



Review Article

Applications and prospects of functional oligosaccharides in pig nutrition: A review

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ABSTRACT

Oligosaccharides are low molecular weight carbohydrates between monosaccharides and polysaccharides, which consist of 2 to 20 monosaccharides linked by glycosidic bonds. They have the effects of promoting growth, regulating immunity, improving the structure of intestinal flora, and are anti-inflammatory and antioxidant. With the comprehensive implementation of the antibiotic prohibition policy in China, oligosaccharides as new green feed additive have been paid more attention. Oligosaccharides can be divided into the following 2 categories according to their digestive characteristics: one is easy to be absorbed by the intestine, called common oligosaccharides, such as sucrose and maltose oligosaccharide; the other is difficult to be absorbed by the intestine and has special physiological functions, called functional oligosaccharides. The common functional oligosaccharides include mannan oligosaccharides (MOS), fructo-oligosaccharides (FOS), chitosan oligosaccharides (COS), xylo-oligosaccharides (XOS) and so on. In this paper, we review the types and sources of functional oligosaccharides, their application in pig nutrition, and the factors limiting their efficacy in recent years. This review provides the theoretical basis for further research of functional oligosaccharides, and the future application of alternative antibiotics in pig industry.

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1. Introduction

Antibiotics have antibacterial, antiviral, and growth-promoting effects. Since the 1940s, antibiotics have been widely used in livestock and poultry production. Their effects of medical treatment, health care, and growth promotion have had a very beneficial impact on the development of animal husbandry (Yin et al., 2021; Murugaiyan et al., 2022). With the improvement of people's living standards, the demand for meat products increases greatly, which also prompts abuse antibiotics in the breeding process, resulting in antibiotic residues, and causing great harm to human health (Liu et al., 2018; Yang et al., 2019; Laloučková and

Skřivanová, 2019). With the progress of science and technology and the improvement of people's safety awareness, the damage of antibiotics to human beings has become increasingly apparent. There are more and more calls to ban antibiotics. The Ministry of Agriculture and Rural Affairs of the People's Republic of China issued Notice 194 prohibiting the addition of antibiotics to feed from January 2020. Therefore, the development and utilization of new green residue-free feed additives have been paid more and more attention, and implementing a comprehensive antibiotic prohibition policy has been implemented.

Oligosaccharides are low molecular polymer composed of 2 to 20 monosaccharide groups connected by the same or different glycosidic bonds, which can be categorized into common oligosaccharides and functional oligosaccharides according to the action mode of oligosaccharides. After entering the gastrointestinal tract, oligosaccharides are digested and absorbed, and thus used as energy sources by the body such as sucrose and maltose (Rajagopalan and Krishnan, 2019; Vieira et al., 2020). Functional oligosaccharides have not only the characteristics of common oligosaccharides, but also a variety of biological functions, which can be used as feed additives to promote the growth and health status of livestock and poultry. Therefore, in recent years, the domestic pig breeding

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industry has been hit hard by the double blow of African swine fever and COVID-19, how to improve the immunity of pigs and reduce the disease rate has become a top priority. Functional oligosaccharides can effectively reduce intestinal pH value, promote mineral absorption, improve animal feed conversion efficiency, maintain intestinal microflora structural homeostasis, improve body immunity, and have the characteristics of green residue-free (Pan et al., 2018). Many animal experiments have shown that functional oligosaccharides have good effects on pigs, poultry and ruminants, which can improve animal performance, reduce feed to meat ratio, improve disease resistance and intestinal health, and thus reduce mortality, so they are regarded as an adequate substitute for antibiotics (Xu et al., 2019; Tiwari et al., 2020).

Functional oligosaccharides are sugars formed by corresponding monosaccharides linked by α -1,6, α -1,3, and α -1,2 glycoside bonds. However, the front part of the digestive tract of monogastric animals can only produce enzymes digesting α -1,4 glycoside bonds. Therefore, functional oligosaccharides are not easily degraded by intestinal digestive enzymes, but directly enter hindgut where many microorganisms live. Beneficial microorganisms can produce enzymes that decompose various glycosidic bonds. Functional oligosaccharides are decomposed and utilized here and converted into small molecules such as short-chain fatty acids to promote the proliferation of beneficial bacteria and inhibit harmful microorganisms (Fig. 1). Common functional oligosaccharides include xylo-oligosaccharides (XOS), mannan oligosaccharides (MOS), chitosan oligosaccharides (COS) and fructo-oligosaccharides (FOS). With the increase of antibiotic prohibition, the development, utilization, and mechanism of new green additives such as functional oligosaccharides are particularly significant. In this paper, we will review the types and sources of functional oligosaccharides, their application in pig nutrition, and the factors limiting their efficacy in recent years. This review will provide the theoretical basis for further research of functional oligosaccharides, and the future application of alternative antibiotics in pig industry.

2. Types and sources of functional oligosaccharides

Functional oligosaccharides mainly include FOS, MOS, XOS and COS (Patel et al., 2011). Because functional oligosaccharides have physical and chemical characteristics such as low calorific value,

stability, safety and non-toxicity, high viscosity, strong hygroscopicity and not being digested by gastrointestinal tract, and also improve the intestinal microflora, reduce serum cholesterol and neutral fat, improve blood sugar, improve the feed efficiency, improve animal immunity, thus it has attracted the attention of the more and more scholars (Pan et al., 2018). The following mainly introduces the related characteristics and sources of FOS, MOS, XOS and COS.

2.1. Fructo-oligosaccharides

The molecular formula of FOS, also known as fructo-oligose, glucose-trisaccharide, is GFn ($n \leq 4$, G for glucose, F for fructose). It is a general term for a group of oligosaccharides formed by binding several D-fructose on the basis of sucrose molecules through β -1,2 glycosidic bonds (Rastall et al., 2010; Rahim et al., 2021). Solid fructo-oligosaccharides are white powdery, easily soluble in water, low in sweetness that only 0.3 to 0.6 of sucrose, and low in energy, which also the only functional oligosaccharide with the dual physiological characteristics of super bifidogenic factors and water-soluble dietary fiber, which widely exists in bananas, potatoes, wheat, barley, onion, garlic, and other plants. Among them, the content of Jerusalem artichoke tuber is the most abundant (Yildiz, 2010; Micciche et al., 2018). It is difficult to extract natural FOS. Commercial production methods of FOS are generally divided into 2 categories, one is the sucrose enzymatic method, and the other is the extraction method (Cano et al., 2020). Relevant studies have shown that FOS can promote the abundance of many beneficial bacteria in the intestinal tract of livestock and poultry, inhibit the growth and reproduction of harmful bacteria, and improve the digestion and absorption of nutrients, and consequently to improve the microecological environment, and improve their immunity and production performance in livestock and poultry.

2.2. Mannan oligosaccharides

In general, MOS consists of mannose-molecules or mannose-glucose, which is formed by α -1,2, α -1,3, α -1,6 glycosidic bonds. Glucose is a phosphorylated glucomannan protein complex extracted by enzymolysis from mannan-rich yeast cell walls

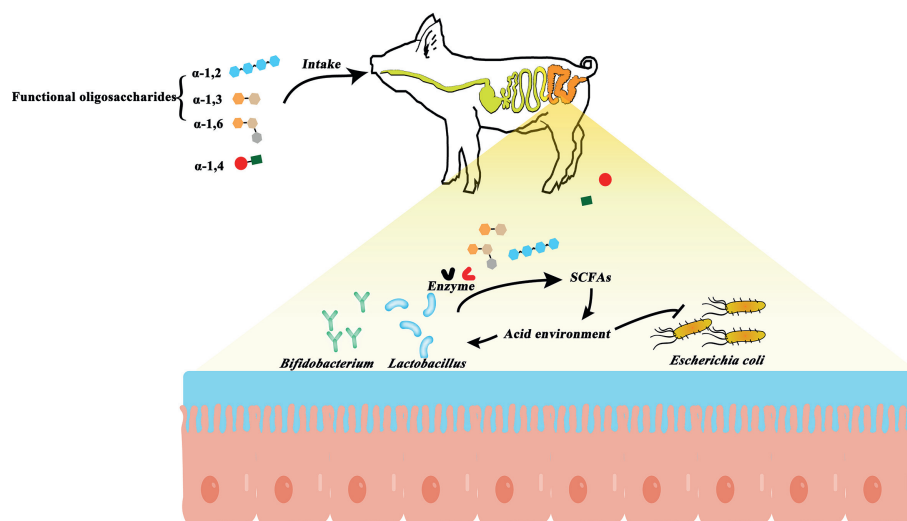


Fig. 1. The beneficial effects of functional oligosaccharides on the intestinal health of weaned piglets through interaction with intestinal microbes. Functional oligosaccharides are broken down by specific enzymes secreted by beneficial bacteria in the gut to produce short-chain fatty acids that maintain intestinal health. SCFAs = short-chain fatty acids.

(Faustino et al., 2021). They widely exist in guar bean gum, sesbania gum, konjac powder, and yeast microbial cell walls, MOS from different sources have different chemical structures. For example, konjac MOS with a molecular ratio of 1:1.6 are synthesized by polymerization of glucose and mannose residues through β -1,4 glycosidic bonds, and its side chain is connected by β -1,3 glycosidic bonds, which has the characteristics of gel (Sohn et al., 2000; Wang et al., 2018). The main chain of oligosaccharides derived from yeast cell wall is mainly arranged by highly branched pyranose residues. The main chain is secured by α -1,6 glycosylases, and the side chain is connected by α -1,2 and α -1,3 bonds. They main composition is a mixture of disaccharide, trisaccharide, and tetrasaccharide, which have the following characteristics: (1) soluble in water, but insoluble in ethanol, acetone and ether and other organic solvents; (2) high temperature resistance, high temperature conditions will not damage its structure and physiological function; (3) easy to absorb moisture, but after moisture absorption does not affect its use value. Commercial MOS are mainly extracted by enzymolysis and then put into production. At present, MOS for feeding mainly come from konjac powder enzymolysis products and yeast cell wall extracts (Yui et al., 1992). In pig breeding, MOS have critical protective effects on the intestinal health and immune performance of pigs. Related studies have shown that mannan oligosaccharides have dual effects of absorbing intestinal pathogens and immune regulation in piglets (Saeed et al., 2017).

2.3. Xylo-oligosaccharides

Xylo-oligosaccharides (XOS) are functional oligosaccharides formed by combining of 2 to 10 xyloses by β -1,4 glycosidic bonds. The main components of xylo-oligosaccharides are xylose, xylobiose, xylotriose, and xylan with a small amount of xylotriose or more, the main effective components are xylobiose and xylotriose (Mäkeläinen et al., 2010; Zhang et al., 2018). Solid XOS are light yellow or light brown powder with high heat and acid resistance and good stability, and the effect of reducing water activity. In addition, compared with other oligosaccharides, the viscosity of XOS is lower, and the processing is more convenient. The primary sources of XOS are corn cob, straw, rice bran, wheat bran, rice husk, cottonseed shell, and other agricultural wastes. These raw materials are rich in xylan hemicellulose (up to 30%) and which also have wide range of sources and low prices. Therefore, reasonable development and application can increase the added value of agricultural and sideline products and reduce the cost of breeding (Carvalho et al., 2013). There are 3 main methods for extracting and preparing XOS: high-temperature cooking, acid extraction, and chemical-enzyme linked method. Chemical-enzyme-linked method is the most popular preparation method in China (Bhatia et al., 2019). XOS contribute to the formation of dominant beneficial flora in the intestinal tract of animals, thus inhibiting the adhesion of harmful bacteria in the intestinal tract, and positively improving the microflora and immune functions of the gastrointestinal tract of animals. Meanwhile, XOS also have specific impact on promoting the digestion and utilization of nutrients in livestock and poultry, thus improving their growth performance and antioxidant capacity (Gobinath et al., 2010; Yang et al., 2015).

2.4. Chitosan oligosaccharides

COS are oligosaccharides linked by β -1,4 glycosidic bonds, and the numbers of glucosamine are usually 2 to 10. As the only natural cationic basic polysaccharide discovered at present, COS are generally less than 3,000 U in molecular weight and have good water solubility, partly soluble in methanol but insoluble in ethanol. Meanwhile, COS have excellent function and high

biological activity, and their metabolites are non-toxic and antigen-free, which can be easily absorbed by the body. COS are not easily decomposed in the animal gastrointestinal tract and are absorbed directly by intestinal cells into blood circulation after entering the intestinal tract. The primary source is abundant marine biological resources, such as shrimp shells and crab shells. Then the oligosaccharides with the required degree of polymerization less than 20 were obtained by enzymic degradation (Singla and Chawla, 2001). COS have many physiological functions including antioxidant, regulating intestinal microecological environment, and improving body immunity. They also have the physiological functions such as anti-bacterial, anti-tumor, and improving animal growth performance etc., and consequently have been widely used in livestock, poultry production, and biomedicine (Ma et al., 2011; Swiatkiewicz et al., 2015).

3. The application of functional oligosaccharides in pig breeding

3.1. Growth performance

Functional oligosaccharides directly enter the intestinal tract of animals in the undegraded form, which can improve the absorption and utilization rate of nutrients in the intestinal tract and promote the overall growth performance of animals (Qiang et al., 2009). Some studies have shown that functional oligosaccharides can improve the intestinal health of pigs during pig breeding, improve feed intake, daily weight gain, and feed conversion rate of pigs, and reduce the diarrhea rate of piglets to a certain extent (Zou et al., 2016; Schokker et al., 2018). Different types of oligosaccharides can promote the growth performance of pigs in the breeding process to a certain time (Table 1). At the same time, the same type of oligosaccharides also has different effects on the growing development and health status of pigs at different growth stages. Diets supplemented with 0.1% FOS increased average daily gain and average daily feed intake, as well as dry matter and nitrogen digestibility of growing pigs from d 0 to 56 of the trial period (Lim et al., 2022). Some studies have found that the average daily gain, average daily feed intake, and weight gain/feed consumption of weaned piglets were significantly improved by adding 100 and 200 mg/kg COS and 80 mg/kg aureomycin in the diet, respectively. Meanwhile, the apparent digestibility of DM, Ca and P was also significantly improved in these 3 groups (Liu et al., 2008). The same conclusion was reached in other experiment, with the increase of dietary COS level, the improvement of average daily gain, average daily feed intake and apparent digestible energy of DM and N increased linearly (Chen et al., 2009). These results indicate that adding a certain amount of COS in the diet can replace antibiotics to improve the growth performance of piglets to a certain extent. For sows, studies have shown that functional oligosaccharides can also reduce their feed to milk ratio to a certain extent (Cheng et al., 2015).

3.2. Immune function

The immune system is the primary weapon of the body to defend against the invasion of pathogens and remove foreign bodies and foreign pathogenic microorganisms. As an immune enhancer, functional oligosaccharides can combine with the surface of some viruses, toxins, and bacteria to improve body's immune function. Functional oligosaccharides can improve B lymphocyte mediated humoral immunity and T lymphocyte mediated cellular immunity, improve mucosal immunity of animals, and thus increase the immune function of animals, which have been used as immune adjuvant in livestock and poultry production (Dawood

Table 1
Effects of functional oligosaccharides on growth performance of pigs.

| Growth stage | Type of oligosaccharides | Adaptation period | Dose, % | Treatment effects, %, difference to control | | | Reference |
|------------------------|--------------------------|-------------------|---------|---|------|-----|----------------------------------|
| | | | | ADG | ADFI | FCR | |
| Weaned pigs | FOS | 28 d | 0.1 | 18 | 13 | -5 | Zhao et al. (2012) |
| | MOS | | | 23 | 15 | -6 | |
| Weaned pigs | MOS | 14 to 35 d | 0.2 | 2 | -6 | -9 | Castillo et al. (2008) |
| Growing pigs | FOS | 42 d | 0.2 | 4 | -1 | -5 | Xu et al. (2002) |
| | | | 0.4 | 8 | 1 | -7 | |
| | | | 0.6 | 7 | -1 | -8 | |
| Weaned pigs | FOS | 19 d | 0.5 | -8 | -1 | 4 | Estrada et al. (2001) |
| Weaned pigs | XOS | 28 d | 0.01 | 4 | 1 | -2 | Chen et al. (2021) |
| | | | 0.05 | 10 | 2 | -7 | |
| | | | 0.1 | 2 | 1 | 0 | |
| Weaned pigs | COS | 42 d | 0.1 | 7 | 0 | -6 | Zhou et al. (2012) |
| | | | 0.2 | 11 | -2 | -12 | |
| Early-weaned pigs | GMOS | 14 d | 0.2 | 31 | 3 | -22 | Yin et al. (2008) |
| | | | 0.025 | 37 | 12 | -18 | |
| Nursery pigs | XOS | 28 d | 0.04 | 33 | 10 | -17 | Hou et al. (2020) |
| Weaned pigs | COS | 21 d | 0.01 | 9 | 6 | -3 | Wan et al. (2017) |
| Weaned pigs | COS | 14 d | 0.02 | 19 | 12 | -8 | Yang et al. (2012) |
| | | | 0.04 | 30 | 18 | -10 | |
| | | | 0.06 | 24 | 16 | -7 | |
| | | | 0.2 | 47 | 11 | -28 | |
| Weaned pigs | MOS | 0 to 14 d | 0.2 | 7 | 6 | 1 | Davis et al. (2002) |
| Growing-finishing pigs | | finisher phase | 0.05 | | | | |
| Weaned pigs | MOS | 35 d | 0.2 | -9 | -16 | -7 | Valpotic et al. (2016) |
| Weaned pigs | COS | 29 to 56 d | 0.0075 | -4 | -10 | -4 | Suthongsa et al. (2017) |
| | | | 0.015 | 16 | -1 | -13 | |
| | | | 0.0225 | 3 | -4 | -4 | |
| Nursery pigs | MOS | 7 to 14 d | 0.2 | 16 | 5 | -8 | Che et al. (2011) |
| Fattening pigs | MOS | 113 to 169 d | 0.1 | - | - | -8 | Giannenas et al. (2016) |
| Weaned pigs | XOS | 28 d | 0.02 | 17 | 2 | -13 | Liu et al. (2018) |
| Nursery pigs | MOS | 42 d | 0.3 | 5 | 0 | -5 | Poeikhampha and Bunchasak (2011) |
| Weaned pigs | XOS | 28 d | 0.75 | 6 | 4 | -2 | Pang et al. (2021) |
| | | | 1.5 | 15 | 14 | -1 | |
| | | | 3 | 10 | 4 | -5 | |

FOS = fructo-oligosaccharides; MOS = mannan oligosaccharide; XOS = xylo-oligosaccharides; COS = chitosan oligosaccharides; GMOS = galactomannus oligosaccharides; ADG = average daily gain; ADFI = average daily feed intake; FCR = feed conversion rate.

et al., 2018; Ashaolu et al., 2020). Serum biochemical index can reflect the animal metabolism in the body and help the livestock and poultry farmers detection and diagnosis of livestock and poultry diseases, further improve the animal growth performance (Wang et al., 2009). Therefore, serum biochemical levels including immune capacity and antioxidant capacity of livestock and poultry were measured as indicators to measure animal health status, so as to reflect the effect of functional oligosaccharides on immune function. Functional oligosaccharides can prevent and treat diseases by stimulating intestinal immune cells and increasing the production of immunoglobulin after ingested by pigs (Choque-Delgado et al., 2011). After antibiotics are forbidden, diarrhea caused by weaning stress of piglets becomes more and more serious, so it is urgent to find a new antibiotic substitute without residue. Therefore, the main research focus of functional oligosaccharides on immune function is their effect on the immunity of weaned piglets (Table 2). When 30 mg/kg or 500 mg/kg COS is added to the diets of weaned piglets, it can be used as an immunomodulator to increase the serum cytokines levels such as IgA, IgM and IgG (Duan et al., 2020; Xu et al., 2018). IgA, IgM, and IgG are antibodies to specific intestinal immune reactions of piglets, which can prevent pathogenic bacteria and other harmful substances from entering the body and act as a barrier. In addition, the increase of immunoglobulin and interleukin content in serum can also promote the development of immune organs. Shao et al. (2000) also showed that MOS could significantly increase the level of IgG and IgA in the serum of suckling piglets, but it had no significant effect on the content of IgM. Meanwhile, the related research shows that short-chain fructooligosaccharides can improve the secretion of cytokines in sows and enhance the immune response of IgA in

serum and intestinal tract. In addition, it can improve the immune barrier function of sows to promote maternal health and maintain the normal growth and development of fetuses. Short-chain fructooligosaccharides can further enhance the immune response of intestinal mucosal cells of weaned piglets by increasing the number of cecal goblet cells (Le Bourgot et al., 2017).

3.3. Antioxidant effect

Under certain conditions, the redox balance of the body is disrupted, and the reactive oxygen species (ROS) production rate exceeds the clearance rate of antioxidant system in the body, which leads to a large accumulation of oxygen free radicals known as “oxidative stress”. It has a dual role, on the one hand which can inhibit microbial infection; on the other hand, if oxidative stress continues, it may lead to the occurrence of chronic inflammatory diseases, and then lead to metabolic disorders and physiological disorders, which adversely affect the growth performance, life span and quality of animal products, and bring huge economic losses to farmers and harm the health of consumers (Fig. 2). Timely regulatory measures can stop losses in time (Lauridsen et al., 2019). Antibiotic therapy is still one of the main treatment methods for animal inflammatory diseases, but the development of antibiotic substitutes is particularly critical in the era of antimicrobial prohibition. Functional oligosaccharides can alleviate oxidative stress by reducing the production of ROS and lipid metabolite malondialdehyde (MDA), and also can improve the body's antioxidant capacity by promoting the body's production of antioxidant enzymes. Therefore, functional oligosaccharides can be added to livestock and poultry feed as an antioxidant to relieve oxidative stress, reduce the occurrence of

Table 2
Effects of functional oligosaccharides on immune function and antioxidant indexes.

| Feed additives | Dose, mg/kg | Feeding object | Main results | Reference |
|----------------|-------------|-------------------|--|---------------------|
| COS | 30 | Weaned pigs | IL-10 and SIgA in small intestine ↑; T-AOC in the duodenum ↑ | Xiong et al. (2015) |
| scFOS | 4,000 | Weaned pigs | IL-1β, IL-6, and TNF-α in serum ↓ | Zhao et al. (2019) |
| XOS | 500 | Weaned pigs | T-AOC, T-SOD, CAT, and IgG in serum ↑; MDA in serum ↓ | Chen et al. (2021) |
| XOS | 15,000 | Weaned pigs | Serum level of IgA, IgG, IgM, and IL-10 ↑; IL-6 and IL-1β ↓ | Pang et al. (2021) |
| COS | 250 | Early-weaned pigs | IL-1β, IL-2, IL-6, IgA, IgG, and IgM in serum ↑ | Yin et al. (2008) |
| GMOS | 2,000 | | | |
| COS | 160 | Weaned pigs | IL-1β in plasma ↓ | Liu et al. (2010) |
| FOS | 1,000 | Weaned pigs | No difference | Zhao et al. (2012) |
| MOS | | | | |
| COS | 250 | Weaned pigs | IgA, IgG, IgM, IL-6, IL-2, and IL-1β in serum ↑ | Sun et al. (2009) |
| GMOS | 2,000 | | | |
| XOS | 400 | Nursery pigs | T-AOC, GSH-Px, CAT, and IgG in serum ↑; MDA in serum ↓ | Hou et al. (2020) |
| MOS | 400 | Sows | IgG in serum ↑ | Czech et al. (2010) |
| MOS | 400/800 | Sow/piglets | IgM in colostrum of sows ↑; IgA and IgG in serum of piglets ↑ | Duan et al. (2016) |
| COS | 100 | Pregnant sows | IL-10, IgA, and IgM in serum ↑ | Wan et al. (2018) |
| COS | – | Gilts | IgM and SIgA in serum of sows and piglets ↑; SIgA in sows' feces ↑ | Ho et al. (2020) |

COS = chitosan oligosaccharides; scFOS = short-chain fructo-oligosaccharides; XOS = xylo-oligosaccharide; GMOS = galactomannan oligosaccharides; FOS = fructo-oligosaccharides; MOS = mannan oligosaccharides; IL = interleukin; SIg = secret immune globulin; T-AOC = total antioxidant capacity; TNF-α = tumor necrosis factor α; T-SOD = total superoxide dismutase; CAT = catalase; Ig = immune globulin; MDA = malondialdehyde; GSH-Px = glutathione peroxidase.

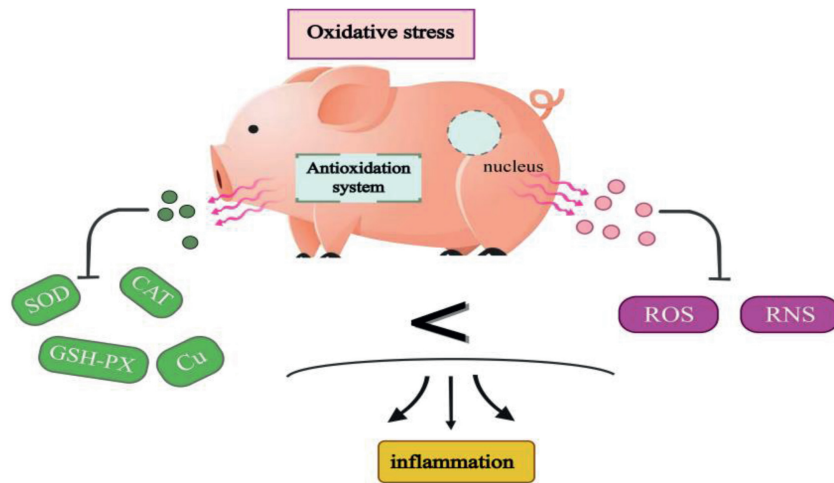


Fig. 2. Antioxidant function of functional oligosaccharides. SOD = superoxide dismutase; CAT = catalase; GSH-Px = glutathione peroxidase; ROS = reactive oxygen species; RNS = reactive nitrogen species.

inflammation and maintain body health (Table 2). There have been increasing reports on oligosaccharides as antioxidants to maintain health in recent years (Vieira et al., 2020). Adding 1% FOS to the diet of weaned piglets can increase the activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) in serum, and reduce the content of MDA in serum, which can relieve the oxidative stress of weaned piglets (Zhang et al., 2022). The same conclusion was also obtained when 2.5 g/kg FOS was added to the diet of piglets challenged with *Escherichia coli* (*E. coli*), confirming that FOS can increase the levels of GSH-Px and catalase (CAT) in plasma and intestinal mucosa of piglets (Luo et al., 2021). The antioxidant capacity and placental amino acid transport capacity of pregnant sows were improved by adding 30 mg/kg COS in the diet, and the activity of GSH-Px in offspring piglets was also increased. Meanwhile, the mRNA expressions of *SOD* and *GSH-Px* in colon of piglets were detected to increase. Therefore, functional oligosaccharides can have a series of beneficial effects on the health of sows and the growth and development of their offspring, promote the intestinal development of piglets, and improve the intestinal antioxidant performance, which can be used as a reference by farmers (Xie et al., 2016a, 2016b). Different types of oligosaccharides can improve the antioxidant properties of pigs at different stages, which strongly proves that

functional oligosaccharides have excellent antioxidant properties and can be used as an “antioxidant” in the future pig breeding process.

3.4. Intestinal health

As a critical part of nutrition and nutrient absorption of livestock and poultry, intestinal health is very essential for livestock growth and disease resistance. Maintaining intestinal health is the key to realizing healthy livestock breeding. Among them, the meaning of “intestinal health” is multi-level, maintaining the integrity of the mucosal layer of the body to play a normal immune function, and includes stable intestinal flora structure and suitable intestinal environment (Jha et al., 2019). Functional oligosaccharides can promote animal intestinal development, improve the intestinal morphology and barrier function, and can be fermented to produce short-chain fatty acids of certain bacteria in the intestine. Thus, forming the intestinal acidic environment, providing a suitable living environment for bacteria, acidic environment is conducive to the intestinal epithelial cell proliferation, which can be beneficial to maintain health, intestinal tract to improve their immunity, ensure the follow-up healthy growth of animals and reduce breeding risks

(Cheng et al., 2017). Different types of functional oligosaccharides have certain effects on the intestinal health of pigs at different stages, mainly in promoting the proliferation of *Bifidobacteria* and *Lactobacillus*, as well as inhibiting the proliferation of *E. coli*. Moreover, the application effects of different types of functional oligosaccharides in animals are not consistent. When they are put into use, it is necessary to analyze the structural characteristics and specific conditions of livestock and poultry to select the appropriate type to achieve the best effect (Table 3). Supplementation of 200 mg/kg COS in the diets of weaned piglets infected with *E. coli* can increase the relative abundance of *Lactobacillus*, decrease the relative abundance of *E. coli*, and increase the villus height of ileum and jejunum, which is beneficial to the digestion and absorption of nutrients and intestinal health of weaned piglets (Liu et al., 2010). The relative abundance of *Lactobacillus*, *Streptococcus*, and *Turicibacter* in intestinal contents of weaned piglets was decreased when 100 mg/kg XOS were added in diets (Yin et al., 2019). Therefore, the application of different oligosaccharides in animal intestinal health should be further studied, and the mechanism underlying needs to be continuously explored to ensure the stabilizing effect of oligosaccharides in livestock and poultry breeding.

4. Influencing factors

The key to pig farming is to improve the growth performance and immune performance, thereby reducing the incidence of disease. The prohibition of antibiotics and the frequent occurrence of African swine fever at home and abroad have caused more attention to the research and application of new feed additives. In recent years, many studies have been reported on the application of functional oligosaccharides in pig breeding, especially in weaned piglets. It plays a significant role in promoting animal growth, improving feed utilization efficiency, and reducing diseases. However, relevant reports have found that adding functional oligosaccharides into the diet of pigs has no significant effect, indicating that the effect of oligosaccharide feed additives is related to many factors, such as animal breeding environment, animal species and age, as well as the supplemental level of oligosaccharide in feed.

4.1. Animal feeding environment

The effect of functional oligosaccharides on healthy pigs is not very significant. MOS can significantly increase the contents of IgA,

IgG, and IgM in serum of germ-free piglets, but in normal healthy piglets, it can only increase the level of IgA, and has no significant effect on the contents of the other 2 immunoglobulins. Only when the intestinal factors have a great influence on the production performance, the growth-promoting effect can be clearly shown (Spring et al., 2015). In addition, only when animals are in a poor feeding environment, the feed hygiene cannot be well guaranteed, resulting in intestinal health and immune system impact, functional oligosaccharides can play a significant antibacterial and immune function, to play a role in regulating intestinal health. In general farms, piglets with 0.3% FOS increased their body weight by 13%, but only 4% in farms with more stringent sanitary conditions (Nakamura et al., 1988). Jeon et al. (2000) found that COS produced by enzymatic hydrolysis of chitosan has bacteriostatic effect. Only 0.5% concentration can completely inhibit the growth of *E. coli*, which can well protect the intestinal health of livestock and poultry.

4.2. Physiological stage

The structure and function of the digestive tract are different in different physiological stages of animals. Functional oligosaccharides generally play a significant role in weaned piglets and diseased piglets. For growing-finishing pig, which have strong immune system and better health status, so adding oligosaccharide to their diets will not show much beneficial effects. Weaned piglets with developing immune system and unstable intestinal microflora are easier to get sick that the main reason of diarrhea is the increase of pathogenic bacteria, so adding functional oligosaccharides after weaning can achieve a better effect. Studies have shown that piglets grow slowly at 1 to 2 wk before and after weaning, and adding mannan oligosaccharides to the diet of weaned piglets improves the growth performance more significantly than pigs at the growth stage (Miguel et al., 2004). Liu et al. (2018) added 200 mg/kg XOS to the diet of weaned piglets. They found that the intestinal microflora structure of piglets was improved, and the relative abundance of *Lactobacillus* increased, and *E. coli* decreased. When the same dose of XOS were added to the diets of growing pigs, the intestinal microbiota structure of pigs was not significantly changed (Sutton et al., 2021). Therefore, when selecting functional oligosaccharides as feed additives, the physiological stage of the feeding target should be considered first to better play the role of functional oligosaccharides and achieve the expected results of the feeding target.

Table 3
Effects of functional oligosaccharides on intestinal microflora of pigs.

| Action stage | Oligosaccharides type | Dose, % | Bacterial source | Main effect | Reference |
|----------------------------|-----------------------|-----------|------------------------|--|----------------------------------|
| Weaned pigs | MOS | 0.04/0.06 | Cecum | <i>Bifidobacterium</i> and <i>Lactobacillus</i> ↑; <i>S. aureus</i> ↓ | Yang et al. (2012) |
| Weaned pigs | FOS | 5 | Colon | <i>Bifidobacterium</i> ↑; <i>E. coli</i> ↓ | Gebbink et al. (2001) |
| Weaned pigs | FOS | 0.6 | Jejunum/ileum | <i>Bifidobacterium</i> and <i>Lactobacillus</i> ↑; <i>Proteobacteria</i> ↓ | Chang et al. (2018) |
| Weaned pigs | scFOS | 0.4 | Colon | <i>Bacteroidetes</i> , <i>Lactobacillus</i> spp., <i>Prevotella</i> spp. and <i>Bifidobacterium</i> spp. ↑ | Zhao et al. (2019) |
| Weaned pigs | FOS | 4 | Gastrointestinal tract | No significant effect | Mikkelsen and Jensen (2004) |
| Weaned pigs | XOS | 1.5 | Intestinal contents | <i>Lactobacillus</i> and <i>Bifidobacterium</i> ↑ | Pang et al. (2021) |
| Weaned pigs | XOS | 0.02 | Rectal feces | <i>Lactobacillus</i> ↑; <i>E. coli</i> ↓ | Liu et al. (2018) |
| Weaned pigs | XOS | 0.025 | Ileum | <i>Bacteroides</i> ↑; <i>Firmicutes</i> ↓ | Ding et al. (2021) |
| Weaned pigs | XOS | 0.01 | Colon | <i>Lactobacillus</i> and <i>Bifidobacterium</i> spp. ↑ | Su et al. (2021) |
| Weaned pigs | COS | 0.1/0.3 | Cecum/colon/rectum | <i>Lactobacillus</i> ↑; <i>E. coli</i> ↓ | Han et al. (2007) |
| Weaned pigs | COS | 0.01 | Ileum/cecum and colon | <i>Bifidobacterium</i> ↑; <i>E. coli</i> ↓ | Wan et al. (2017) |
| Nursery Pigs | MOS | 0.3 | Cecum/rectum | <i>Lactobacillus</i> ↑; <i>E. coli</i> ↓ | Poeikhampha and Bunchasak (2011) |
| Growing pigs | XOS | 0.02 | Intestinal contents | No significant effect | Sutton et al. (2021) |
| Growing and fattening pigs | XOS | 0.01 | Intestinal contents | <i>Proteobacteria</i> and <i>Citrobacter</i> ↓; <i>Firmicutes</i> and <i>Lactobacillus</i> ↑ | Pan et al. (2019) |

MOS = mannan oligosaccharides; FOS = fructo-oligosaccharides; scFOS = short-chain fructo-oligosaccharides; XOS = xylo-oligosaccharides; COS = chitosan oligosaccharides; *E. coli* = *Escherichia coli*.

4.3. Types and dosage of functional oligosaccharides

With a complex structure, widely spread source, and different production process, the functional oligosaccharides produced by different types and manufacturers have significantly different effects. For example, MOS play a role in feeding mainly by absorbing harmful bacteria and toxins and stimulating the immune system of animals. Still, there are relatively few studies on the effects of other oligosaccharides on the immune system. Besides the effect of the type of functional oligosaccharide on pig breeding, the dosage of additives also has a specific effect. When the same functional oligosaccharides were added to the same animal diets, the results varied depending on the amount added. The insufficient number of functional oligosaccharides in the diet had no apparent effect. On the contrary, if the dosage is too large, it will increase feed and feeding cost, and fail to increase beneficial bacteria, reduce harmful bacteria, and cause animal diarrhea. Therefore, the effective concentration of functional oligosaccharides should be fully considered if they are applied in the diets.

4.4. Inherent levels of oligosaccharides in diets

The feed materials are rich in oligosaccharides, while the content of oligosaccharides in corn is very low. Still, the non-digestible sugars such as raffinose and stachyose are rich in barley, wheat, and soybean (Karr-Lilienthal et al., 2005), so the oligosaccharides in barley, wheat and soybean may affect the experimental results of dietary functional oligosaccharides.

5. Application prospects

5.1. Application of functional oligosaccharides in weaned piglets

As a new kind of green feed additive, functional oligosaccharides can improve the nutrients digestibility in the diet for weaned piglets, reduce the ratio of feed to meat, improve the antioxidant capacity of weaned piglets, improve the intestinal microflora structure, reduce the diarrhea rate, and relieve weaning stress. Dietary supplementation of 400 to 600 mg/kg COS can improve the growth rate of weaned piglets, enhance intestinal defense capacity, increase the number of *Lactobacillus* and *Bifidobacterium*, and reduce the number of *Staphylococcus aureus* in cecum (Yang et al., 2012). Adding 500 mg/kg XOS to the diet of weaned piglets can

increase the average daily gain and feed utilization rate of piglets, and improve the serum antioxidant capacity, which is beneficial to the growth performance and survival rate of piglets (Chen et al., 2022). Davis et al. (2000) found that adding MOS can significantly improve piglets' performance (feed intake, daily gain, and feed conversion rate). Functional oligosaccharides improve the growth performance of piglets and have certain effects on the intestinal microflora of piglets. Supplementation of 0.5 g/kg COS can increase the number of beneficial bacteria and the concentration of short chain fatty acids in the ileum and colon of piglets, and reduce the number of harmful bacteria, which has a regulatory effect on the intestinal microbiota structure of piglets (Kong et al., 2014). Supplementation of 4 g/kg short-chain fructo-oligosaccharides in the diet of piglets with intestinal dysfunction can reduce the expression of malondialdehyde and proinflammatory factors in the jejunum and can restore the number of *Lactobacillus* and *Bifidobacterium* in the intestinal tract to the normal level (Yan et al., 2020). At the same time, relevant reports have shown that 2% FOS can increase the average daily gain and the number of *Bifidobacterium* in the ileum of weaned piglets (Shim et al., 2005).

5.2. Application of functional oligosaccharides in sows

The gestation period of sows is a particularly vulnerable physiological stage, and corresponding measures should be taken according to its physiological characteristics to avoid adverse effects before and after delivery, such as insufficient milk production, frequent disease, and other phenomena. This period affects the health of piglets after birth and affects the reproductive cycle of sows. Dietary functional oligosaccharides can improve intestinal microflora structure, feed intake and nutrient digestion and absorption, antioxidant capacity and non-specific immunity. Meanwhile, dietary functional oligosaccharides can encourage better average daily gain, litter weight and healthy litter rate of postpartum weaned piglets (Fig. 3). Duan et al. (2019) added 400 mg/kg MOS in diets of sows and 800 mg/kg MOS in diets of piglets. They found that the relative abundance of *Lactobacillus* in jejunum of sows and piglets increased, while the relative abundance of *E. coli* decreased, and the secret immune globulin (SIgA) content in jejunum mucosa of piglets found an increase. In the piglets, they found that the mRNA expression levels of *IL-8* and Toll-Like receptor ligand (*TLRL*) were decreased, and the contents of pro-inflammatory factors such as *IL-2*, *IL-4* and interferon (*IFN*)- γ in serum of piglets were

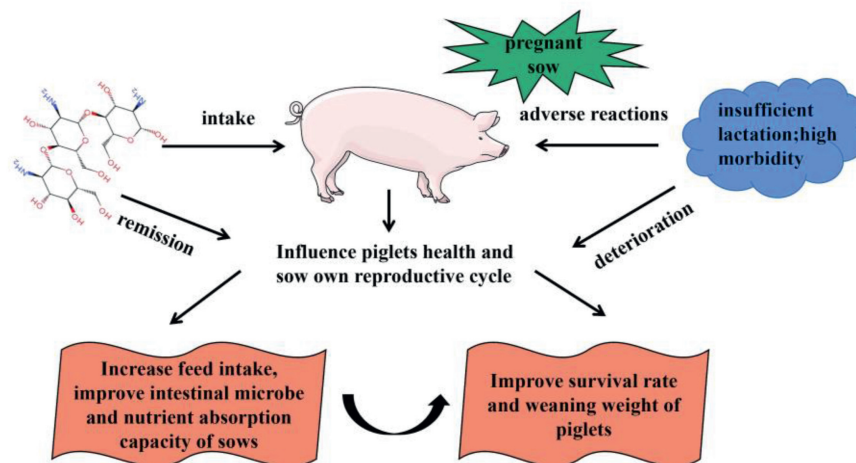


Fig. 3. Effects of functional oligosaccharides on the health of sows. Dietary functional oligosaccharides can improve the intestinal microbiota structure of sows, improve the feed intake and nutrient digestion and absorption, so as to improve the antioxidant capacity and non-specific immunity of sows, and further promote the body health of weaned piglets.

decreased, while the content of anti-inflammatory factor IL-10 was increased, which proved that MOS can improve the intestinal flora structure and immunity of sows and piglets, and it also can inhibit the occurrence of intestinal inflammation and improve the survival rate and growth performance of piglets. Cheng et al. (2015) fed 40 mg/kg COS to sows during oestrus increasing litter size of sows by 18.5% and piglet survival by 19.2%. After feeding 30 mg/kg COS to sows in late gestation and lactation, the amino acid content in milk secreted by sows increased, and the daily gain and weaning weight of offspring increased. At the same time, the blood sugar level and liver glycogen content of piglets are reduced, which further improves the growth efficiency of piglets (Xie et al., 2015). In addition, relevant studies have proved that obesity in sows during late gestation will aggravate perinatal metabolic disorders and affect offspring piglets' performance and intestinal health. Feeding gilts 1000 mg/kg of COS can reduce their final body weight and avoid excessive obesity (Egan et al., 2015). The effects of functional oligosaccharides on alleviating sow obesity and improving offspring survival were further verified. Supplementation of 100 mg/kg COS in the diet of sows increased serum leptin and immunoglobulin content at 35 and 85 d of gestation, and increased fetal survival rate, number of live piglets per litter and average body weight (Wan et al., 2016).

6. Conclusion

In recent years, functional oligosaccharides have attracted more and more attention under the background of antibiotic resistance. There are many functional oligosaccharides, such as COS, XOS, MOS, FOS, etc. They come from a wide range of sources and are green and pollution-free, a good substitute for antibiotics. The physiological functions of functional oligosaccharides and their mechanism of action in pig breeding have also been further recognized. Functional oligosaccharides have certain positive effects on growth performance, immunity, and intestinal health of pigs, but there are still many factors affecting the function of functional oligosaccharides, and how to find a stable role for the use of functional oligosaccharides as feed additives remains to be further explored. All in all, future research should pay more attention to the relevant factors affecting the function of functional oligosaccharides, and study how to eliminate the adverse effects better, to use functional oligosaccharides with maximum efficiency, provide beneficial help for the development of pig breeding industry and provide a reference for the development and utilization of available functional oligosaccharides.

Author contribution

Nian Liu, Haibo Shen and Fan Zhang: Literature collection, Writing-Original draft preparation. **Xiang Liu and Qinrui Xiao:** Format modification. **Qian Jiang:** Writing- Reviewing and Editing. **Bie Tan and Xiaokang Ma:** Funding acquisition.

Declaration of competing interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, and there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the content of this paper.

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References

- Ashaolu TJ. Immune boosting functional foods and their mechanisms: a critical evaluation of probiotics and prebiotics. *Biomed Pharmacother* 2020;130:110625. <https://doi.org/10.1016/j.biopha.2020.110625>.
- Bhatia L, Sharma A, Bachheti RK, Chandel AK. Lignocellulose derived functional oligosaccharides: production, properties, and health benefits. *Prep Biochem Biotechnol* 2019;49:744–58. <https://doi.org/10.1080/10826068.2019.1608446>.
- Cano ME, García-Martin A, Comendador MP, Wojtusik M, Santos VE, Kovensky J, Ladero M. Production of oligosaccharides from agrofood wastes. *Fermentation* 2020;6:31. <https://doi.org/10.3390/fermentation6010031>.
- Carvalho AFA, Neto PDO, Da Silva DF, Pastore GM. Xylo-oligosaccharides from lignocellulosic materials: chemical structure, health benefits and production by chemical and enzymatic hydrolysis. *Food Res Int* 2013;51:75–85. <https://doi.org/10.1016/j.foodres.2012.11.021>.
- Castillo M, Martin-Orue S, Taylor-Pickard J, Perez J, Gasa J. Use of mannanoligosaccharides and zinc chelate as growth promoters and diarrhea preventative in weaning pigs: effects on microbiota and gut function. *J Anim Sci* 2008;86:94–101. <https://doi.org/10.2527/jas.2005-686>.
- Chang M, Zhao Y, Qin G, Zhang X. Fructo-oligosaccharide alleviates soybean-induced anaphylaxis in piglets by modulating gut microbes. *Front Microbiol* 2018;2769. <https://doi.org/10.3389/fmicb.2018.02769>.
- Che T, Johnson R, Kelley K, Van AW, Dawson K, Moran C, Pettigrew J. Mannan oligosaccharide improves immune responses and growth efficiency of nursery pigs experimentally infected with porcine reproductive and respiratory syndrome virus. *J Anim Sci* 2011;89:2592–602. <https://doi.org/10.2527/jas.2010-3208>.
- Chen Y, Kim I, Cho J, Yoo J, Wang Y, Huang Y, Kim H, Shin S. Effects of chitooligosaccharide supplementation on growth performance, nutrient digestibility, blood characteristics and immune responses after lipopolysaccharide challenge in weaning pigs. *Livest Sci* 2009;124:255–60. <https://doi.org/10.1016/j.livsci.2009.02.006>.
- Chen Y, Xie Y, Zhong R, Han H, Liu L, Chen L, Zhang H, Beckers Y, Everaert N. Effects of graded levels of xylo-oligosaccharides on growth performance, serum parameters, intestinal morphology, and intestinal barrier function in weaned piglets. *J Anim Sci* 2021;99(7):skab183. <https://doi.org/10.1093/jas/skab183>.
- Chen Y. The effects of xylo-oligosaccharides on gut barrier function, intestinal microbiota and growth performance in weaned piglets. 2022.
- Cheng LK, Wang LX, Xu QS, Huang LJ, Zhou DS, Li Z, Li SG, Du YG, Yin H. Chitooligosaccharide supplementation improves the reproductive performance and milk composition of sows. *Livest Sci* 2015;174:74–81. <https://doi.org/10.1016/j.livsci.2015.02.003>.
- Cheng W, Lu J, Li B, Lin W, Zhang Z, Wei X, Sun C, Chi M, Bi W, Yang B. Effect of functional oligosaccharides and ordinary dietary fiber on intestinal microbiota diversity. *Front Microbiol* 2017;1750. <https://doi.org/10.3389/fmicb.2017.01750>.
- Choque-Delgado GT, Tamashiro WMSC, Marostica Junior MR, Moreno YMF, Pastore GM. The putative effects of probiotics as immunomodulatory agents. *Food Res Int* 2011;44:3167–73. <https://doi.org/10.1016/j.foodres.2011.07.032>.
- Czech A, Grela E, Mokrzycka A, Pejsak Z. Efficacy of mannanoligosaccharides additive to sows diets on colostrum, blood immunoglobulin content and production parameters of piglets. *Pol J Vet Sci* 2010;13:525.
- Davis E, Maxwell C, Kegley B, de Rodas B, Friesen K, Hellwig D, Johnson Z, Kellogg D. Efficacy of mannan oligosaccharide (Bio-Mos®) addition at two levels of supplemental copper on performance and immunocompetence of early weaned pigs. *Ark Agric Exp Stat Res Ser* 2000:15–8.
- Davis M, Maxwell C, Brown D, De RB, Johnson Z, Kegley E, Hellwig D, Dvorak R. Effect of dietary mannan oligosaccharides and (or) pharmacological additions of copper sulfate on growth performance and immunocompetence of weaning and growing/finishing pigs. *J Anim Sci* 2002;80:2887–94. <https://doi.org/10.2527/2002.80112887x>.
- Dawood MA, Koshio S, Esteban MÁ. Beneficial roles of feed additives as immunostimulants in aquaculture: a review. *Rev Aquacult* 2018;10:950–74. <https://doi.org/10.1111/raq.12209>.
- Ding H, Zhao X, Azad MAK, Ma C, Gao Q, He J, Kong X. Dietary supplementation with *Bacillus subtilis* and xylo-oligosaccharides improves growth performance and intestinal morphology and alters intestinal microbiota and metabolites in weaned piglets. *Food Funct* 2021;12:5837–49. <https://doi.org/10.1039/d1fo00208b>.
- Duan X, Chen D, Zheng P, Tian G, Wang J, Mao X, Yu J, He J, Li B, Huang Z. Effects of dietary mannan oligosaccharide supplementation on performance and immune response of sows and their offspring. *Anim Feed Sci Technol* 2016;218:17–25. <https://doi.org/10.1016/j.anifeedsci.2016.05.002>.
- Duan X, Tian G, Chen D, Huang L, Zhang D, Zheng P, Mao X, Yu J, He J, Huang Z. Mannan oligosaccharide supplementation in diets of sow and (or) their offspring improved immunity and regulated intestinal bacteria in piglet. *J Anim Sci* 2019;97:4548–56. <https://doi.org/10.1093/jas/skz318>.
- Duan X, Tian G, Chen D, Yang J, Zhang L, Li B, Huang L, Zhang D, Zheng P, Mao X. Effects of diet chitosan oligosaccharide on performance and immune response of sows and their offspring. *Livest Sci* 2020;239:104114. <https://doi.org/10.1016/j.livsci.2020.104114>.

- Egan AM, Sweeney T, Hayes M, O'Doherty JV. Prawn shell chitosan has anti-obesogenic properties, influencing both nutrient digestibility and microbial populations in a pig model. *PLoS One* 2015;10:e0144127. <https://doi.org/10.1371/journal.pone.0144127>.
- Estrada A, Drew MD, Van KA. Effect of the dietary supplementation of fructooligosaccharides and *Bifidobacterium longum* to early-weaned pigs on performance and fecal bacterial populations. *Can J Anim Sci* 2001;81:141–8. <https://doi.org/10.4141/A00-037>.
- Faustino M, Durão J, Pereira CF, Pintado ME, Carvalho AP. Mannans and mannan oligosaccharides (MOS) from *Saccharomyces cerevisiae*—A sustainable source of functional ingredients. *Carbohydr Polym* 2021;272:118467. <https://doi.org/10.1016/j.carbpol.2021.118467>.
- Gebbink G, Sutton AL, Williams BA, Patterson JA, Richert BT, Kelly DT, Verstegen MWA. Effects of oligosaccharides in weanling pig diets on performance, microflora and intestinal health[C]/Digestive physiology in pigs. In: Proceedings of the 8th Symposium, Swedish University of Agricultural Sciences, Uppsala, Sweden, 20–22 June 2000. CAB; 2001. p. 269–71.
- Giannenas I, Doukas D, Karamoutsios A, Tzora A, Bonos E, Skoufos I, Tsinas A, Christaki E, Tontis D, Florou-Paneri P. Effects of *Enterococcus faecium*, mannan oligosaccharide, benzoic acid and their mixture on growth performance, intestinal microbiota, intestinal morphology and blood lymphocyte sub-populations of fattening pigs. *Anim Feed Sci Technol* 2016;220:159–67. <https://doi.org/10.1016/j.anifeeds.2016.08.003>.
- Gobinath D, Madhu AN, Prashant G, Srinivasan K, Prapulla SG. Beneficial effect of xylo-oligosaccharides and fructo-oligosaccharides in streptozotocin-induced diabetic rats. *Br J Nutr* 2010;104:40–7. <https://doi.org/10.1017/S0007114510000243>.
- Han K, Kwon I, Lohakare J, Heo S, Chae B. Chito-oligosaccharides as an alternative to antimicrobials in improving performance, digestibility and microbial ecology of the gut in weanling pigs. *Asian-Australas J Anim Sci* 2007;20:556–62. <https://doi.org/10.5713/ajas.2007.556>.
- Ho T, Jahan M, Haque Z, Kracht S, Wynn PC, Du Y, Gunn A, Wang B. Maternal chitosan oligosaccharide intervention optimizes the production performance and health status of gilts and their offspring. *Animal Nutrition* 2020;6:134–42. <https://doi.org/10.1016/j.aninu.2020.02.001>.
- Hou Z, Wu D, Dai Q. Effects of dietary xylo-oligosaccharide on growth performance, serum biochemical parameters, antioxidant function, and immunological function of nursery piglets. *Rev Bras Zootec* 2020;49. <https://doi.org/10.37496/rbz4920190170>.
- Jeon YJ, Kim SK. Production of chitoooligosaccharides using an ultrafiltration membrane reactor and their antibacterial activity. *Carbohydr Polym* 2000;41:133–41. [https://doi.org/10.1016/S0144-8617\(99\)00084-3](https://doi.org/10.1016/S0144-8617(99)00084-3).
- Jha R, Foushe JM, Tiwari UP, Li L, Willing BP. Dietary fiber and intestinal health of monogastric animals. *Front Vet Sci* 2019;6:48. <https://doi.org/10.3389/fvets.2019.00048>.
- Karr-Lilienthal LK, Kadzere CT, Grieshop CM, Fahey Jr GC. Chemical and nutritional properties of soybean carbohydrates as related to nonruminants: a review. *Livest Prod Sci* 2005;97(1):1–12. <https://doi.org/10.1016/j.livprodsci.2005.01.015>.
- Kong X, Zhou X, Lian G, Blachier F, Liu G, Tan B, Nyachoti C, Yin Y. Dietary supplementation with chitoooligosaccharides alters gut microbiota and modifies intestinal luminal metabolites in weaned Huanjiang mini-piglets. *Livest Sci* 2014;160:97–101. <https://doi.org/10.1016/j.livsci.2013.11.023>.
- Laloučková K, Skřivanová E. Antibiotic resistance in livestock breeding: a review. *Sci Agric Bohem* 2019;50:15–22. <https://doi.org/10.2478/sab-2019-0003>.
- Lauridsen C. From oxidative stress to inflammation: redox balance and immune system. *Poultry Sci* 2019;98:4240–6. <https://doi.org/10.3382/ps/pey407>.
- Le Bourgot C, Le Normand L, Formal M, Respondek F, Blat S, Apper E, Ferret-Bernard S, Le Huërou-Luron I. Maternal short-chain fructo-oligosaccharide supplementation increases intestinal cytokine secretion, goblet cell number, butyrate concentration and *Lawsonia intracellularis* humoral vaccine response in weaned pigs. *Br J Nutr* 2017;117:83–92. <https://doi.org/10.1017/S0007114516004268>.
- Lim CB, Muniyappan M, Sanshui G, Kim I. PSIV-11 effects of dietary supplementation of Quillaja saponin or fructooligosaccharide and a mixture of both on the growth performance, nutrient digestibility, fecal microbial, and gas emissions in growing pigs. *J Anim Sci* 2022;100:151. <https://doi.org/10.1093/jas/skac064.256>.
- Liu J, Cao S, Liu J, Xie Y, Zhang H. Effect of probiotics and xylo-oligosaccharide supplementation on nutrient digestibility, intestinal health and noxious gas emission in weanling pigs. *Asian-Australas J Anim Sci* 2018;31:1660. <https://doi.org/10.5713/ajas.17.0908>.
- Liu P, Piao X, Kim S, Wang L, Shen Y, Lee H, Li S. Effects of chito-oligosaccharide supplementation on the growth performance, nutrient digestibility, intestinal morphology, and fecal shedding of *Escherichia coli* and *Lactobacillus* in weanling pigs. *J Anim Sci* 2008;86:2609–18. <https://doi.org/10.2527/jas.2007-0668>.
- Liu P, Piao X, Thacker P, Zeng Z, Li P, Wang D, Kim S. Chito-oligosaccharide reduces diarrhoea incidence and attenuates the immune response of weaned pigs challenged with *Escherichia coli* K88. *J Anim Sci* 2010;88:3871–9. <https://doi.org/10.2527/jas.2009-2771>.
- Liu Y, Espinosa CD, Abellilla JJ, Casas GA, Lagos LV, Lee SA, Kwon WB, Mathai JK, Navarro DM, Jaworski NW. Non-antibiotic feed additives in diets for pigs: a review. *Anim Nutr* 2018;4:113–25. <https://doi.org/10.1016/j.aninu.2018.01.007>.
- Luo Y, Liu L, Chen D, Yu B, Zheng P, Mao X, Huang Z, Yu J, Luo J, Yan H. Dietary supplementation of fructooligosaccharides alleviates enterotoxigenic *E. coli*-induced disruption of intestinal epithelium in a weaned piglet model. *Br J Nutr* 2021:1–27. <https://doi.org/10.1017/S0007114521004451>.
- Ma P, Liu HT, Wei P, Xu QS, Bai XF, Du YG, Yu C. Chitosan oligosaccharides inhibit LPS-induced over-expression of IL-6 and TNF- α in RAW264. 7 macrophage cells through blockade of mitogen-activated protein kinase (MAPK) and PI3K/Akt signaling pathways. *Carbohydr Polym* 2011;84:1391–8. <https://doi.org/10.1016/j.carbpol.2011.01.045>.
- Mäkeläinen H, Forssten S, Saarinen M, Stowell J, Rautonen N, Ouwehand A. Xylo-oligosaccharides enhance the growth of bifidobacteria and *Bifidobacterium lactis* in a simulated colon model. *Benef Microbes* 2010;1:81–91. <https://doi.org/10.3920/BM2009.0025>.
- Micciche AC, Foley SL, Pavlidis HO, McIntyre DR, Ricke SC. A review of prebiotics against *Salmonella* in poultry: current and future potential for microbiome research applications. *Front Vet Sci* 2018;191. <https://doi.org/10.3389/fvets.2018.00191>.
- Miguel JC, Rodriguez-Zas SL, Pettigrew JE. Efficacy of a mannan oligosaccharide (Bio-Mos®) for improving nursery pig performance. *J Swine Health Prod* 2004;12:296–307.
- Mikkelsen LL, Jensen BB. Effect of fructo-oligosaccharides and transgalactooligosaccharides on microbial populations and microbial activity in the gastrointestinal tract of piglets post-weaning. *Anim Feed Sci Technol* 2004;117:107–19. <https://doi.org/10.1016/j.anifeeds.2004.07.015>.
- Murugaiyan J, Kumar PA, Rao GS, Iskandar K, Hawser S, Hays JP, Mohsen Y, Adukkadukkam S, Awuah WA, Maria Jose RA, et al. Progress in alternative strategies to combat antimicrobial resistance: focus on antibiotics. *Antibiotics* 2022;11:200. <https://doi.org/10.3390/antibiotics11020200>.
- Nakamura K. Use of neosugar in piglets and sow. Proceeding of the 3th Neosugar Conference in Japan 1988:145–52.
- Pan J, Yin J, Zhang K, Xie P, Ding H, Huang X, Blachier F, Kong X. Dietary xylo-oligosaccharide supplementation alters gut microbial composition and activity in pigs according to age and dose. *Amb Express* 2019;9:1–10. <https://doi.org/10.1186/s13568-019-0858-6>.
- Pan L, Farouk MH, Qin G, Zhao Y, Bao N. The influences of soybean agglutinin and functional oligosaccharides on the intestinal tract of monogastric animals. *Int J Mol Sci* 2018;19:554. <https://doi.org/10.3390/ijms19020554>.
- Pang J, Zhou X, Ye H, Wu Y, Wang Z, Lu D, Wang J, Han D. The high level of xylooligosaccharides improves growth performance in weaned piglets by increasing antioxidant activity, enhancing immune function, and modulating gut microbiota. *Front Nutr* 2021;8. <https://doi.org/10.3389/fnut.2021.764556>.
- Patel S, Goyal A. Functional oligosaccharides: production, properties and applications. *World J Microbiol Biotechnol* 2011;27:1119–28. <https://doi.org/10.1007/s11274-010-0558-5>.
- Poeikhampha T, Bunchasak C. Comparative effects of sodium gluconate, mannan oligosaccharide and potassium diformate on growth performances and small intestinal morphology of nursery pigs. *Asian-Australas J Anim Sci* 2011;24:844–50. <https://doi.org/10.5713/ajas.2011.10334>.
- Qiang X, Yong LC, Qian BW. Health benefit application of functional oligosaccharides. *Carbohydr Polym* 2009;77:435–41. <https://doi.org/10.1016/j.carbpol.2009.03.016>.
- Rahim MA, Saeed F, Khalid W, Hussain M, Anjum FM. Functional and nutraceutical properties of fructo-oligosaccharides derivatives: a review. *Int J Food Prop* 2021;24:1588–602. <https://doi.org/10.1080/10942912.2021.1986520>.
- Rajagopalan G, Krishnan C. Functional oligosaccharides: production and action[M]// Next generation biomufacturing technologies. American Chemical Society; 2019. p. 155–80.
- Rastall R. Functional oligosaccharides: application and manufacture. *Annu Rev Food Sci Technol* 2010;1:305–39. <https://doi.org/10.1146/annurev.food.080708.100746>.
- Saeed M, Ahmad F, Arain MA, Abd El-Hack ME, Emam M, Butto Z, Moshaveri A. Use of mannan-oligosaccharides (MOS) as a feed additive in poultry nutrition. *J World Poultry Res* 2017;7:94–103.
- Schokker D, Fledderus J, Jansen R, Vastenhouw SA, de Bree FM, Smits MA, Jansman AA. Supplementation of fructooligosaccharides to suckling piglets affects intestinal microbiota colonization and immune development. *J Anim Sci* 2018;96:2139–53. <https://doi.org/10.1093/jas/sky110>.
- Shao L, Zhou L, Li G, Lin F, Fei Z, Jin T, Lin Y, Chen Z, Chen X. Effects of oral administration of mannan-oligosaccharide on immune responses and blood GSH-Px, SOD activities in suckling piglets. *Chin J Vet Sci* 2000;20:257–60. <https://doi.org/10.16303/j.cnki.1005-4545.2000.03.017>.
- Shim S, Verstegen M, Kim I, Kwon O, Verdonk J. Effects of feeding antibiotic-free creep feed supplemented with oligofructose, probiotics or synbiotics to suckling piglets increases the preweaning weight gain and composition of intestinal microbiota. *Arch Anim Nutr* 2005;59:419–27. <https://doi.org/10.1080/17450390500353234>.
- Singla A, Chawla M. Chitosan: some pharmaceutical and biological aspects—an update. *J Pharm Pharmacol* 2001;53:1047–67. <https://doi.org/10.1211/0022357011776441>.
- Sohn K, Kim M, Kim J, Han IK. The role of immunostimulants in monogastric animal and fish-review. *Asian-Australas J Anim Sci* 2000;13:1178–87. <https://doi.org/10.5713/ajas.2000.1178>.
- Spring P, Wenk C, Connolly A, Kiers A. A review of 733 published trials on Bio-Mos®, a mannan oligosaccharide, and Actigen®, a second generation mannose rich fraction, on farm and companion animals. *J Appl Anim Nutr* 2015;3. <https://doi.org/10.1017/jan.2015.6>.
- Su J, Zhang W, Ma C, Xie P, Blachier F, Kong X. Dietary supplementation with xylo-oligosaccharides modifies the intestinal epithelial morphology, barrier function and the fecal microbiota composition and activity in weaned piglets. *Front Vet Sci* 2021:8. <https://doi.org/10.3389/fvets.2021.680208>.

- Sun Z, Tang Z, Yin Y, Huang R, Li T, Tang S, Tan Z. Effect of dietary supplementation of galacto-mannan-oligosaccharides and chitosan on performance and serum immune parameters of 28-day weaned piglets challenged with pathogenic *E. coli*. *J Appl Anim Res* 2009;36:207–11. <https://doi.org/10.1080/09712119.2009.9707061>.
- Suthongsa S, Pichyangkura R, Kalandakanond-Thongsong S, Thongsong B. Effects of dietary levels of chito-oligosaccharide on ileal digestibility of nutrients, small intestinal morphology and crypt cell proliferation in weaned pigs. *Livest Sci* 2017;198:37–44. <https://doi.org/10.1016/j.livsci.2017.02.004>.
- Sutton T, O'Neill HM, Bedford M, McDermott K, Miller H. Effect of xylanase and xylo-oligosaccharide supplementation on growth performance and faecal bacterial community composition in growing pigs. *Anim Feed Sci Technol* 2021;274:114822. <https://doi.org/10.1016/j.anifeeds.2021.114822>.
- Swiatkiewicz S, Swiatkiewicz M, Arczewska-Wlosek A, Jozefiak D. Chitosan and its oligosaccharide derivatives (chito-oligosaccharides) as feed supplements in poultry and swine nutrition. *J Anim Physiol Anim Nutr* 2015;99:1–12. <https://doi.org/10.1111/jpn.12222>.
- Tiwari UP, Fleming SA, Abdul Rasheed MS, Jha R, Dilger RN. The role of oligosaccharides and polysaccharides of xylan and mannan in gut health of monogastric animals. *J Nutr Sci* 2020;9. <https://doi.org/10.1017/jns.2020.14>.
- Valpotic H, Samardzija M, Terzic S, Vince S, Speranda M, Lackovic G, Habrun B, Mas N, Duricic D, Kocila P. Effect of mannan oligosaccharide supplementation on blood and intestinal immune cells, bacteria numbers and performance in weaned pigs. *Acta Vet* 2016;85. <https://doi.org/10.2754/avb201685030267>.
- Vieira TF, Corrêa RC, Peralta RA, Peralta-Muniz-Moreira RF, Bracht A, Peralta RM. An overview of structural aspects and health beneficial effects of antioxidant oligosaccharides. *Curr Pharmaceut Des* 2020;26:1759–77. <https://doi.org/10.2174/1381612824666180517120642>.
- Wan J, Jiang F, Xu Q, Chen D, Yu B, Huang Z, Mao X, Yu J, He J. New insights into the role of chitosan oligosaccharide in enhancing growth performance, antioxidant capacity, immunity and intestinal development of weaned pigs. *RSC Adv* 2017;7:9669–79. <https://doi.org/10.1039/C7RA00142H>.
- Wan J, Xu Q, He J. Maternal chitosan oligosaccharide supplementation during late gestation and lactation affects offspring growth. *Ital J Anim Sci* 2018;17:994–1000. <https://doi.org/10.1080/1828051x.2018.1435313>.
- Wan J, Yang K, Xu Q, Chen D, Yu B, Luo Y, He J. Dietary chitosan oligosaccharide supplementation improves foetal survival and reproductive performance in multiparous sows. *RSC Adv* 2016;6:70715–22. <https://doi.org/10.1039/C6RA13294D>.
- Wang H, Zhang X, Wang S, Li H, Lu Z, Shi J, Xu Z. Mannan-oligosaccharide modulates the obesity and gut microbiota in high-fat diet-fed mice. *Food Funct* 2018;9:3916–29. <https://doi.org/10.1039/C8FO00209F>.
- Wang J, Yoo J, Kim H, Lee J, Kim I. Nutrient digestibility, blood profiles and faecal microbiota are influenced by chitoooligosaccharide supplementation of growing pigs. *Livest Sci* 2009;125:298–303. <https://doi.org/10.1016/j.livsci.2009.05.011>.
- Xie C, Guo X, Long C, Fan Z, Xiao D, Ruan Z, Deng ZY, Wu X, Yin Y. Supplementation of the sow diet with chitosan oligosaccharide during late gestation and lactation affects hepatic gluconeogenesis of suckling piglets. *Anim Reprod Sci* 2015;159:109–17. <https://doi.org/10.1016/j.anireprosci.2015.06.004>.
- Xie C, Long C, Wu X, Yang H, Fan Z, Xiao D, Wang Y, Yin Y. Effect of maternal supplementation with chitosan oligosaccharide on the antioxidant capacity of suckling piglets. *J Anim Sci* 2016a;94:453–6. <https://doi.org/10.2527/jas2015-9611>.
- Xie C, Wu X, Long C, Wang Q, Fan Z, Li S, Yin Y. Chitosan oligosaccharide affects antioxidant defense capacity and placental amino acids transport of sows. *BMC Vet Res* 2016b;12:1–8. <https://doi.org/10.1186/s12917-016-0872-8>.
- Xiong X, Yang H, Wang X, Hu Q, Liu C, Wu X, Deng D, Hou Y, Nyachoti C, Xiao D. Effect of low dosage of chito-oligosaccharide supplementation on intestinal morphology, immune response, antioxidant capacity, and barrier function in weaned piglets. *J Anim Sci* 2015;93:1089–97. <https://doi.org/10.2527/jas.2014-7851>.
- Xu Q, Wang LX, Du YG. The application of oligosaccharides in breeding industry [M]//Oligosaccharides of Chitin and Chitosan. Springer. 2019. p. 325–58. Singapore.
- Xu Y, Wang Z, Wang Y, Yan S, Shi B. Effects of chitosan as growth promoter on diarrhea, nutrient apparent digestibility, fecal microbiota and immune response in weaned piglets. *J Appl Anim Res* 2018;46:1437–42. <https://doi.org/10.1080/09712119.2018.1531763>.
- Xu Z, Zou X, Hu C, Xia M, Zhan X, Wang M. Effects of dietary fructooligosaccharide on digestive enzyme activities, intestinal microflora and morphology of growing pigs. *Asian-Australas J Anim Sci* 2002;15:1784–9. <https://doi.org/10.5713/ajas.2002.1784>.
- Yan H, Zhou P, Zhang Y, Zhang Z, Liu J, Zhang H. Short-chain fructo-oligosaccharides alleviates oxidized oil-induced intestinal dysfunction in piglets associated with the modulation of gut microbiota. *J Funct Foods* 2020;64:103661. <https://doi.org/10.1016/j.jff.2019.103661>.
- Yang C, Ferket P, Hong Q, Zhou J, Cao G, Zhou L, Chen A. Effect of chito-oligosaccharide on growth performance, intestinal barrier function, intestinal morphology and cecal microflora in weaned pigs. *J Anim Sci* 2012;90:2671–6. <https://doi.org/10.2527/jas.2011-4699>.
- Yang H, Paruch L, Chen XJ, Eerde AV, Skomedal H, Wang Y, Liu D, Liu CJ. Antibiotic application and resistance in swine production in China: current situation and future perspectives. *Front Vet Sci* 2019;6:136. <https://doi.org/10.3389/fvets.2019.00136>.
- Yang J, Summanen PH, Henning SM, Hsu M, Lam HM, Huang J, Tseng CH, Dowd SE, Finegold SM, Heber D. Xylooligosaccharide supplementation alters gut bacteria in both healthy and prediabetic adults: a pilot study. *Front Physiol* 2015;6:216. <https://doi.org/10.3389/fphys.2015.00216>.
- Yıldız S. The metabolism of fructooligosaccharides and fructooligosaccharide-related compounds in plants. *Food Rev Int* 2010;27:16–50. <https://doi.org/10.1080/87559129.2010.518295>.
- Yin J, Li F, Kong X, Wen C, Guo Q, Zhang L, Wang W, Duan Y, Li T, Tan Z. Dietary xylo-oligosaccharide improves intestinal functions in weaned piglets. *Food Funct* 2019;10:2701–9. <https://doi.org/10.1039/C8FO02485E>.
- Yin YL, Tang Z, Sun Z, Liu Z, Li T, Huang R, Ruan Z, Deng Z, Gao B, Chen L. Effect of galacto-mannan-oligosaccharides or chitosan supplementation on cytoimmunity and humoral immunity in early-weaned piglets. *Asian-Australas J Anim Sci* 2008;21:723–31. <https://doi.org/10.5713/ajas.2008.70408>.
- Yin J, Wang Y, Xu X, Liu Y, Yao L, Sun Q. The progress of global antimicrobial resistance governance and its implication to China: a review. *Antibiotics* 2021;10:1356. <https://doi.org/10.3390/antibiotics10111356>.
- Yui T, Ogawa K, Sarko A. Molecular and crystal structure of konjac glucomannan in the mannan II polymorphic form. *Carbohydr Res* 1992;229:41–55. [https://doi.org/10.1016/S0008-6215\(00\)90479-8](https://doi.org/10.1016/S0008-6215(00)90479-8).
- Zhang Y, Xia C, Lu M, Tu M. Effect of overliming and activated carbon detoxification on inhibitors removal and butanol fermentation of poplar prehydrolysates. *Biotechnol Biofuels* 2018;11:1–14. <https://doi.org/10.1186/s13068-018-1182-0>.
- Zhang Z, Zhang G, Zhang S, Zhao J. Fructooligosaccharide reduces weanling pig diarrhea in conjunction with improving intestinal antioxidant activity and tight junction protein expression. *Nutrients* 2022;14:512. <https://doi.org/10.3390/nu14030512>.
- Zhao P, Jung J, Kim I. Effect of mannan oligosaccharides and fructan on growth performance, nutrient digestibility, blood profile, and diarrhea score in weanling pigs. *J Anim Sci* 2012;90:833–9. <https://doi.org/10.2527/jas.2011-3921>.
- Zhao W, Yuan M, Li P, Yan H, Zhang H, Liu J. Short-chain fructo-oligosaccharides enhances intestinal barrier function by attenuating mucosa inflammation and altering colonic microbiota composition of weaning piglets. *Ital J Anim Sci* 2019;18:976–86. <https://doi.org/10.1080/1828051X.2019.1612286>.
- Zhou T, Cho J, Kim I. Effects of supplementation of chito-oligosaccharide on the growth performance, nutrient digestibility, blood characteristics and appearance of diarrhea in weanling pigs. *Livest Sci* 2012;144:263–8. <https://doi.org/10.1016/j.livsci.2011.12.009>.
- Zou P, Yang X, Wang J, Li Y, Yu H, Zhang Y, Liu G. Advances in characterisation and biological activities of chitosan and chitosan oligosaccharides. *Food Chem* 2016;190:1174–81. <https://doi.org/10.1016/j.foodchem.2015.06.076>.