Advances in research on solid-state fermented feed and its utilization: The pioneer of private customization for intestinal microorganisms

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ABSTRACT
With sustainable development of biotechnology, increasing attention has been placed on utilization of solid-state fermented feed (SFF). Solid-state fermented feed has been a candidate strategy to alleviate the contradiction between supply and demand of feed resources, ensure food hygiene safety, promoting energy conservation, and emission reduction. In production of SFF, a variety of organic acids, enzymes, vitamins, peptides, and other unknown growth factors are produced, which could affect performance of animals. Solid-state fermented feed produced by different fermentation techniques has great instability on different physiological stages of different animals, which hinders the application and standardized production of SFF. Herein, we summarize the current advances in the role of the characteristics of SFF prepared by different manufacturing technique and its research progress in animal experiments on growth performance, gastrointestinal ecology, and immune system, so as to provide references for further acquiring a relatively perfect set of SFF production and evaluation systems.

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1. Introduction

Fermentation has been used for food processing (Nout, 1994; Soccol et al., 2017; Marco et al., 2017; Şanlier N et al., 2017; De et al., 2018) and preservation (Winsen et al., 2001; Wang et al., 2014a,b; Soccol et al., 2017; Yang et al., 2018) for thousands of years around the world. Moreover, this technique recently gained increasing interest as a tool for adjusting nutritive value of feed and output of livestock products (Chen et al., 2013; Pedersen et al., 2010). Additionally, solid-state fermented feed (SFF) has been defined as a raw feed ingredient or commercial feed in which macromolecular substances and anti-nutritional factors are converted into more efficient and non-toxic nutrients by metabolic activities of microorganisms. Solid-state fermented feed refers to the fermentation of feed substrate by using natural or artificially added microorganisms under artificial control conditions (water content is generally controlled below 70%), so as to change the nutritional characteristics, digestibility, palatability and safety of feed. Meanwhile, SFF is potential to be a candidate strategy for replacing antibiotics in livestock feed (Wang et al., 2011a,b; Ying et al., 2010). The nutritional properties of fermented feed depend on the fermentation starter (bacteria culture used to start fermentation), substrates, and fermentation conditions (temperature and incubation time) used (Awati et al., 2006; Niba et al., 2009; Missotten et al., 2016). Although studies have confirmed that fermentation could be an approach to improve nutritional value of ingredients before being offered to animals (Shimelis and Rakshit (2010); Shi et al., 2017), the quality of feed produced by different manufacturing techniques and their effects on animal performance have not been consistent (Feng et al., 2007a,b; Wang et al., 2014a,b). This inconsistency has encouraged industry professionals to explore SFF.

In recent years, researchers have carried out a large number of experiments in vivo and in vitro to explore applications of SFF (Hu...
et al., 2008; Yu et al., 2010; Wang et al., 2010; Shi et al., 2017). However, a perfect set of SFF production and evaluation systems is unavailable currently because of the instability of SFF. Our review herein summarizes nutritional characteristics of SFF produced by different manufacturing techniques and their effects on growth performance, gastrointestinal ecology, and immune system, hoping to guide researchers to make objective choices in the application of SFF.

2. Manufacturing technique

Interactions among starter cultures, incubation parameters, and substrate characteristics affect end-products of SFF (Fig. 1, Niba et al., 2009). Moreover, the effect of SFF on animals produced by different technologies has been inconsistent (Feng et al., 2007a,b; Kim et al., 2010; Zhang et al., 2013; Liu et al., 2014; Jakobsen et al., 2015a,b). Therefore, to ensure correct management of SFF production to capture its potential, a thorough knowledge of the processes taking place during fermentation is required.

2.1. Starter cultures and substrate characteristics

The most important factors for successful manufacturing of SFF are the choices of substrates and starter culture. Over the past few years, researchers have developed many substrates for SFF such as swill (Zhang et al., 2012; Zeng et al., 2020), seaweed (Zhao et al., 2014), vinasse (Shen et al., 2018), soybean meal (Zhang et al., 2018a,b) and complete feed (Liang et al., 2012; Li et al., 2019), so as to meet manufacturers’ requirements for diverse end-products. Certainly, when the same substrate was fermented by different starter cultures, the end-products different (Table 1).

2.1.1. Starter cultures

Starter cultures that are widely used for SFF are Lactobacillus, Yeast, bacillus, and Moulds. Amylase, protease, lipase, cellulase, pectinase and glucanase, which degrade macromolecular substances into small compounds that are more conducive to animal absorption, are produced during the production of SFF. Effective utilization of fiber by microorganisms is a primary advantage of SFF. Lactic acid, short-chain fatty acid (SCFA) and other metabolites improve palatability of feed, and play an important role in promoting intestinal health. A previous study showed that mixed culture of Cellulose monomomas and Bacillus foecalis alkaligenes reduced cellulose concentration in the substrate (Dawson, 1987). Liao et al. (2009) found that when Aspergillus niger, Trichoderma and yeast were inoculated into corn straw feed at a ratio of 1:2:1 for 6 d (inoculation amount was 12%, incubation temperature was 31 C), crude protein (CP) content in the medium increased 10 times, and content of crude fiber (CF) decreased from 36.2% to 18.47%.

2.1.2. Degradation of non-starch polysaccharides

Recent gradual development and deepening of our understanding of intestinal flora, dietary fiber as “food” of flora has attracted great attention. Microorganisms can decompose dietary fiber during production of SFF, and produce a variety of monosaccharides which are more easily used by intestinal flora. In addition, the monosaccharides can nourish growth of microorganisms, acting as prebiotics and probiotics. Degradation of different types of fiber is closely related to the difference of fiber components. According to characteristics of fiber, we could select microbial strains with high efficiency to degrade a certain component to establish a synergistic degradation system (Table 2).

2.1.3. Substrate characteristics

Many scholars have reported that soybean meal can be fermented by Aspergillus oryzae, Yeast, and Lactobacillus in solid state, which could increase concentration of crude protein (Chen et al., 2011; Rombenso et al., 2013; Hassaan et al., 2015). This concentration increase occurs because microorganisms consume the organic materials, resulting in the “concentration effect” of protein. Furthermore, the effective utilization of ammonium salts and the increase of bacterial protein also contribute to the increase of crude protein. Another study reported that phytic acid, an anti-nutrient factor in soybean meal, can be degraded nearly completely by fermentation with Aspergillus usamii (Hirabayashi et al., 1998). Similarly, fermentation of soybean meal using Bacillus subtilis as the starter culture extensively hydrolyzes protein to amino acids and degrades inhibitors of trypsin and chymotrypsin (Feng et al., 2007a,b). Organisms used in SFF can degrade potentially hazardous raw materials and transform them into products that can improve storage qualities of the ingredient and reduced risk of causing illness (Adams et al., 2002; Guanghui et al., 2017; Yang et al., 2018; Godoy et al., 2018; Dong et al., 2018).

Fig. 1. Interactions in fermented feed among micro-organisms present, fermentation parameters, and substrate quantity and quality that influence final end products.
Table 1
The effect of different starter cultures on the end fermentation products.

| Substrate                | Microorganism            | Product       | Productivity          | References               |
|--------------------------|--------------------------|---------------|-----------------------|--------------------------|
| Wheat straw              | Bacillus sp. BBXS-2      | Amylase       | 6,900 U/g, 5 d        | Qureshi et al. (2016)     |
|                          | Aspergillus lentulus     | Xylanase      | 158.4 U/g, 4 d        | Kaushik et al. (2014)     |
| Wheat bran               | Aspergillus oryzae       | Amylase       | 1,491 U/g, 3 d        | Chen et al. (2014)        |
| Rhizopus oryzae SN5      | Cellulase                | 437 U/g, 5 d  | Pandey et al. (2016)   |
| Aspergillus niger NS-2   | Cellulase                | 395 U/g (CMCase), 28 U/g (FPase), 46 U/g | Bansal et al. (2012)     |
| Wheat straw              | Pleurotus ostreatus      | Laccase       | 32,450 U/g, 7 d       | El-Batal et al. (2015)    |
|                          | Coriolus sp.             | Laccase       | 2,661 U/g, 10 d       | Mathur et al. (2013)      |
| Aspergillus niger LBA 02 | Protease                | 262.7 U/g, 2 d| Castro et al. (2015)  |
| Trichoderma viride-IR5   | Xylanase                 | 72.4 U/g, 168 h| Irfan et al. (2014)   |
| Aspergillus sp. PKD-9    | Xylanase                 | 98,000 U/g, 120 h| Panwar et al. (2014)  |
| Aspergillus oryzae (P6B2)| Xylanase                 | 2,830.7 U/g, 1 d | Pirola et al. (2013)   |
| Mucor petrinuslaris      | β-Carotene               | 8.5 μg/g of β-carotene and 12.1 mg of γ-carotene, 180 h | Certik et al. (2013)     |
| Mucor dimorphosphorus    | and γ-linolenic acid     |               |                       |                          |
| Mucor hiemalis           |                         |               |                       |                          |
| Apple pomace             | Macrophomina             | Amylase       | 3,309 U/g, 120 h      | Kaur et al. (2012)       |
| Aspergillus niger NRRL-567| Cellulase               | 134 U/g (FPase), 60 U/g (β-glucosidase), 172 U/g (CMCase), 2 d | Dhillon et al. (2012a,b) |
| Aspergillus niger NRRL-567| Citric acid             | 294.2 g/kg of dried apple pomace, 5 d | Dhillon et al. (2013)    |
| Rhizopus oryzae 1526     | Fumaric acid             | 52.0 g/kg of dry weight substrate, 21 d | Das et al. (2015)        |
| Saccharomyces             |                         |               |                       |                          |
| Sugarcane bagasse        | Consortium of Aspergillus ornatus | Citric acid | 13.32 mg/g of substrate, 2 d | Ali et al. (2016)       |
| Hostbork liver           | Lipase                   | 72.3 U/g, 4 d| Liu et al. (2016)     |
| Thermomucor indicae      | Lipase                   | 15 U/g, 3 d  | Ferrari et al. (2014) |
| Aspergillus oryzae CPQBA| Pectinase                | 40 U/g, 18 to 24 h| Biz et al. (2016)     |
| 394-12 DRM 01            |                          |               |                       |                          |
| Thermoascus aurantiacus var. | Xylanase             | 176 U/g, 196 h| Chanwicha et al. (2015)|                          |
| levisporus KRU-PN-J2-1   |                          |               |                       |                          |
| Wheat straw              | Pleurotus ostreatus      | Laccase       | 167 U/g, 5 d          | Karp et al. (2012)       |
| Rice straw               | Pyrenophora phaeocornes  | Laccase       | 10,859 U/g, 4 d       | Rastogi et al. (2010)    |
| Aspergillus niger NRRL-2001| Cellulase              | 401 U/g (FPase), 545 U/g (CMCase), 285 U/g | Dhillon et al. (2012a,b) |
| Pleurotus sajor-caju     | Protease                | 85 U/mL, 8 d | Ravikumar et al. (2012) |
| Promicromonaspora sp. MARS| Xylanase               | 85.0 U/g, 4 d| Kumar et al. (2011)   |
| Citrus peel              | Aspergillus niger F3     | Pectinase     | 265 U/g, 4 d          | Rodriguez et al. (2011)  |
| Aspergillus oryzae CPQBA| Pectinase                | 40 U/g, 18 to 24 h| Biz et al. (2016)     |
| Corn cob powder          | Monascus purpureus       | Pigments (red) | 25.42 OD units/g, 7 d| Velmurugan et al. (2011) |
| KACC 42430               |                          |               |                       |                          |
| Aspergillus niger van    |                           | Oxalic acid   | 120 g/kg of dry weight substrate, 7 d | Mai et al. (2016)       |
| Tighem KACC 44333        |                           |               |                       |                          |
| Sorghum straw            | Aspergillus rubiginosus FDNH1| Xylanase | 5,177.23 U/g, 5 d | Adhyau et al. (2016)    |
|                          |                           | Ethanol       | 6.56 g/100 g | Zai et al. (2009)       |
| Saccharomyces cerevisiae |                           |               |                       |                          |
| Bread waste              | Thermomyces sp.          | Amylase       | 39,900 U/g, 4 d       | Cerda et al. (2016)      |
| Aspergillus awamori      | Protease and glycolysase | 102.8 U/g (glucoamylase), 63.7 U/g (protease), 7 d | Melikoglu et al. (2013) |
| Monascus purpureus       | Pigment, glycolysase and protease | 24 AU (absorbance units/g, 8 and 117 U for pigments, glycolysase and protease, respectively, 7 d | Haque et al. (2016)     |

However, the extent to which SFF are safe and how fermentation processes should be conducted to achieve the required level of safety are crucial. Occasionally, the fermentation process can cause loss of nutrients such as vitamins and amino acids, especially synthetic amino acids (Brooks et al., 2003; Niven et al., 2006; Joris et al., 2010; Canibe and Jensen, 2003). Therefore, some investigators proposed that fermentation of complete feed was defective (Joris et al., 2010; Brookst et al., 2003; Scholten et al., 2002; Moran et al., 2006; Canibe et al., 2007).

Numerous investigations strongly suggested that use of multiple substrates and starter cultures will enlarge scope of feed resources that can be developed with SFF, promote directional conversion of feed, and alleviate competition between human beings and livestock for grain. However, what is worth emphasizing is that further studies are needed to assess the underlying mechanisms of the detailed dynamic change regulation process during the during incubation.

2.2. Incubation parameters

Characteristics of SFF are related closely to temperature, moisture content, and time of incubation which leads to diverse quality of feed.

2.2.1. Temperature

Appropriate temperature guarantees proper growth and metabolism of microorganisms. Liu et al. (2010a,b) adjusted temperature from 30 °C (optimal temperature for enzyme production) to 45 °C (optimal hydrolysis temperature for proteases) in fermentation of soybean meal by A. oryzae A-9005. Conversion rate of soybean peptide increased from 50% to 54.51% after 72 h of incubation (Liu et al., 2010a,b). Appropriate temperature can shorten the stable time of fermentation and improve fermentation products (Gu, 2010; Zhang 2010a,b). Appropriate temperature can shorten the stable time of fermentation and improve fermentation products (Gu, 2010; Zhang 2010a,b). Appropriate temperature can shorten the stable time of fermentation and improve fermentation products (Gu, 2010; Zhang 2010a,b).
reaction speed and growth of metabolism of microorganisms (Pandey, 2003). However, the enzyme is easily inactivated by excessive temperature. Also, rapid growth of microorganisms generates additional heat. Poor heat transfer efficiency of solid-state fermentation feed leads to a sharp rise in temperature of substrates. If excess heat cannot be dissipated in time, growth and metabolism of microorganisms is limited. Another interesting study reported that while soybean meal was fermented by compound bacteria, incubation temperature exceeded the optimal temperature (Pandey, 2003). However, the enzyme is easily inactivated by excessive temperature. Also, rapid growth of microorganisms generates additional heat. Poor heat transfer efficiency of solid-state fermentation feed leads to a sharp rise in temperature of substrates. If excess heat cannot be dissipated in time, growth and metabolism of microorganisms is limited.

2.2.2. Moisture content

Moisture content of substrates is also a crucial factor affecting reaction speed and growth of metabolism of microorganisms (Pandey, 2003). However, the enzyme is easily inactivated by excessive temperature. Also, rapid growth of microorganisms generates additional heat. Poor heat transfer efficiency of solid-state fermentation feed leads to a sharp rise in temperature of substrates. If excess heat cannot be dissipated in time, growth and metabolism of microorganisms is limited. Another interesting study reported that while soybean meal was fermented by compound bacteria, incubation temperature exceeded the optimal temperature (Pandey, 2003). However, the enzyme is easily inactivated by excessive temperature. Also, rapid growth of microorganisms generates additional heat. Poor heat transfer efficiency of solid-state fermentation feed leads to a sharp rise in temperature of substrates. If excess heat cannot be dissipated in time, growth and metabolism of microorganisms is limited.

### Table 2

| Items | Typical raw materials | Fermentation strain | Enzymes | Changes in indicators | References |
|-------|-----------------------|---------------------|---------|----------------------|------------|
| Araoxylan | Wheat bran, Rice bran, Maize, Sorghum | Aspergillus niger, Aspergillus awamori, Trichoderma, Fomes lignosus | Endo-β-1,4-D-xylanase, β-D-xylosidase, α-L-arabinofuranase, Xylan acetylesterase, Glucanase | Oligosaccharide †, Glucose †, Viscosity ↓ | Shen et al. (2012); Zhang et al. (2003); Ghoneum (1998); Cui et al. (2005) |
| β-glucan | Barley, Oats, Rye, Brewer’s yeast | Aspergillus niger, Neurospora crassa, Caldicellulosiruptor sp. F32, Phanerochaete sp. 509 | Endo-β-1,3-glucanase, Endo-β-1,4-glucanase, Exo-β-1,3-glucanase, Exo-β-1,4-glucanase | Soluble sugars †, Crude Protein †, Ferulic acid † | Qiao et al. (2018); Ali et al. (2018); Feng et al. (2019); Chen (2014) |
| Mannan and Glucosyranose | Palm meal, Yeast cell wall, Konjac | Enterococcus faecalis, Lactobacillus plantarum, Cladosporium velox, Aspergillus niger, Neurospora crassa, Aspergillus oryzae, Trichoderma virens, Penicillium oxalicum | β-1,4-D-Mannanase, Mannosidase, Glucanase | Short chain fatty acids †, Lactic acid †, Mannose †, Mannosaccharide †, Mannose † | Wang et al. (2016); David et al. (2016); Zhang et al. (2016); Wang et al., 2018a,b; Wang et al., 2014a,b; Sin et al. (2016); Liao et al. (2014); Zhu et al. (2018) |
| Pectin | Sugar beet pulp, Citrus peel, Peanut meal, Ramie | Bacillus cereus, Bacillus megaterium, Pectobacterium, Aspergillus tubingensis, Rahnella aquatilis, Aspergillus niger, Penicillium, Coriolus versicolor | Pectin methyl esterase, Polygalacturonase, Pectin lyase | Utilization of pectin and Pectin acid †, Soluble sugar †, Organic acids † | Mukhopadhyay et al. (2013); Duan et al. (2016); Na et al. (2018); Long et al. (2017); Chang (2020); Debing et al. (2006) |
| Fructan | Chicory, Onion, Jerusalem artichoke | B. subtilis, Lactobacillus plantarum, Leuconostoc, Trichoderma, Penicillium, Pectinophilus simplex, Neonotropha Fischeri, Talaromyces leucettanus, Abycesdulacil, Lactobacillus, Lactobacillus fermentum, Talaromyces flavus | β-fructofuranase | Fructooligosaccharides †, Lactic acid †, Short chain fatty acids † | Cao et al. (2009); Liu et al. (2018); Liu and Cao (1996) |
| Galactomannan | Soybean hulls, Soybean meal, Nut | Aspergillus niger, Aspergillus awamori, Trichoderma, Penicillium simplicissimum, Neonotropha Fischeri, Talaromyces leucettanus, Abycesdulacil, Lactobacillus, Lactobacillus fermentum, Talaromyces flavus | β-(D)-galactosidase, and Pectinolyase | Soluble sugars †, Crude Protein †, Lactic acid †, Mannose †, Mannosaccharide †, Mannan | Wang (2014); Wang (2010a,b); Carrera-Silva et al. (2006); Simesek et al. (2007) |

### References

Studies over the past years have strongly demonstrated that moisture content of fermentation substrates should be adjusted according to properties of substrates (granularity, hydraulics; Nagel et al., 2015; Wang et al., 2016; Qin et al., 2017), microbial characteristics (anaerobic, aerobic or facultative anaerobic; Liu et al., 2017; Wardynski et al., 1993), temperature (Hamidi-Esfahani et al., 2004; Park et al., 2018; Mcquestin et al., 2009), and time (Pojanagaroon et al., 2007; Nagel et al., 2015). Vinegar lees, wheat bran, corn flour and soybean meal were mixed in the ratio of 9:2:1:1, and the moisture content was controlled to 33.8%. After 5 d of anaerobic fermentation at room temperature, the quality of SFF can be guaranteed and the shelf life can be extended to the maximum extent.
The results showed that the optimal fermentation conditions were as follows: initial water content was 40%; sugar content was 0.5%; the ratio of neutral protease to acid protease was 3:1; exogenous protease was 0.3%; anaerobic fermentation at 40 °C for 5 d.

In conclusion, defining more precisely the optima of the environmental variables is required to build a complex kinetic model for the bacterial strains to ensure robust, repetitive, and safe fermentation cycles over long periods of time.

3. Feedback from applied research

In recent years, finding new unconventional feed sources has become a major emphasis in animal husbandry to reduce dependency on conventional feed. Coincidently, interest in SFF for adjusting health of animals increased dramatically after the European Union banned use of antibiotics as antimicrobial growth promoters for swine.

3.1. Growth performance

Under the action of microorganisms, complex macromolecular organic compounds in feed are degraded into small molecular substances which can be easily utilized by animals. Meanwhile, nutritious bacterial proteins and various metabolites are produced (Mao et al., 2020; Yang et al., 2021). Solid-state fermented feed has a sour fragrance, has the potential to stimulate appetite, and logically might improve animal production performance. However, studies on growth performance of animals fed SFF have not yielded consistent responses which confuse nutritionists and livestock farmers (Chi et al., 2019; Tang et al., 2020).

Nevertheless, the vast majority of reports have shown positive effects of SFF. Lu et al. (2014) found that feeding a diet containing 6% fermented soybean meal (FSBM, Streptococcus thermophiles, Saccharomyces cerevisiae and Bacillus subtilis MA139 were used for start culture) resulted in greater average daily gain and average daily feed intake in weanling pigs (Liu et al., 2014). Jiang et al. (2014) fed 10% FSBM instead of soybean meal (SBM) to piglets and observed responses similar to Lu et al. (2014). More attractively is that the palatability of animals ameliorates with the increase of lactic acid in SFF (Kil et al., 2006). Indeed, positive effects of SFF on growth performance of animals have been reported in several studies (Feng et al., 2007a,b; Kim et al., 2010; Zhang et al., 2013).

Because of lack of endogenous hydrolyzing enzymes, non-starch polysaccharides (NSP) cannot be digested by monogastric animals (Jakobsen et al., 2015a,b). Studies reported that NSP could increase viscosity of digesta and reduce nutrient digestibility in intestines (Refstie et al., 1999; Chot et al., 2015; Suhermiyati et al., 2011). Feeding trials have shown that fermentation of rapeseed meal (Chiang et al., 2010), wheat (Steenfeldt et al., 1998; Wei et al., 2019), oats (Svihus et al., 1997; Cui et al., 2019), and barley (Skrede et al., 2003; Huang et al., 2019) improve animal performance compared with unfermented grains, presumably due to a reduction of soluble NSP. Therefore, it seems logical to conclude that degradation of soluble NSP during fermentation improves nutritive value and digestibility of feed components and is an important factor in improving performance of monogastric animals.

Positive effects of SFF for pigs (Lei et al., 2018), broilers (Akinola et al., 2015), rabbits (Li, 2016), Landes goose (Xian et al., 2013), lamb (Zhong et al., 2013) and beef cattle (Shi et al., 2015) also have been reported (Table 3). However, different voices also appeared (Chen et al., 2007; Song et al., 2011; Kim et al., 2010). Some investigators believe that the low pH and high concentration of some metabolites (e.g., acetic acid, biogenic amines) in SFF impair palatability of animals ameliorates with the increase of lactic acid in SFF which could reduce pH of the gastrointestinal tract without a drop in pH alone (Li et al., 2002; Yu et al., 2011). Furthermore, the anion itself may damage the bacteria. In addition, xylitol can promote the transcription of phosphocysteintransferase to increase the production of propionate, thereby reducing the pH value to inhibit the growth of Escherichia coli and Staphylococcus aureus (Liu, 2015; Xiang et al., 2021).

Inhibitory effects of Lactobacillus on Enterobacteriaceae and Staphylococcus aureus were not caused by a drop in pH alone (Li et al., 2009). Lactobacillus can secrete Lactobacillin and produce organic acids, CO2, and H2O2 which can inhibit growth of pathogenic bacteria (Li et al., 2002; Zhang, 2006). Lactobacillin is a bactericidal peptide, that inhibits Gram-positive bacteria by selectively entering the body of pathogenic bacteria and destroying its genetic material or important metabolic pathways (Cleveland et al., 2001; Quan et al., 2006; Turner et al., 2013). In addition, H2O2 can activate the peroxidase-thiocyanate system, combine lactate peroxidase with hydrogen peroxide and react with thiocyanate to produce oxidative intermediates, that inhibit growth of pathogenic bacteria inhibited (Li et al., 2002; Yu et al., 2011). Furthermore, CO2 can inhibit growth of some gram-negative bacteria (Li et al., 2009, Fig. 2). Alternatively, reductions in pathogenic bacteria may be due to a reduction of free amino acids, mainly lysine, by microbial fermentation in SFF was probably the main reason for the negative effect of feeding it on growth performance (Canibe et al., 2012; Pedersen, 2001). Last but not the least, it is worth emphasizing that the safety evaluation of SFF, such as the change regulation of mycotoxin in SFF, should also be paid great attention by investigators, yet this aspect has only scarcely been explored in the field (Yang et al., 2018).

3.2. Gastrointestinal ecology

Increasing attention has been placed to use of SFF which could influence gastrointestinal bacterial ecology (Rene et al., 2001). Effects of SFF on gastrointestinal ecology are reflected mainly in gastrointestinal flora and metabolites.

Intestinal microflora of an animal is the first barrier in protecting the host from diseases caused by colonization of pathogens in the gastrointestinal tract (Patterson et al., 2003). Solid-state fermented feed because of their unique characteristics, lead to acidification of the upper gastrointestinal tract and provide appropriate conditions for establishment of bacteria beneficial to livestock (Niba et al., 2009; Chen et al., 2013). Moreover, SCFA were generated in the production of SFF which could reduce pH of the gastrointestinal tract and create a competitive exclusion against infection by pathogenic bacteria (Engberg et al., 2009; Niba et al., 2009). Several studies have shown that SFF can reduce levels of Enterobacteriaceae (Jiang et al., 2012; Roubovan et al., 2010) and Salmonella (Heres et al., 2003; Mulder et al., 1997) in different segments of the gastrointestinal tract (Rene et al., 2001), yet Lactobacilli increased (Savvidou et al., 2009; Sun et al., 2013). Many scholars believe that these phenomena resulted because that SFF contains increased concentrations of lactic acid and SCFA, leading a lower gut pH (Scholten et al., 2010; Wissen et al., 2001; Missotten et al., 2009; Lyberg et al., 2006; Canibe et al., 2007).

The proposed reduction of Enterobacteriaceae and Salmonella is related to un-dissociated lactic acid and SCFA, because they cross the membrane of bacteria freely but dissociated acids do not (Russell et al., 1998). Inside the bacterial cell, the acid dissociates and pH drops, leading to collapse enzymatic and the proton motive forces. Additionally, the anion itself may damage the bacteria. Several studies have shown that reduction in Enterobacteriaceae and Salmonella are related to concentration of SCFA, yet the correlations were not clear (Shaw et al., 1937; Burnett et al., 1963; Kershaw et al., 1966; Mikkelsen et al., 1997; Mathew et al., 1998). Recent studies have shown that xylitol metabolism key enzymes exist in some bacteria, which form a mutually trophic relationship with other bacteria to increase the production of short chain fatty acids. In addition, xylitol can promote the transcription of phosophocysteintransferase to increase the production of propionate, thereby reducing the pH value to inhibit the growth of Staphylococcus (Liu, 2015; Xiang et al., 2021).

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available substrates for microbial fermentation in the gastrointestinal tract and the increased digestibility of nutrients in the small intestine by feed fermentation, which could partially explain the reduction (Morishita et al., 1970; Urlings et al., 1993; Fransen et al., 1995). All these studies mentioned have explained the finding that SFF may act in a similar manner as antibiotic substitutes, by improving the gastrointestinal ecology and general health of animals.

Because of the differences about nutrient and moisture in SFF, the animal manure would be diversity. If the high-throughput sequencing technology is used alone and the proportion of strains would be overemphasized, the effect of SFF on total bacterial diversity, solid-state fermented feed have a greater impact on the number of intestinal microorganisms, and the environment it would be diversity. If the high-throughput sequencing technology is used alone and the proportion of strains would be overemphasized, the effect of SFF on total bacterial diversity.

In addition, SFF could affect not only the absorption of nutrients, but also appetite. The axis of brain-gut-microorganism (BGM) could link microorganisms to body metabolism. High acetic acid produced in fermentation, which could be absorbed by the brain through the blood-brain barrier, thus promoting the expression of appetite-suppressing neuropeptides, and appetite would be decreased (Kimura et al., 2013). Irregular dietary behavior will lead to obesity or food addiction, accompanied by BGM, and the BGM feedback mechanism would be overemphasized, the effect of SFF on total bacterial diversity.

The combination of multi node therapy targeting BGM may be a desirable way to alleviate obesity or food addiction in the future (Gupta et al., 2020).

In summary, SFF has a great impact on gastrointestinal ecology, including changes in microflora and metabolic behavior, leading a vital role in metabolism to host. Accordingly, it is reasonable that feeding SFF would be also an effective strategy to improve gastrointestinal ecology and reduce the infection vulnerabilities of enteric diseases for animals.

### 3.3. Immune system

The internal environment of the organism is holistic, and changes in composition of enteric microorganisms affect immune responses of animals (Missotten et al., 2013; Nathan, 2008). As an independent antigen, microorganism could play a vital role in stimulating the immune defense function and improving the ability to mitigate oxidative stress. Although only limited data are available, it has been accepted by more and more researchers that feeding SFF decreases mortality rates (Ranjitkar et al., 2016) and positively affects immune responses of animals (Sugiharto et al., 2018; Miao et al., 2013; Ahmed et al., 2016). In Lactobacillus mediated immune responses, SFF also stimulates cellular-mediated immune responses (Xjie et al., 2007; Gao et al., 2009). Feeding SFF leads to an increase in content of Lactobacillus in the intestine, which has been described above. Although the exact mechanism of Lactobacillus mediated immunomodulatory activities is as yet unclear, they may stimulate mucosal immunity in the intestines, humoral immunity, and cellular immunity all of which play a crucial role in the induction and regulation of immune responses (Kabir, 2009; Xiulin et al., 2017).

As resident flora in the intestinal tract, Lactobacillus in SFF could bind to specific receptors on intestinal epithelial surfaces, and

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**Table 3**

The effect of solid-state fermented feed (SFF) on animal production performance.

| Animal | Period | Substrate | Starter culture | Supplementation, % | Effects | References |
|--------|--------|-----------|-----------------|-------------------|---------|------------|
| Pig    | 21 to 42 d | Soybean meal | Lactobacillus Plantarum, Bacillus subtilis | 15 | Diarrhea †, abundance of Lactobacillus and Prevotella † | Xie et al. (2017) |
|        | 19 to 40 d | Wheat grain | Bacillus subtilis | 50 | Short chain fatty acids in intestine † | Le et al. (2016) |
|        | 21 to 30 d | Wheat | Lactobacillus Plantarum; Lactobacillus buchneri | 43.75 | The digestibility of organic matter, starch and phosphorus † | Koo et al. (2018) |
|        | 35.1 ± 1.8 kg | DDGS | Without | 60 | The digestibility of DM, CP and non-starch polysaccharides † | Jakobsen et al. (2015a,b) |
|        | 64 to 144 d | Corn straw | Lactobacillus casei, Bacillus subtilis, Hymenochaete anomala | 10 | There was no difference in growth performance and microbial diversity. | Jang et al. (2016) |
| Poultry | 35 to 65 d | Soybean meal | Lactobacillus casei, Bacillus subtilis, Hymenochaete anomala | 3.75 | Diarrhea †, average daily gain and feed conversion rate † | Yuan et al. (2017) |
|        | 1 to 28 d | Red ginseng | Monascus | 1 | Body weight and feed conversion rate † | Chong and Choi (2016) |
|        | 1 to 35 d | Rice bran | Bacillus amyloliquefaciens | 5 | Body weight and feed conversion rate † | Mussatto et al. (2012) |
|        | 120 to 155 d | Complete feed | Bacillus subtilis, Enterococcus faecium, Bacillus subtilis | 25 | Average daily feed intake †, the digestibility of crude protein and ether extract † | Lian (2016) |
|        | 1 to 21 d | Soybean meal | Bacillus subtilis | 5 | Apparent metabolic rate † | Wang et al. (2011a,b) |
|        | 1 to 42 d | Basal diet | Bacillus subtilis | — | Average daily gain †, average daily feed intake †, feed conversion rate † | Bai et al. (2017) |
|        | 1 to 42 d | Sour cherry kernel | Aspergillus niger | 1 | Structure of intestinal flora † | Gunor et al. (2020) |

**DDGS** – distillers dried grains with solubles.
colonize intestinal epithelial surfaces stably and orderly, which acts as an effective mucosal barrier (Shiyan et al., 2014). In addition, *Lactobacillus* could also promote proliferation of B-cells in small intestinal lymphoid tissue, enhance mucosal immune responses, and induce plasmocyttes to produce a large concentration of IgA, thereby enhancing immune function of animals (Kabir, 2009). Furthermore, reports also indicate that probiotics and their products of metabolism in SFF can stimulate lymphocytes in intestinal mucosa and promote production of interleukin, tumor necrosis factor and interferon (Ko et al., 1962; Roselli et al., 2007; Puwen, 2011; Liu et al., 2014). *Bacillus subtilis* used in SFF can activate development of the immune system and stimulate B lymphocyte which improve antibody levels (Yu et al., 2011). Similar conclusions have been confirmed by other researchers (Wang et al., 2011a,b; Xinju et al., 2013). Different study characteristics, experimental approaches, and levels of SFF seem to partially explain these discrepancies in inferences.

### 4. Challenges

SFF plays an increasingly vital role in today’s ecological animal husbandry. However, the innovative research and industrialization level of SFF still need to be improved, and many problems need to be solved. In terms of starter culture, due to the complexity and diversity of strains for SFF, the contamination of miscellaneous bacteria, the transfer of drug-resistant genes, the generation of toxic metabolites and excessive immunity continue to appear (Ezekiel et al., 2019). In order to ensure the sustainable and healthy development of SFF, strict screening and identification of starter culture are essential.

In addition, improper handled of SFF production process is an important factor limiting the application of SFF. First, the control of moisture. If the water content of SFF is too low, the diffusion of nutrients and metabolites will slow down, and the growth of microorganisms will be limited. On the contrary, excessive moisture content will reduce the porosity of matrix, reduce the transfer of oxygen and heat, and increase the risk of mycotoxin contamination (Lin et al., 2015; Zhao et al., 2015). Secondly, time control. If the fermentation process is terminated too early, the product concentration will be too low. If the time is too long, nutrients will be consumed in large quantities, resulting in the reduction of the number of microorganisms. At the same time, the rapid growth of microorganisms will also lead to the limitation of their own growth and metabolism (Gao et al., 2009; Zhang et al., 2015).

It should be emphasized that if the concentration of acetic acid and biogenic amine in SFF is too high, the palatability of feed will be greatly reduced (Brooks et al., 2001; Moran, 2001). Also, the disappearance of free amino acids during SFF fermentation may also be the main reason for its negative effect on growth performance (Canibe et al., 2012). Therefore, the dialogue mechanism between microorganisms in the fermentation process and the optimization of process parameters need to be further studied to maximize the effectiveness of SFF. In addition, there are still some problems about SFF, such as imperfect product quality standards and feeding mode to be improved. In terms of standards of SFF, there is no unified standard for the quality evaluation of fermented products in the world (Yu et al., 2019). And it is difficult to identify the quality of SFF, such as the type and content of active substances.

In the storage of SFF, the moisture content and the number of microorganisms increase after fermentation. With the increase of storage time, microbial metabolism will consume most of the nutrients in SFF, resulting in the decline of its nutritional value. In the aspect of application technology, the awareness of the synergy and safety of microbial and animal nutrition needs to be improved, the nutrition database and appropriate addition amount need to be further improved. In the future, the research and development of SFF will focus on the screening of characteristic strains with strong antinutritional factor degradation ability, colonization ability and rich metabolites, the evaluation of biological potency for digestion and absorption of raw materials, improvement of body health and improvement of animal product quality, and the dynamic monitoring of fermentation process and product quality. We hope that readers, after understanding the advantages and disadvantages of SFF, can make the right decision on whether and how to apply SFF.

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**Fig. 2.** The regulation mechanism of *Lactobacillus* in solid-state fermented feed (SFF) on gastrointestinal ecology.
5. Conclusions

Our review was mainly motivated by the needs to meet the strong pragmatism toward a better control and insights on SFF for modern agriculture. As a candidate strategy, SFF has positive effects on growth performance, gastrointestinal ecology and immune system. Predictably it is reasonable that a technology so elegantly simple could raise attention of scientists around the globe. More data on the production engineering and application are needed to have a more solid set of results to add to the existing ones.

Author contributions

Lijie Yang: Formal analysis, Investigation, Writing – original draft; Xiangfeng Zeng: Data curation, Software, Writing-Reviewing and Editing, Visualization; Shiyan Qiao: Conceptualization, Methodology, Resources, Supervision, Project administration, Funding acquisition.

Conflict of interest

We declare that we have no financial and personal relationships with other people or organizations that could 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.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (U180220167) and the Beijing Swine Innovation Team of Modern Agriculture Industry Technological System.

References

Adhyaru DN, Bhatt NS, Modi HA, Divecha J. Insight on xylanase from Aspergillus tubingensis FDH101: production, high yield recovery optimization through statistical approach and application. Biocatalysis and Agricultural Biotechnology 2016;6:51–7.

Ahmed ST, Mun HS, Islam MM, Ko SY, Yang CJ. Effects of dietary natural and fermented rapeseed meal on performance, nutrient digestibility, intestinal ecology and immune function. Anim Prod Sci 2015;55:1360–7.

Ali B, Yi Z, Fang Y, Chen LC, Zhao H. Characterization of a fungal thermostable endoglucanase from Chinese Nong-flavor daqu by metatranscriptomic method. Int J Biol Macromol 2018;113:598–605.

Awati A, Williams BA, Bosch MW, Li YC, Verstegen MWA. Use of the in vitro cumulative gas production technique for pigs: an examination of alterations in fermentation products and substrate losses at various time points. J Anim Sci 2006;84:1110–8.

Bai K, Qiang H, Zhang J, He J, Tian W. Supplemental effects of probiotic Bacillus subtilis fmbj on growth performance, antioxidative capacity, and meat quality of broiler chickens. Poultry Sci 2017;96:74–82.

Bansal N, Tewari R, Soni R, Soni SK. Production of cellulases from Aspergillus Niger NS-2 in solid state fermentation on agricultural and kitchen waste residues. Waste Manag 2012;32:1341–6.

Baz A, Finkler AT, Piolet LO, Medina BS, Krieger N, Mitchell DA. Production of pectinases by solid-state fermentation of a mixture of citrus waste and sugarcane bagasse in a pilot-scale packed-bed bioreactor. Biochem Eng J 2016;111:54–62.

Brooks PH, Beal J, Neven S. Liquid feeding of pigs. Potential for improving pig health and food safety. Annu Sci Pap Rep 2003;21:23–9.

Burnett GS, Hanna J. Effect of dietary calcium lactate and lactic acid on faecal Escherichia coli counts in pigs. Nature 1963;197:815.

Canibe N, Jensen BB. Fermented and nonfermented liquid feed to growing pigs: effect on aspects of gastrointestinal ecology and growth performance. J Anim Sci 2003;81:2019.

Canibe N, Hejberg O, Badsberg JH, Jensen BB. Effect of feeding fermented liquid feed and fermented grain on gastrointestinal ecology and growth performance in piglets. J Anim Sci 2007;85:29–58.

Canibe N, Jensen BB, Ravinndran V. Fermented liquid feed-microbial and nutritional aspects and impact on enteric diseases in pigs. Anim Feed Sci Technol 2012;173:17–28.

Cao ZH, Dong YW, Miao JZ. Study on the technological conditions of inulinase production by Aspergillus Niger. Chinese Journal of Bioengineering 2009;29:107–10.

Carreiro EA, Silvestroni A, Leblanc JG, Paard JC, Giori GSD, Sesma F. A thermostable z-galactosidase from Lactobacillus fermentum crf722: genetic characterization and main properties. Curr Microbiol 2006;53:374–8.

Castro RJ, Ohara A, Nishade TG, Bagagil MP, Dias FPG, Sato HH. A versatile system based on substrate formulation for agroindustrial wastes for protease production by Aspergillus Niger under solid state fermentation. Biocatalysis and Agricultural Biotechnology 2015;4:678–84.

Cerda A, El-Bakry M, Gea T, Sanchez A. Long term enhanced solid-state fermentation: inoculation strategies for amylase production from soy and bread wastes by Thermomyces sp. in a sequential batch operation. Journal of Environmental Chemical Engineering 2016;4:2394–401.

Cerf M, Adameczova Z, Guothova L. Simultaneous enrichment of cereals with polyunsaturated fatty acids and pigments by fungal solid state fermentations. J Biotechnol 2013;168:130–40.

Chanwika N, Katekaev S, Aimi T, Boonlue S. Purification and characterization of alkaline xylanase from Thermoasobacter auranticus var. lieviopus KXU-P12-1 cultivated by solid-state fermentation. Mycotechnology 2015;56:309–18.

Chen R. Production of Glucanases by salecan-degrading bacteria. Nanjing University of Science and technology, 2014.

Chen CC, Shih YC, Chou PW, Yu B. Evaluating nutritional quality of single-stage and two-stage-fermented soybean meal (online). Asian-Australas J Anim Sci 2010;23:598–606.

Chen ZT, Zhou AG, Wang ZS, Liu DC, Peng DY. Evaluation of nutritional quality of single-stage meals fermented by Aspergillus oryzae. Chinese Journal of Animal Science 2011;9:40–4.

Chen W, Zhu XZ, Wang JP, Wang XZ, Huang YQ. Effects of Bacillus subtilis var. natto and Saccharomyces cereviesae fermented liquid feed on growth performance, relative organ weight, intestinal microflora, and organ antioxidant status in Landes geese. J Anim Sci 2013;91:978–85.

Chen B, Wu Q, Xu Y. filamentous fungal diversity and community structure associated with the solid state fermentation of Chinese Mouai-flavor liquor. J Int Food Microbiol 2015;179:80–4.

Chen J, Cheng M, Wang L, Zhang L, Zhan C. A vagal-NTS neural pathway that stimulates feeding. Curr Biol 2020;7:1–13.

Chi ZS, Zhang HJ, Guo AH, Li XW, Geng W, Yu YP, et al. Application of fermented chicken production. Guangdong Feed 2015;24:17–20.

Chiang G, Lu WQ, Pao XS, Hu JK, Thacker PA. Effects of feeding solid-state fermented rapeseed meal on performance, nutrient digestibility, intestinal ecology and intestinal morphology of broiler chickens. Asian-Australas J Anim Sci 2010;23:263–71.

Cho JH, Min BJ, Chen YJ, Chen JS, Wang YQ, Kim JD, et al. Evaluation of FSP (fermented soy protein) to replace soybean meal in weaned pigs: growth performance, blood urea nitrogen and total protein concentrations in serum and nutrient digestibility. Asian-Australas J Anim Sci 2007;20:3874–84.

Choc M. Feed non-starch polysaccharides for monogastric animals: classification and function. Anim Prod Sci 2015;55:1360–6.

Chung TH, Choi HI. Growth performance and fatty acid profiles of broilers given diet supplemented with red ginger marc powder combined with red koji. Rev Bras Cienc Avic 2016;18:733–8.

Cleveland J, Montville TJ, Nes IF. Bacteriocins: safe, natural antimicrobials for food preservation. Int J Food Microbiol 2001;71:1–20.

Chyi YH, Wang SC, Huang Y. Evaluation of NSP enzymatic hydrolysis. Feed Industry 2005;2:46–8.

Cui YY, Tian ZM, Lu HJ, Deng D, Ma XY, Chen WD. Nutritional value of bran and application of fermented feed in animal production. Chinese animal husbandry and veterinary 2019;10:2002–15.

Das RK, Brar SK, Verma M. A fermentative approach toward optimizing directed biosynthesis of fumaric acid by Rhizopus oryzae 1526 utilizing apple industry waste biomass. Fungal Biology 2015;119:1279–90.

David RC, Patricia RM, Abelardo M, Miguel G, Clara RG, Nuria S. Intestinal short chain fatty acids and their link with diet and human health. Front Microbiol 2016;7:185.

Dawson KA. Current and future role of yeast culture in animal production. Proceedings of Alltech’s Ninth Annual Symposium 1987:269–92.

De JR, De LV. Acetic acid bacteria in fermented foods and beverages. Curr Opin Biotechnol 2018;40:115.

Debing J, Peunj L, Stagnitti F, Xiong XZ, Li L. Pectinase production by solid state fermentation. Ind Crop Prod 2013;49:115.

Dhillon GS, Kaur S, Verma M. Potential of apple pomace as a solid substrate for fungal cellulase and hemi-cellulase bioproduction through solidstate fermentation of apple pomace. Biomass Bioenergy 2012a;41:165–74.

Dhillon GS, Kaur S, Brar SK, Verma M. Potential of apple pomace as a solid substrate for fungal cellulase and hemi-cellulase bioproduction through solid-state fermentation. Ind Crop Prod 2012b:38–63.

Dhillon GS, Kaur S, Sarma SJ, Brar SK. Integrated process or fungal citric acid fermentation using apple processing wastes and sequential extraction of chitosan from waste steam. Ind Crop Prod 2013;50:346–51.
Dong JJ, Han RZ, Xu GC, Gong L, Xing WR. Detoxification of furfural residues by butanol fermentation by Clostridium saccharobutylicum DSM 3115. Bioresearch 2018;25:495–500.

Dong ZQ, Zhang XS, Dong Q, Guo HF, Gong JS, Shi JS. Breeding, identification and characterization of trehalase producing strain. J Microbiol 2020;40:51–7.

Duan S, Feng X, Cheng L. Bio-degumming technology of jute bast by Pectobacterium sp. DCE-01. Amb Express 2016;6.

Dujardin M, Elain A, Lendormi T, Le FM, Le TY, Sire O. Keeping under control a liquid feed fermentation process for pigs: A reality scale pilot based study. Anim Feed Sci Technol 2014;194:81–8.

El-Batal AI, ElKenawy NM, Yassin AS, Amin MA. Laccase production by Pleurotus sajor-caju in solid state fermentation. Biochemistry and Molecular Biology 2015;5:31–9.

Engberg RM, Hammershøj M, Johansen NF, Abouzekkines MS, Steenfald S, Jensen BB. Fermented feed for dairy cows: effects on egg production, egg quality, Plasma condition and composition and activity of the intestinal microflora. Br Poult Sci 2009;50:228–39.

Ezekiel CN, Ayeni RZ, Ezekiel OT, Solyok M, Deidre ABW, Oluwawatolu AM, Oluwatsono MA, Isomola ECO, Rasheed AA, Ayinl AA, Christopher TE, Rudolf K. High-throughput sequence analyses of bacterial communities and multi-mycotoxin profiling during processing of different formulations of kuma, a traditional fermented beverage. Front Microbiol 2019;9:32–82.

Feng J, Liu X, Xu ZK, Lu YP, Liu YY. Effect of fermented feed mesocnych on intestinal morphology and digestive enzyme activities in weaned pigs. Dig Dis Sci 2007a;52:1845–50.

Feng J, Liu X, Xu ZR. The effect of Aspergillus oryzae, fermented soybean meal on growth performance, digestive capacity of dietary components and activities of intestinal enzymes in weaned pigs. Anim Feed Sci Technol 2007b;134:300–303.

Feng J, Hamed I, Hamouda NA, β-glucan degrading hydrolysates from Caldicellulosiruptor sp. S2 and influence of glycosylation on F2JEG5. Acta Microbiol Sin 2019;59:2144–54.

Ferrarezi AL, Ohe THK, Borges JP, Brito RR, Siqueira MR, Vendramini PH. Production of mannanase from Pleurotus sajor-caju: purification and characterization. J Mol Catal B Enzym 2014;107:106–13.

Franssen NG, Ulringas BA, Bijker PG, Van BCM. Utilization of fermented flocculated poultry sludge as a feed constituent for pigs. Poultry Sci 1995;74:1948–60.

Gao J, Zhang HJ, Wu SY, Yu SH, Yoon I, Moore D, et al. Effect of Saccharomyces cerevisiae fermentation product on immune functions of broilers challenged with Enterococcus. Poult Sci 2009;88:2141–51.

Gloneum M. Enhancement of human natural killer cell activity by modified arabinoxylan from rice bran (MGN-3). Int J Immunother 1998;14:89–99.

Godoy MG, Amorim GM, Barreto MS, Freire DMG. Chapter 12-agar cultures as animal feed :protein enrichment and detoxification. In: Development of Biofuels and Biorefineries. 2018:10;235–56.

Gong R, Xu SZ, Hermundstad A, Yu Y, Stermsorn SN. Hindbrain double-negative feedback mediates palatability-guided food and water consumption. Cell 2018;175:589–95.

Gu B. Research on production of bio-feedstuff with rich peptide from rapeseed meal by mixed solid-state fermentation. Jiangsu University; 2010.

Guanghui Z, Yujie C, Qing K, Ma YX, Yang L. Detoxification of aflatoxin B1 by zygosaccharomyces rouxii with solid state fermentation in peanut meal. Toxins 2020;12:3531–6.

Gungor E, Erener G. Effect of dietary raw and fermented sour cherry kernel (Prunus cerasus) on growth rate and bacterial flora in the intestines of weaned pigs. Vet Rec 1966;79.

Kil DY, Diao LG, Long HF, Lim JS, Kim YY. Effects of organic or inorganic acid supplementation on growth performance, nutrient digestibility and white blood cell counts in weaning pigs. Asian-Australas J Anim Sci 2006;19:252–61.

Kim SW, Van HE, Ji F, Lee CH, Mateo RD. Fermented soybean meal as a vegetable protein source for nursery pigs.1. Effects on growth performance of nursery pigs. J Anim Sci 2010;88:214–24.

Kumar A, Gao Y, Ma J, Li Z. Potential of using solid-state fermentation in rice straw for the production of bioethanol. J Anim Nutr Sci 2014;201:89–95.

Kumar M, Joshi A, Kashyap R, Khanna S. Production of xylanase by Promicromonas sp SARS with rice straw under non sterile conditions. Process Biochem 2011;46:1614–8.

Le MHA, Galle S, Yang Y, Landerio JL, Beltranena E, Ganzle MG, Zijlstra RT. Effects of feeding fermented wheat with or without glycine, intestinal fermentation, nutrient digestibility, and growth performance in weaned pigs. J Anim Sci 2007;85:1467–87.

Lei XJ, Yun HM, Kim IH. Effects of dietary supplementation of natural and fermented herbs on growth performance, nutrient digestibility, blood parameters, meat quality and fatty acid composition in growing-finishing pigs. J Anim Sci 2018;106:761–72.

Li TJ. Advances in bacterial and fungal fermentation of lactic acid bacteria. Microbiology China 2002;29:81–5.

Li ZT. Optimization study on production of fermented feed of fungus chauf of pleurotus nebrodisius with growth performance in rabbit. Hebei University of Engineering; 2016.

Li Z. Inhibitory effects of Lactobacillus metabolites on Escherichia coli and Staphylococcus aureus. China Brew 2009;5:49–52.

Li CH, Xue XL, Yu JX. Research on process parameters and quality of the complex probiotics fermented feed. J Jiangnan Jiao Univ 2010.

Li Z, Chen ZZ, Wang XX. Effect of microbial feeding on growth performance and physiological indexes. Feed Review 2012;4:59–62.

Liang R, Zhen U, Gang Xu, Yang Y. Effects of fermentation feed on layer chicks growth performance and physiological indexes. Feed Review 2012;4:5–8.

Liao XY, Dai Q, Yu HZ. Study on the production of protein feed by mixed fermentation of multi strains. China Feed 2009;16:8–10.

Liu HF, Li SX, Zheng HF, Zheng W, Xu YC. A new aceticidophilic thermostable endo-1,4-β-D-Xylanase from Pseudomonas oxalates GX-7. Cloning, characterization and functional expression in Pichia pastoris. BMC Biotechnol 2014;14:90.

Lin BS, Li J, Li YM, Yang XY. Optimization of key factors influencing microbial fermented feed production and analysis of composition variation during fermentation process. Journal of Agricultural Science Bulletin 2015;31:1–6.

Liu L. Antibacterial effect of xylitol on common pathogenic bacteria of animal origin. Zhejiang University; 2015.

Liu B, Cao YQ. Isolation, Identification and lnulinase production of a basidiomycete strain. J Microbiol 1996;16:14–9.

Irfan M, Nadeem M, Syed Q, One-factor-at-a-time (OFAT) optimization of xylanase production from Trichoderma viride-1R05 in solid-state fermentation. Journal of Food Science and Technology 2014;51:377–83.

Jais A, Paeger L, Sotelo-Hitschfeld T, Wunderlich FT, Peter K, Jens CB. PNOCARC neurons promote hyperphagia and obesity upon high-fat-diet feeding. Neuro 2020;106:1009–25.

Jakobsen GV, Jensen BB, Knudsen KB, Canibe N. Impact of fermentation and addition of non-starch polysaccharide-degrading enzymes on microbial population and on digestibility of dried distillers grains with solubles in pigs. Livest Sci 2015a;178:216–27.

Jakobsen GV, Jensen BB, Knudsen KB, Canibe N. Improving the nutritional value of rapsed cake and wheat dried distillers grains with solubles by addition of enzymes during liquid fermentation. Anim Feed Sci Technol 2015b;208:198–213.

Jiang HL, Sun H, Jiang FC. Application of fermented soybean meal in the production of weaned piglets in Suhuai pigs. China Swine Industry 2014;12:58–60.

Jiang HL, Cai WB, Molkgwa DL. Impact of fermented corn straw on growth performance, digestibility and cecal micro flora of grower pigs. Asian J Anim Vet Adv 2016;11:461–8.

Jirus AM, Missotten JM, Ankeene O. Fermented liquid feed for pigs. Arch Anim Nutr 2010:64:437–66.

Kabir SM. The role of probiotics in the poultry industry. Int J Mol Sci 2009;10:3513–6.

Karp SG, Faraco V, Amore A, Biolo L, Giangrande C, Soccol VT. Characterization of laccase isoforms produced by Pleurotus ostreatus in solid state fermentation of Sugarcane bagasse. BiotechnolBiotechnol 2012;114:773–9.

Kaur S, Kaur B, Shah S, Brar SK, Chandra J. Carbohydrate degrading enzyme production by plant pathogenic mycetiae and microcetiae isolates of Macro- phomina phaseolina through koji fermentation. Ind Crop Prod 2012;36:140–8.

Kaufman M, Wolfa W, Malaka A. Dual application of agricultural residues for production of fermented feed and its effects on performance and nutrient digestibility in growing-finishing pigs. Asian AUralasian Journal of Animal Sciences 2008;21:1635–50.

Koo B, Kim JW, Nyachoti CM. Nutrient and energy digestibility, and microbial metabolites in weaned pigs fed diets containing Lactobacillus-fermented wheat. Animal Feed Ence & Biotechnology 2018;11:27–37.

Kumar M, Joshi A, Kashyap R, Khanna S. Production of xylanase by Promicromonas sp SARS with rice straw under non sterile conditions. Process Biochem 2011;46:1614–8.
Liu BL, Tzeng YM. Water content and water activity for the production of cyclo-
depolymerides in solid-state fermentation by Metarhizium anisopliae. Bio-
otechnology 2019;27:199–207.

Liu C, Sheng JP, Zou JH, Wang HL, Ding Q, Lin S. Effects of microbial changes on
physical and chemical characteristics of agarcous biomass compost during
fermentation. Food Sci (N Y) 2010;7:270–1.

Liu TM, Jue MS, Si SQ. Effect of temperature changes on the production process
of soybean peptides by solid state fermentation of soybean meal. China Brew
2010b;29:111–2.

Liu H, Zhang J, Zhang S. Oral administration of Lactobacillus casei CNRZ 1007 shows
vital enters to enter the intestine and alters the intestinal microflora in formula-fed
piglets. J Agric Food Chem 2014;62:860–6.

Liu Y, Li C, Meng X, Yan Y. Biodiesel synthesis directly catalyzed by the fermented
solid of Burkholderia cepacia via solid state fermentation. Fuel Process Technol
2016;151:141–5.

Liu Y, Ren HH, Ma XM, Xu YF, Zhang J, Yao J, et al. Normal NW. Isolation, identifi-
cation & fermentation condition optimization of an inulinase-producing strain.
J Microbiol 2016;45:79–85.

Long ZD, Chen HR, Liu Z, Zou KS, Sun JS, Li JG, et al. Application of pectin-degrading
enzymes from Bacillus subtilis, Streptomyces sp., and Aspergillus niger. J Biotechnol
2010;152:29–32.

Marco ML, Heeney D, Binda S, Cifelli CJ, Cotter PD, Foligne B, et al. Health bene-
fits of fermented foods: microbially and beyond. Curr Opin Biotechnol 2017;44:
94–102.

Mathews C, Maffett SE, Robbins CM, Golden DA. Effects of a direct-fed yeast culture
on enteric microbial populations, fermentation acids, and performance of
weanling pigs. J Anim Sci 1998;76:2138–45.

Mathur G, Mathur A, Sharma RM, Chauhan RS. Enhanced production of laccase from
Cladosporium sp. using Plackett Burman design. J Pharm Sci 2013;61:1–4.

Mcqueen OJ, Shadbolt CT, Ross T. Quantification of the relative effects of tempera-
ture, pH, and water activity on inactivation of Erichichia coli fermented meat by
meta-analysis. Appl environ Microbiol 2009;75:6963–72.

Melikoglu M, Lin CSK, Webb C. Kinetic studies on the multi-enzyme solution pro-
duction. Process Biochem 2016;51:9

Miao YU, Yan JX, Feng ZL. Effects of microbial fermented feed on immune function
parameter of beef cattle. China Animal Husbandry & Veterinary Medicine
2013;40:114–7.

Mikkelsen LL, Jensen BB. Effect of fermented liquid feed (FLF) on growth perfor-
manace and microbial activity in the gastrointestinal tract of weaned piglets, vol.
80. World Rev Nutr Diet 2011;99:303–17.

Missotan JM, Coris J, Michels J, Collie EV, Herman L, Smet SD, et al. Screening of
isolate lactic acid bacteria as potential beneficial strains for fermented liquid
pig feed production. Anim Feed Sci Technol 2009;150:122–38.

Missotan JA, Michels J, Collie EV, Herman L, Smet SD. Fermented liquid feed for pigs:an
cient technique for the future. J Anim Sci Biotechnol 2016;6:4–12.

Moran CA, Scholten JT, Tricario JM, Brook PH, Verstegen MWA. Fermentation of
what effects of backsliping different proportions of pre-fermented whead on
the microbial and chemical composition. Arch Anim Nutr 2006;60:
158–69.

Morishita Y, Ogata M. Studies on the alimentary flora of pig. 5. Influence of star-
vation on the microbial flora. Nihon Jogaku Jishin no Zasshi the Japanese Journal of
Veterinary Science 1970;32:19–24.

Mukhopadhyay A, Dutta N, Chattopadhyay D, Chakraborti K. Degumming of ramie
fiber and the production of reducing sugars from waste peels using nano-
particle-supported solid-state lyase. Bioreourc Technol 2015;137:202–8.

Mulder RMAW, Havaenra RJH, Veld Huis I. Intervention strategies:the use of pro-
biotics and competitive exclusion microfloras against contamination with pathogens
in pigs and poultry. Probiotics 2, vol. 94. Dordrecht: Springer; 1997.

Niven SJ, Beal JD, Brooks PH. The effect of controlled fermentation on the fate of
synthetic lysine in liquid diets for pigs. Anim Feed Sci Technol 2006;129:
104–15.

Nout MJR. Fermented foods and food safety. Food Res Int 1994;27:291–8.

Pandey A. Solid-state fermentation. Biochem Eng J 2003;13:81–4.

Pandey AK, Edgard G, Negi S. Optimization of concomitant production of cellulase
and xylanase from Rhizopus oryzae using solid-state fermentation. J Biotechnol
2003;2005;82:627–31.

Pedersen A. Fermented liquid feed to piglets, vol. 510. Copenhagen, Denmark:
Danish Bacon and Meat Council; 2000.

Pedersen C, Stein HH. Effects of liquid and fermented liquid feeding on energy, dry
matter, protein and phosphorus digestibility by growing pigs. Livest Sci
2010;134:39–61.

Pirata KDPP, Delabona M, Delabona RF, Paixão DAA, Baleire FCF. Enhancing xylanases
production by a new Amazon Forest strain of Aspergillus oryzae using solid-state fermentation under controlled operation conditions. Ind Crop Prod
2013;43:465–71.

Pillar WA, Leung HK. Effect of moisture content on the development of carbonylic
compounds from traditional malts during fermentation. J Sci Food Agric 2010;33:555–8.

Pooyarojanam S. Effects of pH of fermented water, fermentation and aging time on
Krachai-Dam (Kamep RSA parviflora) honey wines qualities. In: Proceedings of
the 45th KASERTER university annual conference, bangkok, Thailand, 30 january-
February 2011. Subject: Plants; 2007: p. 311–2.

Polce B, Baryga A, Szymanski T, Wolynska W, Tobiola A. Biogas generation capa-
bilities from beef pulp methane fermentation process. Part II. Semi-continuous
bulp fermentation. Gazzetta Tecnol 2003;108:120–5.

Prauwen FX. Fermented liquid feed:effects on weaner piglet intestinal health. Chi-
inese journal of Animal Nutrition 2011;23:2105–8.

Qiao JY, Hongye Y, Jiang ZQ, Liu SQ. A novel thermostable A1,1,4-glucanase from
Thermosaccus aurantiacus and its application in oligosaccharide production from
oat bran. Carbohydr Res 2018;131:7–31.

Qin Y, Kun H, Hong X, Jiang M, Sheng DM. Low-field nuclear magnetic resonance for
online determination of water content during sausage fermentation. J Food Eng
2011;102:291–7.

Quan CS, Hongtao XJ, Jun-Hua W, Liu CJ, Fan SD. Lactobacitsirn-in-safety and
natural food preservative. J Microbiol 2006;26:86–9.

Qureshi AS, Khushk I, Ali CH, Chisti Y, Ahmad N, Mageed H. Coproduction of protease
and amylase by thermophilic Bacillus sp. BBX-2 using open solid-state fer-
mentation of lignocellulosic biomass. Biocatalysis and Agricultural Biotech-
ology 2016;8:146–51.

Ranjkitkar S, Karlsson AH, Petersen MA, Bredie WLP, Engberg RM. The influence of
feeding crimped kernel maize silage on broiler production, nutrient di-
gestibility and meat quality. Br Poultry Sci 2016;57:12–23.

Rastogi S, Soni R, Kaur J, Soni SK. Unravelling the capability of Pyrenophora paeonmum 5-1 for the production of ligno-hemichellulotic enzyme cocktail and
antimicrobial bioactive compounds from rice straw for enhanced enzymatic
saccharification. Bioresour Technol 2016;222:458–69.

Refete S, Sibhus B, Shearer KD, Trond S. Nutrient digestibility in Atlantic salmon and
broiler chickens related to viscosity and non-starch polysaccharide content in
different feed soybean products. Aquacult Nutr 2012;18:311–4.

Ren LVW, Urlings BAP, Lipman IJA. Effect of fermented feed on the microbial
population of the gastrointestinal tracts of pigs. Appl Environ Microbiol
2001;67:3071–6.

Rodriguez-Fernandez DE, Rodriguez-Leon JA, Carvalho JC, Sturm W, Soccol CR. The
behavior of kinetic parameters in production of pectinase and xylanase by
solid-state fermentation. Bioreourc Technol 2011;102:10657–62.

Rombenso A, Crousse C, Trushenski J. Comparison of traditional and fermented
soybean meals as alternatives to fish meal in hybrid striped bass feeds. N Am J
Aquacult 2013;75:197–204.

Roselli M, Finamore A, Britti MS, Konstantinov SR, Smidt H, Willem M, et al. The
novel porcine Lactobacillus salivarius strain protects intestinal cells from en-
erotoxigenic Escherichia coli K88 infection and prevents membrane barrier
damage. J Nutr 2007;137:2797–16.

Roubosvan DHPJ, Nout MJR, Beumer RR, Meulen JVD, Zwietering MH. Fermented
ryzae using solid-state fermentation under controlled operation conditions. Ind Crop Prod
2013;43:465–71.

Russell JB, Diezgonzalez F. The effects of fermentation acids on bacterial growth.
Vet Microbiol 2012;157:45.

Savvidou SE, Beal JD, Brooks PH. Liquid feed fermented with Lactobacillus salivarius
L. Yang, X. Zeng and S. Qiao Animal Nutrition 7 (2021) 905–916
Zhao H, Wang XT, Tang JY, Tang XP, Gang J, Liu GM, et al. Nutritional improvement of sweet potato residue by solid-state fermentation with mixed microbe strains. Animal Nutrition 2015;27:1191–8.

Zhongli P, Chunhua G, Xue B, Zhu WL, Fu XS, Wang YL. Effects of fermented feed on production performance, digestibility of dietary nutrients, blood biochemical indices in goat. J Agric Sci Technol 2013;15:106–13.

Zhu H, Wu WR, He LM, Lei X, Zhou JP, Huang ZX, et al. Biochemical characterization of mannanase produced by Cladosporium velox in culture medium of palm kernal meal. Guangdong Journal of Animal and Veterinary Science 2018;43:43–7.