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Editorial

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Rare Sugars: Applications and Enzymatic Production

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Rare sugars are monosaccharides and their derivatives rarely existing in nature. Of all hexoses and pentoses, only seven (D-glucose, D-galactose, D-mannose, D-fructose, D-xylose, D-ribose and L-arabinose) are present in significant amounts in nature. Despite their low natural abundance, rare sugars have various known biological functions and enormous potential for applications in pharmaceutical, cosmetics, food and flavour industries [1-4]. For example, D-tagatose is a low-calorie sweetener used in food, beverage and diet supplement [5,6]. It was approved as a food additive by the FDA in 2003. Recently D-tagatose has also been proved to be a potentially important drug for treating type 2 diabetes [7,8]. L-nucleoside analogues show increased antiviral activity and good metabolic stability. Some rare sugars are used as building blocks to synthesize the nucleoside analogues which are used as antiviral and anticancer agents [9]. For example, L-ribose, the enantiomer of D-ribose, is used to prepare clevudine, an anti-hepatitis B virus drug [10,11]. L-xylose is use to synthesize 9-(2-deoxy-2-fluro-b-L-arabinofuranosyl) purine nucleosides with anti-hepatitis B virus activity [12]. L-gulose and L-galactose can also be used to produce L-nucleosides [13,14]. D-allose has attracted much attention in recent years due to its various biological functions such as anti-tumor, anti-inflammatory, anti-oxidative and immunosuppressant activities [15]. Rare sugars can also be used as starting materials to synthesize other valuable compounds. For example, D-arabinose is used to synthesize antitumor compounds, such as dehydroamino acid derivatives [16,17].

Because rare sugars occur only in small amounts in nature, their properties have not been fully studied. The research of their synthesis becomes important because it will lead to further evaluation and application of rare sugars. Carbohydrates contain multiple chiral carbons, so their chemical synthesis processes are tedious and time-consuming. The enzyme approach is particular powerful in carbohydrate synthesis due to the high stereospecificity of enzyme catalysis. Prof. Ken Izumori from Kagawa University developed the strategies for preparing all hexoses from the inexpensive sugar glucose [18,19]. In Izumoring strategy, the interconversion of monosaccharides is realized by oxidoreductases, aldose isomerases, D-tagatose 3-epimerase and aldose reductases. The synthesis route of a target rare sugar can be easily designed according to Izumoring strategy. The Izumoring strategy was further updated by adding synthesis strategies of pentoses by Beerens et al. [20]. However, because rare sugars are unnecessary for organisms, in many cases they are the minor products of the enzyme reactions, which implicates that the production of rare sugars is not high enough and can be further improved by enhancing the catalysis efficiency of the enzymes. For example, the D-tagatose manufacturing process includes galactose isomerization by L-arabinose isomerase. As galactose is not the most efficient substrate for L-arabinose isomerase, the yield of D-tagatose needs to be further improved by engineering the substrate binding pocket of the enzyme [21]. In order to produce substantial quantities of rare sugars for further evaluation of their properties or for new applications discovery, the relatively low activities of their synthetic enzymes need to be engineered.

Directed evolution strategies have been proved to be a powerful tool in enhancing the activity or substrate selectivity of various enzymes. It has also been applied in rare sugar synthetic enzyme engineering. Directed evolution of L-arabinose isomerase has yielded the enzyme mutant with 68% increase in isomerization activity for D-galactose [22]. Engineering the recombinant NAD-dependent mannitol-1-dehydrogenase from *Apium graveolens* with random mutagenesis method has improved the thermal stability of this enzyme and thereby improved the production of L-gulose and L-galactose from D-sorbitol and galactitol, respectively [13]. However, so far directed evolution strategy has not been widely used in improving rare sugar production. Engineering enzymes in rare sugar synthesis routes to improve the yield of the rare sugars will become the next important field in rare sugar study.

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References

1. Mu W, Zhang W, Feng Y, Jiang B, Zhou L (2012) Recent advances on applications and biotechnological production of D-psicose. Appl Microbiol Biotechnol 94: 1461-1467.
2. Hoshikawa H, Indo K, Mori T, Mori N (2011) Enhancement of the radiation effects by D-allose in head and neck cancer cells. Cancer Lett 306: 60-66.
3. Granström TB, Izumori K, Leisola M (2007) A rare sugar xylitol. Part II: biotechnological production and future applications of xylitol. Appl Microbiol Biotechnol 74: 273-276.
4. Levin GV, Zehner LR, Saunders JP, Beadle JR (1995) Sugar substitutes: their energy values, bulk characteristics, and potential health benefits. Am J Clin Nutr 62: 1161S-1168S.
5. Oh DK (2007) Tagatose: properties, applications, and biotechnological processes. Appl Microbiol Biotechnol 76: 1-8.
6. Levin GV (2002) Tagatose, the new GRAS sweetener and health product. J Med Food 5: 23-36.
7. Lu Y, Levin GV, Donner TW (2008) Tagatose, a new antidiabetic and obesity control drug. Diabetes Obes Metab 10: 109-134.
8. Espinosa I, Fogelfeld L (2010) Tagatose: from a sweetener to a new diabetic medication? Expert Opin Investig Drugs 19: 285-294.
9. Gumina G, Song GY, Chu CK (2001) L-Nucleosides as chemotherapeutic agents. FEMS Microbiol Lett 202: 9-15.
10. Chu CK, Ma T, Shanmuganathan K, Wang C, Xiang Y, et al. (1995) Use of 2'-fluoro-5-methyl-beta-L-arabinofuranosyluracil as a novel antiviral agent for hepatitis B virus and Epstein-Barr virus. Antimicrob Agents Chemother 39: 979-981.
11. Mathé C, Gosselin G (2006) L-nucleoside enantiomers as antivirals drugs: a mini-review. Antiviral Res 71: 276-281.
12. Ma T, Lin JS, Newton MG, Cheng YC, Chu CK (1997) Synthesis and anti-hepatitis B virus activity of 9-(2-deoxy-2-fluoro-beta-L-arabinofuranosyl) purine nucleosides. J Med Chem 40: 2750-2754.
13. Woodyer RD, Christ TN, Deweese KA (2010) Single-step bioconversion for the preparation of L-gulose and L-galactose. Carbohydr Res 345: 363-368.

doi:http://dx.doi.org/10.4172/jbcbt.1000e105

14. Jeong LS, Schinazi RF, Beach JW, Kim HO, Nampalli S, et al. (1993) Asymmetric synthesis and biological evaluation of beta-L-(2R,5S)- and alpha-L-(2R,5R)-1,3-oxathiolane-pyrimidine and -purine nucleosides as potential anti-HIV agents. J Med Chem 36: 181-195.

15. Lim YR, Oh DK (2011) Microbial metabolism and biotechnological production of D-allose. Appl Microbiol Biotechnol 91: 229-235.

16. Moran EJ, Tellew JE, Zhao Z, Armstrong RW (1993) Dehydroamino acid derivatives from D-arabinose and L-serine: synthesis of models for the azinomycin antitumor antibiotics. J Org Chem 58: 7848-7859.

17. Yoshikawa M, Murakami N, Inoue Y, Hatakeyama S, Kitagawa I (1993) A new approach to the synthesis of optically active pseudo-sugar and pseudo-nucleoside: synthesis of pseudo-α-D-arabinofuranose, (+)-cyclaradine, and (+)-1, pseudo-β-D-arabinofuranosyluracil from D-arabinose. Chem Pharm Bull (Tokyo) 41: 636-638.

18. Izumori K (2006) Izumoring: a strategy for bioproduction of all hexoses. J Biotechnol 124: 717-722.

19. Granström TB, Takata G, Tokuda M, Izumori K (2004) Izumoring: a novel and complete strategy for bioproduction of rare sugars. J Biosci Bioeng 97: 89-94.

20. Beerens K, Desmet T, Soetaert W (2012) Enzymes for the biocatalytic production of rare sugars. J Ind Microbiol Biotechnol 39: 823-834.

21. Kim P (2004) Current studies on biological tagatose production using L-arabinose isomerase: a review and future perspective. Appl Microbiol Biotechnol 65: 243-249.

22. Kim HJ, Kim JH, Oh HJ, Oh DK (2006) Characterization of a mutated *Geobacillus stearothermophilus* L-arabinose isomerase that increases the production rate of D-tagatose. J Appl Microbiol 101: 213-221.

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