健康畜禽 Healthy Livestock

Veterinary presion medicine and reducing veterinary drugs in animal production in China: case study

YANG SHUMING

Institute of Quality Standard and Testing Technology for Agro-Products of CAAS

Funded by:

Ministry of Science & Technology

Horizon2020

Background to the project - China

- Animal husbandry still at low intensity level: **50% of the pigs are produced by farms that sell <500 pigs/yr**
- Chinese pork consumption increased from 37 g/d in 1992 to 64 g/d in 2012.
- Therefore: China shifts towards highly cost-efficient and integrated intensive livestock systems.
- In 2010, China consumed the largest share of global veterinary antimicrobials (23% - 14.5 tonnes). By 2030 expected to be 30%! (personally predicted)
- It has become one of the key issues of concern in Chinese livestock farming.

In 2018, Action on Reduction of Antimicrobial Drugs Use (2018-2021) was initiated by Ministry of Agriculture and Rural Affaires (MARA) with the aim of zero growth of antimicrobial drugs.

Precision Medicine (a smart way?)

- Reducing antibiotics in animal production is not only the interest of scientists, but also the pressing demand of farms especially pilot farms in the list published by MARA.
- Farms are eager to the practical measures: no or less extra costs and maintaining animal or production performances.
- At present, antibiotics use is legal for animal promotion and cure, changing the use modes into a “smart” way is welcome by farms.

Precision Medicine (PM)

a paradigm shif

- According to the National Institutes of Health (NIH), Precision Medicine is 'an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.' This approach will allow doctors and researchers to predict more accurately which treatment and prevention strategies for a particular disease will work in which groups of people. It is in contrast to a 'one-size-fits-all' approach, in which disease treatment and prevention strategies are developed for the average person, with less consideration for the differences between individuals.
- sequencing tens of thousands of genomes becomes simple, not expensive, for human, not for animal specially short life pig and broiler.

Veterinary Precision Medicine (VPM)

- Veterinary Precision Medicine (VPM), defined as an optimized preventive or curative therapeutic approach (right animal, right drug, right dose, right time) based on identification of biomarkers of disease and use of technologies of disease monitoring. (cited from Guillaume Lhermie et.al. of Cornell University, College of Veterinary Medicine, Ithaca, NY, USA)
- Identify the macro-environmental factors that might impact the emergence and development of VPM, in the perspective of veterinary practice. It applied the PESTEL model, commonly used in strategic analysis, as a comprehensive tool of the external environment impacting a system or organization.
- PESTEL means Political, Economic, Social, Technology, environmental and Legal.

VPM approaches at practice (right dose)

- Aim at an optimized preventive or therapeutic approach (right dose)
- Coating/sustained release techniques: such Microcapsules,

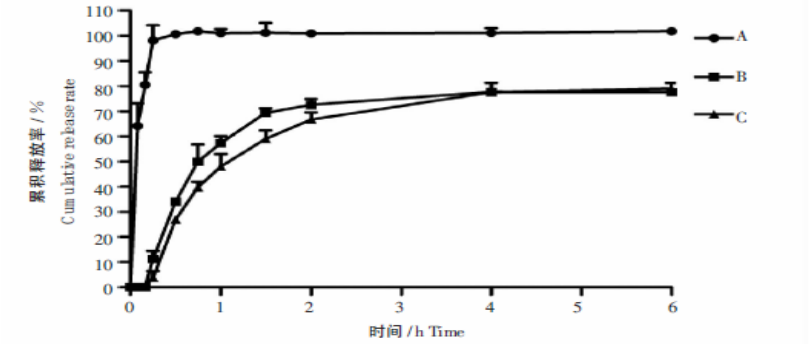
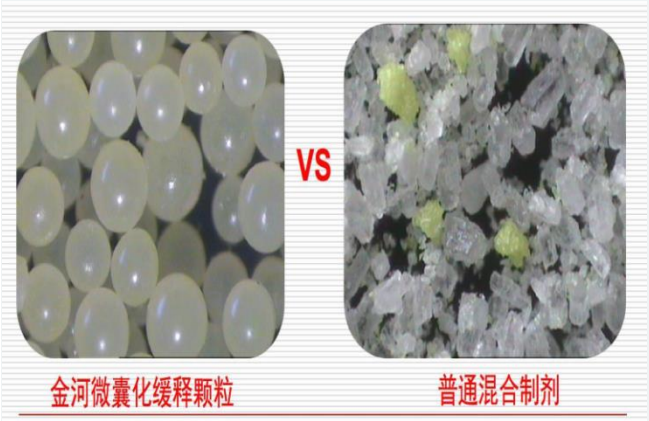


图 4 氟苯尼考微囊的药物体外释放曲线

Figure 4 ***In-vitro*** **release profile of florfenicol from florfenicol microcapsules**

A：氟苯尼考原料药；B：自制氟苯尼考微囊 1；C：自制氟苯尼考微囊 2。

A：The bulk drug of florfenicol；B：Self-prepared florfenicol microcapsules 1；C：Self-prepared florfenicol microcapsules 2.



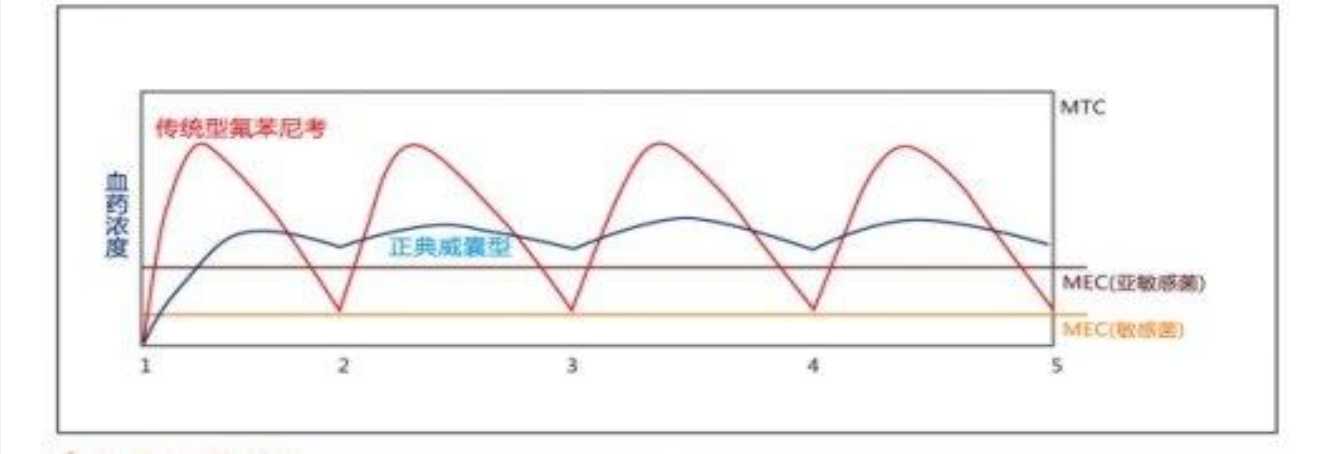
microencapsulated slow-release granules VS common mixture

Table 2 Fitting models or equation of *in vitro* release characteristics of florfenicol microcapsules

拟合模型 Fitting models	自制微囊 1 Self-prepared microcapsules 1		自制微囊 2 Self-prepared microcapsules 2	
	拟合方程 Fitting equation	$R^2_{adjusted}$	拟合方程 Fitting equation	$R^2_{adjusted}$
Zero-order	$Q=0.145\,0t+0.324\,6$	0.534 4	$Q=0.167\,3t+0.220\,3$	0.674 9
First-order	$\ln(1-Q)=-0.336\,8t-0.383\,8$	0.710 2	$\ln(1-Q)=-0.362\,3t-0.195\,4$	0.893 3
Higuchi	$Q=0.419\,7t^{1/2}-0.069\,4$	0.740 2	$Q=0.469\,3t^{1/2}-0.057\,8$	0.852 0
Ritger-Peppas	$\ln Q=0.659\,9\ln t-0.788\,8$	0.799 1	$\ln Q=0.988\,7\ln t-1.078\,9$	0.717 6
Hixson-Crowell	$(1-Q)^{1/3}=-0.108\,7t+0.821\,7$	0.623 5	$(1-Q)^{1/3}=-0.120\,9t+0.890\,8$	0.779 5
Weibull	$(1-Q)^{1/3}=-0.083\,5t+0.877\,8$	0.653 0	$(1-Q)^{1/3}=-0.091\,9t+0.928\,7$	0.812 2

VPM approaches at practice (right dose)

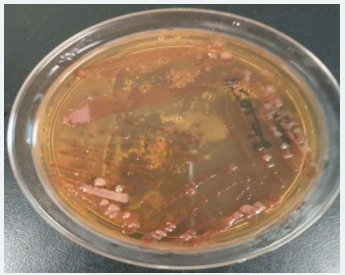
- Behavior of microcapsules of florfenicol in animal bloods

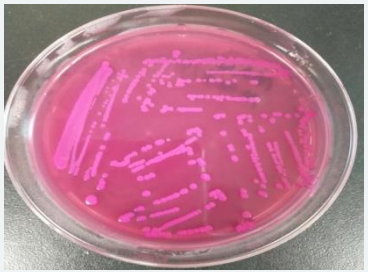


Multiple dose in microcapsules:
keeping a stationary concentration , not high peak or valley ;
Maintaining higher than MEC

VPM approaches at practice : (right drug and time)

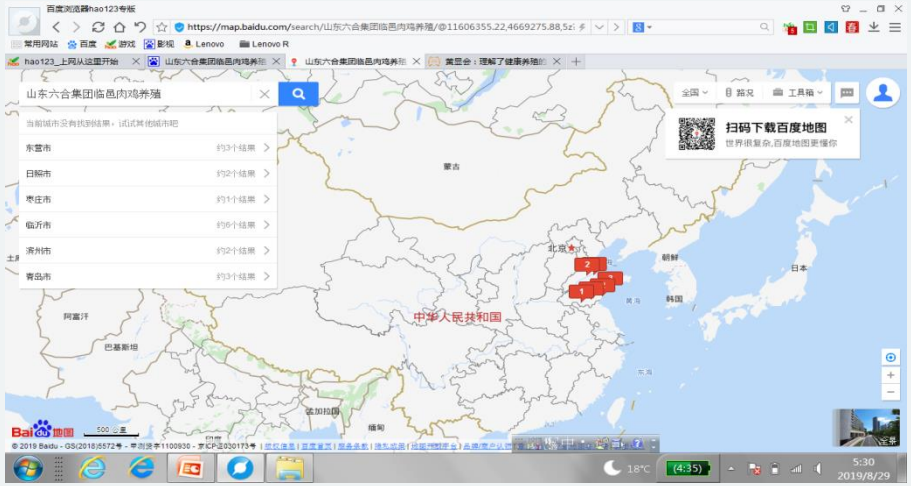
- Aims: an optimized preventive or therapeutic approach (right drug and right time)
- Right time: exposure to pathogen
- Right drugs: sensitive to pathogen
- Need: isolation and susceptibility test





VPM approaches at practice : case I

- Region Liny (LIUHE group), where broiler fed is more than 1 million, contracted farms with LIUHE. Feeding techniques supported from LIUHE.



VPM approaches at practice : case I

- Epidemiological investigation: based on existed data, Bacillary disease led by pathogenic bacteria, E.coli, salmonella , Staphylococcus aureus,
- A survey on main pathogenic bacteria in poultry farms each season,
- Drug susceptibility tests for isolated pathogenic bacteria:
- <50%, drugs are refused

VPM approaches at practice : case I

- Results:
- Drugs costs was reduced by 30%
- Average body weight of broiler up by 1.4%
- Survival rate increased by 1.7%, farms (<90%) reduced by 54.6%.

Case 2: a pig farm

Tianpeng, Beijing, a swine farm with 6 hectares,

Stocking sows : 800

Finished pigs 12000 per year

。Intensive feeding

common diseases : pneumonia

Main used drugs: Amoxicillin+ Doxycycline;

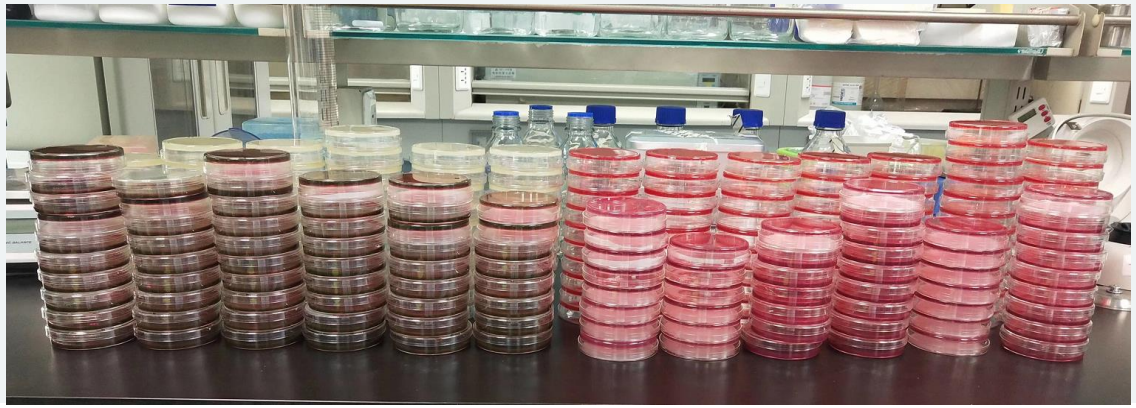
Timicosin + Florfenicol

Technically services by analysis and testing

- it includes production performance, mortality, uses of antibiotics, other index;
- residues in end products and manures
- resistance to antibiotics in bacteria.

Sampling of nasal/anal secretion

	Nasal swab	Anal swab	total
Finish	40		40
sick	10		10
Sow	12	12	24
Total	62	12	74



Isolation of salmonella in BS or XDL culture

	Nasal swab of finish pig	Nasal swab of sick pig	Nasal swab of sow	anal swab of sow	all
Typical salmonella	5	0	0	3	8
Suspected salmonella	0	0	0	0	0
all	5	0	0	3	8

	Nasal swab of finish pig	Nasal swab of sick pig	Nasal swab of sow	anal swab of sow	all
Typical salmonella	5	0	1	3	9
Suspected salmonella	8	0	1	0	9
all	13	0	2	3	18

健康畜禽 Healthy Livestock

Table . Isolation of E. Coli by EMB culture

	Nasal swab of finish pigs	Nasal swab of sick pigs	Nasal swab of sow	Anal swab of sow	all
Typical E. Coli	59	10	5	12	86

Results of susceptibility of E.Coli to drugs

Table 7. Sensitivity of porcine escherichia coli to antimicrobial agents

Names	kind	Sensitive isolate		inter isolate		Resistant isolate	
		strain	%	strain	%	strain	%
Florfenicol	Chloramphenicols	19	22	0	0	67	78
Amoxicillin	Semi-synthetic penicillin broad spectrum beta-lactam antibiotics	5	6	4	5	77	89
Doxycycline	tetracyclines	3	4	2	2	81	94
ENR	quinolones	83	97	0	0	3	3
Erythromycin	macrolides	5	6	60	70	21	4
TMP	Sulfadimidine	19	22	1	1	66	77
GM	aminoglycoside antibiotics	74	86	1	1	11	13
CIP	the third generation of quinoloneantibiotics	80	93	5	6	1	1
Cefotaxime	The third generation of cephalosporin broad-spectrum beta-lactam antibiotics	85	99	0	0	1	1
[Ceftazidime	The third generation of cephalosporin broad-spectrum beta-lactam antibiotics	85	99	0	0	1	1

healthylivestock.net
healthylivestock.net.cn
健康畜禽 Healthy Livestock

Measures after susceptibility

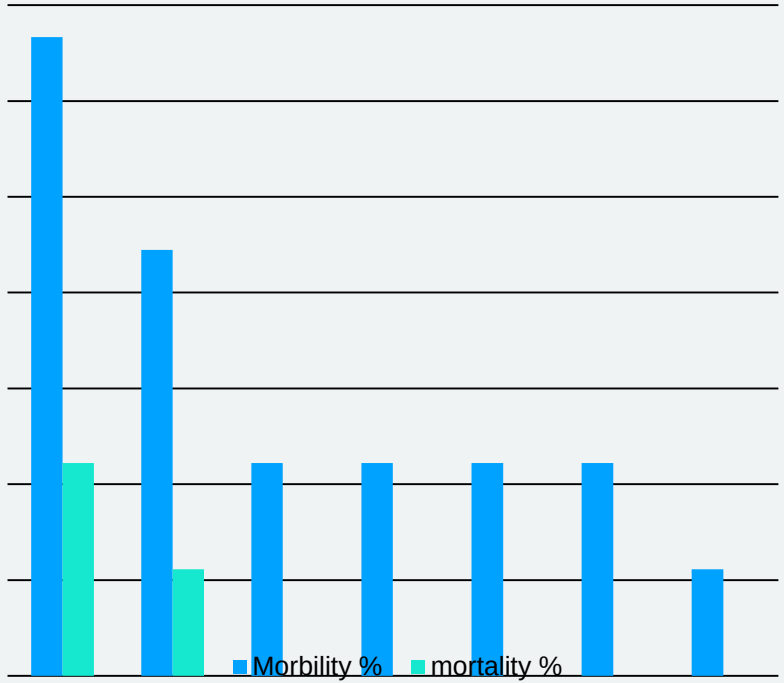
- R-drugs were changed into S-drugs:

  amoxicillin, doxycycline, timicosin and florfenicol to cefotaxime, erythromycin, ENR and CIP,

- Normal dosages can control animal diseases, high dosages were avoided,
- Average morbidity is reduced by 2.5%,
- multi-residues detection is reduced by 21%.

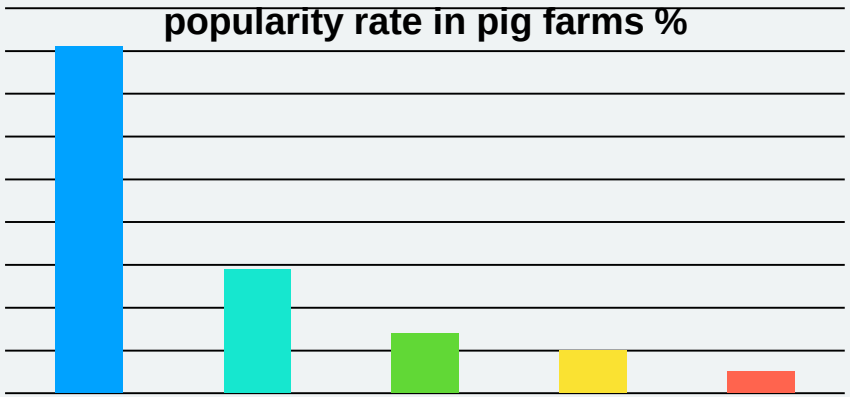
Antibiotics replacers

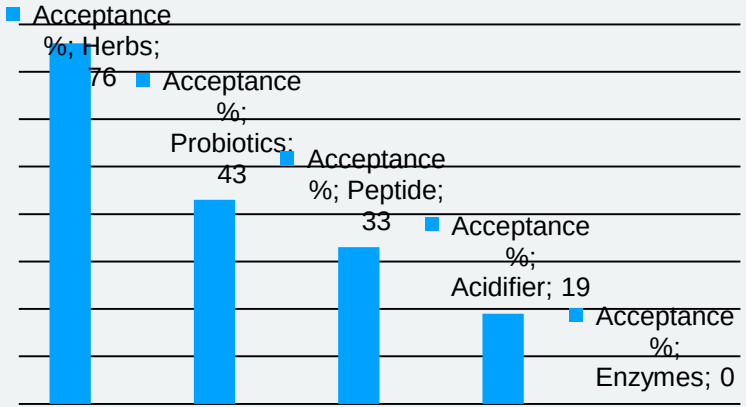
- A feeding broiler trail was done to control infestation of E.Coli, (done by Zhou Shuqin, Heilongjiang agricultural engineering college)
- saccharicter-penin (750 mg/kg) 、yeast culture (0.3%, 0.5%)、probiotics (0.1%)、MOS (750 mg/kg) and flavomycin (5mg/kg) added in basic die.

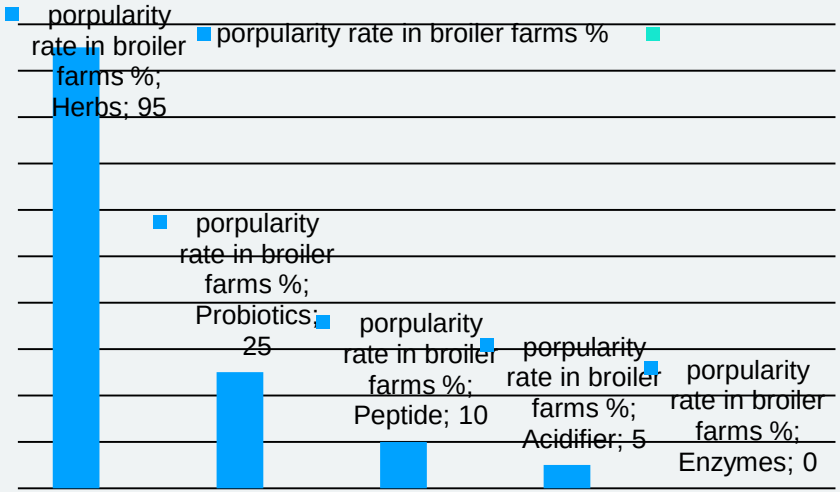


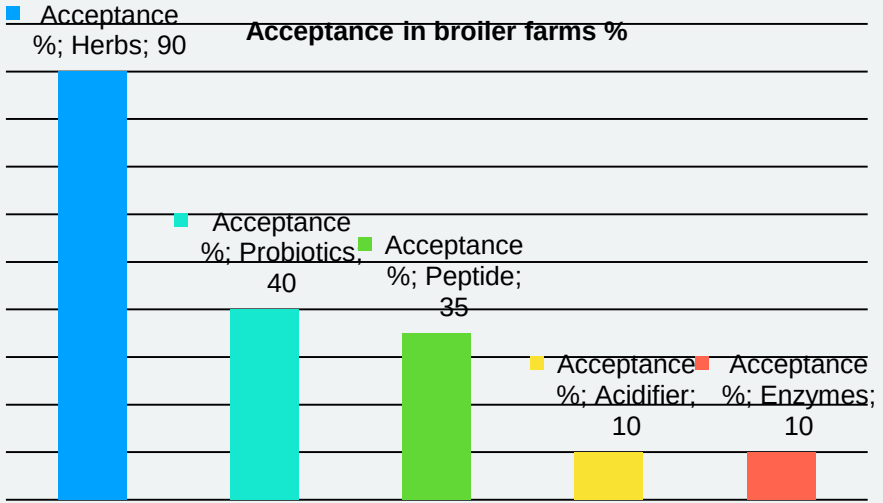
Antibiotics replacers

- A investigation showed situation of antibiotics replacers in Chinese pig and broiler farms.(done by Yu Xiaomen , Beijing Shennongkexin company)
- Popularity rate is number of farms using replacers divided by total number of investigated farms






porpularity rate in broiler farms %; Herbs; 95
porpularity rate in broiler farms %; Probiotics; 25
porpularity rate in broiler farms %; Peptide; 10
porpularity rate in broiler farms %; Acidifier; 5
porpularity rate in broiler farms %; Enzymes; 0


Acceptance in broiler farms %
Acceptance %; Herbs; 90
Acceptance %; Probiotics; 40
Acceptance %; Peptide; 35
Acceptance %; Acidifier; 10
Acceptance %; Enzymes; 10

Conclusions:

- Animal production has more and more pressure on reducing antibiotics use, several practical measures approach to the aim of optimized preventive or therapeutic (right animal, right drug, right dose, right time).
- Limit to use of the practical measures is obvious, innovation is highly recommended.

Thank you!