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MINI-REVIEW

Tagatose: properties, applications, and biotechnological processes

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Abstract D-Tagatose has attracted a great deal of attention in recent years due to its health benefits and similar properties to sucrose. D-Tagatose can be used as a low-calorie sweetener, as an intermediate for synthesis of other optically active compounds, and as an additive in detergent, cosmetic, and pharmaceutical formulation. Biotransformation of D-tagatose has been produced using several biocatalyst sources. Among the biocatalysts, L-arabinose isomerase has been mostly applied for D-tagatose production because of the industrial feasibility for the use of D-galactose as a substrate. In this article, the characterization of many L-arabinose isomerases and their D-tagatose production is compared. Protein engineering and immobilization of the enzyme for increasing the conversion rate of D-galactose to D-tagatose are also reviewed.

Keywords Application · L-Arabinose isomerase · Biotransformation · Properties · Tagatose

Introduction

D-Tagatose, a rare natural hexoketose, is an isomer of D-galactose. The cyclic form of D-tagatose consists of α-D-tagato-2,6-pyranose (79%), β-D-tagato-2,6-pyranose (14%), α-D-tagato-2,5-furanose (2%), and β-D-tagato-2,6-furanose (5%; Köpper and Freimund 2003). D-Tagatose occurs naturally in *Sterculia setigera* gum, and it is also found in small quantities in various foods such as sterilized and powdered cow's milk, hot cocoa, and a variety of cheeses, yogurts, and other dairy products (Mendoza et al. 2005; Richards and Chandrasekhara 1960; Troyono et al. 1992).

D-Tagatose production can be produced from D-galactose by a chemical method using a calcium catalyst (Beadle et al. 1991), but the chemical process has some disadvantages, such as complex purification steps, chemical waste formation, and by-products formation. To overcome these disadvantages, biological manufactures of D-tagatose using several biocatalyst sources have been studied intensively in recent years. Among the biocatalysts, L-arabinose isomerase (EC 5.3.1.4) catalyzes the conversion of D-galactose to D-tagatose as well as the conversion of L-arabinose to L-ribulose, owing to the similar configurations of the substrates (Cheetham and Wootton 1993; Roh et al. 2000a).

In this article, biological production of D-tagatose using L-arabinose isomerase is mainly described. The reaction conditions, protein engineering, and immobilization on L-arabinose isomerase are introduced in the viewpoint of effective D-tagatose production. Moreover, high production of D-tagatose using equilibrium-shifted conversion is suggested.

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Properties

The melting temperature of D-tagatose is 134°C, and it is stable at pH 2–7. D-Tagatose has high solubility [58% (*w*/*w*) at 21°C], which makes it ideal as a flavor enhancer or fiber in soft drinks and yogurts. Its humectant properties are similar to those of sorbitol. D-Tagatose is less hygroscopic than fructose, and it is lower in viscosity [180 cP at 70% (*w*/*w*) and 20°C] than sucrose at the same concentration but slightly higher than fructose and sorbitol. As D-tagatose is a reducing sugar, it is involved in browning reactions during

heat treatment. It decomposes more readily than sucrose at high temperatures (Kim 2004; Levin 2002).

D-Tagatose is a malabsorbing sugar, as it is poorly absorbed in the small intestine (Buemann et al. 1999a, b, 2000; Lærke and Jensen 1999). The unabsorbed fraction of D-tagatose reaches the large intestine where it is completely fermented by the intestinal microflora. The formed short chain fatty acids are absorbed almost completely and are metabolized. During fermentation, there is a relatively low energy recovery, and a certain amount of energy is lost due to increased biomass excretion of the microflora (Bertelsen et al. 2001).

The sweetness of D-tagatose is 92% that of sucrose when compared in 10% solutions. D-Tagatose has a sucrose-like taste with no cooling effect or aftertaste. D-Tagatose is similar to the polyols in having a low caloric value and tooth-friendly property. However, it has no laxative effect unlike polyols (Levin et al. 1995). Although the taste quality of D-tagatose is similar to sucrose, D-tagatose does not contribute to calorie production (Levin 2002; Zehner and Lee 1988). A growth study on rats reports that D-tagatose contributed no net energy (Bar et al. 1999; Livesey and Brown 1996), and human clinical trials shows that subjects gradually and consistently lose weight at medically desirable rates (Levin 2002). As a result of these properties, D-tagatose is considered to be a potential reduced-energy sweetener.

Applications

D-Tagatose have numerous health benefits, including promotion of weight loss (Buemann et al. 2000), no glycemic effect (Donner et al. 1999; Seri et al. 1993), anti-plaque, non-cariogenic, anti-halitosis, prebiotic, and anti-biofilm properties (Bertelsen et al. 1999; Cisar et al. 1979; Lærke et al. 2000; Wong 2000), organ transplants (Paterna et al. 1998), enhancement of flavor (Rosenplenter and Mende 2004), improvement of pregnancy and fetal development (Levin 2000), treatment of obesity (Moore 2006), and reduction in symptoms associated with type 2 diabetes, hyperglycemia, anemia, and hemophilia (Levin 2002; Seri et al. 1993). The heath benefits and application of D-tagatose are summarized in Table 1.

D-Tagatose can be used as a low-calorie sweetener in nonchronic drugs, tooth paste, and mouth wash and in a wide variety of foods, beverages, health foods, and dietary supplements; it can be applied to products of low-carbohydrate diets, cereals, health bars, chocolate, candy, chewing gum, yogurt, soft drink, bakery, milk-based drink, and confectionery. D-Tagatose is also useful as an intermediate for synthesis of other optically active compounds and as an additive in detergent, cosmetic, and pharmaceutical formulation (Ibrahim and Spradlin 2000).

Table 1 Heath benefits and applications of D-tagatose

Health benefits	Applications
Low calorie	Low carbohydrate diets, cereals, health bars, soft drink
No glycemic effect	Diabetic food (type 2)
Anti-halitosis	Anti-hyperglycemic agent, dietary supplement
Prebiotic	Chocolate, candy, chewing gum
Anti-biofilm, anti-plaque	Tooth paste, mouth wash
Flavor enhancement	Yogurt, bakery, milk-based drink, confectionery

Biological production of tagatose

Biological manufactures of D-tagatose have been studied using several biocatalyst sources. *Arthrobacter globiformis* (Izumori et al. 1984), *Gluconobacter oxydans* (Manzoni and Rollini 2001; Rollini and Manzoni 2005), *Mycobacterium smegmatis* (Izumori and Tsuzaki 1988), *Enterobacter agglomerans* (Muniruzzanman et al. 1994), and *Klebsiella pneumoniae* (Shimonishi et al. 1994) have been reported to convert galactitol into D-tagatose. The responsible enzyme for the biotransformation from galactitol to D-tagatose is a sorbitol dehydrogenase (Rollini and Manzoni 2005). *Agrobacterium tumefaciens* D-psicose 3-epimerase (Kim et al. 2006a) and *Pseudomonas cichorii* D-tagatose 3-epimerase convert D-sorbose to D-tagatose (Itoh et al. 1994; Ishida et al. 1997; Yoshida et al. 2007). However, D-sorbose or galactitol is an expensive substrate that seems to have little potential for commercial application.

Various strains of *Mucoraceae* fungi convert D-psicose to D-tagatose (Yoshihara et al. 2006). As the mass production of D-psicose from D-fructose has became industrial feasible in recent years (Kim et al. 2006a; Takeshita et al. 2000), the production of D-tagatose from D-fructose via D-psicose as an alternative method can be proposed in spite of the requirement for further intensive investigation.

A new process to convert D-galactose to D-tagatose is introduced using lactic acid bacteria (Cheetham and Wootton 1993). *Enterobacter agglomerans* also produces D-tagatose from D-galactose when grown on an L-arabinose pre-induced medium (Oh et al. 1998). The cloned L-arabinose isomerases of *Escherichia coli*, *Bacillus subtilis*, and *Salmonella typhimurium* mediate the conversion of D-tagatose from D-galactose (Roh et al. 2000a). L-Arabinose isomerase has been of interest and studied intensively in recent years due to its industrial feasibility in D-tagatose production (Kim et al. 2003a).

Characterization of L-arabinose isomerase

For effective D-tagatose productions using the enzymes, the reaction conditions such as pH, temperature, and metal ion

should be optimized. The optimal reaction conditions of these bacterial L-arabinose isomerases are compared (Table 2). The optimum temperature for L-arabinose isomerase is in the range of 30–50°C in mesophiles such as *Aerobacter aerogenes* (Yamanaka and Wood 1966), *Alicyclobacillus acidocaldarius* (Lee et al. 2005b), *Bacillus halodurans* (Lee et al. 2005a), *Escherichia coli* (Kim et al. 2001a, b; Roh et al. 2000a, b; Yoon et al. 2003), *Lactobacillus gayonii* (Nakamatu and Yamanaka 1969), and *M. smegmatis* (Izumori et al. 1978); of 60–80°C in thermophiles such as *B. stearothermophilus* (Rhimi 2007a, b), *Geobacillus stearothermophilus* (Jung et al. 2005; Kim et al. 2003a; Lee et al. 2005a; Oh et al. 2006a; Ryu et al. 2003), *G. thermodenitrificans* (Baek et al. 2004; Kim and Oh 2005; Oh et al. 2006b), *Thermus* sp. (Kim et al. 2003b), and *Thermoanaerobacter mathranii* (Jørgensen et al. 2004); and of 85-90°C in hyperthermophiles such as *Thermotoga neapolitana* (Kim et al. 2002; Hong et al. 2007) and *T. maritima* (Lee et al. 2004).

The optimum pH for L-arabinose isomerase from *Alicyclobacillus acidocaldarius* is 6.0 (Lee et al. 2005b), while the enzymes from *G. thermodenitrificans* and *Thermus* sp. have optimum pH of 8.5 (Kim and Oh 2005; Kim et al. 2003b). The optimum pHs of the others are in the range 6.0–8.0.

The mesophilic and thermophilic L-arabinose isomerases require Mn^{2+} as a cofactor to enhance the isomerization rate reaction (Patrick and Lee 1968), while the hyperthermophilic L-arabinose isomerases require Co^{2+} (Kim et al. 2002; Lee et al. 2004). Mn^{2+} ion has also been shown to enhance the rate of the arabinose–ribulose isomerization reaction (Nakamatu and Yamanaka 1969; Patrick and Lee 1968).

The kinetic parameters of various bacterial L-arabinose isomerases for L-arabinose or D-galactose as a substrate are presented in Table 3. All reported bacterial L-arabinose isomerases have higher specificity for L-arabinose than D-galactose, suggesting that more research to alter substrate specificity into D-galactose should be needed. The ratio of catalytic efficiency (k_{cat}/K_m) for D-galactose to L-arabinose decreased when the optimum temperature of L-arabinose isomerase was increased; the ratio of k_{cat}/K_m was 128 in the mesophilic enzyme from *B. halodurans*, 51 in the thermophilic enzyme from *G. stearothermophilus*, respectively, and 9 in the hyperthermophilic enzyme from *T. maritima*. These results suggested that substrate specificity at high temperatures altered from L-arabinose into D-galactose.

Tagatose production using L-arabinose isomerase

Protein engineering of L-arabinose isomerase

The three-dimensional structure of *E. coli* L-arabinose isomerase was solved (Manjasetty and Chance 2006). The crystal structure and structural comparison with *E. coli* L-fucose isomerase suggested a possible metal binding site. The crystal structure forms a basis for identifying molecular determinants responsible for isomerization of galactose to tagatose. Based on the solved crystal structure and sequence alignments, the residues for the essential catalytic site and substrate recognition of *G. stearothermophilus* US 100 L-arabinose isomerase was suggested (Rhimi et al. 2007b).

Molecular evolution strategies for improving D-galactose isomerization are proposed as the increases of substrate specificity, thermostability, and optimum temperature and the decrease in optimum pH (Kim 2004). Directed evolution of the L-arabinose isomerase gene has been

Table 2 Biochemical properties of L-arabinose isomerases

Strain for enzyme source	Temp optimum (°C)	pH optimum	Half-life (min)	Metal ion	Reference
Aerobacter aerogenes	50	6.4–6.9	NR	Mn^{2+}	Yamanaka and Wood 1966
Alicyclobacillus acidocaldarius	65	6.0	NR	Mn^{2+}	Lee et al. 2005b
Bacillus halodurans	50	7.5–8.0	20(70°C)	Mn^{2+}	Lee et al. 2005a
B. stearothermophilus US100	80	7.5–8.0	110(75°C)	No requirement	
Escherichia coli	30	8.0	60(50°C)	Fe^{2+}, Mn^{2+}	Yoon et al. 2003
Geobacillus stearothermophilus T6	70	7.0–7.5	52(80°C)	Mn^{2+}	Lee et al. 2005a
G. stearothermophilus	65	7.5	17(70°C)	Mn^{2+}	Kim et al. 2003a
G. thermonitrificans	70	8.5	42(75°C)	Mn^{2+}	Kim and Oh 2005
Lactobacillus gayonii	30–40	6.0–7.0	NR	Mn^{2+}	Nakamatu and Yamanaka 1969
Mycobacterium smegmatis	45	7.0–7.5	10(45°C)	Mn^{2+}	Izumori et al. 1978
Thermoanaerobacter mathranii	65	8.0	NR	Mn^{2+}	Jørgensen et al. 2004
Thermotoga neapolitana	85	7.0	120(90°C)	Co^{2+}	Kim et al. 2002
T. maritima	90	7.0–7.5	185(90°C)	Co^{2+}	Lee et al. 2004
Thermus sp.	60	8.5	NR	Mn^{2+}	Kim et al. 2003b

NR Not reported

Table 3 Kinetic parameters of L-arabinose isomerases

Substrate	Strain for enzyme source	V_{max} (U/mg)	K_m (mM)	k_{cat} (min^{-1})	k_{cat}/K_m (mM^{-1} min^{-1})	Reference
L-Arabinose	*Aerobacter aerogenes*	NR	33	NR	NR	Yamanaka and Wood 1966
	Alicyclobacillus acidocaldarius	35.5	48	1,989	41	Lee et al. 2005b
	Bacillus halodurans	33	36	1,864	51	Lee et al. 2005a
	B. stearothermophilus US100	42	29	2,040	71	
	Escherichia coli	248	60	NR	NR	Yoon et al. 2003
	Geobacillus stearothermophilus T6	37	63	2,048	33	Lee et al. 2005a
	G. stearothermophilus	96	67	4,100	61	Kim et al. 2006b
	G. stearothermophilus (mutant enzyme)	134	100	6,475	65	Kim et al. 2006b
	G. thermonitrificans	86	145	6,960	48	Kim and Oh 2005
	G. thermonitrificans (mutant enzyme)	178	106	14,434	136	Oh et al. 2006b
	Thermoanaerobacter mathranii	NR	80	NR	NR	Jørgensen et al. 2004
	Thermotoga neapolitana	119	116	6,740	58	Kim et al. 2002
	Thermotoga maritima	41	31	2,340	75	Lee et al. 2004
D-Galactose	*Aerobacter aerogenes*	NR	270	NR	NR	Yamanaka and Wood 1966
	Alicyclobacillus acidocaldarius	7.5	129	NR	NR	Lee et al. 2005b
	Bacillus halodurans	1.3	167	120	0.4	Lee et al. 2005a
	B. stearothermophilus US100	8.9	57	438	8.5	
	Escherichia coli	NR	1,480	NR	NR	Yoon et al. 2003
	Geobacillus stearothermophilus T6	9.0	120	516	4.3	Lee et al. 2005a
	G. stearothermophilus	7.8	145	173	1.2	Kim et al. 2006b
	G. stearothermophilus (mutant enzyme)	37.6	578	1,211	2.1	Kim et al. 2006b
	G. thermonitrificans	6.9	408	204	0.5	Kim and Oh 2005
	G. thermonitrificans (mutant enzyme)	35.4	399	1046	3.1	Oh et al. 2006a, b
	Thermoanaerobacter mathranii	NR	120	NR	NR	Jørgensen et al. 2004
	Thermotoga neapolitana	14.3	250	810	3.2	Kim et al. 2002
	T. maritima	8.9	60	504	8.4	Lee et al. 2004

NR Not reported

suggested as a powerful tool for increasing the reaction rate (Kim et al. 2001a). A mutated L-arabinose isomerase from *G. stearothermophilus* was obtained by an error-prone polymerase chain reaction, and it exhibits the change of three amino acids (V322M, A393T, and A408V) compared to the wild-type enzyme. The mutated L-arabinose isomerase shows increases in D-galactose isomerization activity, optimum temperature, catalytic efficiency (k_{cat}/K_m) for D-galactose, and the production rate of D-tagatose from D-galactose (Kim et al. 2006b). A double-sites mutant enzyme, C450S-N475K of L-arabinose isomerase from *G. thermodenitrificans*, was obtained by site-directed mutagenesis. The double-sites mutant enzyme converts D-galactose to D-tagatose with a yield of 58%, whereas a wild type gives 46% of D-tagatose conversion after 300 min at 65°C (Oh et al. 2006b).

Commercial application of L-arabinose isomerase requires an acidic pH range to reduce nonspecific side and browning reactions (Kim 2004). The optimum pHs of Q408V and R408V mutants are shifted to pH 7.5 from 8.5, and the galactose isomerization activities of the mutants are 60 and 30% higher than that of wild type, respectively (Oh et al. 2006a). Using site-directed mutagenesis, comparative studies with the wild type and its mutants are performed, and it is found that the Lys-269 of acidophilic L-arabinose isomerases from *Alicyclobacillus acidocaldarius* has a role to determine pH optimum (Lee et al. 2005b).

Tagatose production using immobilized biocatalyst

To produce D-tagatose effectively, L-arabinose isomerase or cells containing the enzyme should be immobilized, and a bioreactor containing immobilized biocatalyst is used for industrial production of D-tagatose. In terms of the productivity relative to the biomass as specific productivity, the immobilized cells are more efficient than the immobilized enzyme. Using the same mass of cells, D-tagatose production by immobilized cells is higher than that by

immobilized enzyme (Jung et al. 2005). The lower tagatose production of the immobilized enzymes obtained from the same cell mass was due to the decreased activity resulting from enzyme purification process, such as cell lysis, precipitation, and dialysis.

The immobilized enzyme reactor can be used at the highly concentrated enzyme, whereas the immobilized cell reactor cannot be used because at high cell concentrations, immobilized cells contain high levels of other cell materials, which have no tagatose-producing activity and cause steric hindrance (Jung et al. 2005). As a result, the immobilized enzyme reactor has a higher tagatose titer, conversion yield, and volumetric productivity than the immobilized cell reactor, immobilized *G. stearothermophilus* L-arabinose isomerase entrapped by alginate produces D-tagatose at an average D-tagatose productivity of 1,296 g l^{-1} day^{-1} as the reported highest productivity (Ryu et al. 2003). The immobilized *E coli* cells containing *G. stearothermophilus* L-arabinose isomerase in alginate produces a productivity of 70 g l^{-1} d^{-1} in a bioreactor (Jung et al. 2005) while the immobilized *E coli* cells containing *Thermotoga neapolitana* L-arabinose isomerase produces a productivity of 98 g l^{-1} day^{-1} (Hong et al. 2007).

Comparison of tagatose production

A summary of D-tagatose production from D-galactose by various L-arabinose isomerases and cells containing the enzyme is shown in Table 4. The D-tagatose equilibrium from D-galactose is 28.8% at 30°C in *E. coli* L-arabinose isomerase (Kim et al. 2001b), 58% at 65°C in the enzyme from *G. thermodenitrificans* (Oh et al. 2006b), and 68% at 85°C in *Thermotoga neapolitana* (Kim et al. 2002). The content of product of isomerization reaction is determined by the reaction temperature, and it is shifted toward D-tagatose as a product at higher temperatures.

The highest levels of D-tagatose production have been reported 230 g l^{-1} tagatose from 500 g l^{-1} D-galactose using immobilized *G. stearothermophilus* L-arabinose isomerase in continuous recycling mode of a packed-bed bioreactor with a tagatose productivity of 230 g l^{-1} day^{-1} (Kim et al. 2003a). In continuous mode using the immobilized enzyme, 145 g l^{-1} D-tagatose from 300 g l^{-1} D-galactose was produced in the bioreactor with an average tagatose productivity of 1,296 g l^{-1} day^{-1} as the reported highest productivity (Ryu et al. 2003), which was 5.6-fold higher than that in continuous recycling mode. The increase in productivity may be due to the use of 1.5-fold higher amount of enzyme and continuous mode and operation under the optimized conditions such as bead size, length/diameter (L/D) of the reactor, dilution rate, total loaded enzyme amount, and substrate concentration. The highest reported yield of D-tagatose, which is catalyzed by *Thermotoga neapolitana* L-arabinose isomerase using 1.8 g l^{-1} D-galactose, is 68% at 85°C (Kim et al. 2002).

Equilibrium-shifted production of tagatose

The equilibrium between substrate and product cannot be simply changed by protein engineering of the enzyme, as it

Table 4 D-Tagatose production from D-galactose by L-arabinose isomerases and cells containing the enzyme

Biocatalyst	Strain for enzyme source	Temp. (°C)	Galactose (g l^{-1})	Tagatose (g l^{-1})	Yield (%)	Productivity (g l^{-1} d^{-1})	Reference
Enzyme	*Bacillus stearothermophilus*	70	0.9	0.4	48.0	1.5	
Enzyme	*Escherichia coli*	30	100	29	28.8	4.1	Kim et al. 2001b
Immobilized enzyme	*Escherichia coli*	30	500	103	20.5	7.5	Kim et al. 2001b
Immobilized enzyme	*Escherichia coli*	37	100	30	30.0	30	Oh et al. 2001
Enzyme	*Geobacillus stearothermophilus*	60	100	31	30.6	46	Kim et al. 2003a
Immobilized enzyme	*Geobacillus stearothermophilus* (batch)	60	500	230	46.0	319	Kim et al. 2003a
	(continuous)	60	300	145	48.3	1,296	Kim et al. 2003a
Immobilized *E. coli*	*Geobacillus stearothermophilus*	60	300	59	19.7	70	Jung et al. 2005
Enzyme	*Geobacillus thermodenitrificans*	60	300	158	52.7	190	This study
Enzyme	*Thermoanaerobacter mathranii*	65	300	126	42.0	63	Jørgensen et al. 2004
Enzyme	*Thermotoga neapolitana*	80	1.8	1.2	68.0	1.5	Kim et al. 2002
Immobilized *E. coli*	*Thermotoga neapolitana*	70	180	49	27.2	98	Hong et al. 2007
Enzyme	*Thermotoga maritima*	70	1.8	1.0	56.0	4.0	Lee et al. 2004
Enzyme	*Thermus* sp.	60	1.0	0.5	54.0	0.2	Kim et al. 2003b

is controlled by the reaction temperature (Chang et al. 1999). To obtain a higher conversion yield of product than that defined at the specific temperature, the equilibrium should be shifted toward product. If a material binds more specific to product (D-tagatose) than substrate (D-galactose), the addition of a material (like boric acid) causes an equilibrium shift by complex formation between the product and material. Once formed, the product–material complex does not participate in the equilibrium reaction. When residual substrate is converted to product to reestablish the reaction equilibrium, the result is the shifting of the equilibrium toward product formation. The formation of the product–material complex can be proposed as an alternative to high-temperature biotransformation for feasible industrial production of D-tagatose.

Borate forms complexes with carbohydrates (De Muynck et al. 2006) and interacts with enzyme systems and changes the equilibrium of any reaction involving *cis*-diol carbohydrates (Smith and Johnson 1976). Some ketoses such as lactulose, maltulose, and celluobiulose are synthesized from aldoses such as lactose, maltose, and cellobiose, respectively, by the high-yielding isomerization in alkaline solutions containing borate (Hicks et al. 1983; Hicks and Parrish 1980). We found the greater complexing capacity of borate to D-tagatose than D-galactose. In the isomerization reaction between D-galactose and D-tagatose catalyzed by L-arabinose isomerase, the favored formation of D-tagatose/borate complexes shifted the equilibrium toward D-tagatose formation. Now, we attempt high production of D-tagatose using the equilibrium-shifted conversion.

Further research

The three-dimensional structure of *E. coli* L-arabinose isomerase was already solved (Manjasetty and Chance 2006), and the residues for the essential catalytic site and substrate recognition was suggested based on the solved crystal structure and sequence alignments (Rhimi et al. 2007b). Mutation studies for the amino acids on or near the active site should be intensively performed to know the molecular determinants of L-arabinose isomerase activity. The molecular determinants will change the substrate specificity, increase conversion rate, and alter the pH range for activity, and it will provide information for the development of industrial valuable L-arabinose isomerases.

D-Tagatose production by enzyme or cell of non-generally recognized as safe (GRAS) host may cause safety problem (Burdock and Carabin 2004). The problem can be solved by transferring the gene of L-arabinose isomerase to GRAS host such as *Bacillus megaterium*, *Corynebacterium ammonagenes*, and *C. glutamicum*.

In the future, L-arabinose isomerase will be able to produce industrially D-tagatose because the biotransformation has some advantages over the chemical process, such as mild reaction conditions, D-tagatose production without by-products, no salt in waste water, and D-galactose recycling during purification.

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