EU-China expert seminar

Strategies for Intra-cellular protozoosis control

Jiyu Zhang DVM,PhD

infzjy@sina.com

Lanzhou Institute of Husbandry and Pharmaceutical Sciences, CAAS

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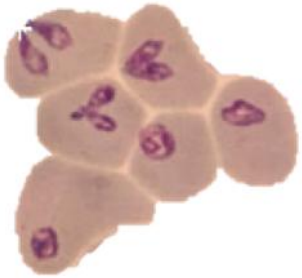
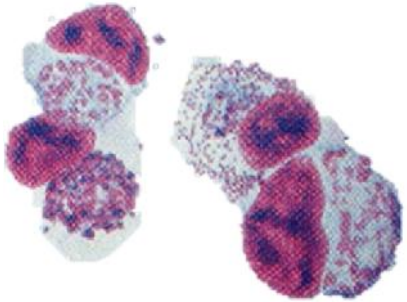
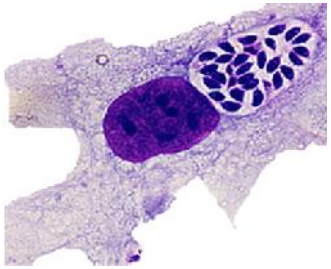
1. Intra-cellular protozoosis in China



Babesia



Theileria



Toxoplasma

Babesiosis (Texas fever)
Feature: fever, inappetence, increased respiratory rate, muscle tremors, anemia, jaundice, and weight loss, hemoglobinemia and hemoglobinuria occur

Bovine theileriosis (East Coast fever)
Feature: high fever, swelling of the lymph nodes, dyspnea, and high mortality, hemorrhages on the serosal and mucosal surfaces of many organs

Toxoplasmosis
Feature: Adult animals toxoplasmosis is usually a subclinical illness. In young animals, usually cause interstitial pneumonia, myocarditis, hepatic necrosis, meningo encephalomyelitis, chorioretinitis, lymphadenopathy, and myositis.

Intra-cellular parasites in clinic

2、Serious threat to animal production and public health

- During the past 15 years, the development of sheep and beef cattle industry is prosperous in China.

- In 2015, China produces 70 million beef cattle and 303 million sheep.

- Piroplasmosis cause serious impact on beef cattle and sheep production.

  It prevail in more than 30 provinces and autonomous regions in China.
- Northwest China, north China, northeast China are high incidence areas.

e.g.:Sheep and goats, recent years in basin area of Yellow River in northwest China,theileria ovis infection rate is 50%. the mortality >10%.

mucosal pallor

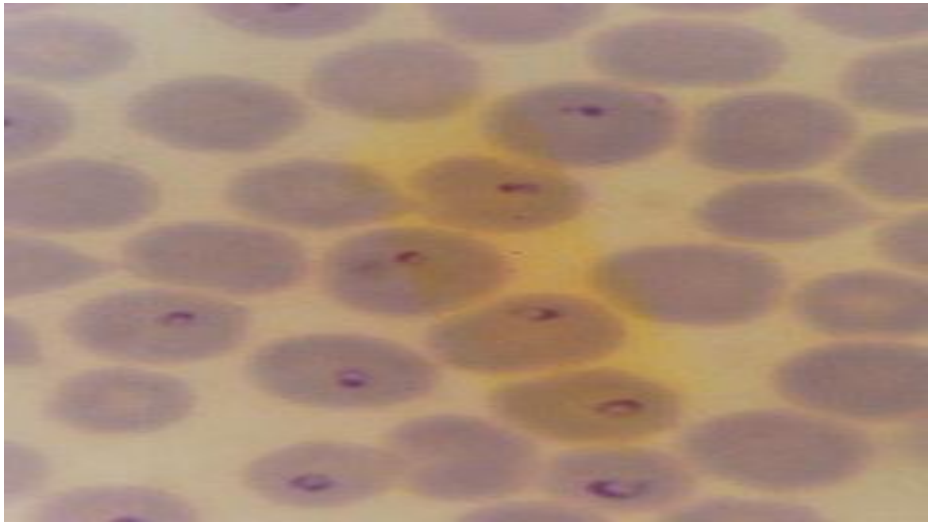
depression

Black stool

Spleen swelling

Myocardial hemorrhage

Skeletal muscle hemorrhage



Theileria annular in blood

Intestinal mucosal bleeding point

Why ?

- Cattle and sheep are transported from epidemic areas to pest free areas (pasturing area to crop growing areas to be fattened for market), healthy animal infected

- Introduction of animal, e.g. cattle Angus(from Australia) about 30,000 heads every year for breed of cattle, the animal lack of resistance to theileria.

- Lack of effective prevention and treatment measures

Prevention and chemotherapy?

- **Currently, there is no effective recombinant vaccine against apicomplexan pathogens.**

- **Some compounds are available for clinical treatment, but the development of drug resistance, reinfection, side effects and residue problems are likely events.**

- **For piroplasmosia**
  - **Trypan (diminazene): Large side effects**
  - **Imidocarb: high levels of toxicity, Long duration of withdrawal**

- **For toxoplasma**

  Sulfanilamide

  Chloramphenicol

  Macrolides and lincosamides

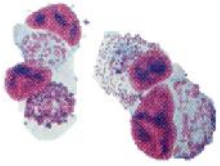
  these antibiotics are often have problems of toxicity or resistance development.

What to do?

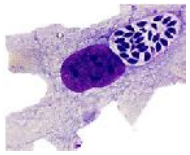
Apicocomplexa

plasmodium

Babesia



Theileria



Toxoplasma

Eimeria

Theoretical basis

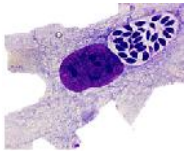
Common characteristics

Apical complex

Isoprene Pathway

Potential target

model of Apicocomplexa



Toxoplasma

Reasearch basis

Traditional Chinese medicine with anti-parasitic ability

Scutellaria baicalensis

Glycyrrhiza uralensis

Stemona japonica

Cyrtomium fortunei

Areca catechu

Brucea javanica

allium sativum

Ranunculus japonicus

Melia azedarach

Reasearch basis

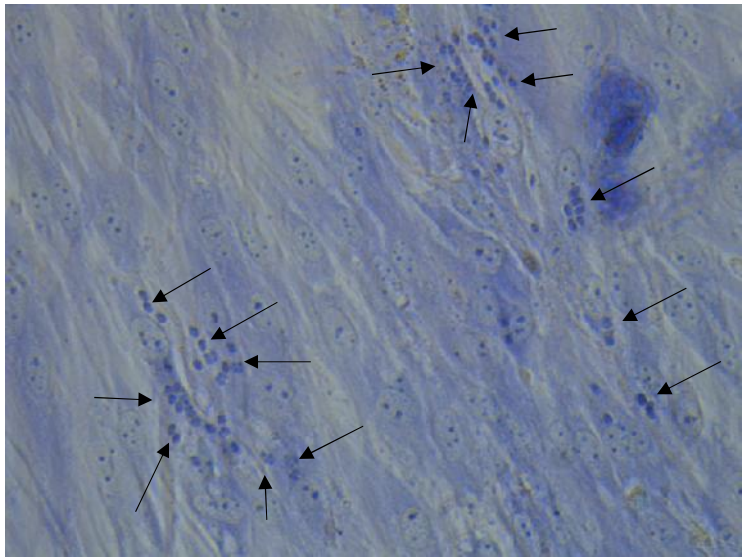
Drug screen

- Baicalin
- Wogonoside
- Licorice glycosides
- Li A
- Arecoline
- Toosendanin
- Tuberostemonine
- Bruceine D
- chlorogenic acid
- Garlicin
- Piperitone
- L-Mandelic acid
- D-Mandelic acid

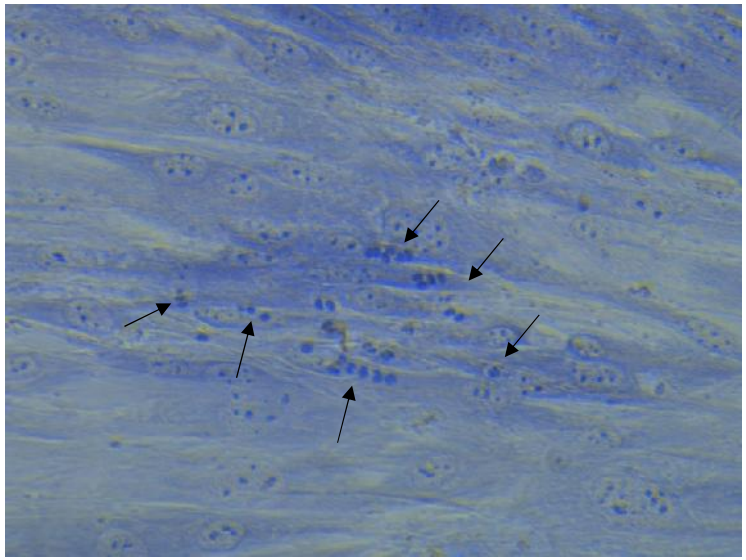
→

May have anti-parasite effect

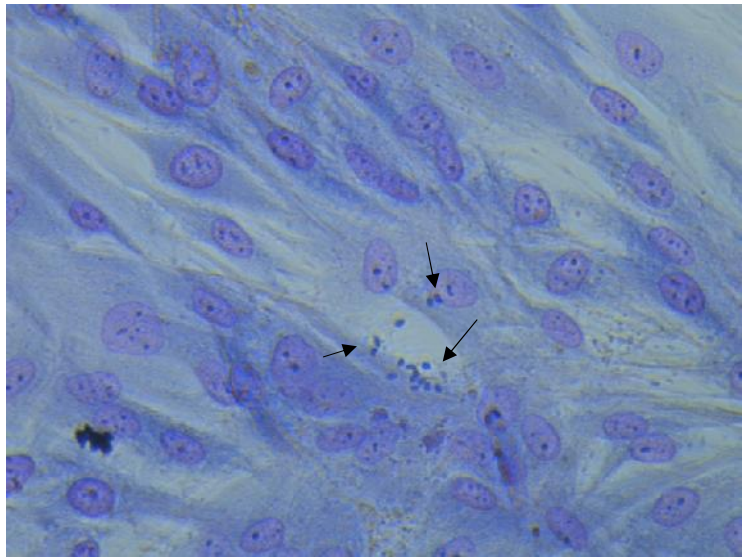
- Li A
- Garlicin
- Piperitone



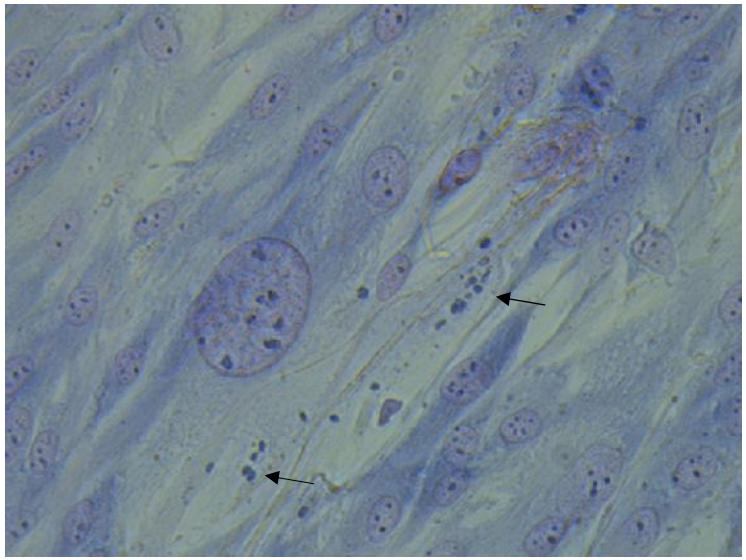
Infect 12h control 24h



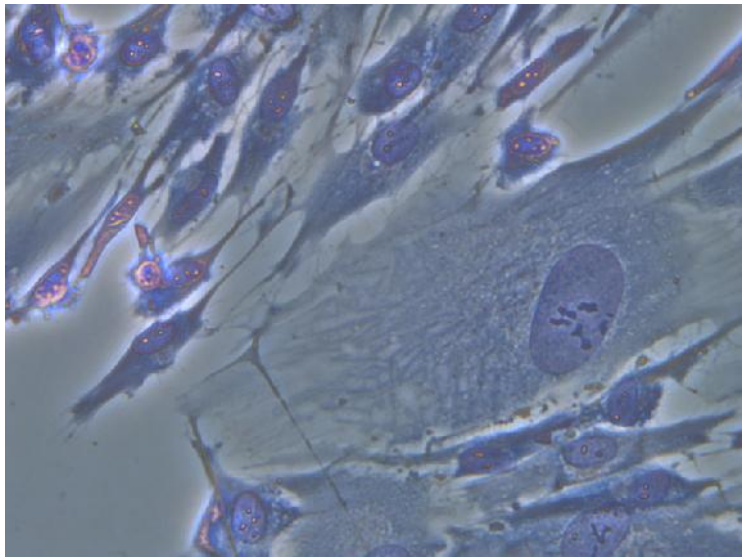
Infect 12h L-A 0.5 ug/mL 24h



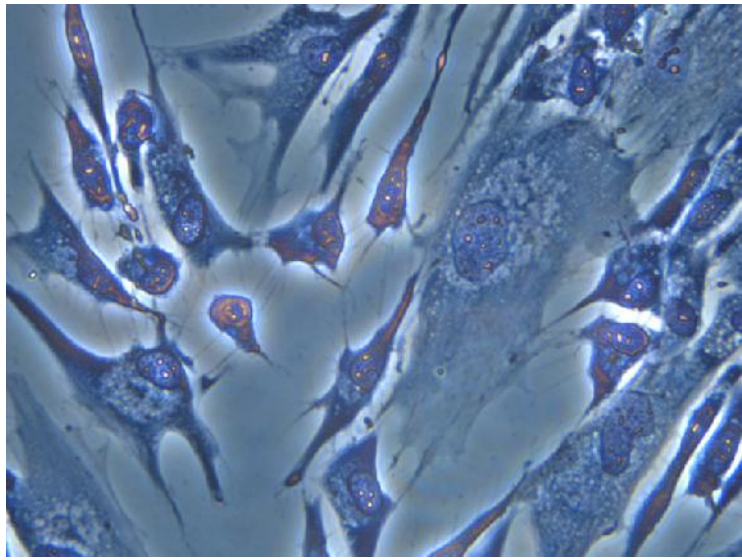
Infect 12h L-A 0.7 ug/mL 24h



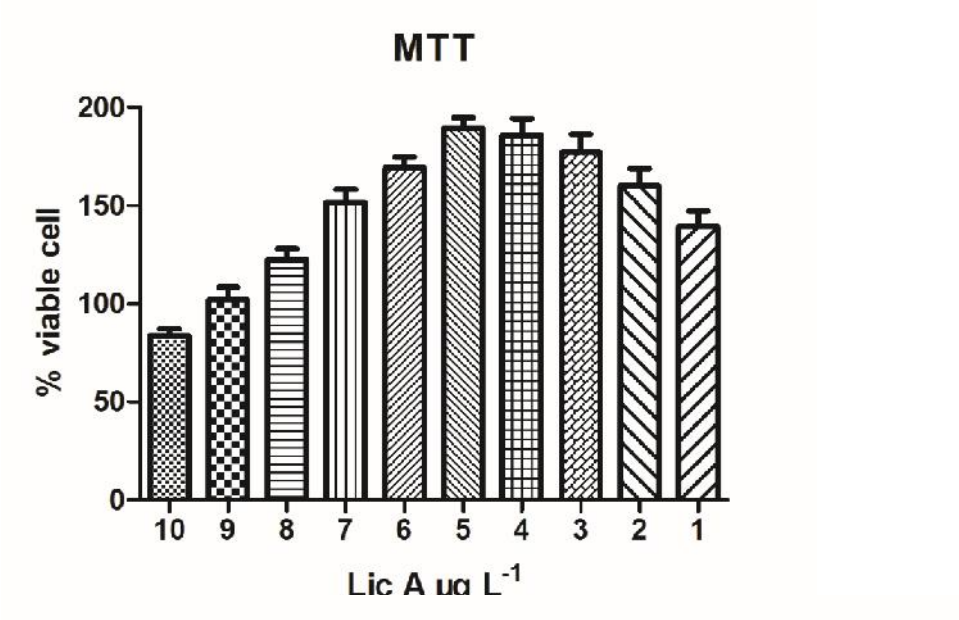
Infect 12h L-A 1 ug/mL 24h

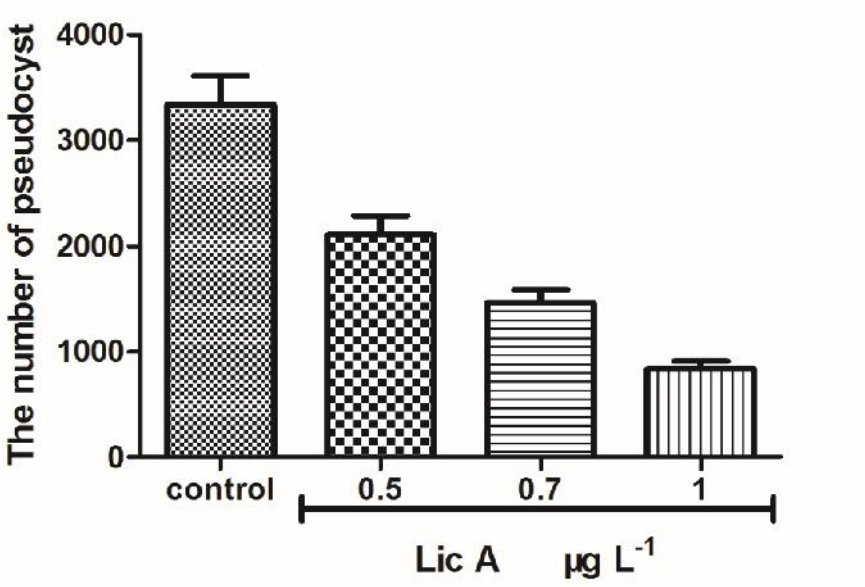


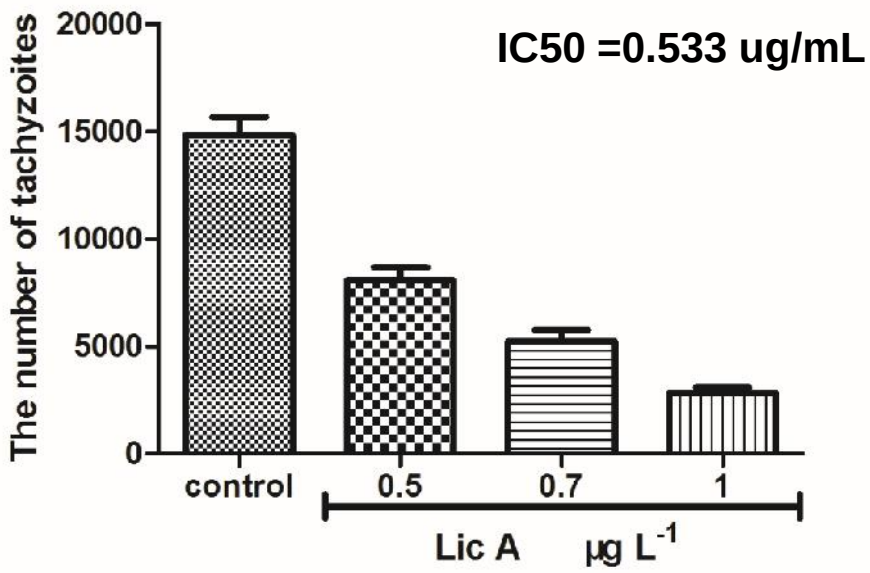
Infect 12h L-A 2 ug/mL 24h

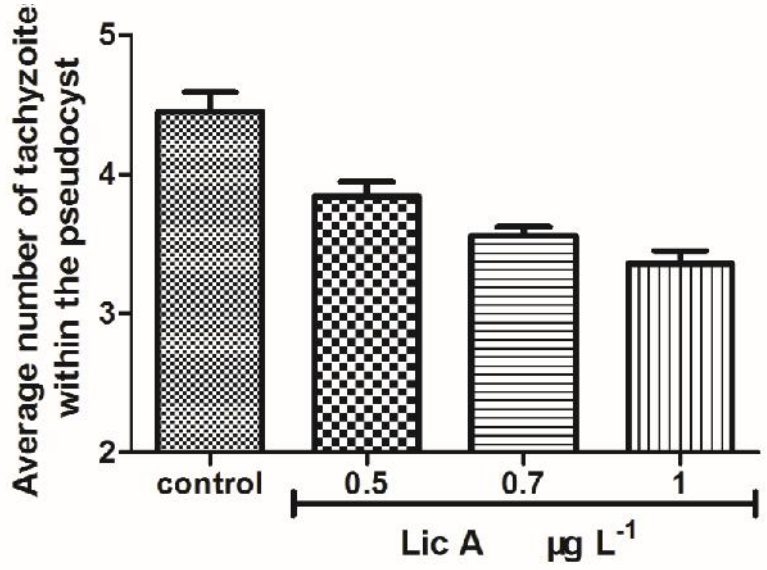


Infect 12h L-A 3 ug/mL 24h


MTT
% viable cell
200
150
100
50
0
10 9 8 7 6 5 4 3 2 1
Lic A µg L-1


The number of pseudocyst
4000
3000
2000
1000
0
control
0.5
0.7
1
Lic A µg L-1


IC50 =0.533 ug/mL
The number of tachyzoites
20000
15000
10000
5000
0
control
0.5
0.7
1
Lic A µg L-1


Average number of tachyzoite within the pseudocyst
5
4
3
2
control
0.5
0.7
1
Lic A µg L-1

Challenges and expectations

1. Epidemiology of immunization of protozoos
2. Structure analysis and bioinformatics of target protein(s)
3. Artificial cultivation method of piroplasma in vitro
4. Comprehensive measures for protozoosis control (Chemical)

Thank you!