Biotechnology Advances 31 (2013) 945–961

Contents lists available at ScienceDirect

Biotechnology Advances

journal homepage: www.elsevier.com/locate/biotechadv

Research review paper

Recent advances in biological production of 3-hydroxypropionic acid

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ARTICLE INFO

Available online 6 March 2013

Keywords:
3-Hydroxypropionic acid
Glycerol
Aldehyde dehydrogenase
Klebsiella pneumoniae
Glycerol dehydratase
Coenzyme/vitamin B_{12}

ABSTRACT

3-Hydroxypropionic acid (3-HP) is a valuable platform chemical that can be produced biologically from glucose or glycerol. This review article provides an overview and the current status of microbial 3-HP production. The constraints of microbial 3-HP production and possible solutions are also described. Finally, future prospects of biological 3-HP production are discussed.

Contents

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0734-9750/$ – see front matter
http://dx.doi.org/10.1016/j.biotechadv.2013.02.008

1. Introduction

3-Hydroxypropionic acid or 3-hydroxypropanoate (3-HP) is an important platform chemical, which is ranked at the top third among twelve platform chemicals selected by the US Department of Energy (DOE) that can be derived from biomass (Werpy and Petersen, 2004). Chemically, 3-HP is a three-carbon, optically inactive (non-chiral) organic compound and a structural isomer of lactic acid (2-hydroxypropanoic acid). 3-HP is also known as hydracrylic acid or ethylene lactic acid (see Fig. 1 for chemical structures of 3-HP and some select precursors/intermediates) (Datta et al., 1995). The bifunctionality of 3-HP owing to the presence of a carboxyl and hydroxyl group (at the β position), makes it a versatile agent for organic synthesis. The compound can be used for the production of chemicals, such as acrylic acid, 1,3-propanediol (PDO), methyl acrylate, acrylamide, ethyl 3-HP, malonic acid, propiolactone and acrylonitrile and can be used as a cross-linking agent for polymer coatings, metal lubricants and antistatic agents for textiles (CEP, 2003; Gokarn et al., 2007). In addition, 3-HP is a starting material for cyclization and polymerization reactions to produce propiolactone, polyesters and oligomers. In particular, the polymer produced from the self-condensation of 3-HP, [poly (3-hydroxypropionic acid)], has good biocompatibility and biodegradability, and can be used for the manufacture of surgical products and drug-releasing materials (Pina et al., 2011; Zhang et al., 2004). Furthermore, the polymer can replace many traditional petroleum-based polymers owing to its excellent glass transition temperature and high melting point (Mochizuki and Hirami, 1997). On the other hand, despite the diverse applications, the commercial production of 3-HP is limited due to the low yield and high production cost (Jiang et al., 2009; Pina et al., 2009; Suthers and Cameron, 2001).

3-HP can be synthesized using a range of chemical routes, and can be produced from acrylic acid, 3-propiolactone, 3-hydroxypropionitrile, ally alcohol, vinyl acetate and 1,3-propanediol. Acrylic acid, an industrially important chemical, was once considered an important precursor for 3-HP. On the other hand, the rapid increase in the price of acrylic acid by an average of 60–63% between December 2009 and December 2010 has made it economically unfavorable (Pina et al., 2011; http://www.icis.com, n.a.). 3-HP can also be produced from the hydrolysis of 3-hydroxypropionitrile, which is derived from a chemical reaction between 2-chloroethanol and sodium cyanide. Cyanide is very toxic and noxious, and its involvement makes the entire process unsuitable for industrial production (Pina et al., 2011). Another chemical route for 3-HP production is the hydrolysis of highly reactive β-propiolactone, which contains a strained four member lactone ring. The main obstacle to this route is the carcinogenicity of β-propiolactone (Long and Purchase, 1950; Pina et al., 2011; Weissermel and Arpe, 1997). A high yield of 3-HP (79–83%) has been achieved using allyl alcohol as a precursor using a gold catalyst (Arceo et al., 2009; Bergman et al., 2008; Weissermel and Arpe, 1997). The major drawback of this process is the sharp decrease in the yield of 3-HP with the repeated use of the catalyst (Pina et al., 2009, 2011). 3-HP can also be prepared from the oxidation of PDO in high yield (Behr et al., 1992). On the other hand, this is also not economically feasible because PDO is expensive (USD 10,000–35,000/ton as of December, 2012; http://www.alibaba.com, n.a). Although many chemical processes have been suggested, none are commercially feasible at present due to the high cost of the starting materials and process, and/or the environmental incompatibility (Jiang et al., 2009).

Studies of the biological production of 3-HP began from the early 2000s. Several recombinant strains of *Escherichia coli* and *Klebsiella pneumoniae* were developed, with glucose and/or glycerol as potential substrates. This review provides an overview of the recent progress in the biological production of 3-HP. First, the various microbial metabolisms that involve 3-HP are presented briefly because they can provide an insight into the synthesis and/or development of efficient biological routes. The existing and possible biological routes for 3-HP production from glucose and glycerol are described. The main focus is given to the current status of biological 3-HP production technologies including the development of various recombinant strains and fermentation processes. Finally, this review discusses the challenges associated

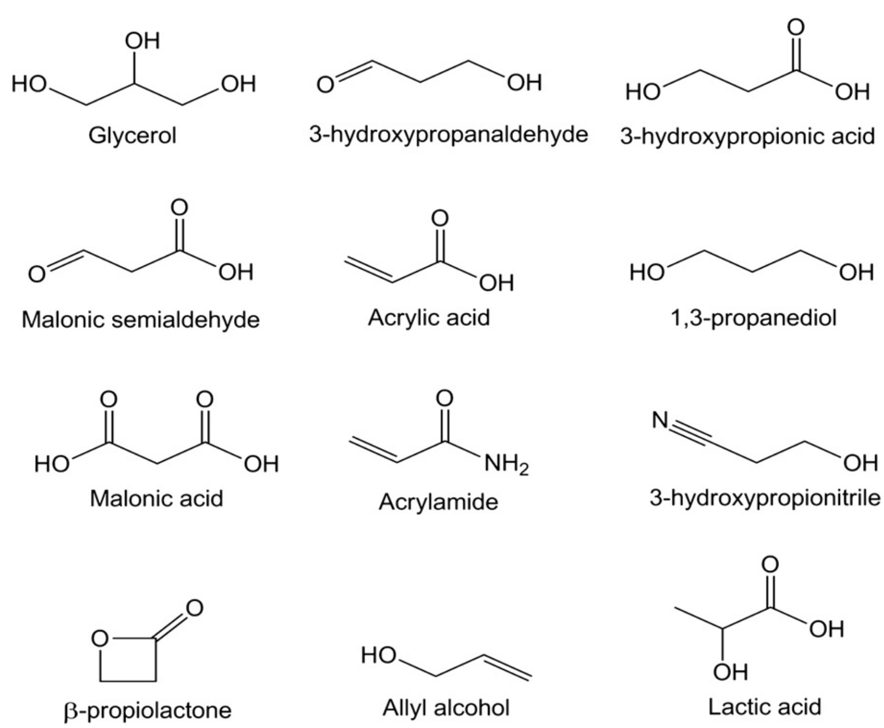

Fig. 1. Chemical structures of 3-HP and some select precursors/intermediates related with biological and chemical production of 3-HP.