

China Invention Patent 201710549846.4
Liaoning Feed Additive No. (2018) H14002

Fatenicon™

The gastrointestinal protector
for antibiotic replacement,
diarrhea prevention,
and African Swine Fever prevention

 UNIVET

肥育康™

有效替抗止泻的胃肠保护剂
替抗 · 替锌 · 防非瘟



 联合华康

About UNIVET China

联合华康(北京)生物科技有限公司

As a nationwide feed additive research group, UNIVET is a joint venture that harnesses the innovative power of its employees to develop high-quality pharmaceutical raw materials, intermediates, veterinary medicines, and feed additives.

It is an exciting time for our company. We established a wide range of technical cooperation networks with Chinese Academy of Sciences, Chinese Academy of Medical Sciences, Chinese Academy of Agricultural Sciences, and University of Illinois at Urbana-Champaign.

Now, we are accelerating the development and promotion of the gastro-intestinal protector, quaternary ammonium oxytetracycline, and acetyl creatine. For the fiscal year 2018, Univet has declared four national invention patents and a national class II new veterinary medicine.

At the end of 2017, UNIVET established UNIVET Liaoning, a production base with 8,000 sqm workshop and 4,000 sqm R&D center. Currently, the factory is mainly engaged in the production of the gastrointestinal protector Fatenicon™, and the promotion of premixes.

UNIVET has always been a reliable innovator of animal health products. Together with our colleagues around the globe, we look forward to creating a more sustainable world for generations to come.



UNIVET Liaoning Production Base

Fatenicon™ 肥育康™

A product of Science and Technology Innovation Project at Chinese Academy of Agricultural Sciences

In October 2017, UNIVET submitted patents for the core technology of Fatenicon™ to the State Intellectual Property Office. The patent number is 201710549846.4. In 2019, the Research of Zinc Oxide Substitutes for Weaning Piglets was listed in the Science and Technology Innovation Project at CAAS. UNIVET led the project and was granted exclusive rights.



Active Ingredients

Cinnamaldehyde 10% + Seaweed Polysaccharide (Patented formula)

Introduction

Fatenicon™ is a condensation preparation of seaweed polysaccharide calcium and cinnamaldehyde. The product is derived from the researches of by UNIVET, which analyzed the mechanism of traditional zinc oxide products for diarrhea control.

Fatenicon™ enhances the function of digestive juices, forms powerful protective barriers, and prevents harmful microorganisms from proliferating in digestive tracts. The product effectively alleviates gastrointestinal inflammatory reactions caused by macromolecular protein antigens and harmful microorganisms, reducing the incidence of gastroenteritis. Fatenicon™ controls diarrhea and promote animal growth.

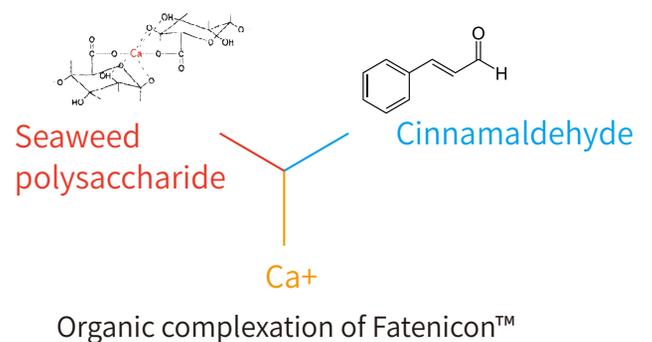
When viruses invade digestive tracts, they destroyed intestinal tissue cells enter the blood circulation, so the gastrointestinal protection is crucial. Fatenicon™ efficiently protects digestive tracts and reduces the incidence of African Swine Fever.

The Chemical Barrier of Fatenicon™

The crystal structure of seaweed polysaccharide in Fatenicon™ is polygonal. This structure enables multiple linear molecules to interact, bond, and crosslink to form a grid-like framework. It promotes and regulates the formation of covalent and ionic bonds between polymer molecular bonds.

Fatenicon™ has a self-supporting polymer dispersion system, which shows both fluidity and shape retention ability. It maintains high affinity with digestive juices through ionic bonding. This function makes Fatenicon™ tightly adhering to the surface of the intestinal mucosa and enhancing intestinal mucosal toughness. Through hydrogen bonding, Fatenicon™ promotes the formation of chyme and reduces the symptoms of diarrhea caused by congenital or exogenous digestive juice deficiency.

Fatenicon™ forms a protective layer on intestinal mucosa, relieving the symptoms of diarrhea. This barrier prevents harmful microbes from replicating and reproducing in intestinal epithelial cells. Fatenicon™'s seaweed polysaccharide component can bind to the glycoprotein on the surface of the virus, blocking the binding site between the virus and the cell receptor, and preventing the infection of the virus.

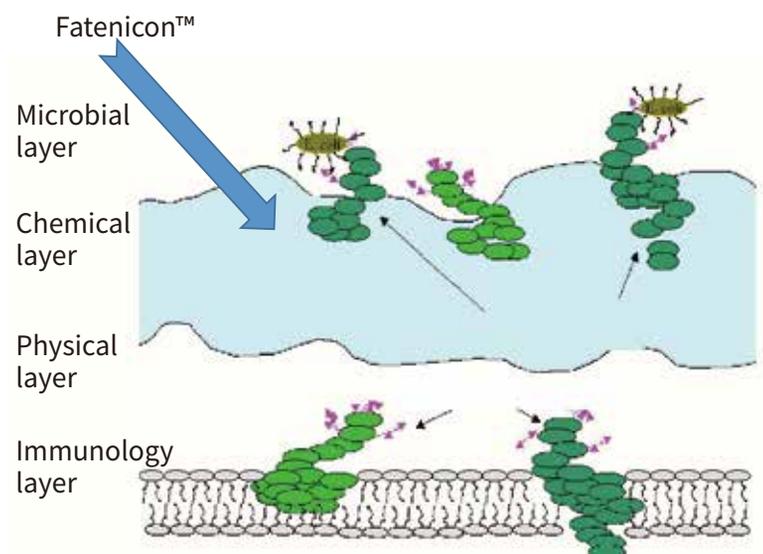


The image on the right shows the process by which mucin in the chemical layer prevents E. coli from adhering to the intestinal mucosa.

The chemical layer maintains a lateral pH gradient in the intestinal tract, preventing the erosion of the intestinal mucosa by acids and proteases, and providing a suitable living environment for the healthy flora.

However, the chemical layer may be degraded by mechanical forces, endogenous microflora, and pepsin, which increases the absorption of macromolecular antigens and adhesion of microbial organisms.

Fatenicon™ is a powerful supplement to the chemical layer.



Strong Antibacterial Activity of Fatenicon™

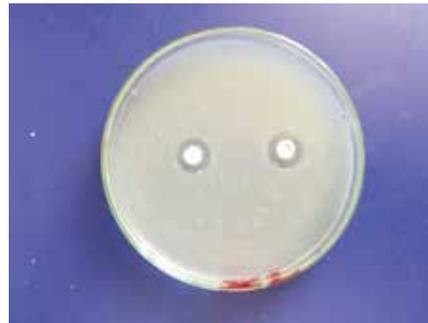
Among the popular antimicrobial plant essential oils, plant aldehydes show the strongest antibacterial activity. Plant aldehydes can alkylate the hydroxy, carboxy, and amino groups of the bacterial protein, causing coagulation and death of the protein. The antibacterial effect of plant aldehyde is broad-spectrum and efficient. In the antibacterial medium in vitro, when the concentration of cinnamaldehyde reaches 1000ug/mL, most bacteria can be killed within 2 hours.

The new preparation process of Fatenicon™ ensures the stability of cinnamaldehyde in the digestive tract, avoids the loss during digestion, and reduces the irritation. The cinnamaldehyde of Fatenicon™ can be carried along with the polysaccharide. By the affinity of the mucus, its concentration can reach 1% on the surface of the intestinal mucosa, which can effectively kill harmful microorganisms and ensure the normal function of the digestive system. This concentration is much higher than that of traditional coated plant essential oil products.

E. coli ATCC25922 / *S. aureus* CMCC(B)26003, Shanghai Luwei Tech.

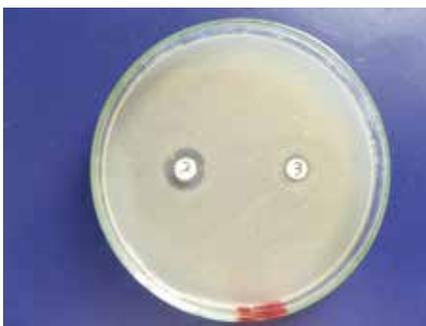


E. coli inhibition zone
 ① Cinnamaldehyde 1% Φ 10.52mm
 ② Fatenicon™ 10% (Cinn. 1%) Φ 12.05mm



S. aureus inhibition zone
 ① Cinnamaldehyde 1% Φ 11.44mm
 ② Fatenicon™ 10% (Cinn. 1%) Φ 11.99mm

The anti-G- and G+ controls showed Fatenicon™ retained the antibacterial activity of the original cinnamaldehyde.



E. coli inhibition zone
 ② Fatenicon™ 10% (Cinn. 1%) Φ 10.93mm
 ③ Colistin sulfate 0.02% Φ 8.57mm

The anti-G- effect of cinnamaldehyde 1% was slightly better than that of colistin sulfate 0.02%, which is similar to the conclusions in papers.



S. aureus inhibition zone
 ② Fatenicon™ 10% (Cinn. 1%) Φ 16.87mm
 ⑤ Guitarmycin 0.02% Φ 22.95

The anti-G- effect of cinnamaldehyde 1% was sensitive, but that of guitarmycin 0.02% is better.

Competitive analysis

Aldehyde disinfectants show better broad-spectrum efficiency.

Feature	Disinfectant						
	Aldehyde	QAS	Chlorine	Iodine	Peroxide	Phenol	Alcohol
Killing Bacteria	++	++/+	+	+	++	++	++
Killing Enveloped Viruses	++	±	+	+	+	±	+
Killing Non-Enveloped Viruses	+	×	+	±	±	×	×
Killing Mold	+	±	+	+	±	+	±
Killing Spores	+	×	+	×	+	×	×
Interfered with Organic Matters	×	√	√	√	√	×	√
Interfered with Soap	×	√	×	×	×	×	×

++ : High activity +: Medium activity ±: Low activity

Source: Iowa State University

E. coli ATCC25922 / *S. aureus* CMCC(B)26003, Shanghai Luwei Tech.



E. coli inhibition zone
 ① Cinnamaldehyde 1% Φ 10.21mm
 ④ Glutaraldehyde 1% Φ 32.99mm



S. aureus inhibition zone
 ① Cinnamaldehyde 1% Φ 12.13mm
 ④ Glutaraldehyde 1% Φ 34.04mm

Experiments have shown that cinnamaldehyde 1% is sensitive to G+ and G-, while glutaraldehyde 1% is extremely sensitive. This result is consistent with other related papers that the ability of glutaraldehyde is 10 times that of other aldehyde disinfectants. Glutaraldehyde 2% disinfectant can kill viruses in 30 minutes, while other aldehyde disinfectants 1% can kill viruses within 2 hours.

Fatenicon™ shows a unique advantage of enhancing the intestinal mucosal protective barrier and eliminate the threat of viruses with the functions of cinnamaldehyde.

Safe and Effective

Hebei Jingdian Group Experimental Farm 2017.11.25 - 2017.12.10

We selected two litters of 30-day-old weaned piglets and divided them into two groups. Each group contained five piglets from the same sow.

* Fatenicon™ group does not use antibiotics in feed.

Group	Initial Wt kg	End Wt kg	Daily gain g	Daily Intake g	Feed Conversion	Diarrhea Rate
Fatenicon™ 1.5kg	8.18	15.44	484.44	788.52	1.63	-
Zinc Oxide 3kg	8.18	14.47	419.63	739.44	1.77	-

Jiangxi Ganzhou 2017.10.6 - 2017.10.23

We selected 100 piglets of 5-week-old and divided them into two groups, three repetitions in each group. In each group, two repetitions contained 20 piglets, while the other one contained 10 piglets. Free feeding.

Group	Initial Wt kg	End Wt kg	Daily gain g	Daily Intake g	Feed Conversion	Diarrhea Rate
Fatenicon™ 1.2kg	8.80±1.31	18.62±2.45	555.56±63.31	802.78±80.16	1.48±0.05	0.67%
Zinc Oxide 2.5kg	8.17±1.25	16.32±2.08	460.00±50.00	740.00±90.88	1.60±0.06	1.00%

Jiangxi Experimental Farm 2019.1.17 - 2019.1.27

We selected 60 Duroc-Landrace-Yorkshire piglets from four columns. These piglets were randomly divided into 2 groups, each group of 2 repetitions, each repetition of 15 heads.

Group	Initial Wt kg	End Wt kg	Total Gain kg	Daily gain g	Intake kg	Feed Conversion	Diarrhea Rate
ZnO 2 kg + Covered ZnO 1 kg	9.83	13.90	4.07	0.37	4.168	1.02	0
ZnO 2 kg + Covered ZnO 1 kg	10.07	14.36	4.29	0.39	4.997	1.16	0
ZnO 2 kg+ Fatenicon™ 1kg	11.73	17.01	5.28	0.48	5.256	1.00	0
ZnO 2 kg+ Fatenicon™ 1kg	10.82	15.66	4.84	0.44	5.058	1.05	0

Fatenicon™ for different animals

In addition to cinnamaldehyde, we have modified the patented seaweed polysaccharide formula and added other components to suit the non-antibiotic needs of different animals. We carefully calculated the costs and returns of our product for animals. In China, we also set up a nationwide market network to provide localized solutions for animal feeders and feed producers, from antibiotic replacement guide to in vivo and in vitro prevention strategies for African swine fever.

For different animals, Fatenicon™ protects the gastrointestinal mucosa against bacteria and viruses. The product kills pathogenic microorganisms in the intestinal mucosa and reduces digestive diseases such as gastroenteritis and gastritis. It can partly or totally replace antibiotics in animal feed. Since China will forbid antibiotics from the beginning of 2020, Fatenicon™ will be a competitive antibiotic alternative for a wide range of animals.

Instructions

The table below listed the recommended dosage of Fatenicon™ in different animals. All of the numbers are carefully tested in the laboratory and by users. Fatenicon™ passed the toxicity test in Chinese Academy of Agricultural Sciences. The result shows that Fatenicon™ is safe even under large additions.

Animal		Dosage (mg/kg feed)
Pigs	Creep Feeding	2000 - 2500
	Nursery Feeding	1000 - 1500
	Fattening	500 - 1000
Chicken		150 - 300
Cattles		500 - 1000
Foxes		500 - 1000
Fishes		300 - 500

Fatenicon™ replaces Zinc Oxide

The single-use or reasonable compatibility of Fatenicon™ can effectively reduce the use of zinc oxide, eliminate the side effects of zinc oxide, and maintain the excellent anti-diarrhea effect. Through in vitro biomimetic safety evaluation, we obtained a qualitative description of the compatibility of Fatenicon™ with traditional zinc oxide products with NPI Chemical Laboratory.

Safety		Fatenicon™ (g/T feed)			
		0	500 (Creep)	1000(Creep)	1500(Nursery)
Zinc Oxide * (g/T feed)	3000	Green	Green	Green	Green
	2500	Yellow	Green	Green	Green
	2000	Orange	Green	Green	Green
	1500	Red	Yellow	Green	Green
	1000	Red	Orange	Green	Green
	500	Red	Red	Yellow	Green
	0	Red	Red	Orange	Green

Qualitative description matrix for in vitro biomimetic safety rating.
NPIC / UNIVET 2017.9

■ Safest
 ■ Medium
 ■ Average
 ■ Dangerous

The zinc oxide used in the test was feed grade, ZnO content $\geq 95\%$, Zn content $\geq 80\%$ ($Pb \leq 0.002\%$, $Cd \leq 0.0008\%$, $As \leq 0.05\%$), and 98% passed the 150 μ m test sieve.



Bacteria Attack Simulation for Fatenicon™ and Zinc Oxide in Piglet Feed

UNIVET Beijing North Laboratory 2018.1.29

Materials and Methods

We inoculated the chyme through different groups to simulate bacterial attacks and compare the damage degree of bacteria on the Fatenicon™ and zinc oxide chyme.

The test used Escherichia coli and Staphylococcus aureus from Shanghai Ruichu Co., Ltd. Zinc oxide is of analytical grade ($ZnO \geq 99\%$).

Test Results

E. coli Attack Simulation

Sample \ Compound Feed (ppm/T)	3000ppm	1500ppm	1200ppm
Fatenicon™	—	Good	Medium
Zinc Oxide	Poor	—	—

S. aureus Attatck Simulation

Sample \ Compound Feed (ppm/T)	3000ppm	1500ppm	1200ppm
Fatenicon™	—	Good	Medium
Zinc Oxide	Average	—	—

Result analysis

This experiment examined the extent of damage to Fatenicon™ and zinc oxide by bacterial challenges in vitro. Among them, the chyme of S.aureus attack is thicker that of E.coli attack. As the concentration of bacteria increased, the surface layer of the zinc oxide group showed hardening. This phenomenon causes zinc oxide to detach from the surface of the intestinal mucosa, resulting in physical damage. The experiment shows that when harmful bacteria reach a specific concentration, the mucous tissue of the intestinal mucosa can be destroyed, and the zinc oxide loses the intestinal protection function.

The Fatenicon™ group showed good chyme complexing ability under the attack of bacteria with different amounts and concentrations. However, with the decrease in the quantity, although the Fatenicon™ group did not show surface hardening, the safety was reduced. Antibacterial substances can only be destroyed when they reach a specific concentration in the mucus of the digestive tract, not in vitro. This test supports Fatenicon™ to replace antibiotics in animals.

Antidiarrheal Test

Zhaojiawa Village, Lulong County, Hebei 2018.12.10

Overview



Day 1
Dec. 10, 2018

Day 2
Dec. 19, 2018

Day 3
Dec. 10, 2018

This litter of piglets was raised five days after birth. All the piglets had diarrhea on day 40. The feeder mixed 0.3% of Fatenicon™ in the feed. No diarrhea was observed by naked eyes after three days.

Moheishi Village, Lulong County, Hebei 2018.11.28

Overview



Day 1
Nov. 26, 2018

Day 2
Nov. 27, 2018

Day 3
Nov. 28, 2018

All the piglets in the litter had diarrhea at the weight of 16kg. The feeder mixed 0.2% of Fatenicon™ in the feed. No diarrhea was observed by naked eyes after three days.



The Reliable Innovator.™

UNIVET China

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