Indian J Microbiol (March 2010) 50(1):2–11
DOI: 10.1007/s12088-010-0017-x

REVIEW ARTICLE

Microbial production and applications of 1,2-propanediol

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Received: 3 December 2008 / Accepted: 4 February 2009

1,2-Propanediol (propylene glycol) is an existing commodity chemical and can be produced from renewable resources using microbes. By virtue of being a natural product, relevant biochemical pathways can be harnessed into fermentation processes to produce 1,2-propanediol. In the present review, the chemical process and different biological strategies for the production of 1,2-propanediol are reviewed and compared with the potentials and limitations of all processes. For the successful commercial production of this diol, it is necessary to establish the metabolic pathways and production hosts (microorganisms), which are capable of delivering final product with high yields and volumetric productivity. Three pathways which have been recognized for 1,2-propanediol production are discussed here. In the first, de-oxy sugars like fucose and rhamnose are used as the carbon sources, while in the other route, the glycolytic intermediate-dihydroxyacetonephosphate (DHAP) is used to produce 1,2-propanediol via the formation of methylglyoxal. A new pathway of 1,2-propanediol production by lactic acid degradation under anoxic conditions and the enzymes involved is also discussed. The production of this diol has gained attention because of their newer applications in industries such as polymers, food, pharmaceuticals, textiles, etc. Furthermore, improvement in fermentation technology will permit its uses in other applications. Future prospect in the light of the current research and its potential as a major bulk chemical are discussed.

Keywords 1,2-Propanediol · Anaerobic fermentation · Renewable resources · De-oxy sugars · Application

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Introduction

In the early 20th century, most bulk chemicals came from microbes, which were produced by fermenting biomass such as corn and potatoes. Subsequently, after learning how to "crack" petroleum into simpler hydrocarbon, chemists took over. They devised complex, multistep processes to convert these building blocks into bulk chemicals as well as smaller scale specialty products [1]. However, the energy crisis during 1970s sparked renewed global interest in the synthesis of bulk chemicals and other materials from bioresources. This paradigm transition not only shifts society's dependence away from petroleum hydrocarbon to highly oxygenized renewable bioresources but also is an important contributor to the development of a sustainable industrial society. Moreover, the use of carbohydrates as chemical raw materials will eliminate the need for several capital-intensive, oxidative processes used in the petroleum industry. Biomass carbohydrates will provide a viable route to products such as alcohols, carboxylic acids and esters. These natural products are stereo- and regiochemically pure, thereby reducing dependence on expensive chiral catalysts and complex synthesis that are currently required to selectively install chemical functionality in petrochemicals [2].

Initially, this transition to renewable feedstocks was impossible due to the lack of appropriate technologies and infrastructure making it less economical. However, in the last two decades, advances in microbial genetics and a new understanding of cell's metabolite pathways helped researchers to perform multiple enzymatic steps to convert renewable feedstocks into industrial chemicals and pharmaceuticals in a more economical way [3]. As a result, there is a demand to reintroduce fermentation as an economical means of producing many bulk chemicals like biofuels (ethanol, butanol, hydrogen), pharmaceuticals

(vitamins, drugs), biofertilizers and diols (1,2-propanediol, 1,3-propanediol, succinic acid, lactic acid) [4]. Producing these chemicals by fermentation not only focuses on its renewable nature but also provides environmental and industrial safety [5].

In this context, 1,2-propanediol (propylene glycol), is a major commodity chemical and has attracted world wide attention due to its application in the synthesis of biodegradable plastics and polymer resins [6]. 1,2-Propanediol is a three-carbon diol with a stereogenic center at the central carbon atom and exists as: (R)-1,2-propanediol and (S)-1,2-propanediol (Fig. 1) [7]. It is a diol with high boiling point and has a strong hydrophilic nature.

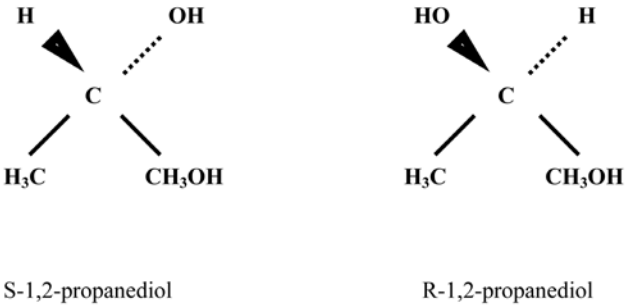

Fig. 1 Chemical structure of 1,2-propanediol.

Annual sale of 1,2-propanediol was estimated over 1 billion pounds in the United States in 1992 [7]. The world consumption of 1,2-propanediol in 2003 was 1.2 million metric tons, the biggest producers being Dow and Lyondell with 35 and 25%, respectively, of the world production [1]. This enormous rise is due to its application which is not restricted in one area but also finds its importance in a wide spectrum of areas such as: (a) in the production of unsaturated polyester resins; (b) as an additive in nutrition products; (c) non-ionic detergents; (d) cosmetics; (e) liquid detergents; (f) as a component of break or hydraulic fluids; (g) as an antifreezing; and (h) as an de-icing agent [1, 6].

Earlier, chemically produced 1,2-propanediol could not make its place in the industrial sector because of its high production cost and the use of petrochemicals. However, with time, science touched all edges in various spheres of life and successfully developed techniques and processes to fulfill the demands of the consumers in terms of 'natural' or 'green' products. In this context, biologically produced 1,2-propanediol must prove as a cost-effective alternative in comparison to the existing chemically synthesized product [6].

Production of 1,2-propanediol by bacteria and yeasts has been known for many years and related pathways are also recognized. Earlier, 1,2-propanediol had negligible market value but with the development of new biological processes, novel strains, metabolic and genetic engineering, the biologically produced 1,2-propanediol can compete with the one produced from the petrochemicals. Moreover, the biological process has the cost-effective potential and economise investment costs, energy demand, disposal costs and consumption of raw materials.

Realizing the importance of all stated above, this article presents an exhaustive review of different strategies, which have been employed for enhancing the production of 1,2-propanediol. Microbial synthesis is discussed in detail as it is an excellent tool to produce this bulk chemical from renewable resources. The present review also gives the broad overview on its biochemical pathway, biochemistry and production yields. Its applications are reviewed by keeping its significance in making biodegradable plastics and other polymers. Outlook and future prospect is discussed under the light of the current research and demand worldwide.

Chemical synthesis of 1,2-propanediol

1,2-Propanediol was earlier manufactured by hydrogenolysis of sugars at high temperature and under pressure in the presence of a metal catalyst which resulted in a racemic mixture of 1,2-propanediol and other polyols [8]. Now, 1,2-propanediol is produced by hydration of propylene oxide [9]. Propylene oxide, a non-renewable petrochemical derivative, is formed chemically either by the chlorohydrin process or by the hydroperoxide process and both the methods are associated with hazardous chemical use. At present enantiomerically pure 1,2-propnediol can be produced by three methods: (a) the catalytic hydrogenation of lactic acid esters [10]; (b) the bioreduction of acetol [6]; and (c) the resolution of racemic 1,2-propanediol [11]. Agribusiness companies such as Archer Daniels Midland have developed another chemical process based on glycerol. Glycerol can be converted to 1,2-propanediol using heterogeneous [12] or homogeneous catalysts [13].

Although it is possible to generate 1,2-propanediol by these chemical methods, these are either capital-intensive and/or generate waste streams containing environmental pollutants. In recent years, some attractive biological processes have been developed for the production of high quality commercial 1,2-propanediol derived from renewable resource at low cost. In this direction, anaerobic and facultative anaerobic microorganisms are interesting entities as these produces 1,2-propanediol as the major end-product of their metabolism [14].

Microorganisms producing 1,2-propanediol

Wide ranges of microorganisms are currently known to ferment sugars to 1,2-propanediol. The production of this diol has been reported from both bacteria and yeasts [15, 16]. Enebo as early as in 1954 reported *Clostridium thermobutyricum* to produce 1,2-propanediol [17]. Suzuki and Onishi were the first to report yeast as a propanediol producing entity [15]. A decade later, *Bacteroides ruminocola* was cited as the producers of this diol by Turner and Roberton [18]. They investigated the metabolism and growth yields of *B. ruminocola* grown on xylose, arabinose and rhamnose, where it was observed that rhamnose was fermented mainly to 1,2-propanediol.

A direct fermentation route to 1,2-propanediol from de-oxy sugars such as fucose and rhamnose from *Escherichia coli* was well studied and reported by Boronat and Aguilar [19]. Furthermore, Altaras and Cameron performed metabolic engineering to increase the substrate spectrum from de-oxy sugars to commonly available sugars [7]. They demonstrated the production of 0.25 g of 1,2-propanediol from 10 g/l of glucose by recombinant *E. coli*.

Tran-Din and Gottschalk in 1985, reported that *Clostridium sphenoides* can produce 1,2-propanediol not only from glucose, rhamnose, fucose, but also from fructose, mannose and cellobiose under phosphate limiting conditions [20]. The considerable higher production was observed from rhamnose and fucose. Fermentation of rhamnose and fucose yielded 72.6 and 68.6 mM of 1,2-propanediol, respectively, with concomitant production of acetate (40–43 mM). However, fermentation of galactose, xylose, mannitol, maltose, sucrose, lactose and raffinose did not yield any production of 1,2-propanediol from this organism.

Cameron and Cooney reported a naturally occurring microorganism, *Thermoanaerobacterium thermosaccharolyticum* to ferment common sugars such as D-glucose and D-xylose to 1,2-propanediol [21]. The highest level of 1,2-propanediol (7.9 g/l) was achieved when glucose was used as a substrate in comparison with the xylose. Sanchez-Rivera and co-workers reported yet higher level of 1,2-propanediol (9.0 g/l) when glucose was used as a substrate from the same organism [22]. Cameron et al. investigated the production of 1,2-propanediol from *T. thermosaccharolyticum* from various substrates such as arabinose and galactose resulted in 4.29 and 3.56 g/l of 1,2-propanediol, respectively [5]. Altaras and co-workers in 2001 investigated the fermentation of the various sugars known to be present in cellulosic biomass [23]. Fermentation of arabinose and glucose produced 0.13 and 0.11 g of 1,2-propanediol per gram of glucose. An interesting reason to use *T. thermosaccharolyticum* for the production of 1,2-propanediol is that, unlike, the synthetic process, which yields a racemic mixture, this fermentation produces enantiomerically pure (R)-1,2-propanediol.

Low levels of this diol have also been detected in several industrial strains of *Saccharomyces cerevisae* [24]. Hoffman was successful in producing 1,2-propanediol from glucose by genetic and metabolic engineering of *S. cerevisae* [25]. He could produce approximately 0.24 g/l of 1,2-propanediol from glucose by this strain.

Salmonella typhimurium has been reported to produce 1,2-propanediol from de-oxy sugars [16]. An equimolar amount of 1,2-propanediol was detected when (methyl pentose), rhamnose or fucose were used as a substrate. However, 1,2-propanediol is not further metabolized in anaerobic cultures, gradually disappears from the medium in *S. typhimurium* cultures maintained under similar conditions [26]. This detailed investigation revealed that when grown on rhamnose, *S. typhimurium* excreted 1 M of 1,2-propanediol/M of sugar into the medium. After exhaustion of the sugar, the diol concentration reached a maximum and gradually disappeared when the culture was kept under the same conditions. Disappearance of the diol did not occur when the cells were removed from the medium by centrifugation.

Veiga da Cunha and Foster reported for the first time that *Lactobacillus brevis* and *L. buchneri* can also produce 1,2-propanediol by degrading lactic acid using glycerol as an electron acceptor [27]. This new pathway of 1,2-propanediol production was further described by Elferink et al. while studying on *L. buchneri* and *L. parabuchneri* [28]. These lactobacilli were able to degrade lactic acid under anoxic conditions, without requiring an external electron acceptor. Here, each mole of lactic acid was converted into approximately 0.5 M of acetic acid, 0.5 M of 1,2-propanediol, and traces of ethanol. Moreover, acidic conditions are required to induce lactic acid degrading capacity of the cells.

Biochemical pathways for the production of 1,2-propanediol

The biosynthesis of 1,2-propanediol occurs within a microbial system through two main pathways. In the first, de-oxy sugars like fucose and rhamnose are used as the carbon sources (Fig. 2) [18], while in the other route, the glycolytic intermediate-dihydroxyacetonephosphate (DHAP) is used to produce 1,2-propanediol via the formation of methylglyoxal (Fig. 3). Subsequently methylglyoxal results in the production of 1,2-propanediol [6]. A new pathway of 1,2-propanediol production by lactic acid degradation under anoxic condition was reported by Elferink et al. in 2001 (Fig. 4) [28].

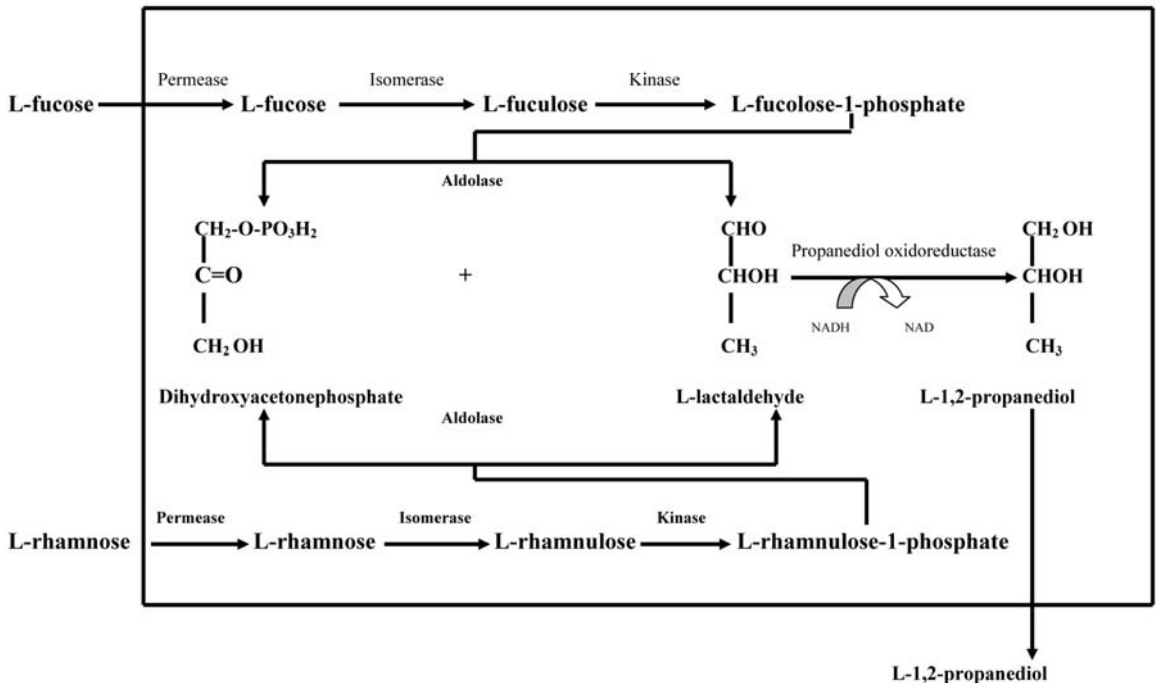

Fig. 2 Schematic representation of metabolic pathways for the production of 1,2-propanediol from fucose/rhamnose.

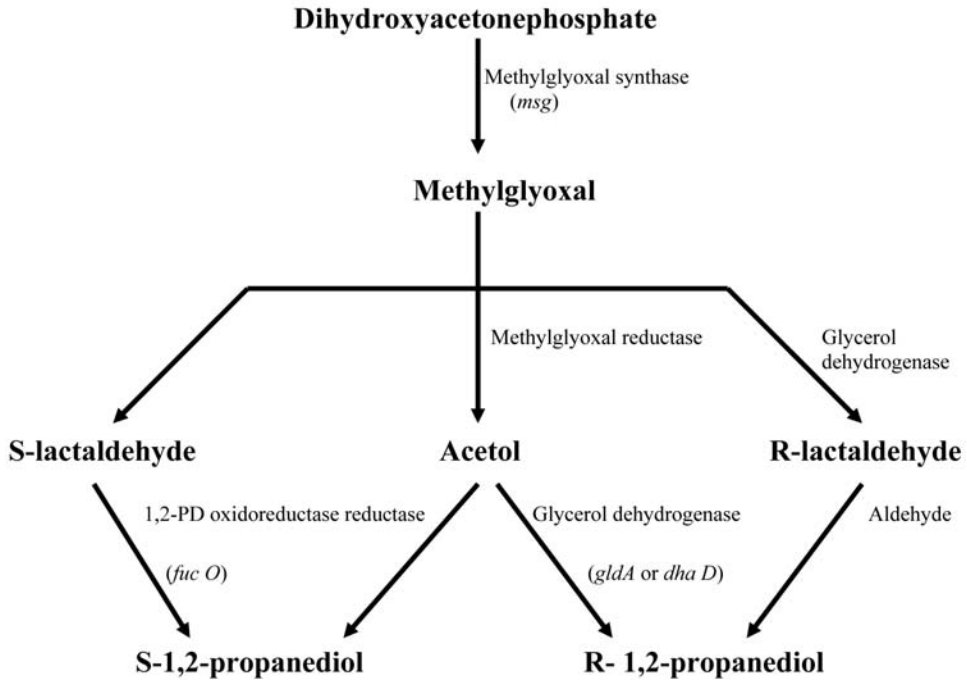

Fig. 3 Schematic representation of metabolic pathway leading to the production of 1,2- propanediol from DHAP.

The first route for the production of 1,2-propanediol uses fucose and rhamnose as a carbon source (Fig. 2). Upon catabolism of L-rhamnose to L-rhamnulose-1-phosphate, the phosphorylated sugar is cleaved to produce DHAP and L-lactaldehyde [16]. Similarly metabolism of fucose can also generate lactaldehyde and DHAP [29]. Fucose is isomerized to L-fuculose and then phosphorylated to L-fuculose-1-phosphate. Subsequently, in both the cases the L-lactaldehyde is reducing to L-1,2-propanediol under anaerobic conditions. It has been reported that L-fucose and L-rhamnose are metabolized through parallel pathways in organisms like *E. coli* [18, 30], *Bacteroides ruminicola* [18], *Bacillus macerans* [31], *S. typhimurium* [16] and various yeasts [15]. However, this route is not commercially feasible, due to the high cost of fucose and rhamnose. The least expensive sugar, L-rhamnose, sells for over $300/kg [7].

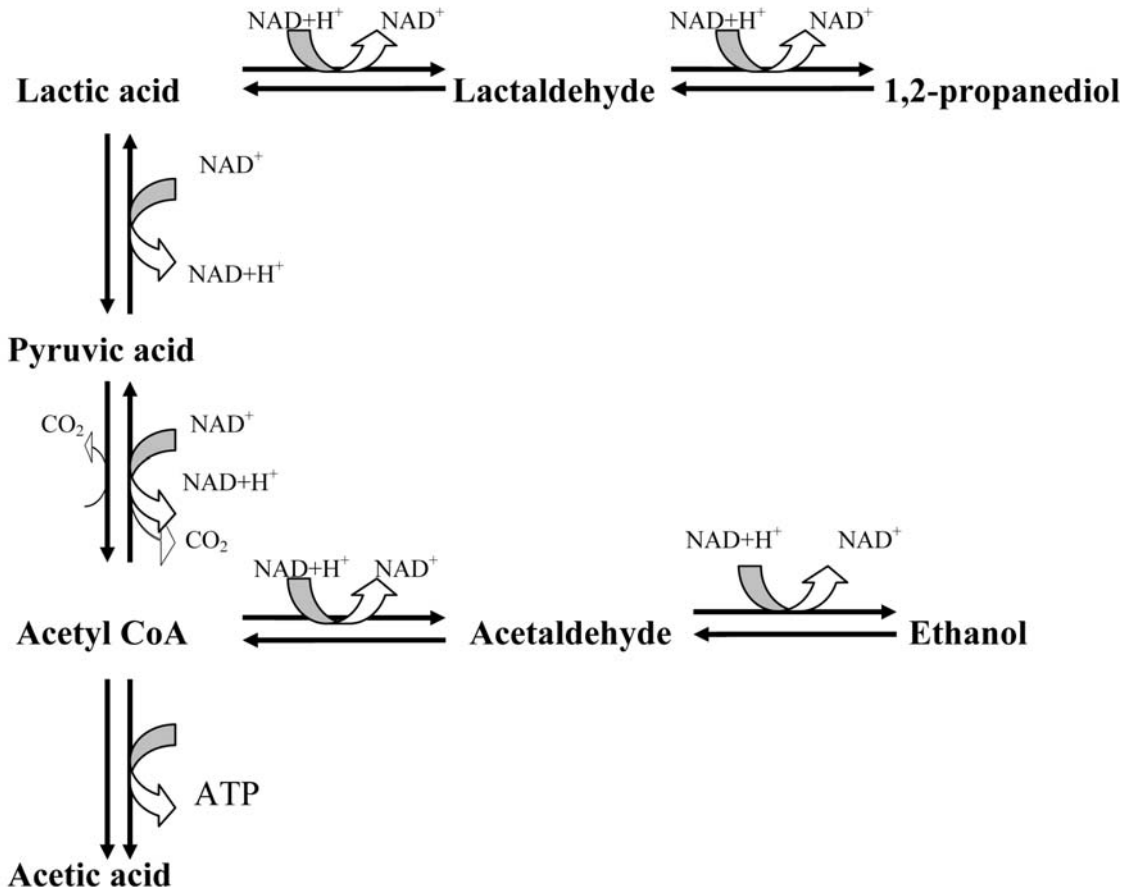

Fig. 4 Pathway for anaerobic degradation of lactic acid by *Lactobacillus buchneri* into 1,2-propanediol, acetic acid and ethanol.

The other route studied for the production of 1,2-propanediol is the utilization of the DHAP, a glycolytic intermediate, to produce 1,2-propanediol via the formation of methylglyoxal (Fig. 3). This methylglyoxal bypass pathway was discovered by Cooper in 1975 where he proposed that methylglyoxal has a role in metabolism [32]. This pathway allows the breakdown of fructose-1,6-bisphosphate under the condition of phosphate limitation [20]. In this process, DHAP is converted to methylglyoxal and provides inorganic phosphate for the glyceraldehyde dehydrogenase reaction. Subsequently methylglyoxal is metabolized further to 1,2-propanediol and D(–)-lactate in the classical bypass. Reduction of methylglyoxal to 1,2-propanediol could proceed either via hydroxyacetone (acetol) [33, 34] or via lactaldehyde [30] (Fig. 4). Lactaldehyde occurs as intermediate in propanediol formation from de-oxy sugars [30], whereas the hydroxyacetone appeared as intermediate in 1,2-propanediol oxidation [33, 34].

Methylglyoxal pathway is found in *T. thermosaccrolyticum* [23], *C. sphenoides* [20] and *S. cerevisiae* [35, 36]. These organisms are reported to ferment common sugars such as glucose, fructose, mannose, galactose, xylose, arabinose, lactose and cellobiose [21, 23]. *T. thermosaccrolyticum* can produce enantiomerically pure (R)-1,2-propanediol which can be used for most of the applications of the racemic mixture and has additional application as a chiral synthon in organic synthesis [21, 37].

Elferink et al. reported another pathway of the production of 1,2-propanediol by lactic acid bacteria [28]. They investigated that *L. buchneri* and *L. parabuchneri* are able to degrade lactic acid to acetic acid with concomitant production of 1,2-propanediol, with traces of ethanol under anoxic conditions without requiring an external electron acceptor (Fig. 4). In addition, this lactate-converting ability is strongly influenced by the pH, and acidic conditions.

Enzymes involved in production of 1,2-propanediol

Enzyme kinetics of 1,2-propanediol formation and studies on their metabolic pathways has been carried out by Forage

and Lin in 1982 [38]. As pointed out earlier, biosynthesis of 1,2-propanediol may occur within microbial system through two main pathways. In the first, L-fucose an L-rhamnose is metabolized through parallel pathways mediated by the sequential action of different enzymes which include a permease [39]; an isomerase [40]; a kinase [41]; and an aldolase [42] (Fig. 2). In this pathway, L-fucose/L-rhamnose get isomerized to L-fuculose/L-rhamnulose and then phosphorylated to L-fuculose-1-phosphate/L-rhamnulose-1-phosphate by respective isomerases and kinases. The phosphorylated molecule is further cleaved to L-lactaldehyde and DHAP by the action of an aldolase (Fig. 2) [43]. Beckmann and Low reported that in the case of *E. coli*, two homologous inducible proteins, each specific for the metabolism of its corresponding sugar are coded by two different gene clusters [44]. The genes of the rhamnose system constitute a well-defined operon with gene for aldolase rha D, whereas, in the fucose system, gene for aldolase encoded by fuc A maintained under separate control [43]. Further, both pathways converge after the corresponding aldolase action. Subsequently, lactaldehyde is reduced to 1,2-propanediol, which is released into the medium by an nicotinamide adenine dinucleotide (NAD)-linked propanediol oxidoreductase, simultaneously regenerating the oxidized co-enzyme (NAD) and allowing the fermentation of fucose or rhamnose to proceed [29, 44].

NAD-linked propanediol oxidoreductase encoded by FucO, is one of the most important enzymes for 1,2-propanediol production and had been described as an enzyme inducible by anaerobic growth on fucose or rhamnose, which is never found under aerobic condition even in the presence of inducers [19]. However, the activity of this enzyme was found to display different characteristics on each sugar. In the rhamnose-grown cells, the increase in enzyme activity under inducing conditions was accompanied by the synthesis of propanediol oxidoreductase, whereas, in fucose-grown cells, the level of propanediol oxidoreductase was high under inducing as well as non-inducing conditions. It suggested that enzyme activity of fucose-grown cells do not depend on the appearance of the specific protein but on the activation of the propanediol oxidoreductase already present in the cells in an inactive form [19]. It is specific for L-isomers and has a molecular weight of 76 kDa. The Km is 0.035 mM for L-lactaldehyde and 1.25 mM for L-1,2-propanediol, at pH 7.0 and 9.5, respectively. This makes released propanediol un-utilizable by the cells even if molecular oxygen becomes available [29, 43].

The other pathway studied for the production of 1,2-propanediol is the utilization of DHAP, a glycolytic intermediate (Fig. 3). This intermediate is converted to methylglyoxal by methylglyoxal synthase enzyme, which subsequently reduced to R-lactaldehyde/S-lactaldehyde by methylglyoxal reductase. This step is followed by the conversion of S-lactaldehyde/acetone to S-1,2-propanediol by oxidoreductase. Similarly, R-lactaldehyde/acetone is converted to R-1,2-propanediol by aldehyde reductase and glycerol dehydrogenase [6].

In this pathway, methylglyoxal synthase is the most important enzyme for 1,2-propanediol production as it links glycolytic intermediate with 1,2-propanediol production. Methylglyoxal synthase catalyzes the conversion of DHAP to methylglyoxal and inorganic phosphate. This enzyme methylglyoxal synthase provides bacteria with an alternative to triosephosphate isomerase for metabolizing DHAP. Phosphate acts as an allosteric inhibitor of this enzyme, which suggests that the methylglyoxal bypass may have significant activity under phosphate starvation conditions [45]. When *C. sphenoids* were grown, propanediol appeared only after the phosphate concentration declined below 80 μM [20].

Hopper and Cooper has purified and characterized this enzyme methylglyoxal synthase from *E. coli*, where it was found that the enzyme has usual pH optima of around 7.5 and a molecular weight of 67 kDa [46]. However, methylglyoxal synthase purified from *S. cerevisiae* is most active in the pH range of 9.5–10.5 and has a molecular weight of 26 kDa [6]. Methylglyoxal activity was also detected in cells of *C. acetobutylicum*, where its native molecular mass was 60 kDa with an optimum pH of 7.5 [45]. This enzyme has also been isolated and crystallized in good yields from *Pseudomonas saccharophila* and *Proteus vulgaris* by Tsai and Gracy [47]. There results showed that this enzyme is specific for DHAP and does not form methylglyoxal from glyceraldehyde-3-phosphate and non-phosphorylated trioses.

The activity of this enzyme has also been detected in the cell extracts of *T. thermosaccrolyticum*. This enzyme is sensitive to phosphate and may resemble the enzyme from *E. coli* [21]. Murata et al. demonstrated the presence of this enzyme in eukaryotes and also suggested that the yeast methylglyoxal is different from prokaryotes in molecular weight and in sensitivity toward various inhibitory chemicals [35]. *E. coli* methylglyoxal synthase is inhibited by phosphate concentrations that were closer to Km value for inorganic phosphate (Pi) as a substrate for 3-phosphoglycerate dehydrogenase. The similar regulation, however, is not applicable to the yeast, since yeast methylglyoxal synthase is somewhat insensitive to Pi concentration.

Besides methylglyoxal synthase, in the production of 1,2-propanediol the two other important enzymes are: methylglyoxal reductase and glycerol dehydrogenase. methylglyoxal reductase reduces the aldehyde group of methylglyoxal to acetol [6]. Phosphate generally has no effect

on its activity in the case of *C. sphenoides*. This enzyme uses NADPH as the reducing co-factor. However, the reduction of the aldehyde group of methylglyoxal to acetol is followed by the stereo specific reduction of the ketone group of the acetol to give R-1,2-propanediol. This reaction is carried out by glycerol dehydrogenase (E.C. 1.1.1.6) [48]. This enzyme may also reduce the ketone group of methylglyoxal to give R-lactaldehyde. It is an NADH dependent enzyme [20].

Hurdles in the development of industrial production of 1,2-propanediol

Although several direct fermentation routes for the production of 1,2-propanediol are documented and many experimental trials have been reported, yet the production is limited and successful schemes for the same are yet to be developed. Most probably, this is because of use of expensive sugars or poorly characterized organisms such as *T. thermosaccharolyticum*. The production processes are yet to be optimized and explored for the economic production of this important diol. Tran-Din and Gottaschalk reported that the strain of *C. sphenoides* produces <2 g/l of 1,2-propanediol from 20 g/l glucose/mannose/cellobiose under phosphorus limited conditions [20]. Similarly, Cameron and Cooney reported that *T. thermosaccharolyticum*, produces up to 7.0 g/l of 1,2-propanediol from 20 g/l of glucose/xylose/mannose/cellobiose [21]. Sanchez-Rivera et al. carried out the batch culture of *T. thermosaccharolyticum* and reported the production of 9.0 g/l of (R)-1,2-propanediol from glucose [22]. Continuous cultures of *T. thermosaccrolyticum* have also been carried out for the production of (R)-1,2-propanediol from either glucose or lactose. Using glucose as a carbon source, the maximum concentration of (R)-1,2-propanediol obtained was only 0.7 g/l under phosphorous-potassium limited conditions. However, when galactose was used as a carbon source, (R)-1,2-propanediol concentration was increased to 3.5 g/l under these conditions. A direct fermentation route to 1,2-propanediol from de-oxy sugars such as fucose and rhamnose from *E. coli* has been reported by Boronat and Anguilar [19], however the yield was quite low. Therefore, if an appropriate enzyme and/or reducing power are provided, the increase in production can be achieved. Genetic and metabolic engineering would result in an increase in propanediol yields as there would be appropriate combination of enzymes in organisms. The optimization of these strains may yield microbial process for the economically viable production of this widely used chemical.

Despite the obvious advantages of a biological production of commodities it is generally expressed that this production mode is not at all economically competitive with a chemical synthetic process due to several disadvantages such as: (a) high costs of the raw materials, (b) low reaction rate and (c) low product concentration.

The relatively high costs of the raw materials are one of the major limitations as the raw material costs are above 50% of the total costs. In this respect, two basic strategies have been used to overcome this problem: (a) to increase the conversion yield and (b) to use cheaper or waste materials. Both of these strategies can be implemented either by a process approach or by a genetic approach. Although, metabolic engineering of 1,2-propandiol production by co-expression of *E. coli*'s glycerol dehydrogense and methylglyoxal synthase gene in *E. coli* BL21 (DE3) was not very successful as it resulted in very low titer (3.9 mM). The possible limitation includes the possibility that the formation of methylglyoxal is metabolically regulated and the substrate specificity and efficiency of the glycerol dehydrogenase may not be optimal [45]. In order to increase the substrate spectrum, *T. thermosaccharolyticum* was grown in presence of simple and complex sugars. In this context, whey permeate was found to be a potential complex sugar, however, it often needed to be supplemented with trace minerals and ammonium sulfate [23].

The second major limitation of bioprocesses is the low reaction rate and reactor productivity, primarily because bioprocesses are carried out at physiological temperature, atmospheric pressure and mostly in batch or fed-batch operation mode. A process approach can have a significant effect on volumetric production rates by increasing cell density in the bioreactor and by developing a continuous process. This is mostly achieved by continuous cultivation with cell recycling or with immobilized cells. However, so far no such reports have been published on cell recycling and immobilized cells.

The third major limitation of bioprocesses is the quite low product concentration compared with chemical processes, resulting in high downstream processing costs. This is mainly caused by product inhibition of cell growth and biosynthesis. Physiological improvements in cell growth and product formation only have a limited impact on this aspect. Chemical or directed mutagenesis may provide better chances for improvement. Recently, *S. cerevisiae* was used as a host strain, where, methylglyoxal synthase (msg) and glycerol dehydrogenase gene (gldA) were inserted. Each gene was cloned in pYES2/CT and pYES3/CT plasmids, respectively and transformed in *S. cerevisiae*. The resultant recombinant was stable [49]. Similarly, Noh et al. demonstrated the expression of both genes in single plasmid (pESC-URA) with two cloning sites in *S. cerevisiae* followed by optimization of 1,2-propanediol production [50].

Economic importance and applications of 1,2-propanediol

Today, it is presumed that in near future the improvements of microbial strains, fermentation and recovery processes will permit the cost-effective production of 1,2-propanediol from renewable resources, and hence will be made available for use in a wide range of applications.

In this regard, typical commercial example of a technology switch with respect to feedstock was demonstrated by a joint venture of the chemical company Ashland Inc. and the food processor Cargill. The aim of this project was the production of propylene glycol out of glycerol from the biodiesel industry at a factory in Europe with an initial capital investment of $80–100 million and a capacity of 65,000 tone/year [2]. Cargill has already presented a process to obtain 1,2-propanediol out of carbohydrates with *E. coli* or *T. thermosaccharolyticum* HG-8 [7, 23].

As bulk commodity chemical 1,2-propanediol is widely used as a feed stock in the preparation of polyester resins for film and fiber manufacture. It is also a cheap commercial product with great potential for microbial processes, since it is water soluble and non-toxic. The mechanism of the enantioselective oxidation of racemic 1,2-propanediol to D-(−)-lactic acid by biotransformation using *Gluconobacter oxydans* has recently been reported [51]. 1,2-Propanediol also finds application as a de-icer and as a non-toxic replacement for ethylene glycol in automobiles, as antifreeze in breweries and dairy establishments. 1,2-Propanediol is also used as airplane deicing fluids. Besides this, it can also be used as an inhibitor of mold growth and as a mist to disinfect air. About 50 million kg were used in food products as an emulsifier, although recent developments have led to the removal of propylene glycol from GRAS status for use in cat food [52].

Enantiomerically pure (R)-1,2-propanediol produced by microbial fermentation, can be used for most of the applications of the racemic mixture and has additional applications as a chiral synthon in organic synthesis [21]. This pure stereoisomer of 1,2-propanediol would also have an importance as chiral starting materials for the synthesis of specialty chemicals, such as optically active propylene oxide and polymers. These compounds may be useful in the manufacture of chiral pharmaceutical products [6]. Besides these, 1,2-propanediol may find some medical applications as well like in the induction of premature centromere separation in oocytes and aneuploidy in one cell zygote in humans [53]. Moreover, antifreeze and de-icing market is growing because of the concern over the toxicity of ethylene glycol-based products. Furthermore, it can be used as a starting material for solvents, emulsifier and plasticizers.

Conclusions and future prospects

Till date, 1,2-propanediol has been commercially produced by synthetic processes starting with petrochemical feedstock and catalysis and involving a variety of chemical intermediates. However, it is now possible that microbiological routes can also potentially produce 1,2-propanediol from renewable feedstocks by processes that would involve benign intermediates.

Furthermore, technological advances for making genetically engineered strains, improvement in measurement of compounds, and theoretical analysis of metabolic fluxes can contribute to the design of production systems for the manufacture of high value-added chemicals. The dual future strategies of optimized hosts and optimized expression, together with the enzymatic properties of the pathway enzymes will allow the continued advancement of such processes. The technique for the removal of competing pathways and the enhancement of desired pathways via genetics and culture manipulation will be important in the development of such process. The potential for integrating a biological process into the downstream processing also seems tractable and economical viable.

Some of the technology developments that are necessary for the successful commercialization of products or chemicals are the integration of metabolic pathway engineering and fermentation production technology. The approach to do so is ever expanding to maximize productivity, improve product purity, expand product line and broaden markets. Knowledge of biochemical pathways and fermentation processes will facilitate metabolic engineering, a rapidly developing technology with great potential to impact dramatically the development of the bio-based economics. It is also notable that a metabolic engineering effort, arguably unprecedented in scope, resulted in the catalyst that is the centerpiece of that process.

The industrial biotechnology vision for the future is based on the belief that every thing from medicine to fuels to clotting fibers and to assorted to other industrial raw materials can be obtained from microorganisms in deed ‘made better’ because unlike chemicals and fossil fuels, biological based industries comprise of infinitely greener and more renewable resources. Thus, it can be concluded that chemical and other industries have reached to new inflection point one in which petroleum and chemistry will solely be supplemented by renewable resource-based industrial biotechnology. It is supposed that this transformation from fossil fuels and chemicals to ‘biofactories’ in not just imminent but it is believed that biotechnological approach will have a hand in the production of at least US$ 50 billion worth of products in the past few years and could by 2010 contribute to US$ 169 billion [14].

Acknowledgements Authors acknowledge with thanks the help of Ms. Kakoli and Mr. Pritesh for critically evaluating the manuscript and Ms. Rekha Kaushik for the technical assistance.

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