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# The biological function of *Atractylodes lancea* and its application in animal husbandry: a review

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*Atractylodes lancea*, is a herbaceous plant of the Asteraceae family which is a traditional Chinese herbal medicine. It is often used for dehumidification, antiemetics, spleen strengthening and antipyretic effects. *Atractylodes lancea* is rich in various bio-active substances and has many biological functions, for instance anti-inflammatory, antioxidant and antiviral effects. Therefore, it is widely used in animal production, such as relieving heat stress, protecting intestinal health and regulating immunity. In recent years, it has received widespread attention in green cultivation. This article reviews the biological functions of *Atractylodes lancea* and looks forward to its application prospects in animal husbandry, in order to provide a theoretical basis for *Atractylodes lancea* to become a new feed additive in animal production.

## KEYWORDS

*Atractylodes lancea*, biological functions, application, animal husbandry, green cultivation

## 1 Introduction

*Atractylodes lancea* (*A. lancea*) is a perennial herb with a light aroma. It is often used for dehumidification, antiemetics, spleen strengthening and antipyretic effects (1–3), as well as relieve pain and diarrhea (4). In recent years, it is widely used to treat vomiting (5) and heatstroke (6), which is one of the traditional Chinese herbal medicine in China. The rhizome of *A. lancea* has been used widely in many countries for various indications. This compound is called “Cangzhu” in China, “Khod-Kha-Mao” in Thailand, and “So-jutsu” in Japan. There are many species of *A. lancea*, which are widely distributed around the world. Studies have found that *A. lancea* has many biological functions, including anti-inflammatory, antioxidant, antiviral, antibacterial, analgesic, so that it can be used for improving gut health, immunity and growth performance of animals (7, 8). Nowadays, with the continuous development and research of new alternative antibiotic products, *A. lancea* and its extracts have been widely used in animal husbandry due to its low cost, high efficiency and low toxicity. This article reviews the main active ingredients and biological functions of *A. lancea*, and looks forward to its application prospects in livestock and poultry production, in order to provide a reference for the efficient use of *A. lancea* in green and healthy cultivation.

## 2 The main biological compounds and their structures of *A. lancea*

*lancea* has a variety of natural bio-active compounds, including sesquiterpenes, enynes, aromatics, polysaccharides, flavonoids, phenols and organic acids (9). The main components of *A. lancea* are sesquiterpenes, including atractylodin, atractylone,  $\beta$ -eudesmol, atractylodes polysaccharides, and atractylenolide (10). The content of active ingredients in *A. lancea* was analyzed by gas chromatography-mass spectrometry (GC-MS). The results showed that the content was as follows: atractylodin (6.22%), hinesol (3.52%), atractylone (1.32%),  $\beta$ -eudesmol (0.81%), and atractylol (0.15%) (11). Wang et al. used a variety of methods to separate the volatile oil of *A. lancea* and found that the contents of atractylodin, atractylol, and atractylone were high, while the contents of atractylenolide and atractylodes polysaccharides were low. At the same time, it was confirmed that *A. lancea* has good pharmacological activities (12). The main bio-active compounds of *A. lancea* and their structures are shown in Figure 1.

## 3 The biological functions of *A. lancea*

### 3.1 Anti-inflammatory

Inflammatory response is a complex physiological response of the immune system to external stimuli, which is regulated by a variety of inflammatory mediators. Appropriate amount of inflammatory factors plays an important role in maintaining the normal physiological functions of animals, but when animals are infected by viruses or bacteria, a large amount of inflammatory factors will be deposited in the body, leading to serious inflammatory damage (13–15). Atractylenolide I and atractylenolide III can reduce the expression level of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and the production of nitric oxide (NO) in animal serum. Atractylenolide I showed a more effective inhibitory effect on the production of TNF- $\alpha$  and NO in peritoneal macrophages activated by lipopolysaccharide (LPS) than atractylenolide III (16). Both nuclear factor- $\kappa$ B (NF- $\kappa$ B) and mitogen-activated protein kinase (MAPK) signaling pathways can regulate the release of inflammatory factors in animals. The study by Jeong et al. (17) showed that atractylenolide I and Atractylenolide III could inhibit the phosphorylation of p38 MAPK, c-Jun N-terminal kinase (JNK), and inhibitor of nuclear factor- $\kappa$ B (I $\kappa$ B) in LPS induced mouse inflammatory macrophages, promote the phosphorylation of extracellular signal-regulated kinase (ERK), block the translocation of NF- $\kappa$ B to the nucleus, and significantly reduce the expression of pro-inflammatory factors such as TNF- $\alpha$ , interleukin-6 (IL-6), and interleukin-1 $\beta$  (IL-1 $\beta$ ). In addition, atractylenolide II can reduce the release of inflammatory factors such as NO, TNF- $\alpha$ , and IL-6 in mouse macrophages induced by LPS, but the effect is not significant (18). In summary, atractylenolide, as the most effective anti-inflammatory component in *Atractylodes lancea*, can reduce the expression level of inflammatory factors and alleviate inflammatory damage by regulating the MAPK and NF- $\kappa$ B signaling pathways, but the inflammatory regulation mechanism of other compounds still needs further study.

### 3.2 Antioxidant

Reactive oxygen species (ROS) are extremely bio-active materials. Excessive levels of ROS in livestock and poultry can cause oxidative stress (19). The phenolic acids and flavonoids contained in *Atractylodes lancea* have metal chelating and free radical scavenging functions, inhibiting the production of ROS (20). The Nrf2-Keap1 signaling pathway plays a pivotal role in the antioxidant response of animals and increase the activity of antioxidant enzymes, among which Nrf2 is the main effector (21). Study had shown that Atractylodes polysaccharide II can increase the activity of glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) in the tissue of mouse liver, significantly reduce the activity of nitric oxide synthase (NOS) and the content of NO and malondialdehyde (MDA) (22). It can be seen that *A. lancea* polysaccharide has good antioxidant activity. On the one hand, *A. lancea* polysaccharide balances the antioxidant system in animals by inhibiting the production of ROS; On the other hand, *A. lancea* polysaccharide can regulate the Nrf2-Keap1 signaling pathway, enhance the activity of antioxidant enzymes SOD and GSH-Px, and improve the ability of animals to clear ROS.

### 3.3 Anti-viral

Viral infections such as swine flu and avian flu are extremely harmful to livestock and poultry production. The clinical manifestations include diarrhea, cough, fever, and lameness. Mild cases can cause breathing and movement difficulties, while severe cases can lead to large-scale deaths, seriously affecting the economic benefits of the breeding industry. *A. lancea* can act on the cell surface to change the protein receptor structure, significantly block the adsorption and penetration of swine influenza virus into cells. Study has shown that *A. lancea* can significantly inhibit the proliferation of swine influenza virus in cells and has a direct effect of inactivating virus (23, 24). In addition, atractylone, as the main antiviral ingredient in *A. lancea*, can block the adsorption and replication of avian influenza virus (25). Toll-like receptor 7 (TLR7) is widely present in immune cells, epithelial cells and nerve cells. When livestock and poultry are invaded by pathogens, TLR7 will immediately transfer to the cell membrane, identify the pathogens, aggregate specific proteins to activate regulatory factors such as I $\kappa$ B, MAPK and interferon (IFN), initiate specific immune responses, and participate in the antiviral process. Atractylone can regulate TLR7 receptors, inhibit the activation of MAPK and NF- $\kappa$ B signaling pathways, relieve epidemic diarrhea and respiratory diseases caused by influenza A virus infection. Chen et al. (26) found that continuous treatment with 10, 20, and 40 mg/kg atractylone for 5 days could alleviate influenza A virus-induced lung injury in mice, significantly reduce serum TNF- $\alpha$ , IL-6, and IL-1 $\beta$  levels, meanwhile increase IFN- $\beta$  levels, indicating that atractylone can promote IFN- $\beta$  production by activating the TLR7 signaling pathway, interfere with viral replication, and recruit immune cells to activate specific immune responses and eliminate viruses. Therefore, *A. lancea* has important application potential in livestock and poultry production because of its antiviral effects.

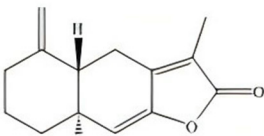
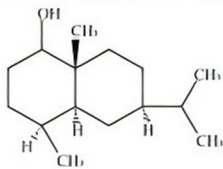
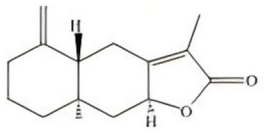
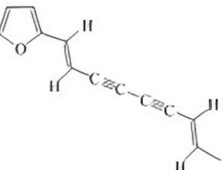
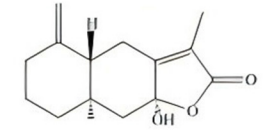
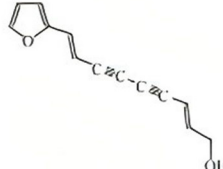
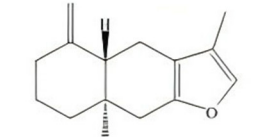
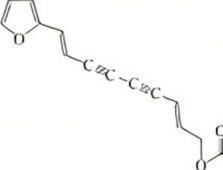
Chemical names	Formula	Molecular structure	Chemical names	Formula	Molecular structure
Atractylenolide I	$C_{14}H_{15}O_2$		$\beta$ -eudesmol	$C_{15}H_{28}O$	
Atractylenolide II	$C_{14}H_{17}O_2$		Atractylodin	$C_{13}H_{10}O$	
Atractylenolide III	$C_{14}H_{17}O_3$		Atractyoldinol	$C_{13}H_{10}O_2$	
Atractylone	$C_{14}H_{17}O$		Acetyla tractlodinol	$C_{15}H_{12}O_3$	

FIGURE 1  
The main bio-active compounds of *A. lancea* and their structures.

### 3.4 Other functions

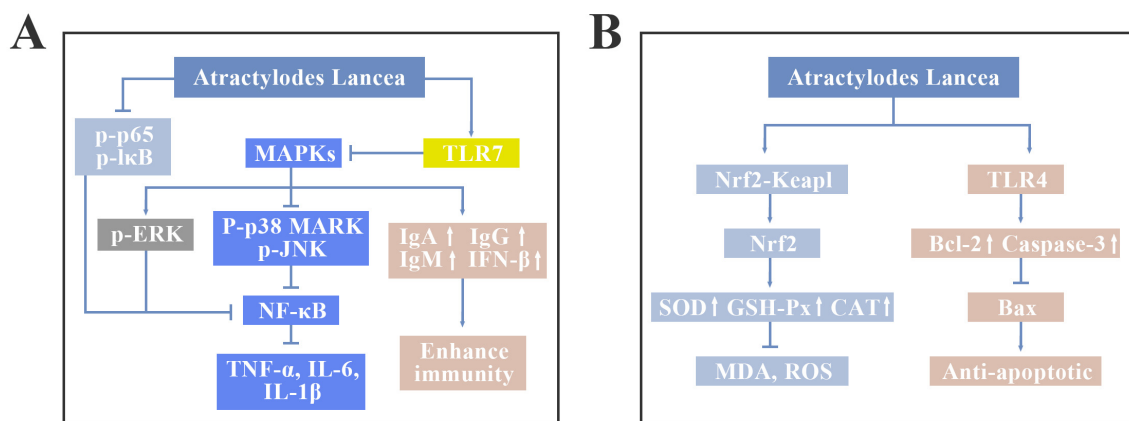
*A. lancea* also has anti-tumor, liver protection, diuretic, glucose metabolism, and lipid metabolism regulating functions. Studies have shown that *A. lancea* polysaccharides have anti-tumor effects, which can activate macrophages through the Toll-like receptor 4 (TLR4) signaling pathway, reduce the expression of B cell lymphoma-2 (Bcl-2), increase the expression of pro-apoptotic factors such as Bcl-2-associated X protein (Bax) and cysteine aspartate proteinase-9 (Caspas-9), finally promote tumor cell apoptosis (27–29). Additionally, *A. lancea* polysaccharides can prevent liver damage caused by harmful chemicals and toxins. Han et al. (22) showed that *A. lancea* polysaccharide can reduce the expression levels of AST, ALT, and MDA in liver, increase the activity of SOD and GSH-Px, and alleviate LPS-induced liver inflammation in mice by inhibiting the NF- $\kappa$ B signaling pathway. It is reported that *A. lancea* has a diuretic effect. Study has found that intravenous injection or oral administration of 1.0 g/kg *A. lancea* solution can significantly increase the urine output of mice (27). In addition, the active ingredients in *A. lancea* can improve glucose uptake, inhibit fat production, and regulate lipid metabolism in animals (30). The regulatory mechanism of *A. lancea* on MAPK, NF- $\kappa$ B, Toll-like receptor (TLR) and Nrf2-Keap1 signaling pathways is shown in Figure 2. The key functions

and associated mechanisms of *Atractylodes lancea* was showed in Table 1.

## 4 Application prospects of *A. lancea* in livestock and poultry production

### 4.1 Improving productive performance

*A. lancea* is rich in natural active substances, which have multiple functions such as improving immunity, resisting stress and promoting digestion. It has great potential in improving the production performance of livestock and poultry. Li et al. (31) found that adding 3, 6, and 9 g/kg of *A. lancea* polysaccharide to the diet could significantly improve the growth performance of early weaned piglets. On the one hand, *A. lancea* polysaccharides can play an antioxidant role and alleviate the adverse effects of stress on growth performance (32). On the other hand, *A. lancea* polysaccharide can stimulate lymphocyte proliferation and antibody production in early weaned piglets, improve disease resistance and reduce diarrhea rate (33). In addition, *A. lancea* also plays an important role in improving the productive performance of poultry and ruminants. Study has found that adding *A. lancea* polysaccharides to laying hen diets can significantly increase egg



**FIGURE 2** The regulatory mechanism of *A. lancea* on MAPK, NF-κB, Toll-like receptor (TLR) and Nrf2-Keap1 signaling pathways. **(A)** MAPK, NF-κB and TLR7 signaling pathways. **(B)** Nrf2-Keap and TLR4 signaling pathways.

**TABLE 1** The key functions and associated mechanisms of *Atractylodes lancea*.

Biological functions	Active ingredients	Relative mechanisms	References
Anti-inflammatory	Atractylenolide I	TNF-α, NO, IL-6, IL-1β↓	(16)
	Atractylenolide III	p38 MAPK, JNK, IκB↓	(17)
			(18)
Antioxidant	Atractylodes polysaccharide II	GSH-Px, SOD↑	(22)
		NOS, NO, MDA↓	(20)
Anti-viral	Atractylone	MAPK and NF-κB signaling pathways↓	(25)
		TNF-α, IL-6, IL-1β↓	(26)
Anti-tumor	Atractylodes polysaccharides	Bcl-2↓	(27–29)
		Bax, Caspas-9↑	
Liver protection	Atractylodes polysaccharides	AST, ALT, and MDA↓	(27)
		SOD, GSH-Px↑	

weight, egg production rate, and feed conversion rate, reduce mortality of laying hens (34). In the ruminants, studies have shown that adding 0.75% of *A. lancea* to the diet can improve the fermentation capacity, increase the efficiency of rumen microorganisms in degrading substances such as protein and cellulose, and promote the synthesis of bacterial protein in the rumen (35). It can be seen that *A. lancea* has good application value and research potential in improving the production performance of livestock and poultry, but its specific addition amount needs further exploration.

### 4.2 Immune regulation

After weaning, piglets lose the protection of maternal antibodies and their immune system is not fully developed, so they are easy to meet with problems such as poor disease resistance, growth retardation and diarrhea. Li et al. (36) added 0.3% purified *A. lancea* polysaccharide, 0.6% crude polysaccharide and 0.6% crude *A. lancea* polysaccharide to the diet of weaned piglets. The results

showed that all three polysaccharides could increase the antibody content in serum, promote lymphocyte proliferation and improve immunity of weaned piglets. Wang et al. (37) found that adding 0.1, 0.2, and 0.3% fermented *A. lancea* to the diet of early weaned piglets could increase the levels of immunoglobulin A (IgA), immunoglobulin G (IgG) and immunoglobulin M (IgM) as well as TP and ALB in the serum, among which 0.2% fermented *A. lancea* had the most significant effect. Interleukin-1 (IL-1) and interleukin-2 (IL-2) are cytokines produced by activated T cells, which can stimulate the proliferation and differentiation of immune cells and enhance animal immunity. The experimental results of Xu et al. (33) showed that adding an appropriate amount of *A. lancea* polysaccharide to the diet of weaned piglets can promote lymphocyte proliferation, increase the levels of antibodies such as IgA and IgG in serum and release cytokines such as IL-1 and IL-2, thereby improving the immunity of weaned piglets. *A. lancea* can significantly increase the spleen and thymus index of livestock and poultry, and it has a positive effect on improving immunity and intestinal health. Li et al. (38) found that *A. lancea* polysaccharide can alleviate cyclophosphamide-induced immune

organ damage in geese. In ruminants, *A. lancea* polysaccharides can induce the proliferation of bovine mammary lymphocytes and activate immune cells (39). In summary, *A. lancea* can be used as an immunomodulator and has important application potential in livestock and poultry production, but its specific mechanism of regulating immunity needs further study.

## 4.3 Improve intestinal health

### 4.3.1 Intestinal barrier

Intestinal health is an important factor affecting the production performance of livestock and poultry, it is also an important indicator for assessing animal welfare. Bose et al. (40) found that fermented *A. lancea* polysaccharide can alleviate LPS-induced intestinal epithelial cell damage and reduce intestinal mucosal permeability through *in vitro* experiments. Shi et al. (41) found that the *A. lancea* can promote the integrity of the intestinal mucosal barrier by inhibiting the phosphorylation of p38 and MAPK signaling pathways and increasing the mRNA expression of *ZO-1*, *Claudin-1*, and *Occludin*. This indicates that *A. lancea* protects the intestinal barrier of animals by reducing the level of inflammatory factors. In addition, adding an appropriate amount of *A. lancea* polysaccharide to the LPS-induced enteritis model can increase the protein level of *ZO-1* and *Occludin*, and alleviate intestinal inflammation in goose (42). In terms of intestinal microbes, *A. lancea* polysaccharides can reduce the relative abundance of *Escherichia coli* in weaned piglets while increasing the level of *Lactobacillus* (36). In addition, Wang et al. (43) reported that *A. lancea* polysaccharides can regulate the structure of intestinal microbes, promote the colonization of probiotics in the intestine, and reduce the abundance of harmful bacteria in mice. Studies on ruminants have shown that adding *A. lancea* to the diet can increase the activity of rumen microbiota, changing the structure of rumen microbes, and promoting rumen fermentation (44, 45). It can be seen that *A. lancea* plays a regulatory role in the intestinal health of animals, but its role in affecting the composition and activity of intestinal microbes still needs further study.

### 4.3.2 Colon health

Colitis often occurs in piglets from 4 to 16 weeks of age after weaning, leading to increasing intestinal mucosal permeability, diarrhea, and reduced the growth performance of piglets (46). Studies have found that *A. lancea* can increase the content of tight junction proteins, thereby reducing diarrhea caused by colitis in mice (3, 47, 48). The mechanism of *A. lancea* in relieving colitis is as follows: on the one hand, *A. lancea* can promote the secretion of mucin by goblet cells, increase the content of *ZO-1* and *Occludin*, reduce intestinal mucosal permeability, and restore the normal physiological function of colon in piglets; On the other hand, *A. lancea* inhibits the phosphorylation of MAPK and NF- $\kappa$ B signaling pathways in the intestine, reduces the expression of inflammatory factors such as TNF- $\alpha$ , IL-6, and IL-1 $\beta$ , alleviates the absorption disorder of sodium ions and chloride ions disturbed by inflammatory factors, improves the water re-absorption capacity in the colon, and reduces diarrhea in piglets. IL-6, which is a reference

indicator of colitis, can increase the permeability of intestinal mucosa (49). Studies have shown that *A. lancea* can inhibit the release of TNF- $\alpha$  and IL-6, up-regulate the expression of autophagy genes, and significantly alleviate colon damage in mice (3, 50, 51). Since colitis is a disease caused by immune system disorders, it is speculated that *A. lancea* can maintain the homeostasis of the internal environment by activating the cell autophagy pathway and ultimately improve colitis.

## 4.4 Relief of heat stress

Heat stress refers to the sum of non-specific physiological responses made by the body to any requirements imposed by the thermal environment at high ambient temperatures (52). In general, there is an isothermal zone in homeothermic animals, and when the ambient temperature is in the range of the isothermal zone, the animal can maintain normal temperature through body temperature regulation; When the ambient temperature is higher than the upper limit of the isothermal zone, the animal will be subjected to heat stress (64). When heat stress occurs, animals typically show increased breathing, increased heart rate, and impaired electrolyte balance (53). Therefore, heat stress can effect the growth performance and reproductive performance. Under the influence of heat stress, animals' appetite decreases, resulting in a decrease in feed intake, which seriously affects production performance (54). Studies have shown that heat stress can lead to oxidative stress, adding *A. lancea* to pig diets can increase the activity of antioxidant enzymes in serum, reduce MDA and ROS levels, and thus alleviate heat stress (55, 56). *A. lancea* can terminate lipid peroxidation by removing ROS and hydrogen peroxide, improve ROS-induced intestinal epithelial cell shedding, and restore the digestive and absorptive functions of the intestine. Xu et al. found that adding *A. lancea* polysaccharides to broiler diets can significantly improve the antioxidant capacity, enhance immunity, and alleviate the damage caused by heat stress (57). In addition, *A. lancea* also has a good effect in alleviating heat stress in ruminants. It has been reported that under heat stress conditions, adding *A. lancea* to cattle diets can significantly improve immunity and antioxidant capacity, promote rumen digestion and absorption of nutrients in the feed, and improve production performance (57). It can be seen that *A. lancea* plays an important role in alleviating heat stress in animals, but its effective components and optimal additive dosage need further study.

## 4.5 Other application prospects

### 4.5.1 Antimicrobial agents

Studies have shown that *A. lancea* has antibacterial effects on a variety of microbes, including *Escherichia coli*, *Candida albicans* and *Staphylococcus aureus* (2, 58). Peng et al. reported that 5–40 mg/mL Atractyoldinol had a significant inhibitory effect on *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis* (59). The antibacterial mechanism of *A. lancea* is that on the one hand, *A. lancea* can destroy the protein structure in the bacterial cell membrane, causing the cell contents to flow out; On the

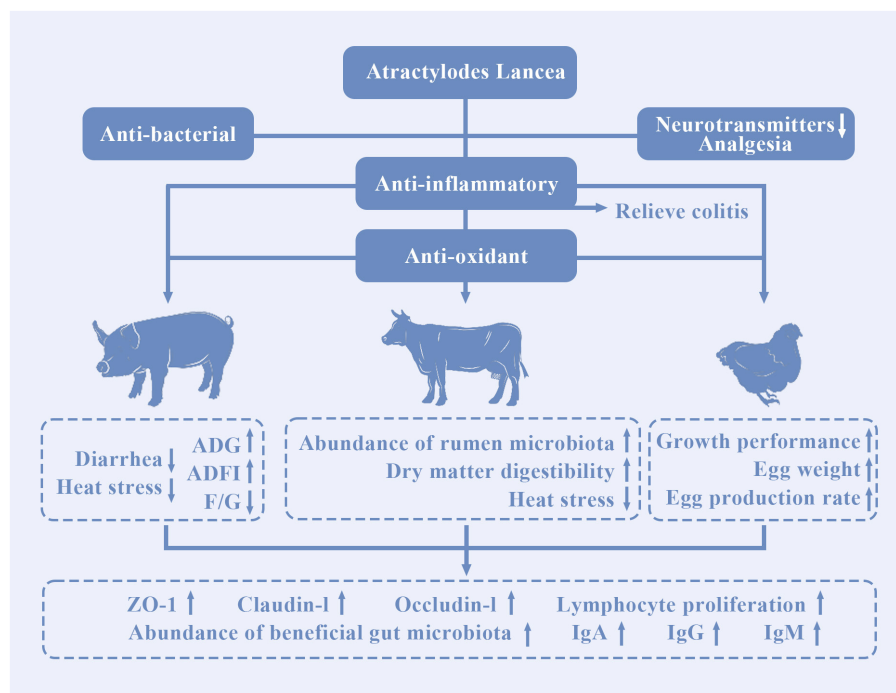


FIGURE 3  
The application of *A. lancea* in livestock and poultry production.

other hand, adding *A. lancea* to animal feed as a feed additive can directly remove aflatoxin and improve the digestibility of nutrients in the feed. It can be seen that *A. lancea* has important application value in livestock and poultry production as an antibacterial agent.

#### 4.5.2 New type of analgesic agents

Ohara et al. found that atractyoldinol and  $\beta$ -eudesmol have analgesic effects, which can inhibit the function of the nervous system, and reduce the sensitivity of animals to external stimuli (60). Atractylodesinol is used as an analgesic in livestock and poultry production. On the one hand, atractylodesinol can inhibit the release of neurotransmitters (61, 62); On the other hand, atractyoldinol can block acetylcholine receptor channels, weaken nerve signal transmission, and relieve pain caused by production processes such as sow farrowing, piglet castration and rectal prolapse suture (63). Therefore, atractyoldinol has a good analgesic effect which can be used as a new analgesic. However, it is currently rarely used in livestock and poultry, the specific dosage needs further experimental research to explore. The application of *A. lancea* in livestock and poultry production is shown in Figure 3.

## 5 Conclusion and perspectives

Under the background of “total ban on antibiotics,” optimizing livestock and poultry feed formula and finding new green feed

additives have become research hotspots. *A. lancea* can inhibit the phosphorylation of MAPK and NF- $\kappa$ B signaling pathways, reduce the level of inflammatory factors, and alleviate the inflammatory response of livestock and poultry; At the same time, *A. lancea* can reduce the level of ROS and oxidative stress damage in animals by regulating the Nrf2-Keap1 signaling pathway; *A. lancea* can also inhibit the TLR signaling pathway to exert antiviral function. Adding *A. lancea* to animal diet can improve their growth performance and immunity, improve intestinal health and relieve heat stress. In addition, *A. lancea* can also be used as an antibacterial agent and analgesic, which has important application prospects in livestock and poultry production. However, the production process of *A. lancea* still needs to be optimized. Therefore, in the future, we should further develop *A. lancea* as a feed additive, promote its application in livestock and poultry production, explore the appropriate amount of addition at different growth stages, so as to promote the development of green ecological farming.

## Author contributions

YG: Funding acquisition, Writing – original draft. DoW: Writing – review & editing, Validation, Software. XM: Software, Writing – review & editing. JL: Supervision, Writing – review & editing. DiW: Supervision, Writing – review & editing. BC: Supervision, Writing – review & editing. XY: Supervision, Writing – review & editing. HL: Resources, Software, Writing – original draft.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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