

Bioactives for efficient, sustainable high quality meat production

If their use as a supplement in feed has been a defining characteristic of modern livestock farming, antibiotic growth promoters were introduced during the industrialisation of livestock farming, especially in poultry feed during the 1940s. In addition to the imprecise mechanisms of growth promotion triggered by antimicrobial agents, the use of AGPs is now very controversial.

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Indeed, the rise to prominence of AGPs in the animal industry came with its own share of criticism and controversy. In 1969 the Swann committee report (focusing on transferable oxytetracycline resistance from animals to humans) suggested that intensive use of antibiotics in animal husbandry had led to a surge in the rates of antibiotic-resistant bacteria.

Are things falling apart?

During the 1990s, further evidence continued to pour in (for example reports on vancomycin-resistant enterococcus (VRE) detected in patients).

In the 2000s in Europe, the growing awareness surrounding the risk of feed antibiotics, and the ensuing outbreaks of several animal diseases (bovine spongiform, swine fever sanitary crisis) led to the introduction of a range of new measures to ensure food safety.

Europe enacted a total ban on the use of AGPs in animal feed, and restricted the use of antibiotics in animals to health reasons with a veterinary prescription.

The drop in sales volume of antibiotics that followed the ban of AGPs in Europe was matched by a reduction in actual exposure to antibiotics, which was measured by calculating the Animal Level of Exposure to Antimicrobials (ALEA) index.

The ALEA index is obtained by examining factors such as the Population Correction Unit (PCU) to control for animal

	Negative control	AGP treatment	XTRACT 6930	P-value
Feed intake (g/d)	81.99	84.04	84.09	0.40
Average daily gain (g/d)	48.9 ^b	50.4 ^a	51.3 ^a	0.001
FCR (g/g)	1.73 ^a	1.71 ^{ab}	1.68 ^b	0.01

Table 2. Summary of meta-analysis of 38 broilers trials.

demographics, the administered dose of antibiotics and the duration of treatment, to control the fact that antibiotics today are far more efficient and require a lower dose and shorter treatment time.

However, despite these improvements, the challenges associated with drug-resistant bacteria in animals persist, and continue to grow.

A change of paradigm?

In February 2019, Mr Andriukaitis, EU Commissioner for Health and Food Safety, stated that “antimicrobial resistance shows no signs of slowing down” and that treatment for campylobacteriosis and salmonellosis are becoming less and less effective.

Additionally, multidrug resistance (resistant to 2-3 antibiotics) is now found in about 30% of salmonella in man.

A review on antimicrobial resistance has already reported an alarming increase in deaths related to antimicrobial resistant infections. An estimation of 10 million deaths in 2050 was given, putting this problem at the top of the reasons for deaths worldwide and the associated costs will soar to \$100 trillion. Nowadays, all specialists agree that responsibilities for this problem are shared. From the agricultural point of view, an AGP ban by itself is not a sustainable, long-term solution, and it needs to be accompanied by appropriate biosecurity, monitoring and disease control, supported by the use of modern nutritional strategies in the agricultural sector.

Biosecurity is like a wake-up call

In essence, biosecurity is all about preventing contact and the spread of microbes between animals. Barns that house commercial birds should be considered a restricted access zone eligible for a tough cleaning programme.

● Avoiding visitors is a must:

If a visit is required, visitors should have previously showered and changed clothing and footwear before entering barns. A field study led by the Research Group on the Epidemiology of Zoonoses and Public Health from Montreal University was able to demonstrate that poultry operations that used external teams to remove litter or to vaccinate were, respectively, eight and thirteen times more at risk of having a flock infected than operations who use their internal and trained teams.

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Table 1. Deaths from antimicrobial resistant infections are set to rise by 2050 (Review on Antimicrobial Resistance).

Cause of death	Amount
Antimicrobial resistant infections	10.0m
Cancer	8.2m
Diabetes	1.5m
Diarrhoeal disease	1.4m
Road traffic accidents	1.2m
Measles	130,000
Cholera	120,000
Tetanus	60,000

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● **A proper cleaning and disinfection programme is essential:**

A complete cleaning programme between every productive cycle might require up to three entire days of work. Nevertheless, this time investment is critical to reduce the pathogenic load in the building.

All steps in this process are important from wet to dry cleaning, soaking, washing, drying and disinfecting all installations (from the roof to individual equipment such as feeder and water pipe systems prone to biofilm development).

The successive use of detergent and disinfectant will respectively guarantee the removal of all traces of organic matter together with elimination of pathogens.

There is no global biosecurity guideline and development of a regional approach is needed most of the time.

Management

Management comprises a wide range of actions to be set up once birds are placed in the barn. Some critical ones for antibiotic reduction are highlighted below:

● **Management of density:**

For decades, high stocking density coupled with the preventive use of antibiotics has been applied to maximise productivity. In certain regions of the globe (such as Europe) this is no longer permitted.

This necessary change points out that a high stocking density has a negative effect on performance creating stress for the animals and to their intestinal microbiota. A reduction in stocking density can accompany the reduction of use of preventive antibiotics, limiting pathogenic challenges.

● **Environmental management with ventilation:**

Daily monitoring of the temperature, the humidity and associated ventilation inside the building is highly recommended. Indeed, pathogenic development is first dependent on these two parameters, that, if well controlled, will avoid any over-proliferation and limit the use of therapeutic antibiotics.

As this monitoring is mostly computerised the frequency of visits into the barn should not be underestimated.

● **Vaccination programme:**

Infectious disease management with the use of vaccination is important. Vaccination programmes represent an important cost and may not totally protect birds. It also represents a particular stress for birds, inducing a reaction of the immune system most of the time and generating a temporary inflammation.

Circulating pro-inflammatory cytokines are known to affect voluntary feed intake. Even if this phenomenon lasts only a few days, it may entail delays in growth performance first and depletion of gut mucosa by lack of nutrients.

Birds will then divert energy from

production to maintain gut integrity. Certain natural solutions based on plant compounds are now proven to limit the negative subclinical effects of vaccination programmes. The addition of such additives made of turmeric and chilli pepper oleoresins (XTRACT Nature) as an adjuvant to the vaccination programme, was first evaluated by the USDA (United State Department of Agriculture) Animal Parasitic Diseases Laboratory in 2011.

Results in broilers have demonstrated a boosting effect of coccidiosis vaccination and an increase in the pool of antibodies produced in reaction to a second infection.

A well-controlled coccidiosis programme also opens up possibilities for reducing the use of coccidiostats. Similar results were obtained with other types of vaccination programmes in pullets.

Nutrition deeply involved in intestinal health

Nutrition is no longer just a matter of meeting the birds' nutritional requirements. Nutrition plays an important role in birds' metabolic functions and represents an important angle of attack for a sustainable use of antibiotics.

● **Water: aka 'the first nutrient':**

Water quality and accessibility are the first factors to be considered. Beyond its nutritional value, proper monitoring of the quantity of water consumed can be a first indicator of upcoming pathogenic outbreaks. A delicate balance between shortage of water (negatively impacting FCR) and wasted water (negatively impacting litter quality) must be found. Water management is a tool to reduce the use of both preventive and therapeutic antibiotics.

● **Precision feeding:**

In common practice, safety margins in nutrients are used to make sure all animals' requirements are covered. This impacts the formulation costs, increased excretion in manure and sometimes too high levels of nutrients that can affect intestinal health and requires the use of antibiotics.

The withdrawal of antibiotics is frequently associated with a change in protein sources. Indeed, recent formulation models tend to recommend the use of individual synthetic amino acids in order to reduce crude protein inclusion.

This change aims to reduce the intestinal challenges associated with the digestion of proteins (intestinal inflammation, generation of heat) and to orientate to more bioavailable amino acids, limiting their availability for microbial fermentation.

● **Modern additives to complement precision feeding.**

Limiting the use of antibiotics is critical to the general health status of poultry and their intestinal health. Indeed it is now commonly accepted that mucosal tissues and microbial populations (super organism) are all connected.

● **Acidifiers**

The use of acidifiers to control pH has become a common practice worldwide. There is no doubt they are essential in the elimination of antibiotics.

● **Additive targeting intestinal lumen**

Probiotic, prebiotic and post-biotic metabolites are mainly intended to equilibrate gut microflora acting on the content of the intestinal lumen. Directly providing beneficial strains or organic substrate to their development, their inclusion in feed is providing a potential competitive exclusion to pathogenic floras.

● **Additive targeting intestinal structure and immune functions.**

In addition to lumen microbiota balance, optimal gut integrity is crucial. Among selected mode of actions, antioxidant and anti-inflammatory substances can be beneficial. Some natural compounds encompass these properties and thus also support the poultry immune system and its capacity to cope with any challenges.

Studies show that a selected blend of phytomolecules consisting of carvacrol (from oregano), cinnamaldehyde (from cinnamon) and capsicum oleoresin (from red chilli pepper) has the potential to be an alternative solution to antibiotics used as growth promoters.

Data gathered for over 20 years from field trials has shown that the inclusion in poultry diets enables chickens to achieve similar levels of growth and performance compared to diets supplemented with antibiotic growth promoters (be they avilamycin, bacitracin, flavophospholipol, or enramycin).

A comprehensive overview of the effects of this blend is presented under a meta-analysis format (see Table 2), taking into account 38 broiler trials, comparing negative controls or AGP-supplemented poultry feed.

Conclusion

Poultry meat is the most popular source of animal protein around the world, owing to its affordability. However, although AGPs have long been considered the most efficient solution to minimise production costs, their detrimental effects on the development of antibiotic-resistant strains of bacteria with tremendous implications for human health are concerning.

The European experience has shown that a simple ban on AGPs is not enough to restrict their use and that additional measures are required to provide a comprehensive solution. In light of the total AGP ban in Europe, the potential of phytomolecules to provide an alternative solution to AGPs in promoting growth and improving feed conversion ratio, while remaining a viable economical alternative, are promising.

The results of these studies are yet more interesting in its application as an alternative to AGPs, in light of signs suggesting tighter regulations or a near total ban on AGPs in other parts of the world. ■