Applied Microbiology and Biotechnology (2018) 102:8145–8152
https://doi.org/10.1007/s00253-018-9241-9

MINI-REVIEW

Recent progress on biological production of α-arbutin

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Received: 18 May 2018 / Revised: 11 July 2018 / Accepted: 11 July 2018 / Published online: 21 July 2018

Abstract

Arbutin, a glucoside of hydroquinone, is used as a powerful skin lightening agent in the cosmeceutical industry because of its strong inhibitory effect on the human tyrosinase activity. It is a natural compound occurring in a number of plants, with a β-anomeric form of the glycoside bond between glucose and hydroquinone. α-Arbutin, which glycoside bond is generated with α-anomeric form, is the isomer of natural arbutin. α-Arbutin is generally produced by transglucosylation of hydroquinone by microbial glycosyltransferases. It is interesting that α-arbutin is found to be over 10 times more effective than arbutin, and thus biological production of α-arbutin attracts increasing attention. Seven different microbial enzymes have been identified to be able to produce α-arbutin, including α-amylase, sucrose phosphorlase, cyclodextrin glycosyltransferase, α-glucosidase, dextransucrase, amylosucrase, and sucrose isomerase. In this work, enzymatic and microbial production of α-arbutin is reviewed in detail.

Keywords Arbutin · Glucoside · Glycosyltransferase · Transglucosylation · Tyrosinase inhibitor

Introduction

Arbutin (4-hydroxyphenyl β-D-glucopyranoside, CAS No. 497-76-7) is a natural glucoside of hydroquinone occurring in a number of plants and refers in particular to the glucoside with a β-anomeric form of the glycoside bond between glucose and hydroquinone. α-Arbutin (4-hydroxyphenyl α-D-glucopyranoside, CAS No. 84380-01-8), the isomer of arbutin with an α-anomeric form of the glycoside bond, is unnatural and can be biosynthesized by microorganisms or microbial enzymes.

Arbutin is traditionally used as a urinary antiseptic and diuretic for treating urinary tract infections (Gemot et al. 2002), kidney stones, and cystitis (Abascal and Yarnell 2008). It also shows anti-oxidative (Ioku et al. 1992; Bang et al. 2008), antimicrobial (Jurica et al. 2017; Tabata et al. 1982), and anti-inflammatory effects (Lee and Kim 2012). More importantly, arbutin has been widely used as a powerful skin lightening agent in cosmeceutical industry due to its strong inhibitory effect on the tyrosinase activity (Han et al. 2014). Tyrosinase (EC 1.14.18.1) plays a crucial role in controlling melanin generation as a rate-limiting enzyme (Kanteev et al. 2015). It is a multifunctional oxidase and initiates two rate-limiting steps in melanogenesis, by catalyzing the hydroxylation of tyrosine to β-3,4-dihycroxyphenylalanine (DOPA) firstly and the subsequent oxidation of DOPA to DOPA quinine. DOPA quinine is eventually converted to melanin by several further reactions. A number of tyrosinase inhibitors have been identified from both natural and synthetic sources and commercially used for melanin-reducing and skin-whitening effects in the cosmeceutical industry (Chang 2009). Arbutin is the most prominent natural compound used as an effective skin-lightening agent commercially because it prevents melanin formation without melanocytotoxicity effect, compared to traditional depigmenting compounds such as hydroquinone and kojic acid (Maeda and Fukuda 1996; Zhu and Gao 2008).

Arbutin is a natural compound occurring in a number of edible berry-producing plants such as blueberry, cranberry, marjoram, and most pear species (Cho et al. 2011b; Lukas et al. 2010; Pop et al. 2009). It is generally extracted from the fruit peels and the leaves of various plants (Cho et al. 2011b; Lee and Eun 2009; Pop et al. 2009). Recently, plant cell culture methods are widely studied for exogenous biosynthesis of arbutin from hydroquinone by using various plant cells, including *Ruta graveolens* L., *Hypericum perforatum* L. (Piekoszewska et al. 2010), *Aronia melanocarpa* (Kwiecien et al. 2013), *Ruta graveolens* ssp. *divaricate* (Skrzypczak-

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Pietraszek et al. 2005), *Rauwolfia serpentine* (Lutterbach and Stockigt 1992), and *Catharanthus roseus* (Inomata et al. 1991). An arbutin synthase (EC 2.4.1.218) from *R. serpentine* was expressed in *Escherichia coli* and identified as a novel member of the Class IV glycosyltransferases belonging to the Nucleotide Recognition Domain type 1β (NRD1β) family of glycosyltransferases. It is a unique multifunctional enzyme for converting various natural products and xenobiotics. It shows broad acceptor substrate specificity with the highest activity toward hydroquinone, but uses only pyrimidine nucleotide activated glucose as a donor substrate with the highest activity toward uridine diphosphate glucose (UDPG) (Hefner et al. 2002). In plant, arbutin is generally produced from hydroquinone and UDPG by arbutin synthase (Fig. 1). An engineered *E. coli* was constructed for high-level biosynthesis of arbutin by introducing two exogenous genes, a 4-hydroxybenzoate 1-hydroxylase from *Candida parapsilosis* CBS604 and an arbutin synthase from *R. serpentina*. This work provides an efficient approach to produce plant-derived arbutin in an engineered microorganism (Shen et al. 2017).

Arbutin is produced from plant sources; however, α-arbutin is generally produced by microorganisms or microbial glycosyltransferases (Fig. 2). Interestingly, α-arbutin is much more effective than natural arbutin for inhibiting tyrosinase activity. The 50% inhibitory concentration (IC_{50}) of α-arbutin on human tyrosinase is 2.0 mM, whereas that of natural arbutin is higher than 30 mM (Kazuhisha et al. 2007; Sugimoto et al. 2003). Inhibitory effects of α-arbutin on melanin biosynthesis were examined in cultured human melanoma cells and a human skin model, and the results showed that α-arbutin efficiently inhibited melanin synthesis without cytotoxicity effect (Kazuhisha et al. 2007; Sugimoto et al. 2004). Therefore, biosynthesis of α-arbutin has attracted increasing attention. In this work, biosynthesis of α-arbutin by enzymatic transglucosylation and microbial techniques were reviewed in detail.

Enzymatic production of α-arbutin by transglucosylation

As early as 60 years ago, α-arbutin was successfully synthesized by the chemical reaction of penta-*O*-acetyl-β-D-glucopyranose and hydroquinone under high temperature and reduced pressure with a yield of 16% (Tatsuo et al. 1952). Chemical synthesis of α-arbutin generally results in some disadvantages including low regioselectivity, vigorous reaction conditions, and formation of by-products (Seo et al. 2012b). α-Arbutin is able to be efficiently produced by enzymatic transglucosylation. At least seven different kinds of microbial enzymes have been used for α-arbutin biosynthesis. They all use hydroquinone as an acceptor substrate, and different enzyme uses different glucosyl donor substrate for α-arbutin biosynthesis (Fig. 2 and Table 1).

Sucrose phosphorlase

Sucrose phosphorlase (EC 2.4.1.7) catalyzes the reversible conversion of sucrose and phosphate to fructose and glucose-1-phosphate. It is a member of glycosyltransferases and belongs to GH13 enzymes, and catalyzes transglucosylation in addition to phosphorolysis (Sugimoto et al. 2008). When acting as a glycosyltransferase, sucrose phosphorlase has a strict glycosyl donor substrate specificity and transfers glucose moiety from only sucrose, glucose-1-phosphate, and glucose-1-fluoride. However, it shows a rather broad glucosyl acceptor specificity and transfers the glucosyl residue to various acceptors such as sugars and sugar alcohols (Kitao and Sekine 1992). It is also able to catalyze the glucosylation of some carboxylic acid compounds, including benzoic acid (Sugimoto et al. 2007) and acetic acid (Nomura et al. 2008).

Sucrose phosphorlase is the first enzyme used for studying enzymatic biosynthesis of α-arbutin. In 1994, Kitao and Sekine studied α-glucosyl transfer to phenolic compounds by *Leuconostoc mesenteroides* sucrose phosphorlase and found that the enzyme was able to transfer the glucosyl residue to all 23 kinds of tested phenolic and related compound substrates. It showed high transfer efficiency toward hydroquinone for α-arbutin production and the transfer ratio in molar reached approximately 65% after optimization of transglycosylation (Kitao and Sekine 1994).

α-Amylase

α-Amylase (EC 3.2.1.1), a member of glycosyl hydrolase family 13 (GH13), catalyzes the hydrolysis of internal α-1,4-glycosidic linkages in starch and converts starch to glucose, maltose, and short-chain oligosaccharides. Some α-amylases exhibit glucosyl transfer activity to both starch hydrolysis products (maltooligosaccharides, MOS) and non-carbohydrate chemical compounds as glucosyl acceptors (Moreno et al. 2010). *Trichoderma viride* α-amylase shows glucosyl transfer activity toward a wide variety of flavonoids

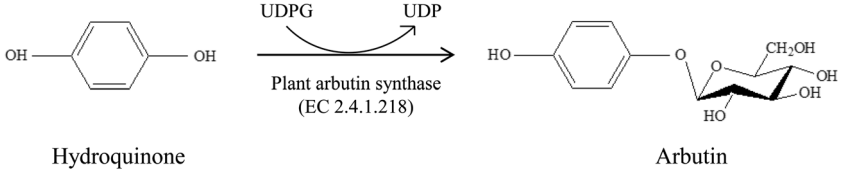

Fig. 1 Arbutin biosynthesis by arbutin synthase in plants

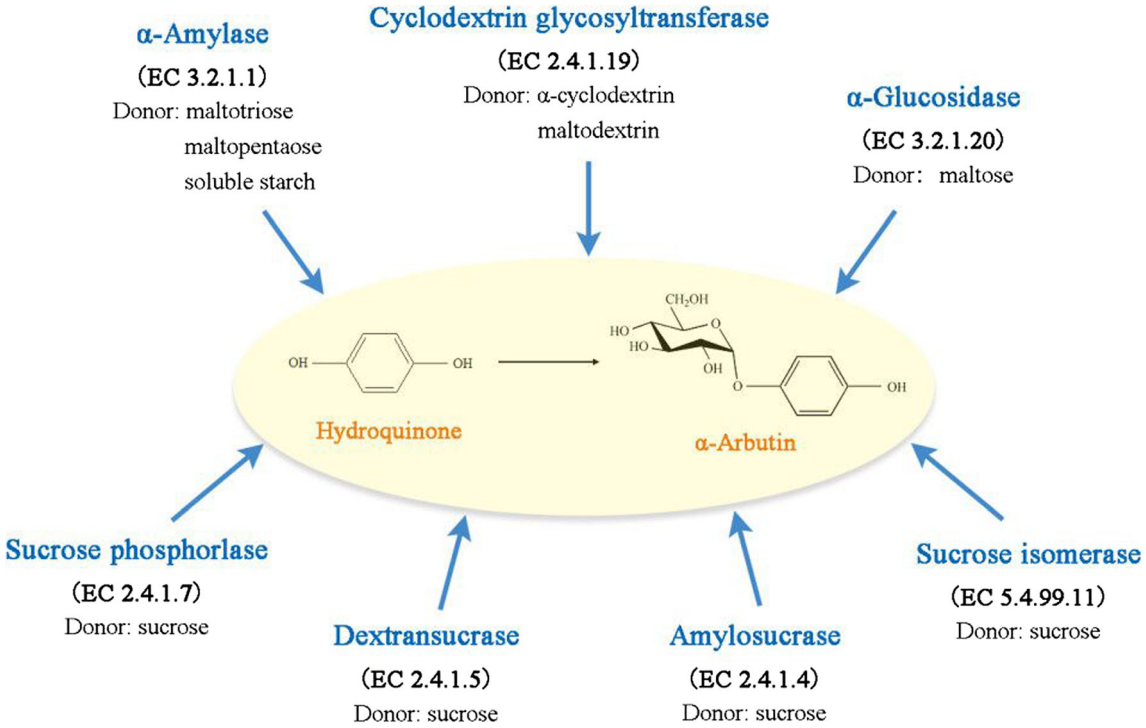

Fig. 2 Biological production of α-arbutin from hydroquinone by various microbial enzymes

and coumarin. Epigallocatechin gallate (EGCG) is the optimum acceptor among the tested ones, and the enzyme also shows appreciable activities toward daidzein, (+)-catechin, quercetin, genistein, naringenin, esculetin, and kaempferol (Noguchi et al. 2008). *Aspergillus oryzae* α-amylase is able to synthesize alkyl glycosides from starch and alcohols through glucosyltransferation (Larsson et al. 2005). Stevia is used as glucosyl acceptor to produce stevia glycosides by *A. oryzae* α-amylase (Ye et al. 2014). In addition, *Bacillus subtilis* α-amylase displays efficient catalytic activity for glucosylation of caffeic acid (Nishimura et al. 1995) and kojic acid (Nishimura et al. 1994).

Table 1 Enzymatic synthesis of α-arbutin from hydroquinone by various microbial enzymes

Enzyme	Microbial source	Donor	Hydroquinone	Molar yield (%)	Reference
Sucrose phosphorlase	*L. mesenteroides*	Sucrose (500 g L^{-1})	10 g L^{-1}	~65	Kitao and Sekine 1994
α-Amylase	*B. subtilis* X-23	Soluble starch (100 g L^{-1})	20 g L^{-1}	32.4	Nishimura et al. 1994
		Maltopentaose (100 g L^{-1})	20 g L^{-1}	24.8	
		Maltotriose (100 g L^{-1})	20 g L^{-1}	22.4	
		Maltose (100 g L^{-1})	20 g L^{-1}	9	
CGTase	*Thermoanaerobacter* sp.	α-Cyclodextrin (50 g L^{-1})	9.08 mM	23.3	Mathew and Adlercreutz 2013
		Maltodextrin (50 g L^{-1})	9.08 mM	21.7	
		Maltotriose (50 g L^{-1})	9.08 mM	20.0	
		Maltose (50 g L^{-1})	9.08 mM	15.7	
α-Glucosidase	*X. campestris* WU-9701[a]	Maltose (1.2 M)	45 mM	93	Kurosu et al. 2002
α-Glucosidase	*S. cerevisiae*	Maltose (1.5 M)	50 mM	4.6	Prodanovic et al. 2005b
		Maltose (1.5 M)	9 mM	28	Prodanovic et al. 2005a
Dextransucrase	*L. mesenteroides*	Sucrose (215 mM)	450 mM	0.4	Seo et al. 2009
Amylosucrase	*D. geothermalis*	Sucrose (2.3 mM)	2.3 mM	1.3	Seo et al. 2012a
		Sucrose (23 mM)	2.3 mM	90[b]	
Amylosucrase	*C. carboniz*	Sucrose (20 mM)	5 mM	44.7	Yu et al. 2018
Sucrose isomerase	*E. rhapontici*	Sucrose (1 M)	50 mM	33.2	Zhou et al. 2011

[a] Lyophilized cells harboring the enzyme activity were used for α-arbutin biosynthesis

[b] L-Ascorbic acid (0.2 mM) was added as an oxidant to prevent the oxidation of hydroquinone and improve the α-arbutin production

In 1994, Nishimura et al. screened a highly hydroquinone glucosylating enzyme-producing strain, *B. subtilis* X-23, from 600 strains of soil microorganisms. The enzyme was purified and identified as α-amylase. When maltotriose, maltopentaose, and soluble starch used as glucosyl donors, the molar production yield of α-arbutin by purified *B. subtilis* α-amylase from hydroquinone was measured to be 22.4, 24.8, and 32.4%, respectively (Nishimura et al. 1994).

Cyclodextrin glycosyltransferase

Cyclodextrin glycosyltransferase (CGTase, EC 2.4.1.19), also a GH13 member, catalyzes the breakdown of starch and linear maltodextrin substrates to produce cyclodextrins. CGTase is a multifunctional enzyme catalyzing four related bioreactions including cycling, coupling, disproportionation, and hydrolysis and has versatile applications in food, pharmaceutical, and chemical industries (Han et al. 2014). The disproportionation activity of CGTase is widely used for transglycosylation of various carbohydrates and non-carbohydrate compounds. A highly disproportionating CGTase is used for enhanced synthesis of 2-O-α-D-glucopyranosyl-L-ascorbic acid by transglucosylation of L-ascorbic acid (Gudiminchi et al. 2016). Many other bioactive compounds, including stevioside (Lu and Xia 2014), rutin (Sun et al. 2011), and resveratrol (Shimoda et al. 2015), could be biologically modified by transglucosylation using CGTases to improve their properties.

Recently, *Thermoanaerobacter* sp. CGTase was used for glycosylation of hydroquinone to produce α-arbutin. When α-cyclodextrin and maltodextrin were used as glucosyl donor substrates, the transfer efficiency of hydroquinone glycosylation was measured to be 31.8 and 29.2%, respectively. The major glycoside products from these two reactions were both identified as α-arbutin and the molar yield was calculated to be 23.3 and 21.2%, respectively. In addition, a two-step enzymatic reaction system comprising CGTase and amyloglucosidase was performed to improve the molar yield of α-arbutin to 30% (Mathew and Adlercreutz 2013).

α-Glucosidase

α-Glucosidase (EC 3.2.1.20) catalyzes the hydrolysis of α-1,4 linkages with a substrate preference for maltose, maltotriose, and maltotetraose. This enzyme generally has transglucosylation activity toward some carbohydrates and non-carbohydrate compounds, and is used for oligosaccharide production (Zhao et al. 2017) and biosynthesis of bioactive glucosides (Pavlovic et al. 2013; Seo et al. 2011).

In 2000, *Xanthomonas campestris* WU-9701 was screened for showing α-anomer-selective glucosylation of some organic compounds having alcoholic groups, including l-menthol (Nakagawa et al. 2000) and (+)-catechin (Sato et al. 2000). Lyophilized cells of *X. campestris* WU-9701 also showed high glucosylation activity from maltose to hydroquinone to produce α-arbutin. After reaction for 36 h at 40 °C, 42 mM α-arbutin was produced from 45 mM hydroquinone and 1.2 M maltose, with a molar ratio of 93% (Kurosu et al. 2002). The α-glucosyl transfer enzyme responsible for hydroquinone glucosylation from *X. campestris* WU-9701 was purified and identified showing typical α-glucosidase properties. The encoding gene was obtained and cloned in *E. coli* for expression and the recombinant enzyme was proved to be α-glucosidase (Sato et al. 2012).

Prodanovic et al. tested hydroquinone glucosylation activity from invertase, amyloglucosidase, and α-glucosidase, and found that only α-glucosidase was able to produce hydroquinone glycoside. After reaction with 50 mM hydroquinone and 1.5 M maltose for 20 h at 30 °C, α-arbutin was produced by α-glucosidase from baker's yeast (*Saccharomyces cerevisiae*) with a molar conversion yield of 4.6% with respect to hydroquinone (Prodanovic et al. 2005b). And the conversion yield was further improved to 28% after optimization of reaction conditions (Prodanovic et al. 2005a).

Dextransucrase

Dextransucrase (EC 2.4.1.5), a member of GH70 enzymes, catalyzes the biosynthesis of dextran from sucrose with release of fructose. It is able to catalyze three distinct reactions, including polymerization, hydrolysis, and transglucosylation (Naessens et al. 2005). Through transglucosylation, dextransucrase produces various beneficial oligosaccharides (Kothari and Goyal 2015) and bioactive glucosides of many compounds including stevioside (Ko et al. 2016), ampelopsin (Woo et al. 2012), puerarin (Ko et al. 2012), and various alcohols (Kim et al. 2009).

Leuconostoc mesenteroides dextransucrase was used for α-arbutin biosynthesis from hydroquinone as a glucosyl acceptor and sucrose as a donor. After optimization of reaction conditions using a response surface methodology, 544 mg mL^{-1} α-arbutin was produced from 450 mM hydroquinone and 215 mM sucrose, with a bioconversion yield of 0.4% based on the hydroquinone supply (Seo et al. 2009).

Amylosucrase

Amylosucrase (EC 2.4.1.4), a member of GH13 family, catalyzes the α-glucosyl transfer from sucrose to non-reducing terminal residue of α-glucan to produce α-(1,4)-glucan. It is also a versatile enzyme and is able to catalyze transglucosylation from sucrose as a donor to appropriate glucosyl acceptor substrates (Tian et al. 2018). Due to efficient transglucosylation activity, amylosucrase has been used for biosynthesis of various bioactive α-glucosides, including those of rutin (Kim et al. 2016), (+)-catechin (Cho et al.

2011a), glycerol (Jeong et al. 2014), phloretin (Overwin et al. 2015), and salicin (Jung et al. 2009).

Amylosucrase from *Deinococcus geothermalis* was used for biosynthesis α-arbutin with sucrose as a glycosyl donor and hydroquinone as an acceptor. The conversion yield of hydroquinone to α-arbutin was extremely low (only 1.3%) probably due to the instability of hydroquinone in the reaction mixture, and the yield was significantly enhanced in presence of L-ascorbic acid. A highest yield of 90% was obtained from an optimized reaction system including 23 mM sucrose, 2.3 mM hydroquinone, and 0.2 mM L-ascorbic acid (Seo et al. 2012a). Among all characterized amylosucrases, the one from *Cellulomonas carboniz* displays transglucosylation activity prominently and has a remarkably higher transglucosylation/hydrolysis ratio than others, and thus has a good potential for transglucosylation tool enzyme (Wang et al. 2017). *C. carboniz* amylosucrase efficiently produced α-arbutin without the addition of L-ascorbic acid. A conversion yield of 44.7% was obtained using a reaction system including 20 mM sucrose and 5 mM hydroquinone (Yu et al. 2018).

Sucrose isomerase

Sucrose isomerase (EC 5.4.99.11) catalyzes sucrose isomerization to isomaltulose through the rearrangement of the α-1,2 linkage between glucose and fructose to an α-1,6 linkage, by a mechanism of intramolecular transglycosylation (Mu et al. 2014). It has been commercially used for large-scale production of isomaltulose, also known by the trade name Palatinose, which is considered as a beneficial sucrose substitute for food industry.

In 2011, Zhou et al. reported the α-arbutin production by transglycosylation of *Erwinia rhapontici* sucrose isomerase using hydroquinone and sucrose as substrates. The wild-type produced 16.6 mM α-arbutin from 50 mM hydroquinone and 1 M sucrose with molar transfer ratio of 33.2%. Site-directed mutagenesis in the catalytic pocket was carried out to improve its hydrolytic activity and α-arbutin productivity. Under the same reaction conditions, the variants F185I, F321I, and F321W produced 36.1, 43.6, and 44.1 mM α-arbutin, with molar transfer ratio of 72.2, 87.25, and 88.2%, respectively (Zhou et al. 2011).

Biological production of α-arbutin by microorganisms

In addition to enzymatic biosynthesis, α-arbutin can be produced from hydroquinone by some microorganisms. For example, in a previous work, approximately 600 strains of microorganisms isolated from soil were cultured and screened for potential α-arbutin producer. Using hydroquinone as an acceptor and maltopentaose as a donor, a highly hydroquinone glucosylating enzyme-producing strain, *B. subtilis* X-23, was screened and the enzyme was identified as extracellular α-amylase (Nishimura et al. 1994).

As mentioned above, lyophilized whole cells of *X. campestris* WU-9701 was used for efficient biosynthesis of α-arbutin from maltose to hydroquinone. After reaction for 36 h at 40 °C, 42 mM α-arbutin was produced from 45 mM hydroquinone and 1.2 M maltose, with a molar ratio of 93% (Kurosu et al. 2002). The α-arbutin-producing enzyme was characterized as α-glucosidase and the encoding gene and the protein were deposited in GenBank as accession numbers AB081949.1 and BAC87873.1, respectively (Sato et al. 2012). In 2006, surface display of α-arbutin-producing enzyme on *E. coli* was constructed for α-arbutin production. A transglucosidase gene from *X. campestris* BCRC12608 was fused to a truncated gene of a surface anchoring motif, the ice nucleation protein (INP) of *X. campestris* BCRC12846. The truncated INP consisting of N- and C-terminal domains (INPNC) directed the recombinant protein fused with α-arbutin-producing transglucosidase to *E. coli* cell surface. The engineered *E. coli* displaying transglucosidase produced 83.4 mM α-arbutin from 100 mM hydroquinone and 1.2 M maltose after reaction at 40 °C for 1 h, with a molar conversion of 83.4%. By comparison, the wild strain of *X. campestris* BCRC12608 only produced 16 mM α-arbutin under the same reaction conditions (Wu et al. 2006). Furthermore, a fed-batch culture strategy was developed for high cell density cultivation of recombinant *E. coli* cells anchoring surface displayed transglucosidase. The hydroquinone transglucosylation activity of recombinant cells using lactose as an inducer was slightly lower than that induced by isopropyl-β-D-thiogalactoside (IPTG) in batch fermentation; however, lactose was a better inducer for transglucosidase expression in fed-batch fermentation. Cell density using fed-batch culture induced by lactose was improved to 17.6 g L^{-1}, compared to that of 1.9 g L^{-1} using batch culture induced by lactose, and thus total transglucosylation activity and α-arbutin productivity were remarkably enhanced by the fed-batch culture (Wu et al. 2008). The authors did not show the detailed transglucosidase-encoding gene sequence and only described that the gene showed 95% homology with α-glucosidase from *X. campestris* ATCC33913 (GenBank accession no. NP637823) (Wu et al. 2006). Therefore, the transglucosidase responsible for α-arbutin production from *X. campestris* BCRC12608 could be α-glucosidase, which is the same as the one from *X. campestris* WU-9701 (Kurosu et al. 2002).

In addition, highly α-arbutin-producing microbial strains were screened by physical and chemical mutation breeding treatments. An α-arbutin-producing microorganism, *Xanthomonas maltophilia* 1.1788, was selected for a series of mutation breeding approaches including ultraviolet (UV) light, *N*-methyl-*N*-nitro-*N*-nitroso-guanidine (NTG) treatment, and quick neutron mutation. A positive mutation, *X. maltophilia* BT-112, was screened with 15-fold enhanced α-arbutin

productivity compared to the parent strain. After microbial fermentation for 15 h, 120 mM hydroquinone and 240 mM sucrose were added to the fermenter for reaction, and 30.6 g L^{-1} α-arbutin was produced after reaction for 72 h, with a molar conversion of 93.6% (Liu et al. 2013a). Several kinds of fed-batch strategies were studied to develop a cost-effective method for improved α-arbutin production by *X. maltophilia* BT-112 fermentation, and dissolved oxygen-control pulse fed-batch showed a higher α-arbutin yield. Using dissolved oxygen-control fermentation feeding with hydroquinone and yeast extract, a maximum α-arbutin yield of 61.7 g L^{-1} with a molar conversion of 94.5% were obtained after optimization of fermentation conditions (Liu et al. 2014). To reduce toxic effect of hydroquinone on *X. maltophilia* BT-112 cells, hydroquinone was immobilized on non-polar macroporous adsorbent H107 resin for producing α-arbutin. A maximum α-arbutin yield of 64.7 g L^{-1} with a molar conversion of 93.5% was obtained by reaction of fermentation broth with immobilized hydroquinone. The α-arbutin productivity reached 0.9 g L^{-1} h^{-1}, which was 526% higher than that produced from free hydroquinone, and fermentation broth could be reused for three consecutive batch reactions without obvious activity loss (Liu et al. 2013b). When whole cells of *X. maltophilia* BT-112 was used for producing α-arbutin from immobilized hydroquinone, a maximum α-arbutin yield of 65.9 g L^{-1} with a molar conversion of 95.2% was obtained; the α-arbutin productivity was 202% higher than that produced from free hydroquinone, and the whole cells could be reused for six times without obvious activity loss (Liu et al. 2013c). Further, a fermentation scale-up of a 30 L jar to a 3000 L pilot was developed for large-scale production of α-arbutin. A surfactant Tween-80 showed a positive effect on α-arbutin production. α-Arbutin produced in the presence of 0.4% (*w*/*v*) Tween-80 was 124.8% higher than that of the control. An α-arbutin yield of 38.2 g L^{-1} was finally obtained in 3000 L fermenter, with a molar conversion ratio of 93.7%, which was comparable to the laboratory-scale results (Wei et al. 2016). In addition, isolation of α-arbutin from *X. maltophilia* fermentation broth was reported by one-step macroporous resin adsorption chromatography. A polar macroporous adsorbent resin S-8 offered the best adsorption and desorption capacities for α-arbutin among all the tested resins, and finally, α-arbutin was efficiently isolated with a purity of 97.3% (*w*/*w*) and a recovery of 90.9% (*w*/*w*) (Liu et al. 2013d).

Conclusions and future prospects

α-Arbutin attracts increasing attention because of its great potential for use as a powerful skin-lightening agent in the cosmeceutical industry. It is generally produced by enzymatic or microbial transglucosylation of hydroquinone. Seven kinds of different enzymes possessing transglucosylation activity have been employed for conversion of hydroquinone to α-arbutin. These enzymes use different substrates as transglycosylation donors and show different productivities of α-arbutin. Finding novel enzymes with potential transglucosylation activity toward hydroquinone would be tried for α-arbutin production in the future. Molecular modification of α-arbutin-producing enzymes using directed evolution or structure-based site-directed mutagenesis would also be performed to improve the substrate specificity toward hydroquinone and enhance α-arbutin productivity.

For α-arbutin production by microorganisms, various recombinant expression systems could be tried for enhancing the expression level of α-arbutin-producing enzymes, fermentation engineering could be deeply studied to increase the total fermentation activity, the bioprocess of α-arbutin production by the engineered microorganisms could be further optimized, and the downstream process researches would be also strengthened.

Acknowledgements This work was supported by the Support Project of Jiangsu Province (No. 2015-SWYY-009), the Research Program of State Key Laboratory of Food Science and Technology, Jiangnan University (Nos. SKLF-ZZA-201802 and SKLF-ZZB-201814), and the National First-Class Discipline Program of Food Science and Technology (No. JUFSTR20180203).

Compliance with ethical standards

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

Conflict of interest The authors declare that they have no conflict of interest.

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