Artykuł przeglądowy *Review*

Biological activity of *Macleaya cordata* and its application in pig industry*

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Summary

***Macleaya cordata* is rich in alkaloids and exhibits diverse biological activities, which explains its worldwide distribution and utilization. This paper provides an overview of those alkaloids, their solubility and stability, as well as various biological activities, including antibacterial, anti-inflammatory, anticancer, and insecticidal properties. It also focuses on research into *Macleaya cordata* and on the application of that plant and its bioactive components in the pig industry as potential alternatives to antibiotics in feed, as well as in prevention and treatment of diseases, especially diarrhea. This paper reviews the alkaloids contained in *Macleaya cordata*, their biological characteristics and application in the pig industry, hoping to provide a valuable reference for further research on the utilization of *Macleaya cordata* and its bioactive ingredients in the pig industry and in animal husbandry in general.**

Keywords: *Macleaya cordata*, alkaloids, biological activities, pig industry

The administration of antibiotics can effectively inhibit or eradicate pathogenic microorganisms, thereby preventing and controlling animal diseases, reducing morbidity and mortality rates, as well as promoting animal growth. The utilization of antibiotics in animal husbandry facilitates the development of intensive farming practices, safeguards animal health, and yields substantial economic benefits to the industry. However, the misuse of antibiotics gives rise to a range of issues, including drug residues and environmental pollution, as well as decreased immunity and bacterial resistance, which have sparked widespread concern among the public. The use of antibiotics in animal feed is being restricted or banned by an increasing number of countries and regions. The European Union (EU) initiated the regulation of antibiotic use in 1973. In 2006, all EU member states officially implemented a ban on the inclusion of antibiotics in animal feed. Japan and South Korea followed suit in 2008 and 2011, respectively, prohibiting the utilization of antibiotics as growth promoters in animal feed. Since July 1, 2020, China has prohibited the use of growth-promoting drugs other than traditional Chinese medicine in animal feed. The United States introduced the Veterinary Feed Directive (VFD) in early 2015, which mandates veterinary supervision over the application of essential antimicrobials in animal feed and restricts their usage solely to cases when they are necessary to ensure animal health (12). In order to ensure a stable development of global animal husbandry and safeguard human health, it is imperative not only to further regulate antibiotic usage, but also to urgently study and develop effective alternatives. Among the various alternatives available, plant extracts have garnered significant attention in recent years. Plants play a pivotal role in numerous medicinal practices, such as Chinese traditional medicine, Ayurvedic medicine, or Unani medicine. The utilization of medicinal plants continues to be prevalent today, with an estimated 80% of the global population

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relying on herbal products and supplements as their primary sources of medication. In the United States, approximately 18% of adults and 5% of children have utilized natural products (8, 16).

The perennial herb *Macleaya cordata*, belongs to the genus *Macleaya*, which comprises two species: *Macleaya cordata* (Wild.) R. Br. and *Macleaya microcarpa* (Maxim.) Fedde. It grows in North America, East Asia, and Europe. In North America, it is distributed mainly in the northern temperate zone, east of the Mississippi River, while in China, it occurs mainly in Shanxi, Guizhou, Yunnan, Jiangsu, Zhejiang, and other middle and lower reaches of the Yangtze River. *Macleaya cordata* is also widely cultivated as an ornamental plant in Europe (33). It is commonly used as a medicine in North America, mainly for the treatment of insect bites and psoriasis. In China, *Macleaya cordata* has a medicinal history of more than 1,000 years. The earliest records of *Macleaya cordata* can be found in *A Supplement to Materia Medica* written by Chen in the Tang Dynasty. In addition, there are records about *Macleaya cordata* in Chinese medicine books such as *Compendium of Materia Medica* written by Li in the Ming Dynasty. According to records of traditional Chinese medicine, *Macleaya cordata* can be used for detoxification, removing congestion, reducing swelling, and killing insects. It is commonly used to treat suppurative infection, scalding, intractable dermatosis, rheumatism and other conditions. The use of *Macleaya cordata* extract as livestock feed has been prevalent in numerous countries for several decades. In Europe, it has obtained approval from the European Food Safety Authority (EFSA) as a permissible ingredient for animal feeding. In China, products containing sanguinarine and chelidonine as primary components have been developed into officially licensed traditional Chinese veterinary drugs and pharmaceutical feed additives (42). In animal husbandry, *Macleaya cordata* and its active ingredients have been used to treat many diseases, such as avian pasteurellosis, piglet colibacillosis, swine salmonellosis, and swine transmissible gastroenteritis. Modern studies have shown that the main bioactive substances in *Macleaya cordata* are isoquinoline alkaloids, such as sanguinarine (SA), chelerythrine (CHE), protopine (PRO), allocryptopine (ALL), and berberine (BER), which have, among others, anti-microbial, insecticidal, antiviral, anti-inflammatory, and anti-tumor activities, in addition to improving liver function and enhancing immunity. As a traditional herbal medicine resource, *Macleaya cordata* has numerous beneficial biological activities due to its alkaloids, which have demonstrated significant efficacy in various research studies and practical applications. Rational development and utilization of this plant is of enormous importance for production and research, especially for reducing the reliance on antibiotics during breeding processes and for eliminating antibiotic supplementation in animal feed (27). This paper reviews the alkaloids contained in *Macleaya cordata*, their biological characteristics and application in the pig industry, hoping to provide valuable insights for further study on their utilization in the pig industry and in animal husbandry in general.

Alkaloids in *Macleaya cordata*

The main active ingredients of *Macleaya cordata* are alkaloids. At present, 147 alkaloids, including SA, CHE, PRO, ALL, and BER, have been identified or isolated from *Macleaya cordata* (23), and, in terms of their chemical structure, most of them belong to the isoquinoline group. The alkaloid content varies in different parts of the plant. According to Zhang et al. (43), the above-ground parts of *Macleaya cordata* exhibited a descending order of alkaloid content for the same growth period and planting area, with fruit having the highest content (2.103%), followed by leaf (1.017%), and stem (0.820%). Zhong (45) discovered that the fruit pod of *Macleaya cordata* contained the highest concentration of alkaloids compared with its roots, stems, leaves. The predominant alkaloid component of the fruit pod was identified as SA. The alkaloid content of *Macleaya cordata* varied depending on the source of the plant, with wild *Macleaya cordata* having higher alkaloid levels than those of cultivated plants (37). The leaf alkaloid profiles also differed between different species of *Macleaya.* Specifically, the leaves of *Macleaya cordata* contained higher amounts of PRO and ALL, whereas the leaves of *Macleaya microcarpa* had higher levels of SA and CHE (11). The stability of alkaloids can be influenced by various factors. Li et al. (19) investigated the solubility and stability of alkaloids in *Macleaya cordata*, revealing that both SA and CHE exhibited excellent solubility and stability in methanol and ethanol solutions. Moreover, these compounds demonstrated remarkable stability in distilled water and rainwater, while their stability was compromised when exposed to tap water. The presence of oxidants exerted a significant influence on the stability of SA and CHE. Notably, SA and CHE remained

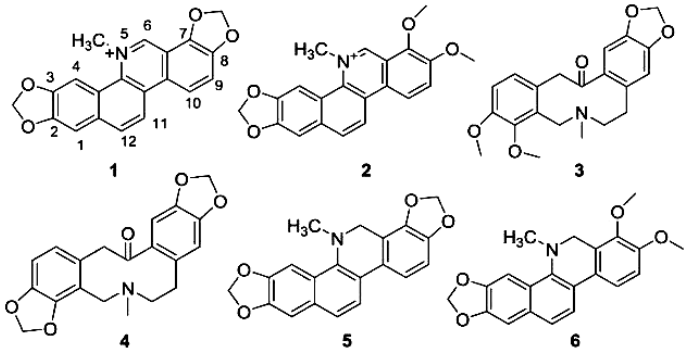

Fig. 1. Structures of sanguinarine (1), chelerythrine (2), allocryptopine (3), protopine (4), dihydrosanguinarine (5), and dihydrochelerythrine (6), abundant benzo[c]phenanthridine alkaloids found in *Macleaya cordata* (16)

stable in a temperature range from room temperature to 54°C. Additionally, SA maintained its stability in a pH range of 2.5~7.0, whereas CHE remained stable in a pH range of 2.5~8.0.

Biological activities of *Macleaya cordata* and its active ingredients

The main active components in *Macleaya cordata* are alkaloids, the most abundant of which are SA, CHE, PRO, and ALL. Modern pharmacological studies have demonstrated that extracts of *Macleaya cordata* and its active ingredients possess significant anti-inflammatory, antibacterial, anticarcinogenic, and antioxidant properties. They also exhibit insecticidal and maggot-killing effects, as well as provide relief from coughs and asthma symptoms. Furthermore, they display analgesic properties and improve liver function as well as intestinal health and immunity.

Anti-inflammatory activity

The occurrence of inflammation, which is an immune response to external stimuli and a crucial part of various pathophysiological processes, can be triggered by tissue damage or microbial invasion. Numerous studies have confirmed the anti-inflammatory properties of the alkaloids found in *Macleaya cordata*. SA exerts an anti-inflammatory effect by inhibiting the activation of the nuclear factor kappa B (NF-κB) and phosphorylation of IκB-α, thereby reducing the expression of inflammatory factors (2). In addition, SA present in *Macleaya cordata* enhances the mRNA and protein levels of Heme oxygenase-1 (HO-1) through the activation of p38 MAPK/Nrf2 pathway in mouse macrophage RAW264.7, causing an increase in antioxidant capacity (35).

The alkaloids present in *Macleaya cordata* are the active constituents of the phytogenic feed additive Sangrovit, which effectively mitigates colonic mucosal damage induced by Dextran sulfate sodium (DSS). This is achieved through a reduction in the expression of Cyclooxygenase-2 (COX-2) triggered by DSS, as well as a significant decrease in myeloperoxidase activity within colon tissue and reduced glutathione levels in erythrocytes (36). Supplementation of broiler feed with plant-derived isoquinoline alkaloids (IQA) resulted in a significant reduction in lesions observed in the duodenum ($P < 0.05$), jejunum ($P < 0.001$), and ileum ($P < 0.001$). This supplementation effectively protects broilers from necrotic enteritis, as demonstrated by Xue et al. (38). *Macleaya cordata* extract (MCE) has a strong anti-inflammatory activity and can significantly reduce the expression of inducible NO synthase in the jejunal mucosa of broilers (15). The inclusion of 50 mg/kg SA in fish feed resulted in a significant reduction in serum IL-1β and IL-6 levels, indicating a favorable anti-inflammatory effect (41).

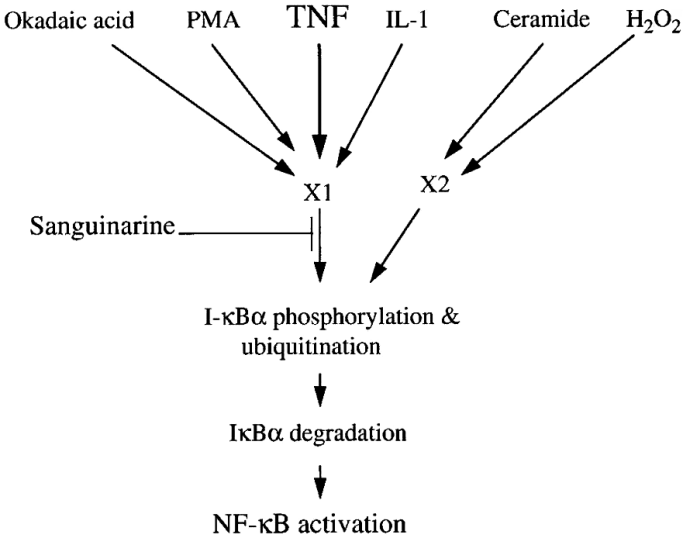

Fig. 2. Site of action of sanguinarine in the pathway leading to NF-κB activation by a variety of agents (2)

Antimicrobial activity

Macleaya cordata contains many alkaloids, such as SA and CHE, which possess antibacterial and antifungal properties. Additionally, MCE and its active alkaloids demonstrate significant antibacterial efficacy. The antibacterial activity of *Macleaya cordata* and its alkaloids is one of the numerous activities exhibited by this plant, and it is particularly important in animal breeding. Investigations of its antibacterial effects contribute to its increased use in animal breeding. A study conducted by Pan et al. (28) revealed that SA and CHE inhibited to a varying degree 12 plant pathogens, with inhibition rates exceeding 50% for 7 pathogens. These findings provide evidence for the broad-spectrum antibacterial properties of SA and CHE. Kosina et al. (17) used standard reference bacterial strains, including *Staphylococcus aureus* CCM 3953, *Staphylococcus aureus* CCM 4223, P*seudomonas aeruginosa* CCM 3955, two strains of *Escherichia coli* (CCM 4225 and CCM 3954), and *Streptococcus agalactiae*, as indicator bacteria in their *in vitro* bacteriostatic tests of *Macleaya cordata* and its alkaloids. The study revealed that the antibacterial activity of PRO or ALL was lower than that of SA and CHE, while the antibacterial activity of MCE increased with higher content of SA and CHE, albeit remaining relatively low.

Zhang et al. (44) investigated the inhibitory effect and minimum inhibitory concentration of MCE for nine commonly used feed probiotics, including *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, and *Enterococcus faecalis*. The findings revealed that the recommended concentration of MCE (60 μg/mL) was significantly lower than the minimum inhibitory concentration required to inhibit the growth of these nine probiotics. These results provide experimental evidence supporting the use of MCE. The antibacterial activity of SA and CHE against drug-resistant

Tab. 1. Minimum inhibitory concentrations (μg mL^{-1}) of *Macleaya cordata* extracts and pure alkaloids for selected bacterial strains (17)

Extract/Alkaloid	*S. aureus* CCM 3953	*S. aureus* CCM 4223	*P. aeruginosa* CCM 3955	*E. coli* CCM 4225	*E. coli* CCM 3954	*S. agalactiae*
Aerial part	125.0	125.0	125.0	125.0	125.0	125.0
Seeds	125.0	125.0	62.5	250.0	62.5	125.0
Capsules	62.5	62.5	62.5	125.0	62.5	125.0
Sanguinarine	31.3	31.3	250.0	31.3	62.5	15.6
Chelerythrine	31.3	31.3	500.0	125.0	125.0	7.8
Protopine	250.0	250.0	125.0	125.0	125.0	125.0
Allocryptopine	250.0	250.0	125.0	125.0	125.0	125.0
Dihydrochelerythrine	N.E.	N.E.	N.E.	N.E.	N.E.	N.E.
Dihydrosanguinarine	N.E.	N.E.	500.0	N.E.	500.0	N.E.

Explanations: CCM – labeling of bacterial strains; N.E. – no effect. MICs of selected antimicrobial agents are published for CCM standard reference bacterial strains directly from standard method used.

bacteria has also been observed. Khin et al. (16) demonstrated that SA and CHE completely inhibited the growth of wild type (Sa1199), methicillin-resistant (Ah1263), and multiply-resistant (IA116) strains of *Staphylococcus aureus* in the concentration range of 3~10 μg/mL, with their antibacterial efficacy being comparable to or even surpassing that of the reference compound chloramphenicol. Li et al. (20) conducted an *in vitro* antibacterial activity assay on *Macleaya cordata* essential oil, and found that the essential oil exhibited significant antibacterial activity against all 10 microorganisms tested, including Gram-positive bacteria, Gram-negative bacteria, fungi, and yeasts. Remarkably, *Staphylococcus aureus* was most sensitive to the essential oil, with a minimum inhibitory concentration (MIC) value of 125 mg/mL. The inhibition zones of the essential oil for *Staphylococcus aureus* had diameters of 17.2 ± 1.2 mm. Analysis of the scanning electron microscopy images revealed significant changes in the cell membrane structure, resulting in severe damage and loss of cellular morphology.

The *in vitro* antibacterial activity and mechanism of Sanguinarine chloride hydrate (SGCH) against *Staphylococcus aureus* CMCC(B)26003 were investigated by Gu et al. (9). The results demonstrated that SGCH was medium-sensitive against *Staphylococcus aureus*, with minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values of 128 and 256 μg/mL, respectively. In the bactericidal activity curve, SGCH at 8 × MIC completely eradicated *Staphylococcus aureus* within 24 h. Furthermore, SGCH was found to disrupt the integrity and permeability of the SA cell wall and membrane.

Investigation of the bacterial inhibitory mechanism of SA revealed that the presence of SA can impede bacterial division by disrupting the assembly dynamics of filamentous temperature-sensitive protein (Fts Z) in the Z ring (1). Additionally, it has the ability to stimulate the release of membrane-bound cellwall autolytic enzymes, ultimately leading to cellular lysis (26). In addition to antibacterial activity, MCE and its active components exhibit inhibitory activity against fungi, including *Trichophyton rubrum*, *Trichophyton schoenleini*, *Trichophyton rosaceum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccos*. Inhibition is particularly evident for five species of *Epidermophyton* pathogenic fungi. Moreover, the strength of inhibition increases with higher concentrations (34). Sanguinarine hydrochloride exhibits a broad spectrum of bacteriostatic activity and exerts a potent inhibitory effect, with a minimum bacteriostatic concentration of less than 40 μg/mL, against *Aspergillus niger*, *Trichoderma*, *Aspergillus oryzae*, *Rhizopus*, *Mucor*, *Aspergillus flavus*, and yeast. Additionally, MCE demonstrates inhibitory activity against *Penicillium digitatum*, responsible for postharvest rot in citrus fruits, with an inhibitory zone diameter of 30.02 mm (5).

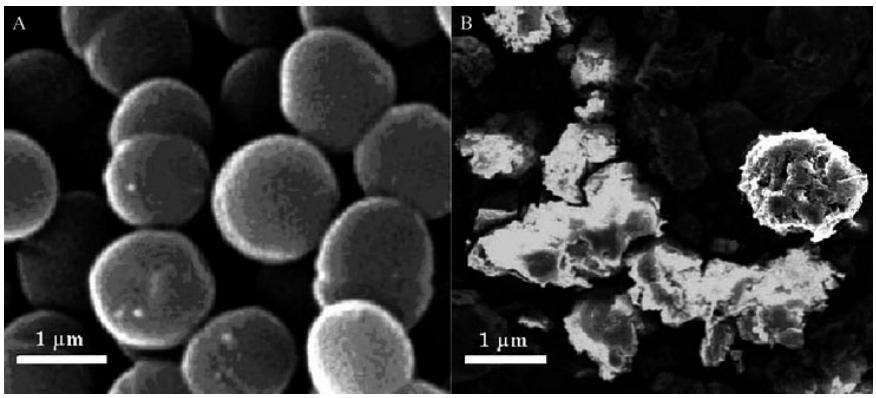

Fig. 3. Action of the essential oil of *Macleaya cordata* on the structures of *S. aureus* cells observed by SEM (20)
Explanations: (A) cell structure of native *S. aureus* (B) cell structure of *S. aureus* treated with 100 mg/mL essential oil.

Anticancer activity

The efficacy of *Macleaya cordata* alkaloids in inhibiting cancer cell pro-

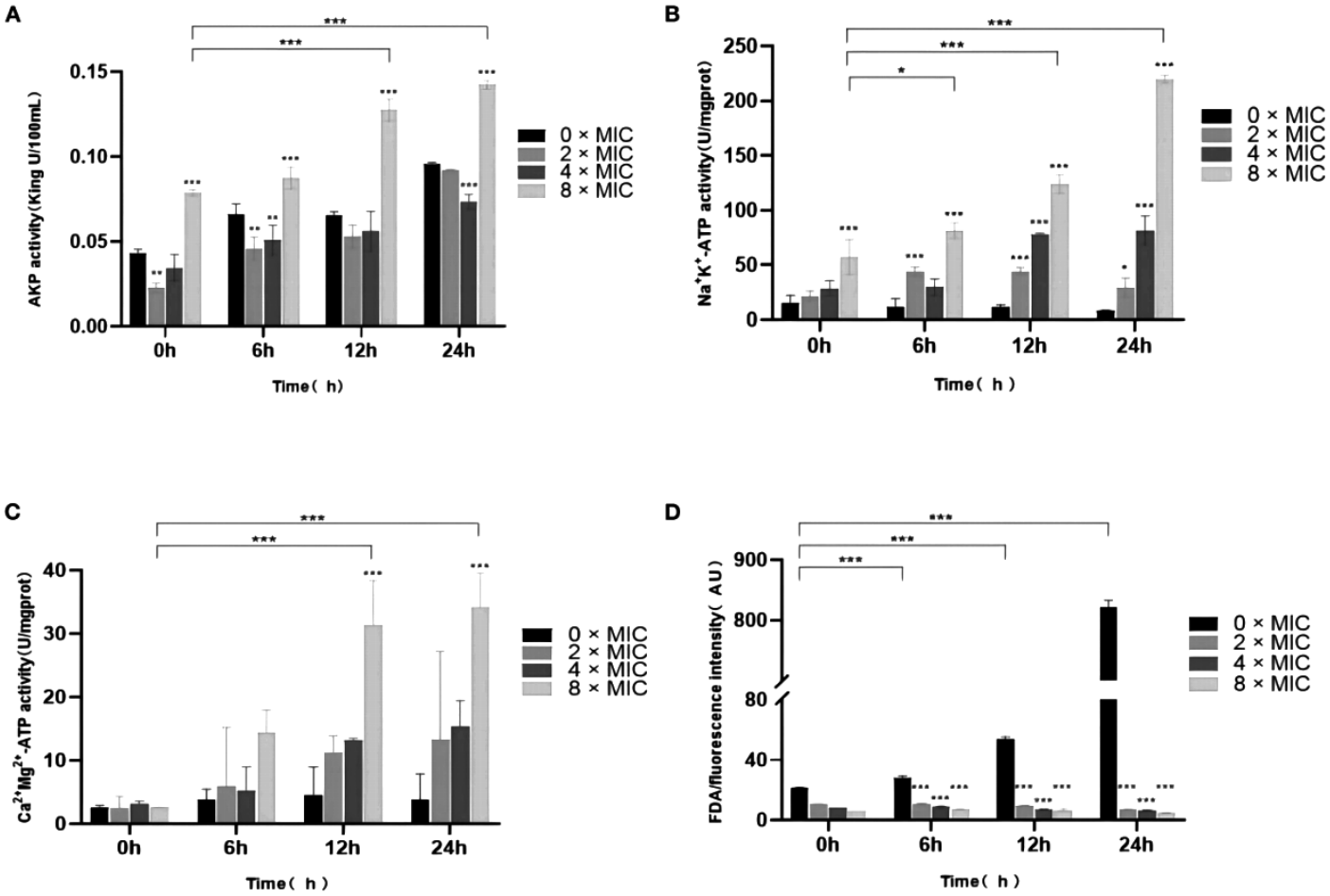

Fig. 4. E^+ K^+, Ca^{2+} Mg^{2+}-ATP activities and FDA of SA

Explanations: (A) Impact of SGCH on AKP activity of SA. (B) Determination of SA Na^+ K^+-ATP activity by SGCH. (C) Determination of SA Ca^{2+} Mg^{2+}-ATP activity by SGCH. (D) Fluorescein diacetate (FDA) staining experiment. *$p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$ (9)

liferation and their *in vivo* and *in vitro* anti-cancer effects have been substantiated by several studies. PRO and CHE exhibited potent inhibitory activity against the growth of human promyelocytic leukemia cells (HL-60), human lung cancer cells (A-549), and human breast adenocarcinoma cells (MCF-7), which are representative of acute myeloid leukemia, human lung cancer epithelial cells, and human breast cancer cells, respectively. Notably, the inhibition of the proliferation of HL-60 cells by these compounds may be attributed to the induction of apoptosis through a mitochondria-related pathway that disrupts S phase cell cycle progression (31, 32). The administration of SA can stimulate the generation of reactive oxygen species -dependent ceramide (Cer) and dephosphorylation of AKT, thereby inducing apoptosis in human leukemia cells. Additionally, SA can trigger reactive oxygen species-dependent phosphorylation of extracellular signal-regulated kinase 1/2 (ERK1/2) and division of the prostate apoptosis response factor-4 (Par-4), leading to apoptosis in human prostate cancer cells (30). Colorectal cancer (CRC) is the third most prevalent and deadly cancer in the United States as of 2017. Overexpression of serine-threonine kinase receptor-associated protein (STRAP) and maternal embryo leucine zipper kinase (MELK) may serve as markers for CRC. SA can dephosphorylate STRAP and MELK, inhibiting their interaction and triggering intrinsic apoptosis (7). The cytotoxic activity of extracts from different parts of *Macleaya cordata* on cancer cells shows significant variation, attributed mostly to their different alkaloid composition. Furthermore, the synergistic interplay between these alkaloids can influence the overall efficacy of the extracts. Notably, MCE from the leaf demonstrates remarkable cytotoxicity against human pharyngeal squamous carcinoma cells (FaDu), human tongue squamous carcinoma cells (SCC-25), and the human breast adenocarcinoma cell line (MCF-7). MCE exhibited the highest cytotoxic activity against the human triple-negative breast denocarcinoma cell line (MDA-MB-231). At a concentration of 100 μg/mL, the cytotoxic activity of MCE was superior to that of the anticancer drug etoposide against Fadu, SCC-25, MCF-7, and MDA-MB-231 (29).

Insecticidal activity

Studies have found that the alkaloids of *Macleaya cordata* can kill or repel various agricultural pests, such as tobacco aphids, *Ectropis obliqua hypulina* Wehrli, *Plutella xylostella* (Linnaeus), and *Pieris rapae*.

Furthermore, it exhibits insecticidal activity against a wide range of other insects, including flies, maggots, and fecal nematodes (10). Four isoquinoline alkaloids, namely SA, CHE, PRO, and ALL, were isolated from the crude alkaloid extract of the aerial parts of *Macleaya cordata* by Kui et al. (18). Among them, SA, CHE, and ALL exhibited nematocidal activity against *Bursaphelenchus xylophilus*, *Caenorhabditis elegans*, and *Meloidogyne incognita*. Three alkaloids, SA, CHE and ALL, showed nematicidal activity with median lethal concentration (LC_{50}) values of 28.52, 34.50, and 37.45 μg/ml, respectively, against *Bursaphelenchus xylophilus*; 22.78, 40.25, and 38.90 μg/ml, respectively, against *Caenorhabditis elegans*; and 67.52, 61.00, and 76.56 μg/ml, respectively, against *Meloidogyne incognita* at 24 h.

The ciliate *Ichthyophthirius multifiliis* is one of the most pathogenic parasites of fish maintained in captivity. *In vitro* antiparasitic efficacy tests showed that SA was 100% effective against *Ichthyophthirius multifiliis* at a concentration of 0.7 mg/L, with LC_{50} and LC_{90} values of 0.437 and 0.853 mg/L, respectively, after 4 h of exposure. *In vivo* antiparasitic efficacy tests showed that the number of *Ichthyophthirius multifiliis* on the gills in the treatment group (in 0.9 mg/L SA) was reduced by 96.8%, in comparison to the untreated group at 25°C after 48 h (39). Ke et al. (13) tested the molluscicidal activity of alkaloids extracted from different parts of *Macleaya cordata*. The alkaloid component AN2 was found to be most toxic against the snail *Oncomelania hupensis*, with 48 h LC_{50} and LC_{90} values of 6.35 mg/L and 121.23 mg/L, respectively. These results indicated that AN2 not only inhibited protein synthesis and respiratory chain oxidative phosphorylation, but also caused hepatocellular injury and reduced the detoxifification ability of the liver, which resulted in the death of *Oncomelania hupensis*.

Later, Ke et al. (14) extracted quaternary benzo[c] phenanthridine alkaloids (QBAs) from the *Macleaya cordata* fruit. In the treatment of *Oncomelania hupensis* with QBAs, the lethal concentration (LC_{50}) was 2.89 mg/L for 48 h and 1.29 mg/L for 72 h. The molluscicidal activity of QBAs was close to that of niclosamide (ethanolamine salt), indicating that QBAs have a potential development value as novel biogenic molluscicides. Further analysis of the mechanism of physiological toxicity showed that glutathione S-transferase (GST), carboxylesterase (CarE), alkaline phosphatase (AKP), and acid phosphatase (ACP) activity in the liver of snails treated with LC_{50} of QBAs for 120 h decreased by 62.3%, 78.1%, 59.2%, and 68.6%, respectively. These enzymes were seriously inhibited by QBAs, and the detoxification and metabolic functions of the liver gradually weakened, leading to poisoning, which could have been the main cause of the death of *Oncomelania hupensis*.

The utilization of *Macleaya cordata* and its bioactive compounds in the pig industry

Antibiotics have long played a pivotal role in ensuring and promoting the advancement of the swine industry. However, the escalating issue of antibiotic misuse has become increasingly evident, impeding the sustainable development of this sector. Researching and employing antibiotic alternatives is an efficacious approach to ensuring a robust, enduring, and sustainable growth of the pig industry. Herbal extracts possess the inherent attributes of being derived from nature, exhibiting minimal toxicity, leaving negligible residues, and not inducing resistance, which makes them optimal substitutes for antibiotics. Over an extended period of time, numerous studies have consistently demonstrated that *Macleaya cordata* extract and its active constituents exhibit antibacterial, anti-inflammatory, antioxidant, anticancer, and insecticidal properties, while also protecting the liver, enhancing immunity, and promoting growth. The investigation of MCE and its active constituents as potential alternatives to antibiotics in pig farming has significant research value and production implications. *Macleaya cordata* and its bioactive compounds have the potential to enhance growth performance at various stages of pig development, while also serving as effective prophylactic and therapeutic agents against diseases prevalent in the pig industry. In the white scour of piglets, the cure rate of *Macleaya cordata* oral liquid was 26.7% higher than those of penicillin and streptomycin, and 13.3% higher than that of a 2% Norfloxacin injection (40). Man et al. (25) discovered that the inclusion of MCE in the diet of weaned piglets resulted in a significant increase in serum IgG and NO levels, as well as enhanced lysozyme (LSZ) activity. This improvement in immune response not only significantly enhanced disease resistance, but also positively affected growth performance. Remarkably, the efficacy of MCE surpassed that of oxytetracycline. When investigating the application of MCE in piglet feed, Li et al. (21) discovered that the supplementation of MCE at 5.0 mg/kg significantly enhanced piglets' average daily gain and feed intake ($P < 0.05$), while simultaneously reducing the feed to gain ratio ($P < 0.05$). Furthermore, MCE caused a significant improvement in the serum levels of IgG and LSZ in weaned piglets ($P < 0.01$), along with a notable reduction in serum MDA content ($P < 0.01$). Liu et al. (24) observed that the inclusion of MCE supplements at 40 mg/kg in the diet of growing piglets improved intestinal barrier function by reducing diarrhea incidence and increasing levels of ZO-1 and Claudin-1 in the jejunum.

Liang et al. (22) conducted a pharmacokinetic study on the oral and rectal administration of SA to pigs, which revealed a rapid absorption and metabolism of SA, with elimination occurring within approximately

2 hours. However, its metabolite dihydrosanguinarine (DHSA) exhibited an extended retention time in the body. Goodarzi et al. (8) demonstrated that dietary supplementation of MCE at 120 mg per kg could enhance the growth performance and nutrient digestibility of weaned piglets, while causing no significant jejunal histomorphological changes. Chen et al. (4) investigated the impact of dietary supplementation with Sangrovit, containing a minimum SA content of 1.5%, on the growth performance, intestinal morphology, intestinal flora, and metabolites of early weaned piglets. The results indicated that SA supplementation has the potential to enhance both growth performance and intestinal morphology in early weaned piglets, while positively influencing the intestinal environment. Chen et al. (3) discovered that the inclusion of MCE in the diet increased the average daily gain and decreased the feed to gain ratio and the diarrhea rate of weaned piglets during a 21-day feeding trial. Furthermore, serum IgG levels were significantly higher ($P < 0.05$) in MCE-fed piglets compared to control piglets. Additionally, MCE supplementation led to a significant increase ($P < 0.05$) in serum total antioxidant capacity (T-AOC), glutathione peroxidase (GSH-Px), and superoxide dismutase (SOD) activity when compared to the control group. The inclusion of MCE significantly increased the abundance of *Lactobacillus* spp. ($P < 0.05$), while decreasing the prevalence of *Salmonella* spp. ($P < 0.05$) and showing a tendency to reduce the population of *Escherichia coli* ($P < 0.10$). Dietary supplementation with MCE increased the villus height and improved the villus height to crypt depth ratio in the duodenum, jejunum, and ileum, as well as reduced the crypt depth in the jejunum of piglets ($P < 0.05$).

Zhukova et al. (46) discovered that the administration of *Macleaya cordata* supplements exclusively during 30 and 60-day studies significantly increased the erythrocyte count, by 16.7% and 23.2%, respectively ($P < 0.05$), and hemoglobin concentration, by 30.7% and 37.9%, respectively ($P < 0.01$). Additionally, this supplementation activated anaerobic glycolysis, which was demonstrated by a substantial rise in glucose concentration, ranging from 96.4% to 48.0% ($P < 0.01$), lactate levels increasing by 71.4% to 55.2%, ($P < 0.01$), an increase in lactate dehydrogenase activity of 18.6% to 29.4% ($P < 0.05$), and a reduction in pyruvate.

Tab. 2. Effects of dietary MCE supplementation on the immune response of weaned piglets (3)

	Treatments[#]				
Items[*]	Control	MCE	ABO	SEM[†]	P-value
IgA, g/L	1.77	1.53	1.66	0.28	0.743
IgG, g/L	6.77[b]	11.53[a]	6.86[b]	1.01	0.017
IgM, g/L	0.63	0.78	0.65	0.05	0.275

Explanations: * IgA – Immunoglobulin A; IgG – Immunoglobulin G; IgM – Immunoglobulin M. [#] Treatments consisted of (1) Control; basal diet, (2) MCE – basal diet + 50 mg/kg MCE and (3) ABO – basal diet + 20 mg/kg flavomycin + 100 mg/kg aureomycin. [†] SEM – pooled standard error of mean. a, b – Means with different superscripts in the same row differ significantly ($P < 0.05$).

Macleaya cordata exhibits numerous important biological activities, including anti-inflammatory, antibacterial, anticancer, and insecticidal properties. In the pig industry, both *Macleaya cordata* and its active constituents can mitigate inflammatory responses, regulate the intestinal flora balance, enhance intestinal barrier function, reduce diarrhea incidence rates, as well as improve immunity levels and productivity. Further investigation of *Macleaya cordata* and its active components as potential alternatives to antibiotics in the pig industry, as well as in animal husbandry in general, has significant scientific value and production implications for clinical disease control and treatment.

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