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# Co-production of 3-hydroxypropionic acid and 1,3-propanediol by *Klebseilla pneumoniae* expressing *aldH* under microaerobic conditions

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## HIGHLIGHTS

- *Klebseilla pneumoniae* expressing *E. coli aldH* was cultured under microaerobic conditions.
- Aeration enhanced 3-hydroxypropionate production but lowered 1,3-propanediol formation.
- The highest 3-hydroxypropionate was 48.9 g/L in 28 h at the aeration rate of 1.5 vvm.
- The specific formation rates of metabolites were compared.
- Carbon and redox balances were performed.

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## ABSTRACT

Fed-batch cultures of *Klebsiella pneumoniae* expressing *Escherichia coli aldH* were performed under microaerobic conditions to investigate the effects on metabolites production. Increasing the aeration rate enhanced cell growth and 3-hydroxypropionic acid (3-HP) production, but reduced 1,3-propanediol (1,3-PDO) formation. The recombinant strain *K. pneumoniae*/pUC18*kan-aldHec* produced 48.9 g/L of 3-HP and 25.3 g/L of 1,3-PDO with an overall yield of 0.66 mol/mol in 28 h at an aeration rate of 1.5 vvm; however, under fully aerobic condition, no 3-HP and 1,3-PDO were produced due to the repression of *dha* operon. The flux through the reaction catalyzed by glycerol dehydratase and the split ratio of 1,3-PDO were negatively correlated with the aeration rate, even though the 3-HP level showed a positive trend. This study demonstrated that the relative amounts of 3-HP and 1,3-PDO can be controlled by the aeration rate.



## 1. Introduction

1,3-Propanediol (1,3-PDO) is a bulk chemical widely used in cosmetics, foods, lubricants, medicines, and the polymer polytrimethylene terephthalate (PTT) (Deckwer, 1995). Another platform chemical, 3-hydroxypropionic acid (3-HP), also has a wide range of industrial applications for synthesis of such specialty chemicals as acrylic acid, methyl acrylate, propiolactone, malonic acid, acrylamide and so on. Both 1,3-PDO and 3-HP are classified in the third group of top value added chemicals that can be derived from biomass (Werpy and Petersen, 2004). Since the biodiesel industry produces a surplus of glycerol (Andrea et al., 2010; Forrest et al., 2010), conversion of this chemical to higher-value products is essential for economic reasons.

*Klebsiella pneumoniae* is a facultative anaerobic organism that produces 1,3-PDO from glycerol under anaerobic and microaerobic conditions (Ruch et al., 1974; Ruch and Lin, 1975). In the oxidative route, glycerol is dissimilated to pyruvate via dihydroxyacetone phosphate (DHAP) and NADH is formed. Pyruvate is further converted to acetate, lactate, ethanol and other compounds. In the reductive route, glycerol dehydratase (GDHt), a coenzyme $B_{12}$-dependent enzyme, converts glycerol to 3-hydroxypropionaldehyde (3-HPA), which is subsequently reduced to 1,3-PDO by 1,3-propanediol oxidoreductase (PDOR) concomitant with oxidation of NADH to regenerate $NAD^+$ (Zeng et al., 1996). When an $NAD^+$-dependent aldehyde dehydrogenase is over-expressed, 3-HPA is converted to 3-HP and the formed NADH can be used for 1,3-PDO production (Zhu et al., 2009), and the amount of byproducts from the oxidative route can be reduced.

GDHt is a critical enzyme for 1,3-PDO and 3-HP production. It is expressed under anaerobic conditions and undergoes inactivation by oxygen in the absence of substrate (Wanger et al., 1966). Although GDHt is sensitive to oxygen, some studies indicated that 1,3-PDO production was improved in microaerobic cultures (Chen et al., 2003). It was also reported that transcription of the *dha*

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