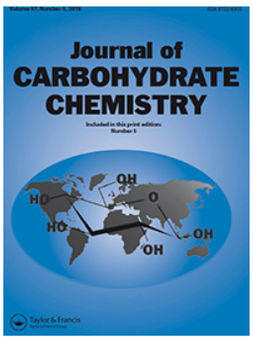

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Novel approaches for biotechnological production and application of L-arabinose

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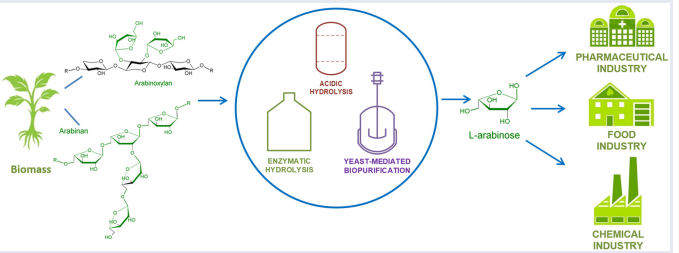
ABSTRACT

L-arabinose is found in biopolymers such as hemicellulose, pectin, arabinogalactan-protein complexes, and polysaccharides of exudate plant gums. Recent studies have revealed many possible applications of L-arabinose in the fields of pharmaceutical, food and chemical industries. Novel approaches to obtain L-arabinose are focused on the utilization of lignocellulosic by-products, purified polysaccharides, and residual hydrolysates containing a mixture of sugars. L-arabinose can be released from lignocellulosic biomasses by acid-catalysed or enzymatic hydrolysis. L-arabinose-enriched solutions can be obtained from residual hydrolysates by yeast-mediated biopurification. The most promising, novel processes to obtain L-arabinose have combined the advantages of different methods but technological barriers still exist impeding the industrial implementation.

GRAPHICAL ABSTRACT



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Introduction

Shifting the dependence of our society from petroleum-based to renewable biomass-based resources is considered to be crucial to the development of a sustainable industry, energy independence and the effective management of greenhouse gas emissions.[1,2] Plant-based raw materials have the

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potential to replace a large fraction of fossil resources as feedstocks for industrial productions, addressing both the energy and non-energy, i.e., chemicals and materials, sectors.[3] The vast majority of the plant biomass resources is lignocellulose, which is composed of three major constituents: cellulose, hemicellulose and lignin. Lignocellulosic materials have the greatest potential to be used as renewable sources to produce value-added materials and chemicals due to their low commercial value and abundant availability. The sustainable use of lignocellulosic biomass requires integrated manufacturing which has led to the development of the term biorefinery, analogous to oil refinery. The biorefinery concept embraces a wide range of technologies that are able to separate biomass resources such as wood, grass, crop residues, etc. into their building blocks such as carbohydrates, proteins, oils, etc. and convert those into a wide spectrum of marketable products and energy.[4,5] In particular, the carbohydrate fraction of lignocellulosic biomass is expected to play the major role in producing bio-based chemicals, since it can be effectively hydrolysed to monosaccharides which can then be converted into an array of value-added molecules via fermentations or chemical synthesis.[3] Major research efforts in the field of lignocellulose utilization over the last few decades have been focused on the extraction of the main sugar components like glucose and xylose from the lignocellulosic biomass and convert them into value-added products. In contrast, less attention has been accorded to the valorisation of the minor sugar components like L-arabinose. However, L-arabinose is the second most abundant pentose beside D-xylose. It is mainly found in hemicellulose, pectin and other plant polysaccharides. Although L-arabinose has many interesting properties and possible applications, the recent utilization of L-arabinose is limited partly due to the fact that high quality L-arabinose have not been produced yet as commodity chemical.[6] Recently there are commercial interest and accelerating research effort to investigate the potential of L-arabinose for the development and production of high-value bio-products and to develop new, high-performance methods for obtaining high purity grade L-arabinose.[7,8]

Therefore, in this review the structure and properties, the potential applications in different fields and the new approaches in the biotechnological production of L-arabinose are described. The proposed methods and achieved results are detailed and the advantages and disadvantages of each method are critically evaluated. The structure and chemical composition of the plant polysaccharides containing L-arabinose, in particular the anomers, enantiomers and ring structure, the main features of the process of acid-catalysed release of L-arabinose and the main properties and mode of action of the enzymes hydrolysing arabinosyl linkages are also reviewed to provide wide and up-to-date background for the novel methods of L-arabinose production.

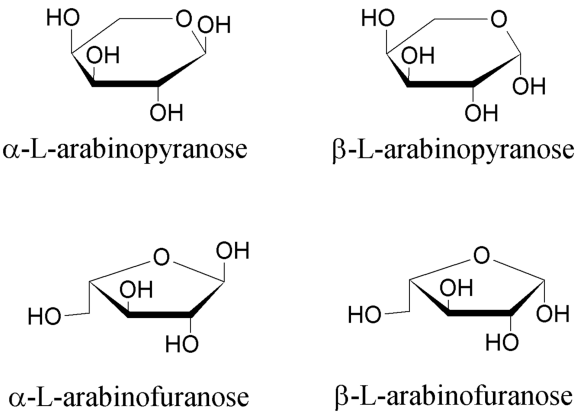

Figure 1. Different forms of L-arabinose presented in Haworth projection.

L-arabinose

L-arabinose ($C_5H_{10}O_5$, molar mass of 150.13 g/mol, Fig. 1) is an aldopentose, the second most abundant pentose next to D-xylose in nature. L-arabinose is widely found in plant cell walls as a component of biopolymers including hemicellulose[9] and pectin,[10] in arabinogalactan-protein complexes[11] and in exudate plant gums.[12] Although most of the monosaccharides in plant biopolymers are normally present in their D-form, arabinose is a rare exception, as their L-configuration is more common.[13] Conversely, arabinose is present in the D-form in the cell wall[14,15] and exopolysaccharides[16,17] of some bacteria. L-Arabinose is named after gum arabic from which it was first isolated.[8] The furanose form of L-arabinose outnumbers the form of pyranose in natural polysaccharides. However, in aqueous solution the pyranose form of free L-arabinose is more stable,[7,18] although it possesses various isomers: α- and β-pyranose and α- and β-furanose (Fig. 1) as well as a trace amount of the open-chain aldehyde at equilibrium, hence giving more complex spectra than the most monosaccharides.[19] However, the nature of solvent and the presence of a particular substituent appear to have an effect on the equilibrium composition of L-arabinose in a solution. The anomeric effect is stronger in nonpolar solvents and therefore in these solvents the α-anomer is present in higher proportion. Besides the pyranose/furanose ratio also depends on the nature of the solvent.[19,20]

Possible utilizations of L-arabinose

As a natural sweetener and a starting material for the production of flavour

L-arabinose can be used in the food and flavour industry as a dietary, natural sweetener or as a raw material to produce different flavours by Maillard reaction.[8,21] L-arabinose has a very similar taste to sucrose, but

with approximately half the sweetness of sucrose. Animal studies in chickens and pigs indicate that the metabolizable energy of L-arabinose is significantly less than that of D-glucose.[22,23] The apparent metabolizable energy (AMEn) value of L-arabinose, which is corrected to zero nitrogen balance, was found to be 60% and 40% of that of D-glucose at 5% and 10% dietary inclusion levels, respectively, in the case of chickens.[22] Therefore, it has shown great merits as a sweetener and a food additive to prevent obesity and maintain good health.[24,25]

As a blood-sugar-reducing agent and functional food additive

L-Arabinose has been reported to have highly interesting properties in blood sugar reduction and for the treatment of human diabetes. In vitro studies performed with porcine intestinal mucosa[26] and in vivo studies in rats,[27] mice[26] and pigs[28] fed by sucrose in combination by L-arabinose revealed the inhibitory effect of L-arabinose on intestinal sucrase activity resulting in a delayed digestion of sucrose and consequently a slower absorption of glucose that leads to a delayed and decreased blood glucose and insulin responses. Krog-Mikkelsen et al.[29] investigated the dose-response effects of L-arabinose on intestinal sucrase activity in vitro and glucose tolerance, appetite, and energy intake in humans. The in vitro studies showed that L-arabinose inhibited the brush border enzyme sucrase in an uncompetitive dose-dependent manner. The in vivo human study with 3 different doses of L-arabinose in sucrose beverages (250 g/L sucrose supplemented by 0, 1, 2, 3 g/L arabinose) showed that L-arabinose supplementation suppressed the increases in blood glucose, insulin, and C-peptide concentrations in plasma after sucrose ingestion and also augmented the postprandial increase in the incretin hormone glucagon-like peptide-1 response in dose-dependent manner. No effects on triacylglycerol, gastrointestinal symptoms, appetite ratings, or energy intake were observed. These results are in great accord with the results of the study of Inoue et al.[30] which was performed in both healthy subjects and in patients with type 2 diabetes to investigate the effects of the addition of L-arabinose to a sucrose-containing beverage or meal. Kaats et al.[31] reported that consumption of formula containing L-arabinose and trivalent chromium after a 70-gram oral challenge of sucrose was effective in safely lowering both circulating glucose and insulin levels in humans. Hence, L-arabinose is a promising additive for functional foods and for the treatment of human diabetes.

As an antioxidative agent with protective activities against hyperglycemia

Hyperglycemia is the main characteristic of diabetes mellitus, in which oxidative stress is one of the important risk factors of diabetic complications.

Antioxidants to attenuate oxidative stress are considered as effective therapeutic agents to prevent pathological conditions associated with hyperglycemia under diabetes mellitus.[32,33] Song et al.[32] investigated the radical scavenging activity of pure L-arabinose and arabinan-rich sugar beet pulp in vitro and their protective effects against high glucose-induced oxidative stress using LLC-PK_1 porcine renal epithelial cells. L-arabinose and sugar beet pulp significantly inhibited the high glucose-induced cytotoxicity and lipid peroxidation and also inhibited the formation of nitric oxide compared with high glucose-treated control. The superoxide anion production of groups treated with L-arabinose or sugar beet pulp was significantly lower than that of the control treated with high glucose. Furthermore, L-arabinose and sugar beet pulp elevated the glucose uptake, resulting in lower glucose concentration compared with the non-treated control. L-arabinose or sugar beet pulp treatment down-regulated the expressions of proteins related to high glucose-induced oxidative stress in LLC-PK_1 cells. Hence the results of the study indicated that L-arabinose and sugar beet pulp are promising antioxidative agents with protective activities against hyperglycemia.

As a precursor for antiviral drug development

Unlike other L-sugars, L-arabinose is relatively ample monosaccharide in nature, hence it is a promising raw material for biotechnological production of L-ribose.[34] L-ribose is a rare and expensive sugar that can be used as a precursor for the production of L-nucleoside analogues which are used as antiviral drugs.[35] L-ribose can be formed from L-ribulose, D/L-ribitol and L-arabinose by enzymatic conversion using isomerases, oxidoreductases and epimerases, respectively.[36] Recently, significant research efforts have been made to investigate the biotechnological production of L-ribose from naturally abundant L-arabinose. Helanto et al.[35] described a novel way of L-ribose production from L-arabinose by using metabolically engineered bacterial cells. For this purpose, an L-ribose isomerase was introduced into L-ribulokinase-deficient mutants of *Escherichia coli* and *Lactobacillus plantarum*. Resting cells of these mutants were used for the production of L-ribose, while the use of protein precipitates for converting L-arabinose to L-ribose was also achievable. Yeom et al.[37] demonstrated the production of L-ribose from L-arabinose via a two-enzyme system from *Geobacillus thermodenitrificans*, in which L-ribulose was first produced from L-arabinose by L-arabinose isomerase and subsequently converted to L-ribose by mannose-6-phosphate isomerase. Du et al.[38] developed a practical chemical synthesis of 2′-deoxy-2′-fluoro-5-methyl-β-L-arabinofuranosyl uracil (L-FMAU) from L-arabinose through the intermediate of L-ribose with 8%

overall yield. L-FMAU is a potential antivirial agent against hepatitis B virus.

As a precursor for the production of other molecules with potential therapeutic applications

Ketoheptoses are seven-carbon sugars with significant pharmacological potential as inhibitors of sugar metabolism. L-gluco-heptulose is a rare, naturally occurring ketoheptose that may have potential therapeutic applications in hypoglycaemia and cancer.[39] Subrizi et al.[39] reported efficient, stereo-selective, one-step, biocatalytic preparation of L-gluco-heptulose from L-arabinose using trans-ketolase variants of *E. coli* mutants on a preparative laboratory scale.

As raw material for non-ionic surfactant production

The potential use of L-arabinose as the starting material in the synthesis of non-ionic surfactants was reported by Bouquillon.[40] Due to the increasing importance of carbohydrates as cheap and renewable starting material, the use of these compounds as nucleophile agents in telomerisation reaction is of great interest in regard to the production of biodegradable non-ionic surfactants. Bouquillon[40] succeeded in the preparation of D-xylose-based and L-arabinose-based surfactants using telomerisation of butadiene, glycosylation or esterification reactions. The considered surfactants had excellent amphiphilic properties and their syntheses and purification were described to be clean and easy to handle. Derivatization of the surfactants was also explored.

As a precursor for the production of amino acids

Corynebacterium glutamicum is a non-pathogenic, Gram-positive, soil bacterium which is primarily used for the biotechnological production of amino acids. Amino acid production by using *C. glutamicum* is typically based on media containing glucose from starch hydrolysis or fructose and sucrose as present in molasses.[41] Schneider et al.[41] described the engineering of recombinant *C. glutamicum* strains for the production of L-glutamate, L-lysine, L-ornithine and L-arginine from L-arabinose as sole or combined carbon and energy source with D-glucose. The *araBAD* operon from *E. coli* was successfully expressed in wild-type, L-lysine-, L-ornithine- and L-arginine producing strains of *C. glutamicum* to enable the utilisation of L-arabinose in the production of amino acids.

Other possible applications

Other possible applications of L-arabinose were also reported. For example, it was used for bacteriological diagnostics,[42] for the photo-chemical conversion of solar energy into electrical energy by a photogalvanic cell containing Eosin-Arabinose system,[43] as raw material in second generation biohydrogen production by using anaerobic mixed-cultures under extreme thermophilic conditions,[44] for analytical purposes[45] to identify, differentiate and characterize pentose sugar isomerases,[46] and as a precursor of other bio-active compounds and platform molecules, e.g. arabinitol, for the bio-renewable chemical industry.[47,48]

Production of L-arabinose

Exudate plant gums such as gum arabic and mesquite gum are considered to be suitable raw materials for L-arabinose production. On an industrial scale L-arabinose can be produced from gum arabic by acid hydrolysis followed by multiple purification procedures containing neutralization reaction, ion exchange and other chromatographic separations. However, the high cost of gum arabic and the expensive purification steps required result in high cost of pure L-arabinose which limits its widespread industrial applications.[8,49] According to Cheng et al.,[8] in 2010 China produced about 500 tons of L-arabinose at the cost of more than 70 USD/kg. L-arabinose could also be industrially produced from other arabinan-, arabinoxylan- or arabinogalactan-containing plant materials, including wood materials, vegetable and fruit processing by-products or agro-industrial residues such as corncob and sugar beet pulp. There are many patents about the production of crystalline L-arabinose from sugar beet pulp. Generally these processes start with the alkaline extraction of arabinan. Purification of the arabinan fraction can occur by ion-exchange chromatography or ultrafiltration. The arabinan fraction is hydrolysed into arabinose monomers under acidic conditions at elevated temperature. The arabinose solution can be purified by ion-exchange chromatography and adsorbent resins or ultrafiltration. The neutralised and purified arabinose solution is concentrated and pure L-arabinose is recovered by crystallization.[50–52]

Recently, L-arabinose has become a valuable product with growing market worldwide. However, it seems to be more common and widespread in China compared to other countries. Hence, many of the significant manufacturers are also located in China. The following companies are considered the main manufacturers of L-arabinose: Danisco (US), Futaste (CN), Shandong Xieli Bio-technology (CN), Shandong Longlive Bio-technology (CN), Healtang Co. Ltd. (CN), Tangchuan Biotechnology (CN), Zhejiang Huakang Pharmaceutical (CN), and Shandong Lujian Biological Technology (CN).

Complex plant polysaccharides that are possible alternative sources to produce L-arabinose

Pectins and hemicelluloses comprise a wide range of structurally different polysaccharides from which several are considered as plant polysaccharides that can be suitable sources of L-arabinose. In the following section the structures of pectin and hemicellulose polysaccharides containing considerable amount of L-arabinose are detailed. Other arabinose-containing molecules of plant biomass are also described briefly.

Pectins

Pectins represent a family of complex polysaccharides that contain 1,4-linked α-D-galactopyranosyluronic acid residues.[53] Pectins are highly diverse polysaccharides regarding their chemical composition and structure which also differs depending on many factors such as the plant source, cell type and physiological state of the cell. Depending on the composition of backbone and side chains, pectins can be divided into distinct structural groups: homogalacturonan, rhamnoglacturonan I and substituted galacturonans such as rhamnogalacturonan II, xylogalacturonan and apiogalacturonan.[54] Arabinose is present in the pectin polymers of rhamnogalacturonans I and II. Rhamnogalacturonan II contains a homogalacturonan backbone of 1,4-linked α-D-galactopyranosyluronic acid units with complex side chains attached onto the O-2 or O-3 positions.[55] The side chains are composed of 12 types of glycosyl residues which are connected to each other by at least 22 different glycosidic bonds. Arabinose is present in the side chains of rhamnogalacturonan II in the form of β-L-arabinofuranose and α-L-arabinopyranose.[56] The rhamnogalacturonan I contains a backbone of 1,2-α-L-rhamnopyranose-1,4-α-D-galactopyranosuronic acid repeats in which the rhamnopyranose units can be decorated with various side chains at O-4 position and the galactopyranosuronic acid units may be acetylated on O-2 and/or O-3 position.[53,54] The predominant side chain of rhamnogalacturonan I contains individual, linear or branched α-L-arabinofuranosyl and β-D-galactopyranosyl residues.[53] Rhamnogalacturonan I side chain arabinan consists of a backbone of 1,5-linked α-L-arabinofuranosyl residues which can be decorated with α-L-arabinofuranose units on O-2 and O-3 positions and with 1,3-linked disaccharide of α-L-arabinofuranosyl residues on O-3 position,[57] moreover the arabinan chains may connect to each other forming diverse branched structure.[58] Rhamnogalacturonan I side chain arabinogalactan (usually called arabinogalactan I) also includes oligosaccharides with diverse structure. It is composed of 1,4-linked β-D-galactopyranosyl backbone with or without decorations of α-L-arabinofuranosyl residues at O-3 position. Moreover internal, 1,5-linked α-L-arabinofuranosyl[59] and 1,3-linked β-D-galactopyranosyl residues[60] were also

identified in the β-D-galactopyranose backbone, as well as terminal α-L-arabinopyranose substitution at the non-reducing end.[59] Another type of arabinogalactan, called arabinogalactan II, is also part of most of the cell walls however there is no accordance in the literature regarding the question whether it is part or not of the pectin structure. Arabinogalactan II can also occur as part of arabinogalactan-proteins of the cell wall and as a polysaccharide of exudate plant gums. A recent study has demonstrated that arabinogalactan II of arabinogalactan-protein can be covalently linked to rhamnogalacturonan I and also to arabinoxylan of the hemicellulose, forming a so-called arabinoxylan-pectin-arabinogalactan-protein complex.[61] Arabinogalactan II is composed of a 1,3-linked β-D-galactopyranose backbone having side chains of 1,6-linked β-D-galactopyranose oligosaccharides attached to the backbone at O-6 position.[10] The side chains of arabinogalactan II are usually highly decorated with L-arabinose residues however other moieties can also attach to the side chain such as L-rhamnose, D-mannose, D-xylose, D-glucose, L-fucose, D-glucosamine, D-glucuronic acid and D-galacturonic acid.[11] The arabinose decorations of the side chain mainly exist in the form of 1,3-linked α-L-arabinofuranose monomers however short oligosaccharides containing α-1,3- or α-1,5- linked L-arabinofuranose units may also be formed in some cases.[62] Moreover, further substitution of a single α-L-arabinofuranose branch by β-L-arabinopyranosyl residue at O-3 position has been suggested recently.[18,63] The 1,6-linked β-D-galactopyranose side chain may also be terminated by β-L-arabinopyranosyl residues attached to the final galactopyranosyl residue at O-3 position.[63]

Hemicelluloses

Hemicelluloses are heterogeneous polymers with diverse structure which can contain pentoses such as β-D-xylose and α-L-arabinose, hexoses such as β-D-mannose, β-D-glucose and α-D-galactose, uronic acids such as α-D-glucuronic and 4-O-methyl-α-D-glucuronic acids, and other organic acids such as acetic acid and hydroxycinnamic acids. Rarely, other sugars such as α-L-rhamnose and α-L-fucose can also be present in small quantities.[64,65] Hemicelluloses are traditionally referred to as polysaccharides extractable from lignocellulose biomass by aqueous alkaline solutions; however, this kind of determination is not exact. According to another definition, hemicelluloses are polysaccharides in plant cell walls that have β-1,4-linked backbones with an equatorial configuration at C1 and C4 carbons.[9] This definition excludes β-1,4-galactans with an axial configuration, callose having a backbone of β-1,3-linked glucoses, and arabinogalactans comprised of a β-1,3-linked galactose backbone.[9] In this article, in concern with this definition, arabinogalactans are considered as pectin polysaccharides however certain

arabinogalactans, e.g. arabinogalactan II, can be covalently linked to hemicellulose and pectins at the same time, as it was described previously. According to the composition of the backbone chain and the presence and ratio of their sidechain constituents, different type of hemicelluloses can be distinguished such as arabinoxylan, glucuronoarabinoxylan, arabinoglucuronoxylan, glucuronoxylan, homoxylan, xyloglucan, arabinoxyloglucan, homomannan, glucomannan, galactomannan and galactoglucomanan. Considerable amount of L-arabinose is present in arabinoxylan, glucuronoarabinoxylan, arabinoglucuronoxylan and arabinoxyloglucan.

Arabinoxylans have a backbone of 1,4-linked β-D-xylopyranosyl residues which are highly decorated with monomeric sidechains of α-L-arabinofuranose linked to O-2 or O-3 positions however double substituted xylose residues can also occur. Acetyl groups can also attach to the xylose units of the backbone at position O-2 and/or position O-3. The presence of hydroxycinnamic acids, e.g., ferulic acid, p-coumaric acid and ferulic acid-containing phenolic dimers and trimers, linked to O-5 position of α-L-arabinofuranose moieties is a common feature of the arabinoxylan structure. Dimerization of the phenolic compounds can lead to intra-molecular cross-links of arabinoxylans and covalent interactions with other cell wall constituents.[65] However, the phenolic compounds can also be referred to as building block of the lignin structure instead of the hemicellulose fraction.[64] Arabinoxylans often contain side chains of α-D-glucopyranosyluronic acid and/or 4-O-methyl-α-D-glucopyranosyluronic acid linked at O-2 position to the xylose units. Those arabinoxylans are referred to as arabinoglucuronoxylans or glucuronoarabinoxylans, depending on the molar ratio of glucopyranosyluronic acid to arabinose. Generally that ratio is higher than one for arabinoglucuronoxylans and less than one for glucuronoarabinoxylans.[64] Some arabinoxylans – that sometimes are also referred to as hetero-xylans – have even more complex structure. In those cases along the previously described decorations different oligomeric sidechains – mainly containing α-L-arabinofuranose, β-D-xylopyranose, α-D-galactopyranose and hydroxycinnamic acids linked to α-L-arabinofuranose – can be attached to the homoxylan backbone.

Xyloglucans have a linear backbone containing 1,4-linked β-D-glucopyranose residues which are frequently decorated with α-D-xylopyranose residues attached at O-6 position. The xylose moieties are frequently further elongated at O-2 position by other sugars forming short side chains with wide structural varieties. The xylose units can be substituted by β-D-galactopyranose or α-L-arabinofuranose, and the β-D-galactopyranose unit can be further elongated at O-2 position by α-L-fucopyranose.[9] Alpha-L-arabinofuranose can be directly attached to the glucose residues at O-2 position too.[66] However, other less common structural variants of the side-chains are also exist in which the following sugars can also be part of the structure: β-L-arabinofuranose,

α-L-arabinopyranose, β-D-galactopyranoslyuronic acid,[67] β-D-xylopyranose,[68] α-L-galactopyranose.[69] In addition, xyloglucans can contain O-linked acetyl groups too. In some plants, such as tobacco, tomato, and potato, the xyloglucan is highly substituted with L-arabinose moieties, hence that polymers are referred to as arabinoxyloglucans. In arabinose containing xyloglucans the arabinose moieties are preferably located as terminal residues.[70]

Other arabinose-containing molecules

Hydroxyproline-rich glycoproteins occur in the extracellular matrix of land plants and green algae and their carbohydrate content, varied from 2 to 95% of their dry weight, is predominantly present as oligoarabinosides and/or as heteropolysaccharides which are O-linked to the hydroxyproline residues. Short arabinofuranoside oligosaccharides occur in every type of hydroxyproline-rich glycoproteins examined thus far, including the Ser-Hyp_4-containing extensins, arabinogalactan-proteins, gum arabic glycoprotein, repetitive proline-rich proteins and the solanaceous lectins.[71] Small glycoconjugates can also contain arabinose residues such as flavonols or saponin constituents.[18]

Release of arabinose from polysaccharides

Chemical hydrolysis to release arabinose from complex polysaccharides

During chemical hydrolysis of polysaccharides to decompose them into monomeric constituents, a complex series of chemical reactions happen that disrupt molecular interactions within the polysaccharide and with other cell wall components.[72] The presumed mechanism of acid-catalysed hydrolysis of the glycosidic linkage is initiated by protonation of either glycosidic oxygen or oxygen of the ring to form carbonium cation. Subsequently, a water molecule is added to form two monomeric sugars and release the proton. Thus, the polysaccharide hydrolysis involved multiple steps: generation of protons, migration of protons to the reaction site, disruption of molecular interactions, diffusion of hydrolysis products through pores in lignocellulose particles, and mass transfer of products into and within the bulk solution.[72] Hydrolysis is usually conducted with either water/steam (autohydrolysis) or dilute acid solution. During autohydrolysis, dissociation of water at high temperature generates proton, while for hydrolysis in dilute acid the added acid dissociates into proton(s) and anion.[72] The reaction rate and selectivity of the chemical hydrolysis of the polysaccharide fraction are influenced by the temperature, reaction time, pH as determined by acid concentration and type and buffer capacity of the feedstock, chemical structures of the polysaccharides, reactor design,

substrate loading and particle size of the feedstock.[73,74] One of the main challenges of efficient hydrolysis is to identify the proper reaction conditions and catalysts to completely decompose the polysaccharide into monomers and at the same time avoid further degradation of released sugars.[75]

Several studies have reported preferential hydrolysis of arabinose attached as side group compared to the backbone chain of the hemicellulose. Kusema et al.[76] investigated the kinetics of homogenous mineral acid, e.g. hydrochloride acid, hydrolysis of arabinogalactans and concluded that it is easier to hydrolyse the arabinose units from the side chains of arabinogalactan compared to the release of galactose from the main chain, the activation energies for the release of arabinose and galactose were 126 kJ/mol and 135 kJ/mol, respectively. Kusema et al.[75] also investigated the hydrolysis of arabinogalactans by using solid acid catalysts of Smopex-101 and Amberlyst 15 (cation exchangers). The experimental results revealed that the hydrolysis of arabinogalactan by the heterogeneous catalyst of Smopex-101 does not occur randomly, but starts from the arabinose side chains followed by the gradual hydrolysis of galactose residues. Faster release of arabinose compared to xylose during acidic hydrolysis was also reported in the case of nitric acid hydrolysis of sugar cane bagasse[77] and sulphuric acid hydrolysis of wheat straw.[78]

Mäki-Arvela et al.[74] reviewed that the rate of acid hydrolysis of hemicellulose is partially determined by the structure of the anhydrosugar, for example, whether it is α- or a β-anomer or it is furanose or pyranose. The acid hydrolysis proceeds faster for furanose sugars compared with pyranose ones. The reason for the faster furanose hydrolysis rate compared with that of pyranose is the higher structural angle strains in the furanose sugar units, whereas pyranose rings are strain-free.[74] It is also widely agreed that in general the α-glycosidic linkages hydrolyse more readily compared to β-glycosidic ones.[73,79] These properties could explain the facilitated arabinose release from hemicellulose-containing biomass that was observed in the above mentioned investigations, since arabinose is mainly present in furanose form connected by α-glycosidic bond as side chain to the hemicellulose backbone.

Enzymatic release of arabinose moieties from complex polysaccharides

O-Glycoside hydrolases refer a group of enzymes that cleavage the O-glycosidic linkages of carbohydrate containing molecules, such as di-, oligo- and polysaccharides. They can be classified into various glycoside hydrolyse (GH) families based on amino-acid sequence and structure similarities. These families are available on the continuously updated carbohydrate-active enzyme (CAZy, http://www.cazy.org) database.[80–82] Glycoside hydrolases can attack within the oligo/polymeric chain or at one of the

Table 1. Enzymes involved in hydrolysis of L-arabinose-containing molecules derived from the CAZy database.[82]

	EC number	Systematic name	Reaction	GH family
endo-1,5-α-L-arabinanase	EC 3.2.1.99	5-α-L-arabinan 5-α-L-arabinanohydrolase	Endohydrolysis of 1,5-α-arabinofuranosidic linkages in 1,5-arabinans	GH43
exo-1,5-α-L-arabinanase	EC 3.2.1.-	ns	Release 1,5-α-L-arabinobiose from the nonreducing end of its substrate	GH93
α-L-arabinofuranosidase	EC 3.2.1.55	α-L-arabinofuranoside non-reducing end α-L-arabinofuranosidase	Hydrolysis of terminal non-reducing α-L-arabinofuranoside residues in α-L-arabinosides	GH2, GH3, GH43, GH51, GH54, GH62
α-L-arabinopyranosidase	EC 3.2.1.-	ns	ns	GH42
β-L-arabinofuranosidase	EC 3.2.1.185	β-L-arabinofuranoside non-reducing end β-L-arabinofuranosidase	Hydrolysis of β-L-arabinofuranosyl-(1,2)-β-L-arabinofuranose linkages of its substrate	GH127, GH137, GH142, GH121
β-L-arabinopyranosidase	EC 3.2.1.88	β-L-arabinopyranoside non-reducing end β-L-arabinopyranosidase	Removal of a terminal β-L-arabinopyranose residue from the non-reducing end of its substrate	GH27

ns, not specified.

ends of the chain as well as at terminal side decorations, thus endo-acting and exo-acting enzymes can be distinguished.[83] Enzymatic hydrolysis of the glycosidic linkages takes place via general acid catalysis which requires two critical residues: a proton donor and a nucleophile/base. It can occur via two mechanisms resulting in either net retention or inversion of anomeric configuration.[84,85] Glycoside hydrolases that are involved in the hydrolysis of arabinosyl linkages can be referred to as arabinanolytic enzymes.[7]

As it was previously described, arabinose can occur in several forms and can be attached with different types of linkages in plant polysaccharides. As a consequence, several types of enzymes that are involved in the hydrolysis of L-arabinosyl linkages exist in nature (Table 1).

However, arabinose is predominantly present in the form of α-L-arabinofuranose connecting with 1,2-; 1,3- or 1,5-linkages to each other or to other sugar moieties in the plant polysaccharides that have the potential for arabinose production. Thus, in this section arabinanolytic enzymes involved in the cleavage of α-1,2-; α-1,3- and α-1,5-linkages of L-arabinose-containing molecules are detailed with particular attention to α-L-arabinofuranosidases (Fig. 2).

Endo-arabinanases (EC 3.2.1.99, 5-α-L-arabinan 5-α-L-arabinanohydrolase) are endo-acting enzymes that hydrolyse the 1,5-α-arabinofuranosidic linkages within the arabinan backbone mainly resulting in arabino-oligosaccharides

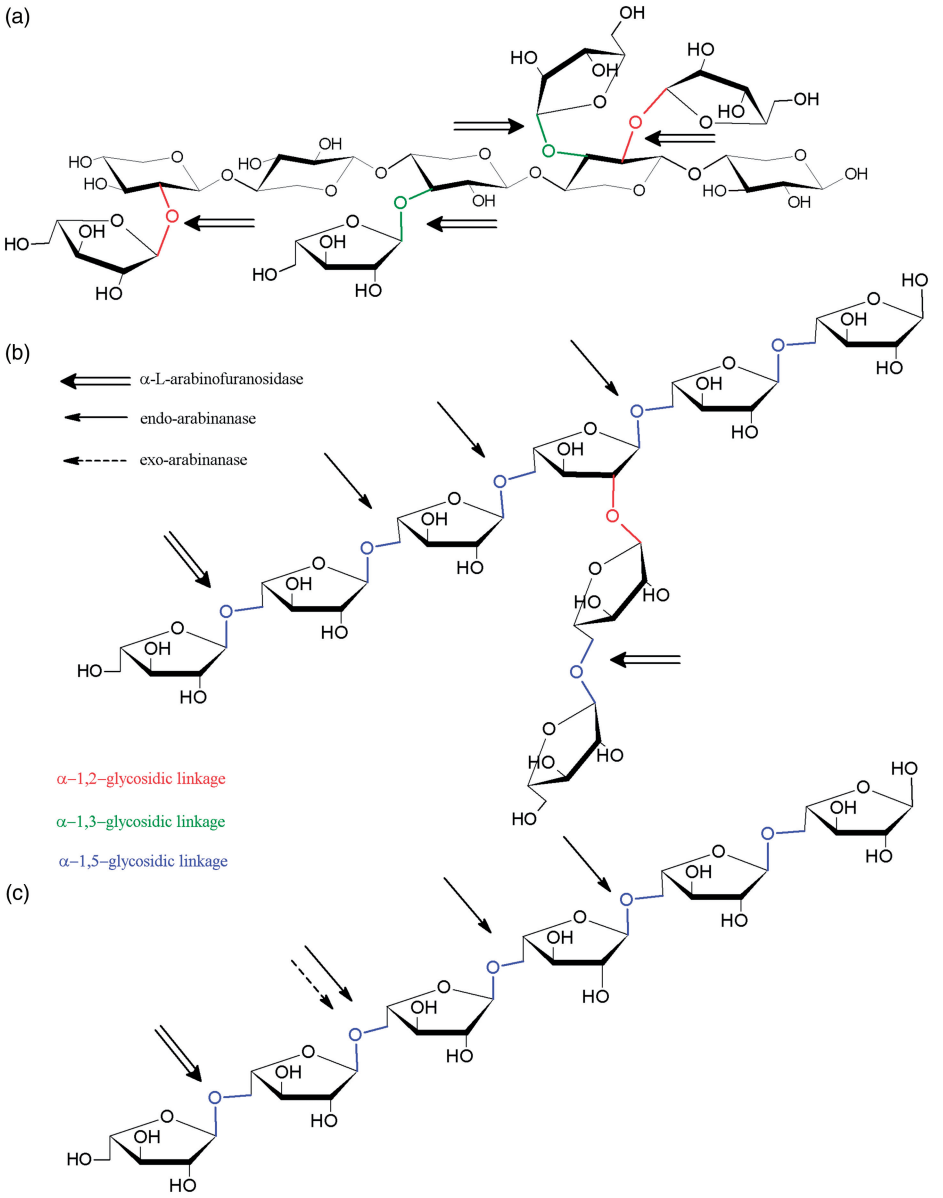

Figure 2. Typical modes of action of arabinanolytic enzymes involved in the cleavage of α-L-arabinofuranosidic linkages of arabinoxylan (a), branched arabinan (b) and linear arabinan (c) oligomers

with different length (Fig. 2b,c). Endo-arabinanases have thus far only been described in GH 43 family. GH 43 also contains α-L-arabinofuranosidases and other enzyme activities like xylosidase and galactosidase.[7] Endo-arabinanases can act on both linear and branched arabinan however more slowly on the latter.[86,87] Park et al.[88] reported that endo-arabinanase from

Bacillus licheniformis DSM13 (BLABNase) could hydrolyse debranched and linear arabinan with over 500 times higher activity when compared to branched sugar beet arabinan. The enzyme was found to be typical endo-1,5-α-L-arabinanase that specifically hydrolyses branchless arabinan polymers to produce mainly arabinobiose and arabinotriose, and small amounts of various arabino-oligosaccharide intermediates. Slightly higher activity against debranched arabinan (100% relative specific activity) compared to branched arabinan (48.4% relative specific activity) was published in the case of endo-arabinanase from *Rhizomucor miehei* (RmArase) by Chen et al.[89] However, in contrast with a typical endo-arabinanase, this enzyme resulted in significant amount of monomer arabinose beside arabinobiose at the end of arabinan hydrolysis.[89]

Exo-arabinanases (EC 3.2.1.-, exo-1,5-α-L-arabinanase) release mainly arabinobiose units from linear arabinan chain (Fig. 2c). Carapito et al.[90] reported the production, biochemical characterization and structural analysis of an exo-1,5-α-L-arabinanase of *Fusarium graminearum* which belongs to GH 93. The enzyme releases 1,5-α-L-arabinobiose from the non-reducing end of linear 1,5-α-L-arabinan with net retention of the anomeric configuration. Sakamoto et al.[91] reported the characterization of the exo-1,5-α-L-arabinanase of *Penicillium chrysogenum* (produced by recombinant *E. coli*) which catalysed the release of arabinobiose from debranched 1,5-α-L-arabinan however the enzyme was found to be structurally distinct from known arabinan-degrading enzymes based on its amino acid sequence and a hydrophobic cluster analysis. McKie et al.[92] described and arabinanolytic enzyme (ArbA) of *Pseudomonas fluorescens* subsp. *cellulosa* which predominantly releases arabinotriose from linear arabinan and arabino-oligosaccharides suggesting that the enzyme displays significant exo-activity. The authors suggested that the enzyme have sufficient endo-activity also as the ratio of released reducing sugar to the decrease in viscosity during hydrolysis of linear arabinan was very similar to that observed for the well-documented endo-arabinanase (ABNA) of *Aspergillus niger*. Sequence comparisons between ArbA and proteins of other glycosyl hydrolases showed that ArbA exhibits greatest sequence identity with ABNA, placing the enzyme in GH 43.

Alpha-L-arabinofuranosidases (EC 3.2.1.55, α-L-arabinofuranoside non-reducing end α-L-arabinofuranosidase) are exo-acting enzymes that catalyse the hydrolysis of terminal, non-reducing α-L-1,2-, α-L-1,3- and α-L-1,5-arabinofuranosyl residues from different arabinose-containing oligosaccharides, polysaccharides (e.g. arabinoxylan, arabinogalactan, arabinan) and molecules (Fig. 2a–c).[6,93] Substrate specificity of α-L-arabinofuranosidases is determined by activity measurements under certain environmental conditions on different model substrates which are predominantly the

followings: linear arabinan polymer and oligomer, branched arabinan polymer and oligomer, arabinoxlyan polymer and oligomer, arabinogalactan polymer and oligomer and the artificial substrate of p-nitrophenyl-α-L-arabinofuranoside (pNPA). Beyond their substrate specificity, α-L-arabinofuranosidases can be distinguished regarding their linkage specificity too. Linkage specificity determines the type of the cleavable linkages (α-L-1,2-, α-L-1,3- and α-L-1,5-arabinofuranosyl linkages) and specifies that the removable arabinose moieties are attached to mono- or di-substituted subunit of the carbohydrate chain. The latter is predominantly important in terms of the arabinofuranosidases that specifically act on arabinoxylans – those enzymes are sometimes referred to as arabinoxylan arabinofuranohydrolases –, hence arabinoxylans often contain xylan units bearing two side decorations of arabinose attached at O-3 and O-2 positions. The use of the synthetic substrate of pNPA to determine α-L-arabinofuranosidase activity is quite general however recent studies have revealed that many α-L-arabinofuranosidases are not able to act on pNPA but show high activity against their natural substrates.[94–96] Moreover some xylanases show significant activity against pNPA resulting in the specification of those xylanases as a bifunctional enzyme that displays both arabinofuranosidase and xylosidase activities. However, the activity against pNPA does not prove the activity against natural substrates, hence that kind of determination is debatable. Nevertheless, true bifunctional enzymes have been reported which are able to release arabinose from arabinoxylans and hydrolyse xylo-oligosaccharides.[97,98]

Previously, there have been attempts to classify α-L-arabinofuranosidases based on their source and substrate specificity or their mode of action and substrate specificity. However these kinds of classifications seemed to be ineffectual, because they are too broad to usefully characterise the properties of the enzymes classified in one group. Newly isolated enzymes often show different properties than that of classified before which would require the addition of several new subclasses, making the classification too complex for the effective use.[93] Recently, the CAZy classification is generally accepted however enzymes within a single GH family usually show wide variety regarding their substrate specificity. According to the CAZy classification α-L-arabinofuranosidases are present in six GH families: GH 2, GH 3, GH 43, GH 51, GH 54 and GH 62. Arabinofuranosidases show broad variety in their substrate and linkage specificity. Arabinofuranosidases belonging to GH3, GH51, GH54 and GH93 result in hydrolysis of the glycosidic linkages with retention of the anomeric configuration. Arabinofuranosidases belonging to GH43 and GH62 result in the inversion of the anomeric configuration during hydrolysis of the glycosidic bonds.[13]

Table 2. Arabinose content of agro-industrial by-products.

Raw material	Arabinose content (expressed as arabinan polymer in percentage of dry matter)	References
corn fibre	12.0	[103]
corn cob	2.4	[104]
corn stover	2.7	[105]
wheat bran	10.6	[106]
wheat straw	3.0	[107]
barley husk	5.7	[108]
barley straw	3.0	[109]
rice husk	1.7	[110]
rice straw	3.4	[111]
sunflower stalk	0.8	[112]
sugar beet pulp	18.0	[113]
brewer's spent grain	8.7	[114]
sugar cane bagasse	1.3	[115]

Alpha-L-arabinofuranosidases play key role during the decomposition of arabinoxylan- containing biomass, since the L-arabinose side chains can hinder the action of xylanases[99] and can also act as substrate specificity determinants.[100] Alpha-L-arabinofuranosidases can act in synergy with endoxylanases, since endo-xylanases usually hydrolyse more effectively the xylan chains from which arabinose moieties are removed, while most of the α-L-arabinofuranosidases are more active on soluble arabinose-substituted xylo-oligosaccharides obtained after xylanase treatment.[6] The activity of different α-L-arabinofuranosidases is strongly influenced by the type of the glycosidic bond (α-1,2, α-1,3 or α-1,5), the location of the arabinose unit (connect to mono- or di-substituted xylose subunit), the frequency of the arabinose moieties and the presence of other side decorations.[93,101,102]

L-arabinose-containing lignocellulosic residues

L-arabinose presents in the side chains of the hemicellulose and pectin polymers, and in smaller quantities compared to the backbone-forming sugar components. However, there are some biomasses, mainly available from the agro-industrial and food sector as by-products, which contain significant amount of L-arabinose making them promising raw materials for arabinose production. Table 2 summarizes the arabinose content of some widely available lignocellulosic agro-industrial by-products. L-arabinose content of the cell wall in a certain plant can vary in a broad range depending on the type of the plant tissue. Promising agro-industrial by-products for L-arabinose production are corn fibre, wheat bran, brewer's spent grain and sugar beet pulp containing around 12%, 11%, 9% and 18% of L-arabinose, respectively (Table 2). In comparison, plant gums such as flaxseed gums of Norman, Omega, Foster and Arabic gum contain around 14%, 9%, 11% and 24% of L-arabinose, respectively.[12]

Novel methods of biotechnological production of L-arabinose

Dilute acid catalysed hydrolysis of corn fibre, wheat bran and pinewood

Dilute acid hydrolysis of destarched corn fibre was investigated by Shibanuma et al.[116] for the purpose of studying L-arabinose production. The concentrations of oxalic acid, hydrochloric acid and sulphuric acid were varied between 0.01–2 N, 0.01–0.1 N and 0.05–0.5 N, respectively at 100 °C using 10% (w/w) dry matter content, and the reaction time was changed from 0.5 to 6 h at the selected acid concentrations. Oxalic acid hydrolysis was concluded as the most suitable method regarding the preferential release of L-arabinose. During oxalic acid hydrolysis of destarched corn fibre, arabinose was liberated rapidly at the beginning of hydrolysis and then slowed down when the yield reached 50–54% of theoretical. Arabinose yield then slowly increased until around 70% of theoretical. Conversely, xylose liberation was relatively slow but linearly increased to more than 66% of theoretical. (Throughout section entitled novel methods of biotechnological production of L-arabinose, theoretical yields for the hydrolyses are calculated based on raw material composition by assuming complete liberation of the relevant component.) The authors concluded that the most suitable conditions for preferential release of arabinose were 0.3–1 N oxalic acid concentration and 1 hour reaction time. Hydrolysis with 1 N oxalic acid concentration and 1 hour reaction time resulted in an arabinose yield of 62% and xylose yield of around 40%, based on theoretical. Although significant amount of oligosaccharides were also produced during the acidic treatments, data about the amount of solubilised oligomers were not published.

Dilute acid catalysed hydrolysis of enzymatically destarched wheat bran using water bath or microwave irradiation for heating was investigated by Aguedo et al.[48] Experiments using water as heating medium were carried out at pH 1, 2, 3 adjusted by hydrochloride acid, at 80 °C and 100 °C using 10% (w/w) dry matter for 2, 6, and 24 hours reaction times. The arabinose yield changed according to a saturation curve as a function of the reaction time, and an arabinose yield of 70% of theoretical was reached at 100 °C and pH 1 within 6 hours. During these conditions significant amount of xylose was also recovered, but the exact amount of the solubilised xylose was not published. Microwave heating was investigated at 4.75% (w/w) dry matter content according to a Box-Behnken experimental design in which the effect of temperature (130, 140, 150 °C), irradiation duration (1, 3, 5 minutes) and pH of the medium (1, 2, 3) on the arabinose yield was examined. Microwave heating for 4–5 minutes at 150 °C and pH 1 appeared as a fast and highly efficient method to recover more than 90% of the arabinose content of destarched wheat bran. The experimental design gave an

adequate model to describe the release of xylose and arabinose. According to the proposed model a range of conditions could be selected to minimise xylose release and hydrolyse around 50% of the total arabinose, yielding a high purity arabinose fraction, whereas when an arabinose yield of 80–90% was achieved the xylose yield was more than 80% of theoretical. The microwave treatment at 140 °C and pH 2 for 3 minutes resulted in an average arabinose yield of 46% and xylose yield of 3% of theoretical. Sugar oligomers were probably produced along the sugar monomers however oligosaccharides were not analysed in this study.

Soft acid hydrolysis of *Pinus* sp. sawdust in order to selectively recover arabinose and/or hemicellulose was investigated by Bravo et al.[117] First a one-step hydrolysis was studied in which experiments were carried out at different temperatures (60, 65, 70 and 80 °C), reaction times (4 and 18 hours, with sampling at selected times) and hydrochloric acid concentrations (1%, 2% and 3%). Fifty grams air-dried sawdust (with 9.6% moisture content) with an average diameter of 0.6 mm was mixed with 500 mL water in glass reactor and stirred at 500 rpm. According to the authors the best result was obtained at 65 °C, 3% hydrochloric acid and 18 hours reaction time resulting in 52% arabinose recovery in monomeric form which corresponds to 3.81 g/L arabinose concentration. The arabinose selectivity was 52% in this case. Arabinose selectivity was probably calculated as the ratio of arabinose to all monosaccharides solubilised however definition was not provided by the authors. During the acidic hydrolysis oligomer sugars were also produced in relevant concentration (5.4 g/L) resulting in total (oligomers and monomers) hemicelullose recovery of 41.3%. The sugar composition of the oligomers was not studied. Under the same reaction conditions higher arabinose selectivity was achieved (almost 70%) at 4 hours reaction time however the arabinose recovery was only 20% in that case. As a second alternative a two-step acidic hydrolysis was also tested resulting in liquid streams with much lower arabinose concentration compared with the one-step process.

These results implied that the α-1,2 and α-1,3 bonds connecting arabinofuranose moieties to the xylan backbone are more sensitive to the effects of pH and temperature than the β-1,4 bonds of the xylopyranose units in the backbone. This is in accord with the results of previous investigations – detailed in section entitled chemical hydrolysis to release arabinose from complex polysaccharides. – proposing the preferential hydrolysis of arabinose side moieties over the hemicellulose backbone. Acid hydrolysis under mild conditions seems to be an appropriate method to selectively release a significant part of the arabinose from the hemicellulose of lignocellulosic residues. Nevertheless, restricted information is available in the literature about selective arabinose hydrolysis by mild acid treatments, especially in

terms of the determination of all hydrolysis products including monomer and oligomer sugars. The main advantages of these methods are the cheap and readily available raw materials used and the simple process applied. The main disadvantages are the relatively low arabinose concentrations and purity achieved in the obtained solutions from which the recovery of pure arabinose crystals requires further purification steps (Table 3). The recovery process of arabinose was not investigated in these studies.

Enzymatic hydrolysis of purified sugar beet pulp arabinan or corn hull arabinoxylan

Lim et al.[118] investigated arabinose production from purified debranched arabinan and sugar beet arabinan using thermostable α-L-arabinofuranosidase and endo-α-1,5-arabinanase of *Caldicellulosiruptor saccharolyticus* simultaneously. The enzymes were produced by recombinant *E. coli*, and after cell disruption the enzymes were purified through a multistep process involving chromatography and dialysis. The effects of the dosage and ratio of the enzymes, the temperature, the pH and the substrate concentration on the arabinose yield and productivity were examined. In the case of sugar beet arabinan the most favourable conditions were the following: pH 6.0, 75 °C, 20 g/L sugar beet arabinan, 3 U/mL endo-1,5-α-L-arabinanase and 24 U/mL α-L-arabinofuranosidase. Under these conditions 16 g/L arabinose was obtained after 2 hours, resulting in a volumetric productivity of 8 g/(L × h). (One unit (U) of endo-1,5-α-L-arabinanase activity was defined as the amount of enzyme required to liberate 1 μmol arabinose per minute at 75 °C and pH 6.5 from debranched arabinan. One unit of α-L-arabinofuranosidase activity was defined as the amount of enzyme required to liberate 1 μmol of *p*-nitrophenyl per minute at 80 °C and pH 5.5 from *p*-nitrophenyl-α-L-arabinofuranoside.) Based on these results Kim et al.[21] developed a continuous process of arabinose hydrolysis from sugar beet arabinan by immobilised enzymes in a packed-bed bioreactor that resulted in a productivity of 9.9 g/(L × h) (Table 3).

Kurakake et al.[119] investigated arabinose production from purified corn hull arabinoxylan using α-L-arabinofuranosidase of *Arthobacter aurescens* MK5. The cells were grown in a liquid medium containing corn hull arabinoxylan in which the arabinose/xylose ratio was 0.6. The suspension of the separated and washed cells of *Arthobacter aurescens* MK5 was used in the determination of enzyme activities and the hydrolysis of corn hull arabinoxylan. The cell suspension had relatively high arabinoxylan hydrolase activity, while its α-L-arabinofuranosidase and *β*-xylosidase activities were low. Enzymatic hydrolysis of the soluble corn hull arabinoxylan was performed at pH 7 and 40 °C for 43 hours using 1 U/mL arabinoxylan hydrolyse

Table 3. Summary of the novel methods of biotechnological production of L-arabinose.

Method	Raw material	Results	Downstream processes	Product	Advantages	Disadvantages	Comments	References
Dilute acid catalysed hydrolysis	Corn fibre (destarched)	62% arabinose yield and 40% xylose yield (based on theoretical), calculated concentrations: 15 g/L arabinose and 12 g/L xylose	Not investigated	arabinose-containing solution	cheap raw material, simple process	relatively low arabinose concentration and low arabinose purity (based on total sugar solubilised)	–	[116]
	Wheat bran (destarched)	46% arabinose yield and 3% xylose yield (based on theoretical), calculated concentartions: 3 g/L arabinose, 0.3 g/L xylose	Not investigated	arabinose-containing solution	cheap raw material, fast and simple process, high arabinose purity	low arabinose concentration	–	[48]
	Pinewood sawdust	52% arabinose yield 17% other hemicellulosic sugar yield (based on theoretical), arabinose concentration of 3.8 g/L.	Not investigated	arabinose-containing solution	cheap raw material, simple process	low concentartion and low purity of arabinose	–	[117]
Enzymatic hydrolysis	Arabinan (purified from sugar beet pulp)	80% arabinose yield (based on theoretical), arabinose concentration of 16 g/L, arabinose volumetric productivity of 8 g/(L × h) in batch process	Not investigated	arabinose-containing solution	only arabinose is released as monomeric sugar, mild reaction conditions	purification of arabinan and arabinanolytic enzymes could be labour-intensive and costly	A continuous process using immobilised enzymes in a packed-bed bioreactor was also developed resulting in arabinose volumetric productivity of 9.9 g/(L × h)	[21,118]
	Arabinoxylan (purified from corn hull)	45%, 44% and 16% arabinose yields (based on theoretical) at 2%, 4.5% and 16% substrate concentrations, respectively, xylose is not released	Not investigated	arabinose-containing solution	only arabinose is released as monomeric sugar, mild reaction conditions	purification of arabinoxylan and arabinanolytic enzymes could be labour-intensive and costly, long reaction time	–	[119]

(*continued*)

Table 3. Continued.

Method	Raw material	Results	Downstream processes	Product	Advantages	Disadvantages	Comments	References
Biopurification	Xylose mother liquor	arabinose purity of 86% (based on total sugars), calculated concentration of arabinose in the biopurified fermentation medium: 30 g/L	Consecutive process steps of activated carbon treatment, ion-exchange, concentration and crystallization	arabinose crystals: 99% purity, 69% recovery (based on theoretical)	pure and crystalline product, mild conditions	other sugars can not be valorized, long fermentation	–	[8]
Combined process of enzymatic hydrolysis and biopurification	Arabinoxylan (purified from corn fibre)	Enzymatic hydrolysis: 9.7 g/L arabinose, 8.5 g/L xylose, calculated arabinose yield: 76%, calculated xylose yield: 57% (based on theoretical). Biopurification: 9.7 g/L arabinose concentration.	Consecutive process steps of activated carbon treatment, cation- and anion-exchange, concentration, crystallization and recrystallizations	Pure arabinose crystals: 35% recovery (based the on arabinose conetent of the raw material)	pure and crystalline product, mild conditions	purification of arabinoxylan could be labour-intensive and costly, long hydrolysis and fermentation	–	[120]
Combined process of acid hydrolysis and biopurification	Corn fibre	Acid hydrolysis: 74% arabinose yield, 32% xylose (glacatose) yield, 40% glucose yield, concentrations: 10.5 g/L arabinose, 8.4 g/L xylose (glacatose), 15 g/L glucose. Biopurification: 9.2 g/L arabinose concentration, arabinose purity of 90% (based on total sugars)	Not investigated	arabinose-containing solution	cheap raw material, integrated process in a biorefinery scheme, more effective sugar utilisation	low arabinose concentration, long fermentation	Arabinose biopurification was aslo performed in 3-L benchtop bioreactor by using *Ogataea zsoltii* NCAIM Y.01540, resulting in arabinose purity of 90% of total sugars	[103,121]

activity at different substrate concentrations (2%, 4.5% and 16% (w/w)). (One unit was defined as the amount of the cell suspension that could produce 1 μmol of reducing sugar (glucose base) in 1 minute from corn hull arabinoxylan.) The arabinose yields achieved were 45%, 44% and 16% of theoretical at 2%, 4.5% and 16% (w/w) substrate concentrations, respectively (Table 3). During the hydrolysis only arabinose was released.

The advantages of these methods are the mild reaction conditions applied and the pure arabinose solution obtained, considering the solubilised monosaccharides. The drawbacks are that the production of the investigated starting materials (purified arabinan and arabinoxylan) and the purification of the applied enzymes (α-L-arabinofuranosidase and endo-α-1,5-arabinanase) require complex and expensive processes. Moreover, the purification and recovery of arabinose from the hydrolysates can be challenging since the starting materials are also soluble in water.

Biopurification of hemicellulose hydrolysis-derived products

Hydrolysis of the whole hemicellulose content of lignocelluloses generally results in a mixture of xylose, arabinose and other sugars from which the arabinose can be separated by chromatographic methods. However, on an industrial scale it might be difficult and expensive. Biopurification of hemicellulosic hydrolysate is an interesting and inexpensive strategy to produce pure arabinose solution through the depletion of other sugars (e.g. glucose, xylose, galactose) using the adequate microorganisms.[8,120]

Cheng et al.[8] performed yeast-mediated arabinose biopurification on xylose mother liquor using *Pichia anomala* Y161 which was selected by screening of 306 strains of yeasts. Xylose mother liquor is an acid hydrolysate by-product derived from the preparation of xylose from corncob or sugarcane bagasse. It generally contains 350–400 g/L xylose, 150–180 g/L arabinose and 150–180 g/L glucose and galactose. Biopurification experiments were carried out with a mixture of yeast extract-containing fermentation medium and xylose mother liquor under aerobic conditions in shake flasks. In order to determine the optimal conditions of the arabinose biopurification response surface methodology was employed. The fermentation time (50, 60, 70, 80, 90 hours), temperature (30, 31, 32, 33, 34 °C) and concentration of xylose mother liquor in the medium (15, 20, 25, 30, 35% (v/v)) were investigated according to central composite experimental design in terms of the purity of arabinose solution obtained. Under the optimised condition of biopurification (32.5 °C, 75 hours and 21% (v/v) xylose mother liquor) an arabinose purity of 86% (of total sugars) was achieved. Biopurification under the optimised condition was also accomplished in a 3-L bioreactor. After cell removal, the fermentation broth subjected to

consecutive process steps of activated carbon treatment, ion-exchange treatment, concentration and crystallization. The yeast-mediated arabinose biopurification and the downstream processes resulted in arabinose crystals with a purity of 99% and with a recovery of 69% of theoretical (Table 3).

Biopurification of arabinose-rich residual streams seems to be an effective method with the potential to implement on an industrial scale. Nevertheless, the main drawback of arabinose biopurification is wasting the other sugars convertible into value-added products. Utilisation of the cell mass obtained as by-product of the biopurification is also an issue to be solved.

Enzymatic hydrolysis of purified corn fibre arabinoxylan combined with hydrolysate biopurification

Park et al.[120] developed a method to produce arabinose from purified corn fibre arabinoxylan by enzymatic hydrolysis followed by arabinose biopurification. Commercially available enzyme preparation (Cellulase C-0901) derived from *Penicillium funiculosum* was used for the enzymatic hydrolysis of the purified arabinoxylan containing 28% (w/w) arabinose and 33% (w/w) xylose. The purified arabinoxylan was obtained from alkali treatment of corn fibre however the conditions of extraction and purification were not published. Enzymatic hydrolysis was performed at 40 °C, 3.5 pH and 45.5 g/L substrate concentration using an enzyme dosage corresponding to 5940 units β-xylanase, 9 units β-xylosidase and 21 units α-L-arabinofuranosidase in a 5-L jar fermenter. (One unit of the enzyme activity was defined as the amount of enzyme which released 1 µmol xylose from soluble 4-*O*-methyl-D-glucurono-D-xylan or *p*-nitrophenyl from the corresponding *p*-nitrophenyl-glucosides per minutes.) At the end of the hydrolysis (72 hours) the resultant supernatant contained xylose, arabinose and small amount of other mono- and oligosaccharides. The arabinose and xylose concentrations were 9.7 g/L and 8.5 g/L, respectively. *Williopsis saturnus* var. *saturnus* yeast was cultured on the hydrolysate aerobically at 30 °C, 4.5 pH and 96 hours residence time. After 72 hours of biopurification almost all of the xylose was consumed without any loss of arabinose however the concentrations of other components were not reported. The solution obtained after biopurification was decolorized with activated carbon, deionized with cation- and anion-exchange resins, concentrated under reduced pressure and then subjected to crystallization. Finally, 57% of the arabinose of initial arabinoxylan was obtained as crude crystals. However, in order to get pure crystals further purification was performed by recrystallization 3 times using ethanol-water mixture, resulting in 61% (w/w) yield based on the crude crystalline arabinose. Hence in the final pure product 35% of the arabinose content of the raw material was recovered (Table 3).

Although this is a promising method to produce crystalline arabinose, the difficulties of the production of purified arabinoxylan which was used as raw material, and the significant arabinose loss during the downstream processes might cause a strict barrier in terms of industrial implementation.

Acidic hydrolysis of corn fibre combined with hydrolysate biopurification for biorefining

Fehér et al.[103] invented an integrated biorefinery process based on a two-step acidic fractionation of corn fibre and microbial conversions by using *Candida boidinii* NCAIM Y.01308 in which pure arabinose solution and xylitol solution were produced. The fractionation process of corn fibre included two sequential hydrolyses catalysed by sulphuric acid. In the first step of fractionation corn fibre was treated under mild acidic conditions (90 °C, 1.1% (w/w) sulphuric acid, 51 minutes, 10% (w/w) dry matter) which is followed by an oligomer hydrolysis step on the liquid fraction (120 °C, 1.1% (w/w) sulphuric acid, 60 minutes). After the oligomer hydrolysis step a glucose- and arabinose-rich liquid fraction was obtained containing 15 g/L glucose, 8.4 g/L xylose (+galactose), 10.5 g/L arabinose and 0.9 g/L acetic acid. After the first acidic and the oligomer hydrolysis steps the yields of glucose, xylose (+galactose), arabinose and acetic acid were 40%, 32%, 74% and 27% of theoretical, respectively. In the second hydrolysis step (120 °C, 1.1% (w/w) sulphuric acid, 30 minutes,10% (w/w) dry matter) the solid residue of the first step was utilised to produce xylose-rich supernatant (3 g/L glucose, 28 g/L xylose (+galactose), 6.6 g/L arabinose and 2.3 g/L acetic acid.) for xylitol production. The glucose- and arabinose-rich hydrolysate was utilised to produce pure arabinose solution through aerobic biopurification using *Candida boidinii* NCAIM Y.01308. Biopurification was carried out at 30 °C in rotary shaker (220 rpm) for 96 hours in 100-mL cotton-plugged Erlenmeyer flasks containing 20 mL of pH-adjusted (pH =6) glucose- and arabinose-rich hydrolysate. After three days of biopurification the glucose, xylose and acetic acid content of the hydrolysate were completely depleted and 43% of the initial galactose was consumed. Sugar alcohols (e.g. xylitol) were not produced during the biopurification due to the aerobic conditions. The arabinose concentration was constant through the whole biopurification process. This process resulted in a supernatant containing 9.2 g/L arabinose and 1 g/L galactose, which corresponds to the arabinose purity of 90% of total sugars (Table 3). The cell mass was separated and part of that was reused as inoculum in the xylitol fermentation step of the biorefinery process. Arabinose biopurification of the glucose- and arabinose-rich hydrolysate of corn fibre was also tested in 3-L benchtop bioreactor by using *Ogataea zsoltii* NCAIM Y.01540 yeast.[121] The biopurification was carried out in 1.2 L reaction volume at 37 °C and pH 6 using 1 vvm aeration and

400 rpm stirring speed. The arabinose concentration was constant during the fermentation and after three days of biopurification the supernatant contained 1.3 g/L xylose (+galactose) and 11.6 g/L arabinose, corresponding to the arabinose purity of 90% of total sugars (Table 3).

The proposed process does not require expensive purifications to obtain appropriate starting material and the acidic fractionation enables to minimize the loss of valuable sugars during the biopurification. Furthermore, that kind of integration of the xylitol fermentation and the arabinose biopurification enables the utilization of the by-product cell mass of biopurification and results in a more effective carbon utilization regarding the xylitol fermentation step. The main drawback of the process is the relatively low concentration of arabinose in the biopurified supernatant which could cause high downstream costs in the case of industrial implementation.[122]

Conclusions

L-arabinose can be used as natural sweetener, blood-sugar-reducing and antioxidative agent, precursor for drugs syntheses, raw material for surfactant, amino acid and other platform molecules. Novel approaches to obtain L-arabinose focus on the utilisation of lignocellulosic by-products, purified polysaccharides and sugar-containing residual streams and are based on the methods of mild acidic hydrolysis, enzymatic hydrolysis or yeast-mediated biopurification however the most promising ones combine the advantages of different methods. The main challenge of effective L-arabinose production is to obtain an arabinose solution with sufficiently high concentration and acceptable purity through a relatively short process.

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