# TRICOLIN

COMPLEX ORAL ANTIBIOTIC OF SYSTEMIC ACTION

## ACTS STRONG,

## HITS THE TARGETS!

ENROFLOXACIN
COLISTIN SULFATE
TRIMETHOPRIM

*Salmonella spp.*

*Pasteurella spp.*

*E.coli*

# SOLUTION HERE AND NOW!

## Field trials in poultry farming

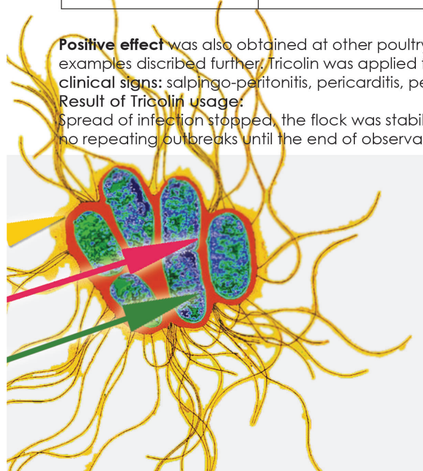
At one of the poultry farms for treatment of broilers of COBB 500 cross with violation of the functions of the gastrointestinal tract, broad-spectrum drugs were used: tricolin and preparation No. 2 containing doxycycline and colistin. In this case, birds in one house obtained tricolin, in another house - preparation №2, both starting from 23rd day of life, according to product leaflet. Bacteriological studies were done, resulting in pathogenic microflora isolation.
Isolated bacteria, according to results of studies, proved to be sensitive to amoxicillin, doxycycline and fluorophenicol. Application results of test preparations are given in Table 4.

**In spite of the fact that sensitivity was low to the active ingredients of TRICOLIN separatly, and the product No. 2 included doxycycline, the sensitivity to which was high, the best results were obtained in the poultry house treated with TRICOLIN.**

Table 4. Comparative characteristics of production indicators.

| Indicators | TRICOLIN | DOXY+COLISTIN | TRICOLIN effect |
|---|---|---|---|
| Number of birds | 14967 | 14905 | |
| Mortality | 298 | 411 | +113 |
| Liveability | 98,01 | 97,31 | + 0,7% |
| Average daily weight gain | 51,28 | 50,88 | + 0,8% |
| FCR | 1,824 | 1,842 | - 0,018 |
| Efficiency Index | 290,04 | 283,34 | + 2,4% |

**Positive effect** was also obtained at other poultry farms in different clinical situations with one of examples discribed further. Tricolin was applied for 12000 laying hens in age of 300 days with clinical signs: salpingo-peritonitis, pericarditis, perihepatitis.
Result of Tricolin usage:
Spread of infection stopped, the flock was stabilized. After treatment protocol was fulfilled, there were no repeating outbreaks until the end of observation period of 500 days of life.



**TRICOLIN**
**IS HIGHLY EFFECTIVE**
**AGAINST**
***Salmonella spp.***

## Acidity

In production of oral antibiotics with enrofloxacin, an alkaline formula is often used.
It may result in problems with sedimentation of a drug, if dissolved in hard water.

**TRICOLIN** ACIDIC **pH** FORM
FOR IDEAL ACTION IN HARD WATER

## Toxicity

Synergistic effect of selected active ingredients made it possible to reduce their concentration without loss of efficiency and to minimize overal toxicity of the product.

Table 5. Study of toxicity of TRICOLIN.

| groups of 10 mice | dose of the drug, mg / mouse | 04.05.12 | | 05.05.12 | | 06.05.12 | |
|---|---|---|---|---|---|---|---|
| | | alive | dead | alive | dead | alive | dead |
| 1 | 1000 | 10 | - | 10 | - | 10 | - |
| 2 | 2000 | 10 | - | 10 | - | 10 | - |
| 3 | 2500 | 10 | - | 10 | - | 10 | - |
| 4 | 5000 | 8 | 2 | 7 | 3 | 7 | 3 |
| 5 | 10000 | 6 | 4 | 6 | 4 | 5 | 5 |
| 6 | 15000 | 7 | 3 | 7 | 3 | 8 | 2 |
| 7 control | 0 | 10 | - | 10 | - | 10 | - |

Low toxicity data indicate that TRICOLIN belongs to 4th toxicity class - low-toxic products.
For white mice with oral administration route, **$LD_{50}$ is 10,000 mg / kg.**
**TRICOLIN IS SAFE and not toxic in doses, 8 times higher than therapeutic.**

## TRICOLIN – COMPLEX UNIVERSAL ANTIBIOTIC OF SYSTEMIC ACTION

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# GENERALIZED INFECTION?

Today, the issue of resistance of pathogenic microorganisms to antibacterial drugs is urgent, as their resistance determines the choice of strategies for treatment and prevention. Resistance is one of factors that determine possibilities to increase economic efficiency of livestock sectors.

**Bacterial infections often have an associated course,** so usage of complex drugs with a wide spectrum of action remains appropriate. **The use of complex drugs in accordance with principles of rational antibiotic therapy allows to:**
- **Prevent occurrence of resistant strains of microorganisms**
- **Reduce likelihood of side effects when using several synergistic substances.**

## Sensitivity

Table 1 shows results of sensitivity studies of bacterial infectious pathogens to most frequently used antibacterial substances.

Table 1. Sensitivity of bacterial pathogens to antibiotics, Ukraine, 2011.

| Detected bacteria | E. Coli 71 | Salmonella 21 | Staphylococcus spp. 9 | Streptococcus spp. 15 | P.Haemolytica 1 | Pasteurella spp. 1 | Pseudomonas spp. 5 | Proteus spp. 3 |
|---|---|---|---|---|---|---|---|---|
| | % | % | % | % | % | % | % | % |
| **Colistin** | **94** | **100** | 0 | 0 | **100** | **100** | **100** | 0 |
| **Enrofloxacin** | **59** | **100** | 44 | 41 | **100** | **100** | **100** | 33 |
| **Trimethoprim** | **54** | **95** | 44 | 7 | **100** | **100** | 0 | 0 |
| Gentamicin | 52 | 95 | 56 | 27 | 100 | 100 | 100 | 67 |
| Doxycycline | 61 | 95 | 56 | 53 | 100 | 100 | 80 | 0 |
| Oxytetracycline | 44 | 90 | 11 | 7 | 0 | 0 | 40 | 0 |
| Flumequin | 14 | 48 | 0 | 13 | 0 | 0 | 0 | 33 |
| Florfenicol | 76 | 95 | 44 | 53 | 100 | 100 | 0 | 100 |
| Spectinomycin | 15 | 33 | 0 | 0 | 100 | 100 | 20 | 0 |
| Amoxicillin | 39 | 95 | 89 | 89 | 100 | 100 | 0 | 0 |
| Amoxicillin + Clavulanic acid | 32 | 86 | 67 | 47 | 100 | 100 | 0 | 33 |

According to research by Dreval DV, Center of Modern Diagnostics, Kiev, Ukraine. A total of more than 200 samples.

Based on modern scientific data about sensitivity of pathogens, BioTestLab team developed a new complex drug TRICOLIN.

## Mechanism of action

**Colistin sulphate**
Breaks mechanisms of cytoplasmic membrane, leading to loss of vital cell components by bacterial cell.

**Enrofloxacin**
Inhibits activity of bacterial cell's DNA-gyrase enzyme.

**Trimethoprim**
Folic acid antagonist, inhibits activity of dihydrofolate reductase enzyme in synthesis of tetrahydrofolic acid.

# ACUTE FORM? POLYINFECTION?

# TRICOLIN
Oral solution

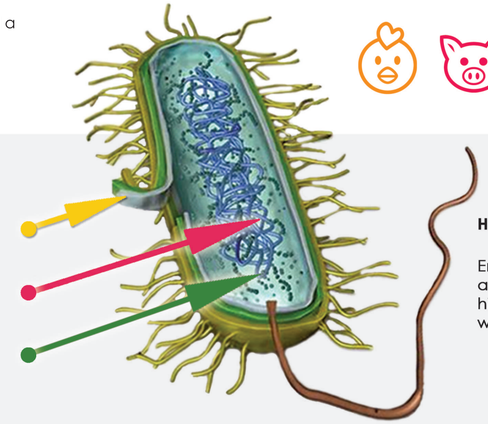
## UNIVERSAL DRUG
- in case of mixed bacterial etiology
- in case of increased resistance
- in case when there's no time to wait for sensitivity results


## Route of administration and doses

TRICOLIN is recommended for use in poultry, pigs, livestock with respiratory and gastrointestinal tract diseases.

Table 2. Application protocol of TRICOLIN.

| | |
|---|---|
| **Route of administration** | Orally |
| **Dosage** | **Poultry:** 1 ml/L of water **Calves, pigs:** 0,5-1 ml/L of water or 0,3 ml/kg of body weight |
| **Duration of treatment** | 3-5 days, salmonellosis - 5-7 days |
| **Withdrawal period: meat (calves, poultry, pigs)** | 7 days |



**HIGH BIOAVAILABILITY**

Enrofloxacin and trimethoprim bind to blood proteins and quickly spread through body tissues, reaching high concentrations in cytoplasm of bacterial cells, where they act directly on bacterial DNA.

# SOLUTION HERE AND NOW!

In practice, cases of synergism are known, with increase in effecacy of combined preparations, even with a combination of active substances, to which (if used separately) sensitivity of microflora was low or even absent.

## Synergies of components

Synergistic effect is clearly demonstrated in results of studies comparing sensitivity to Tricoline, bivalent and monovalent antibiotics in Table 3.

Table 3. Sensitivity determination of bacterial infectious pathogens in animals and poultry.

| Bacteria (cattle, pigs, poultry) | №ER* | Growth inhibition in mm | | | |
|---|---|---|---|---|---|
| | | TRICOLIN | Enro+Trimetho | Enrofloxacin | Trimethoprim |
| **Staph. aureus** | 1404 | 30 | 29 | 29 | 6 |
| **Staph. aureus** | - | 22 | 25 | 22 | 11 |
| **Staph. aureus** | - | 35 | 33 | 33 | 6 |
| **Staph. aureus** | 250 | 15 | 17 | 15 | 10 |
| **E. Coli** | 240 (13) | 18 | 15 | 15 | 6 |
| **E. Coli** | 194 | 26 | 27 | 13 | 6 |
| **E. Coli** | 244 (1) | 26 | 29 | 18 | 20 |
| **E. Coli** | 240 (13 ж) | 19 | 15 | 17 | 6 |
| **Salmonella spp.** | 240 (18) | 30 | - | 20 | 22 |
| **Salmonella spp.** | 196 (12) | 33 | 30 | 32 | 23 |
| **Strep. spp.** | 158 | 25 | 23 | - | - |

*ER - expert report. According to research by Dreval DV, Center of Modern Diagnostics, Kiev, Ukraine. disco-diffusion method.

Results of the study (Table 3) show that the complex drug **TRICOLIN showed the highest or close to it efficacy against *Staphylococcus aureus*, *Streptococcus spp.*** despite the fact, that according to the data in Tables 2 and 3, the components in its composition, individually, were less effective against coccus infections.

COLISTIN
ENROFLOXACIN
TRIMETHOPRIM

SYNERGY

LESS TOXICITY

LESS DOSES

RESISTANCE PREVENTION