泰妙菌素防控支原体肺炎的药物敏感性测定与应用实践

Susceptibility Determination and Application of Tiamulin for the Control of Mycoplasma hyopneumoniae

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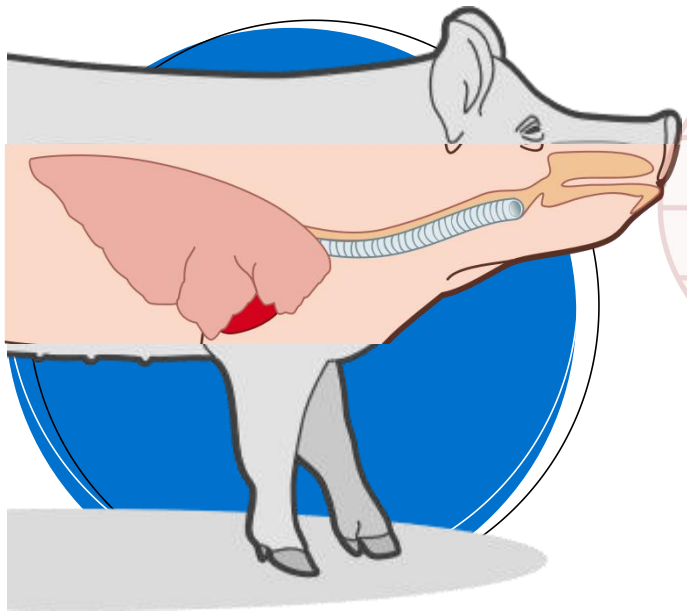
1. Background 背景介绍

1.1 Porcine Respiratory Diseases Complex (PRDC) 猪呼吸道疾病综合征

--Multifactorial syndrome
--多种因素导致的综合征



Primary agents 原发病原

- PRRSV
  猪繁殖与呼吸综合征病毒
- PCV-2
  圆环病毒2型
- Influenza
  猪流感病毒
- Aujeszky
  伪狂犬病毒
- *Mycoplasma hyopneumoniae*
  猪肺炎支原体

Secondary agents 继发病原

- Actinobacillus pleuropneumoniae
  胸膜肺炎放线杆菌
- Haemophilus parasuis
  副猪嗜血杆菌
- Streptococcus suis
  猪链球菌
- *Mycoplasma hyorhinis*
  猪鼻支原体

1. Background 背景介绍

1.2 Mycoplasma hyopneumoniae 猪支原体肺炎

Clinical signs

临床症状

Lesions

病理损伤

--Often subclinical 常呈现亚临床感染

--Clinical 临床症状

- non-productive cough 干咳
- increasing the FCR 提升饲料转化率
- decreasing the ADG 降低平均日增重
- more heterogeneous weights between pigs 均匀度变差
- increasing cull rate and mortality 淘汰率和死亡率增加

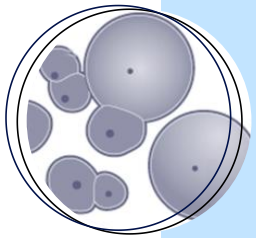
--Infections with M. hyopneumoniae can cause different lesions according to how the illness progresses. 根据病程发展，导致不同程度的病理损伤

- Red to purple-coloured areas of consolidation in the cranial ventral part of the apical, cardiac, accessory, and diaphragmatic lobes. 在肺尖叶、心叶、副叶和膈叶的颅腹侧出现红色实变区。

1. Background 背景介绍

1.3 Mycoplasma hyopneumoniae control strategies 猪支原体肺炎的防控策略

--Diagnosis 诊断



PCR is the most common diagnostic test done on lung tissue, nasal swabs, and samples obtained using tracheobronchial brushing or lavage.
PCR是最常见的诊断方法，可用于检测肺组织、鼻拭子、气管灌洗液样本

ELISA tests, antibodies against M. hyopneumoniae can be detected in serum, which can arise from maternal antibodies, infection, or vaccination. ELISA检测可检测血清中的抗体，可能来自母源抗体、感染或疫苗接种

--Treatment and control 治疗与控制

Antimicrobial agents that work against this bacteria include: tetracyclines, macrolides, pleuromutilin and fluoroquinolones.
有效的抗菌药物包括四环素类、大环内酯类、截短侧耳素类和氟喹诺酮类。

--Vaccination 免疫

Widely used, since it reduces clinical symptoms and pulmonary lesions and improves productivity. In addition, it reduces the bacterial load in the airways and the prevalence of the infection on the farm.
疫苗免疫广泛使用，可减轻临床症状和肺部病变，提高生产性能，降低呼吸道中的细菌载量和感染率。

--Eradication 净化

2. Objectives of study 研究目的

- 2.1 Highly effective antibacterial for clinical eradication and control of **M. hyopneumoniae** were screened through drug susceptibility testing.

通过药敏试验筛选对猪肺炎支原体高效抗菌药物，用于净化与临床控制。

- 2.2 Determine the susceptibility of M. hyopneumoniae to tiamulin. Minimum inhibitory concentration (MIC), MIC Range, MIC_{50}, and MIC_{90} values were calculated.

测定泰妙菌素对猪肺炎支原体的敏感性，计算与统计最小抑菌浓度（MIC）、MIC范围、MIC_{50}和MIC_{90}值。

- 2.3 Based on the PD and PK data of Tiamulin, combined with the results of susceptibility tests, the precise dosage of Tiamulin to control M. hyopneumoniae was determined.

结合泰妙菌素的药效学（PD）和药代动力学（PK）数据，确定控制猪肺炎支原体的精准用药剂量。

- 2.4 Through precise medication, the dosage of antibacterial drugs is reduced, and the impact of M. hyopneumoniae on the production performance is reduced.

通过精准用药，减少抗菌药物用量，降低猪肺炎支原体对生产性能的影响。

3. Materials 试验材料

3.1 Test drugs 受试药物

Tiamulin: with a purity of 98.9%, batch number ERS10050， provided by ELANCO (Shanghai) Animal Health Co., Ltd.

泰妙菌素：纯度98.9%，批号ERS10050，由礼蓝（上海）动物保健有限公司提供。

Table. Preparation for each test drug 表 测试药物的准备方法

Test drugs 测试药物	Solvent 溶剂	Purity(%) 纯度	Initial concentration(μg/mL) 初始浓度	Volume(mL) 体积	Quality(mg) 质量	Weighing Quality(mg) 称重质量
Tiamulin 泰妙菌素	Water 水	98.9	1280	10	12.8	12.94

3.2 Culture medium 培养基

--The KM2 liquid medium (batch number 20250616) was developed by the Animal Mycoplasma Innovation Team, Veterinary Research Institute, Jiangsu Academy of Agricultural Sciences.

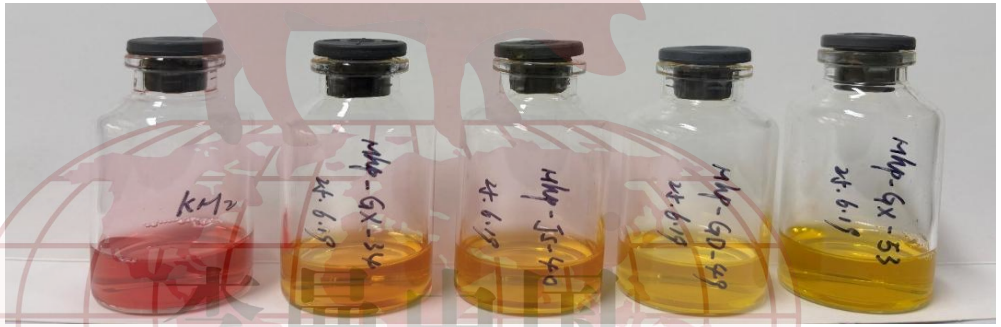
KM2液体培养基（批号20250616），由江苏省农业科学院动物卫生研究所动物支原体创新团队开发。

4. Method 试验方法

4.1 Preparation of bacterial storage solution 细菌储存液制备

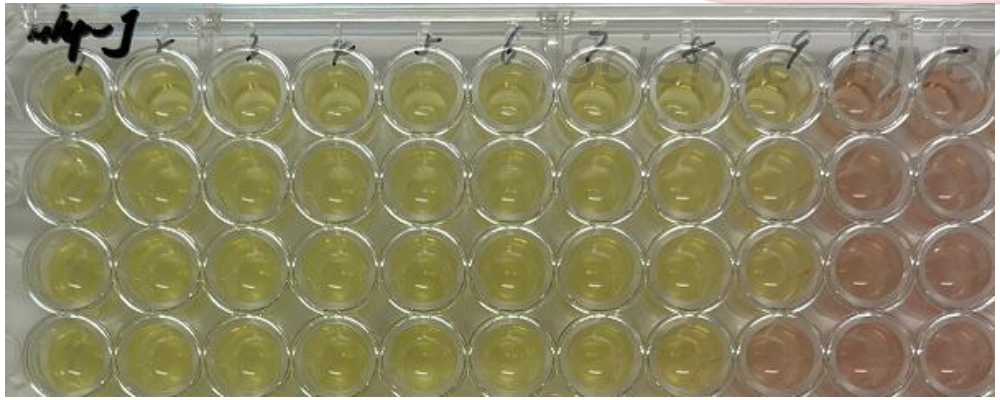
--M. hyopneumoniae were inoculated in KM2 liquid medium.

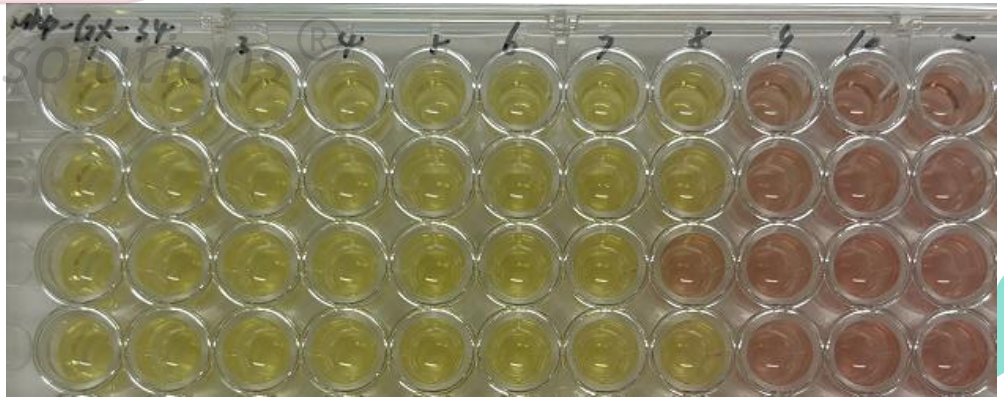
将猪肺炎支原体接种于KM2液体培养基



--The CCU titers of 21 strains of M. hyopneumoniae were determined by the microtiter plate method

通过微量滴定板法测定21株猪肺炎支原体的CUU滴度





4. Method 试验方法

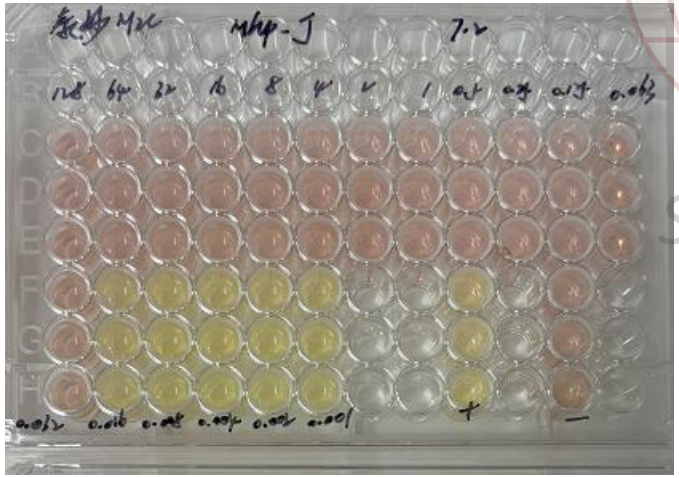
4.2 Determination of Minimum Inhibitory Concentration (MIC) MIC值的测定

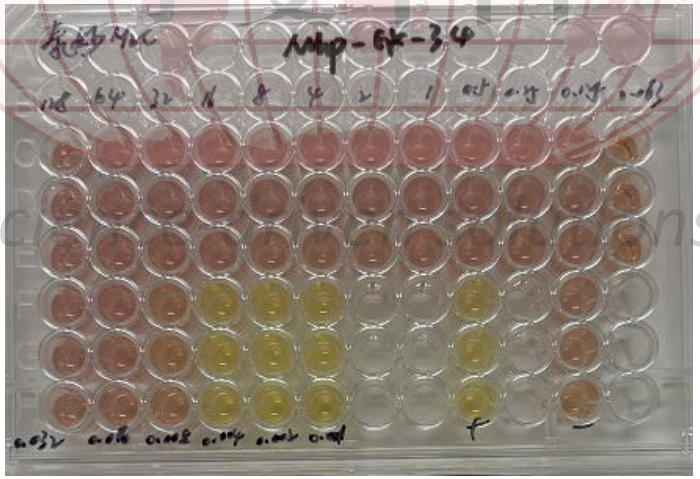
--MIC of tiamulin against M. hyopneumoniae and were determined by the broth microdilution method.

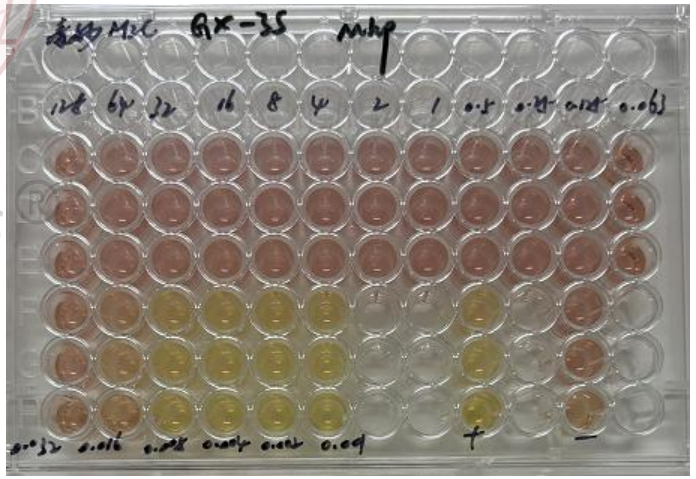
采用肉汤微量稀释法测定泰妙菌素对猪肺炎支原体的MIC 值

--The experimental procedures were set referring to the literature of Hannan, P. C., Vet Res. 2000.

实验步骤参考Hannan, P. C.的文献（Vet Res. 2000）

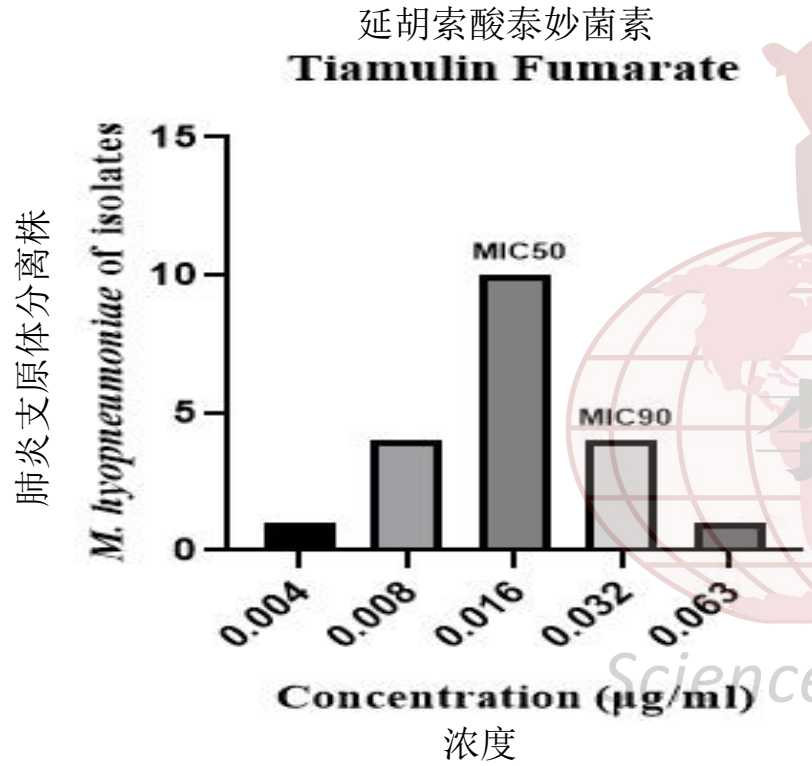






5.Results and Analysis 结果与分析

5.1 MIC results for Tiamulin against M. hyopneumoniae 泰妙菌素对肺炎支原体MIC 测定结果



Items 项目	MIC values（μg/mL） MIC值
MIC Range	0.004-0.063
MIC_{50}	0.016
MIC_{90}	0.032

--For M. hyopneumoniae, MIC range of tiamulin was 0.004 to 0.063 μg/mL, with MIC50 at 0.016 μg/mL and MIC90 at 0.032 μg/mL.

针对肺炎支原体，MIC范围是0.004到0.063μg/mL，MIC50为0.016 μg/mL ，MIC90为0.032 μg/mL

5.Results and Analysis 结果与分析

5.2 MIC results for 2025 VS 2020 2020年与2025年MIC 测定结果对比

Items 项目	MIC values（μg/mL） MIC值	
	Year 2025	Year 2020
MIC Rang	0.004-0.063	0.03-0.25
MIC_{50}	0.016	0.06
MIC_{90}	0.032	0.12

--For M. hyopneumoniae strains isolated in China show high and consistent sensitivity to tiamulin; there is no evidence of a resistance pattern developing to tiamulin.

结论：中国分离的猪肺炎支原体菌株对泰妙菌素表现出高度一致的敏感性，未发现耐药性

6. Applications and Practices 猪场应用与实践

6.1 Determined dosage of Tiamulin to control M. hyopneumoniae was determined
确定使用泰妙菌素控制猪肺炎支原体的剂量

Tiamulin inclusion level THF (ppm) 泰妙菌素添加剂量	Calculated daily dose tiamulin (mg/kg) 计算每日剂量	Lung concentration (μg/g) 肺组织浓度	Colon mucosa concentration (μg/g) 结肠粘液浓度	Colon content contenttration (μg/g) 结肠内容物浓度	Ileum content concentration (E) (μg/g) 回肠内容物浓度
38.5	1.98	a	a	a	---
110	6.6	1.46	a	2.84	0.8
220	13.2	1.99	1.57	8.05	2.4
LOQ		0.94	0.92	1.62	---

Key: a=below the limit of quantification (LOQ, in μg/g); a表示，低于最低检测限
E=estimate ICC (colon contents conc. x 29% = ileum contents conc.) E为估测值，结肠内容物浓度的29%为回肠内容物浓度

--Tissue concentrations in target tissues such as lung achieved with oral dosages of >6.6mg/kg body weight, is high and exceeded the MIC values for key respiratory pathogens e.g. M. hyopneumoniae.

—当口服添加泰妙菌素的剂量超过6.6毫克/公斤体重时，在肺脏等靶器官中达到的药物浓度较高，超过了关键呼吸道病原如肺炎支原体的MIC值

Tiamulin activity (Denagard®) in certain swine tissues following oral and intramuscular administration. Proc. AASV Chicago p.115-118

6. Applications and Practices 猪场应用与实践

6.1 Determined dosage of Tiamulin to control M. hyopneumoniae was determined
确定使用泰妙菌素控制猪肺炎支原体的剂量

Tiamulin inclusion level THF (ppm) 泰妙菌素的添加剂量	Calculated daily dose tiamulin (mg/kg) 每剂量用记录	Lung con-centration (μg/g) 肺组织浓度	M. Hyopneumoniae 猪肺炎支原体	M. Hyorhinis 猪鼻支原体
137.5(Body weight:25kg) 143.5(Body weight:50kg) 165.0(Body weight:75kg) 206.3(Body weight:100kg)	6.6	Lung 1.46	0.01-0.05 (Windsor 1996) 0.06-1.0 (Stipkovits 2004) 0.048 (Thongkamkoon 2002) <0.015-0.12 (Vicca 2004) 0.015-0.12 (Maes 2007) 0.03-0.125 (Kobayashi 2008) 0.048 - 0.19 (Thongkamkoon 2010) 0.03-0.125 (Tavio 2014) 0.002-0.125 (Klein 2016) 0.03-0.25(China 2020) 0.004-0.063 (China 2025)	0.024-0.39 (Thongkamkoon & Makhanon 2005) 0.048 - 0.097 (Thongkamkoon 2010) 0.256 - 1.0 (Makhanon 2015)

6. Applications and Practices 猪场应用与实践

6.1 Determined dosage of Tiamulin to control M. hyopneumoniae was determined
确定使用泰妙菌素控制猪肺炎支原体的剂量

6.1.1 M. hyopneumoniae strains isolated in China show high and consistent sensitivity to tiamulin; there is no evidence of a resistance pattern developing to tiamulin.

从中国分离的肺炎支原体菌株对泰妙菌素高度敏感，未发现耐药性。

6.1.2 Recommended dose rates of tiamulin for feed medication (treatment period 7-14 consecutive days, 6.6mg/kg bw) give tiamulin levels in plasma and lung in excess of the MIC 90（0.032μg/mL）for M. hyopneumoniae.

建议饲料中添加泰妙菌素的剂量6.6mg/kg体重，治疗时间7~14天，血浆和肺组织中的药物浓度超过MIC90（0.032μg/mL ）

6.1.3 According to 6.6mg/kg bw , calculate the amount of tiamulin per ton of feed according to the feed intake of pigs of different weights.

按照6.6mg/kg体重的标准，根据不同猪群的采食量，确定每吨饲料中泰妙菌素的添加量。

6.1.4 Controlling SDR, it is recommended to use tiamulin in combination with tetracycline drugs to increase efficiency.

控制呼吸道问题时，建议与四环素类药物联合使用，提高药效。

6. Applications and Practices 猪场应用与实践

6.2 Clinical application and field trial data of tiamulin 临床应用和田间试验数据

--Chronic wasting disease continuous improvement program 慢性消耗性疾病改善方案

Type of pig 猪的类型	Health challenges 健康挑战	Improvement program 改善方案
Grow-finish farm 生长育肥猪 -Low feed cost of per kilogram of gain 降低斤猪饲料成本 -Low cost of per kilogram of gain 降低斤猪成本	**Porcine Respiratory Diseases Complex猪呼吸系统疾病综合征** -Primary agents: PCV-2 PRRSV MPH ect. 原发病原：圆环病毒2型、蓝耳病毒、肺炎支原体等 -Secondary agents: APP etc. 继发病原：胸膜肺炎放线杆菌等	**Respiratory disease control program** 呼吸道疾病改善方案 -Feed medication: Tiamulin +CTC+（Florfenicol） 饲料添加：泰妙菌素+金霉素+（氟苯尼考）
	Intestinal diseases肠道疾病 -Ileitis 回肠炎 -Dysentery 猪痢疾	**Intestinal diseases control program** 肠道疾病改善方案 -Feed medication: Tiamulin +CTC 饲料添加：泰妙菌素+金霉素

- Please follow the drug label and instructions, and choose the course of treatment according to the actual situation of the pig farm under the guidance of a licensed veterinarian.
  The dosage of the drug should be converted according to the actual kilogram weight of the pig.
  Pay attention to the washout period for each drug and follow it closely.

6. Applications and Practices 猪场应用与实践

6.2 Clinical application and field trial data of tiamulin 临床应用和田间试验数据

--Field trial results and economic benefits (221 farms) 田间应用结果及经济效益（221个农场）

- The feed additive tiamulin effectively controls chronic wasting diseases such as respiratory diseases and intestinal diseases in fattening pigs, bringing the following effects

  饲料中添加泰妙菌素，有效的控制猪呼吸道和肠道疾病

- FCR reduced by 0.2

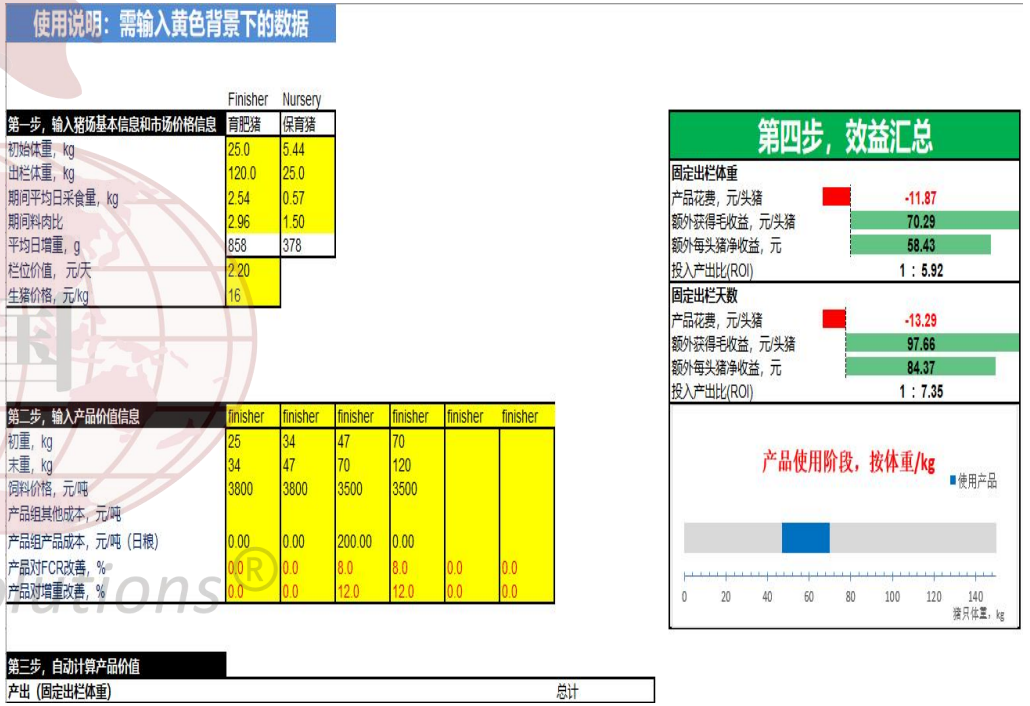
  料肉比降低0.2

- Improved growth performance: ADG and uniformity

  改善生长性能：日增重和均匀度

- Reduce deaths and culls

  降低死亡和淘汰



使用说明：需输入黄色背景下的数据

第一步，输入猪场基本信息和市场价格信息	Finisher 育肥猪	Nursery 保育猪
初始体重，kg	25.0	5.44
出栏体重，kg	120.0	25.0
期间平均日采食量，kg	2.54	0.57
期间料肉比	2.96	1.50
平均日增重，g	858	378
栏位价值，元/天	2.20	
生猪价格，元/kg	16	

第二步，输入产品价值信息	finisher	finisher	finisher	finisher	finisher	finisher
初重，kg	25	34	47	70		
末重，kg	34	47	70	120		
饲料价格，元/吨	3800	3800	3500	3500		
产品组其他成本，元/吨						
产品组产品成本，元/吨（日粮）	0.00	0.00	200.00	0.00		
产品对FCR改善，%	0.0	0.0	8.0	8.0	0.0	0.0
产品对增重改善，%	0.0	0.0	12.0	12.0	0.0	0.0

第三步，自动计算产品价值

产出（固定出栏体重） 总计

ROI:1:7.315

投入产出比 1:7.315

Summary
总结

- For M. hyopneumoniae strains isolated in China show high and consistent sensitivity to tiamulin; there is no evidence of a resistance pattern developing to tiamulin.

  从中国分离的肺炎支原体菌株对泰妙菌素高度敏感，未发现耐药性。

- Tissue concentrations in target tissues such as lung achieved with oral medication at dosages of >6.6mg/kg bw, is high and exceeded the MIC values for key respiratory pathogens e.g. M. hyopneumoniae.

  当口服中添加泰妙菌素的剂量超过6.6毫克/公斤体重时，在肺脏等靶器官中达到的药物浓度较高超过了关键呼吸道病原如肺炎支原体的MIC值。

- Chronic wasting bacterial disease continuous improvement program：Tiamulin + CTC+ Florfenicol

  慢性消耗性疾病改善方案：泰妙菌素+金霉素+（氟苯尼考）。

- Feed additive tiamulin effectively controls chronic wasting diseases, thereby delivering benefits: 饲料添加泰妙菌素有效控制慢性消耗性疾病，因此有以下收益：
  - Reduces FCR by 0.2 料肉比降低0.2
  - Improves growth performance: ADG and uniformity 改善生长性能：日增重和均匀度
  - Reduces mortality and culling losses 降低死亡和淘汰

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