



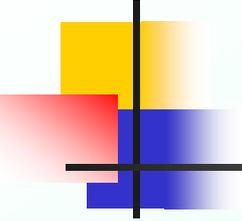
# Approach to Authorization of novel technologies on alternatives to antibiotic in China

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**Deputy President  
President  
General Director**

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National Feed Industry Economy Committee  
Feed Research Institute of the CAAS**

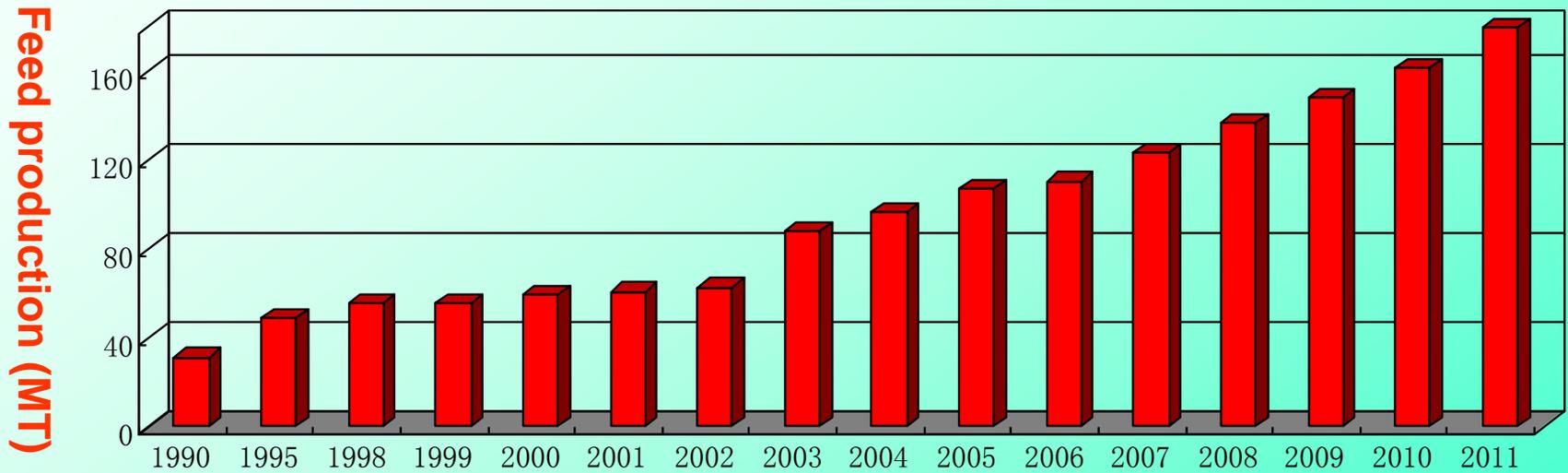




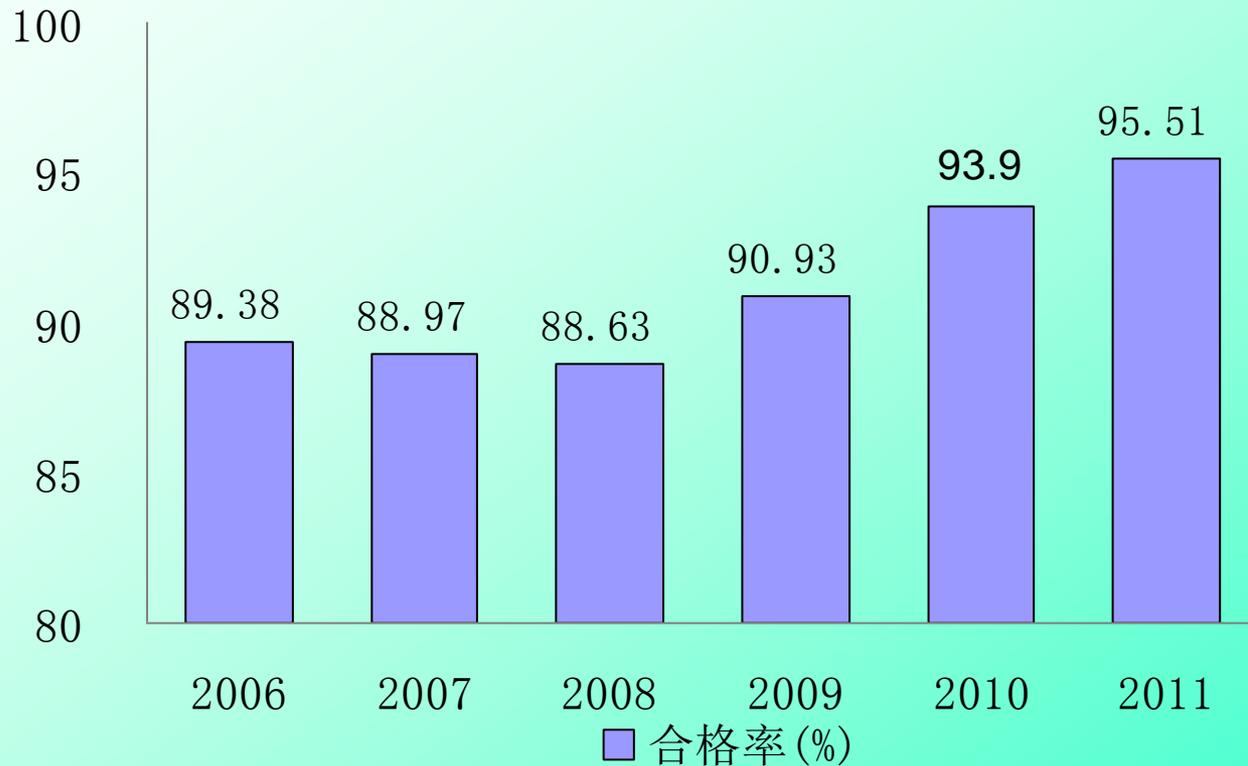
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# **1. Animal husbandry and feed industry of china**

# Feed production (MT) in China (1990-2011)

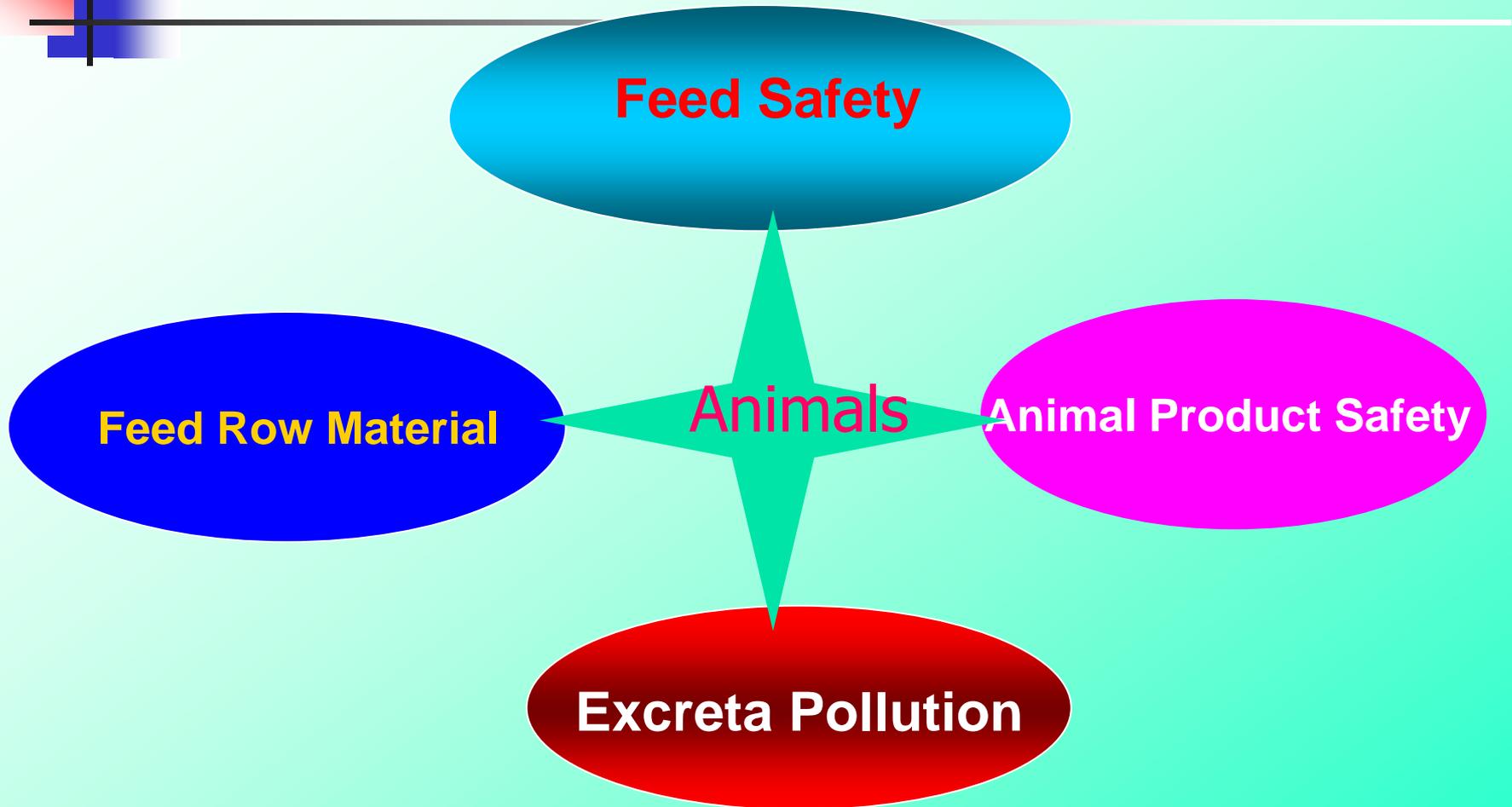


# Compound feed product pass rate are steadily increasing

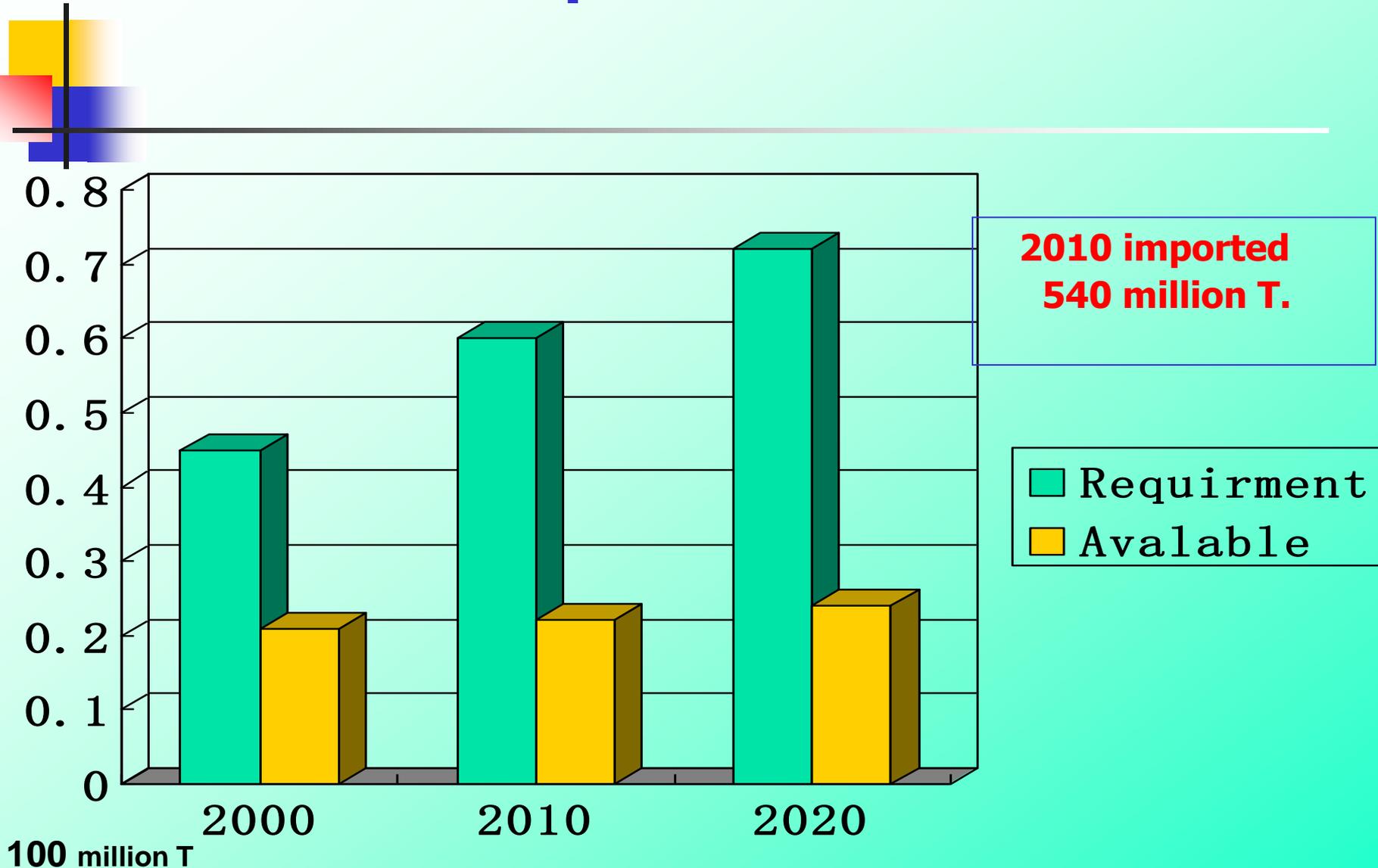


● **Feed quality improved**

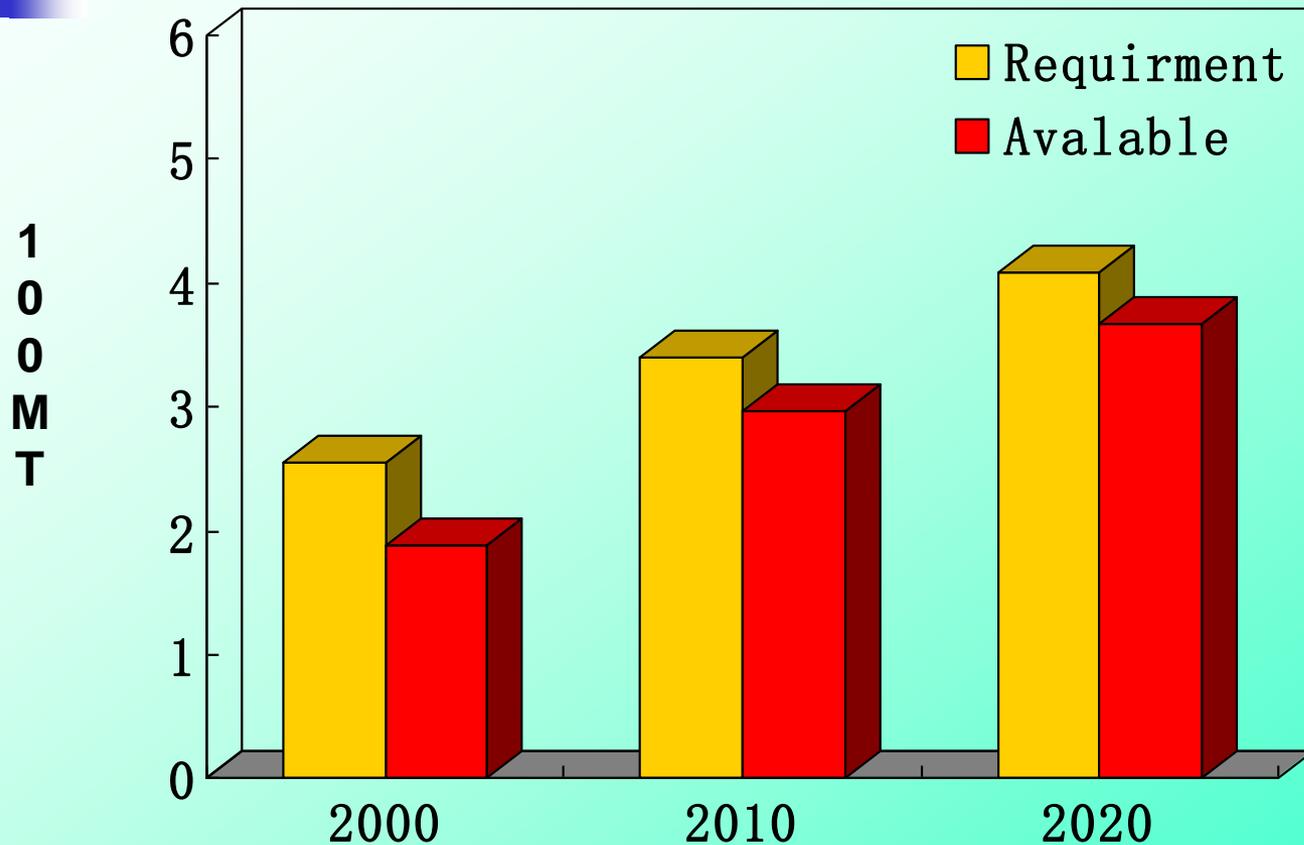
# Today's Challenges

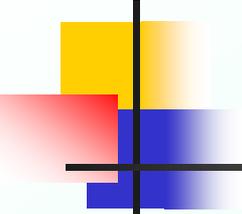


# The balance of protein resources



# The balance of energy resources

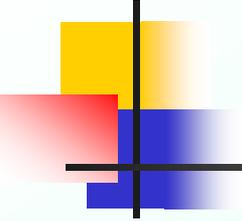




# New technology adoption

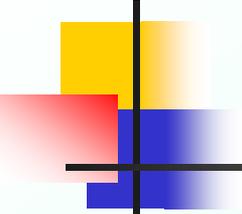
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- Government now encourage the feed industry enterprises adopt new high technology to go along with a professional, standard and the industrial model, the animal farm scale will grow bigger and bigger. Integrator farm play an important role in our country and will keep growing.
- New technology such as producing biofeed, nonpolluting feed, no residue feed, and functional feed will be developed to meet overcoming the environment pollution and the animal product quality improving.



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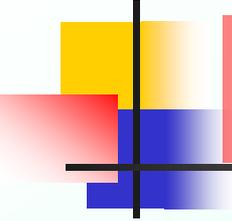
## **2. General situation on alternatives to antibiotic**



# Fear of the antibiotics use

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- Over 90 percent of antibiotics consumption are used for feed all over world.
- 50 percent of the world feed antibiotics were consumed in China.
- The increased use of antibiotics has given rise to a fear of the development of resistant pathogenic bacterial strains and residual contamination of the food chain with antibiotics.



## Growth promoting effect of antibiotics

Animal	Daily gain	FCR
piglet	+4.2~136% (15%)	+1.7~42.7% (6.5%)
Growing pig	+0~8.9% (3.6%)	-1.8~3.8% (2.4%)

Source: Thaler & Miller, 2000

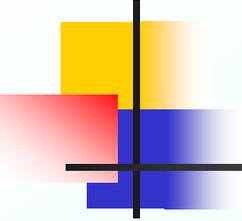
# Growth promoting effect of antibiotics in China

(1994—2008 trials)

<b>Animals</b>	<b>Daily gain</b>	<b>FCR</b>
<b>4-20kg piglet (62trials)</b>	<b><math>11.12 \pm 1.19\%</math></b>	<b><math>8.15 \pm 0.82\%</math></b>
<b>20-60kg growing pig (73trials)</b>	<b><math>9.80 \pm 0.80\%</math></b>	<b><math>8.02 \pm 0.70\%</math></b>
<b>60-90kg finish pig (39trials)</b>	<b><math>6.24 \pm 1.68\%</math></b>	<b><math>8.15 \pm 1.36\%</math></b>
<b>chicken (73trials)</b>	<b><math>4.36 \pm 0.44\%</math></b>	<b><math>3.88 \pm 0.47\%</math></b>
<b>Broiler medium (61trials)</b>	<b><math>3.81 \pm 0.44\%</math></b>	<b><math>3.93 \pm 0.44\%</math></b>
<b>Broiler large (35trials)</b>	<b><math>4.21 \pm 1.01\%</math></b>	<b><math>4.12 \pm 0.87\%</math></b>
<b>Duck (41trials)</b>	<b><math>5.31 \pm 0.84\%</math></b>	<b><math>3.88 \pm 0.61\%</math></b>

# Development of alternative strategies in China

- **Many countries have a comprehensive ban of antibiotics in feed.**
- **The feeding environment in China is different.**
- **Feed antibiotics is still a meaningful option to prevention of animal diseases.**
- **China will have to face the antibiotic disabling problem.**
- **Intensive research has focused on the development of alternative strategies with the aim of maintenance of animal health and performance.**



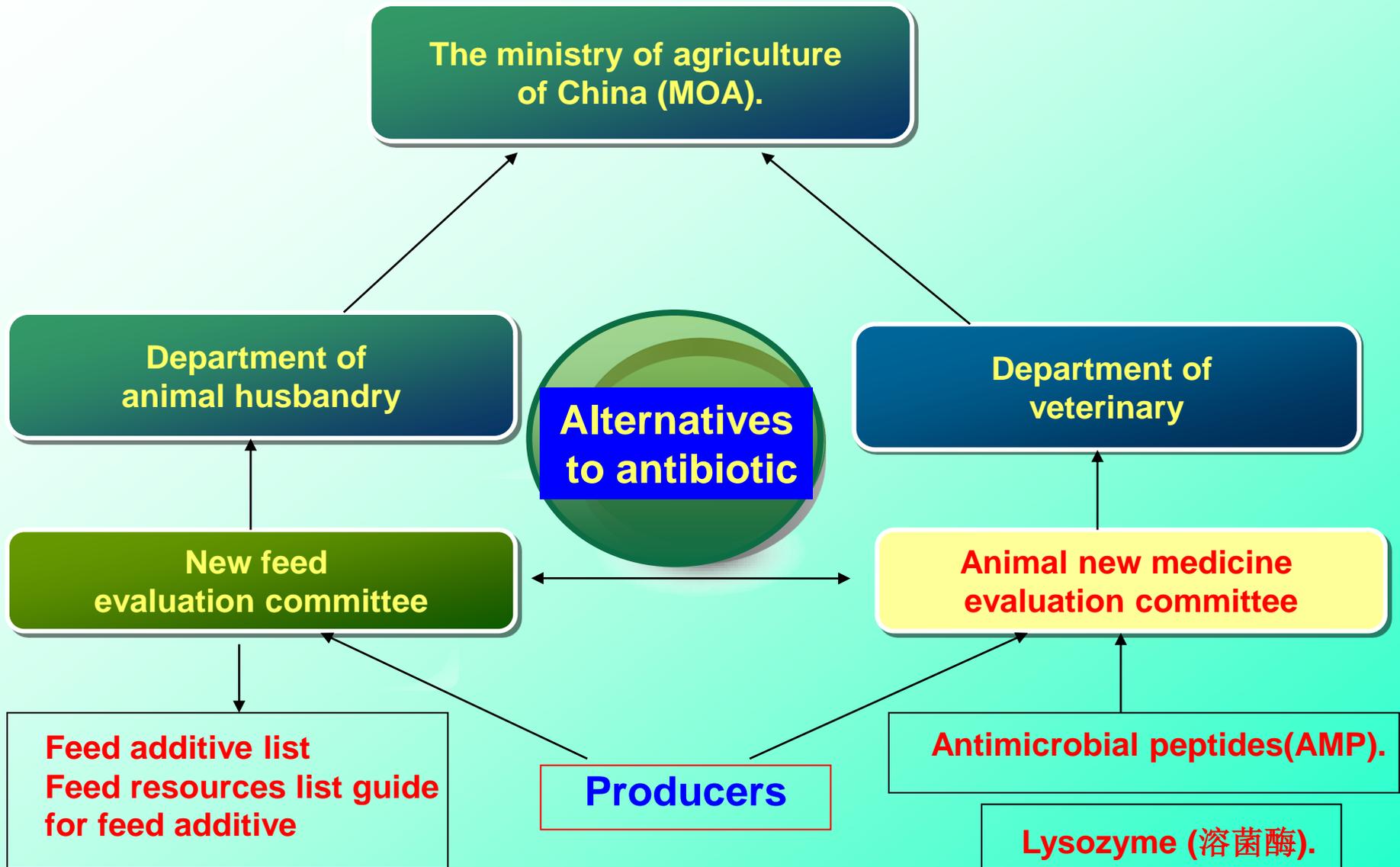
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### **3. Management on alternatives to antibiotic**

# The organization of feed additives and animal medicine in china

- **The management for feed ingredient and feed additive are under the animal husbandry department, MOA.**
- **Any new feed additives have to be approved by the new feed evaluation committee , the ministry of agriculture of china (MOA).**
- **Presently china has published a< feed additive list>, <the use guide for feed additive> and <feed ingredient list >.**

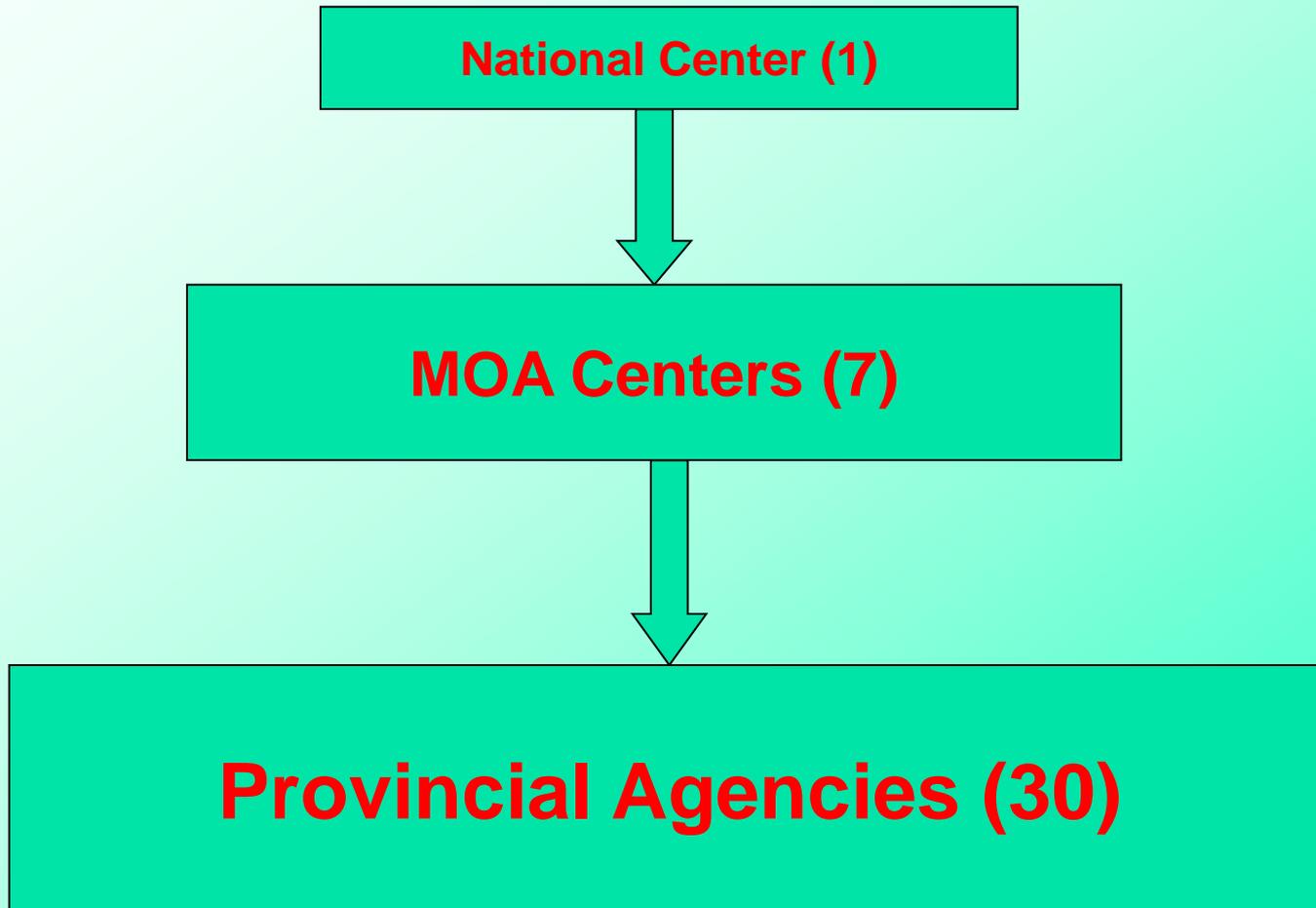
# Organization of feed additives and animal medicine in china



# Feed quality supervision & detecting system

In order to control the feed quality, China has established the Feed quality supervision & detecting system.

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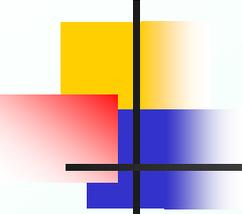


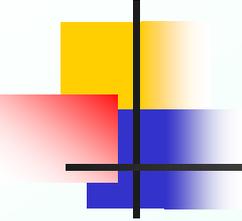
# Feed quality supervision & detecting items by MOA

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- **General feed safety.**
- **Detecting of nutrients and hygiene criteria.**
- **Detecting of clenbuterol and ractopamine.**
- **Detecting of illegal additives: e.g. melamine etc.**
- **Detecting of cattle, sheep & goat derived ingredients in ruminant feed.**

# Feed Additives Supervision items by MOA

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- Routine supervision and management
  - Administrative law enforcement
  - Reporting complaints
  - Information feedback and the Urgent events.



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## **4. Novel technologies on alternatives to antibiotic**

# Current situation and future development

**Antibiotics 抗生素**

**Residue  
残留**

**Resistance  
耐药性**

**Harmful to animal and human health  
影响动物和人类的健康**

**Reduce the use of antibiotics**

**减少抗生素的使用**

**EU  
欧盟**

**China  
中国**

# Alternatives to antibiotics in China

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- Various natural materials have been investigated as efficient alternatives to antibiotic growth promoters. Many of which are commercially available.



# Alternatives to Antibiotics in China

**Probiotics**

**Antimicrobial Peptides**

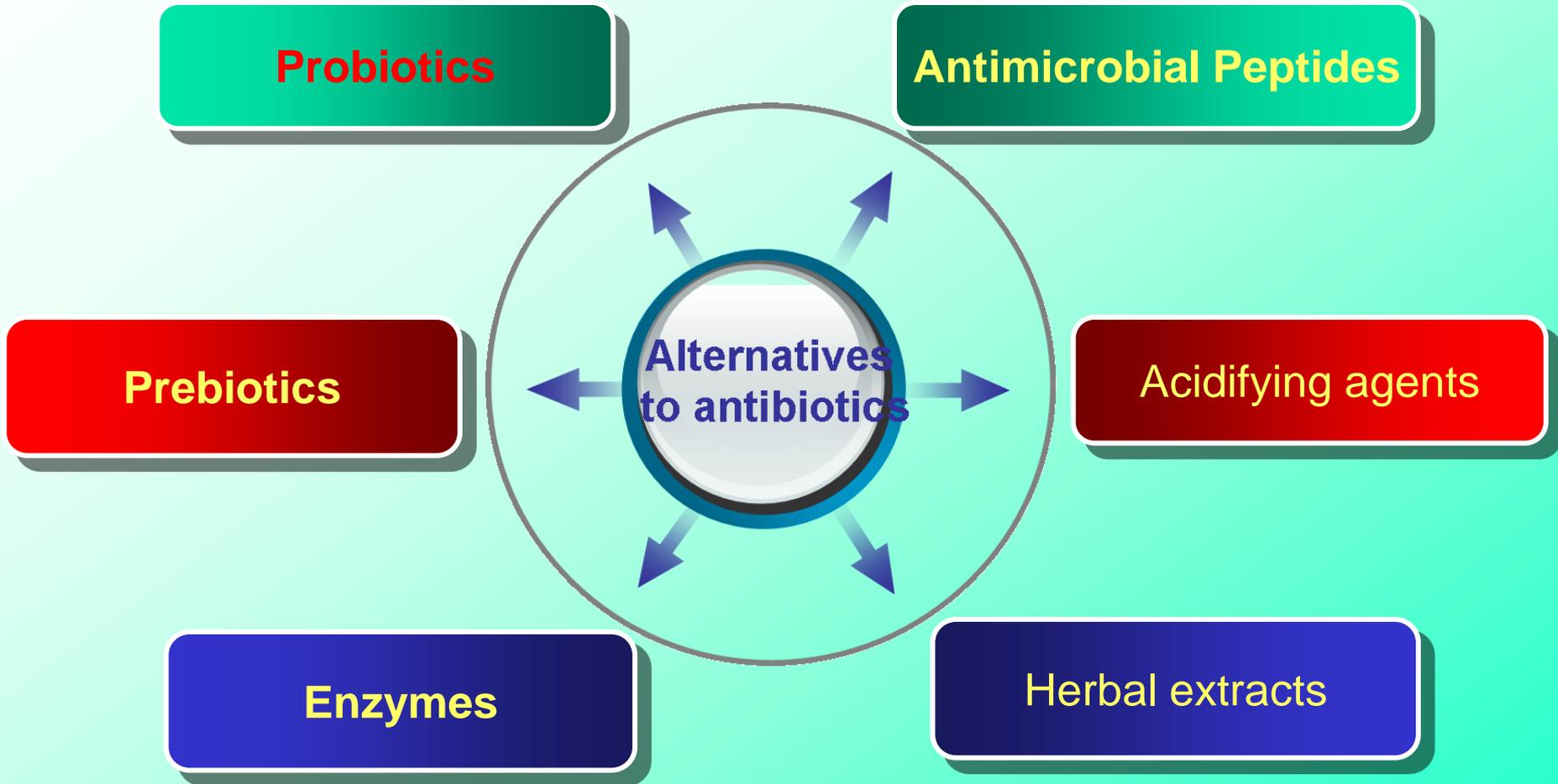
**Prebiotics**

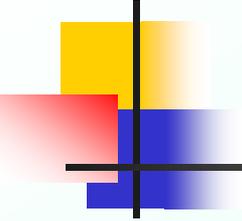
**Alternatives  
to antibiotics**

**Acidifying agents**

**Enzymes**

**Herbal extracts**





# 1. Probiotics

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- **Probiotics are one of the most important alternatives to antibiotic in China., which was widely used in feed mills and animal farms.**
- **Its output is about 50000 tons a year.**
- **Focused on three categories:**  
*Bacillus, Lactic acid bacteria & Yeasts.*

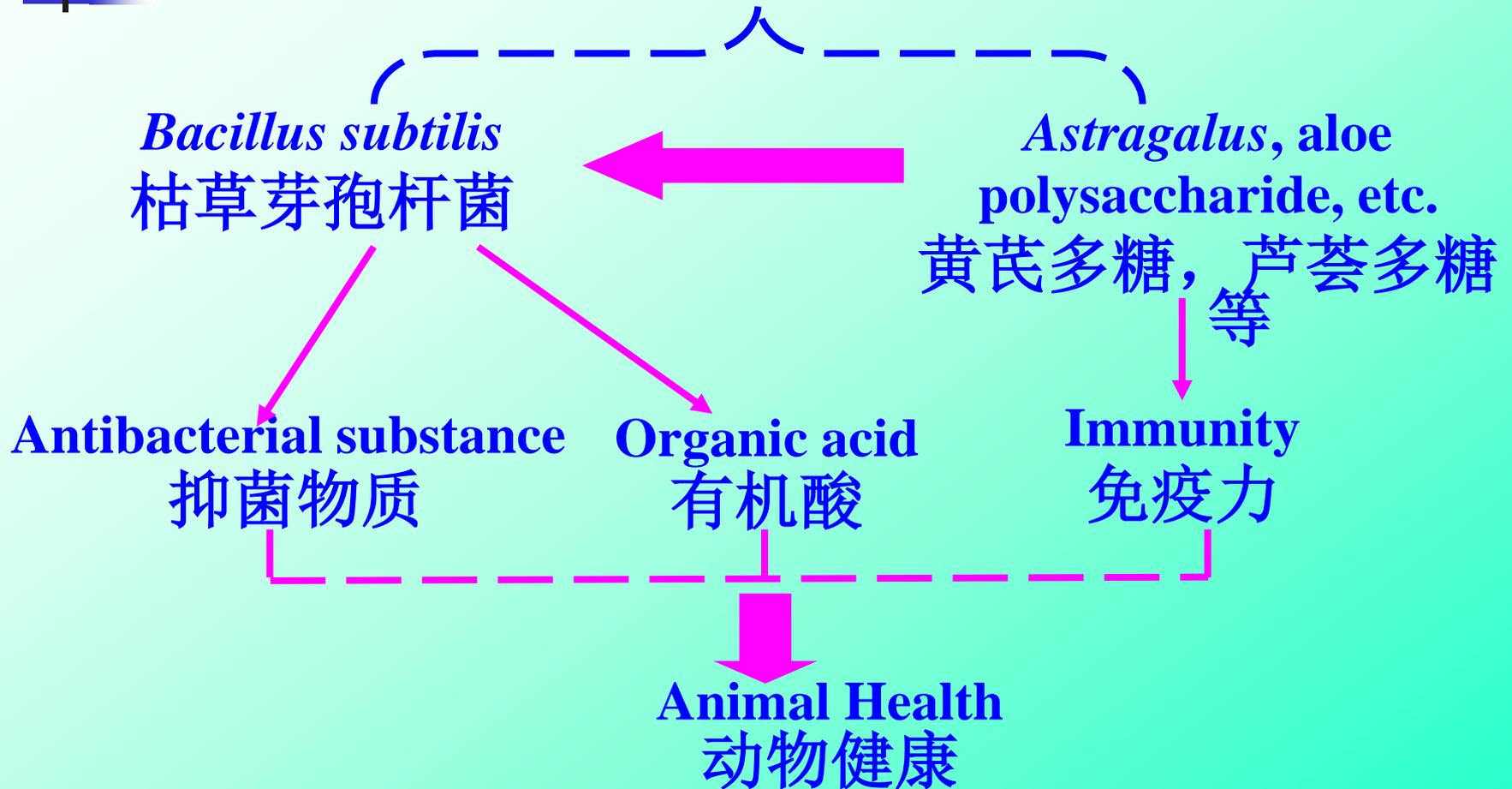
# Direct-fed microorganisms by MOA

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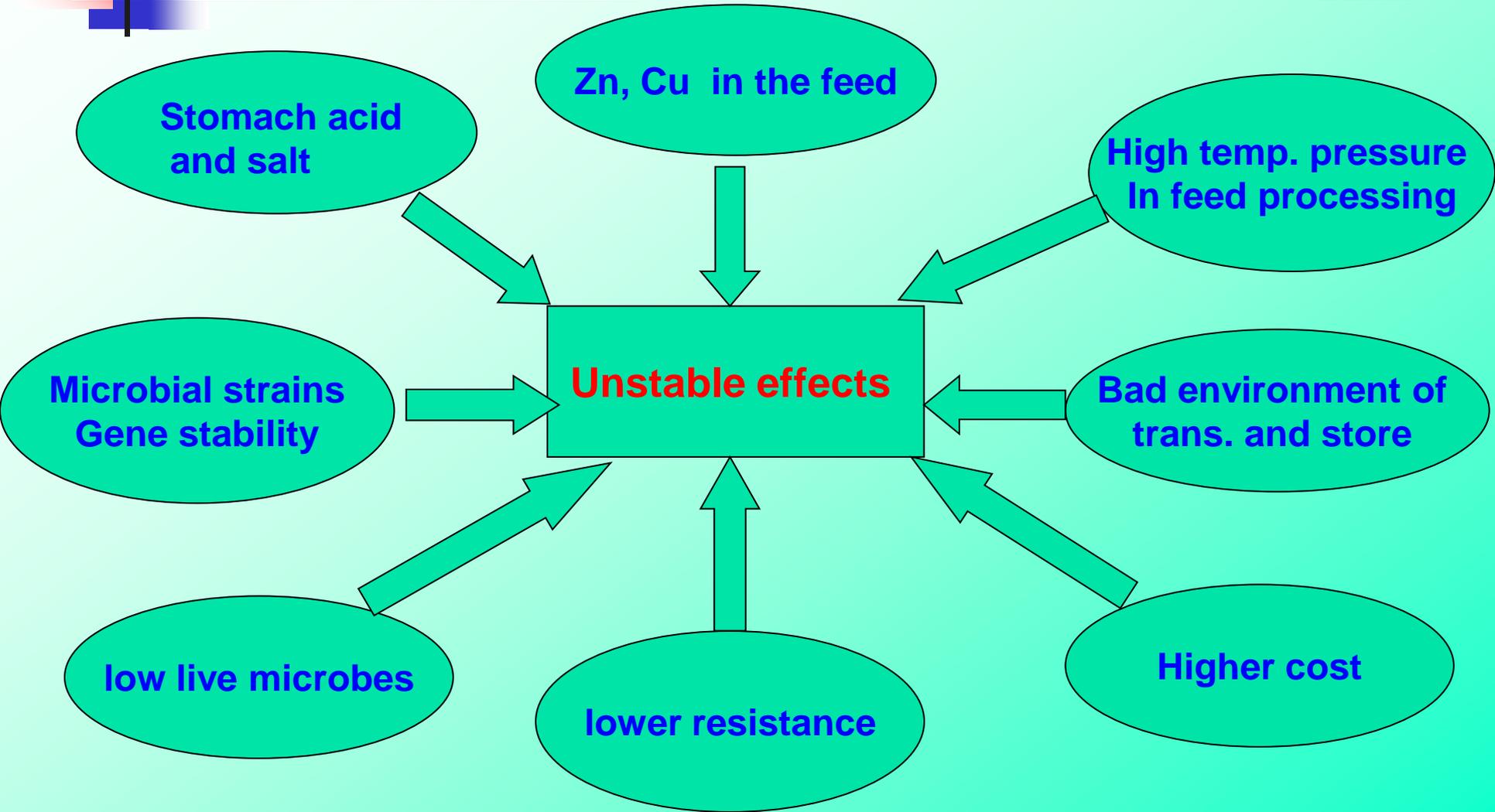
1. *Lactobacillus casei* (干酪乳杆菌)
2. *Streptococcus faecalis* (粪链球菌)
3. *Pediococcus acidilacticii* (乳酸片球菌)
4. *Bacillus natto* (纳豆芽孢杆菌)
5. *Streptococcus lactis* (乳链球菌)
6. *Candida utilis* (产朊假丝酵母)
7. *Lactobacillus Plantarum* (植物乳杆菌)
8. *Streptococcus faeciun* (屎链球菌)
9. *Bacillus subtilis* (枯草芽孢杆菌)
10. *Lactobacillus acidophilus* (嗜酸乳杆菌)
11. *Sacchaeomyces cerevisiae* (啤酒酵母)
12. *Rhodopseudomonas palustris* (沼泽红假单胞菌)

# Functional synbiotics

## Synbiotics



# Challenge of the probiotics use



# New processing: pre-fermentation- encapsulation

**Pre-fermentation- encapsulation**

**Realized the integration of fermentation  
and micro-capsules**

① **High live microbes**

② **Higher Micro encapsulation of efficiency**

③ **Higer stability**

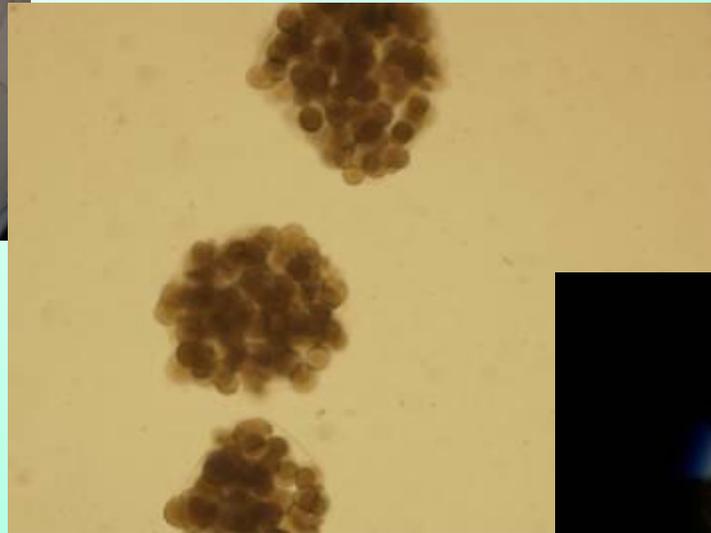
④ **Lower cost**

**Make the probiotics industrialization possible**

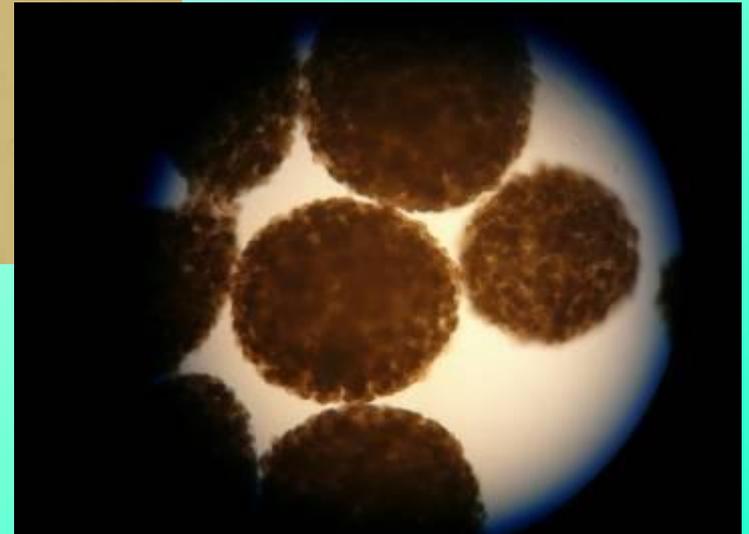
# Microscopy photos for preparation of micro-capsule



1 h



8 h

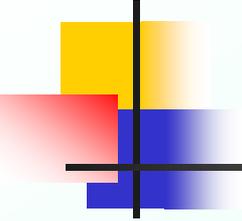


10 h

# Comparison of Encapsulation techniques

<b>Encapsulation technique</b>	<b>Processing characteristic</b>
<b>Pre-fermentation encapsulation</b>	<ol style="list-style-type: none"><li>1. High efficiency of Micro encapsulation</li><li>2. Effective living bacteria content in the product of up to <math>10^{11}</math>cfu/g.</li><li>3. Simplify post-processing and easier to industrialization</li><li>4. Low cost and versatile device</li><li>5. Well product uniformity</li></ol>
<b>Post-fermentation-coating</b> (fluidized layer coating and spray coating)	<ol style="list-style-type: none"><li>1. Easier to industrialization</li><li>2. Low rate of embedding</li><li>3. Effective living bacteria content in the product of up to <math>10^9 \sim 10^{10}</math>cfu/g</li><li>4. Large energy-consuming, high cost</li></ol>

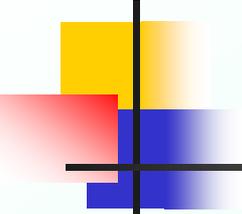
Under the same conditions, consumes the same fermentation raw materials, but 10–100 times live bacteria available



## 2. Prebiotics

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- **In China, most of the studied on prebiotic oligosaccharides are focused:**
  - **Fructo oligosaccharides (FOS)**
  - **Mannan oligosaccharides (MOS)**
  - **Arabinoxyl- oligosaccharides**
  - **Xylo-oligosaccharide.**
- **Oligosaccharides can be available on the market. Some of the feed mills start to use.**



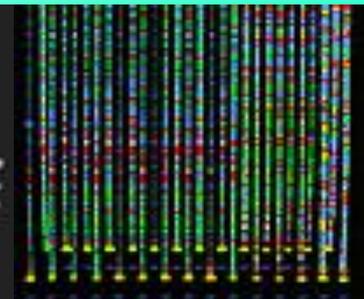
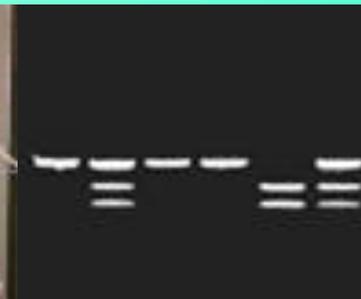
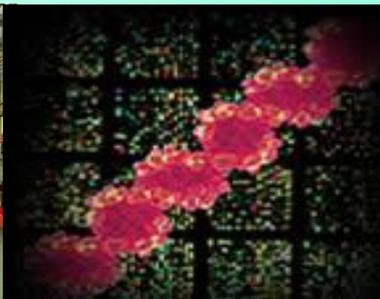
# **Study on preparative technology of pectic oligosaccharides(果胶寡糖) and chito-oligosaccharide(壳寡糖)**

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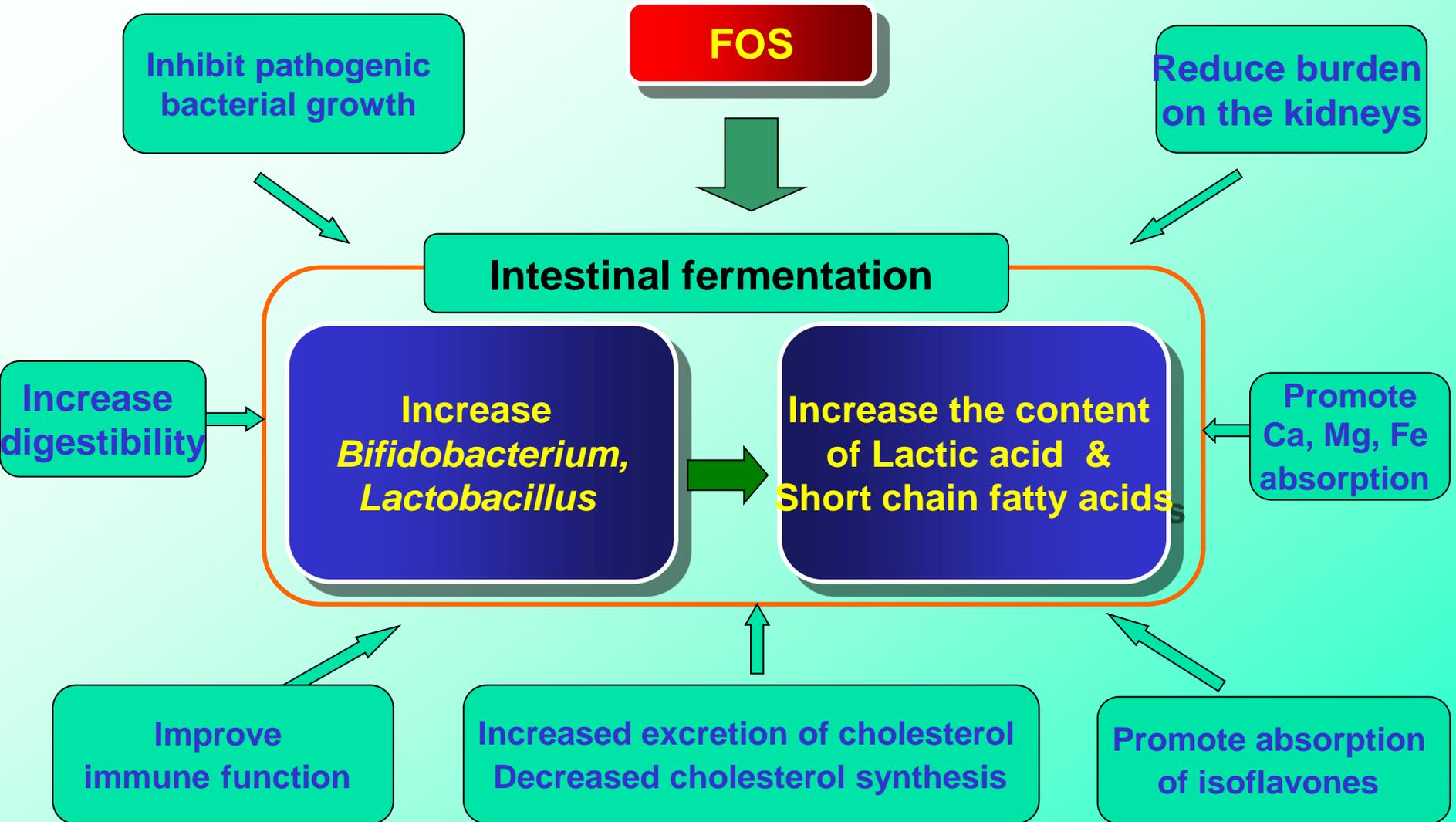
- **On the basis of structure-activity relationships study to pectin and oligosaccharides, Endo-pectate lyase and commercialization were selected respectively for Apple pectin and Chitosan papain degradation, and through targeted monitoring of polymerization degree of degradation products, access to the desired target saccharides.**

# Fructo oligosaccharides (FOS)

- **FOS can be found naturally in some cereal crops and onions.**
- **Widely used in swine, poultry and aquatic feed in China.**

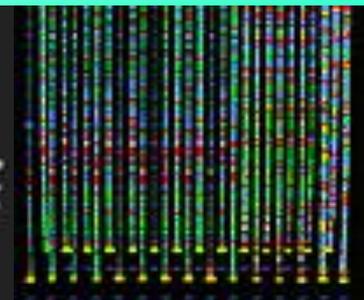
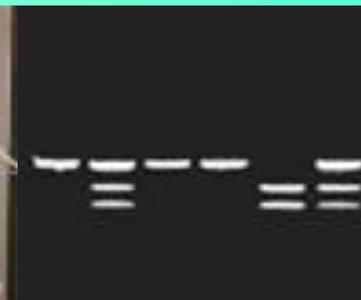
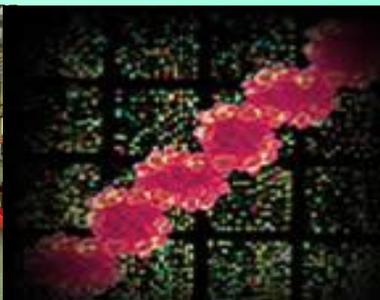


# Effects of FOS



# Mannan oligosaccharides(MOS)

- MOS is obtained from the cell wall of yeast (*Saccharomyces cerevisiae*).
- In recent years, with the development of hemicellulose resources in feed industry and aquaculture, the application and research of  $\beta$  – mannanase enter a new stage.



# Effects of MOS

## 1. Regulation of immune defense

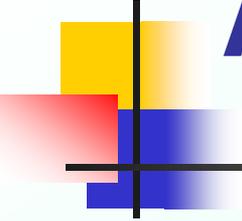
- a. Activated macrophages
- b. Improve the antibody response ability, strengthening the protection of vaccine efficacy
- c. Stimulation of hepatic secretion of mannose binding protein, affects the immune system.

## 2. Regulation of non-specific immune defense

Interference with intestinal pathogen colonization, prompted the bacteria become intestinal predominant flora.

## 3. Adsorption of mycotoxin

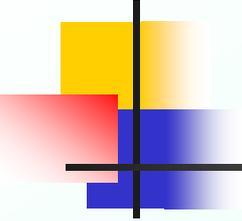
Through physical adsorption or direct binding of mycotoxin, eliminate toxin on the body of the harmful effects



# Arabinoxylo-oligosaccharides

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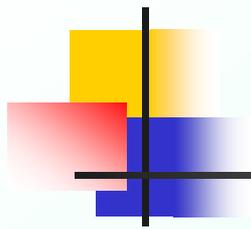
- **A new oligosaccharides, has been highlighted oligosaccharide on the basis of current state at home and domestic.**
- **Considered as food ingredients, arabinoxylo-oligosaccharides have favorable technological properties and cause prebiotic effects derived from their ability to modulate the intestinal function.**



# Xylo-oligosaccharide

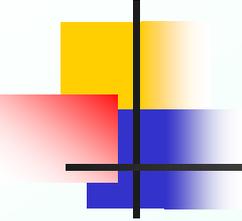
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- Xylo-oligosaccharide, a kind of prebiological substance, which can't be digested but can **selectively activate bacterial reproduction** within intestines.
- It can obviously improve intestinal micro ecological balance, proliferate bifid bacteria and gastric function.



# 3.Enzyme preparations

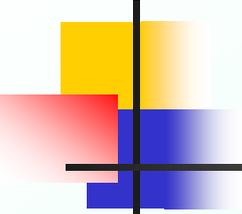
## 酶制剂



## 3. Enzyme preparation

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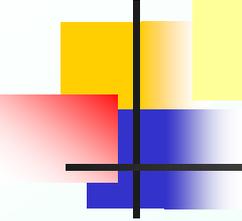
- **The feed enzymes developed in recent 10 years in china, there are a lot of reports about their application .**
- **Enzymes can degrade the anti-nutrient factors in feedstuff, increase nutrient digestibility, and reduce pollution to environment, and have been widely supplemented in animal feed.**



# 12 kinds feed enzyme preparations

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- Presently, 12 kinds feed enzyme preparations are used in China: amylase, cellulase,  $\beta$ -glucanase, glucose oxidase, lipase, maltase, mannanase, pectinase, protease, amylase, amylopectinase, phytase, xylanase.
- Although the enzyme preparation on the microbial itself does not have significant impact, but it can improve the feed digestibility, reduced nutrient residues in digestive tract weight, shorten the residual time, indirect reduction of pathogen growth opportunities, and realize the effect of disease prevention.
- The use of feed enzymes as antimicrobial growth promoters will need to be studied further before this strategy finds widespread use within the feed industry.



# Phytase

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- **Phytase is now most important enzyme because of its relatively easy manufactured and be used in all kind feed of animals.**
- **There are 4 companies have set up a international business with 40 countries.**
- **Granular, powder, Instant Soluble.**  
**5,000u/g - 200,000u/g are avaiable.**

# Instant Soluble Phytase

SPECIFICATIONS 99.99% soluble. (see the left solubility test picture) Colour: Buff or white powder Odour: Normal fermentation odour Enzymatic Activity: 100,000u/g Activity Temperature:20-70°C,favorable at 50°C Carrier Material: Instant soluble Mineral.



# Heat-resistant acid Phytase

图2：耐高温植酸酶最适温度

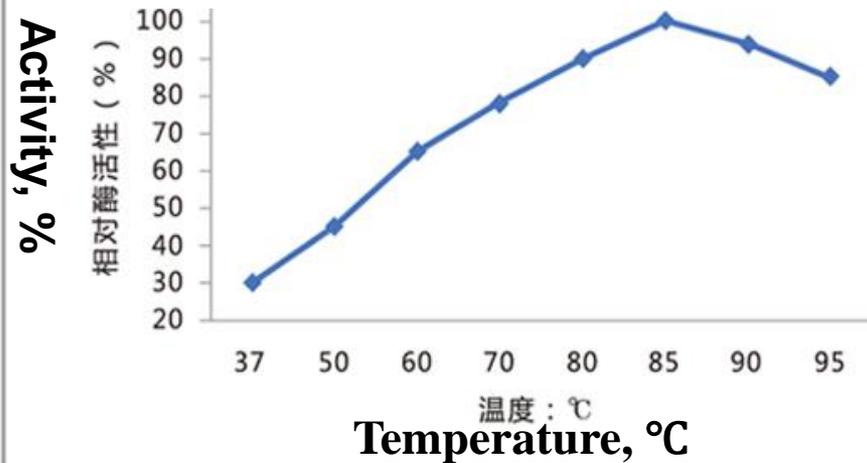
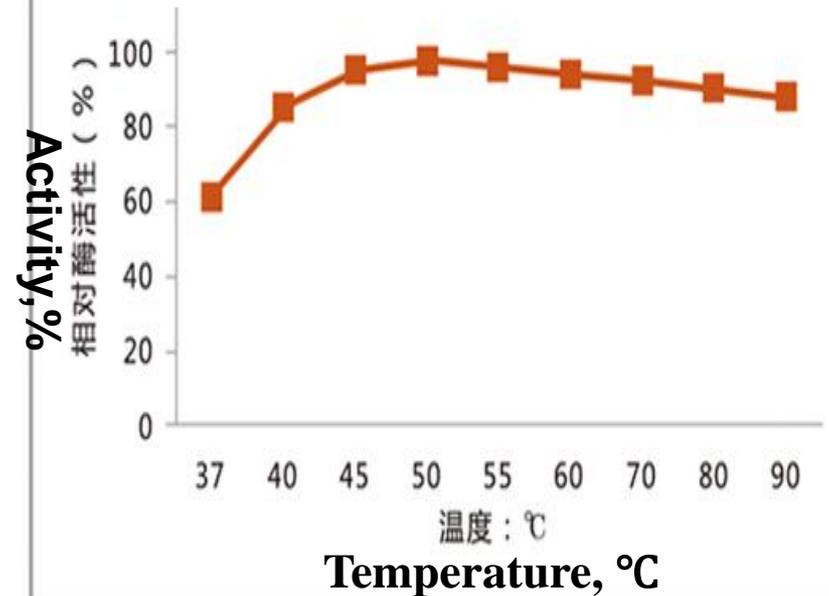
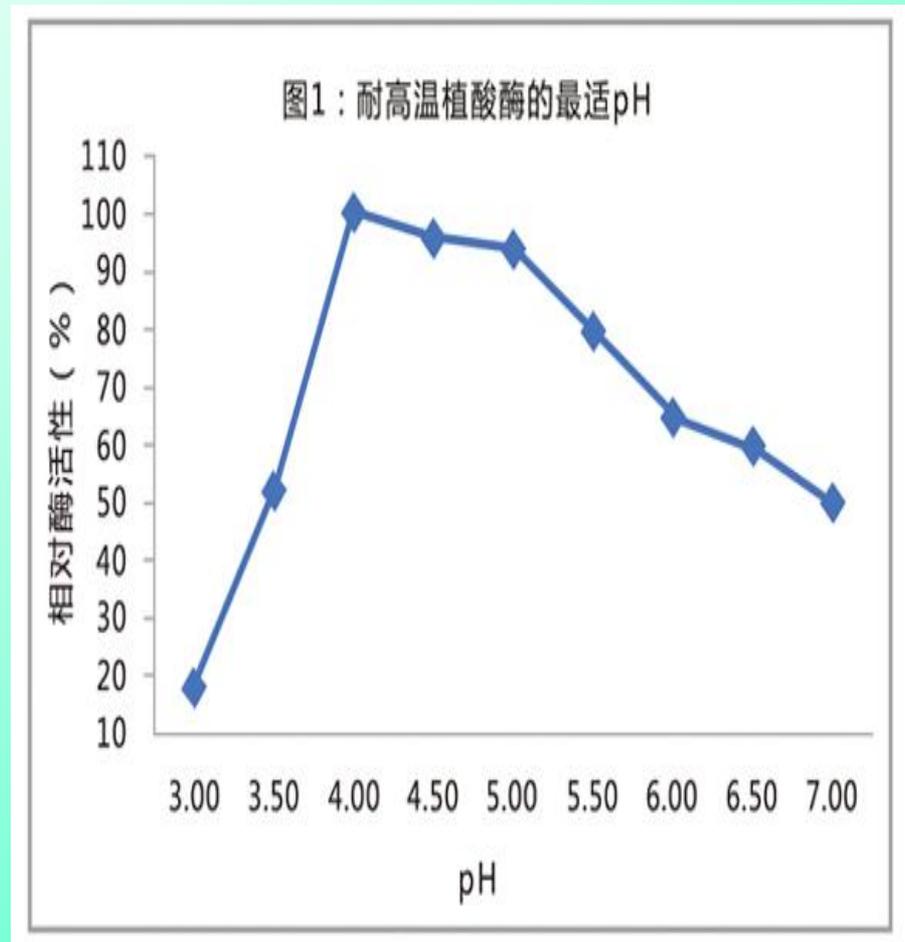


图3：耐高温植酸酶的热稳定性



# Heat-resistant acid Phytase

- High temperature resistant acid Phytase
- pepsin and trypsin-resistant features,
- pH3.5~pH7.0 range
- optimum pH4.0, have a higher stability.



# $\beta$ -mannanase

## Existing questions and the methods to increase the yield of $\beta$ -mannanase 存在问题及提高 $\beta$ -甘露聚糖酶产量的方法

✓ Low yield and enzymatic activity, difficult for massive application of  $\beta$ -mannanase

产量低，酶活力不高，使 $\beta$ -甘露聚糖酶不能大量推广使用

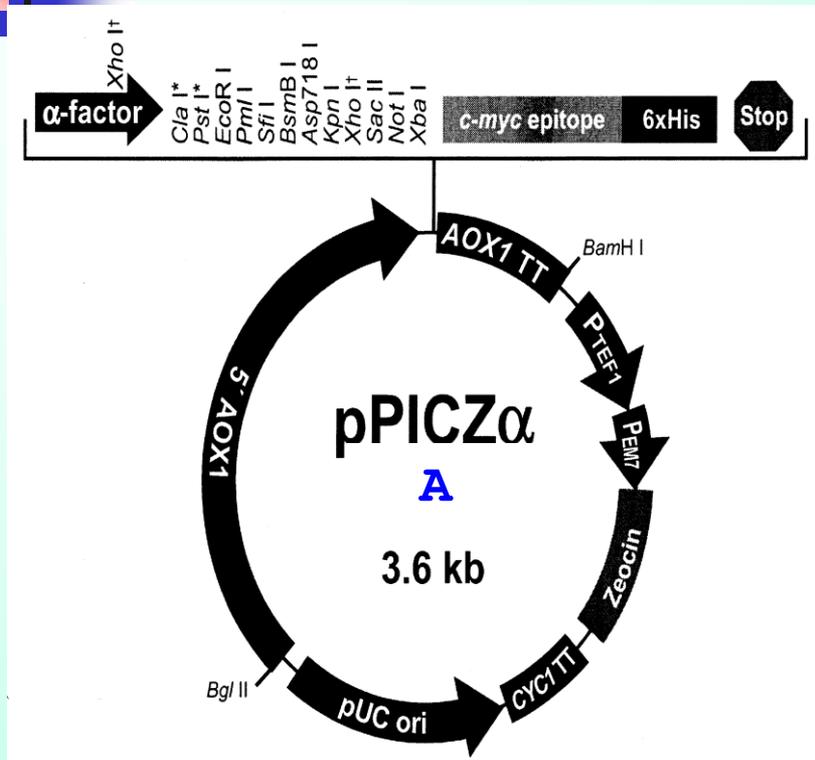
◆ Screening high yielding *A. sulphureus* mannanase strains by a mutant treatment

诱变选育高产硫色曲霉MAFIC001  $\beta$ -甘露聚糖酶菌种

◆ Modifying  $\beta$ -mannanase gene sequence according to codon bias

根据密码子偏好性，优化 $\beta$ -甘露聚糖酶基因序列

- ✓ Highest protein expression level (最高蛋白浓度): 3 g/L
- ✓ Highest enzymatic activity (最高酶活力): 1100 U/mL
- ✓ Purity (纯度): 96%



*Pichia pastoris* expression vector  
毕赤酵母表达载体



Fermentation device (10 L)  
发酵装置 (10升)

# Xylanase木聚糖酶

✓ *Aspergillus niger* Xylanase gene

● Realization of expression in  
Escherichia coli and pichia pastoris

# Thermostability of the modified recombinant xylanase 改造的重组木聚糖酶热稳定性研究

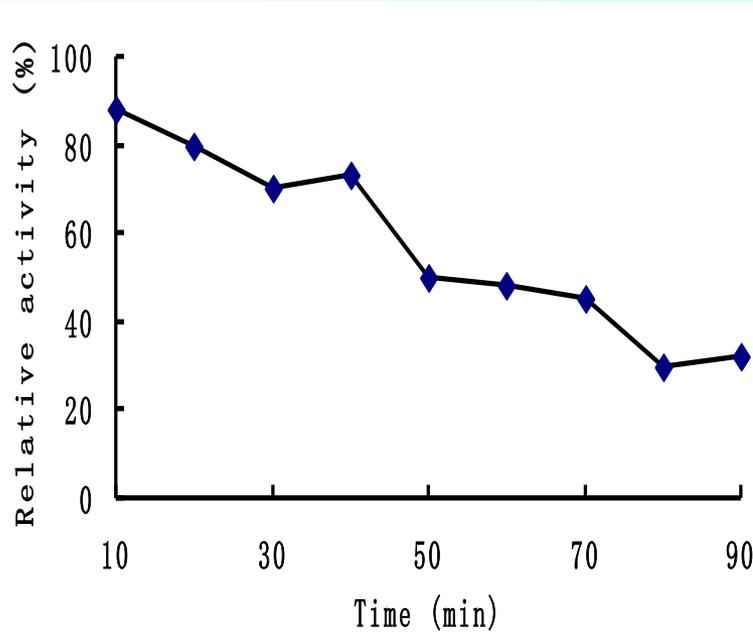
*Aspergillus sulphureus* 硫色曲霉

Modified xynA  
改造xynA

+

pGAPZ $\alpha$ A  
载体

expression in *Pichia pastoris*  
毕赤酵母中表达



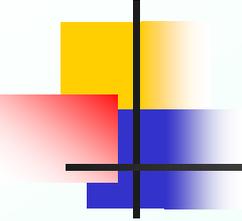
- **Good stability: 80°C for 90 min**  
热稳定性好, 80°C保持90 min
- **Enzymatic activity: 120 U/mL**  
最高酶活力达120 U/mL
- **Protein concentration: 3.78 mg/mL**  
蛋白浓度为3.78 mg/mL

# Alpha-Galactose glucoside enzyme

- **Alpha-Galactose glucoside enzyme could resistant the degradation of neutral and alkaline protease. it has high specific activity under the condition of PH value 2-8, and can withstand 80 °C high temperature.**
- **Experimental results show that addition in the broiler diet with different levels of Galactose glucoside enzyme (150 U/kg, 300 U/kg, 1500 U/kg group), it improves FCR, increase energy, protein apparent metabolic rate as compared with the control group.**

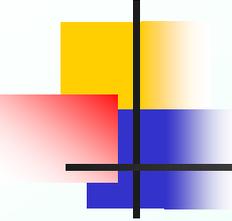
# High cell density fermentation of recombinant pichia pastoris yeast production technology Established

- **Established the high level expression of recombinant strain of Alpha-Galactose glucoside enzyme, Cellulase and Pectinase.**
- **The expression of 3 kinds of enzyme in the fermentation tank is up to 10000U/ml, 30000 U/ml and 10000 U/ml respectively.**



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## 4. Antimicrobial peptides (AMPs)抗菌肽



## 4. Antimicrobial peptides (AMPs)

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- AMPs are another major group of promising novel alternatives to antibiotics based on their effectiveness, safety, and enormous diversity.
- ✓ **AMPS : Important components of the innate immune system** 先天免疫系统的重要组成成分
- ✓ **Abundant and diverse groups of molecules that are encoded by definite genes**  
特定编码基因产生的一类小分子多肽

# Current situation and existing problems

## 现状及存在问题

- **Research of higher structure and antibacterial mechanism of AMPs**

研究抗菌肽高级结构和抗菌机理

- **Short half-life, easy to lose activity**

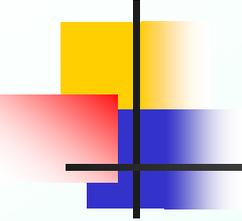
半衰期短，易失活

- **Toxicity toward prokaryotic cell**

抗菌肽对原核细胞的毒性

- **Low yield, difficult to purify**

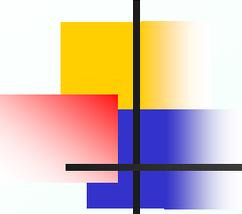
天然抗菌肽纯化难度大，产量低



## Key points for product development

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- **Modify the molecule of AMPs**  
优化抗菌肽分子
- **Select definite strain, and fusion expression**  
原核系统中选育特定抗性菌株，真核系统中采用融合表达以提高其表达率
- **Special induction mode, reduce product cost**  
以特殊的诱导模式，降低生产成本

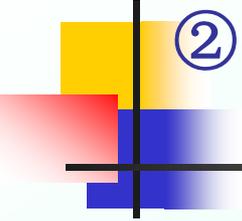


# Antimicrobial peptides-activity feed products development

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① Two Antimicrobial Peptide expression platform establishment of *Bacillus subtilis* and Yeast .

- Through the *Bacillus subtilis* modified system, antibacterial peptide expression volume reached 1.8mg/ml above.
- The key technology to the low expression volume and low stability solved.

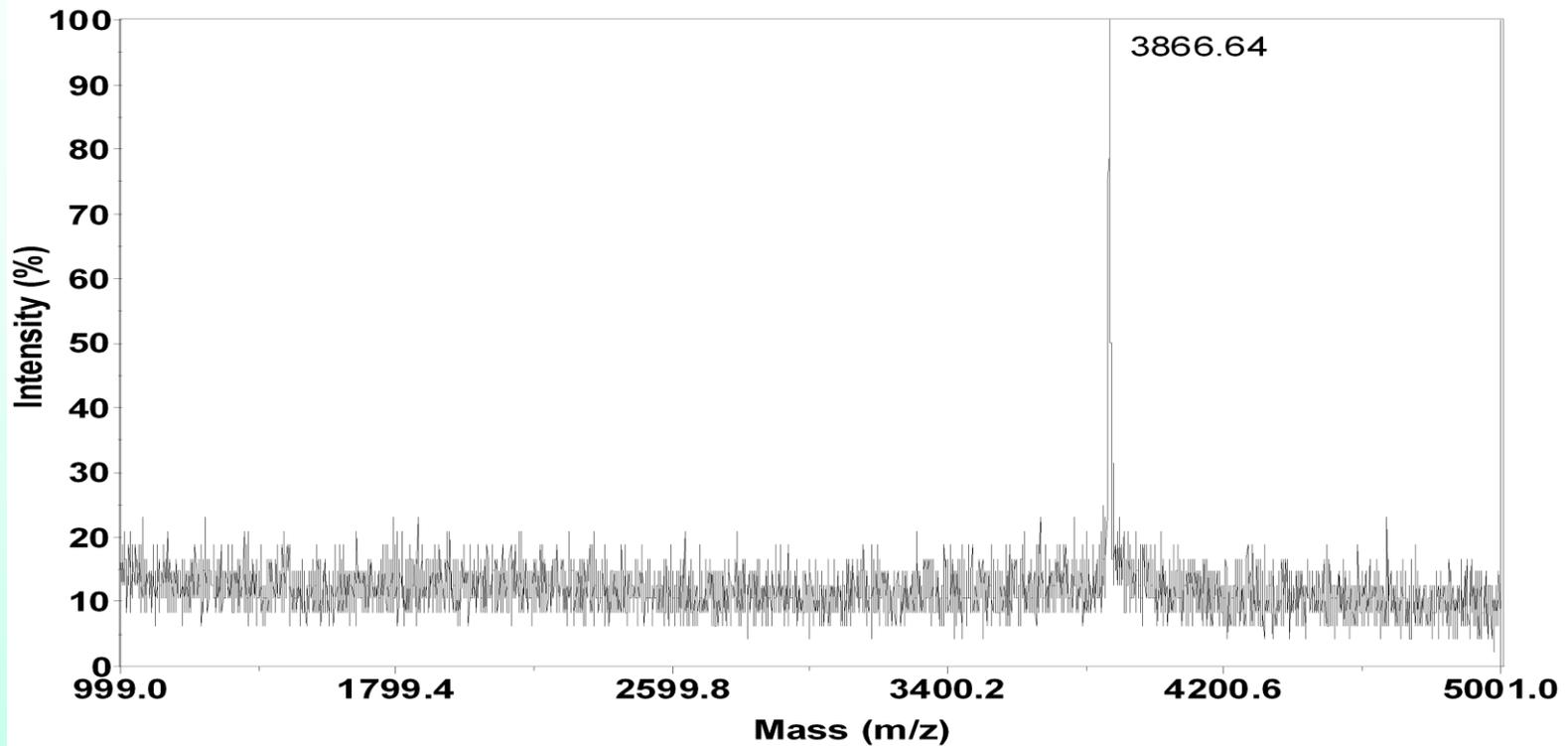


## ② Clear features molecular structure is available.

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- **The mass spectrometric analysis for Antibacterial peptide :**
- **cecropin consists of 37 amino acid composition, molecular weight of 3.866KD.**
- **Bacillus subtilis consists of 37 amino acid, molecular weight: 3.879KD, its amino acid sequence is:**  
**GLGKAQCAALWLQCASGGTIGCGGGAVACQNYRQFCR.**

# Figure 1. Antibacterial peptide cecropin mass spectra

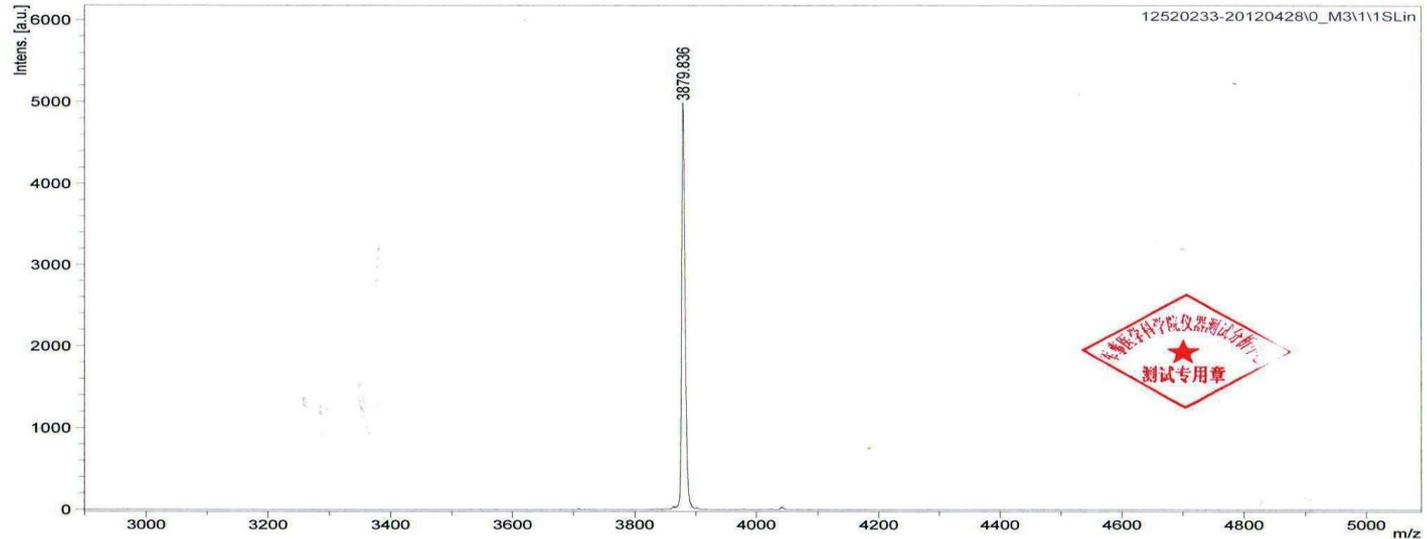


# Figure 2. Bacillus subtilis bacteria antimicrobial peptide mass spectra

D:\lby\lby2012\20120518\12520233-20120428\0\_M311

Comment 1

Comment 2



Bruker Daltonics flexAnalysis



### ③ Complete the antibacterial peptide cecropin and subtilin part antimicrobial **spectrum and stability** test

**Table 1, cecropin antibacterial peptides against pathogenic bacteria of the minimum inhibitory concentration**

<b>Division bacteria</b>	<b>Minimum inhibitory concentration(<math>\mu\text{g/ml}</math>)</b>
<i>E.coli</i> K12D31 (大肠杆菌K12D31)	1.8
<i>E.coli</i> K88 (大肠杆菌K88)	2.0
<i>E. coli</i> K99 (大肠杆菌K99)	2.0
<i>Salmonella typhimurium</i> (鼠伤寒沙门氏菌)	8.0
<i>Salmonella enteritidis</i> (肠炎沙门氏菌)	16.0
<i>Staphylococcus aureus</i> (金黄色葡萄球菌)	0.2
<i>Streptococcus faecalis</i> (粪链球菌)	24.0

## Table 2. Minimum inhibitory concentration of the *Bacillus subtilis* against pathogenic bacteria

Division bacteria	Gram attributes	Minimum inhibitory concentration( u g/ml)
<i>Staphylococcus aureus</i> CMCC26003	G <sup>+</sup>	1.3
<i>Staphylococcus aureus</i> CVCC1882	G <sup>+</sup>	4.69
<i>Staphylococcus aureus</i> ATCC29213	G <sup>+</sup>	23.43
<i>Staphylococcus aureus</i> ATCC25923	G <sup>+</sup>	11.7
<i>Staphylococcus aureus</i> ATCC43300	G <sup>+</sup>	187.5
<i>Staphylococcus aureus</i> 野生株（吉林）	G <sup>+</sup>	23.43
<i>Staphylococcus aureus</i> 野生株（华中）	G <sup>+</sup>	11.7
<i>A. hydrophila</i> （嗜水气单胞菌）	G <sup>-</sup>	46.9
<i>B. cereus</i> （蜡样芽孢杆菌）	G <sup>+</sup>	0.2
<i>Vibrio anguillarum</i> （鳃弧菌）	G <sup>-</sup>	12.8
<i>C. perfringens</i> （魏氏梭菌）	G <sup>+</sup>	1.4

# pH value effect on the activity of two antibacterial peptide

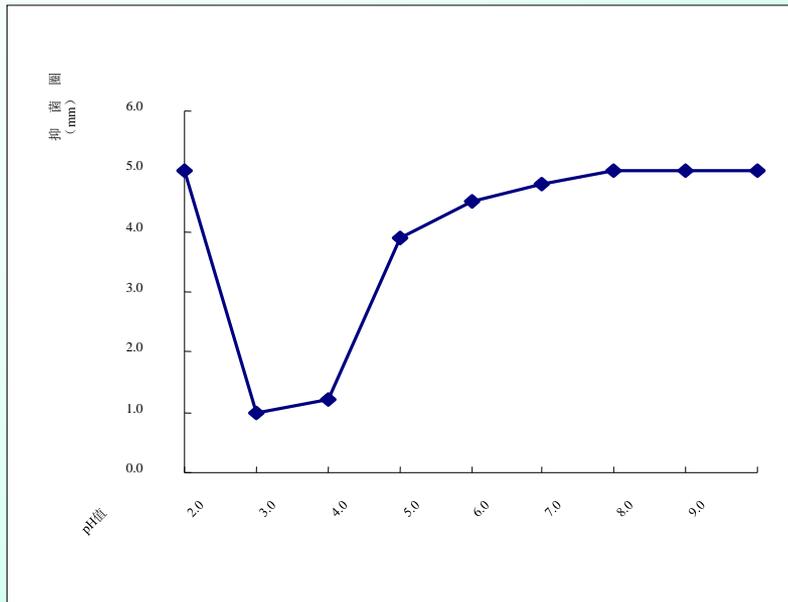


Figure 9 pH value effect on the activity of antibacterial peptide cecropin

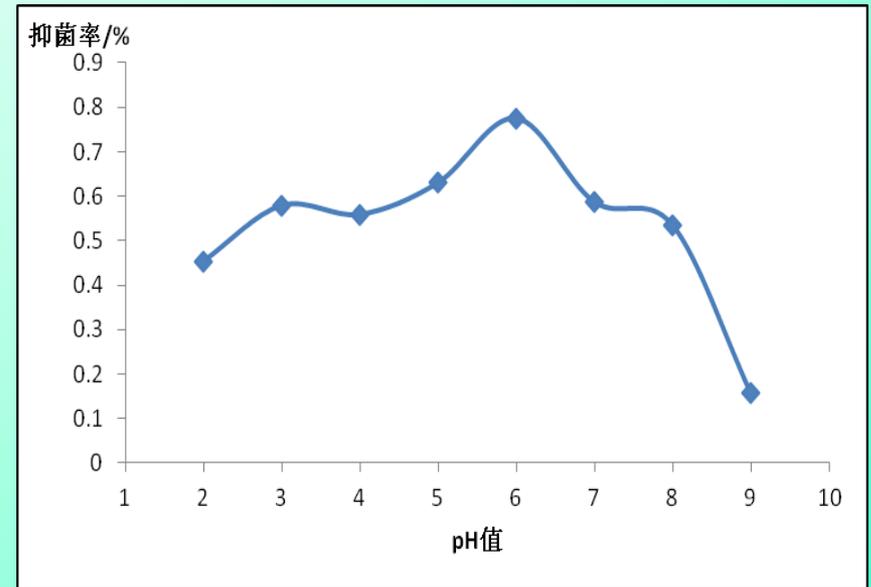


Figure 10 pH value on effect of *Bacillus subtilis* bacteria activity

## Antimicrobial peptides-activity feed products development

- **④ Obtained pure purity greater than 99.5% of antibacterial peptide, established two methods for detection of antimicrobial peptides, complete isolation and purification of antibacterial peptide cecropin pilot**
- **⑤ Completed the feed safety evaluation of antibacterial peptide cecropin, established product quality standards.**

# Antibacterial assay 抑菌分析

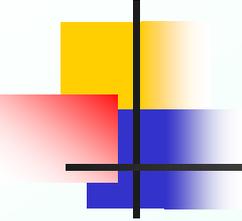
***E. coli* K12D31**

↓  
AMPs-sensitive strain  
抗菌肽敏感菌株



1: control with no insert; 2-6: positive recombinants induced 72 h

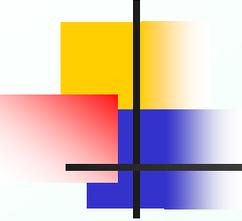
1: 对照; 2-6: 重组菌诱导72 h的正对照组 (抗菌肽)



# Studies on other bioactive peptides and defense peptides

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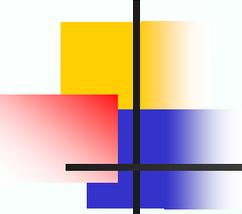
- **① Recombinant expression of host defense peptides of Palustrin-OG2**
- Improved OG2 peptide expression in Escherichia coli , purification and activity determination.
- **② Recombinant expression of Apidaecin(蜜蜂肽) and Spheniscin(企鵝防禦肽).**
- **③ Recombinant expression of BuforinII(牛乳鐵蛋白素) in the photorhabdus luminescens .**



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## 5. Herbal extracts

(*Astragalus polysaccharide*, APS)  
天然提取物（黄芪多糖）



## 5. Chinese herbal extracts

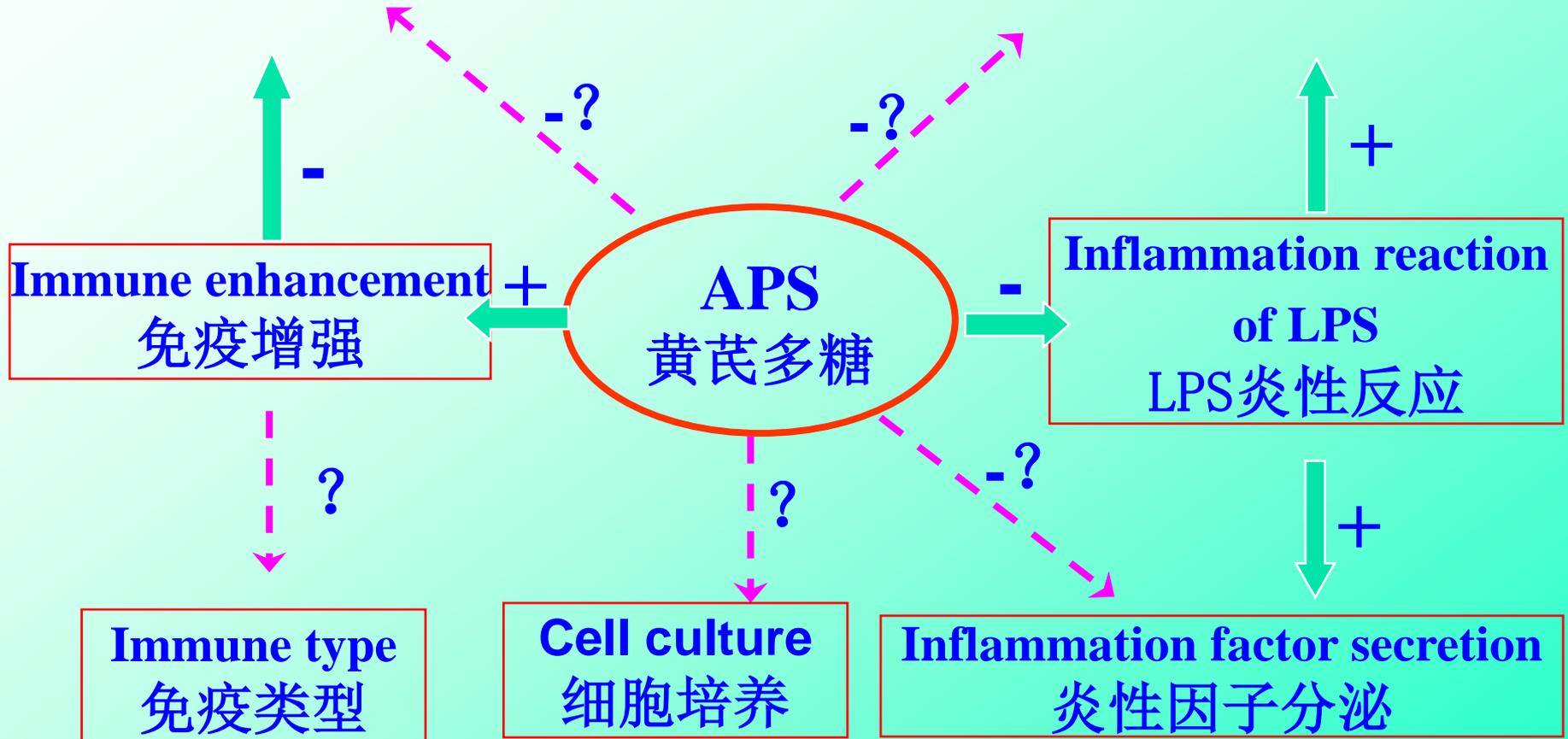
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- Practice has proved it can promote appetite, enhance immunity, prevent and cure diseases etc..
- Traditional Chinese medicine additives is over 50 kinds.
- Slow effect ,Much required dose and antibiotics-like effects.
- the main problems : bad palatability and high cost.
- two important representatives : oregano oil and *Astragalus polysaccharide*.

# APS Hypothesis

Immune suppress (cyclophosphamide)  
免疫抑制 (环磷酰胺, CY)

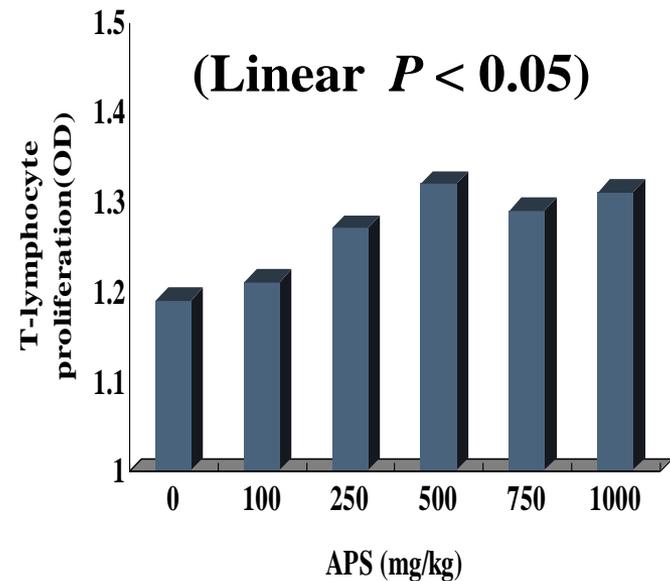
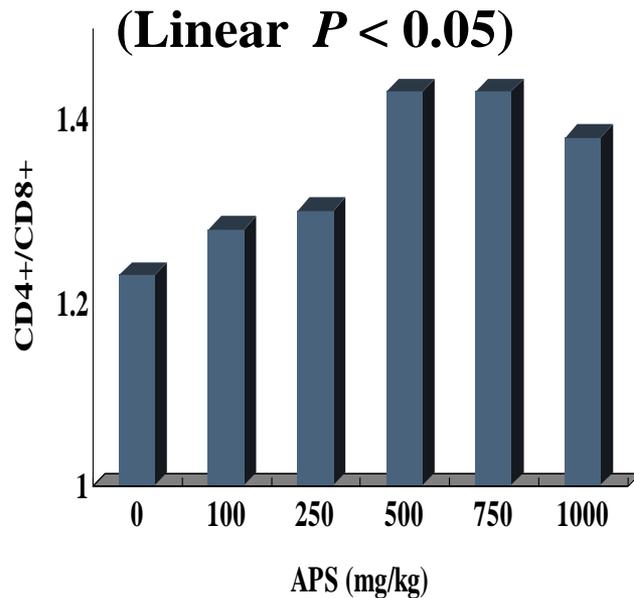
Disorder of GH/IGF-I axis  
GH / IGF-I轴异常



# Effects of APS on ratio of $CD4^+/CD8^+$ and Lymphocyte proliferation in piglets

$CD4^+/CD8^+$

淋巴细胞增殖



◆ Improve cell immune function, the optimal APS level was 500 mg/kg

APS在断奶仔猪日粮中的最适添加量为500 mg/kg

# Effects of dietary supplement of APS on serum cytokines in weaned pigs received cyclophosphamide (CY)

APS (注射环磷酰胺, CY) 对断奶仔猪血清细胞因子的影响 (pg/mL)

	-CY		+CY	
	-APS	+APS	-APS	+APS
<b>d 14</b>				
<b>IL-2</b>	<b>55.4</b>	<b>79.8</b>	<b>50.6</b>	<b>77.8</b>
<b>IFN-<math>\gamma</math></b>	<b>133.3</b>	<b>160.1</b>	<b>111.7</b>	<b>138.9</b>

➤ **Reverse CY-induced cell immune suppress and humour immune suppress**

● 环磷酰胺免疫抑制模型研究发现, APS可促进猪的正常细胞免疫, 也可逆转CY造成的免疫抑制

# Effects of APS on serum index in piglets

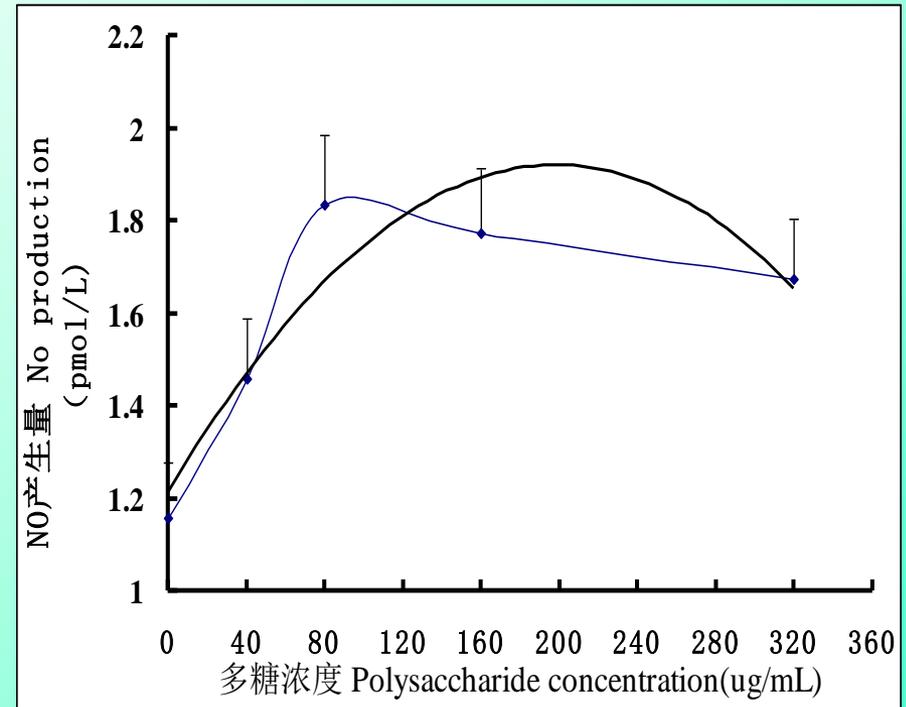
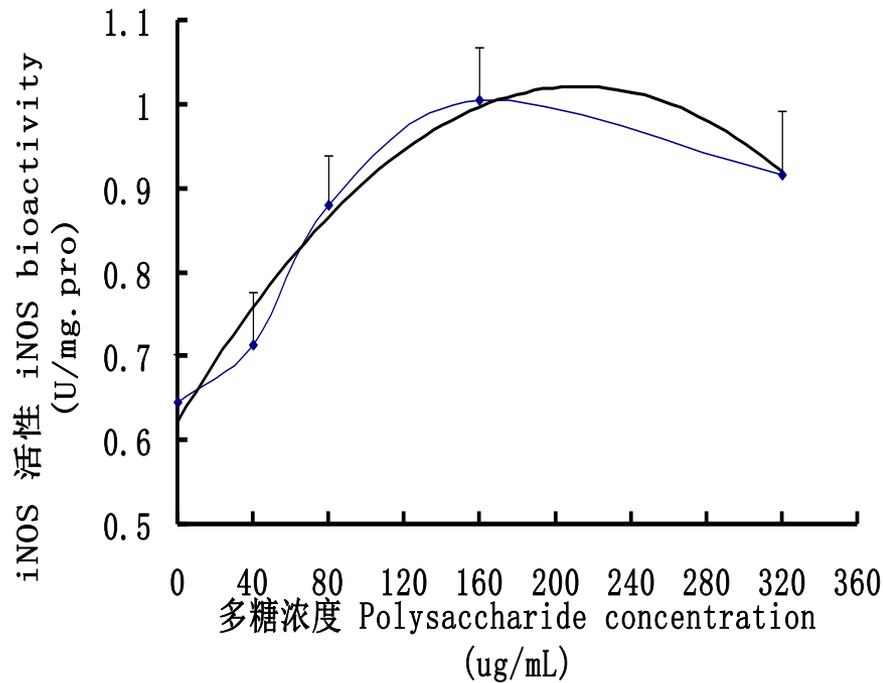
## APS对仔猪血清指标的影响

	-LPS		+LPS	
	-APS	+APS	-APS	+APS
d 14				
Cortisol	115.3	113.0	155.5	136.0
GH	3.82	3.83	4.56	3.94
IGF-I	235.6	240.0	215.9	224.9

- **Recover the normal function of GH/IGF-I axis**
  - ❖ APS通过降低炎性细胞因子、GH和皮质醇的含量，增加抗炎性因子的合成，恢复GH/IGF-I轴的正常而发挥其免疫抗炎作用

# Effects of APS on NO and iNOS activity in piglets

APS对仔猪NO和iNOS的影响

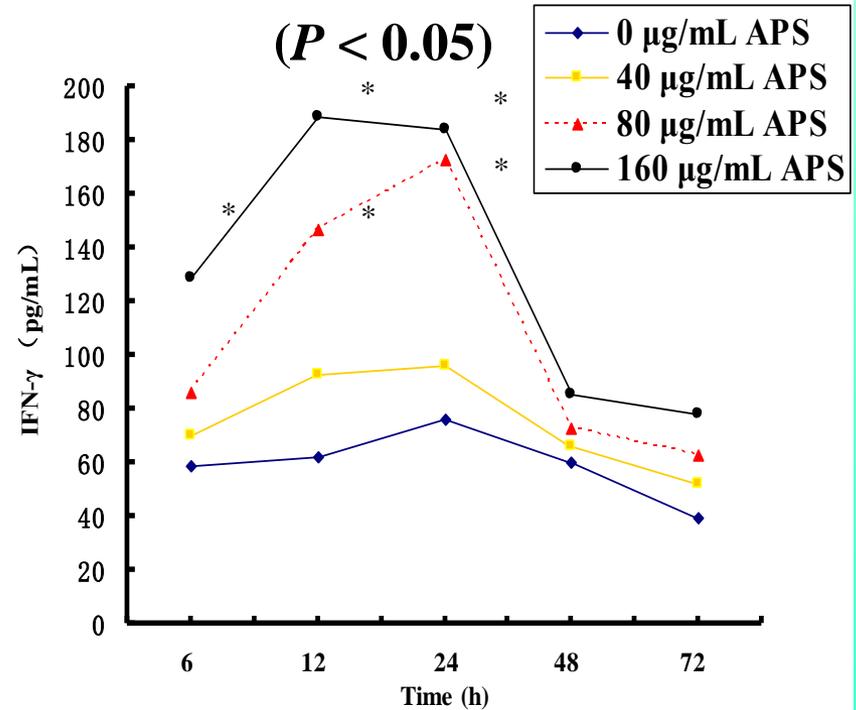
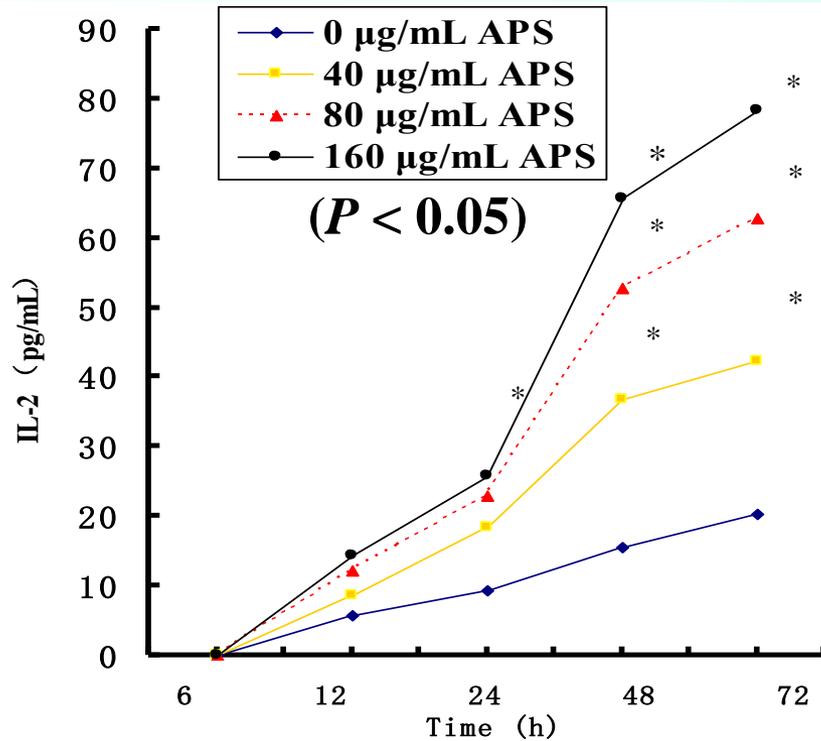


➤ Increase NO and iNOS activity of the peripheral blood lymphocytes in piglets

■ APS显著增加仔猪外周血淋巴细胞NO和iNOS的活性，并呈剂量依赖性

# Effects of APS on different cytokines

## APS对不同细胞因子的影响

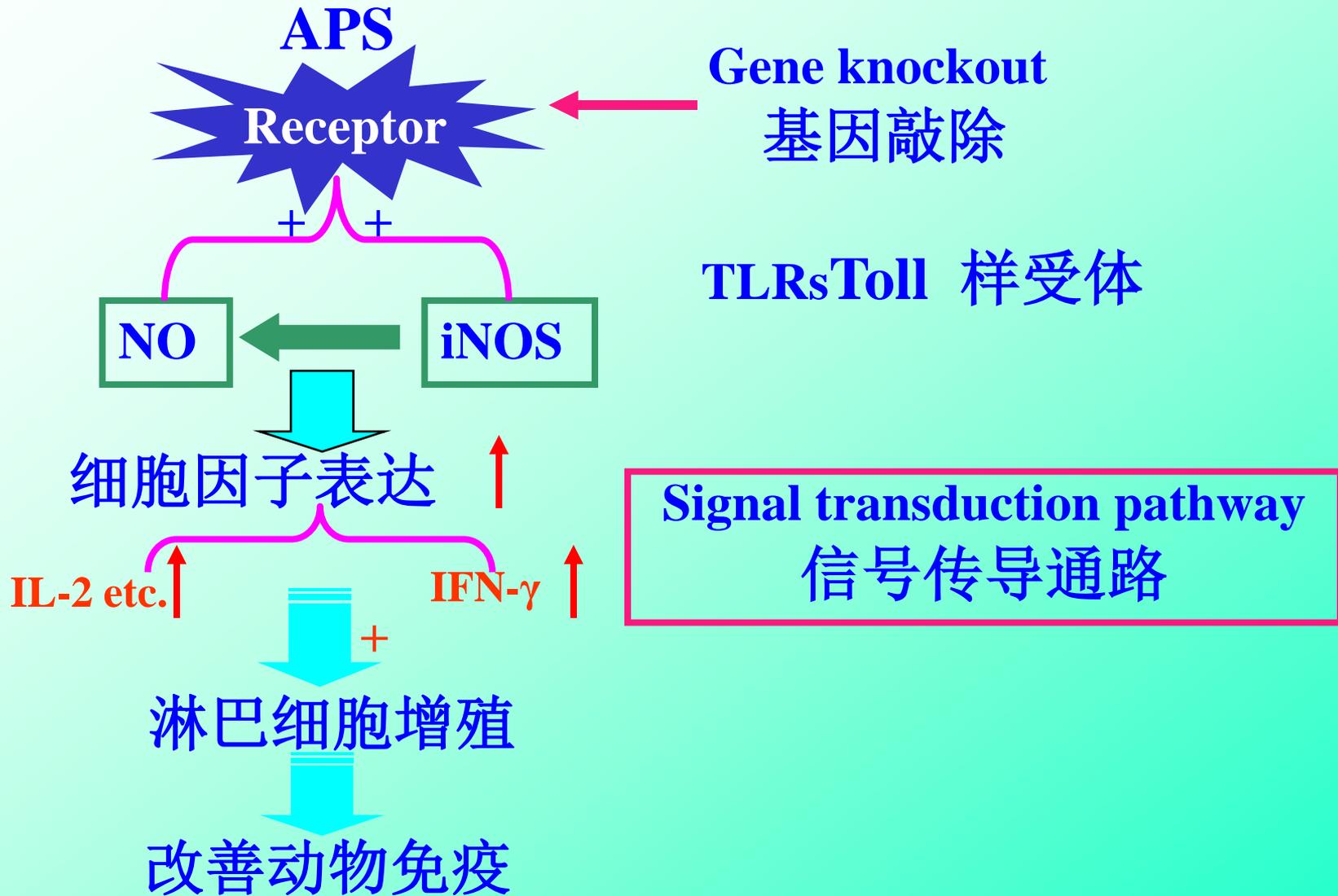


➤ Increase the IL-2 and IFN-γ secretion

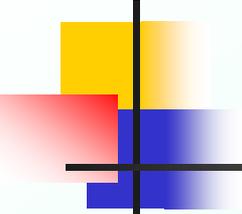
❖ APS可在体外促进细胞因子IL-2和IFN-γ的分泌，这可能是APS的免疫调节作用之一

# Mechanism of immune function of APS

## APS的免疫作用机理

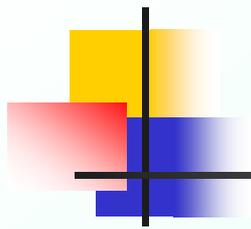


## 6. Acidifying agent

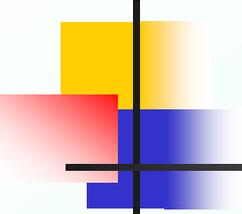


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- Research shows, lactic acid, citric acid or acetic acid and other organic acids can promote the animal appetite, improve weight gain and feed conversion. However, there are some problems of feed supply organic acids must be considered, such as corrosion of equipment and higher cost.
- **Acidification agent application in China feed industry is still in the initial stage, usage and methods have not yet be standardized.**
- Organic acid is added in feed and feed formula to consider the compatibility, high protein and salt minerals will be of the acid buffer action; moreover some special acidification agent will cause the animal reduction of feed intake



# 5. Conclusions



## Conclusions

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- 1. Wide variety of antibiotic replacements available.**
- 2. Each product or class has distinct characteristics, responses, advantages, and disadvantages.**
- 3. Scientific literature increasing worldwide, and effectiveness of products is continually improving.**

# Conclusions

Recombinant technique  
重组DNA技术

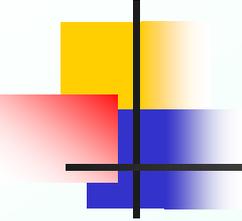
Extraction  
提取

Microbiology  
微生物学

Probiotics, Antimicrobial peptides, Prebiotics, Herbal  
extracts, Enzyme preparations, Acidifying agents  
酶制剂, 天然提取物, 益生菌, 抗菌肽, 寡糖, 酸化剂

Safety Animal products  
绿色畜产品

~~Antibiotics~~  
~~抗生素~~



Thank you for your attention!  
The End

