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MINI-REVIEW

L-Rhamnose isomerase and its use for biotechnological production of rare sugars

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Abstract L-Rhamnose isomerase (L-RI, EC 5.3.1.14), catalyzing the isomerization between L-rhamnose and L-rhamnulose, plays an important role in microbial L-rhamnose metabolism and thus occurs in a wide range of microorganisms. It attracts more and more attention because of its broad substrate specificity and its great potential in enzymatic production of various rare sugars. In this article, the enzymatic properties of various reported L-RIs were compared in detail, and their applications in the production of L-rhamnulose and various rare sugars including D-allose, D-gulose, L-lyxose, L-mannose, L-talose, and L-galactose were also reviewed.

Keywords L-Rhamnose isomerase · Rare sugar · D-Allose · Monosaccharide · Substrate specificity

Introduction

L-Rhamnose isomerase (L-RI, EC 5.3.1.14) is an aldose isomerase reversibly catalyzing the isomerization between L-rhamnose and L-rhamnulose. L-RI exists in a wide range of microorganisms due to its important role in L-rhamnose metabolism. L-RI exhibits very broad specificity toward various aldoses and ketoses and thus displays a great potential in biological production of many expensive rare sugars (Leang et al. 2004b). Rare sugars are defined by International Society of Rare Sugars as monosaccharides and their derivatives existing in nature in very limited quantities (Izumori 2002). Recently, plenty of literatures have focused on the unique physiological effects and medical potential of rare sugars, and they are proven to be of paramount significance in the food industry, nutraceuticals, pharmaceuticals, and other applications. D-Tagatose (Kim 2004), D-psicose (Mu et al. 2012), and some polyols have been formally approved by US Food and Drug Administration (FDA) as Generally Recognized As Safe (GRAS) and allowed to be used in food and medical industries.

Microbial L-RI has been used for enzymatic production of D-allose and various L-monosaccharides. D-Allose, a C3 epimer of D-glucose, has been proven to be of potential medical benefits, including cryoprotective (Sui et al. 2007), antioxidative (Nakamura et al. 2011), anti-hypertensive (Kimura et al. 2005), immunosuppressant (Hossain et al. 2000), anti-inflammatory (Gao et al. 2013), anti-tumor (Malm et al. 2015), and anti-cancer activities (Indo et al. 2014). L-form monosaccharides attract increasing attention because they can be potentially used as important starting materials to synthesize many high-value pharmaceutical compounds (Ahmed 2001). L-Sorbose has been used as the industrial precursor for chemical synthesis of L-ascorbic acid for decades (Pappenberger and Hohmann 2014) and was used as a substrate for synthesis of the potential glycosidase inhibitor 1-deoxygalactonojirimycin (Furneaux et al. 1993). L-Ribose is an important precursor for the synthesis of L-nucleoside analogs (Hu et al. 2011).

Although L-RI displays great potential for use in production of rare sugars, there is still no available literature reviewing the recent studies of L-RIs. In this work, all the reported microbial L-RIs are compared in detail, and the

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biotechnological production of various rare sugars by L-RI is reviewed.

Role in microbial sugar metabolism

L-Rhamnose is an important component of mycobacterial cell walls of some microorganisms (Southard et al. 1959). The anabolism and catabolism of L-rhamnose have been studied. It is normally generated by microorganism through D-fructose and D-mannose metabolism (Kanehisa and Goto 2000). L-RI plays a major role in microbial catabolism of L-rhamnose. Three structural genes are involved in L-rhamnose metabolism in *Escherichia coli*, including rhaA, rhaB, and rhaD, encoding L-RI, L-rhamnulose kinase (EC 2.7.1.5), and L-rhamnulose-1-phosphate aldolase (EC 4.1.2.19), respectively (Egan and Schleif 1993; Moralejo et al. 1993; Power 1967). L-RI catalyzes L-rhamnose to L-rhamnulose firstly; L-rhamnulose is further phosphorylated by L-rhamnulose kinase; and finally, L-rhamnose-1-phosphate is hydrolyzed by L-rhamnulose-1-phosphate aldolase to dihydroxyacetone phosphate and L-lactaldehyde (Fig. 1). The former product enters tricarboxylic acid (TCA) cycle for glycolysis. In *E. coli*, L-lactaldehyde is converted to L-lactate by lactaldehyde dehydrogenase (EC 1.2.1.22) under aerobic conditions, while it is reduced to L-1, 2-propanediol by propanediol oxidoreductase (EC 1.1.1.77) to be transported extracellularly (Baldoma and Aguilar 1988).

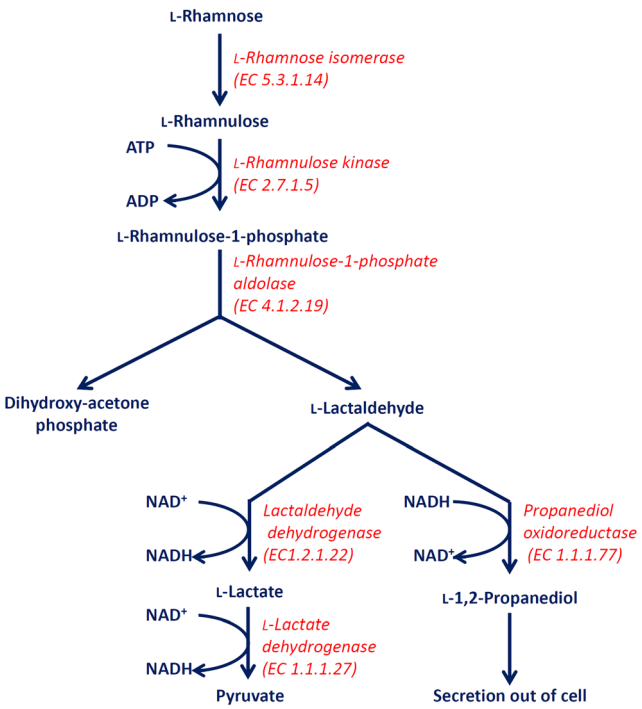

Fig. 1 Microbial catabolism of L-rhamnose

Comparison of various L-RIs

So far, L-RI has been characterized from *E. coli* (Takagi and Sawada 1964), *Lactobacillus plantarum* (Domagk and Zech 1966), *Pseudomonas* sp. strain LL172 (Bhuiyan et al. 1997b), *Pseudomonas stutzeri* (Leang et al. 2004b; Leang et al. 2004c), *Bacillus pallidus* Y25 (Poonperm et al. 2007), *Thermoanaerobacterium saccharolyticum* NTOU1 (Lin et al. 2010), *Thermotoga maritima* ATCC 43589 (Park et al. 2010), *Caldicellulosiruptor saccharolyticus* ATCC 43494 (Lin et al. 2011), *Bacillus halodurans* ATCC BAA-125 (Prabhu et al. 2011), *Mesorhizobium loti* Tono (Takata et al. 2011), *Dictyoglomus turgidum* DSMZ 6724 (Kim et al. 2013), *Bacillus subtilis* ATCC 23857 (Park 2014), and *B. subtilis* str. 168 (Bai et al. 2015). The enzymatic properties of the different L-RIs are listed in Table 1.

Comparison of the amino acid sequences

The comparison of amino acid sequences of various microbial L-RIs was shown in Table S1. Based on the comparison data, the L-RIs could be divided into two groups. Group I members, including L-RIs from *E. coli*, *B. halodurans* ATCC BAA-125, *B. subtilis* str. 168, *T. saccharolyticum* NTOU1, *C. saccharolyticus* ATCC 43494, and *B. pallidus* Y25 exhibited 40–80 % amino acid residue identity with each other. Group II members, including L-RIs from *P. stutzeri*, *M. loti* Tono, and *D. turgidum* DSMZ 6724 also displayed 40–80 % identity with each other. However, interestingly, relatively low identity (only 15–25 %) was shown between groups I and II members (Table S1). In addition, the phylogenetic tree of L-RIs also provided two regions with groups I and II members (Fig. 2). Multiple sequence alignment of various L-RIs was shown in Fig. S1. Although the reported L-RIs showed much difference in the residue sequence with each other, especially between groups I and II, there were still some residues that are completely identical in all of the displayed sequences. The crystal structures of L-RIs from *E. coli* (Korndorfer et al. 2000), *B. halodurans* ATCC BAA-125 (Doan et al. 2010), and *P. stutzeri* (Yoshida et al. 2007) have been determined and released in Protein Data Bank (PDB) database with no. of 1D8W, 3UXI, and 2I57. The available structural information suggested that L-RI catalyzes the isomerization by a metal-mediated hydride-shift mechanism, like D-xylose isomerase. According to the *E. coli* L-RI structure, two metal ions were observed. One was "structural" metal to help substrate binding, coordinated by Glu234, Asp267, His294, and Asp334, and the other was "catalytic" metal to help the hydride shift, coordinated by Asp294 and His262 (Korndorfer et al. 2000). It was found that these six residues were completely conserved in all reported L-RIs (Fig. S1).

Table 1 Comparison of biochemical properties of various L-RIs[a]

L-RI from	GenBank accession no.	Subunit molecular mass (kDa)	Total molecular mass (kDa)	Opt. pH	Opt. temp. (°C)	Opt. metal	Half-life (h, °C)	Reference
B. subtilis str. 168	CAB15096.1	48	NR	8.5	70	Mn^{2+}	6 h, 65°C 10 h, 60°C	Bai et al. 2015
B. subtilis ATCC 23857	NR	49	194	8.0	60	Mn^{2+}	~2 h, 70°C	Park 2014
D. turgidum DSMZ 6724	ACK41729.1	47	185	8.0	75	Mn^{2+}	4.5 h, 85°C 12.7 h, 80°C 28 h, 75°C 52.7 h, 70°C 71.3 h, 65°C	Kim et al. 2013
M. loti Tono	BAK52808.1	47	NR	9.0	60	Mn^{2+}	>1 h, 50°C	Takata et al. 2011
B. halodurans ATCC BAA-125	Q9LCL9	48	121	7.0	70	Mn^{2+}	0.08 h, 80°C 0.42 h, 70°C	Prabhu et al. 2011
C. saccharolyticus ATCC 43494	ABP66492.1	48	193.4	7.0	90	Co^{2+}	~1 h, 90°C	Lin et al. 2011
T. maritima ATCC 43589	NR	46	184	8.0	85	Mn^{2+}	773 h, 75°C	Park et al. 2010
T. saccharolyticum NTOU1	ADF43732.1	49	NR	7.0	75	Co^{2+}	>2 h, 75°C	Lin et al. 2010
B. pallidus Y25	BAF80456.1	48	NR	7.0	65	Mn^{2+}	1 h, 65°C	Poonperm et al. 2007
P. stutzeri	BAD14073.1	42	NR	9.0	60	Mn^{2+}	NR	Leang et al. 2004b; Leang et al. 2004c

[a] *NR* not reported

Effect of metal ions

In general, L-RIs require Mn^{2+} or Co^{2+} as a divalent metal cofactor for activation (Table 1). The three-dimensional structures of both *E. coli* (Korndorfer et al. 2000) and *P. stutzeri* L-RI (Yoshida et al. 2007; Yoshida et al. 2010) reveal the clear existence of metal-binding sites and bound metals, and the mechanism of aldose-ketose isomerization by L-RI has been proposed as a metal-mediated hydride-shift biocatalysis process based on the reported structure information.

Effect of pH

The L-RIs from *B. halodurans* ATCC BAA-125 (Prabhu et al. 2011), *C. saccharolyticus* ATCC 43494 (Lin et al. 2011), *T. saccharolyticum* NTOU1 (Lin et al. 2010), and *B. pallidus* Y25 (Poonperm et al. 2007) showed pH optima at neutral pH (7.0), and others showed pH optima at slightly alkaline side up to pH 9.0 (Table 1). However, for practical applications, aldose isomerases are expected to have slightly acidic pH optima, because acidic pH conditions may reduce non-enzymatic browning reaction leading to the unwanted byproducts (Friedman 1996). Many researches have focused on the isolation of acidic aldose isomerase and ketose epimerases or the molecular modification to reduce the pH optima of these enzymes, such as D-glucose isomerase (Bhosale et al. 1996), L-arabinose isomerase (Fan et al. 2015; Xu et al. 2014), and D-psicose epimerase (Zhang et al. 2015).

Effect of temperature

A major consideration for the practical use of biotransformation is the development and improvement of the satisfied enzymes (Polizzi et al. 2007; Plou and Ballesteros 1999). Reaction at high temperatures can enhance the solubility of substrates and products, provide a higher reaction rate, and reduce the microbial contamination (Mozhaev 1993).

As shown in Table 1, most of the L-RIs show highest activities at relatively high temperatures (not less than 60 °C); however, significant difference of thermostability is seen among different sources of L-RIs. The one from *M. loti* Tono retains 70 % of initial activity after incubation at 50 °C for 1 h (Takata et al. 2011). The ones from *B. pallidus* Y25 (Poonperm et al. 2007) and *B. subtilis* str. 168 (Bai et al. 2015) show half-lives at 65 °C of 1 and 6 h, respectively. The one from *B. halodurans* ATCC BAA-125 can retain >90 % of activity after 15 h of incubation at 60 °C but only shows half-lives at 70 and 80 °C of 25 and 5 min, respectively (Prabhu et al. 2011). The one from *B. subtilis* ATCC 23857 has a half-life of approximately 2 h at 70 °C (Park 2014). By comparison, the ones from some thermophiles exhibit very good thermostability (Table 1). The half-lives of *D. turgidum* L-RI at 75, 80, and 85 °C are 28, 12.7, and

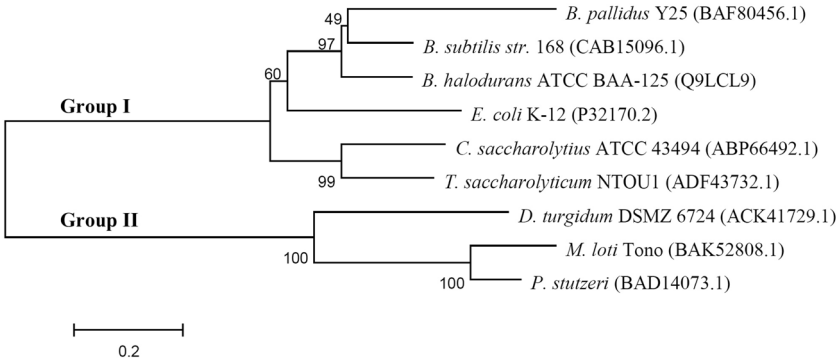

Fig. 2 A phylogenetic tree of the already identified L-RIs with known GenBank accession number. The tree was generated by the neighbor-joining method using ClustalW software. The amino acid substitution per position was indicated by scale bar. The bootstrap values were indicated by the numbers on each clade. The GenBank numbers of various enzymes were shown after each microbial source of L-RI

4.5 h, respectively (Kim et al. 2013). The one from *T. maritima* ATCC 43589 has a half-life of 773 h at 75 °C (Park et al. 2010). The one from *C. saccharolyticus* ATCC 43494 is strongly stable at 80 and 85 °C and exhibits a half-life of 65 min at 90 °C (Lin et al. 2011).

Substrate specificity and kinetics

L-RI has recently attracted much attention due to its wide substrate specificity toward various aldoses and ketoses and its potential applications for production of various rare sugars (Tables 2 and 3). All the reported L-RIs showed the optimum substrate as L-rhamnose, and among them, the *C. saccharolyticus* L-RI had the highest specific activity (380 U mg^{-1}) toward L-rhamnose. L-Lyxose was the second favored substrate of the reported L-RIs because L-lyxose had similar configuration with L-rhamnose, and the enzyme from *T. saccharolyticum* NTOU1 showed much higher specific activity (130 U mg^{-1}) toward L-lyxose than other L-RIs.

E. coli L-RI was specific for L-rhamnose, L-lyxose, and L-mannose (Korndorfer et al. 2000) while it showed null activity toward D-allose and D-ribose, but other reported L-RIs had broader specificity including D-allose and D-ribose (Table 2). From the crystal structure information, both *E. coli* (Korndorfer et al. 2000) and *P. stutzeri* (Yoshida et al. 2007) L-RIs showed highly conserved amino acid residues involved in the interactions between the protein and the O1, O2, and O3 of the L-rhamnose, which were responsible for the metal-binding and catalytic mechanism, while significant structural differences were found in the recognition of the atoms at 4, 5, and 6 positions of the substrate, which were responsible for the substrate specificity. In *E. coli* L-RI, Val53, Leu63, Ile67, and Phe336 created a unique hydrophobic pocket to recognize the substrate and it thus led to the narrow substrate specificity (Korndorfer et al. 2000). The residues of *P. stutzeri* L-RI involved in the interactions with substrate at 4, 5, and 6 positions (Yoshida et al. 2007) were interestingly very highly conserved compared to *Astragalus missouriensis* D-xylose isomerase (Jenkins et al. 1992), which had relatively loose substrate recognition and was able to isomerize a wide variety of substrates.

The comparison of kinetic parameters of various reported L-RIs was shown in Table 3. The L-RI from *B. subtilis* str. 168 exhibited the lowest K_m (0.49 mM) toward L-rhamnose (Bai et al. 2015); however, the enzyme from *C. saccharolyticus* ATCC 43494 showed the highest catalytic efficiency (k_{cat}/K_m) toward L-rhamnose, which reached 100.32 mM^{-1} s^{-1} (Lin et al. 2011). In addition, the kinetic parameters toward various substrates significantly varied among various reported L-RIs (Table 3).

Biotechnological applications of L-RI for production of rare sugars

Production of D-allose from D-psicose

As mentioned above, the rare sugar D-allose attracts increasing attention because of its physiological effects and commercial interest. D-Allose can be produced from another rare sugar D-psicose, which is easily produced from D-fructose by ketose 3-epimerase (Mu et al. 2012). Bioconversion of D-psicose to D-allose can be catalyzed by D-galactose-6-phosphate isomerase, D-ribose-5-phosphate isomerase, and L-RI (Mu et al. 2015). *Lactococcus lactis* D-galactose-6-phosphate isomerase efficiently converts D-psicose to D-allose and D-altrose (Park et al. 2007b). The reported D-allose-producing D-ribose-5-phosphate isomerases include the ones from *Clostridium thermocellum* (Park et al. 2007a), *Clostridium difficile* (Yeom et al. 2010), *Thermotoga maritime* (Yeom et al. 2010), and *Thermotoga lettingae* TMO (Feng et al. 2013), and they generate no byproduct but only D-allose from D-psicose.

The biological production of D-allose was first reported using L-RI from *P. stutzeri* LL172 (Bhuiyan et al. 1997b). The immobilized whole cells of *P. stutzeri* were used to convert D-psicose to within 20 days, with the conversion yield of 40 % (Bhuiyan et al. 1998). D-Allose production was also performed by the recombinant *P. stutzeri* L-RI, which was immobilized by cross-linking with glutaraldehyde and L-lysine; however, it produced 25 % D-allose together with 8 % D-altrose as byproduct from D-psicose after bioconversion and ethanol crystallization (Menavuvu et al. 2006). Large-scale

Table 2 Specific activities (U mg^{-1}) of L-RIs from different bacterial sources for various substrates[a]

Substrate	*B. pallidus* Y25	*T. maritima* ATCC 43589	*P. stutzeri*	*B. subtilis* ATCC 23857	*T. saccharolyticum* NTOU1	*M. loti*	*C. saccharolyticus* ATCC 43494
L-Rhamnose	77.2	55	244	3.58	203	76.1	380
L-Lyxose	19.3	203	110	2.58	130	60.9	65
L-Mannose	4.52	15	81.6	0.92	6	2.27	38
D-Allose	2.58	6.7	7.5	0.467	5.7	3.03	21
D-Ribose	6.33	2.8	16	0.094	1.6	7.53	4.9
D-Glucose	NR	5.3	0.01	0.136	NR	NR	NR
D-Xylose	NR	NR	1.2	NR	NR	NR	NR
D-Arabinose	NR	NR	0.07	NR	NR	6.92×10^{-3}	NR
D-Altrose	NR	NR	0.02	NR	NR	NR	NR
L-Xylose	NR	NR	0.007	NR	NR	6.56×10^{-3}	NR
L-Talose	NR	NR	NR	0.029	NR	5.23	NR
Reference	Poonperm et al. 2007	Park et al. 2010	Leang et al. 2004b	Park 2014	Lin et al. 2010	Takata et al. 2011	Lin et al. 2011

[a] *NR* not reported

production of D-allose from D-psicose was performed using a continuous column bioreactor containing the recombinant *P. stutzeri* L-RI immobilized on BCW-2510 Chitopearl beads. When 50 % (*W*/*W*) D-psicose was applied to the column, approximately 30 % D-psicose was isomerized to D-allose for 17 days but still with a very small amount of byproducts (Morimoto et al. 2006).

Enzymatic production of D-allose from D-psicose has also been studied using the L-RIs from *B. pallidus* Y25 (Poonperm et al. 2007), *T. saccharolyticum* NTOU1 (Lin et al. 2010), *C. saccharolyticus* ATCC 43494 (Lin et al. 2011), and *B. subtilis* str. 168 (Bai et al. 2015), and they produce D-allose without any byproduct, with maximal conversion yield of 35, 34, 33, and 37.5 %, respectively.

Enzymatic production of D-gulose from D-sorbose

D-Gulose has been produced from D-sorbose by both the free (Leang et al. 2004b) and the immobilized P. stutzeri L-RI (Bhuiyan et al. 1999), with the same of conversion yield of 10 %.

Enzymatic production of L-sugars

L-Rhamnulose

L-Rhamnulose (6-deoxy-L-sorbose) is a precursor of the strawberry aroma furaneol and has been used in the flavor industry (Hecquet et al. 1996). Most of L-RIs show the optimal substrate as L-rhamnose producing L-rhamnulose. Free L-RI from *B. pallidus* Y25 produces L-rhamnulose from L-rhamnose with a turnover ratio of 45 % (Poonperm et al. 2007). L-Rhamnulose has also been continuously produced by immobilized L-RI from *D. turgidum* DSMZ 6724 in a packed bed bioreactor, and an average of 130 g L^{-1} L-rhamnulose can be produced from 300 g L^{-1} L-rhamnose, with a productivity of 78 g L^{-1} h^{-1} and a conversion yield of 43 % (Kim et al. 2013).

L-Lyxose

The recombinant *P. stutzeri* L-RI catalyzed the isomerization of L-xylose to L-xylulose and L-lyxose, with the final equilibrium between L-xylose/L-xylulose/L-lyxose of 61:35:4 (Leang et al. 2004b); however, the equilibrium ratio was 26:53:21 when the same enzyme was used in immobilized form using L-xylulose as substrate (Granstrom et al. 2005). The immobilized recombinant *P. stutzeri* L-RI produced 4.06 g L^{-1} L-lyxose and 4.94 g L^{-1} L-xylose from 19.2 g L^{-1} L-xylulose (Granstrom et al. 2005). Unlike *P. stutzeri* L-RI, the ones from *B. subtilis* ATCC 23857 (Park 2014) and *T. maritima* ATCC 43589 (Park et al. 2010) produced L-lyxose from L-xylulose without any byproduct, and the final equilibrium ratio between L-lyxose and L-xylulose was 40:60 and

Table 3 Comparison of kinetic parameters of L-RIs from various bacterial sources

	Substrate	*B. pallidus*[a]	*T. maritima*	*P. stutzeri* [a]	*B. subtilis* ATCC 23857	*B. subtilis* str. 168	*T. saccha-rolyticum*	*D. turgidum*	*B. halodurans*[a]	*M. loti* [a]	*C. saccharolyticus*
K_m (mM)	L-Rhamnose	4.89	37	11	53	0.49	3.53	24.6	528	5	1.03
	L-Mannose	28.9	76	54	97	8.01	58.9	36.8	119	23.4	3.64
	L-Lyxose	16.1	69	61	86	NR [b]	45.2	33.4	771	23.5	3.65
	D-Allose	41.8	NR	42	NR	5.98	121	61.5	NR	7.11	14.3
	D-Ribose	34.9	NR	38	NR	8.64	148	54.5	NR	6.18	33.5
	L-Xylulose	NR	111	NR	NR	NR	NR	63.0	NR	NR	NR
	L-Fructose	NR	123	NR	NR	NR	NR	73.2	NR	NR	NR
k_{cat} (s^{-1})	L-Rhamnose	68	146	171.67	153	7.72	179.32	195	149.52	50.5	99.9
	L-Mannose	76.83	442	89.67	37	10.49	30.04	155	88.88	9.98	78.7
	L-Lyxose	31	462	100.33	53	NR	240	200	216	73.83	186
	D-Allose	34.5	NR	5.02	NR	0.72	33.9	81	NR	1.33	68.1
	D-Ribose	14.18	NR	15.77	NR	30.76	21.5	49	NR	4.73	118
	L-Xylulose	NR	281	NR	NR	NR	NR	130	NR	NR	NR
	L-Fructose	NR	274	NR	NR	NR	NR	116	NR	NR	NR
k_{cat}/K_m (mM^{-1} s^{-1})	L-Rhamnose	13.91	3.94	15.61	2.88	15.76	20.8	7.93	0.28	10.1	100.32
	L-Mannose	2.66	5.82	1.67	0.381	1.31	0.51	4.21	0.75	0.43	21.63
	L-Lyxose	1.93	6.70	1.664	0.62	NR	5.3	5.99	0.28	3.14	51.14
	D-Allose	0.83	NR	0.12	NR	NR	0.28	1.33	NR	0.19	4.765
	D-Ribose	0.41	NR	0.415	NR	3.56	0.15	0.90	NR	0.77	3.525
	L-Xylulose	NR	2.53	NR	NR	NR	NR	2.065	NR	NR	NR
	L-Fructose	NR	2.23	NR	NR	NR	NR	1.59	NR	NR	NR
Reference		Poonperm et al. 2007	Park et al. 2010	Leang et al. 2004b	Park 2014	Bai et al. 2015	Lin et al. 2010	Kim et al. 2013	Prabhu et al. 2011	Takata et al. 2011	Lin et al. 2011

[a] The values were recalculated based on the original references after unit conversion

NR not reported

45:55, respectively. The *B. subtilis* ATCC 23857 L-RI produced 40 g L^{-1} L-lyxose from 100 g L^{-1} L-xylulose (Park 2014), and the one from *T. maritima* ATCC 43589 produced 225 g L^{-1} L-lyxose from 500 g L^{-1} L-xylulose (Park et al. 2010).

L-Mannose

The enzymatic production of L-mannose from L-fructose was first studied using immobilized *P. stutzeri* L-RI with turnover yield of 30 % (Bhuiyan et al. 1997a). Recently, L-mannose production was also reported using free L-RIs from *B. subtilis* ATCC 23857 and *T. maritima* ATCC 43589. Twenty-five grams per liter of L-mannose was produced from 100 g L^{-1} L-fructose by 15 U mL^{-1} *B. subtilis* L-RI after 80 min (Park 2014), while 175 g L^{-1} L-mannose was produced from 500 g L^{-1} L-fructose by 100 U mL^{-1} *T. maritima* L-RI after 5 h (Park et al. 2010).

L-Talose

Enzymatic production of L-talose from L-tagatose was performed by *P. stutzeri* L-RI immobilized on Chitopearl beads BCW 2603 (Bhuiyan et al. 1999) and *M. loti* L-RI immobilized on BCW 2510 (Takata et al. 2011), and both could convert L-tagatose to L-talose with production yield of 12 %. *P. stutzeri* L-RI produced L-galactose as byproduct (Leang et al. 2004b), while *M. loti* L-RI produces no byproduct but only L-talose from L-galactose (Takata et al. 2011).

L-Galactose

Leang et al. reported the production of L-galactose from L-tagatose by *P. stutzeri* L-RI immobilized on BCW 2510, and the conversion ratio was 60:30:10 (L-tagatose/L-galactose/L-talose) at equilibrium. In addition, the authors also performed the L-galactose from L-sorbose by two reactions catalyzed by D-tagatose 3-epimerase followed by *P. stutzeri* L-RI, with an overall yield of 7.5 % L-galactose obtained from L-sorbose (Leang et al. 2004a).

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Compliance with ethical standards This article does not contain any studies with human participants or animals performed by any of the authors.

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