, A. Pramanik, S.K. Maji, S. Haldar, U.K. Mukhopadhyay, J. Mukherjee

Utilization of vinasse for production of poly-3-(hydroxybutyrate-co-hydroxyvalerate) by *haloferax mediterranei*

AMB Express, 2 (1) (2012), p. 34, 10.1186/2191-0855-2-34 ↗

Google Scholar ↗

Bhattacharyya et al., 2014 A. Bhattacharyya, J. Saha, S. Haldar, A. Bhowmic, U.K. Mukhopadhyay, J. Mukherjee

Production of *poly-3-(hydroxybutyrate-co-hydroxyvalerate)* by *haloferax mediterranei* using rice-based ethanol stillage with simultaneous recovery and re-use of medium salts

Extremophiles, 18 (2) (2014), pp. 463-470, 10.1007/s00792-013-0622-9 ↗

View in Scopus ↗ Google Scholar ↗

Blank et al., 2002 L. Blank, J. Green, J.R. Guest

AcnC of *escherichia coli* is a 2-methylcitrate dehydratase (*prpd*) that can use citrate and isocitrate as substrates

Microbiology, 148 (1) (2002), pp. 133-146, 10.1099/00221287-148-1-133 ↗

View in Scopus ↗ Google Scholar ↗

Cal et al., 2016 A.J. Cal, W.D. Sikkema, M.I. Ponce, D. Franqui-Villanueva, T.J. Riiff, W.J. Orts, A.J. Pieja, C.C. Lee

Methanotrophic production of polyhydroxybutyrate-co-hydroxyvalerate *with high hydroxyvalerate* content

Int. J. Biol. Macromol., 87 (2016), pp. 302-307, 10.1016/j.ijbiomac.2016.02.056 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Cavalheiro et al., 2009 J.M.B.T. Cavalheiro, M.C.M.D. de Almeida, C. Grandfils, M.M.R. da Fonseca

poly(3-hydroxybutyrate) production by *cupriavidus necator* using waste *glycerol*

Process Biochem., 44 (5) (2009), pp. 509-515, 10.1016/j.procbio.2009.01.008 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Cerruti da Costa et al., 2025 R. Cerruti da Costa, P.R. Oliveira, L.G. Nandi, D.M. Bobermin, M. Miotto, I.C. Bellettini, J. da Silva Crespo, T. Daitx, S. da, C. Teixeira, S. da, L.N. Carli

Green active food packaging films based on nanocomposites of PHBV/sepiolite/essential oils

Sustain. Food Technol., 3 (2) (2025), pp. 470-481, 10.1039/D4FB00232F ↗

View article View in Scopus ↗ Google Scholar ↗

Chang et al., 2025 Y.-C. Chang, M.V. Reddy, Y. Mawatari, O. Sarkar

Enhanced polyhydroxyalkanoate biosynthesis by *cupriavidus sp.* Cy-1 utilizing CO2 under controlled non-explosive conditions

Chemosphere, 373 (2025), Article 144181, 10.1016/j.chemosphere.2025.144181 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Chen, 2009 G.Q. Chen

A microbial polyhydroxyalkanoates (PHA) based bio- and materials industry

Chem. Soc. Rev., 38 (2009), pp. 2434-2446, 10.1039/b812677c ↗

View in Scopus ↗ Google Scholar ↗

Chen et al., 2019 Y. Chen, X.-Y. Chen, H.-T. Du, X. Zhang, Y.-M. Ma, J.-C. Chen, J.-W. Ye, X.-R. Jiang, G.-Q. Chen

Chromosome engineering of the TCA cycle in *halomonas bluephagenesis* for production of copolymers of *3-hydroxybutyrate* and *3-hydroxyvalerate* (PHBV)

Metab. Eng., 54 (2019), pp. 69-82, 10.1016/j.ymben.2019.03.006 ↗

View PDF View article Google Scholar ↗

Chen et al., 2006 C.W. Chen, T.-M. Don, H.-F. Yen

Enzymatic extruded starch as a carbon source for the production of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) by *haloferax mediterranei*

Process Biochem., 41 (11) (2006), pp. 2289-2296, 10.1016/j.procbio.2006.05.026 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Chen et al., 2018 J. Chen, W. Li, Z.-Z. Zhang, T.-W. Tan, Z.-J. Li

Metabolic engineering of *escherichia coli* for the synthesis of polyhydroxyalkanoates using acetate as a main carbon source

Microb. Cell Factor., 17 (1) (2018), p. 102, 10.1186/s12934-018-0949-0 ↗

View PDF View article Google Scholar ↗

Choi and Lee, 1999 J. Choi, S.Y. Lee

High-Level production of Poly(3-Hydroxybutyrate-co-3-Hydroxyvalerate) by Fed-Batch culture of recombinant *escherichia coli*

Appl. Environ. Microbiol., 65 (10) (1999), pp. 4363-4368, 10.1128/AEM.65.10.4363-4368.1999 ↗

View in Scopus ↗ Google Scholar ↗

Choi et al., 2005 J.-H. Choi, Kim Tae-Kang, Kim Tae-Kang, Kim Won-Chan, Joo Gil-Jae, Yeoll Lee Kyeong, Rhee In-Koo

Cloning and characterization of cyclohexanol dehydrogenase gene from *rhodococcus* sp. Tk6

J. Microbiol. Biotechnol., 15 (6) (2005), pp. 1189-1196

View in Scopus ↗ Google Scholar ↗

Ciesielski et al., 2021 S. Ciesielski, E.O. Adu, J. Mozejko-Ciesielska, T. Pokoj, A. Wilke

Wood juice valorization through production of Poly(3-hydroxybutyrate- *co* -3-hydroxyvalerate) using *bacillus* sp. G8_19

ACS Sustain. Chem. Eng., 9 (50) (2021), pp. 16870-16873, 10.1021/acssuschemeng.1c06856 ↗

View in Scopus ↗ Google Scholar ↗

Claes et al., 2002 W.A. Claes, A. Pühler, J. Kalinowski

Identification of two *prpdbc* gene clusters in *corynebacterium glutamicum* and their involvement in propionate degradation via the 2-Methylcitrate cycle

J. Bacteriol., 184 (10) (2002), pp. 2728-2739, 10.1128/JB.184.10.2728-2739.2002 ↗

View in Scopus ↗ Google Scholar ↗

CORDIS, 2013 CORDIS, 2013. *Final Report Summary - ECOBIOCAP (Ecoefficient Biodegradable Composite Advanced Packaging)*. https://doi.org/https://cordis.europa.eu/project/id/265669/reporting.

Google Scholar ↗

Coutinho de Paula et al., 2019 F. Coutinho de Paula, S. Kakazu, C. Bilia Chimello de Paula, A.F. de Almeida, J.G. Cabrera Gomez, J. Contiero

Burkholderia glumae MA13: a newly isolated bacterial strain suitable for polyhydroxyalkanoate production from crude glycerol

Biocatal. Agric. Biotechnol., 20 (2019), Article 101268, 10.1016/j.bcab.2019.101268 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Datahorizzon, 2025 Datahorizzon, 2025. *Global Biodegradable Plastic PBAT Market*. Retrieved October 10, 2025, from https://www.google.com/search?q=Global+Biodegradable+Plastic+PBAT+Market&sourceid=chrome&ie=UTF-8 ↗.

Google Scholar ↗

De Crescenzo et al., 2023 C. De Crescenzo, S. Sabbarese, C. Amabile, T. Abate, A. Migliaccio, C. De Blasio, S. Chianese, D. Musmarra

Modelling the growth of a PHB producer methanotrophic bacterial strain using a computational fluid dynamic approach: discontinuous methane feeding strategy

Curr. Res. Biotechnol., 6 (2023), Article 100146, 10.1016/j.crbiot.2023.100146 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

de Eugenio et al., 2007 L.I. de Eugenio, P. Garci´a, J.M. Luengo, J.M. Sanz, J.S. Roma´n, J.L. Garci´a, M.A. Prieto

Biochemical evidence that phaz gene encodes a specific intracellular medium chain length polyhydroxyalkanoate depolymerase in *pseudomonas putida* KT2442

J. Biol. Chem., 282 (7) (2007), pp. 4951-4962, 10.1074/jbc.M608119200 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Dedieu et al., 2022 I. Dedieu, C. Aouf, S. Gaucel, S. Peyron

Mechanical recyclability of biodegradable polymers used for food packaging: case study of polyhydroxybutyrate-co-valerate (PHBV) plastic

Food Addit. Contam. Part A, 39 (11) (2022), pp. 1878-1892, 10.1080/19440049.2022.2122589 ↗

View in Scopus ↗ Google Scholar ↗

Dedieu et al., 2023 I. Dedieu, C. Aouf, S. Gaucel, S. Peyron

Recycled Poly(hydroxybutyrate-co-valerate) as food packaging: effect of multiple melt processing on packaging performance and food contact suitability

J. Polym. Environ., 31 (3) (2023), pp. 1019-1028, 10.1007/s10924-022-02600-4 ↗

View in Scopus ↗ Google Scholar ↗

Divya, 2013 G. Divya

Polyhydroxy alkanoates - a sustainable alternative to Petro-Based plastics

J. Pet. Environ. Biotechnol., 04 (2013), 10.4172/2157-7463.1000143 ↗

Google Scholar ↗

Doi et al., 1992 Y. Doi, Y. Kanesawa, N. Tanahashi, Y. Kumagai

Biodegradation of microbial polyesters in the marine environment

Polym. Degrad. Stab., 36 (2) (1992), pp. 173-177, 10.1016/0141-3910(92)90154-W ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Doineau et al., 2023 E. Doineau, C. Perdrier, F. Allayaud, E. Blanchet, L. Preziosi-belloy, E. Grousseau, N. Gontard, H. Angellier-Coussy

Designing poly(3-hydroxybutyrate-co-3-hydroxyvalerate) P(3HB-co-3HV) films with tailored mechanical properties

Mater. Today Commun., 36 (2023), 10.1016/j.mtcomm.2023.106848 ↗

Google Scholar ↗

Du and Yu, 2002 G. Du, J. Yu

Green technology for conversion of food scraps to biodegradable thermoplastic polyhydroxyalkanoates

Environ. Sci. Technol., 36 (24) (2002), pp. 5511-5516

View in Scopus ↗ Google Scholar ↗

EmergenResearch, 2024 EmergenResearch, 2024. *Bioplastics Market Size*. Retrieved October 10, 2025, from https://www.emergenresearch.com/industry-report/bioplastics-market ↗.

Google Scholar ↗

Eschenlauer et al., 1996 A.C. Eschenlauer, S.K. Stoup, F. Srienc, D.A. Somers

Production of heteropolymeric polyhydroxyalkanoate in *eschericha coli* from a single carbon source

Int. J. Biol. Macromol., 19 (1996), pp. 121-130, 10.1016/0141-8130(96)01114-2 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Ezhov et al., 2013 V.A. Ezhov, N.V. Doronina, Yu.A. Trotsenko

Biosynthesis of polyhydroxybutyrate/valerate with different molecular weights during the growth of *methylobacterium extorquens* G-10 on a methanol-pentanol mixture

Appl. Biochem. Microbiol., 49 (2) (2013), pp. 150-153, 10.1134/S0003683813020038 ↗

View in Scopus ↗ Google Scholar ↗

Farah et al., 2011 Nadia Omar Farah, Mumtaz Tabassum, Abdul Rahman Nor'Aini, Saadiah Hafid Halimatun, Lai Yee Phang, Ali Hassan Mohd

Utilization of kitchen waste for the production of Green thermoplastic polyhydroxybutyrate (PHB) by *cupriavidus necator* CCGUG 52238

Afr. J. Microbiol. Res., 5 (19) (2011), pp. 2873-2879

Crossref ↗ Google Scholar ↗

Feijoo et al., 2022 P. Feijoo, K. Samaniego-Aguilar, E. Sánchez-Safont, S. Torres-Giner, J.M. Lagaron, J. Gamez-Perez, L. Cabedo

Development and characterization of fully renewable and biodegradable polyhydroxyalkanoate blends with improved thermoformability

Polym. (Basel), 14 (2022), 10.3390/polym14132527 ↗

Google Scholar ↗

Feng et al., 2010 B. Feng, S. Cai, J. Han, H. Liu, J. Zhou, H. Xiang

Identification of the phab genes and analysis of the PHBV precursor supplying pathway in *haloferax mediterranei*

Wei Sheng Wu Xue Bao, 50 (2010), pp. 1305-1312

View in Scopus ↗ Google Scholar ↗

Ferre-Guell and Winterburn, 2018 A. Ferre-Guell, J. Winterburn

Biosynthesis and characterization of polyhydroxyalkanoates with controlled composition and microstructure

Biomacromolecules, 19 (2018), pp. 996-1005, 10.1021/acs.biomac.7b01788 ↗

View article View in Scopus ↗ Google Scholar ↗

Ferri et al., 2023 M. Ferri, K. Papchenko, M. Degli Esposti, G. Tondi, M.G. De Angelis, D. Morselli, P. Fabbri

Fully biobased Polyhydroxyalkanoate/Tannin films as multifunctional materials for smart food packaging applications

ACS Appl. Mater. Interfaces, 15 (23) (2023), pp. 28594-28605, 10.1021/acsami.3c04611 ↗

View in Scopus ↗ Google Scholar ↗

Future Market Insights, 2025 Future Market Insights, 2025. *Biodegradable Packaging Market*. https://www.futuremarketinsights.com/reports/biodegradable-packaging-market?utm_source ↗.

Google Scholar ↗

Gahlawat and Soni, 2019 G. Gahlawat, S.K. Soni

Study on sustainable recovery and extraction of polyhydroxyalkanoates (PHAs) produced by *cupriavidus necator* using waste glycerol for medical applications

Chem. Biochem. Eng. Q., 33 (1) (2019), pp. 99-110, 10.15255/CABEQ.2018.1471 ↗

View in Scopus ↗ Google Scholar ↗

Ganzeveld et al., 1999 K.J. Ganzeveld, A. van Hagen, M.H. van Agteren, W. de Koning, A.J.M. Schoot Uiterkamp

Upgrading of organic waste: production of the copolymer poly-3-hydroxybutyrate-co-valerate by ralstonia eutrophus with organic waste as sole carbon source

J. Clean. Prod., 7 (6) (1999), pp. 413-419, 10.1016/S0959-6526(99)00159-6 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Gao et al., 2022 Q. Gao, H. Yang, C. Wang, X.Y. Xie, K.X. Liu, Ying Lin, S.Y. Han, M. Zhu, M. Neureiter, Yina Lin, J.W. Ye

Advances and trends in microbial production of polyhydroxyalkanoates and their building blocks

Front. Bioeng. Biotechnol., 10 (2022), 10.3389/fbioe.2022.966598 ↗

Google Scholar ↗

García-Chumillas et al., 2024 S. García-Chumillas, T. Guerrero-Murcia, M. Nicolás-Liza, F. Monzó, A. Simica, L. Simó-Cabrera, R.M. Martínez-Espinosa

PHBV cycle of life using waste as a starting point: from production to recyclability

Front. Mater., 11 (2024), 10.3389/fmats.2024.1405483 ↗

Google Scholar ↗

Garcia-Gonzalez and De Wever, 2018 L. Garcia-Gonzalez, H. De Wever

Acetic acid as an indirect sink of CO2 for the synthesis of polyhydroxyalkanoates (PHA): comparison with PHA production processes directly using CO2 as feedstock

Appl. Sci., 8 (9) (2018), p. 1416, 10.3390/app8091416 ↗

View in Scopus ↗ Google Scholar ↗

Ghosh et al., 2019 S. Ghosh, R. Gnaim, S. Greiserman, L. Fadeev, M. Gozin, A. Golberg

Macroalgal biomass subcritical hydrolysates for the production of polyhydroxyalkanoate (PHA) by haloferax mediterranei

Bioresour. Technol., 271 (2019), pp. 166-173, 10.1016/j.biortech.2018.09.108 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Ghysels et al., 2018 S. Ghysels, Md.S.I. Mozumder, H. De Wever, E.I.P. Volcke, L. Garcia-Gonzalez

Targeted poly(3-hydroxybutyrate-co-3-hydroxyvalerate) bioplastic production from carbon dioxide

Bioresour. Technol., 249 (2018), pp. 858-868, 10.1016/j.biortech.2017.10.081 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

GlobeNewsWire, 2023 GlobeNewsWire

Global Biodegradable Plastic Market Size is Estimated to Reach USD 6.97 Billion by 2031, Growing at a CAGR of 13.5%

Straits Research (2023)

https://www.globenewswire.com/en/news-release/2023/11/29/2787665/0/en/Global-Biodegradable-Plastic-Market-Size-is-Estimated-to-Reach-USD-6-97-Billion-by-2031-Growing-at-a-CAGR-of-13-5-Straits-Research.html?utm_source= ↗

Google Scholar ↗

Grimek et al., 2003 T.L. Grimek, H. Holden, I. Rayment, J.C. Escalante-Semerena

Residues C123 and D58 of the 2-Methylisocitrate lyase (PrpB) enzyme of *salmonella enterica* are essential for catalysis

J. Bacteriol., 185 (16) (2003), pp. 4837-4843, 10.1128/JB.185.16.4837-4843.2003 ↗

View in Scopus ↗ Google Scholar ↗

Guo et al., 2013 M. Guo, D.C. Stuckey, R.J. Murphy

Is it possible to develop biopolymer production systems independent of fossil fuels? Case study in energy profiling of polyhydroxybutyrate-valerate (PHBV)

Green. Chem., 15 (3) (2013), p. 706, 10.1039/c2gc36546d ↗

View in Scopus ↗ Google Scholar ↗

Gupta et al., 2024 S. Gupta, P. Janmeda, P. Chaudhary

Methylene chloride: a carcinogen with its origin, adverse effects and preventive measures

Biochem. Cell. Arch., 24 (2) (2024), 10.51470/BCA.2024.24.2.1833 ↗

Google Scholar ↗

Han et al., 2013 J. Han, J. Hou, F. Zhang, G. Ai, M. Li, S. Cai, H. Liu, L. Wang, Z. Wang, S. Zhang, L. Cai, D. Zhao, J. Zhou, H. Xiang

Multiple propionyl coenzyme a-supplying pathways for production of the bioplastic poly(3-Hydroxybutyrate-co-3-Hydroxyvalerate) in *haloferax mediterranei*

Appl. Environ. Microbiol, 79 (2013), pp. 2922-2931, 10.1128/AEM.03915-12 ↗

View in Scopus ↗ Google Scholar ↗

Han et al., 2015 J. Han, L.-P. Wu, J. Hou, D. Zhao, H. Xiang

Biosynthesis, characterization, and hemostasis potential of Tailor-Made Poly(3-hydroxybutyrate- *co* -3-hydroxyvalerate) produced by *haloferax mediterranei*

Biomacromolecules, 16 (2) (2015), pp. 578-588, 10.1021/bm5016267 ↗

View article View in Scopus ↗ Google Scholar ↗

Heinrich et al., 2015 D. Heinrich, M. Raberg, A. Steinbüchel

Synthesis of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) from unrelated carbon sources in engineered *rhodospirillum rubrum*

FEMS Microbiol. Lett., 362 (2015), 10.1093/femsle/fnv038 ↗

Google Scholar ↗

Hermann-Krauss et al., 2013 C. Hermann-Krauss, M. Koller, A. Muhr, H. Fasl, F. Stelzer, G. Braunegg

Archaeal production of polyhydroxyalkanoate (PHA) Co- and terpolyesters from biodiesel Industry-Derived By-Products
Archaea, 2013 (2013), pp. 1-10, 10.1155/2013/129268 ↗
Google Scholar ↗

Hofherr et al., 2009 S.E. Hofherr, J.S. Senac, C.Y. Chen, D.J. Palmer, P. Ng, M.A. Barry
Short-Term rescue of neonatal lethality in a mouse model of propionic acidemia by gene therapy
Hum. Gene Ther., 20 (2) (2009), pp. 169-180, 10.1089/hum.2008.158 ↗
View in Scopus ↗ Google Scholar ↗

Hou et al., 2015 J. Hou, H. Xiang, J. Hana
Propionyl coenzyme a (Propionyl-CoA) carboxylase in *haloferax mediterranei*: indispensability for propionyl-CoA assimilation and impacts on global metabolism
Appl. Environ. Microbiol, 81 (2015), pp. 794-804, 10.1128/AEM.03167-14 ↗
View in Scopus ↗ Google Scholar ↗

Huang et al., 2006 T.-Y. Huang, K.-J. Duan, S.-Y. Huang, C.W. Chen
Production of polyhydroxyalkanoates from inexpensive extruded rice bran and starch by *haloferax mediterranei*
J. Ind. Microbiol. Biotechnol., 33 (8) (2006), pp. 701-706, 10.1007/s10295-006-0098-z ↗
View in Scopus ↗ Google Scholar ↗

Huang et al., 2023 Z. Huang, Q. Wang, I.A. Khan, Y. Li, J. Wang, J. Wang, X. Liu, F. Lin, J. Lu
The methylcitrate cycle and its crosstalk with the glyoxylate cycle and tricarboxylic acid cycle in pathogenic fungi
Molecules, 28 (18) (2023), p. 6667, 10.3390/molecules28186667 ↗
View in Scopus ↗ Google Scholar ↗

Huong et al., 2017 K.-H. Huong, K. Shantini, R. Sharmini, A.A. Amirul
Exploring the potential of 1-Pentanol and oleic acid for optimizing the production of Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) copolymer by *cupriavidus* sp. Usmaa1020
Arab. J. Sci. Eng., 42 (6) (2017), pp. 2313-2320, 10.1007/s13369-017-2473-7 ↗
View in Scopus ↗ Google Scholar ↗

Ingram and Winterburn, 2022 H.R. Ingram, J.B. Winterburn
Influence of emulsified plant oil composition on growth and biopolymer production of *cupriavidus necator* DSM 545
Food Bioprod. Process., 132 (2022), pp. 23-34, 10.1016/j.fbp.2021.12.005 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Jain and Tiwari, A., 2010 Kosta Jain, S. Tiwari, A
Polyhydroxyalkanoates: a way to sustainable development of bioplastics
Chronicles Young Sci., 1 (2010), p. 10
View in Scopus ↗ Google Scholar ↗

Jang et al., 2017 S.H. Jang, H.A. Jang, J. Lee, J.U. Kim, S.A. Lee, K.-E. Park, B.H. Kim, Y.H. Jo, B.L. Lee
PhaR, a negative regulator of PhaP, modulates the colonization of a *burkholderia* gut symbiont in the midgut of the host insect, riptortus pedestris
Appl. Environ. Microbiol., 83 (11) (2017), 10.1128/AEM.00459-17 ↗
Google Scholar ↗

Jin et al., 2023 A. Jin, L.J. del Valle, J. Puiggalí
Copolymers and blends based on 3-Hydroxybutyrate and 3-Hydroxyvalerate units
Int. J. Mol. Sci., 24 (24) (2023), p. 17250, 10.3390/ijms242417250 ↗
View in Scopus ↗ Google Scholar ↗

Jo et al., 2024 S.Y. Jo, S.H. Lim, J.Y. Lee, J. Son, J. Choi, Il, S.J. Park
Microbial production of poly(3-hydroxybutyrate-co-3-hydroxyvalerate), from lab to the shelf: a review
Int. J. Biol. Macromol., 274 (2024), 10.1016/j.ijbiomac.2024.133157 ↗
Google Scholar ↗

Kachrimanidou et al., 2014 V. Kachrimanidou, N. Kopsahelis, S. Papanikolaou, I.K. Kookos, M. De Bruyn, J.H. Clark, A.A. Koutinas
Sunflower-based biorefinery: Poly(3-hydroxybutyrate) and poly(3-hydroxybutyrate- co -3-hydroxyvalerate) production from crude glycerol, sunflower meal and levulinic acid
Bioresour. Technol., 172 (2014), pp. 121-130, 10.1016/j.biortech.2014.08.044 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Kemavongse et al., 2008 K. Kemavongse, P. Prasertsan, A. Upaichit, P. Methacanon
Poly-β-hydroxyalkanoate production by halotolerant rhodobacter sphaeroides U7
World J. Microbiol. Biotechnol., 24 (10) (2008), pp. 2073-2085, 10.1007/s11274-008-9712-8 ↗
View in Scopus ↗ Google Scholar ↗

Kerketta and Vasanth, 2019 A. Kerketta, D. Vasanth
Madhuca indica flower extract as cheaper carbon source for production of poly (3-hydroxybutyrate-co-3-hydroxyvalerate) using *ralstonia eutropha*
Process Biochem., 87 (2019), pp. 1-9, 10.1016/j.procbio.2019.09.013 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Keskin et al., 2017 G. Keskin, G. Klzll, M. Bechelany, C. Pochat-Bohatier, M. Öner
Potential of polyhydroxyalkanoate (PHA) polymers family as substitutes of petroleum based polymers for packaging applications and solutions brought by their composites to form barrier materials
Pure Appl. Chem., 89 (2017), pp. 1841-1848, 10.1515/pac-2017-0401 ↗
View in Scopus ↗ Google Scholar ↗

Kim et al., 1999 S.-W. Kim, P. Kim, J.H. Kim
Production of Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) from methylobacterium organophilum by potassium-limited fed-batch culture

Enzym. Microb. Technol., 24 (8–9) (1999), pp. 555-560, 10.1016/S0141-0229(98)00160-4 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Kim et al., 2022 J. Kim, K.Y. Kim, J.K. Ko, S.M. Lee, G. Gong, K.H. Kim, Y. Um

Characterization of a novel acetogen *clostridium* sp. Js66 for production of acids and alcohols: focusing on hexanoic acid production from syngas

Biotechnol. Bioprocess Eng., 27 (2022), pp. 89-98, 10.1007/s12257-021-0122-1 ↗

Google Scholar ↗

Koller, 2015 M. Koller

Recycling of waste streams of the biotechnological Poly(hydroxyalkanoate) production by *haloferax mediterranei* on whey

Int. J. Polym. Sci., 2015 (2015), pp. 1-8, 10.1155/2015/370164 ↗

Google Scholar ↗

Koller et al., 2007 M. Koller, P. Hesse, R. Bona, C. Kutschera, A. Atlić, G. Braunegg

Potential of various Archae- and eubacterial strains as industrial polyhydroxyalkanoate producers from whey

Macromol. Biosci., 7 (2) (2007), pp. 218-226, 10.1002/mabi.200600211 ↗

View in Scopus ↗ Google Scholar ↗

Krueger et al., 2012 C.L. Krueger, C.M. Radetski, A.G. Bendia, I.M. Oliveira, M.A. Castro-Silva, C.R. Rambo, R.V. Antonio, A.O.S. Lima

Bioconversion of cassava starch by-product into bacillus and related bacteria polyhydroxyalkanoates

Electron. J. Biotechnol., 15 (3) (2012), 10.2225/vol15-issue3-fulltext-6 ↗

Google Scholar ↗

Kuntanoo et al., 2015 K. Kuntanoo, S. Promkotra, P. Kaewkannetra

Fabrication of novel polyhydroxybutyrate-co-hydroxyvalerate (PHBV) mixed with natural rubber latex

Key Eng. Mater., 659 (2015), pp. 404-408, 10.4028/www.scientific.net/KEM.659.404 ↗

View in Scopus ↗ Google Scholar ↗

Kuo, 2019 G. Kuo

When fossil fuels run out, what then? - MAHB

MAHB. (2019)

Google Scholar ↗

Lee et al., 2008 W.-H. Lee, C.-Y. Loo, C.T. Nomura, K. Sudesh

Biosynthesis of polyhydroxyalkanoate copolymers from mixtures of plant oils and 3-hydroxyvalerate precursors

Bioresour. Technol., 99 (15) (2008), pp. 6844-6851, 10.1016/j.biortech.2008.01.051 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Leimann et al., 2013 F.V. Leimann, L. Cardozo Filho, C. Sayer, P.H.H. Araújo

Poly(3-hydroxybutyrate-co-3- hydroxyvalerate) nanoparticles prepared by a miniemulsion/solvent evaporation technique: effect of phbv molar mass and concentration

Braz. J. Chem. Eng., 30 (2) (2013), pp. 369-377, 10.1590/S0104-66322013000200014 ↗

View in Scopus ↗ Google Scholar ↗

Li et al., 2009 X. Li, K.L. Liu, M. Wang, S.Y. Wong, W.C. Tjiu, C.Bin He, S.H. Goh, J. Li

Improving hydrophilicity, mechanical properties and biocompatibility of poly[(R)-3-hydroxybutyrate-co-(R)-3-hydroxyvalerate] through blending with poly[(R)-3-hydroxybutyrate]-alt-poly(ethylene oxide)

Acta Biomater., 5 (2009), pp. 2002-2012, 10.1016/j.actbio.2009.01.035 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Li et al., 2021 H.-F. Li, M.-R. Wang, L.-Y. Tian, Z.-J. Li

Production of polyhydroxyalkanoates (PHAs) by vibrio alginolyticus strains isolated from salt fields

Molecules, 26 (20) (2021), p. 6283, 10.3390/molecules26206283 ↗

View in Scopus ↗ Google Scholar ↗

Longo et al., 2024 A. Longo, F. Fanelli, M. Villano, M. Montemurro, C.G. Rizzello

Bioplastic production from Agri-Food waste through the use of *haloferax mediterranei*: a comprehensive initial overview

Microorganisms, 12 (2024), 10.3390/microorganisms12061038 ↗

Google Scholar ↗

Luo et al., 2016 H. Luo, D. Zhou, X. Liu, Z. Nie, D.L. Quiroga-Sánchez, Y. Chang

Production of 3-Hydroxypropionic acid via the Propionyl-CoA pathway using recombinant *escherichia coli* strains

PLOS ONE, 11 (5) (2016), Article e0156286, 10.1371/journal.pone.0156286 ↗

View in Scopus ↗ Google Scholar ↗

Ma et al., 2018 W. Ma, J. Wang, Y. Li, L. Yin, X. Wang

Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) co-produced with l-isoleucine in *corynebacterium glutamicum* WM001

Microb. Cell Factor., 17 (1) (2018), p. 93, 10.1186/s12934-018-0942-7 ↗

Google Scholar ↗

Machado and da Silva, 2023 T.F.G. Machado, R.G. da Silva

Employing deuterium kinetic isotope effects to uncover the mechanism of (R)-3-hydroxybutyrate dehydrogenase

In Methods in Enzymology, 685, ELSEVIER (2023), pp. 225-240, 10.1016/bs.mie.2023.03.004 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Martla et al., 2018 M. Martla, K. Umsakul, K. Sudesh

Production and recovery of poly(3-hydroxybutyrate- *co* -3-hydroxyvalerate) from biodiesel liquid waste (BLW)

J. Basic Microbiol., 58 (11) (2018), pp. 977-986, 10.1002/jobm.201800279 ↗

View in Scopus ↗ Google Scholar ↗

Masani et al., 2009 M.Y.A. Masani, G.K.A. Parveez, A.M.D. Izawati, C.P. Lan, A. Siti Nor Akmar

Construction of PHB and PHBV multiple-gene vectors driven by an oil palm leaf-specific promoter

Plasmid, 62 (3) (2009), pp. 191-200, 10.1016/j.plasmid.2009.08.002 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Matsumoto et al., 2022 A. Matsumoto, S.J. Kawai, M. Yamada

Utilization of various carbon sources for poly(3-hydroxybutyrate) [P(3HB)] production by *cobetia* sp. Iu180733jp01 (5-11-6-3) which is capable of producing P(3HB) from alginate and waste seaweed. J

Gen. Appl. Microbiol, 68 (2022), pp. 207-211, 10.2323/jgam.2021.11.002 ↗

View in Scopus ↗ Google Scholar ↗

Mavaddat et al., 2014 P. Mavaddat, S.M. Mousavi, E. Amini, H. Azargoshasb, S.A. Shojaosadati

Modeling and CFD-PBE simulation of an airlift bioreactor for PHB production

AsiaPac. J. Chem. Eng., 9 (4) (2014), pp. 562-573, 10.1002/apj.1785 ↗

View in Scopus ↗ Google Scholar ↗

McAdam et al., 2020 B. McAdam, M. Brennan Fournet, P. McDonald, M. Mojicevic

Production of polyhydroxybutyrate (PHB) and factors impacting its chemical and mechanical characteristics

Polymers, 12 (12) (2020), p. 2908, 10.3390/polym12122908 ↗

Google Scholar ↗

Melendez-Rodriguez et al., 2018 B. Melendez-Rodriguez, J.L. Castro-Mayorga, M.A.M. Reis, C. Sammon, L. Cabedo, S. Torres-Giner, J.M. Lagaron

Preparation and characterization of electrospun food biopackaging films of Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) derived from fruit pulp biowaste

Front. Sustain. Food Syst., 2 (2018), 10.3389/fsufs.2018.00038 ↗

Google Scholar ↗

Mezzina and Pettinari, 2016 M.P. Mezzina, M.J. Pettinari

Phasins, multifaceted polyhydroxyalkanoate Granule-Associated proteins

Appl. Environ. Microbiol., 82 (17) (2016), pp. 5060-5067, 10.1128/AEM.01161-16 ↗

View in Scopus ↗ Google Scholar ↗

Miscevic et al., 2020 D. Miscevic, K. Srirangan, T. Kefale, S. Kilpatrick, D.A. Chung, M. Moo-Young, C.P. Chou

Heterologous production of 3-hydroxyvalerate in engineered *escherichia coli*

Metab. Eng., 61 (2020), pp. 141-151, 10.1016/j.ymben.2019.11.005 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Napathorn, 2014 S.C. Napathorn

Biocompatibilities and biodegradation of poly(3-hydroxybutyrate-co-3-hydroxyvalerate)s produced by a model metabolic reaction-based system

BMC Microbiol., 14 (1) (2014), p. 285, 10.1186/s12866-014-0285-4 ↗

View in Scopus ↗ Google Scholar ↗

Naresh Kumar et al., 2020 A. Naresh Kumar, S. Chatterjee, M. Hemalatha, A. Althuri, B. Min, S.-H. Kim, S. Venkata Mohan
Deoiled algal biomass derived renewable sugars for bioethanol and biopolymer production in biorefinery framework
Bioresour. Technol., 296 (2020), Article 122315, 10.1016/j.biortech.2019.122315 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Naser et al., 2021 A.Z. Naser, I. Deiab, B.M. Darras
Poly(lactic acid) (PLA) and polyhydroxyalkanoates (PHAs), Green alternatives to petroleum-based plastics: a review
RSC Adv., 11 (2021), pp. 17151-17196, 10.1039/d1ra02390j ↗
View article View in Scopus ↗ Google Scholar ↗

Ng et al., 2011 K.-S. Ng, Y.-M. Wong, T. Tsuge, K. Sudesh
Biosynthesis and characterization of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) and poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) copolymers using jatropha oil as the main carbon source
Process Biochem., 46 (8) (2011), pp. 1572-1578, 10.1016/j.procbio.2011.04.012 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Nhu et al., 2024a T.T. Nhu, L. Boone, V. Guillard, L. Chatellard, M. Reis, M. Matos, J. Dewulf
Environmental sustainability assessment of biodegradable bio-based poly(3-hydroxybutyrate-co-3-hydroxyvalerate) from agro-residues: production and end-of-life scenarios
J. Environ. Manag., 356 (2024), Article 120522, 10.1016/j.jenvman.2024.120522 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Nielsen, 2014 J. Nielsen
Synthetic biology for engineering acetyl coenzyme a metabolism in yeast
MBio, 5 (6) (2014), 10.1128/mBio.02153-14 ↗
Google Scholar ↗

Novackova et al., 2019 I. Novackova, D. Kucera, J. Porizka, I. Pernicova, P. Sedlacek, M. Koller, A. Kovalcik, S. Obruca
Adaptation of cupriavidus necator to levulinic acid for enhanced production of P(3HB-co-3HV) copolyesters
Biochem. Eng. J., 151 (2019), Article 107350, 10.1016/j.bej.2019.107350 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Obruca et al., 2010 S. Obruca, I. Marova, O. Snajdar, L. Mravcova, Z. Svoboda
Production of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) by *cupriavidus necator* from waste rapeseed oil using propanol as a precursor of 3-hydroxyvalerate
Biotechnol. Lett., 32 (12) (2010), pp. 1925-1932, 10.1007/s10529-010-0376-8 ↗
View in Scopus ↗ Google Scholar ↗

Ojha and Das, 2020 N. Ojha, N. Das
Fabrication and characterization of biodegradable PHBV/SiO 2 nanocomposite for thermo-mechanical and antibacterial applications in food packaging
IET Nanobiotechnology, 14 (9) (2020), pp. 785-795, 10.1049/iet-nbt.2020.0066 ↗
View in Scopus ↗ Google Scholar ↗

Padovani et al., 2016 G. Padovani, P. Carlozzi, M. Seggiani, P. Cinelli, S. Vitolo, A. Lazzeri
PHB-rich biomass and BioH2 production by means of photosynthetic microorganisms
Chem. Eng. Trans., 49 (2016), pp. 55-60, 10.3303/CET1649010 ↗
View in Scopus ↗ Google Scholar ↗

Paduvari and Somashekara, 2025 R. Paduvari, D.M. Somashekara
Advancements in genetic engineering for enhanced polyhydroxyalkanoates (PHA) production: a comprehensive review of metabolic pathway manipulation and gene deletion strategies
Bioengineered, 16 (1) (2025), 10.1080/21655979.2025.2458363 ↗
Google Scholar ↗

Park and Damodaran, 1994 C. Park, V.K. Damodaran
Biosynthesis of Poly(3-hydroxybutyrate- *co* -3-hydroxyvalerate) from ethanol and pentanol by *alcaligenes eutrophus*
Biotechnol. Prog., 10 (6) (1994), pp. 615-620, 10.1021/bp00030a006 ↗
View in Scopus ↗ Google Scholar ↗

Pernicova et al., 2019 I. Pernicova, D. Kucera, J. Nebesarova, M. Kalina, I. Novackova, M. Koller, S. Obruca
Production of polyhydroxyalkanoates on waste frying oil employing selected *halomonas* strains
Bioresour. Technol., 292 (2019), Article 122028, 10.1016/j.biortech.2019.122028 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Plastictoday, 2023. Plastictoday, 2023. *Greening of an Industry: PHBV gets food-contact approval.* https://doi.org/https://www.plasticstoday.com/industry-trends/greening-of-an-industry-phbv-gets-food-contact-approval.
Google Scholar ↗

Pmarketresearch, 2023 Pmarketresearch, 2023. *Current commercial applications of Polyhydroxybutyrate-Valerate (PHBV) in global industries.* https://pmarketresearch.com/chemi/polyhydroxybutyrate-valerate-phbv-market/ ↗.
Google Scholar ↗

Policastro et al., 2021 G. Policastro, A. Panico, M. Fabbricino
Improving biological production of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) co-polymer: a critical review
Rev. Environ. Sci. Biotechnol., 20 (2021), pp. 479-513, 10.1007/s11157-021-09575-z ↗
View in Scopus ↗ Google Scholar ↗

Poomipuk et al., 2014 N. Poomipuk, A. Reungsang, P. Plangklang
Poly-β-hydroxyalkanoates production from cassava starch hydrolysate by *cupriavidus* sp. Kku38
Int. J. Biol. Macromol., 65 (2014), pp. 51-64, 10.1016/j.ijbiomac.2014.01.002 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Priya et al., 2022 A. Priya, Z. Hathi, M.A. Haque, S. Kumar, A. Kumar, E. Singh, C.S.K. Lin
Effect of levulinic acid on production of polyhydroxyalkanoates from food waste by *haloferax mediterranei*
Environ. Res., 214 (2022), Article 114001, 10.1016/j.envres.2022.114001 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Riedel et al., 2013 S.L. Riedel, C.J. Brigham, C.F. Budde, J. Bader, C. Rha, U. Stahl, A.J. Sinskey
Recovery of poly(3-hydroxybutyrate- *co* -3-hydroxyhexanoate) from *ralstonia eutropha* cultures with non-halogenated solvents
Biotechnol. Bioeng., 110 (2) (2013), pp. 461-470, 10.1002/bit.24713 ↗
View in Scopus ↗ Google Scholar ↗

Rivera-Briso and Serrano-Aroca, 2018 A.L. Rivera-Briso, Á. Serrano-Aroca
Poly(3-Hydroxybutyrate-co-3-Hydroxyvalerate): enhancement strategies for advanced applications
Polymers, 10 (2018), 10.3390/polym10070732 ↗
Google Scholar ↗

Rodríguez-Cendal et al., 2023 A.I. Rodríguez-Cendal, I. Gómez-Seoane, F.J. de Toro-Santos, I.M. Fuentes-Boquete, J. Señarís-Rodríguez, S.M. Díaz-Prado
Biomedical applications of the biopolymer Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV): drug encapsulation and scaffold fabrication
Int. J. Mol. Sci., 24 (2023), 10.3390/ijms241411674 ↗
Google Scholar ↗

Sakthiselvan and Madhumathi, 2018 P. Sakthiselvan, R. Madhumathi
Kinetic evaluation on cell growth and biosynthesis of polyhydroxybutyrate (PHB) by *bacillus safensis* EBT1 from sugarcane bagasse
Eng. Agric. Environ. Food, 11 (3) (2018), pp. 145-152, 10.1016/j.eaef.2018.03.003 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Salgaonkar et al., 2019 B.B. Salgaonkar, K. Mani, J.M. Bragança
Sustainable bioconversion of cassava waste to Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) by *halogeometricum borinquense* strain E3
J. Polym. Environ., 27 (2) (2019), pp. 299-308, 10.1007/s10924-018-1346-9 ↗
View in Scopus ↗ Google Scholar ↗

Sandhya et al., 2013 M. Sandhya, J. Aravind, P. Kanmani
Production of polyhydroxyalkanoates from ralstonia eutropha using paddy straw as cheap substrate

Int. J. Environ. Sci. Technol., 10 (1) (2013), pp. 47-54, 10.1007/s13762-012-0070-6 ↗

View in Scopus ↗ Google Scholar ↗

Sangkharak et al., 2021 K. Sangkharak, N. Paichid, T. Yunu, S. Klomklao, P. Prasertsan

Utilisation of tuna condensate waste from the canning industry as a novel substrate for polyhydroxyalkanoate production

Biomass Convers. Biorefinery, 11 (5) (2021), pp. 2053-2064, 10.1007/s13399-019-00581-4 ↗

View in Scopus ↗ Google Scholar ↗

Saratale et al., 2019 R.G. Saratale, G.D. Saratale, S.K. Cho, D.S. Kim, G.S. Ghodake, A. Kadam, G. Kumar, R.N. Bharagava, R. Banu, H.S. Shin

Pretreatment of kenaf (*hibiscus cannabinus* L.) biomass feedstock for polyhydroxybutyrate (PHB) production and characterization

Bioresour. Technol., 282 (2019), pp. 75-80, 10.1016/j.biortech.2019.02.083 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Schmidt et al., 2024 A. Schmidt, B. Bittmann-Hennes, D. Moncada, B. Montero

Self-Reinforced biocomposites made from Poly(3-hydroxybutyrate- *co* -3-hydroxyvalerate) (PHBV): an innovative approach to sustainable packaging production through melt processing

ACS Omega, 9 (52) (2024), pp. 51073-51088, 10.1021/acsomega.4c05957 ↗

View in Scopus ↗ Google Scholar ↗

Senila et al., 2024 L. Senila, E. Kovacs, M.-A. Resz, M. Senila, A. Becze, C. Roman

Life cycle assessment (LCA) of bioplastics production from lignocellulosic waste (Study Case: PLA and PHB)

Polymers, 16 (23) (2024), p. 3330, 10.3390/polym16233330 ↗

View in Scopus ↗ Google Scholar ↗

Shantini et al., 2021 K. Shantini, N.A. Azami, H. Kai-Hee, A.R.M. Yahya, A.A. Amirul

Poly(3-hydroxybutyrate-co-3-hydroxyvalerate) copolymer synthesis by using 1-pentanol and oleic acid: process optimization and polymer characterization

J. Polym. Res., 28 (7) (2021), p. 247, 10.1007/s10965-021-02608-9 ↗

View in Scopus ↗ Google Scholar ↗

Shantini et al., 2012 K. Shantini, A.R.M. Yahya, A.A. Amirul

Empirical modeling development for integrated process optimization of poly(3-hydrxybutyrate- *co* -3-hydroxyvalerate) production

J. Appl. Polym. Sci., 125 (3) (2012), pp. 2155-2162, 10.1002/app.36345 ↗

View in Scopus ↗ Google Scholar ↗

Sharma et al., 2022 K. Sharma, K. Malik, S. Chaudhary, S. Kumar, N. Dhull, S. Sujeeta

Polyhydroxybutyrates (PHBs): an eco-friendly alternative to petroleum-based plastics for diminution of their detrimental effects on the environment

Int. J. Agric. Appl. Sci., 3 (2022), pp. 8-18, 10.52804/ijaas2022.322 ↗

Google Scholar ↗

Sheng et al., 2001 D. Sheng, D.P. Ballou, V. Massey
Mechanistic studies of cyclohexanone monooxygenase: chemical properties of intermediates involved in catalysis
Biochemistry, 40 (37) (2001), pp. 11156-11167, 10.1021/bi011153h ↗
View in Scopus ↗ Google Scholar ↗

Sheu et al., 2009 D.-S. Sheu, W.-M. Chen, J.-Y. Yang, R.-C. Chang
Thermophilic bacterium *caldimonas taiwanensis* produces poly(3-hydroxybutyrate-co-3-hydroxyvalerate) from starch and valerate as carbon sources
Enzym. Microb. Technol., 44 (5) (2009), pp. 289-294, 10.1016/j.enzmictec.2009.01.004 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Shi et al., 2020 L.-L. Shi, Y.-Y. Da, W.-T. Zheng, G.-Q. Chen, Z.-J. Li
Production of polyhydroxyalkanoate from acetate by metabolically engineered *aeromonas hydrophilia*
J. Biosci. Bioeng., 130 (3) (2020), pp. 290-294, 10.1016/j.jbiosc.2020.05.003 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Silano et al., 2019 V. Silano, J.M. Barat Baviera, C. Bolognesi, B.J. Brüschweiler, A. Chesson, P.S. Cocconcelli, R. Crebelli, D.M. Gott, K. Grob, E. Lampi, A. Mortensen, I. Steffensen, C. Tlustos, H. Van Loveren, L. Vernis, H. Zorn, L. Castle, J. Cravedi, R. Franz, ..., G. Rivière
Safety assessment of the substance poly((R)-3-hydroxybutyrate-co-(R)-3-hydroxyhexanoate) for use in food contact materials
EFSA J., 17 (1) (2019), 10.2903/j.efsa.2019.5551 ↗
Google Scholar ↗

Singh Saharan et al., 2014 B. Singh Saharan, A. Grewal, P. Kumar
Biotechnological production of polyhydroxyalkanoates: a review on trends and latest developments
Chin. J. Biol., 2014 (2014), pp. 1-18, 10.1155/2014/802984 ↗
Google Scholar ↗

Sohn et al., 2022 Y.J. Sohn, J. Son, H.J. Lim, S.H. Lim, S.J. Park
Valorization of lignocellulosic biomass for polyhydroxyalkanoate production: status and perspectives
Bioresour. Technol., 360 (2022), 10.1016/j.biortech.2022.127575 ↗
Google Scholar ↗

Sudesh et al., 2000 K. Sudesh, H. Abe, Y. Doi
Synthesis, structure and properties of polyhydroxyalkanoates: biological polyesters
Prog. Polym. Sci., 25 (2000), pp. 1503-1555, 10.1016/S0079-6700(00)00035-6 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Suhazsini et al., 2020 P. Suhazsini, R. Keshav, S. Narayanan, A. Chaudhuri, P. Radha

A study on the synthesis of poly (3-hydroxybutyrate-co-3-hydroxyvalerate) by *bacillus megaterium* utilizing cheese whey permeate

J. Polym. Environ., 28 (5) (2020), pp. 1390-1405, 10.1007/s10924-020-01687-x ↗

View in Scopus ↗ Google Scholar ↗

Tabassum Mumtaz et al., 2009 Suraini Abd-Aziz Tabassum Mumtaz, Abdul Rahman Nor'Aini, Phang Lai Yee, Yoshihito Shirai, Mohd Ali Hassan

Fed-batch production of P(3HBco3HV) copolymer by *comamonas* sp EB 172 using mixed organic acids under dual nutrient limitation

Eur. J. Sci. Res., 33 (3) (2009), pp. 374-384

Google Scholar ↗

Tao et al., 2021 G.-B. Tao, B.-W. Tan, Z.-J. Li

Production of polyhydroxyalkanoates by a moderately halophilic bacterium of salinivibrio sp. Tgb10

Int. J. Biol. Macromol., 186 (2021), pp. 574-579, 10.1016/j.ijbiomac.2021.07.038 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Tian et al., 2022 L. Tian, H. Li, X. Song, L. Ma, Z.-J. Li

Production of polyhydroxyalkanoates by a novel strain of photobacterium using soybean oil and corn starch

J. Environ. Chem. Eng., 10 (5) (2022), Article 108342, 10.1016/j.jece.2022.108342 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Tsuji et al., 2005 H. Tsuji, T. Ono, T. Saeki, H. Daimon, K. Fujie

Hydrolytic degradation of poly(ε-caprolactone) in the melt

Polym. Degrad. Stab., 89 (2) (2005), pp. 336-343, 10.1016/j.polymdegradstab.2005.01.018 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Van Thuoc et al., 2019 D. Van Thuoc, D.N. My, T.T. Loan, K. Sudesh

Utilization of waste fish oil and glycerol as carbon sources for polyhydroxyalkanoate production by *salinivibrio* sp. M318

Int. J. Biol. Macromol., 141 (2019), pp. 885-892, 10.1016/j.ijbiomac.2019.09.063 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Verlinden et al., 2011 Rob A.J. Verlinden, Zofia Piotrowska-Seget, David J. Hill, Melvin A. Kenward, Craig D. Williams, Iza K. Radecka

Production of polyhydroxyalkanoates from waste frying oil by *cupriavidus necator*

AMB Express, 1 (2011), p. 11

Google Scholar ↗

Vermeer et al., 2022 C.M. Vermeer, M. Nielsen, V. Eckhardt, M. Hortensius, J. Tamis, S.J. Picken, G.M.H. Meesters, R. Kleerebezem

Systematic solvent screening and selection for polyhydroxyalkanoates (PHBV) recovery from biomass

J. Environ. Chem. Eng., 10 (6) (2022), Article 108573, 10.1016/j.jece.2022.108573 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Volova et al., 2001 T.G. Volova, G.S. Kalacheva, O.V. Altukhova
The autotrophic synthesis of polyhydroxyalkanoate by alcaligenes eutrophusin the presence of carbon monoxide
Microbiology, 70 (6) (2001), pp. 640-646, 10.1023/A:1013175413013 ↗
View in Scopus ↗ Google Scholar ↗

Volova et al., 2021 T. Volova, E. Kiselev, I. Nemtsev, A Lukyanenko, A. Sukovatyi, A. Kuzmin, G. Ryltseva, E. Shishatskaya
Properties of degradable polyhydroxyalkanoates with different monomer compositions
Int. J. Biol. Macromol., 182 (2021), pp. 98-114, 10.1016/j.ijbiomac.2021.04.008 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Wagle et al., 2019 A.R. Wagle, Y.M. Dixit, B.V. Vakil
Scale up studies for polyhydroxyalkanoate production by a bacillus flexus strain with industrial potential
Indian J. Microbiol, 59 (2019), pp. 383-386, 10.1007/s12088-019-00807-z ↗
View in Scopus ↗ Google Scholar ↗

Wong et al., 2022 H.S.J. Wong, N.A. Azami, A.-A.A. Amirul
Enhanced production of polyhydroxyalkanoate with manipulable and reproducible 3-hydroxyvalerate fraction by high alcohol tolerant *cupriavidus malaysiensis* USMAA2-4 transformant
Bioprocess Biosyst. Eng., 45 (8) (2022), pp. 1331-1347, 10.1007/s00449-022-02748-2 ↗
View in Scopus ↗ Google Scholar ↗

Wongmoon and Napathorn, 2022 C. Wongmoon, S.C. Napathorn
Optimization for the efficient recovery of poly(3-hydroxybutyrate) using the Green solvent 1,3-dioxolane
Front. Bioeng. Biotechnol., 10 (2022), 10.3389/fbioe.2022.1086636 ↗
Google Scholar ↗

Woo et al., 2024 J.-M. Woo, H.-J. Kim, S. Hwang, E.-J. Seo, J.-B. Park
Structure modeling-based characterization of ChnD, the 6-hydroxyhexanoate dehydrogenase from *acinetobacter* sp. Strain NCIMB 9871
J. Biotechnol., 392 (2024), pp. 90-95, 10.1016/j.jbiotec.2024.06.008 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Xu et al., 2010 Y. Xu, R.-H. Wang, A.A. Koutinas, C. Webb
Microbial biodegradable plastic production from a wheat-based biorefining strategy
Process Biochem., 45 (2) (2010), pp. 153-163, 10.1016/j.procbio.2009.09.001 ↗
View PDF View article View in Scopus ↗ Google Scholar ↗

Yin et al., 2020 F. Yin, D. Li, X. Ma, J. Li, Y. Qiu

Poly(3-hydroxybutyrate-3-hydroxyvalerate) production from pretreated waste lignocellulosic hydrolysates and acetate co-substrate

Bioresour. Technol., 316 (2020), Article 123911, 10.1016/j.biortech.2020.123911 ↗

View PDF View article View in Scopus ↗ Google Scholar ↗

Yuan et al., 2015 Q. Yuan, R. Sparling, J. Oleszkiewicz

Polyhydroxybutyrate production from municipal wastewater activated sludge with different carbon sources

Air Soil Water Res, 8 (2015), pp. 53-58, 10.4137/ASWR.S27218 ↗

View in Scopus ↗ Google Scholar ↗

Zhang and Cronan, 1998 Y. Zhang, J.E. Cronan

Transcriptional analysis of essential genes of the *escherichia coli* fatty acid biosynthesis gene cluster by functional replacement with the analogous *salmonella typhimurium* gene cluster

J. Bacteriol., 180 (13) (1998), pp. 3295-3303, 10.1128/JB.180.13.3295-3303.1998 ↗

View in Scopus ↗ Google Scholar ↗

Zhang et al., 2022 L. Zhang, Z. Jiang, T.H. Tsui, K.C. Loh, Y. Dai, Y.W. Tong

A Review on Enhancing *Cupriavidus necator* Fermentation for Poly(3-hydroxybutyrate) (PHB) Production From Low- Cost Carbon Sources

Front. Bioeng. Biotechnol. (2022), 10.3389/fbioe.2022.946085 ↗

Google Scholar ↗

Zhang et al., 2015 Y.-Z. Zhang, G.-M. Liu, W.-Q. Weng, J.-Y. Ding, S.-J. Liu

Engineering of *ralstonia eutropha* for the production of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) from glucose

J. Biotechnol., 195 (2015), pp. 82-88, 10.1016/j.jbiotec.2014.12.014 ↗

View PDF View article Google Scholar ↗

Zheng et al., 2020 C. Zheng, Z. Yu, C. Du, Y. Gong, W. Yin, X. Li, Z. Li, U. Römling, S. Chou, J. He

2-Methylcitrate cycle: a well-regulated controller of <scp> bacillus </scp> sporulation

Environ. Microbiol., 22 (3) (2020), pp. 1125-1140, 10.1111/1462-2920.14901 ↗

View in Scopus ↗ Google Scholar ↗

Cited by (0)