

Colistin Sulfate in poultry and swine Production

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The use of antibiotics is an important tool for controlling various bacterial diseases that cause economic losses when they affect livestock production. In order to make better use of this tool, it is necessary to have an accurate diagnosis to find the right and effective treatment, preventing the emergence of bacterial resistance.

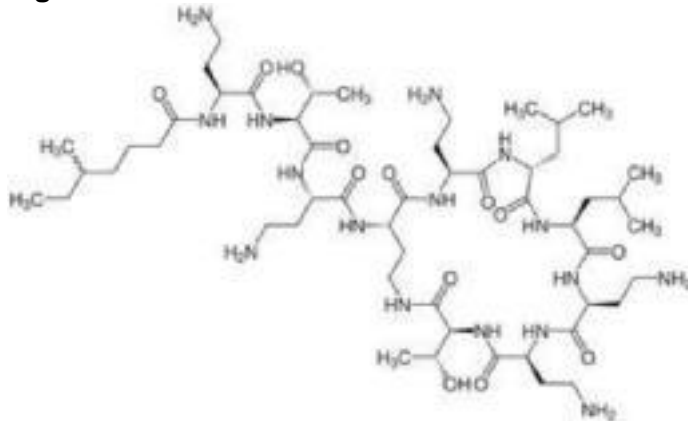
Currently, the use of antibiotic growth promoters has become a common practice in livestock production, although its use is being restricted. The favorable results obtained in animal production parameters may be due primarily to the beneficial effect produced by the intestine in various forms (Colín et al., 1994; Pérez y Gasa, 2002):

- a. Favoring growth in the gastrointestinal tract of microorganisms that synthesize nutrients or inhibit nutrient destroying organisms.
- b. Inhibiting the growth of organisms that produce excessive amounts of ammonia and other toxic compounds.
- c. Improving nutrient absorption.
- d. Improving animal welfare by reducing immune stress and expense of nutrients to produce an inflammatory response in the intestine due to bacterial attack (Roura et al., 1992)

A growth promoter used in Peru in poultry and pork production is sulfate colistin, an antibiotic belonging to the polymyxin group. This group was discovered in 1947 and isolated from *Bacillus polymyxa*, a bacterium that has five different compounds: polymyxin A, B, C, D and E; but only B and E are therapeutic use. E polymyxin or colistin sulfate was discovered in 1949 by non-ribosomal synthesis, from *Bacillus polymyxa*, subspecies *colistinus* Koyama (Coria et al., 2011).

Colistin sulfate is an antibiotic polypeptide which possesses activity mainly against Gram negative bacteria and in veterinary medicine is used orally for the treatment or prevention of enteritis in production animals (EMA, 2002). It is highly effective against strains of *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella* spp., *Haemophilus* spp., *Shigella* spp., *Pasteurella* spp., *Brucella* spp., *Aerobacter aerogenes* and *Bordetella bronchiseptica*. Gram positive bacteria are generally less sensitive, but there are some sensitive strains such as *Staphylococcus* spp., *Bacillus* spp., *Streptococcus pyogenes* and *Corynebacterium* spp. (FAO, 2006, Sumano y Ocampo, 2006).

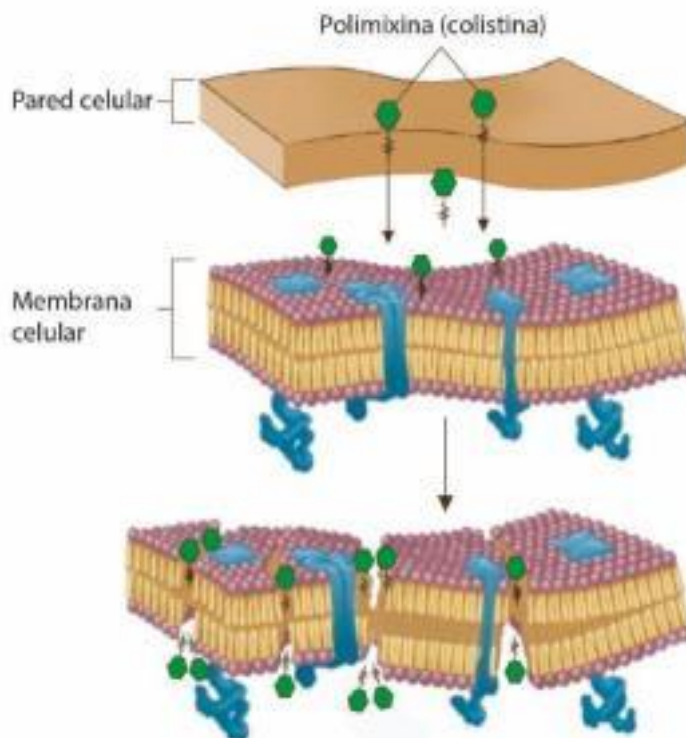
Figure 1. Chemical structure of colistin



Source: Mendes, C.A.C.; Aburdmann, E. 2009. Polimixinas: revisão em ênfase na sua nefrotoxicidade. Rev. Assoc. Med. Bras. Vol. 55, Nº 6: 752-9 p.

The mechanism of action of colistin sulfate is to alter the permeability of the cell membrane of bacteria. This process occurs by electrostatic interactions between the cationic polypeptide (colistin) and anionic molecules of lipopolysaccharide of the outer membrane of Gram negative bacteria, favoring the derangement of the bacterial cell membrane. This way the colistin displaces magnesium (Mg^{2+}) and calcium (Ca^{+2}), which destabilizes the lipopolysaccharide molecule of negatively charged part producing an alteration of the outer membrane. The result of this process is an increase in the permeability of the cell envelope, leakage of contents and subsequently cell death (FAO, 2006; Coria et al, 2011).

Figure 2. Mechanism of action of colistin sulfate



One of the characteristics of colistin sulfate is that administered orally it almost isn't absorbed in the gastrointestinal tract, this favors it having a selective and specific activity in the intestinal lumen against enterobacteria (Sumano and Ocampo, 2006; Collell and Segura, 2013). However, although colistin is very poorly absorbed in the intestine, defects in the function of the intestinal barrier associated with gastrointestinal infections produce increased intestinal permeability (Camilleri et al., 2012). Also, Rhouma and colleagues in 2015, found that colistin when in contact with gastric fluid decreased antimicrobial activity. It is so, that the use of a protective cover using the cyclic oligosaccharide microencapsulation process reduces the amount absorbed in the intestine; optimizing its action at the intestinal lumen. Similarly, it has been shown that the use of this protective cover in antibiotics increases their effectiveness because of the improved interaction of the antibiotic with the cell wall of the bacteria due to it being chemically similar (Sinha et al., 2002; Shastri et al., 2004).

In the poultry and swine production, colistin sulfate is indicated for the prevention and control of gastrointestinal diseases caused by Gram negative bacteria, as is the case of *Escherichia coli* and *Salmonella* spp. These last two bacteria cause diseases of great importance in the livestock industry (Mejía, 2003; Bozorgmehri, 2004; FAO, 2006; Gilbert, 2010; Collell y Segura, 2013).

Colibacillosis is produced by *Escherichia coli*, the predominant bacterial species of normal digestive microbiota of most animals. The importance of colibacillosis in poultry and pig production lies in the large economic losses generated by the high costs of treatment and by decreasing certain production parameters such as weight loss, increased conversion rates and mortality (Gilbert, 2010; Turcas et al., 2012).

Studies have been conducted of sensitivity of clinical isolates of *E. coli* in birds against colistin sulfate, obtaining in most of these studies results of 100% sensitivity (Gilbert, 2010). Also, Richez in 2007 got very low results of colistin sulfate resistance by *E. coli* isolated from pig farms, occurring in only 3 of the 100 strains faced with this antibiotic (Collell and Segura, 2013). Similarly, in a study by Urema in 2004 it concluded that colistin reduced the growth of *E. coli* and the production of toxins (Collell y Segura, 2013).

Salmonellosis is an important disease in poultry and pork production, because of the implications that arise in Public Health, the restrictions on the marketing of products from infected farms and the impact on health programs of farms (flowers, 1981). The most common clinical manifestation of this disease is enteritis, which is often presented as a bloody or profuse watery diarrhea accompanied by fever, but you can see a broad spectrum of clinical symptoms, such as acute septicemia, abortion, arthritis, necrosis on extremities and respiratory disease (OIE, 2008).

Bozorgmehri in 2004 assessed the effect of the use of colistin sulphate in feed to control *Salmonella enteritidis* in a broiler farm. In this study, the addition of colistin sulfate to the feed of chickens, reduced contamination of *Salmonella enteritidis* in the flock and housing. Also, a 14% increase in live weight gain and 8% in feed conversion was observed. Moreover, several studies of sensitivity to colistin sulfate conducted with different isolates of *Salmonella* sp. in pig farms in Spain, showed very low percentage of resistance to this active, performing in most results of 100% sensitivity (Mejía, 2003; García, 2011).

In the poultry and pig industry it has become very important the use of antibiotic and/or non-antibiotic growth promoters, because by using them you get better health, growth and feed conversion. That is why the use of oral colistin sulphate has become a very good alternative to

improve production parameters and prevent the presence of diseases such as colibacillosis and salmonellosis.

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