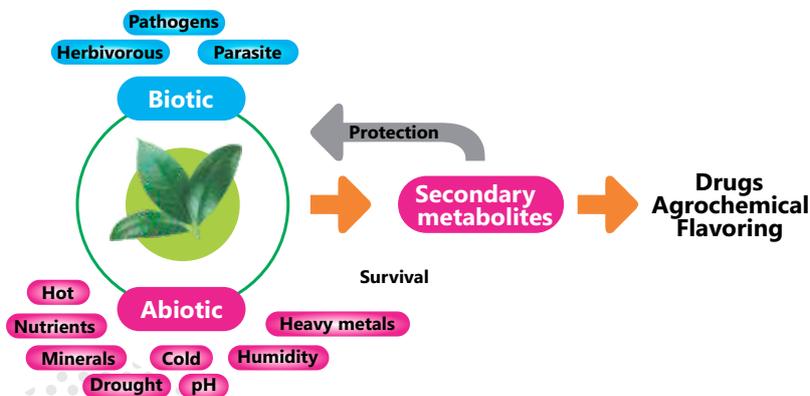


ADDITIVES

THE APPEARANCE OF NATURAL ADDITIVES AS PERFORMANCE ENHANCERS - THE HOP

Nature has always produced almost every organic substance known. The plant kingdom is responsible for contributing with secondary metabolites administration; many of them offer a great added value due to their application in medicine, cosmetics, aliments and agrochemicals. Plants have their own defenses that normally protect them from other plants and predators. These defenses have a chemical nature and, generally, involve substances of secondary metabolism (CROTEAU et al., 2000; PINTO et al., 2002).

Influence of secondary metabolites accumulation



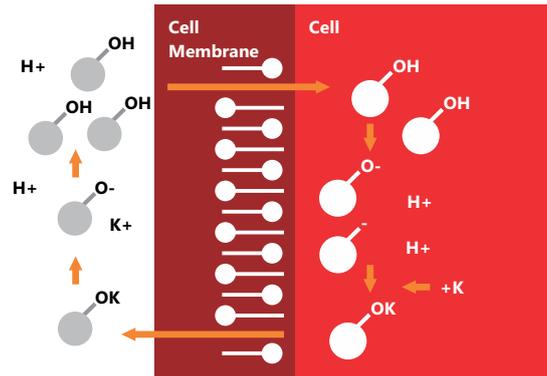
Secondary products have an important role in plants' adaptation to their environment. These molecules contribute to the interaction of the plants with different ecosystems (AERTS et al., 1991; HARBORNE, 1988). These products increase the survival probability, because they are responsible for different biological activities such as antibiotic, antifungal and antiviral in order to protect the plants from the pathogens, and some of them present antigerminative or toxic activities for other plants (LI et al., 1993). The concept of secondary metabolism has been briefly defined as less abundant compounds, with a frequency of less than 1% of the total carbon, due to their storage in organs or in specific cells. The primary metabolism is described as the vital functions for the survival of the plant, such as cell division, growth, breathing, storage and reproduction.

The phytogetic additives are substances mainly volatile and lipophilic (SIMÕES C.M.O., SPITZER V., 1999), the majority of which are terpene hydrocarbons, simple alcohols, ketones, phenols and esters with pharmacologically active compounds. These additives present a significant variation in the chemical composition of the vegetal, depending on climate conditions, incidence of light, phase of harvest, localization or storage conditions (APPLEGATE et al., 2010).

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When we think about industrial poultry farming, 100% of professionals in the area agree that the intestinal integrity in birds has a direct impact on the efficiency of their production. It is necessary to adopt measures in order to increase the longevity of enterocytes. Birds spend between 20 and 25% of the gross energy consumed in the maintenance of the intestinal epithelium, which represents a high demand of energy. When this tissue is damaged, apart from a reduction of the volume of substrate digested and absorbed, there is a higher demand of energy for cell renewal. The energy that could be used for production is used for tissue repair, resulting in a minor weight gain and in a high feed conversion (FRANCO, 2010).

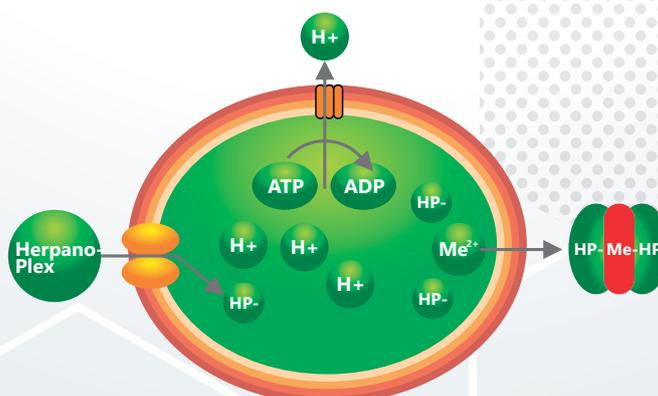
Mechanism of action of secondary metabolites in the target bacteria



The use of antimicrobials in animal feeding is being more and more restricted, due to the problems related, in most cases, to public health. In January 2006, the use of antibiotic growth promoters (AGP) in animal feeding was prohibited by the European Union. This trade bloc is a big influencer for important importers such as the Asian and Middle East blocs. In consequence, Brazil has tried to adapt to the international export rules and to apply the laws in force. In many countries, consumers of poultry products request that meat should be produced without antibiotics.

The components of bitter substances of hop (*Humulus lupulus*) have a strong antimicrobial activity against a variety of microorganisms (GERHAUSER, 2005; SRINIVASAN et al., 2004; LEWIS et al., 1994). Antimicrobial applications of hop include antiprotozoal and anti-clostridial activities and antiviral activities, apart from various applications in feeding as additives for animal ration and their use as a potential source for new antibiotics (CORNELISON et al., 2006; MITSCH et al., 2004; LEWIS K., AUSUBEL F.M., 2006). Bacterial species with susceptibility to hop include *Clostridium perfringens*, *Clostridium difficile*, *Clostridium botulinum*, *Mycobacterium tuberculosis*, and strains resistant to antibiotics of *Staphylococcus aureus* and *Helicobacter pylori* (SRINIVASAN et al., 2004).

Picture of the mechanism of action of Herbanoplex



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The hop substances are divided into two groups: α -acids and β -acids, but there are other compounds that appear in a natural way or during the dry and storage process of the plant (BIENDL M., PINZL C., 2008). The α -acid (Humulone) and its isomers soluble in water and the iso- α -acids (isohumulones) are the main components that generate the bitter flavor of this vegetal. These substances act as ionophores in the gram-positive bacteria cell wall, producing an alteration of the transmembrane potential, resulting in the leakage of ATP and the cell death (TEUBER M., SCHMALRECK A.F., 1973; SCHMALRECK A.F., TEUBER M., 1975). The antimicrobial activities of β acids are attributed to a series of similar compounds, such as lupulone and its congeners (adlupulone, colupulone, among others); they contribute less to the bitterness than the α -acids, but they have an important antimicrobial activity due to their hydrophobic nature (SIRAGUSA et al., 2008). Their antimicrobial effect happens in the bacterial cell wall, denaturing and coagulating proteins. They alter the permeability of the cytoplasmic membrane for hydrogen and potassium ions, producing the interruption of the vital processes of the cell, such as transport of electrons, protein translocation, phosphorylation and other reactions that depend on enzymes, fact that cause a lack of chemiosmotic control of the cell, leading to the death of the bacteria (DORMAN et al., 2000).

Different studies have shown that hop compounds can replace the AGPs in poultry diets (BOZKURT et al., 2009). CORNELISON et al., 2006 compared the effects of penicillin and hop and found that the body weight of birds was similar in both treatments at 42 days of age. After that, BOZKURT et al., 2009 added hop extracts to broiler's feed and found that, at 21 days of age, the body weight of the birds was higher compared to the birds that were fed with avilamycin.

A lot have been discussed about the use of AGPs in the selection of microorganisms with gens resistant to antimicrobials that affect antibiotic therapy in humans. In consequence, the use of AGPs in animal feeding is being reduced or, in some countries, even prohibited (BEDFORD, 2000).

The lupulone is a strong anti-clostridial agent that proves that the β -acids of hop extract reduce or inhibit the proliferation of *C. perfringens* in the intestine. So, it is a natural alternative that is reliable and economically sustainable for global poultry production.

Influence of accumulation of secondary metabolites

