Journal of
Applied Microbiology

Journal of Applied Microbiology ISSN 1364-5072

REVIEW ARTICLE

# *Saccharomyces cerevisiae* as a probiotic feed additive to non and pseudo-ruminant feeding: a review

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**Keywords**
live cells, microflora, monogastric, probiotic additive, *Pseudo-ruminant*, *Saccharomyces cerevisiae*.

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2019/0712: received 21 April 2019, revised 6 July 2019 and accepted 25 July 2019

doi:10.1111/jam.14416

## Abstract

The production of livestock and poultry faces major challenges to meet the global demand for meat and dairy products and eggs due to a steady increase in the world's population and the ban of antibiotics in animal production. This ban has forced animal nutritionists to seek for natural alternatives to antibiotics. In this context, the yeast *Saccharomyces cerevisiae* has received considerable attention in the last decade. It has been reported that feed supplementation with live yeast cells improve feed efficiency, enhance feed digestibility, increase animal performance, reduce the number of pathogenic bacteria, improve animal health and reduce the negative environmental impacts of livestock production. The current review sheds light on the effects of the use of live *S. cerevisiae* cells in the diets of nonruminant and pseudo-ruminant's animals and the mechanisms by which they exert its effects. This review work revealed that the addition of *S. cerevisiae* in poultry feed causes a phenomenon called competitive exclusion of pathogenic bacteria capable of causing disease adhere to the yeast surface, and so removing a large amount of harmful microorganisms and allowing the Animal defend more effectively, the production of antimicrobial agents, the balancing the gut microbiota and stimulation of host adaptive immune system and improving gut morphological structure, thus these benefits are reflected on the overall poultry health. In addition, in the presence of live *S. cerevisiae* cells, the immunity of rabbits was improved due to the high number of white blood cell. In addition, apparent digestibility of acid and neutral detergent fibre was improved in horses and rabbits. *Saccharomyces cerevisiae* in pig diets augment mucosal immunity by increasing IgM and IgA activity against pathogens, enhance intestinal development and function, adsorb mycotoxins, modulate gut microbiota and reduce postweaning diarrhoea.

## Introduction

Within the last 30 years, the development of strategies to improve livestock production, to lower production cost and to reduce the negative environmental impacts of livestock production was of utmost importance for nutritional scientists, microbiologists and biochemists. Supplementation of livestock feed with, for example antibiotics as well as a number of probiotics and/or probiotics have been exploited to achieve the aforementioned goals (Al-Khalaifah 2018). However, in the past 14 years, application of antibiotics in animal production has faced decreasing social acceptance due to toxic effects in animals, the development of bacterial resistance, side effects on human health and a negative impact on the safety and quality of products derived from livestock and poultry such as meat, dairy and eggs. Within the European Union, application of antibiotics in livestock is prohibited today (Official Journal of the European Union Regulation 2006). In United States, the use of antibiotics or antimicrobial drugs as feed additives to help livestock or poultry grow faster or gain weight or cause conversion of feed efficiency are prohibited (FDA 2015). The Guidance for Industry #209 recommended that the use of antibiotics or antimicrobial drugs in livestock production is only to ensure animal health (FDA 2012). Therefore probiotics such as yeast *S. cerevisiae* have been evaluated among others as potential feed supplements to improve feed utilization, enhance feed digestibility, reduce the number of pathogens (Haldar *et al.* 2011), improve animal performance and health (Cheng *et al.* 2014). Yeast is known to induce positive effects in both ruminants and nonruminants; yeast supplementation also reduces the negative environmental impacts of livestock production (Ogbuewu *et al.* 2018). In available scientific literature, supplementation of monogastric feed with live yeast cells did not show uniform results. Beneficiary effects on animal health and performance (Medina *et al.* 2002; Van der Peet-Schwering *et al.* 2007; Kowalik *et al.* 2012) as well as no effects (Kornegay *et al.* 1995; Sanaa 2013) in the presence of yeast have been reported. The reasons for the variations in the results could be explained by the use of different types and doses of live yeast cells as well as differences in feed composition, animal species, physiological status and age of the animals (Wagner *et al.* 1990). Moreover, differences in the digestive system among monogastric species can be found. Structures such as gizzard, crop and functional caecum are not common to all monogastric animals whereas stomach, small and large intestine are structures of the gastrointestinal tract of all monogastric animals. In addition, digestion may differ among animal species. Rabbits, for example use a process called coprophagy to utilize fibre from the feed to a greater extent. In the caecum, rabbits use massive quantities of bacteria to convert indigestible fibre to digestible nutrients. In horses, fibre digestion is performed by bacterial fermentation in the hindgut. In poultry, a positive effect on fibre digestion in the gizzard is achieved by reducing particle size by grinding with grit While in pigs, soluble fibre was fermented either in the small intestine or in the caecum, whereas fermentation of insoluble fibre occurred in the colon. Thus, *Saccharomyces* might act via different mechanisms in different animal species. This review gives an overview on the impact of dietary live *S. cerevisiae* cells in nonruminant and pseudo-ruminant's animals.

## *Saccharomyces cerevisiae*

Yeasts are an important source for obtaining products with probiotic activity, either live strains or derivatives of their cell walls. These preparations demonstrated a proven immunosuppressant activity in livestock as well as improvements in gastrointestinal physiology, which contributed to improved production results (Morales 2004). Yeast strains are more well-known in their use as probiotics belonging to the genera *Saccharomyces*, *Kluyveromyces, Hansenula, Pichia and Candida* and within these genera, species *S. boulardii, S. cerevisiae, K. fragilis, K. lactis, C. saitoana and C. pintolopesii* (Coenen 2000; Bovill *et al.* 2001; Campeanu 2002; Kumura *et al.* 2004). The most prominent yeast used as a feed additive in livestock is *S. cerevisiae*. It is rich in digestible proteins, vitamins (vitamin B6, thiamin, biotin, riboflavin, nicotinic acid and pantothenic acid), magnesium and zinc (Haiman and Frank 1994). Its calcium content, however, is low (Haiman and Frank 1994). The polysaccharides α-D-mannan, chitin and β-D-glucan are the main constituents of the *S. cerevisiae* cell wall. The immunological specificity of yeasts is determined by mannoproteins and β-D-mannan (Ruiz-Herrera 1992; Li *et al.* 2006). Yeasts are not a natural host of gut micro-organisms in monogastrics; therefore, *S. cerevisiae* flows along the gastrointestinal tract as alive and active without adhering to its walls. The strains that do not have the ability to adhere to the intestinal epithelium are effective as bio regulators and their action based on the ability of colonization through several mechanisms (Rodriguez *et al.* 2000; Baptista 2002) referred in their work that the use of live yeast cells to act as detoxification agents against mycotoxins and other bacterial toxins and their receptors in the mucous membrane and *Vibrio cholera* toxin. Severe damage to organs has been eliminated due to diets that may contain these toxins in the presence of *S. cerevisiae* for their ability to reduce animal stress, providing vitamins, enzymes and proteins (Baptista *et al.* 2005). The use of probiotics in the case of yeast is given by their bio regulatory action, which occurs by various mechanisms including microbial antagonism suppression of pathogenic bacteria, stimulation of the animal's immune system, attachment and removal of pathogens and increased activity-specific enzyme bacteria. From the standpoint of biomedical therapy, these mechanisms can be classified as pharmacodynamics and Pharmacokinetics (Perez 2007), as shown in (Fig. 1).

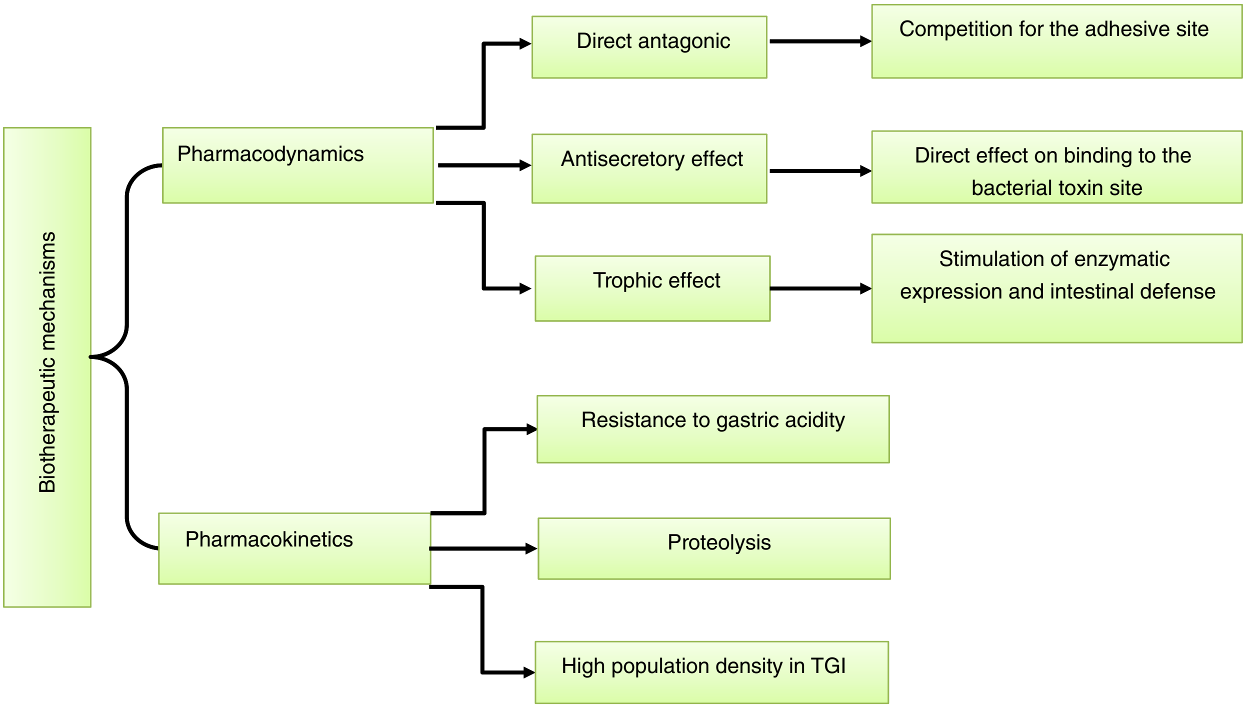

**Figure 1** Mechanisms of action biotherapeutics used by the yeast for the control of pathogens adapted from (Suarez and Guevara, 2018). [Colour figure can be viewed at wileyonlinelibrary.com]

## Mode of action of *Saccharomyces cerevisiae* as an additive

Care should be taken to select a probiotic strain, based on the requirements of the animal to be delivered, and must ensure the diversity of the organisms in the gut and provide the stability of their ecology, which can be affected by changes in diet and hard exercise (Amaral 2006). The potential mechanisms have been demonstrated for health benefits of yeasts as efficient probiotics in the animal production can be identified and are attributed to the ability to be involved in highlighting these criteria (Fig. 2): (i) adhesion capacity to intestinal cells (ii) improvement in feed digestibility and enhancement of beneficial micro-organisms in the gut, (iii) promotion of digestive enzyme activity, (iv) immunostimulant effect, (v) tolerance to high acidity (vi) resistance to bile salts (vii) improving gut morphological structure (Pourabedin *et al.* 2014) and (viii) direct antagonistic effect on enterobacteria and other yeasts and inhibition of the formation of destructive bacteria (Ogbuewu *et al.* 2018) (Fig. 2). Supplementation of yeast as a probiotics in livestock production uses the following pathways to exert their positive effects; immunomodulation, metabolic effects, changes in intestinal microbiota and removal of oxygen.

i Immunomodulation: Supplementation of *Saccharomyces cerevisiae* modulates and alters cytokines and activates immune system in livestock. This improves the immunity of the livestock and helps in prevention of diseases.
ii Metabolic effects: *S. cerevisiae* inhibits toxins, improve microflora, feed digestibility, supply nutrients and lower the cholesterol levels.
iii Changes the intestinal microbiota: *S. cerevisiae* inhibits pathogenic micro-organisms, improves digestibility and animal performance by altering the microbiome of the gastrointestinal tract.
iv Removal of oxygen: *S. cerevisiae* removes oxygen this increases the proliferation of viable anaerobic bacteria which helps to reduce $CH_4$ and lactate productions. It also improves the pH stability, increases microbial protein and changes volatile fatty acid, which results in the increase in feed intake, improves animal productivity and health (Fig. 2).

In monogastrics, inclusion *S. cerevisiae* into the diets of the animals was reported to stimulate immune response (Buts *et al.* 1986). Majtán *et al.* (2005) observed that dietary *S. cerevisiae* promotes the synthesis and release of pro-inflammatory cytokines from macrophages. *Saccharomyces cerevisiae* was also reported to affect the immune

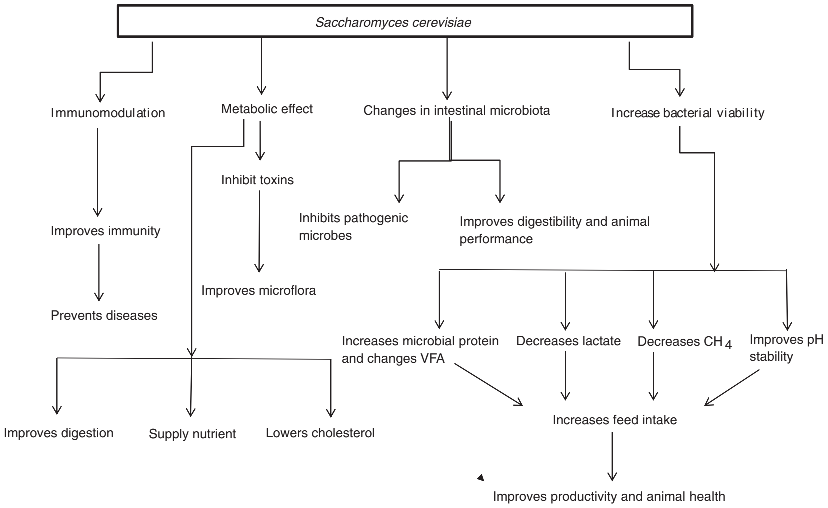

**Figure 2** Mechanism of action of *Saccharomyces cerevisiae* as feed additives in livestock production.

response by stimulating the IgA response to pathogenic micro-organisms (Qamar *et al.* 2001). In addition, the high amount of glucans present in the inner *S. cerevisiae* cell wall was linked to the stimulation of the immune system by a so far unknown mechanism (Song and Di Luzio 1979). Dietary *S. cerevisiae* was also shown to inhibit pathogen adhesion to the cell wall of the animal mucosa (Castagliuolo *et al.* 1999). This anti-adhesive effect was ascribed to the presence of mannan in the outer cell wall of *S. cerevisiae* (Ofek *et al.* 1977; Gedek, 1989). Furthermore, supplementation of the animal diet with *S. cerevisiae* was found to reduce the adverse action of toxins (Parlat *et al.* 2001). Secretion of a serine protease capable of hydrolysing toxin A from *Clostridium difficile* was observed with some *S. cerevisiae* strains (Castagliulo *et al.* 1996) and the high content of methionine enables *S. cerevisiae* to suppress the harmful effects of aflatoxins in animals (Stanley *et al.* 1993). Dietary *S. cerevisiae* was found to alter the gut pH of the animals (Makled, 1991). The yeast is capable of decreasing the pH of the intestine by secretion of organic acid such as lactic and acetic acid. This creates a more favourable environment for the inherent gut microbiota, thereby decreasing the probability of the colonization with pathogens (Servin and Coconnier 2003) (Fig. 2). The diet of chickens supplemented with *S. cerevisae* could be also used for egg-yolk coloration due to the production of *Phaffiarhodozyma* carotenoids by the yeast (Çelik *et al.* 2003).

## Application of probiotic yeast in monogastrics

The benefits of adding yeast as a probiotic to livestock diets were reviewed by (Vohra *et al.* 2016). Most studies have evaluated live yeast as a probiotics in ruminants, poultry, swine, rabbits, with fewer studies in horses. Generally, studies have shown that the addition of live yeast may improve fibre digestibility, inhibit the growth of pathogens, produce antibacterial compounds, stimulate the immune system and improve gut morphological structure. Furthermore, Broadway *et al.* (2015) reviewed the literature on live yeast and yeast cell wall supplements to food-producing animals and pointed that yeast cell wall components interact directly with immune cells, bind bacteria to prevent colonization of pathogens, may possess antioxidant and antitumour properties, promote growth performance and alter metabolism (Fig. 2).

## Probiotic yeast for poultry

Microbial communities inhabiting in the digestive tract of chickens are essential for gut homeostasis, host metabolism and affect many physiological functions within the bird and their health. They play an important role in digesting nutrients, inhibiting pathogens and interacting with each other as well as with the gut-associated immune system (Borda-Molina *et al.* 2018). In modern production of broilers, there are many factors that can cause stressors (food changes or imbalances, processing at the hatchery and high stocking density) during the post hatching period, (Pinchasov and Noy 1993) which ultimately affect pathogens colonization in the digestive tract result in weaken the immune system, posing a threat to bird health and food safety. *Salmonella*, *Campylobacter jejuni* and *Clostridium perfringens* appear to infect chickens and hens increasing the risk of contamination through the food chain, resulting in a harmful condition for poultry and humans (Holzapfel and Schillinger 2002; Van Immerseel *et al.* 2004; Humphrey *et al.* 2007). The gut microbiota is one of the main defence components in the digestive tract against enteric pathogens. The disturbance of the gut microbiota–host interaction plays a crucial role in the development of intestinal disorders. There have been significant changes in caecal microbiota in chickens infected with *C. perfringens* (Feng *et al.* 2010; Stanley *et al.* 2012; Skraban *et al.* 2013), *Eimeria* species (Perez *et al.* 2011; Stanley *et al.* 2014; Wu *et al.* 2014) and *Salmonella* Enteritidis (Nordentoft *et al.* 2011; Juricova *et al.* 2013; Videnska *et al.* 2013). Therefore, probiotics act as a biological alternative in controlling *Salmonella, Campylobacter, C. perfringens* or *Escherichia coli* (Holzapfel and Schillinger 2002; Patterson and Burkholder 2003; Siragusa and Ricke, 2012). In poultry, the benefits of yeast probiotic supplements are shown in the production performance of broilers and increased chickens resistance to enteric pathogens infection (*Salmonella, Campylobacter jejuni, C. perfringens* or *E. coli*) (Banjeree and Pradhan, 2006; Higgins *et al.* 2007; Higgins *et al.* 2008). Furthermore, the frequency of colonization of *salmonella* was significantly decreased by yeast probiotic supplementation, whereas unfinished birds had higher levels of colonization of *Salmonella* (Line *et al.* 1997).

Supplementation of birds diets with yeast has been shown to modulate the birds' intestinal microflora, to inhibit the colonization of the gastrointestinal tract by bacterial pathogens, to enhance the immune response of the birds, and to improve the sensory and quality characteristics of the animal-derived meat (Aksu *et al.* 2005; Zhang *et al.* 2005; Kabir, 2009; Afsharmanesh *et al.* 2010; Javadi *et al.* 2012) - (Table 1).

A decrease in serum cholesterol and serum albumin with increasing dietary yeast levels in broiler diets was observed and no detrimental effects on the birds performance occurred up to an inclusion level of 1% (w/w) (Ahmed *et al.* 2015) (Fig. 3). Furthermore, Oyedeji *et al.* (2008) reported that inclusion of 200, 250 and 300 mg of *S. cerevisiae* (Levucel SB) per kg diet resulted in an increase in total body weight gain, low feed conversion ratio and a reduction mortality rate in broilers after 4 weeks. Abdelrahman (2013) observed that inclusion of dry fat together with 3 kg of *S. cerevisiae* per ton of feed had no effect on total feed intake but increased total weight gain, reduced feed conversion ratio and low blood cholesterol levels were obtained in broilers compared to the control when using corn oil as the energy source.

Increase in antibody titre against influenza disease virus, daily body weight gain, final body weight, feed intake and serum high-density lipoprotein level, but low serum cholesterol level were observed in 3-day-old male broilers when supplementing their diet with 0·1, 0·2 and 0·3% (w/w) of live *S. cerevisiae* powder compared to the control (Gheisari and Kholeghipour, 2006).

It was also reported that *S. cerevisiae* could modulate or neutralize the effect of aflatoxin B1 (Parlat *et al.* 2001). A reduction in deleterious effects of aflatoxins on body weight gain, on feed intake and on feed conversion ratio were observed in Japanese quails with 1 g of yeast per kg of feed contaminated with 2·5 mg aflatoxin, similar results were obtained for broilers by (Pizzolitto *et al.* 2013). Drinking water supplemented with $5 \times 10^9$ cells per liter of *S. cerevisiae* CECT 1891 resulted in better animal performance when feeding a diet contaminated diet with 1·2 mg of aflatoxin B1 per kg of feed. In the study of (Koc *et al.* 2010) stated that supplementation of feed with 2 kg per ton *S. cerevisiae* NCYC R618 (4 billion CFU per g) resulted in an increase in weight gain and feed intake by 12·4 and 9·4%, respectively, in 21-d-old broilers. Furthermore, yeast supplements have improved the microbial population of the ileum substantially; a 93% increase in lactic acid bacteria and a 152% decrease in *E. coli* population were obtained. The more balanced gastrointestinal microbial population is associated with improving the health and performance of the broilers (Thongsong *et al.* 2008). Supplementation of feed with live yeast was also reported to lipopolysaccharide effect in birds. Lipopolysaccharides, cell wall components of gram-negative bacteria were shown to imitate bacterial infection and to induce inflammatory responses in broilers (Takahashi *et al.* 2008; Munyaka *et al.* 2013). Thus, nutrients are need for the inflammatory responses of the birds and therefore not available for growth (Roura *et al.* 1992). Wang *et al.* (2016a) observed that supplementation of the feed of lipopolysaccharide-induced broilers with 0·5 g $kg^{-1}$ of *S. cerevisiae* NCYC 47Hr+ ($10^{10}$ CFU per g) resulted in lower serum nitric oxide levels and lower serum myeloperoxidase activity in 21-day-old birds. In addition, a lower number of interleukin-1β receptors in the spleen on day 21 and 27 were obtained. A further study by (Wang *et al.* 2016b) with *E. coli* challenged broilers resulted in a 38% decrease in serum diamine oxidase activity and a 22·63% decrease in ileal myeloperoxidase activity when the feed was supplemented with 0·5 g $kg^{-1}$ *S. cerevisiae* ($10^{10}$ CFU per g). A lower diamine oxidase activity points to an improved intestinal integrity, since the enzyme is secreted by the intestinal villi into the blood stream upon leakage of the intestinal barrier (Luk *et al.* 1980). In addition, a 14·38% increase in the ratio of ileal villus height to crypt depth was observed as well as a lower expression of inflammation-related genes in the intestine such as interleukin-1β, interleukin-8, NF-κB and Toll-like receptor 4. The reduced expression of intestinal inflammation-related genes suggests that yeast supplementation alleviates the

**Table 1** Impact of supplementation of poultry diets with live *Saccharomyces cerevisiae*

| Live *S. cerevisiae* doses | Poultry species | Impacts | References |
|---|---|---|---|
| 0·1, 0·2 and 0·3% in powdered form | Broiler | higher final body weight, higher daily body weight gain, higher feed intake, lower serum cholesterol levels, higher serum high-density lipoprotein concentrations, lower heterophil to lymphocyte ratio | Gheisari and Kholeghipour (2006) |
| 1 g/kg of feed | Japanese quails | Lower deleterious effects of aflatoxins | Parlat *et al.* (2001) |
| 2 kg/ton of feed | Broiler | higher daily weight gain, higher feed intake, higher numbers of ileal LAB, lower counts of ileal *E. coli* | Koc *et al.* (2010) |
| 1, 2 and 3 g/kg of feed | Broiler | No effect on feed intake, lower final body weight and lower daily weight gain, higher feed conversion | Ahmed *et al.* (2015) |
| 0·5 g/kg of feed | Broiler | Lower serum concentration of nitric oxide, lower serum myeloperoxidase activity, lower number of interleukin-1β receptors in the spleen | Wang *et al.* (2016a) |
| 0·5 g/kg of feed | Broiler | Lower serum diamine oxidase activity, lower ileal myeloperoxidase activity, higher ratio of villus height to crypt depth in the ileum, down-regulation of inflammation-related genes (IL-1β, interleukin-8, NF-κB and Toll-like receptor 4) | Wang *et al.* (2016b) |
| 200, 250 and 300 mg/kg of feed | Broiler | Higher daily weight gain, lower feed conversion ratio, lower mortality | Oyedeji *et al.* (2008) |
| 3 kg/ton of feed | Broiler | Higher total weight gain, lower blood cholesterol concentrations, lower feed conversion ratio | Abdelrahman (2013) |
| $5 \times 10^9$ cells/l drinking water | | Higher feed intake, higher body weight gain, lower feed conversion ratio, higher total serum protein levels, higher serum albumin levels, higher serum globulin levels | Pizzolitto *et al.* (2013) |

effect of toxins in the body, improves gut structure resulting in a better absorption of nutrients and improves crypt depth.

A probiotic *S. cerevisiae* enriched with Se could increase egg weight, quality of eggshell and improves egg quality (low cholesterol level in egg yolk) (Invernizzi *et al.* 2013). On the other hand, (Zhang *et al.* 2005) investigated the effect of *S. cerevisiae* cell on the meat quality in male broilers and stated that the tenderness of meat improved by the whole yeast or *S. cerevisiae* extract. Yeast cell wall products have been shown to affect the richness of species and bacterial intestinal diversity (Roto *et al.* 2015). However, there is limited information on the effect of yeast nucleotides on intestinal microbiota of chickens. Recently, (Wu *et al.* 2018) found that feeding dietary yeast nucleotides into pathogen-free chickens increased the diversity of intestinal microbiota and abundance of *Lactobacillus* (Wu *et al.* 2018). *Eimeria* impaired gut function, shifted gut microbiome and performance; yeast nucleotides improved performance independently, attenuated *Eimeria* damage on indices of gut function and modulated caecal microbiome. In the study of (Ahiwe *et al.* 2019) reported that whole yeast and its derivatives can improve meat yield of broilers and through its effect on white blood cell, lymphocyte and monocyte counts, may be linked to an amelioration of stress induced by *Salmonella* lipopolysaccharide in broilers. They also noted that autolysed yeast, yeast cell wall and its enzymatically hydrolysed components when supplemented at $2\ \text{g kg}^{-1}$ diet may act as an appropriate alternative to antibiotics in broilers production. The enzymatic hydrolysis of yeasts produces cell-free culture supernatant that show activity against Gram-negative bacteria. Previous studies have shown that refined functional carbohydrates can agglutinate as well as inhibit adherence of several species of *Salmonella* to the intestinal epithelium inhibiting them from colonizing the digestive tract (Walker *et al.* 2017, 2018). Singh *et al.* (2019) also showed that refined functional carbohydrates have effects on cytokine gene expression, including the genes encoding for pro-inflammatory cytokines and T helper (T1and T2), which enhances the immune function of sexually mature hens. Furthermore, increased apoptotic functions in the presence of prebiotic reduce the numbers of colonized bacteria in chicks' caeca. The adhesion of pathogens onto the surface of yeast-derived refined functional carbohydrates rather than intestinal receptors can be responsible for reduced activation of pro-inflammatory signalling pathways and thus the translocation of bacteria. Prebiotics such as refined functional carbohydrates could benefit during sexual maturity in hen by enhancing the immune response while also providing protection from infection.

## Probiotic yeast for rabbits

Rabbits are both monogastric animals, but also herbivores, with particular digestive and physiological characteristics. Intensive breeding of rabbits could cause physiological stress with 24% of mortality rate and

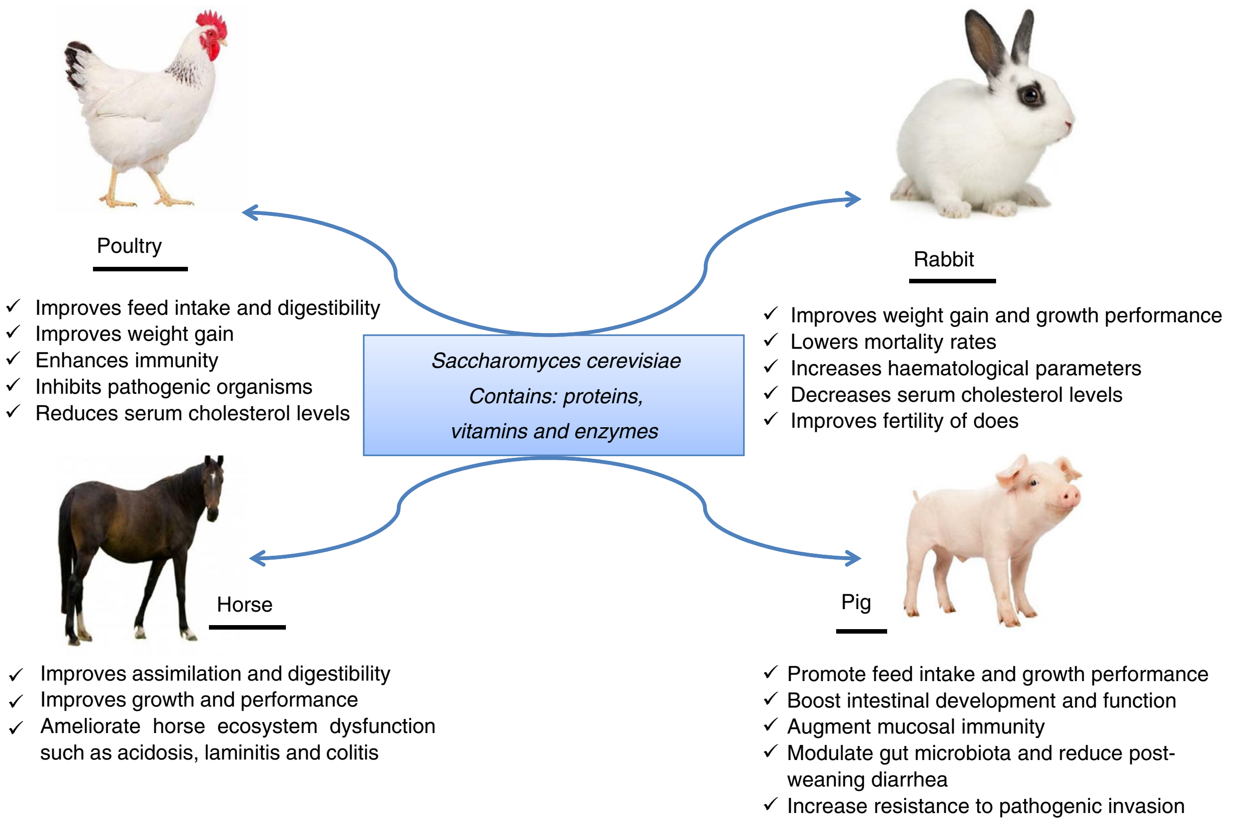

**Figure 3** Positive effects of *Saccharomyces cerevisiae* supplementation on nutrition of poultry, rabbits, pigs and horses. [Colour figure can be viewed at wileyonlinelibrary.com]

morbidity. About 75% of deaths were due to incidence of enteric disease resulting in a lower efficiency of production and reproduction of rabbit does (Belhassen *et al.* 2016). The high incidence of gastrointestinal diseases in rabbits is often related to abnormalities in the composition of bacteria (Combes *et al.* 2011; Bauerl *et al.* 2014). Any imbalance of microflora can lead to pH alteration, dysbiosis and pathogens proliferation, with adverse effects on animal health (Michelland *et al.* 2010). The establishment of a healthy, stable and diverse microflora in gastrointestinal tract is of great significance for rabbits to resist intestinal diseases.

Micro-organisms in rabbit caecum can ferment foregut-undigested cellulose, other nutrients, volatile fatty acids, ammonia nitrogen, vitamins and other nutrients. The volatile fatty acids are rapidly absorbed in the intestine and can then provide 40% energy to maintain adult rabbits, in which butyric acid is a direct source of energy to hindgut, whereas acetic acid creates cholesterol and fat metabolism in the liver in metabolism (Gidenne, 1997). In addition, microbes in the caecum can also use ammonia nitrogen to synthesize bacterial proteins, and these proteins are used twice by rabbits in the form of soft faeces (Kohl *et al.* 2011). Normal intestinal flora is beneficial to host's digestion and metabolism of nutrients, thereby promoting the rabbits' growth and development. Feed provides the nutrients and energy for intestinal ecosystem of animals, which is a major factor affecting the microbial balance of the adult animal. The bacterial structure affects feed degradation and therefore affects the physicochemical parameters of intestinal pH, the concentration of metabolite and redox potential. On the contrary, the dietary composition also affects the balance of intestinal flora (Zhu *et al.* 2015). The physiology of the digestive system of rabbits is largely depends on its caecal microbial population, characterized by the presence of an abundant microflora. According to (Ezema and Eze 2015) who reported that rabbits fed diets supplemented with *S. cerevisiae* improved average weight gain and daily feed intake compared to those in the control group. However, as observed in the rabbits study by (Emmanuel *et al.* 2019). *Saccharomyces cerevisiae* was reported to primarily act on the microbiota in the caecum and proximal colon of rabbits (Carabaño *et al.* 2006; Fortun-Lamothe and Boullier 2007). The effects of supplementation with live *S. cerevisiae* in the rabbit rations are summarized in

**Table 2** Impact of supplementation of rabbit diets with live *Saccharomyces cerevisiae*

| live *S. cerevisiae* doses | Impacts | References |
|---|---|---|
| 1 g/kg of feed | Lower mortality of kits in the first reproductive cycle, no effect on viability of kits in the first reproductive cycle, but higher viability in the second reproductive cycle, improved fertility of does in the second reeproductive cycle | Belhassen *et al.* (2016) |
| 1 g/kg of feed | No effect on growth rate, short chain fatty acid and caecal microbiota | Belhassen *et al.* (2016) |
| 300 and 600 mg/kg of feed | Lower apparent neutral detergent fibre and acid detergent fibre digestibility, higher caeca yeast and mould population, higher slaughter weight, no negative effects on meat quality parameters | Rotolo *et al.* (2014) |
| 0·1% (w/w) | Higher final body weight, higher daily body weight gain, higher nitrogen utilization, improve feed conversion efficiency | El-Badawi *et al.* (2017) |
| 10 g/kg of feed | Reduced mortality, higher redox potential in the caeca content | Kimsé *et al.* (2008) |
| 2 g/kg of feed | Increased haematocrit and haemoglobin concentration and decreased serum cholesterol | Seyidoglu *et al.* (2013) |
| $2 \times 10^8$ CFU/animal/day | Negatively affect digestibility of dry matter, organic matter and neutral detergent fibre, and also increased mortality rate | Campos-Morales *et al.* (2015) |
| Equal dose of $5 \times 10^8$ cells/animal/day lactic acid bacteria and *S. cerevisiae* | No effect on feed intake, body weight gain, feed conversion efficiency and digestibility of dry matter. Crude protein digestibility improved | Kamra *et al.* (1996) |
| 3·0 g/kg of feed | Improved growth performance and haematopoiesis. Reduced serum cholesterol level | Onifade *et al.* (1999) |
| $5 \times 10^8$ cells/animal/day | No effect on body weight and nutrient digestibility | Chaudhary *et al.* (1995) |
| 1 and 10 g/kg feed | No effect on total tract digestibility of nutrients and growth rate | Kimsé *et al.* (2012) |

(Table 2). Inclusion of *S. cerevisiae* Sc47 ($10^8$ CFU per g) in the rabbits diet with a dose of 0·1% (w/w) resulted in an increase in final body weight by 22% and an increase in body weight by 36·9%, whereas feed conversion was found to be 24% less (El-Badawi *et al.* 2017). Furthermore, nitrogen intake and nitrogen digestibility were increased by 16·68 and 10·98%, respectively, in the presence of yeast. Rotolo *et al.* (2014) observed a lower apparent neutral and acid detergent fibre digestibility as well as a higher caeca yeast and mould population when supplementing the rabbit diet with live yeast ($10^{10}$ CFU per g) at 0, 300 and 600 mg kg$^{-1}$. Yeast supplementation had also a tendency to increase slaughter weight (1–6%). Furthermore, no negative effect on meat quality parameters and chemical composition were obtained.

No effect was observed on mortality of does and the length of gestation in both reproductive cycles. However, improvement in fertility of does (95·8 *vs* 66·7% in the control) was observed when rabbits diet supplemented with live *S. cerevisiae* of 1 g per dose per kg feed (Belhassen *et al.* 2016) in the second reproductive cycle. In addition, yeast supplementation resulted in a 7·8% increase in viability rate of the kits in the second reproductive cycle, and also showed a decrease in mortality rate of kits in the presence of *S. cerevisiae* in the first 21 days of the first reproductive cycle. Emmanuel *et al.* (2019) showed that dietary inclusion of *S. cerevisiae* at 0·12 g kg$^{-1}$ of feed, improved epididymal sperm characteristics and testicular morphometrism of rabbit bucks.

An increase in the concentrations of haematocrit and haemoglobin, whereas a reduction in cholesterol was observed in rabbits fed *S. cerevisiae* supplemented diet with 2 g kg$^{-1}$ feed (Seyidoglu *et al.* 2013) (Fig. 3). However, (Campos-Morales *et al.* 2015) reported that inclusion of *S. cerevisiae* with $2 \times 10^8$ CFU per day per animal negatively affects digestibility of dry matter, organic matter and neutral detergent fibre, as well as increased mortality rate of rabbits.

## Probiotic yeast for pigs

The level of increased use of probiotics started since a ban on the use of antibiotics as promoters of antimicrobial growth in pig feeds in 2006, efforts have been directed towards natural alternatives to feed additives with growth promoting and/or immunomodulatory properties has augmented dramatically. The most of the researches showed a health beneficial effect of a probiotic yeast applied in piglets; yeast or yeast product supplement may promote average daily feed consumption and pig growth performance, augment mucosal immunity by increasing IgM and IgA activities against pathogens, boost intestinal development and function, adsorb mycotoxins, modulate gut microbiota and reduce postweaning diarrhoea (Kogan and Kocher 2007; Shen *et al.* 2009; Sauer *et al.* 2011; Jiang *et al.* 2015). In gestating sows, *S. cerevisiae* supplementation to sows had no beneficial effects on body weight and feed intake of gestating sow, but the total number of piglets born and born alive was greater than in un supplemented sows (Di Giancamillo *et al.* 2007; Agazzi *et al.* 2015). Shen *et al.* (2009) demonstrated that there was no difference between pigs fed antibiotic growth promoters and pigs fed diets supplemented with yeast on growth performance, nutrient digestibility and intestinal morphology, indicating that yeast products may be an effective substitute for antibiotic growth promoters. It also has been shown that the immune-potentiating costs of yeast-based supplements had no adverse impact on pig growth performance (Molist *et al.* 2014). However, it has also been reported that yeast cultures have no effect on pig growth performance or apparent total tract digestibility of dry matter, crude protein, neutral detergent fibre and acid detergent fibre (Kornegay *et al.* 1995). The effects of adding yeast products to diets for pigs are not fully understood, but it is believed that yeast products may have a number of positive effects if added to pig diets and there is some evidence that yeast products can be used as partial or fully alternatives to antibiotic growth promoters. The benefits of intestinal health and immunomodulatory effects of yeast cells are important and represent the most likely benefits of supplementing pig diets with yeast (Liu *et al.* 2018). Live yeast, finely ground live yeast and yeast fermentation products may lead to increased villus heights and villus-to-crypt ratios (Bontempo *et al.* 2006; Shen *et al.* 2009; Jiang *et al.* 2015). Furthermore, significant longer villi and deeper crypts were found in the ileum of piglets receiving diets supplemented with *S. cerevisiae* spp. (Domeneghini *et al.* 2004; Di Giancamillo *et al.* 2008). In addition, live yeast supplement may increase gut cell proliferation and increase glycoconjugates concentration in the mucin of supplemented pigs, thereby increasing their resistance to pathogenic invasion (Bontempo *et al.* 2006). Many beneficial effects of yeast and yeast products are suggested to stimulate the immune-modulation because the b-D-glucans in the walls of yeast cells enhances the function of macrophages and neutrophils by binding to their receptors causing cascades cytokines and increasing the production of antibodies (Kogan and Kocher 2007; Kim *et al.* 2017). In the study of (Kogan and Kocher 2007; Shen *et al.* 2009) who demonstrated the mechanism by which yeast cells can provide these benefits is the result of the composition of the yeast cells. The specific sugar types that form large parts of the cell walls of yeast, notably a-D-mannans and b-D-glucans, are thought to be responsible for the effects of yeasts cells. In addition, the requirement for yeast extracts containing nucleotides may be increased under certain conditions, such as high stress, during disease, or rapid growth (Waititu *et al.* 2016). The weaning itself causes villus atrophy and reduces replacement of enterocytes both of which inhibit the absorption of nutrients, a part of easing the transition around weaning of pigs involves preparing the intestine to change in diet form that caused a possible deficiency of nucleotides and in that case, yeast cells may be potentially beneficial (Jiang *et al.* 2015).

Indeed, pigs that were challenged with *E. coli K88* and fed diets containing a yeast fermentation product have higher concentrations of serum tumour necrosis factor-alpha, less diarrhoea, higher appetite and decreased adherence of *E. coli* to the intestinal mucosa than pigs fed an un-supplemented control (Kiarie *et al.* 2011, 2012). Likewise, pigs fed on diets supplemented with live yeast and exposed to enterotoxigenic *E. coli* were observed to have reduced disease-related stress, reduced diarrhoea scores, reduced duration of diarrhoea, and reduced shedding of *E. coli* (Trckova *et al.* 2014). Jiang *et al.* (2015) reported that feeding of live yeast and finely ground live yeast increases serum concentrations of IgA, IL-2 and IL-6. The a-D-mannans in the yeast have potential antioxidant effects (Kogan and Kocher 2007). Particularly, a-D-mannans are thought to bind to mannose-specific receptors that are present on many bacteria such as *E. coli* and *Salmonella* spp., which inhibit adhesion of these pathogens to the mannose-rich glycoproteins lining the intestinal lumen (Kogan and Kocher 2007).

## Probiotic yeast for horses

One of the major concerns in the production of horses is the disruptions of the composition and/or activity of hindgut microbiota that lead to altered digestive health and onset of colic (Sadet-Bourgeteau and Julliand 2012). The digestive system of the horse has a faster passage rate, leaving the microflora of the large intestine with less time to carry out fermentation, this leads to accumulation of lactate and reduction in pH leading to subclinical acidosis in the caecum-colon, consequently increasing the horses' susceptibility to colic pain or laminitis (Jouany *et al.* 2008; de Rezende *et al.* 2012). The effects of a probiotic yeast to the digestive compartment mainly caecum-colon. Increase fibre digestibility in the horse's colon and modulated the balance of hindgut bacterial communities through live yeast supplement, thus reduced the risk of lactic acidosis (Medina *et al.* 2002; Jouany *et al.* 2008). Yeast supplements in a diet for horses improve digestion and assimilation of the diet and encourage horse growth performance (Julliand *et al.* 2006; de Rezende *et al.* 2012) (Fig. 3). Live *S. cerevisiae* (Sc 47 Biosaf®) in a dose of 20 g resulted in a 2·1% greater apparent digestibility of digestible energy and a 1·4% higher hemicellulose digestion in horses (de Rezende *et al.* 2012). In addition, a better digestion of nutrients was reported by (Morgan *et al.* 2007), as well as a higher intestinal microbial

**Table 3** Impact of supplementation of horse diets with live *Saccharomyces cerevisiae*

| Live *S. cerevisiae* doses | Impacts | References |
|---|---|---|
| 10, 20 and 30 g/kg of diet | No positive effect feed digestibility | Gobesso *et al.* (2012) |
| 1 and 3 g/kg of diet | No effect on dry matter, crude protein, crude fat, neutral detergent fibre and acid detergent fibre digestibility, no effect on short chain fatty acid production | Mackenthun *et al.* (2013) |
| 2 g/head/day | Higher dry matter, organic matter, neutral detergent fibreand acid detergent fibre digestibility | Agazzi *et al.* (2009) |
| 20 g/head/day | Higher apparent digestibility of digestible energy, hemicellulose digestion and speed of horses | de Rezende *et al.* (2012) |
| 11 g/head/day | Higher dry matter, organic matter, neutral detergent fibre and acid detergent fibre intake, higher dry matter, organic matter, neutral detergent fibre and acid detergent fibre digestibility | Salem *et al.* (2016) |
| 5 g/head/day | No effect on average daily gain, lowers dry matter intake and improves feed efficiency of forage | Moura (2011) |
| 20 g/head/day | Weight gain, increase in milk and faster growth rate | Glade (1991) |
| 10 g/kg of diet | No effect on microbial counts in the caecum and colon, modified pH, concentrations of lactic acid and ammonia | Medina *et al.* (2002) |
| 56 g/head/day | Increase dry matter intake and improves digestibility | Morgan *et al.* (2007) |
| 4 mg/g of feed dry matter | Improves fermentation of feed and fibre digestion | Elghandour *et al.* (2016) |
| 1 ounce twice daily of feeds | No effect on weight but increases forage digestibility and gut health | Nerlich *et al.* (2018) |
| $10 \times 10^{9}$ and $10 \times 10^{10}$ CFU/ animal/day | No effect on gastric pH but reduced lactate-utilizing bacteria | Julliand *et al.* (2018) |
| 10 g/head/day | Improves fibre digestibility and growth | EFSA (2009) |
| 10, 20 and 30 g ($5 \times 10^{8}$ CFU per g)/animal/day | No changes in the microbiota and no improvement on cellulolytic population and fibre digestion | Taran *et al.* (2015) |
| 2 g/head/day | No effect on digestibility, feacal pH and blood parameters | Palagi *et al.* (2018) |
| 10 g/head/day | Higher dry matter intake, neutral detergent fibre intake and hemicellulose intake | Jouany *et al.* (2008) |

population and a more constant caecal pH (Medina *et al.* 2002). Salem *et al.* (2016) observed a 42·75% higher dry matter intake, a 43·73% higher organic matter intake, a 50·31% higher neutral detergent fibre intake and a 62·75% higher acid detergent fibre intake when mare obtained 11 g of Biocell F53 yeast culture per day as a feed supplement. The corresponding increase in dry matter, organic matter, neutral detergent fibre and acid detergent fibre digestibility was found to be 15·52, 14·74 27·73 and 50·72% respectively. Feed supplement with 10 g of yeast per day per horse resulted in a 2·5% higher dry matter intake, a 3·75% higher neutral detergent fibre intake and a 3·33% higher hemicellulose intake using a high fibre diet, however, no effect on the intakes using a high starch diet were observed (Jouany *et al.* 2008). Gobesso *et al.* (2012) observed that supplementing forage diet with 0, 10, 20 and 30 g $\text{kg}^{-1}$ of live yeast ($5 \times 10^{8}$ CFU per g) did not improve feed digestibility, however, lower digestibility of organic matter, crude protein, acid detergent and neutral detergent fibre were observed with 10 and 20 g $\text{kg}^{-1}$ doses, whereas 30 g $\text{kg}^{-1}$ dose was similar to the control. Mackenthun *et al.* (2013) reported that inclusion of 1 and 3 g of yeast ($2 \times 10^{10}$ CFU per g) into the diet of horses had no effect on dry matter, crude protein, crude fat, neutral detergent fibre and acid detergent fibre digestibility. Additionally, no effect on the concentration of short chain fatty acids in the faecal water on day 5 of digestibility trial was found. Agazzi *et al.* (2009) noted that feeding the horses with a diet containing a 70 : 30 forage to concentrate supplemented with 2 g of yeast per day per head, recorded a the highest dry matter, organic matter, neutral detergent fibre and acid detergent fibre digestibility (7·25, 7·37, 18·47 and 30·46%) respectively. however, no effect on crude protein and ether extract digestibility was observed. This implies that yeast exhibited its effect in the caecum to aid feed/nutrient digestibility. Julliand *et al.* (2018) reported that inclusion of ($10 \times 10^{9}$ and $10 \times 10^{10}$ CFU per animal per day of *S. cerevisiae*) in horses' diet had no effect on gastric pH but reduces the lactic acid utilizing bacteria. Palagi *et al.* (2018) reported that supplementation of 2 g per head per day of *S. cerevisiae* in horses' diet did not produce any effect on digestibility, feacal pH and blood parameters. However, (Efsa, 2009) reported that the inclusion of 10 g of *S. cerevisiae*/head/day improved fibre digestibility and growth. Elghandour *et al.* (2016) opined that supplementation of 4 mg of *S. cerevisiae* per g of feed dry matter improved fermentation of feed and fibre digestion. The administration of *S. Cerevisiae* to mature horses fed high-fibre diet increased apparent nutrient digestion rate, the apparent digestion rates of dry matter and organic matter improved significantly in treated horses compared to un supplemented control, but the most relevant difference between the experimental groups had a positive effect on live yeast over the fibrous fractions such as neutral detergent fibre and acidic detergent fibre (Agazzi *et al.* 2011) (Table 3).

## *Saccharomyces cerevisiae* and greenhouse gases emissions in non and pseudo-ruminant

Greenhouse gases (GHGs) emitted during livestock production cause global warming effect and also lead to loss of metabolic energy (Velazqnez *et al.* 2019). Indeed, up to 20% of the global anthropogenic CH4 is emitted by ruminants (Bhatta *et al.* 2007). Ruminants and monogastrics emit $CH_4$, but the former emits much more $CH_4$ than the latter (Franz *et al.* 2010, 2011; Cabezas Garcia, 2017). It has been speculated that this difference in $CH_4$ emission may be due attributable primarily to differences in the microbiota of the rumen and the hindgut of nonruminant (Yang *et al.* 2016). However, the microbiological peculiarity for the different $CH_4$ emissions by these two groups of ruminants and monogastric is largely unknown. The identification of these responsible microbes and the relationship to $CH_4$ emission and the fermentation properties of the rumen and the caecum will help to understand the factors affecting the production of $CH_4$ in rumen and develop dietary strategies to effectively reduce $CH_4$ emission from ruminants (Mi *et al.* 2018). Supplementation of *S. cerevisiae* in livestock diets to reduce GHGs such as $CH_4$, $CO_2$ and $NO_2$ is a recent area of interest in the production of livestock (Fig. 2). The use of *S. cerevisiae* to decrease $CH_4$ in livestock production has be investigated and positive effect established in ruminants. The mechanism is associated with the ability of supplemented *S. cerevisiae* to induce acetogen growth and completes with the methanogens for $H_2$ (Hristov *et al.* 2013). However, the effect of *in vitro* or *in vivo* studies on the supplemented *S. cerevisiae* to reduce $CH_4$ is low and inconsistent (Beauchemin *et al.* 2008). To the best of our knowledge there is no published work on the use of *S. cerevisiae* to reduce GHGs in poultry, rabbit and horse experiment both *in vitro* and *in vivo*. Therefore, more research is required to evaluate the impacts of supplementation of *S. cerevisiae* to reduce GHGs emitted from these animals.

In conclusion, supplementation of *S. cerevisiae* in the diets of nonruminants has the potentials to improve feed intake, enhance digestibility, reduce pathogenic microbes, improves animal health and performance. *Saccharomyces cerevisiae* plays these roles in nonruminant animal production through various mechanisms. However, the common functions of *S. cerevisiae* in monogastric are linked to an improvement of immunity, the stimulation of beneficial microbes in the gastrointestinal tract and an improvement of fibre digestibility. Gut villi stimulation especially in the jejunum is very likely the mechanism by which *S. cerevisiae* improve growth rate.

However, there is no published information on the effect of *S. cerevisiae* supplementation on the greenhouse gases (GHGs) in nonruminant animals. Therefore, there is need to carryout *in vitro and in vivo* studies on the effect of *S. cerevisiae* on GHGs from nonruminants to gain insights on its effect.

## Conflict of Interest

The authors declare no conflict of interest.

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