Current status of xylooligosaccharides: Production, characterization, health benefits and food application

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Highlights

- Enzymatic hydrolysis of xylan produces high xylooligosaccharides yields and limits by-product formation.
- Xylooligosaccharides of high degree of polymerization range can be produced by *in situ* methods.
- Xylooligosaccharides is a potential prebiotic; mechanism of action with gut mirobiomeis required.
- The potential biological activity of xylooligosaccharides is of interest for developing new functional foods.

Abstract

Background: Functional foods are receiving high interest and attracting global attention due to their therapeutic health benefits. Xylooligosaccharides (XOS) are potential prebiotics that has attained commercial interest due to their prospective application in the food industry and its beneficial effects on human wellness. The demand to create alternate natural sources is steadily increasing to meet the consumer and industry needs for safe foods.

Scope and approach: The review summarizes the various strategies employed in xylan extraction, XOS production (chemical and enzymatic) and characterization. The study also critically views the physiological importance and biological effects described through various *in vitro* and *in vivo* intervention studies. The technological properties, food-based applications and the future perspectives of XOS are presented.

Key findings and conclusions: A better utilization of XOS to exert a positive impact on health would help to the functional foods and nutraceuticals future markets.

Keywords: Lignocellulosic biomass; Xylan; Xylooligosaccharides; Prebiotics; Functional foods

1. Introduction

The occurrence of non-communicable diseases (NCD's), particularly hypertension and obesity, are considered as a severe public health problem. Based on the consumers' awareness for a diet that links health and nutrition; the functional food market is proliferating to increase the value of the ingredients added to food. In this line, consumers look around for products with reduced fat and salt contents, along with functional food ingredients (prebiotics and probiotics), that aids in health care (Ferrao et al., 2018). Food industries are witnessing an upsurge for functional foods as they are considered as "Foods for Specified Health Uses" (FOSHU) with potential therapeutic health benefits. Japan has been a pioneer in leading and developing the functional food market. Recently, European countries like United Kingdom, France, Germany and Netherlands are showing an increase in the need for functional foods (Farid et al., 2019).

Prebiotics are non-digestible food ingredients that benefit the host by selective stimulation of the growth of beneficial colonic bacteria (Roberfroid, 2000). Prebiotic ingredient selective global market was valued at USD 3.4 billion in 2018 and is further expected to rise to USD 8.34 billion by 2026 with a compound annual growth rate (CAGR) of 10.1% (Watson, 2019). Non-digestible oligosaccharides (NDOs) are prebiotic carbohydrates made up of low molecular weight compounds. Non-digestible oligosaccharides can be differentiated based on the type of monomeric sugars: (i) Fructo-oligosaccharides (FOS), a sucrose-related oligosaccharides (ii) Galactooligosaccharides (GOS) and Lacto-sucrose, a lactose-related oligosaccharides (iii) Malto-oligosaccharides (MOS), Isomaltooligosaccharides (IMO), Trehalose and Cyclodextrins, a starch-related oligosaccharides (iv) Others-oligosaccharides including Xylooligosaccharides (XOS), Soybean oligosaccharides (SOS), Algal derived marine oligosaccharides (ADMO), Pectin-derived acidic oligosaccharides (pAOS), Human milk oligosaccharides (HMO). Fructooligosaccharides and Galactooligosaccharides have received much attention as prebiotic oligosaccharides at the research level and are commercially produced (Costa, Guimarães, & Sampaio, 2012; Crittenden & Playne, 1996; Prapulla, Subhaprada, & Karanth, 2000; Sangwan, Tomar, Singh, Singh, & Ali, 2011). XOS, IMO, MOS, SOS, pAOS and lactulose are considered as novel health promoting oligosaccharides (Meyer, Miguel, Fernandez, & Ortiz, 2015; Pan, Chen, Wu, Tang, & Zhao, 2009).

Among the different prebiotic oligosaccharides, XOS appears to be a promising candidate. They are produced from abundant, inexpensive and renewable sources like agricultural crops and their residues/by-products (Aachary & Prapulla, 2011). XOS occupies an important position due to their multi-dimensional influence on human health, and they are potential agents against several gastrointestinal disorders. There is a growing awareness on the role of human gut microflora in maintaining the host health, within the gastrointestinal tract as well as systemically by the absorption of metabolites. The intake of XOS improves the immune system (Chen, Chen, Chang, & Lin, 2012), modulates intestinal microbiota (Lin, Chou, Chien, Chang, & Lin, 2016) and reduces the risk of cancer (Maeda, Ida, Ihara, & Sakamota, 2012). XOS is stable to both heat and acidity during food processing, paving their way for application in low-pH food products compared to other prebiotic like inulin (Courtin, Swennen, Verjans, & Delcour, 2009; Vazquez, Alonso, Dominguez, & Parajo, 2000).

Additionally, XOS has shown to exhibit sweetness characteristics with prebiotic properties (Kim, Yoo, Jung, Park, & Hong, 2015). XOS is less documented in terms of production with substantial differences in chemical structure, degree of polymerization and technologies for producing oligosaccharides in high yields. There is a need to develop alternative approaches to enhance the process efficiency to meet the increasing demand with reduced costs.

The review aims to deliver an in-depth knowledge available from the vast literature of scientific investigations reported till date on the different aspects of XOS. XOS is majorly produced from xylan, in that line the extraction strategies involved for xylan production has been discussed briefly. The state of art developments of XOS from xylan using different methods from conventional processes to biotechnological approaches, its limitations and advantages has been detailed in production. The improvisations in the area of purification and characterization of XOS from qualitative analysis to quantitative analysis using high end sophisticated techniques is described. The physiological benefits and its various food applications are also explained. The originality of the review lies in the fact that it encompasses and compares the data from the research knowledge present till date in this field and with a detailed report.

2. Xylooligosaccharides (XOS)

'XOS is linear oligosaccharides composed of d-xylose units that are linked by β-1, 4 glycosidic bonds. The degree of polymerization (DP) of XOS ranges between 2 and 12 (Fig. 1), consisting of xylobiose, xylotriose, xylotetraose, xylopentose, xylohexose and xylohepatose (Carvalho, de Oliva Neto, Da Silva, & Pastore, 2013; Samanta et al., 2012). XOS with less than 4 monomers are considered important as prebiotics but may not be vital (Gullon et al., 2008). Nevertheless, by nature, XOS is present in vegetables, fruits, honey, milk and bamboo shoots in a limited quantity making it economically unsuitable for large scale production and purification (Vazquez, Alonso, Dominguez, & Parajo, 2000). Chemical synthesis or enzymatic hydrolysis of a suitable substrate such as xylan to produce XOS is the most preferred process on an industrial scale.
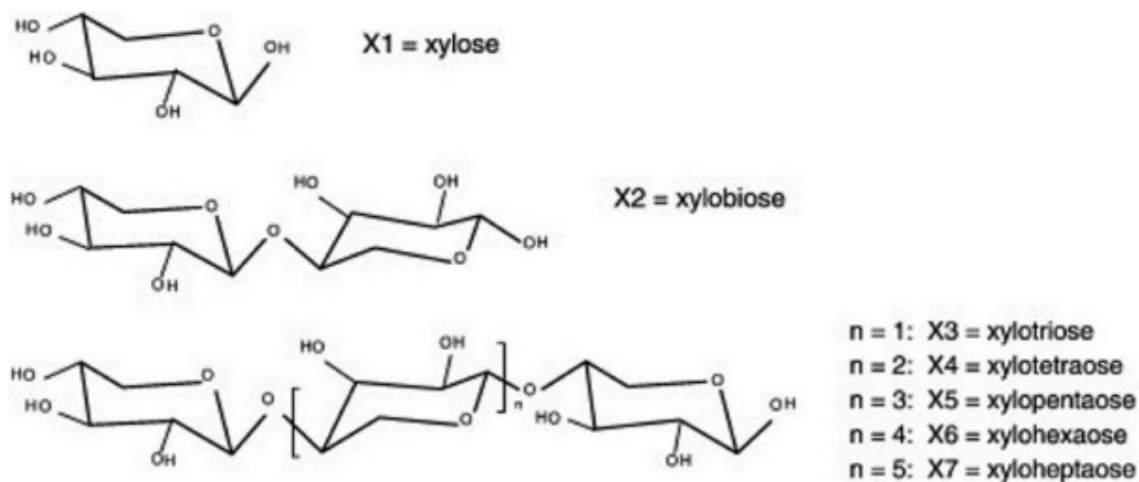

Fig. 1. Chemical structures of xylooligosaccharides (Carvalho et al., 2013).

2.1. Xylan as substrate

Xylan, a hemicellulose is abundantly present in the plant cell wall. They have branched polymers of (1 → 4) linked β-d-xylopyranosyl backbones, which may be substituted with arabinose, 4-O-methyl glucuronic acid (MeGlcA), ferulic acid, *p*-coumaric acid or an acetyl side group (Saha, 2003) (Fig. 2). Xylan is a low molecular weight (MW) polymer with a degree of polymerization (DP) in range of 80–200 (Ebringerova & Heinze, 2000), found universally in annuals, hardwoods, softwoods and seaweeds in marine environments (Linares-Pasten, Aronsson, & Karlsson, 2018). Plant hemicelluloses consist of two predominant monosaccharides: xylose and arabinose termed as arabinoxylans along with small contents of uronic acid (glucuronic acid and 4-O-methyl derivative). Plant hemicellulose (hardwood and softwood) also contain other type of xylan like gluco-xylan (glucose linked xylans) (Muralikrishna & Subba Rao, 2007; Scheller & Ulvskov, 2010). On the contrary, xylan from cereals and grasses consist of α-l-arabinofuranose residues that are linked to the backbone as single-unit side-chains, to the third position of xylose (Ebringerova & Heinze, 2000). Depending on the different sources used for the production of XOS, the structure differs, in terms of the degree of polymerization as well as the type of linkages present.
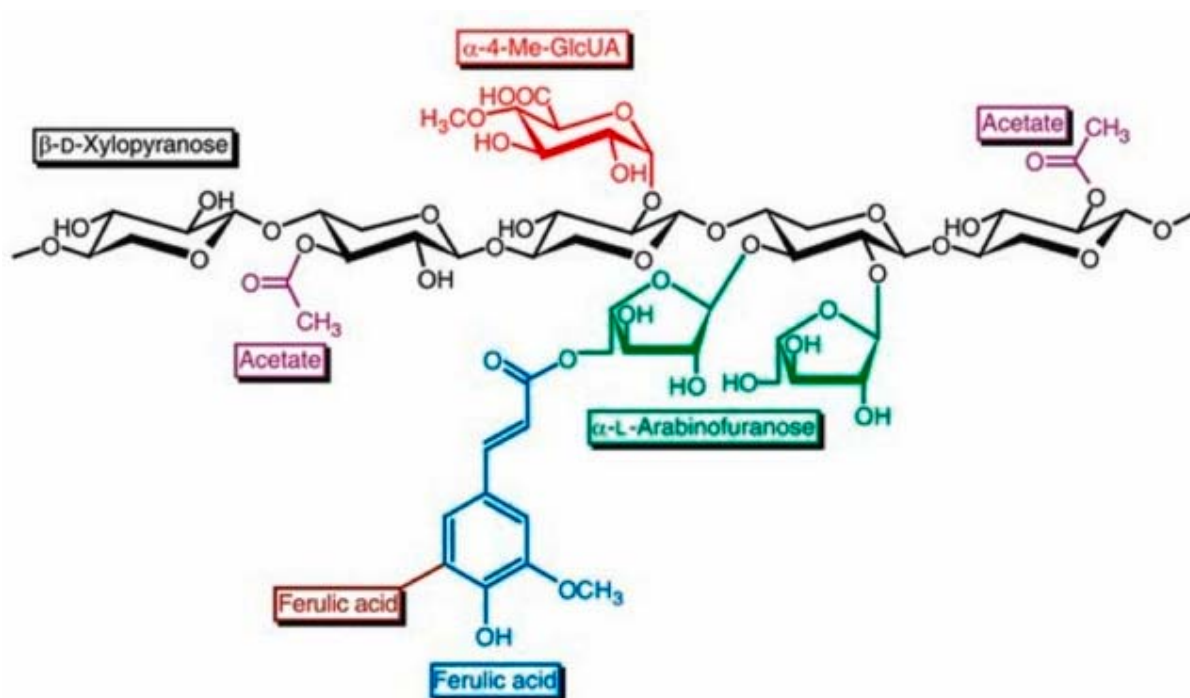

Fig. 2. Chemical structure of xylan (Saha, 2003).

Xylan extraction from the plant cell wall can be carried out using water (Manisseri & Gudipati, 2010; Palaniappan, Yuvaraj, Sonaimuthu, & Antony, 2017), alkali (de Mattos, Colodette, & de Oliveira, 2019; Khat-Udomkiri et al., 2018; Prashanth & Muralikrishna, 2014; Samanta et al., 2012), using dimethyl sulfoxide (DMSO) (de Carvalho et al., 2017; Fu et al., 2018; Rowley, Decker, Michener, & Black, 2013), hot water under pressure (Kilpelainen et al., 2012) and cold water under pressure (Ayyappan & Antony, 2017).

A major challenge during the extraction of xylan is the recalcitrance of biomass as it is highly bound to other cell wall components such as cellulose and lignin through chemical bonds and physical barrier (Zoghlami & Paës, 2019). Hemicellulose bonding with cellulose is mostly weak (hydrogen bonds), whereas, lignin forms ester linkage that are sensitive to hydrolysis with limited resistant ester/ether linkages. The limitation in alkali extraction is the use of salts such as sodium hydroxide, potassium hydroxide and barium hydroxide solutions at high temperature (90 °C). This leads to deacetylation, thereby shrinking the original structures and changing the swelling coefficient of hemicelluloses (Nilsson, Saulnier, Andersson, & Aman, 1996). Xylan derived naturally contains O-acetyl groups located at the hydroxyl ends of the xylan backbone. The acetyl groups in the isolated hemicelluloses need to be preserved as they maintain the water solubility; however, during alkali extractions, these groups are removed (Gabrielli, Gatenholm, Glasser, Jain, & Kenne, 2000). Water extraction aids in the isolation of high molar mass, water-soluble hemicelluloses (xylan) with less arabinose substitution. They help in preserving the hemicellulose structure; however, the resulting yield is relatively low (Ebringerova & Heinze, 2000). Such low yields of xylan by water extraction were reported by Rao and Muralikrishna (2004) from Bengal gram husk (2.78%) and wheat bran (4.8%). Even-though the method is advantageous in retaining the structure of xylan, and using green solvents that create a minimal environmental impact for food applications; the yields should be improvised by any pre-treatment process.

2.2. Production strategies of XOS

The production of XOS from xylan of lignocellulosic biomass (LCB) can be carried out by chemical synthesis, enzymatic hydrolysis (Aachary & Prapulla, 2011; Samanta et al., 2015) or by combining both chemical and enzymatic treatments (Izumi, Azumi, Kido, & Nakabo, 2004; Yang, Xu, Wang, & Yang, 2005). The enzymatic hydrolysis is commonly followed due to its reproducibility and high yield (Charalampopoulos & Rastall, 2012). At present, XOS is commercially produced by the enzymatic hydrolysis of corn cob xylan (Aachary & Prapulla, 2011; Wako, Osaka, Japan; Mitmesser & Combs, 2017). In contrast, other sources such as sugarcane bagasse, corn husk, cereal straw flax shives, wheat bran, almond shells, bamboo etc., are yet to be commercialized (Samanta et al., 2015).

XOS production through chemical methods can be carried out by autohydrolysis, hydrothermal treatment, steam, micro-wave assisted and dilute solutions of mineral acids or alkaline solutions. During the aqueous processing of xylan, the hydronium ions (generated from water auto-ionization and from *in situ* generated organic acids) progressively breaks the hemicellulosic chains by hydrolytic action. The reaction yields soluble products but leaves behind both cellulose and lignin with a little chemical alteration. As acid hydrolysis releases toxic and undesired products such as furfural, that have reported to affect the functionality of the oligosaccharide (Akpinar, Erdogan, & Bostanci, 2009); green extraction technology using enzyme-based methods are appreciated as they are environmentally friendly alternatives.

Enzymatic hydrolysis of XOS using endoxylanase is highly regarded in the food industry as it does not require special equipment, high temperatures and pressure to operate, as well as produce any undesirable by-products in contrast to autohydrolysis (Akpinar et al., 2009; Samanta et al., 2015). The glycosidic linkages of the xylan backbone are cleaved by xylanase

to produce small fragments such as xylose, xylotriose and xylobiose. The bacterial and fungal enzymes of the glycoside hydrolase (GH) families; GH10 and GH11 are extensively used for the production of different types of XOS. Mostly, the GH10 endoxylanases utilize small substrates to produce xylose, whilst, GH11 enzymes preferably attack the lengthier chains of xylan and inhibit xylose production (Juturu & Wu, 2012; Palaniappan, Balasubramaniam, & Antony, 2017). Xylanase act on the β-1,4- (or β-1,3) linkages and can be endo-acting (differently substituted xylan backbone are hydrolyzed) or exo-acting (xylan from reducing or non-reducing end get hydrolyzed). Endo-1,4-β-xylanases (EC 3.2.1.8) cleaves the β-1,4-linked backbone of xylan randomly and are the most commonly investigated. Endoxylanase are the key enzymes for the production of XOS and have been widely studied. The increased knowledge of endoxylansase on the diverse specificity at a structural level helps in the production with improvised yields (by enzyme combinations) and different types of XOS (using specific enzymes).

The enzymatic degradation of complex hemi-cellulosic biomass into desired components (XOS), necessitates the cooperative action of different enzymes due to their complex chemical compositions, physicochemical properties and physical structures. Many studies state that a synergy of two enzymes have been implemented for the hydrolysis of xylan that results in better and improved XOS yield (Kiran, Akpinar, & Bakir, 2013). Azelee et al. (2016) studied the effect of mixture of xylanase:arabinofuranosidase (Xyn2:AnabfA) in pretreated kenaf stems and showed a 95.03% of XOS yield, compared to single enzymes (30%). This could be because of the action of AnabfA, that degrades the arabinose branching sites leaving more spaces for the action of Xyn2 to degrade the xylan backbone into smaller polymers. However, some important factors should be considered for the use of synergistic enzymes for XOS production: raw material selection, type of pre-treatment and the choice of primary and accessory enzymes (Van Dyk & Pletschke, 2012). Commercial Xylanase preparations contain a mixture of various xylanolytic enzymes such as endo-1,4- -xylanases, 1,4--d-xylosidases, -l-arabinofuranosidase, -d-glucuronidase, galactosidase and acetyl xylan esterases at different levels and they have wide applications in different industries. Literature provides enough knowledge in this field so as to increase the possibilities to choose an enzyme candidate, or a cocktail of enzymes that improve the overall yield of XOS by enzymatic hydrolysis of xylan.

Table 1 presents a comprehensible literature available on the recent techniques (autohydrolysis, chemical and enzyme hydrolysis) used for the production of XOS. It can be seen from Table 1, that XOS production from chestnut shells by autohydrolysis (non-isothermal) resulted in the least yield (5.7%), while acid hydrolysis showed the highest yield (86.6%). It can also be noted that the chemical methods have been improvised with the aid of pretreatment processes. Pre-treatment of the lignocellulosic biomass with helps in hydrolysis of hemicellulose backbone linked to cellulose microfibril into soluble oligosaccharides (Qing, Li, Kumar, & Wyman, 2013). Microwave assisted acid hydrolysis enhanced the yield by 5-fold, while acetic acid pretreatment by 10-fold, when compared to the auto hydrolysis. Dry steaming can also be initiated as a pre-step for increasing the efficiency of enzymatic hydrolysis by volatilizing furfural. Ultrasound as a pre-treatment has great potential for extraction of xylooligomers and other oligosaccharides. The chemical and physical effects produced by ultrasonic waves enhance the delignification and surface erosion of the lignocellulosic biomass (Bussemaker & Zhang, 2013).

Table 1. Production of XOS from various substrates by different methods.

Substrates	Methods	Yield (%)	Reference
Physicochemical			
Corn cob	Acid hydrolysis, 10 mL of 0.25 M H_2SO_4, 90 °C, 15–30 min	86.60	Samanta et al. (2012)
Sugarcane bagasse hemicelluloses	Microwave-assisted acid hydrolysis, dilute H_2SO_4 (0.1–0.3M), at 90 °C, 20–40 min	29.02	Bian et al. (2014)
Beechwood xylan	Acid hydrolysis, 0.7 M H_2SO_4, 90 °C, 45 min	22.10	Chemin et al. (2015)
Hazelnut Shells	Autohydrolysis, Isothermal 190 °C, 5 min (heating), 5 min (holding) up to 45 min at 300 rpm Liquid to Solid Ratio (LSR) = 10, Logarithmic values of severity factor (Log R_0) = 3.92	10.00	Surek and Buyukkileci (2017)
Chestnut Shells	Autohydrolysis, non-isothermal 180 °C LSR = 8, Severity factor (S_0) = 3.08	5.70	Gullon et al. (2018)
Corn cobs	Steam explosion using acidic electrolyzed water, *Paenibacillus barengoltzii* (PbXyn10A) xylanase, 12 h	75.00	Liu et al. (2018)
Almond Shells	Autohydrolysis, Isothermal 200 °C, 20 min (heating), 5 min (holding), LSR = 10, S_0 = 3.94	High DP (>4) XOS 7.70 Low DP XOS (<4) 3.30	Singh, Talekar, Muir, and Arora (2019)
(Populus) poplar	Acetic acid treatment, pre-treatment at 170 °C, 5% Acetic acid, and 30 min	55.80	Wen, Zhang, Wang, Lian, and Zhang (2019)
Enzymatic hydrolysis			
Wheat bran	0.28 U Endoylanase, Finger millet (*ragi* malt), 50 °C, 2 h	14.40	Manisseri and Gudipati (2010)
Bengal gram husk and wheat bran	0.28 U Driselase (endoxylanase), *Basidiomycetes* sp,50 °C, 2 h	5.80 & 14.40	Madhukumar and Muralikrishna (2012)
Corn cob	pH - 4.0, 5.0 and 6.0, Temperature - 30, 40 and 50 °C, Endoxylanse, *Trichoderma viridae* - 2.65, 6.625 and 13.25 U, Incubation time - 8, 16 and 24 h	50.00	Samanta et al. (2012)
Sugar Cane bagasse	2.65 U Endoxylanase, *Trichoderma viridae*, pH 4, 40 °C, 8 h	0.17	Jayapal et al. (2013)
Wheat straw	0.48 U Endoxylanase A (mutated at K80R), *Bacillus halodurans* S7, 50, 55, 60 and 65 °C, 7 h	39.77	Faryar et al. (2015)
Sugarcane bagasse	Aqueous ammonia PTT, β-xylosidase-free xylanase of *B. subtilis* (KCX006), 40 U of endoxylanase and 4.3U of α-l-arabinofuranosidase, 50 °C, 30h	67.00	Reddy and Krishnan (2016)

Pretreated corn cob	Ultra-high-pressure PTT, 100 U Endoxylanase, *Streptomyces thermovulgaris* (TISTR1984), 55 °C, 24h	10.66	Seesuriyachan, Kawee-ai, and Chaiyaso (2017)
Wheat bran	Washing with sodium acetate buffer followed by alkali extraction. Recombinant *Bacillus amyloliquefaciens* xylanase A, 0.4 U, 40 °C, 24 h	16.14	Liu, Huo, Xu, and Weng (2017)
Finger millet Seed coat (CO9 *v*)	Sodium acetate buffer (0.1 M, pH 4.8) 50 °C, 125 U commercial endoxylanase from *Trichoderma longibrachiatum*, 7 h	72.00	Palaniappan, Balasubramaniam, and Antony (2017)
Rice bran	Sodium acetate buffer (0.1 M, pH 4.8) 50 °C, 125 U commercial endoxylanase from *Trichoderma longibrachiatum*, 7 h	68.00	Ayyappan and Antony (2017)
Coconut husk	Crude xylanase concentration -1–5%, pH - 4–6, temperature - 45–65 °C, incubation time - 6–18 h	82.50	Jnawali, Kumar, Tanwar, Hirdyani, and Gupta (2018)
Hemicellulose dissolving pulp	Incubation time - 1, 2, 6, 8, 10, 12, 20, and 24 h, endoxylanase dosage - 50, 80, 120, and 150 IU g^{-1} substrate, pH 5, 50 °C in a 50 mM sodium acetate buffer solution in the incubator (150 rpm)	45.18	Wang et al. (2018)
Brewers' spent grain	Commercial endo xylanase from *Trichoderma longibrachiatum*, 20 g/L, 12 h	44.43	Amorim et al. (2018)
Beechwood xylan	Reaction mixture consisted of 3.0% (w/v) xylan in 0.05 M sodium citrate buffer at pH 5.3, endo-xylanase concentration 200 U/g of substrate, at 50 °C and 180 rpm for 36 h	0.92	Guido, Silveira, and Kalil (2019)

From Table 1, XOS production using enzymes showed varied yields ranging from as low as 5.8%–82.5%. A higher yield can be achieved by optimizing the processing conditions such as enzyme stability and its pH, temperature, and reaction time accordingly (Akpinar et al., 2009; Linares-Pasten, Aronsson, & Nordberg Karlsson, 2018). Enzymes are more effective after a thermal treatment as the active sites of the enzymes have improved access to the substrate. The hydrolyzing ability however decreases with enzymes at higher quantities which could be due to feedback inhibition by the enzymes (Sun, Yoshida, Park, & Kusakabe, 2002). With the advent of biotechnological approaches, some novel techniques have been developed for the improvisation of XOS production both chemically and enzymatically.

The cost of enzymes is a major drawback in the production of XOS as they are expensive due to their isolation and multi-step purification steps. However, a recent strategy is the use of immobilized enzymes that increases the catalyst efficiency, continuous operation of enzymatic processes, allow the easy recovery of both enzymes and products, rapid termination of reactions and multiple reuse of enzymes (Homaei, Sariri, Vianello, & Stevanato, 2013; Illanes et al., 2016). Immobilized enzymes can optimize a process as well as help to achieve affordable commercialization of XOS production (Goldman, 2009). The ultimate challenge for researchers is to maximize the yield of XOS with fewer impurities and unwanted by-products. To overcome the limitations faced during the production of XOS, there is an increasing need to develop an innovative, convenient and efficient production technology by applying process integration strategies.

3. Characterization of XOS

3.1. Purification and separation

The purification of XOS with desired degree of polymerization (DP) range is achieved by removing the monosaccharide or non-saccharide compounds. Based on the degree of purity; purification and separation of XOS may require multistep down-stream processing which directly impacts the cost of production (Vazquez, Garrote, Alonso, Dominguez, & Parajo, 2005). A number of purification techniques such as solvent extraction, adsorption techniques, membrane separation and chromatography have been assessed (Illanes et al., 2016; Qing et al., 2013; Vazquez, Alonso, Dominguez, & Parajo, 2000). Membrane technology is gaining importance as a promising downstream strategy for the production of high-purity XOS at industrial scale (Crittenden & Playne, 1996). Ultrafiltration, requires low energy and is easy to scale-up for the separation of oligosaccharides produced from higher molecular-weight compounds effectively (Czermak et al., 2004). Yet, Cordova, Astudillo, and Illanes, (2019) indicate that ultrafiltration is more of a pre-treatment step of XOS rather than purification step. To aid the removal of small contaminants from almond shell XOS (autohydrolysis and enzymatic treatment); Singh, Nadar, Muir, and Arora (2019) utilized both ultrafiltration and nanofiltration for purification. Ultrafiltration helped in removing high molecular weight compounds, while the nanofiltration step concentrated the XOS mixture and removed the monosaccharides. This synergistic approach led to XOS of fractional purity (57%).

The adsorption-based purification techniques use various adsorbents such as aluminum hydroxide or oxide, activated carbon, silica, titanium, bentonite and porous synthetic

materials (Qing et al., 2013). Activated charcoal treatment is an option for the elimination of lignin and carbohydrate-based degradation compounds from the XOS mixtures (Montane, Nabarlatz, Martorell, Torne-Fernandez, & Fierro, 2006). A study by Chen et al. (2014) showed that 10% activated carbon with ethanol/water elution aided in recovering 47.9% XOS from *Miscanthus x giganteus*, followed by elution with ethanol. Otieno and Ahring (2012) reported that higher purity of XOS could be obtained by pretreating the liquor containing xylose to filtration, decolouration, membrane filtration, centrifugation, and spray drying. Besides, the purification of liquid media depends on the molecular weight, solubility and intermolecular bonding.

Ion-exchange resins in combination with other purification processes have been applied to remove the negatively/positively charged organic compounds, salts, heavy metal ions and other pigments present in XOS mixtures (Chen, Bowman, et al., 2016). Chen, Bowman, et al. (2016) evaluated the purification of XOS using adsorption with activated charcoal simultaneously with ethanol elution followed ion-exchange adsorption involving three steps (different charged resin in each step). The treatment caused no change to the composition of oligomer with high XOS recovery yields of 91% as well as the XOS mixture was highly fermented by *Bifidobacterium catenulatum* and *Bifidobacterium adolescentis*, proving that the addition of ion exchange resin step for the purification was crucial for the prebiotic effect of the end product.

Capillary electrophoresis (CE) has been successful for the separation of XOS compounds since the mid-1990s (Khandurina & Guttman, 2005; Rydlund & Dahlman, 1997; Sartori et al., 2003). Yet the lack of chromophores and charged groups in XOS limits the application of CE to separate the essential oligosaccharides (Arentoft, Michaelsen, & Sorensen, 1993; Zemann, Nguyen, & Bonn, 1997). Gel-permeation chromatography (GPC) is commonly used and easily adapted separation technique. Depending on the pore size of the Bio-Gel used, XOS of high-purity fractions with different DP ranges can be collected; the performance of the separation can be further improved by connecting more columns in a series. Although Gel-permeation chromatography separation of oligosaccharides is relatively sound, the limitation lies in its high cost for large-scale production of XOS (Manisseri & Gudipati, 2010). Chromatographic techniques are generally used for purification prior to structural characterization of XOS. The popularity of the purification techniques is attributed to its low energy requirements, easy scale-up and easy to manipulate operational variables, i.e., temperature, pressure agitation and rate of feed flow. The separation techniques are required to produce high purity XOS fractions with the desired DP ranges for industrial food applications.

3.2. Analytical characterization

Structural information on monosaccharide composition and the glycosidic linkages of methylated XOS can be measured by nuclear magnetic resonance (NMR) spectroscopy, gas chromatography-mass spectrometry (GC–MS) and high-performance anion-exchange chromatography with pulsed amperometric detection (HPAEC-PAD). Matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS) is an efficient tool for determining the molecular weight distribution of XOS (Qing et al., 2013). Structure of derivatized XOS can be analyzed utilizing a Reverse-phase high-performance liquid chromatography (RP-HPLC) in

combination with MS/MS (Bowman, Dien, Vermillion, & Mertens, 2014). Quemener, Ordaz-Ortiz, and Saulnier (2006) structurally characterized the arabinoxylooligosaccharides (AXOS, neutral deprotonated) by electrospray ionization quadrupole time-of-flight mass spectrometry (ESI-QTOFMS) and electrospray ionization ion trap mass spectrometry (ESI-ITMS). The results exhibited that the negative ion MS/MS technique could differentiate the mono- or di-substituted AXOS, giving precise structural information.

High Performance Liquid Chromatography (HPLC) is widely used for analysis, as there is no requirement for sugar derivatization. HPLC with a refractive index detector (RID) determines the components of monosaccharides released from chemical or enzymatic hydrolysis. The detection of oligosaccharides by HPLC-RID is mainly limited to products with a DP of 2–5 (Li, Converse, & Wyman, 2003). HPLC-RID, HPAEC-RID (PAD) have been used to detect and quantify XOS of varying DP derived from several sources. Yet, the methods cannot be applied if XOS is produced from hemicelluloses of lignocellulosic biomass, as they have low solubility due to the number compositions of side chains (Qing et al., 2013). However, evaporative light scattering detector (ELSD) have higher sensitivity and less susceptible to temperature change induced difference in sensitivity as observed with refractive index detector (Alltech, 2005). Ohara, Owaki, and Sonomoto (2006) characterized XOS (up to DP 6) through a cation-exchange column (Sugar KS-802; Showa Denko, Tokyo) equipped with RI detector. Palaniappan, Balasubramaniam, and Antony (2017) used an amino columns NH_2P (Ashipak NH_2P-50 4E - Shodex, HPLC) with ELSD detector for the characterization of XOS (enzymatic hydrolysis (endoxylanase) of finger millet seed coat xylan) with a DP up to 3. An ultrahigh-performance liquid chromatography (UPLC) with a BEHHILIC (unbonded ethylene bridged hybrid efficient hydrophilic interaction chromatography) column and 4000 QTrap MS detector was also utilized for the characterization of XOS (Tomkins, Van Berkel, Emory, & Tschaplinski, 2010).

The analytical techniques such as HPLC, GC-MS are sufficient for characterizing the glycosyl residue compositions for oligosaccharides. Nevertheless, they are unable to provide detailed structural information such as the configuration of glycosyl linkages, a sequence of glycosyl residues and the anomeric arrangement. NMR has shown to be a potential technology for the understanding of oligosaccharide structures, using ^{1}H and ^{13}C isotopes. With the usage of different combinations of ionizations and analyzers like coupling to MS with chromatography techniques such as Gas chromatography-Mass spectrometry (GC-MS), High performance liquid chromatography-Mass spectrometry (HPLC-MS), High performance anion-exchange chromatography-Mass spectrometry (HPAEC-MS) and Electro-spray Ionization-Mass spectrometry (ESI-MS); there is a better characterization of the structural features; however, challenges remain unaddressed.

At present, some chromatographic methods are utilized for oligosaccharide analysis to facilitate retention, separation and detection of analytes; as the separation of α/β anomers results in the splitting and congestion of peaks in the chromatogram. Recent technological advances in glycomics help in the qualitative and quantitative determination of oligosaccharides even in the presence of complex matrices. XOS of permeate and retentate streams from each separation step, along with the liquid extract from the ion exchange step, and the final dry product is assayed for certain specifications. The identity and quality of the product are standardized by parameters such as levels of total oligosaccharides,

carbohydrate monomers (glucose, fructose and sucrose up to 12%), XOS with a DP range of >75%, xylose of <1%), polyphenols less than 2% and organic acids (<1%) (GRAS Notice (GRN) No. 816, 2018). The final product needs to meet these specifications and further evaluate the prebiotics potential and released for packaging.

4. Health benefits of XOS

The properties of XOS relies on the structure, the type of sugars present and their degree of polymerization (DP) (Brienzo, Carvalho, Figueiredo, & Oliva Neto, 2016). Several research with initial investigations reveals the beneficial effects of XOS for its bifidogenic activity, maintenance of gastrointestinal health, reduction of blood cholesterol, increase in mineral absorption, immune stimulation, glucose reducing ability, antioxidant and anticancer activity (Aachary & Prapulla, 2009; Ando et al., 2004; Madhukumar & Muralikrishna, 2010; Swennen, Courtin, Van der Bruggen, Vandecasteele, & Delcour, 2005).

Till date, the mechanisms of action of prebiotics like fructans, lactulose and galactansare the most studied and delineated in the literature (Guarino et al., 2020). Whereas further investigations are required to understand the possible health benefits of other prebiotics, such as XOS, Soybean oligosaccharides and Resistant Starch (Guarino et al., 2020). Thus, although the mechanism of XOS is not research or known, the general mechanism of action of certain health benefits of prebiotics are as follows:

a. Prebiotics reduce adiposity by decreasing the expression of G-protein coupled receptor in the subcutaneous adipose tissue, leading to in a dip in the concentration, and thereby resulting in lipolysis (Dewulf et al., 2011). Prebiotic also decrease the size of adipocytes as the large-sized adipocytes have increased level of fatty acids, insulin resistance and Tumor necrosis factor-alpha (TNF-α).
b. The prime focus of any prebiotic is to stimulate the growth and activity of the gut beneficial bacteria which in turn metabolizes the prebiotics to release fermentation by-products such as short chain fatty acids (SCFA). SCFA's influence the cell integrity of the Gastrointestinal tract (GI) tract, help in glucose homeostasis and modulation of immune function (Koh, De Vadder, Kovatcheva-Datchary, & Bäckhed, 2016). For an example, SCFA's reduces the luminal and fecal pH, which helps in the inhibition of the growth of pathogenic bacteria. They also reduce the formation of phenolic compounds, toxic nitrogen (ammines ammonia) and lessens the activity of undesirable bacterial enzymes (Slavin, 2013).
c. Prebiotics helps in reducing the energy intake by altering satiety hormones like ghrelin, peptide YY (PYY), and Glucagon-like peptide (GLP-1), thereby resulting in reversing weight gain (Parnell & Reimer, 2012).

It should be noted that the prebiotics action on colon microbiome diversity is still under debate. At present, more profound investigations are necessary for understanding in detail the molecular mechanisms underlying the favorable effect of each separate type of oligosaccharides (Lovilloa, Luna, & Fernández, 2020).

Table 2. Prebiotics efficacy of XOS by *in vitro* fermentation.

Studies	Major findings	Fermentation Products	Reference
Prebiotic activity of corn cob XOS	Higher growth in the order: *E. faecium, E. fecalis, L. maltromicus, L. viridescens*	Not stated	Samanta et al. (2012)
XOS utilization for the growth of *Weissella* strains (6 different strains)	•*Weissella* strains growth utilizing XOS evident •Lactate and acetate majorly produced	Lactate (9 mM) and acetate (11 mM) was predominant.	Patel et al. (2013)
Corn cob XOS tested for prebiotics activity of *Lactobacillus plantarum*	High growth rates with dense cells seen	Acetate was the major SCFA with varying levels (1.50–1.78 mg/mL).	Yu et al. (2015)
XOS fermentation with pig faecal inoculum in the presence of *Salmonella*	XOS was little fermented	150 mg SCFA/g after 24 h	Tran, Boudry, Everaert, and Bindelle (2016)
In vitro* fermentation of XOS from *Miscanthus giganteus (MA-G)	•Decrease in the pH •Increase in beneficial bacteria •High production of SCFA	Total SCFA (289 mg/g) Acetic acid - 194 mg/g and 95 mg/g lactic acid	Chen et al. (2016)
XOS syrup from wheat bran	*Lactobacillus brevis* showed maximum growth with 0.5% XOS syrup	Not stated	Geetha and Gunasekaran (2017)
XOS from finger millet seed coat	Prebiotics activity was strain-specific *L. plantarum > L. acidophilus > L. casei > L. lactis*	Not stated	Palaniappan, Balasubramaniam, and Antony (2017)
Corn cobs and sugar cane XOS inoculated with adult faecal microbiota	•Positive shifts in gut microbiome composition •Increased SCFA production	XOS produced the highest level of SCFAs than the other fibers Corn cob (127.4 mg/mL); Sugar cane (180.3 mg/mL)	Fehlbaum et al. (2018)
XOS from *Moso* bamboo pre-hydrolyzate	•Increased counts of intestinal *Bifidobacteria adolescents* •Stimulates the production of SCFA's by *Lactobacillus acidophilus*	Lactic acid was the main product 1.5 g/L.	Huang et al. (2019)
Fermentation of beech wood XOS with *Bacillus subtilis* 3610 and human faecal inocula from two healthy donors.	Increased growth of *Bacteroides*	Highest production of Butyrate (Donor 1 = 9.0 ± 0.6 mM; Donor 2: 10.5 ± 0.8 mM)	Amorim et al. (2020)

4.1. A brief discussion on prebiotic efficacy of XOS

Research efforts are oriented at aspects that can positively contribute to animal and human health. In this regard, ways to stimulate beneficial microbiota and repress the growth of pathogenic organisms in the colon have received much attention. In the early 1990s, Japan was the first country to use prebiotics as a food ingredient for gastrointestinal health. The potential health benefits of non-digestible oligosaccharides, particularly the activity as prebiotics have been demonstrated through various *in vitro* methods, animal models and clinical trials (Crittenden & Playne, 1996; Rycroft, Jones, Gibson, & Rastall, 2001).

In vitro studies prove that XOS can stimulate the growth of probiotic strains; however, the utilization of XOS was strain-specific, attributed to its homo-fermentative property (Table 2). Table 2 details the prebiotic efficacy of XOS by *in vitro* fermentation evident from different studies. The studies cited in the table clearly shows that XOS aids in the selective stimulation of beneficial non-pathogenic organisms; *Lactobacillus* family showing maximum growth. Fehlbaum et al. (2018) reported XOS and beta-linked galactooligosaccharides resulted in the positive shifts in gut micrbiome. In comparison to other prebiotics such as galacto-oligosaccharides, fructo-oligosaccharides and inulin, XOS showed high resistance to digestion in the upper gastrointestinal tract, better ability to stimulate the growth of *Bifidobacteria* and *Lactobacillus* and the production of SCFA and lactate to a greater extent (Huang et al., 2019; Madhukumar & Muralikrishna, 2012). XOS are potential prebiotic candidates in the promotion of normal microbiota balance, particularly species of *Bifidobacteria*, are more efficiently grown on XOS than fructooligosaccharides (official prebiotics). Huang et al. (2019) observed that several species of *Lactobacillus*, *Bifidobacterium* and *Bacteroides* exhibited growth with XOS (2–5 units of xylose) as a sole carbon source in the *in vitro* fermentation culture media. XOS has shown to inhibit the pathogenic microorganisms such as *Enterococcus* spp., *Escherichia coli*, *Clostridium difficile* and *Clostridium perfringens* (Crittenden et al., 2002) and prevents the adhesion of *Listeria monocystogenes* on the intestinal epithelium (Ebersbach, Andersen, Bergström, Hutkins, & Licht, 2012).

Table 3 shows the beneficial effects of XOS incorporated in different animal models. The studies illustrated in the table exhibited the following results: improved body weight, better intestinal health, increased count of beneficial bacteria and the SCFA content. It should be noted that the reduction in the cecal pH could be credited to the rise in the content of SCFA produced from the selective fermentation by *Bifidobacteria* and *Lactobacilli*. The presence of feruloyl substituent's in XOS might help in the growth of beneficial bacteria and produces higher butyric acid due to the slow fermentation of branched XOS while fructooligosaccharides and galactooligosaccharides with longer DP's still produce lower amounts of butyrate (Patel & Prajapati, 2015). Butyrate, an SCFA regulates the gene expression in colonocytes, pro-differentiation, anti-proliferation, maintains the gut barrier function, intestinal metabolism and anti-inflammatory (Cheng et al., 2018; Gibson & Wang, 1994). Gobinath Madhu, Prashant, Srinivasan, & Prapulla, (2010) showed that oligosaccharides has potential to render beneficial effects on the metabolic abnormalities associated with diabetes. Ding et al. (2018) reported the enhanced intestinal health of White Lohmann laying hens when administered with XOS in the diet. Fei et al. (2019) have reported the protective effects of XOS against obesity-induced colonic inflammation by

Table 3. Prebiotics efficacy of XOS demonstrated by animal studies.

Studies			Findings	Reference
Dosage	**Type/Sex/Age/Sample no's**	**Time/duration**		
XOS dosage at 10% (w/w)	Wistar rats, Weight: 150–160g Sex: male,	6 weeks	Improved body weight, reduced hyperglycaemia, cholesterol, severe glucosuria, diabetic nephropathy, proteinuria, blood creatinine and urea concentration	Gobinath Madhu, Prashant, Srinivasan, and Prapulla (2010)
XOS dosage at 0.2% & 0.5%	Ross 308-Broiler chickens Age: 1-day Male N: 192 Female N: 192	6 weeks	Increase in the •length of the villus in the ileum •abundance of *Lactobacillus crispatus* and *Anaerostipesbutyraticus* in the colon and cecum •*Clostridium cluster* XIVa in the cecal •gene copies for butyrate production, butyryl-CoA:acetate CoA29 transferase in the caeca	de Maesschalck et al. (2015)
XOS at dosage 0, 1250, 2500, and 5000 mg/kg per day	Purebred Beagle dogs Age:7–8 months Male N: 16 Female N: 16	26 weeks	•The administration of XOS resulted in any major chronic toxicity in all the groups •No observed adverse effect level (NOAEL) of XOS is 2500 mg/kg body weight (BW)/day	Gao et al. (2017)
XOS at dosage of 0, 0.01, 0.02, 0.03, 0.04, 0.05%	White Lohmann laying hens Age: 28 weeks N: 1080	8 weeks	An increase in •villus height and the VH: CD ratio of the jejunum and length of the jejunum •*Bifidobacteria* and SCFA's content (butyrate) was in the cecum •the content of $1,25(OH)_2D_3$ in plasma •contents of IgA, TNF-α, IgM, and IL-2 XOS enhanced the intestinal health and immune function of laying hens	Ding et al. (2018)
Group 1- Normal diet Group 2-high fat diet (HFD) Group 3-HFD + XOS (2 g/kg)	Sprague Dawley rats Weight: 280 ± 20 g Age/sex: 8weeks/male N: 30	15 weeks	HFD + XOS treatment reduced the •plasma levels of monocyte chemoattractant protein-1, •TNF-α mRNA expression, •overall microbial abundance in the faeces XOS-treated rats increased the •beneficial bacteria •SCFA content	Fei et al. (2020)

			•increased in the gut and occludin mRNA expression in the rat colon XOS can alleviate colonic inflammation by regulating gut microbial composition and enhancing SCFA content in the gut.	
1) XOS - 100 mg/kg **2)IAPS – 600 mg/kg** **3)XOS (100 mg/kg) + IAPS (600 mg/kg**	Ross-308 chicks Weight: 44.00 ± 0.45 g Age: 1 day old N: 240	21 days	XOS + IAPS – •higher average daily gain and lower feed-to-gain ratio •lower plasma d-lactic acid •higher mRNA expression of claudin-1, claudin-3, and occludin in the jejunum *XOS, IAPS, and XOS + IAPS –* •increased the villus height (VH) of all intestine segments, jejunal goblet cell numbers •increased the mRNA expression of zonula occludens-1 and occludin of the jejunum	Wang et al. (2020)

Note: IAPS - gamma-irradiated Astragalus polysaccharides; BW – Base weight.

improving the intestinal microbial structure and increasing the abundance of SCFA-producing microbes in Dawley rats. Gao et al. (2017) showed that high dosage (2500 mg/kg) XOS had No observed adverse effect level (NOAEL) on beagle dogs; based on body surface area (conversion factor of 0.54 for dogs to human) corresponds to 81–108g XOS in human adults weighing 60–80 kg. In a recent study, Wang et al. (2020), experimented the combination of XOS and gamma-irradiated Astragalus polysaccharides and reported their potential as a chlortetracycline substitute that helps in improving the growth performance, intestinal barrier function and intestinal morphology of broilers. The literature reported in this review exhibits evidence of potential effects of XOS on various clinical disorders, paving a better way for their use in human subjects.

Studies elucidating the prebiotic efficacy of XOS from human intervention models are explained in Table 4. XOS at a dose of 8–12 g/day is recommended for human consumption (Xiao, Ning, & Xu, 2012). With various clinical trials using XOS, the bifidogenic effect and health benefits where generally observed at a least dose of less than 4 g/day, while fructooligosaccharides, inulin and resistant starch required approximately 10–20 g/day, 15 g/day and 30 g/day respectively to show a bifidogenic effect (Alfa et al., 2018; Bouhnik et al., 1999; Whelan, 2013). However, there has been a low incidence of adverse effects associated with high consumption of XOS resulting in minor gastrointestinal effects of physiological nature. Human intervention trials involving colonic fermentation of XOS showed a significant increase in the count of *Bifidobacteria*, a concomitant rise in faecal moisture and decrease of faecal pH. Further, at such concentration (8–12 g/day) XOS did not show any negative effects such as gastrointestinal disorders like belching, flatulence, rumbling and faecal smelling. Still, studies examining the prebiotics effect on gastrointestinal microbiota in human populations is scarce, investigations are essential to delineate the mechanisms involved in biological effects. The effects of XOS on metabolic disorders have been demonstrated through human intervention models: Childs et al. (2014) demonstrated that a 10% risk of reduction in coronary artery disease was achieved by XOS treatment; while Yang et al. (2015) reported that XOS modified the gut microbiota in healthy and Pre-diabetic mellitus subjects; however, future studies involving large sample size are required to learn about the metabolic impact of XOS and their connection between XOS-mediated gut microbiota changes and the pathogenesis of Type 2 Diabetes mellitus (T2DM). The influence of gut bacteria on human metabolism is mainly by regulating the host's immune response, intestinal glucose absorption, energy extraction and lipid metabolism (Musso, Gambino, & Cassader, 2011). Finegold et al. (2014) carried out studies in healthy people and stated that XOS administered at a dosage of 2.8 g/day, showed good tolerance and modified the composition of gut bacteria without any gastrointestinal side effects. Studies from the humans and animal models validate that XOS is an effectual prebiotic having the ability to alter the microbiota even at a lower level of 1.4 g/day in adults, which is lower than levels required by fructooligosaccharides (10 g/day) or galactooligosaccharides (10 g/day). However, further clinical studies with long-term administration of XOS is required determine the potential of XOS in the area of metabolic disorders.

The scientific evidence from an array of *in vitro* and *in vivo* studies demonstrates the ability of XOS possess the hallmarks of prebiotics such as showing resistance to gastrointestinal hydrolysis, fermentation by colonic microbiota, and selective stimulation of intestinal

Table 4. Prebiotics efficacy of XOS tested on human.

Studies				Findings	Reference
Dosage	Participant/Age/Sex	Type of study	Time period		
AXOS-10 g/day	Twenty healthy adults (women N: 14 Men N: 6 Age: 24 ± 5 years,	Randomized, placebo controlled cross-over Study	3 weeks	•Increased Bifidobacteria mainly *B. adolescentis* (+0·41 log to +0·81 log bifidobacteria/g dry faecal weight) •After 3 weeks, reduced urinary *p*-cresol (five to ten times higher before XOS consumption)	Cloetens et al. (2010)
XOS-5g, Inulin + XOS - 3 g inulin +1 g XOS	Sixty healthy volunteers Men N: 34 Women N: 26 Age: 18–24 years	A double-blind, randomized, placebo-controlled study	4 weeks	•XOS increased *Bifidobacterium* (1 log difference) •Propionic and butyric acid contributions were higher in the XOS and INU–XOS groups (50% higher) •Protein metabolism was only affected for p-cresol in the XOS group •70% higher faecal expression of s-IgA at V3 in the INU–XOS (1629 ng/mL faecal water) •XOS did not affect the LPS-induced ex vivo inflammation profile •Activity of α-glucosidase and β-glucuronidase were increased (170·9–270 mg/g DM)	Lecerf et al. (2012)
Wheat bran extract (WBE) containing AXOS - 3, 10 and 0 g/days	Sixty-three healthy adults Men N: 33 Women N: 30 Age:18–85 years,	Double blind randomized placebo controlled crossover trial	6 weeks	•Increased Bifidobacteria in 10 g WBE/d by over 2-fold; 3 g/d by 1.3-fold compared to placebo •High WBE increased the total level of faecal SCFA - acetic acid, butyric acid andpropionic acid by 8% relative to placebo •WBE decreased the *p*-cresol by 37% •Increased stool frequency and reduced constipation by 91% in WBE treatment groups compared to placebo (81%) •Reduced LDL (P = 0.168)	Francois et al. (2012)
XOS - 1.4g and 2.8g	Thirty-two healthy adults Men N: 11 Age: 23–34 years Women N: 21 Age: 21–49 years	A double-blind, randomized, placebo-controlled study	10 weeks	•Count of *Bifidobacterium,* total anaerobic counts and *Bacteroides fragilis was* increased in both XOS groups. •XOS intervention had no significant effect on stool pH, SCFA or lactic acid	Finegold et al. (2014)
XOS: 8 g/day Synbiotic formulation: XOS + Bi-07 (*B. animalis subsp. lactis*, 109 cfu/d)	44 healthy volunteers Age: 25–65 years	Double-blind, placebo-controlled, randomised, factorial cross-over study	3 weeks	*Immune parameters* •XOS deceased the expression of the CD16/56 on NKT cells by 1-fold (4.7 to −4.7 ΔMFI) •XOS and XOS + Bi-07 resulted in lower expression of CD19 on B cells (18.0 to −0.5 ΔMFI)	Childs et al. (2014)

				•XOS lowered IL-10 production •Faecal IgA was increased in XOS supplements (−147.5 to 209 µg/g wet-weightfaeces) in comparison to control *Biochemical parameters* •XOS resulted in high fasting HDL concentrations by 0.07 mM compared to control (−0.1 to 0.07) and lower total cholesterol:HDL-cholesterol ratio •Increased bowel movements per day by 1-fold •XOS + Bi-07 supplement significantly increased bifidobacterial content compared with the placebo (0.1–0.4 log_{10} cells/g dry-weight faeces) •Faecal isovaleric acid concentrations were increased •during the XOS + Bi-07 (−0.3 to 0.6 µmol/g wet-weight faeces)	
XOS 2 g/day	Pre-DM N: 13 (placebo: n = 6; XOS: n = 7) Healthy N: 16 (placebo: n = 9; XOS: n = 7)	A double-blind, randomized, placebo-controlled study	8 weeks	•XOS intervention reduced the abundance of Firmicutes •Infectious disease related to Streptococcus and Subdoligranulum in placebo groups was largely inhibited by XOS in healthy subjects •XOS diminished or reversed the magnitude of population decline in all four genera-*Blautia, Anaerotruncus, Dialister, and Oscillospira* •XOS decreased the abundance of *Enterorhabdus*in pre-DM, *Howardella*and *Slackia*in healthy subjects •XOS increased the count of *Blautia hydrogenotrophic* in pre-DM •XOS reduce serum leptin and serum TNFα by 50% in pre-DM after 8 weeks	Yang et al. (2015)
Rice porridge containing XOS - 1.2g	Twenty healthy subjects XOS N: 10 Placebo N: 10 Male-2, Female-8 Age: 23–25 years	A double-blind, randomized, placebo-controlled study	8 weeks	•XOS group had significantly higher Lactobacillus spp. counts compared to the placebo group (5.5–7.5 log cfu/g of faeces) •A decrease in the count of *Clostridium perfringens* (5.1–3.5 log cfu/g of faeces), total anaerobic bacterial count unaltered (11.8–11 log cfu/g of faeces)	Lin et al. (2016)

Bifidobacterium spp. Although, data from *in vitro* and *in vivo* studies support the effects of XOS as a bifidogenic agent that modifies the composition and activity of the gut microbiota, however, more information is required to elucidate further the mechanisms involved. Even though experimental evidence supports the hypothesis of XOS physiological benefits, still, human intervention studies are limited to prove these effects. Suggestively more information from human intervention studies is required to include XOS in the prebiotic list of ingredients.

5. Physico-chemical properties and food applications of XOS

The physicochemical properties of XOS are varied and interesting: water-soluble, low calorie (Vazquez, Alonso, Dominguez, & Parajo, 2000), less sweet, highly hygroscopic (Alonso, Dominguez, Garrote, Parajo, & Vazquez, 2003), highly stable in acidic media (pH 2.5–8.0), resistant to heat (above 100 °C) (Mano et al., 2018), exhibit water retention capacity, anti-freezing property (Moure, Gullon, Dominguez, & Parajo, 2006), acceptable organoleptic properties (mouthfeel, taste, texture and colour) (Hirayama, 2002), and non-carcinogenic (Kazumitsu, Boseki, Norio, & Yoshimasa, 1997), makes it much suitable for incorporation into foods.

XOS can be widely utilized in agriculture, pharmaceutical, food and cosmetic industries. The current and potential market applications of XOS correspond to their use as functional food ingredients. The recommended dietary allowance of XOS is a minimum of 0.7–1.4g (Vazquez, Alonso, Dominguez, & Parajo, 2000; Finegold et al., 2014) and a maximum of 12 g/day (Xiao et al., 2012) for different age groups (≤11 months to ≥ 65 years). Some of the cited literature is documented in Table 5. They can be utilized as sugar/fat replacer, taste/texture enhancer, for mineral absorption, weight management, diabetic foods and for immune health improvement (Samanta et al., 2015; Zhao et al., 2017) based on the Generally Recognized as Safe (GRAS) status issued by Food and Drug Administration (FDA) (2019), Foods for Specified Health Uses (FOSHU) and European Food Safety Authority (EFSA) (2018). The XOS syrup that is commercially available exhibits sweetness qualities that is 50% equivalent to that of sucrose along with physicochemical stability during processing conditions; this paves the way for the successful application as alternative sweeteners in food systems (Kyung et al., 2014). It can be utilized as sugar replacers, for the retention of moisture and to increase the fibre content in beverages, bakery and dairy products, chocolates and fruit jellies. Wu and Lin (2011) demonstrated a new role for XOS as cryoprotective agents for the preservation of Chinese meat balls and was successful in retaining the quality and sensorial attributes at a least concentration of 1% XOS. XOS as texture modifier showed their efficacy in producing strong gels (biopolymers) with increased shear stress (Penksza, Juhász, Szabó-Nótin, & Sipos, 2019). It has been seen that from view point of food processing, XOS had benefits over other functional oligosaccharides (fructooligosaccharides, inulin, galactooligosaccharides) as it was resistant to low pH and high temperatures. This feature allows XOS to be used in low-pH juices, carbonated drinks and acidic foods (Gupta et., 2016). The development of symbiotic foods with probiotics and prebiotics are seeing an increasing trend; for e.g. Bikkle manufactured by Suntory Ltd. Japan since 1993 is a drink comprising of XOS, whey minerals, oolong tea extract and *Bifidobacteria*, has received much attention among the consumers in the market (Gupta et., 2016).

Table 5. Application and functional properties of XOS in food systems.

S. No.	Functional Properties	Food system	Level of XOS addition	Major findings	Reference
1	Viscosity	Yoghurts	1.5, 2.5, 3.5 and 4.5%	XOS up to 3.5% showed strengthening effect on viscosity and decreased whey separation	Mumtaz, Rehman, Huma, Jamil, and Nawaz (2008)
2	Sugar replacer	Cookies	30.0%	Cookies with comparable diameter, height and slightly darker color compared to control	Pareyt, Finnie, Putseys, and Delcour (2011)
3	Prebiotics	*Idli*, a cereal-based fermented cake	0.2, 0.4 and 0.6% w∕v	0.4% XOS resulted in enhanced fermentation time (6 h), texture, color and sensory characteristics *Idli* with XOS showed higher moisture content and a softer texture	Aachary and Prapulla (2011)
4	Cryoprotective agent	Chinese meatball (20% fat)	XOS, sorbitol and sucrose (1% XOS+ 3% sucrose)	XOS resulted in high sensory juiciness of the product	Wu and Lin (2011)
5	Sweetener	Non-alcoholic carbonated drink	48.0%	XOS enhanced the full-bodied character of beverage without any drawback of off flavor, perception or mouthfeel	Gupta, Agarwal, and Hegde (2013)
6	Sugar replacer	Cookies	5–15%	5% of XOS enriched cookies highly acceptable in terms of physicochemical properties	Ayyappan et al. (2016)
7	Sweetness index	Oral Administration	XOS (8, 10, 12, 14, and 16%) and luohanguo (LHGE) extract (0.02–0.1%)	XOS and LHGE extract was 0.25- and 75.76-fold sweeter than 5% sucrose solution	Kim et al. (2015)
8	Sugar replacer	Bread	10–40%	Decrease in the loaf volume with increased XOS levels XOS incorporated at 30% resulted in a dough of excellent stability and better loaf volume	Ayyappan and Antony (2017)
9	Fat replacer, sodium reduction, flavour enhancer (yeast extract and arginine)	Processed cheese	3.30%	Improved physicochemical and rheological properties: increased melting rate, decreased viscosity and particle size, decrease in the consistency, increase in elasticity (G′) and firmness (G*) Sensory characteristics: low bitter taste,	Ferrao et al. (2018)

				improvised salt and acid taste, and high homogeneity	
10	Viscosity	Yoghurt	70% XOS (powder and liquid) levels 1, 3 and 5%	Liquid form XOS decreased the shear stress value and viscosity Powder XOS had nil effects	Penksza et al. (2018)
11	Prebiotics	Yoghurt	Inulin, xylooligosaccharides, iso-malto-oligosaccharides (3 or 5 g/kg milk)	Prebiotics (up to 5 g/kg) resulted in insignificant impact on the quality attributes and fermentation characteristics	Li, Ding, and Zhao (2019)
12	Rheology - rotational technique (flow curve)	Aqueous solution	XOS, FOS and Sucrose (0.5, 1, 2, 3, 4, 5, 10, 20, 30, 40, 50, 60, and 70% dry material)	At low concentration: XOS showed thickening effect similar to sucrose and lower than FOS At high concentration: XOS consistency was higher due to differences in the water-binding mechanism of powder form products	Penksza, Juhasz, Szabo-Notin, and Sipos (2019)
13	Rheology - rotational technique (constant shear rate)	Aqueous solution	XOS 70L, 70P, 95P, sucrose, and FOS - 50% dry material	The viscosity of XOS (70P) higher than sucrose and FOS	Penksza, Juhasz, Szabo-Notin, and Sipos (2019)
14	Texture modifier	Aqueous solution	1.0 g locust bean gum (LBG) + 1.0 g xanthan gum/5.0 g of gelatin mixed with XOS (70L, 70P,95P) 1 and 3% in aqueous solution	No influence of XOS on hardness or stability of the xanthan gels Low concentration XOS resulted in stronger initial gel Higher concentration XOS resulted in a gel more stable against increasing shear stress	Penksza, Juhasz, Szabo-Notin, & Sipos (2019)
15	Rheological properties - Ultra-high temperature/High-temperature short time (UHT/HTST)	Strawberry puree	5% w/w	No changes the rheological properties of XOS added strawberry puree during the storage	Dai, Leung, Corradini, Xiao, and Kinchla (2020)

6. Concluding remarks, future challenges and trends for XOS

The study delivered a comprehensive review on the production, characterization, health benefits and applications of XOS in food systems that gives a distinct direction to future research. According to the demand of the consumers for safe and quality foods, the industry is facing an upsurge to introduce new, natural and cost-effective functional ingredients. XOS has caught the attention of scientists around the globe for its diverse functional properties and can be administered at a dose less than 3 g/day. XOS have different facets and possibilities for the development of novel functional foods and a promising upcoming to fit into the food industry. A study conducted by the Global Info Research (GIR) in 2018, showed that the international market of XOS, projected a growth from 94 million USD in 2017 to 130 million USD in 2025, at a compound annual growth rate of 4.1% (e-Market Research, USA, 2018). This shows the opportunity in research, development and commercialization of XOS.

Based on the review discussed here, the future of XOS in food and pharmaceutical industries relies on the challenges and trends that can be stated as follows;

> ➤ The technological and financial feasibility of XOS production must be established.
> ➤ Enzymes have been regarded as a potential platform to yield XOS with the absence of toxic by-products, however, more insights into appropriate use of enzymes are required.
> ➤ A pre-treatment process prior to extraction is promising method as it increases the extraction yield as seen from this review.
> ➤ Challenges and opportunities exist in exploring the improved knowledge of the symbiotic relationships between XOS and colonic microbiota.
> ➤ It is necessary to study the structure-function relationship and to examine the bioavailability of XOS; as the non-digestible oligosaccharides are mainly metabolized/fermented by the colonic microflora; to produce metabolites/byproducts that exert beneficial biological effects.
> ➤ Research and development on metabolomics, have the potential to outstrip the molecular mechanisms between the XOS and gut microbiology. Nevertheless, the capabilities of XOS induced gut microbiota changes are now known, as is the potential to determine metabolome impact.
> ➤ The actual scenario of XOS as functional food ingredients in food applications is limited to laboratory scale experiments and needs to be scaled-up.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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