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Efficient conversion of 1,2-butanediol to (*R*)-2-hydroxybutyric acid using whole cells of *Gluconobacter oxydans*

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ABSTRACT

(*R*)-2-Hydroxybutyric acid ((*R*)-2-HBA) is an important building block for azinothricin family of antitumour antibiotics and biodegradable poly(2-hydroxybutyric acid). However, optically active (*R*)-2-HBA could not be produced through microbial fermentation or chemical synthesis. Several biocatalytic methods have been reported for the production of (*R*)-2-HBA. Those processes used expensive and scarce substrates and would not be suitable for practical application. In this work, *Gluconobacter oxydans* DSM 2003 was confirmed to have the ability to produce (*R*)-2-HBA from 1,2-butanediol, a non-toxic and inexpensive compound that had a great potential for biotechnological processes. Under the optimal conditions, the biocatalytic process produced (*R*)-2-HBA at a high concentration (18.5 g l^{-1}) and a high enantiomeric excess (99.7%). The biocatalysis process introduced in this study may provide a technically and economically interesting route for production of (*R*)-2-HBA.

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1. Introduction

Optically active (*R*)-hydroxy monocarboxylic acids, such as (*R*)-2-hydroxybutyric acid ((*R*)-2-HBA) and (*R*)-lactic acid, are important building blocks for the production of biodegradable material (Tsuji and Okumura, 2009; Zhao et al., 2010). Those polymers are susceptible to hydrolytic degradation and thus can be utilized as materials for biomedical, pharmaceutical, and environmental applications (Tsuji and Okumura, 2009; Matuana, 2008). In particular, (*R*)-2-HBA has also been found application for the production of azinothricin family of antitumour antibiotics (Karl et al., 1995; Nakagawa et al., 2007). However, different from (*R*)-lactic acid, (*R*)-2-HBA could not be produced through microbial fermentation (Zhao et al., 2010; Gao et al., 2009; Tanaka et al., 2006; Lu et al., 2009; Zhou et al., 2003; Okino et al., 2008). 2-HBA produced by chemical synthesis from petrochemical resources is a mixture of two optical isomers. Thus, biocatalysis has been emerged as a practical tool for (*R*)-2-HBA synthesis in recent years (Adam et al., 1995, 1997; Nakagawa et al., 2007; Simon et al., 1989; Gao et al., 2011).

Butanediols are non-toxic and inexpensive compounds that have a great potential for biotechnological processes (Nakajima et al., 1994; Ji et al., 2009a,b; Zhang et al., 2010). There have been some reports on value added chemicals production from 1,3-, 2,3- and 1,4-butanediols by biocatalysts (Harada and Hirabayashi, 1968; Shigeno et al., 1992; Ji et al., 2011; Xiao et al., 2010). Production of (*S*)-2-HBA and racemic 2-HBA from 1,2-butanediol was also acquired through biocatalytic methods (Wong and Matos, 1985; Nakajima et al., 1994). However, the biocatalytic production of (*R*)-2-HBA from 1,2-butanediol has never been studied in previous works. It thus would be desirable to find an effective biocatalyst for the (*R*)-2-HBA production from 1,2-butanediol.

Gluconobacter oxydans, an obligate aerobic Gram-negative bacterium, has a respiratory metabolism characterized by incomplete oxidation of sugars, alcohols and acids (Prust et al., 2005). The partially oxidized organic compounds (aldehyde, ketone and organic acid) would be rapidly accumulated in the medium (Gao and Wei, 2006). This property makes *G. oxydans* an important biocatalyst for industrial use (Wei et al., 2009; Su et al., 2004; Gupta et al., 2001).

In a previous report, *G. oxydans* DSM 2003 could efficiently catalyze the (*R*)-isomer of the racemic 1,2-propanediol into (*R*)-lactic acid (Su et al., 2004). Thus, the strain might also have the ability to produce (*R*)-2-HBA from the (*R*)-1,2-butanediol. In this work, the product of *G. oxydans* DSM 2003 catalyzing racemic 1,2-butanediol oxidation was identified as (*R*)-2-HBA and then the reaction conditions were optimized. Production of (*R*)-2-HBA from racemic 1,2-butanediol using the strain was acquired.

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