Belorkar and Gupta *AMB Expr (2016) 6:82*
DOI 10.1186/s13568-016-0253-5

AMB Express

MINI-REVIEW

Open Access

Oligosaccharides: a boon from nature's desk

Seema A. Belorkar[1*] and A. K. Gupta[2]

Abstract

This article reviews the varied sources of oligosaccharides available in nature as silent health promoting, integral ingredients of plants as well as animal products like honey and milk. The article focuses on exotic and unfamiliar oligosaccharides like Galactooligosaccharides, Lactulose derived Galactooligosaccharides, Xylooligosaccharides, Arabinooligosaccharides and algae derived Marine oligosaccharides along with the most acknowledged prebiotic fructooligosaccharides. The oligosaccharides are named as on the grounds of the monomeric units forming oligomers with functional properties. The chemical structures, natural sources, microbial enzyme mediated synthesis and physiological effects are discussed. An elaborate account of the different types of oligosaccharides with special reference to fructooligosaccharides are presented. Finally, the profound health benefits of oligosaccharides are rigourously discussed limelighting its positive physiological sequel.

Keywords: Oligosaccharides, Prebiotics, Functional food and applications

Introduction

Food industry is presently witnessing an upcoming market for edible products having health benefits apart from nutrition, now well recognized as functional foods. The market of functional foods is facing an increasing demand also because of consumer awareness about health. According to the Global Industry Analyst (GIA) report on the demand of prebiotics, based on studies in market trends in countries like US, Canada, Japan, Europe (France, Germany, Italy, UK, Spain, Russia and rest of Europe), Asia–Pacific (China, India and Rest of Asia–Pacific) and rest of World, the industry is likely to flourish to a tune of US $4.8 billion by 2018 from US $1.0 billion in 2011 (Spinner 2013).

Japan is one of the leading countries giving importance to functional food market focusing on "Food of Specified Health Use" (FOSHU). Many European countries like Germany, France, United Kingdom and Netherlands have also showed an extended demand for functional foods (Katapodis et al. 2004; Menrad 2003).

Since past three decades there has been constant evaluation of market trend of western countries witnessing increased demand of functional foods. Even in developing country like India, where the dairy industry is one of the main industries supporting economy, there has been a significant rise in demand of value added dairy products encompassing health benefits to the consumers (Gour 2013).

Prebiotics and probiotics have raised as best option for quench of the increasing need of functional food. Roberfroid (2000) studied probiotics and prebiotics food and reviewed their properties to be rightly labeled as functional foods. He explained that prebiotics are non-digestible food ingredients that benefit the host by selectively stimulating the growth or activity of one or limited number of bacteria in colon.

Food ingredients which naturally offer resistance to digestion, when reach the intestine exhibit a favoring effect on normal flora of the colon are called as prebiotics. Prebiotics encompass several health benefits like the calorie-free nature, act as artificial sweeteners, have non-carcinogenic nature and stimulate the growth of *Bifidobacterium* and probiotic *Lactobacilli* in the colon (Saminathan et al. 2011). They possess preventive effect against colon cancer (Moore et al. 2003). They have

*Correspondence: seema.belorkar@gmail.com
[1] Department of Microbiology and Bioinformatics, Bilaspur University, 206, Budhiya complex, Sarkanda, Bilaspur, Chhattisgarh 495004, India
Full list of author information is available at the end of the article

ability to decrease cholesterol levels in the serum (Fernandez et al. 2003). Phospholipids and triglyceride levels are also found to be regulated in the serum by prebiotic food (Katapodis et al. 2004). Fructooligosaccharides (FOS) are gaining wide acceptance as prebiotics (Belorkar et al. 2013). This mini review presents an overview of the types of oligosaccharides existing in nature, their sources and major thrust applications.

Oligosaccharides: types, sources and applications

Extensive research has been done on various types of oligosaccharides. They differ in their nature of monomeric sugars and are named so. They have varied sources of origin and differ in their benefits imparted to the consumer. The most popular oligosaccharides are FOS, Galactooligosaccharides (GOS), Lactulose derived galactooligosaccharides (LDGOS), Xylooligosaccharides (XOS), Arabinooligosaccharides (AOS), algae derived marine oligosaccharides (ADMO). Other oligosaccharides occurring in nature are Pectin-derived acidic oligosaccharides (pAOS), Maltooligosaccharides (MOS), Cyclodextrins (CD) and human milk oligosaccharides (HMO) with specific acknowledged benefits. The oligosaccharides have great industrial applications (Crittenden and Playne 1996; Prapulla et al. 2000). The chemical structure of some important oligosaccharides are given in Fig. 1.

Structure of fructooligosaccharides

FOS consist of a fructose units polymerized to different extent. Oligomers with two fructose units are called as 1-kestose. Oligomers with three fructose units are called as 1-nystose. Oligomers with four fructose units are called as 1-fructofuranosyl-nystose. The sugars are linked by β-2, 1 position of sucrose (Sangeetha et al. 2005).

Occurrence of FOS

Varieties of sources cater fructooligosaccharides in varying concentrations as its natural component like wheat, honey, onion, garlic and banana (Roberfroid and Slavin 2000). Barley and tomato contains 0.15 % of fructooligosaccharides. Banana and brown sugar has 0.30 % fructooligosaccharides. Honey has 0.75 % of fructooligosaccharides (Flamm et al. 2001).

Bornet et al. (2002) recorded the occurrence of short chain FOS in many edible plants. Fructooligosaccharides expresses degree of polymerization from 1 to 5

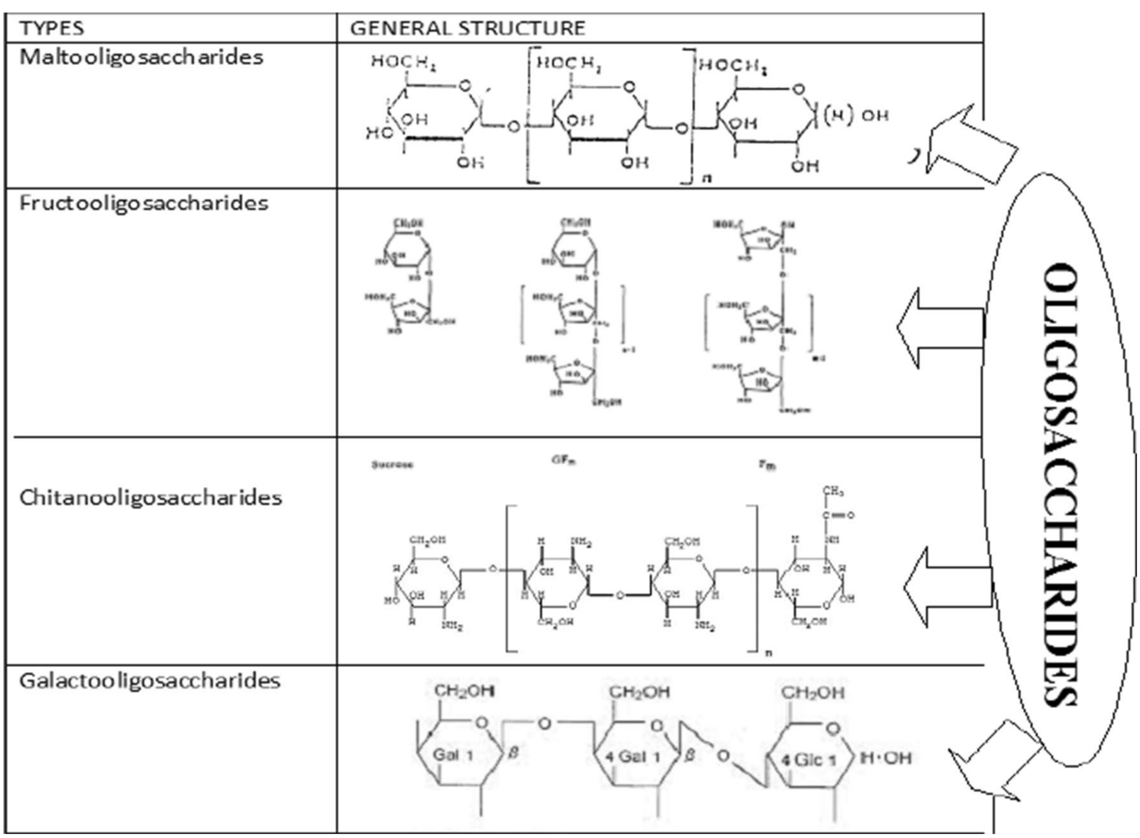

Fig. 1 Overview of structure of some common oligosaccharides

units of fructose. Short chain oligosaccharides are similar to dietary fibers in resisting digestion in intestine and getting converted to acetate, propionate, butyrate and gas in colon. Fructooligosaccharides also add up to the fecal matter and gives improved bowel movement. In the digestive tract they promote *Bifidobacterium* and on other hand have an inhibitory effect on *Clostridium perfringes* in colon.

FOS are found abundantly in nature as a component of cereals, fruits and vegetables next to starch specified in Fig. 2 (Sangeetha et al. 2005). These exhibit resistance to basic enzymes involved in digestion like alpha amylase, saccharase and maltase when investigated in humans (Losada and Olleros 2002).

Johnson et al. (2013) reported that lentils are rich in prebiotics. There is a significant variation in prebiotic carbohydrate composition of different types of lentils. They analyzed Raffinose-family oligosaccharides, sugar alcohols, fructooligo-saccharide and resistant starch carbohydrates. They recorded the occurrence of Raffinose-family oligosaccharides, sugar alcohols, fructooligosaccharides and resistant starch as 4071, 1423, 62 and 7500 mg per 100 g dry matter, respectively.

Fructosyltransferase enzyme

Some plants and microorganisms express fructosyltransferase enzyme naturally. The activity of this enzyme empowers these organisms to synthesize fructooligosaccharides (Sanchez et al. 2008). Fructosyltransferase enzyme from different sources exhibit different mechanisms of action and produce different mixtures of oligosaccharides.

Beneficial health effects of FOS on consumers

FOS are receiving attention and importance not merely because of their application as alternative sweeteners but rather for the accompanied desirable characteristics. The earlier known health benefits of FOS were inhibitory effect on pathogens and stimulatory effect on *Bifidobacterium*. The FOS was analyzed further to highlight its detailed interaction with *Bifidobacterium* (probiotics) which paved a pathway for the concept of synbiotics (Perrin et al. 2001; Vander et al. 2004). The health benefits of FOS have been reviewed by many workers (Antosova and Polakovic 2001; Hernandez et al. 2009; Patel and Goyal 2011; Ganaje et al. 2014).

Some of the evident health benefits observed by consumption of fructooligosaccharides include the following:

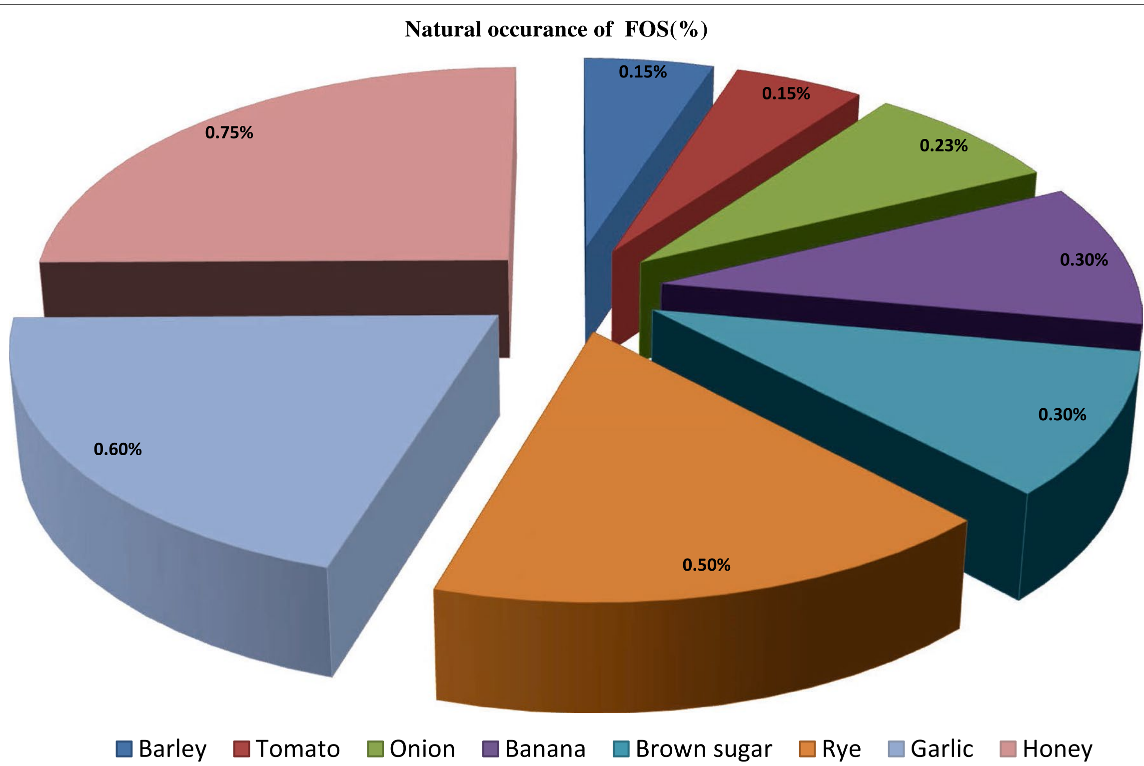

Fig. 2 Distribution of FOS in various natural products

Promotes growth of the gut micro flora

Studies on *Bifidobacterium* species revealed that fructooligosaccharides preferred those carbohydrates which allow maximum growth and metabolic activities of this beneficial flora in human intestine (Palframan et al. 2003). The diet and its composition have an impact on gut and its microflora. It has been observed that any kind of change in the diet affects the metabolism of the inhabitants. The dietary fibres like oligosaccharides exert a combined effect on both the pH environment of the gut and the metabolism of bacterial community (Chen et al. 2000; Flint et al. 2007).

Prebiotics have multidimensional effect on host-bacteria interaction

It is now well established fact that host bacteria interactions are highly specific with varied dimensions. The digestion resistant carbohydrates in the gut are fermented in the colon which causes increase in the serum lactate levels. The study was conducted on horses by injecting fructooligosaccharides directly in caecum and acidotic state was maintained. Its effect on caecum bacteria and metabolites were analyzed. *Streptococcal* species (EHSS) showed positive relation with caecum lactate and negative response with serum lactate; however, serum lactate has a positive influence on *Enterobacteriaceae* (Rudi 2010).

Genetic features direct the probiotic effect of bacteria

Excellent studies on genomics of lactic acid bacteria in relation to their role in functional foods have been done by Klaenhammer et al. (2005). Their findings discovered that many genetic features exert control over the bacterial metabolic and probiotic process.

Development of resistance to ill effects of bile salts

Fructooligosaccharides and their monomeric derivatives offer resistance against the ill effects of bile salts on Bifidus group of intestinal inhabitants. Perrin et al. (2001) studied the inhibitory effect of bile salts on three strains of *Bifidobacterium* in medium containing any carbohydrate source. In presence of fructooligosaccharides in the medium the *Bifidobacterium* improved their resistance and demonstrated better growth in presence of bile salts. Macfarlane et al. (2008) studied the effect of inulo, galacto and fructooligosaccharides was extremely favorable for *Bifidobacterium* and also *Lactobacilli* but to a lesser extent. Their health benefits encompass features like putative anti-cancer properties, mineral absorption, lipid metabolism, anti-inflammatory and other immune effects such as atopic disease.

Promotes preferential growth of Bifidus

A statistical model was used by Shuhaimi et al. (2009) for the study of growth of *Bifidobacterium pseudocatenulatum* G4 under the influence of prebiotic. The physiological effect of inulin and fructooligosaccharides were investigated with sorbitol, arabinan and inoculum rate. Fractional factorial design was used to determine their effect on growth of selected bacterium in skimmed milk. They optimized their growth conditions and concluded that in 1 L fermentor, the yield increase and Central Composite Design was very effective in optimization of medium for growth of Bifidus. In a similar study, Ketabi and Dieleman (2011) investigated the effect of isomalto-oligosaccharides on intestinal microflora of rats and inferred that it specifically stimulated the growth of *Lactobacilli*.

Removal of cholesterol

Cholesterol was found to be evidently removed by *Lactobacillus acidophilus* ATCC 4962 in the presence of prebiotics in a study conducted by Liong and Shah (2005). The effect of six prebiotics including fructooligosaccharides was used to investigate the best combination for effective removal of cholesterol. The first-order model, the second-order polynomial regression model and quadratic models were used in their study.

Artificial sweetness

Apart from all the above stated prime health benefits fructooligosaccharides also has artificial sweetness and low caloric value. Artificial sweeteners are constantly in demand due to need of diabetics and health conscious consumers. Initially the demand was satisfied by aspartame agent or natural sweeteners like palatinose. Due to their popular use all types of oligosaccharides remained poorly exploited despite their functional properties (Mussatto et al. 2009).

Role in osteoporosis

The most recent trial of fructooligosaccharides supplemented with calcium in post menopausal women have registered beneficial effects in bone mineral density which is highly significant in osteoporosis (Slevin et al. 2014).

Galactooligosaccharides (GOS) and Lactulose derived galactooligosaccharides (LDGOS)

Mammalian milk is the natural source of GOS. Industrially trans galactosylation of lactose present in whey catalysed by β-galactosidases is gaining momentum as an promising alternative for synthesis of GOS (Affertsholt-Allen 2009).

β-Galactosidase is a hydrolase that attacks the o-glucosyl group of lactose. The general mechanism of enzymatic lactose hydrolysis has a transgalactosylic nature, involving a multitude of sequential reactions with disaccharides (other than lactose) and higher saccharides, collectively named galacto-oligosaccharides (GOS), as intermediate products (Wallenfels and Malhotra 1960; Goulas et al. 2007). Non digestible oligosaccharides have wider applications (Sako et al. 1999).

The GOS are complex mixtures of oligosaccharides ranging from two to eight moieties, and different glycosidic linkages: β-(1,1), β-(1,2), β-(1,3), β-(1,4) and β-(1,6) (Playne and Crittenden 2009). The hydrolytic enzymes preferentially expressed by *Bifidobacterium* species specifically target β-glycosidic linkages of GOS in the intestine (Macfarlane et al. 2008).

Microbes are exuberant sources of the enzymes producing Lactulose and GOS (Nguyen et al. 2009; Splechtna et al. 2006, 2007; Maischberger et al. 2008; Placier et al. 2009). The operation conditions are to be properly monitored for optimal ratio of lactulose and GOS for potential synthesis of prebiotics (Guerrero et al. 2013; 2015).

The main physiological effects of GOS are related with their composition and activities of the intestinal microbiota (Algieri et al. 2014). The human intestinal tract harbors a complex community of bacteria, eukaryotic microorganisms, archaea, viruses, and bacteriophages, collectively referred to as the intestinal microbiota. Bacteria account for the majority of these microorganisms: their total number in the human gut is estimated at 1014 cells mainly present in the colon (Backhed et al. 2005; Lupp and Finlay 2005). The wide applications of GOS and LDGOS are represented in Fig. 3.

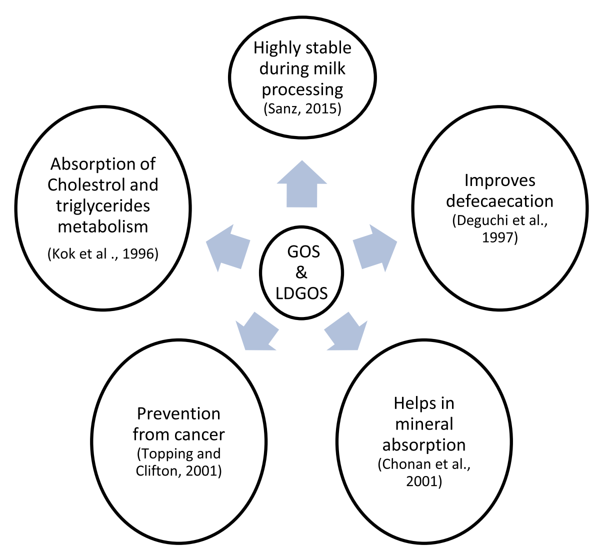

Fig. 3 Functions of GOS and LDGOS

Xylooligosaccharides (XOS)

Xylooligosaccharides or feruloyl oligosaccharides are known to be produced by *Aspergillus*, *Trichoderma*, *Penicillium*, *Bacillus* and *Streptomyces*. It is found in plant sources like Bengalgram husk, wheat bran and straw, spentwood, barley hulls, brewery spent grains, almond shells, bamboo and corn cob. XOS mainly exerts prebiotic effect in consumers.

These unusual oligosaccharides are composed by chains of xylose moieties linked by β-(1,4) bonds, with a polymerization degree ranging from two to ten monosaccharides.

It is also known to act as a plant growth regulator. It has multidimensional applications as antioxidant and gelling agent in food products, beneficial for diabetes, in treatment of arteriosclerosis, reduces total cholesterol and LDL in patients with type 2 diabetes mellitus and in colon cancer (Chung et al. 2007; Sheu et al. 2008; Lecerf et al. 2012; Moure et al. 2006; Katapodis and Chistakopoulos 2008; Madhukumar and Muralikrishna 2010). Figure 4 is a diagrammatic representation of applications of XOS.

Arabinooligosaccharides (AOS)

Arabinooligosaccharides are yet another class of oligosaccharides which hold the potential of being labelled as prebiotics. The exuberant source of AOS is arabinan polysaccharide a branched pectic polysaccaharide exhibiting linkage of 1,3 and 1,5 α L -arabinofuranosyl residues (Vogel 1991). Arabinose occurs naturally in arabinans, arabinogalactans or arabino xylans present in plants cell wall components. The nature of linkages differ depending upon the sources. The brush border epithelial cells of the intestine are inefficient to degrade the polysaccharides present in plant cell wall. This resistance of cell wall polysaccharides towards intestinal hydrolysis confer them the potential to be used as prebiotics (Yoo et al. 2012; Rastall and Hotchkiss 2003). The efficacy of the prebiotic effect of AOS is structure dependent (Casci et al. 2006; Gullón et al. 2011).

Initially the extraction was practiced by hot alkali treatment (Cibe 2003) of sugar beet dried pulp (5.5 million tons) a major coproduct of beet sugar industries residue in European countries.

AOS can also obtained by enzymatic hydrolysis of Arabinose containing polymers. Beldman et al. (1997) classified the Arabinan degrading enzymes in six classes-

(i) α-L-Arabinofuranosidase (EC 3.2.1.55), which is not active with polymers (Komae et al. 1982; Weinstein and Alber sheim 1979).

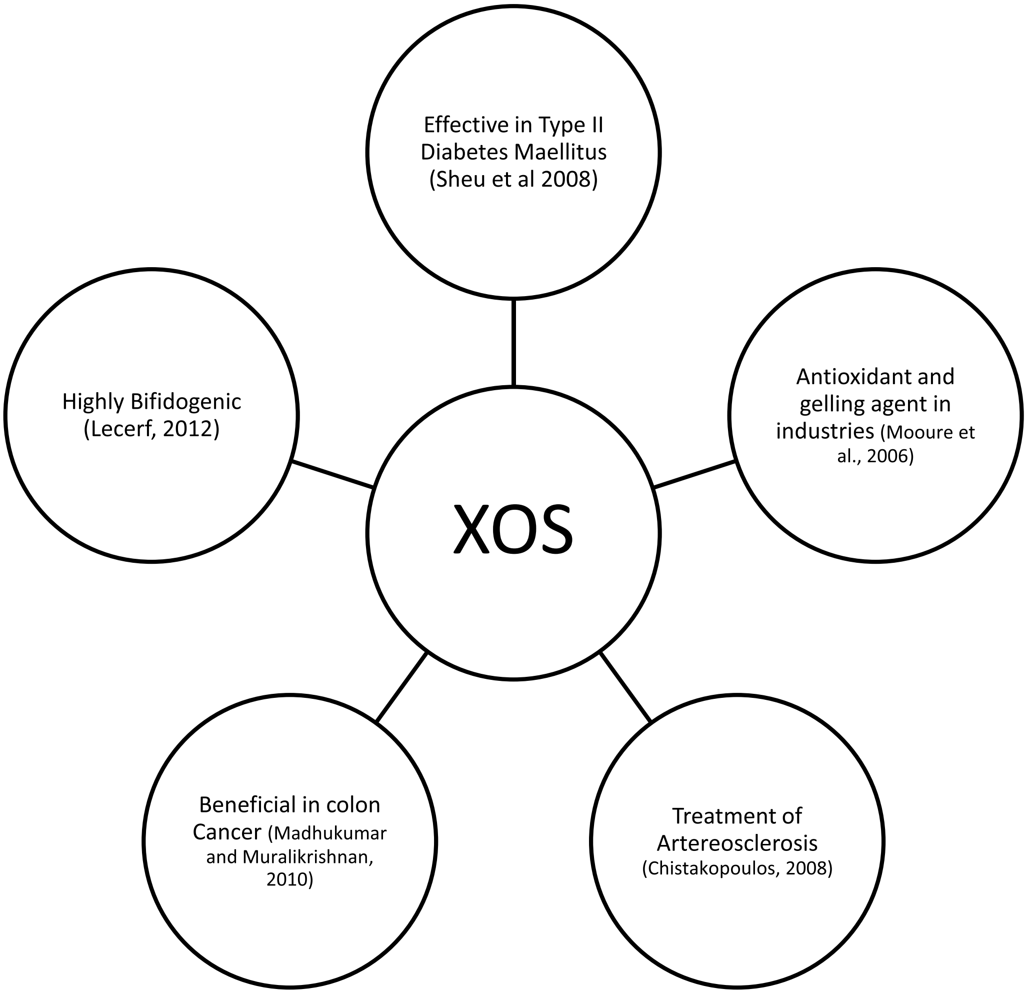

Fig. 4 Functions of XOS

(ii) α-L-Arabinofuranosidase, which is active with polymers (Kaji and Tagawa, 1970; Rombouts et al. 1988).
(iii) α-L-Arabinofuranohydrolase, which is specific for arabinoxylans (Kormelink et al. 1991; Van Laere et al. 1997).
(iv) exo-α-L-Arabinanase, which is not active with *p*-nitrophenyl-α-L-arabinofuranoside (Kaji and Shimokawa1984; McKie et al. 1997).
(v) β-L-Arabinopyranosidase (Dey 1983; Kaji and Saheki 1975).
(vi) endo-1, 5-α-L-Arabinanase (EC 3.2.1.99) (Voragen et al. 1987).

The various degree of polymerization (dp) are obtained when subjected to ultrafiltration can produce Oligosaccharides of uniform molecular weight (Matsubara et al. 1996; Jian et al. 2013). AOS derived from sugar beet pectin (Al-Tamimi et al. 2006) and lemon peel (Hotchkiss et al. 2010) support the intestinal bifidus flora nearly equal to FOS and Inulooligosaccharides (Gómez et al. 2015; Palframan et al. 2002; Rycroft et al. 2001; Sanz et al. 2005). The extent of response is directly proportional to the dp of the oligosaccharide (Sulek et al. 2014; Westphal et al. 2010).

Apart from the normal benefits, AOS is reported to reduce the inflammatory conditions in Ulcerative colitis patients. Invitro experiments have proved about specific stimulation of *Bifidobacterium* and *Lactobacillus* accompanied by production of SCFA acetate which is well known stimulator of anti inflammatory response. AOS can prove to be a boon for patients suffering from Ulcerative colitis after in vivo confirmation (Vigsnæs et al. 2011).

Algal-oligosaccharides lysate (AOL) and neoagarooligosaccharides (NAOS) occur in the algal polysaccharide extracts (APEs) of *Gracilaria* and *Monostroma*and inenzymatic hydrolysis of agarose. They have a prebiotic effect and also act as an antioxidant (Wu et al. 2005; Hu et al. 2006).

Algae-derived marine oligosaccharides

Recently, algae are reported to contain bipolysaccharides (Stengel et al. 2011; Barra et al. 2014). The bioactive components mainly include glucose, starch and other polysaccharides (Hamed et al. 2015). Besides these, oligosaccharides are another group of carbohydrates with small dp containing 3–10 sugar units, ranging from disaccharides and/or carbohydrates with up to 20 residues with defined functions (Patel and Goyal 2010).

The chemical structure and conformation decides the classification of algae-derived marine oligosaccharides namely chitosan-, laminarin-, alginate-, fucoidan-, carrageenan- and ulvan-oligosaccharides.

The note worthy bioactive compounds in Marine macroalgae or seaweeds is namely polysaccharides, tannins, and diterpenes. (O'sullivan et al. 2010). These ingredients may lead a pivitol role in nutraceuticals (Milinki et al. 2011). The functions of ADMO are given in Fig. 5.

Other oligosaccharides

Mannanoligosaccharides (MOS) are mainly isolated from cell wall fragments of yeast. It was found to alter the gut microflora in fishes. It has been used as an alternative to antibiotics and added to improve the nutritive value of broiler diets (Dimitroglou et al. 2010; Eseceli et al. 2010). Chitosanoligosaccharides (COS) has been recorded to be produced by depolymerisation of chitosan. They are mainly used as an antioxidative agent, anti-tumor agent and anti-microbial agent. Chitosan oligosaccharides have been recorded to protect normal cells from apoptosis (Liu et al. 2010). Human milkoligosaccharide (HMO) naturally occurs in human breast milk. It signifies the preferential growth of *Bifidobacterium* and *Lactobacilli* in the colon of mother fed babies (Quigley 2010). Gentiooligosaccharides (GeOS) is produced by digestion of starch and mainly used as a prebiotic (Cote 2009; Fujimoto et al. 2009).

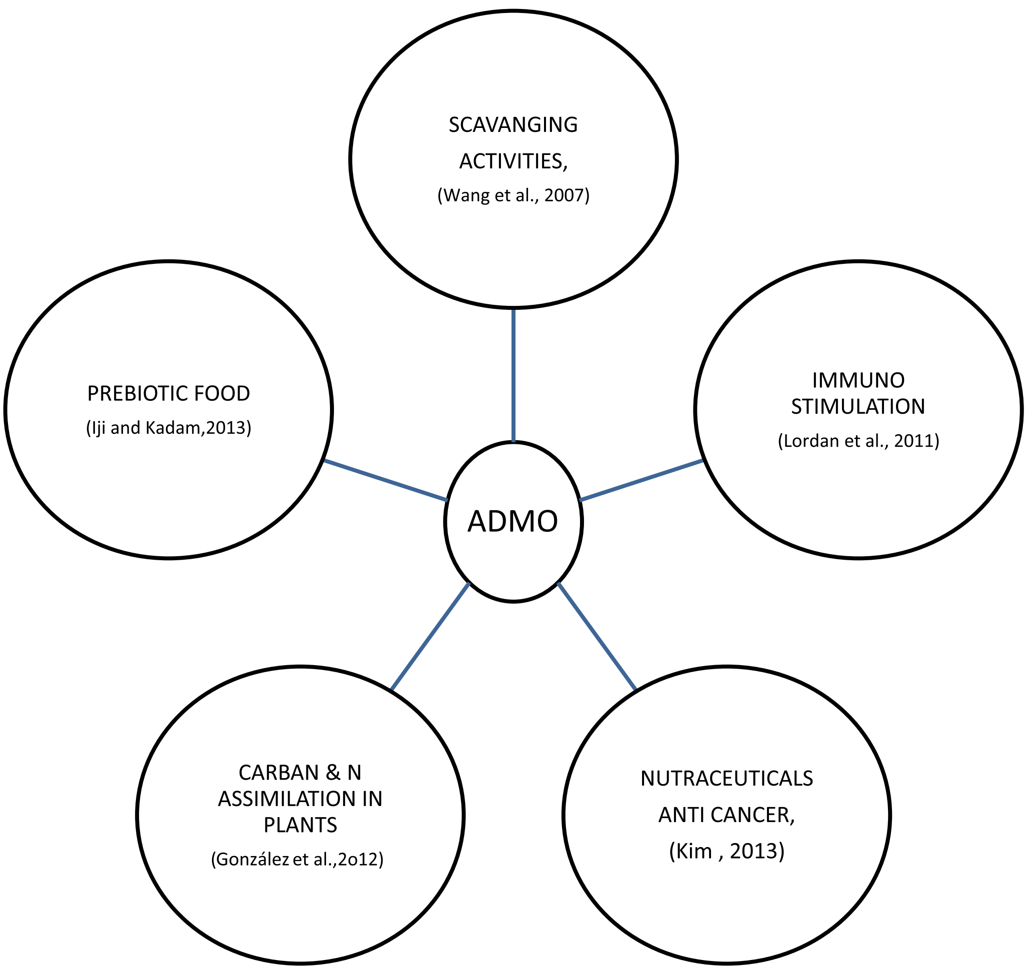

Fig. 5 Functions of AOS

Pectin-derived acidic oligosaccharides (pAOS) occur in higher plant products like fruits and vegetables. It mainly finds its applications in infant formulae to subside diarrhoea, increase absorption of minerals and calcium ions and also has antioxidant effects (Liu et al. 2010). pAOS also successfully helped in the lung infections by modulating the intestinal microbiota and the inflammatory and immune responses (Bernard et al. 2015). Cyclodextrins (CDs) are produced by transformation of starch by *Bacillus macerans*. It is used as a stabilizer for volatile compounds in food preparations and chemicals. It acts as an antioxidant. It is used as taste enhancers in bitter medicines and food items (Astray et al. 2009; Courtois 2009).

Although all oligosaccharides are exhibiting prebiotic properties but fructo-oligosaccharides has gained much attention as artificial sweeteners because they provide sweet taste to the consumer and do not increase the blood glucose level. Therefore, they find important place in the food of diabetics. Thus, fructooligosaccharides act as artificial sweeteners with functional properties apart from sweetness similar to that of natural sweeteners.

Oligosaccharides from various sources have been considered as boon due to health benefits they encompass along with property of being used as an artificial sweetner. Due to the diversified health benefits conferred by them, they have earned a prominent recognition as Nutraceuticals presently limelighted in the health market. The microbial production of enzymes catering the catalysis of oligosaccharides are now targeted by the biotechnologists for their optimum synthesis. Microorganisms, especially molds have been the most prominent microbe for enzymatic synthesis of the prebiotic oligosaccharides. Since 1980s teeming research work was focused towards isolation of potent microbes for oligosaccharide synthesis. The oligosaccharide production has been successfully attempted employing diverse approach viz. SmF, SSF, immobilization of the intact microbial cells or derived enzymes. The successful attempts have been made to improve the strain through mutations.

These laboratory processes have although recorded successful production of oligosaccharides but scaling up introduces exuberant increase in the cost of production of oligosaccharides. The bio process improvement should be inculcated using cheaper agro-industrial wastes as substrates for oligosaccharide production. To decrease the cost of production following issues have to be addressed: (i) a potent and stable microbial enzyme source is to be fetched (ii) scrutinizing agro-industrial wastes befitting the oligosaccharide production (iii) cheaper alternatives for purification strategies of synthesized oligosaccharides.

Future prospects

As stated in the introduction of the review the demand of health promoting food is expected to rise up to US $4.8 billion by 2018. The hike in the demand is indicative of the future directions towards which the food industry is fastly marching. The so called health promoting food or pro and prebiotics under the unanimous label of "Nutraceuticals" will be a focus of attraction for every such layman growing conscious about health in near future. The present scenario of the health market trend is facing certain health issues pertaining to intake of the prebiotics viz. aggravation of intolerance to lactose, increments in allergic responsiveness of sensitive individuals as reported in several human based case studies.

Looking forward with this setback associated with probiotics, prebiotic are coming up as more promising option. Above all the prebiotic effect of oligosaccharides are now extended to their antidiarrheal, antiobesity and presently towards suppression of type 2 diabetes. The future would really depend on the synergistic effect developed by combinational use of prebiotics and probiotics. The incremental benefits of synbiotics would be auxiliary to the nature's boon.

Abbreviations

ADMO: algae derived marine oligosaccharides; AOS: arabinooligosaccharides; CD: cyclodextrins; dp: degree of polymerization; FOSHU: food of specified health use; FOS: fructooligosaccharides; GOS: galactooligosaccharides; GIA: Global Industry Analyst; HMO: human milk oligosaccharides; LDGOS: lactulose derived galactooligosaccharides; MOS: maltooligosaccharides; pAOS: pectin-derived acidic oligosaccharides; XOS: xylooligosaccharides.

Authors' contributions

The corresponding author has prepared script under the guidance of co author. Both authors read and approved the final manuscript.

Author details

[1] Department of Microbiology and Bioinformatics, Bilaspur University, 206, Budhiya complex, Sarkanda, Bilaspur, Chhattisgarh 495004, India. [2] Pt. Ravishankar Shukla University, Raipur, CG 492010, India.

Acknowledgements

The author's acknowledge the support of SOS in Life Sciences, Pt. Ravishankar Shukla University, Raipur and Department of Microbiology and Bioinformatics, Bilaspur University, Bilaspur for supporting the work for which the topic was reviewed.

Competing interests

The authors declare that they have no competing interests.

Funding

The present review is not funded by any funding agency.

Received: 4 April 2016 Accepted: 15 September 2016

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