Soon after the therapeutic use of antibiotics was introduced, the growth-promoting effect of these products in chickens was discovered. Several antibiotics have been in use as growth promoters of farm animals ever since.

Antimicrobial resistance

The widespread use of antimicrobials in food animal production has been linked to the development of antimicrobial resistance (AMR) in bacterial populations. AMR has emerged as a global health crisis. When antimicrobials are administered to food animals for disease prevention or growth promotion, they are commonly administered at lower doses and for longer durations than when these drugs are used for disease treatment and control; administration of low doses for extended periods can increase selective pressure for AMR. In these cases, antimicrobials are usually administered via medicated feed or drinking water on a herd- or flock-wide basis, leading to imprecise dosing when animals can choose what quantity of feed or water to consume and potentially enhancing selection for AMR. Additionally, although veterinary oversight of antimicrobial use has been associated with reduced selection for AMR, veterinary involvement in the use of antimicrobials by the US food animal industry is often limited.

Consumer pressure

Since 2015, NRDC and their allies—Friends of the Earth, Consumers Union, Food Animal Concerns Trust, and Center for Food Safety—together representing millions of consumers, have reviewed and rated the top 25 fast-food and casual restaurant chains in the United States on their antibiotics use policies and practices. They also looked at overall transparency in their meat and poultry supply chains. The results are published annually in a report called Chain Reaction. The 2016 results are shown in Fig. 1.

For the affluent consumers in the West, particularly in Europe, animal welfare, quality, safety and sustainability are important considerations. Retailers on the other hand are keeping close tabs on these developments and for them traceability and certifications are a must to stay in business.

Voluntary commitments from top restaurant chains to shift away from the routine use of antibiotics in their large meat and poultry supply chains are an important lever in changing how these drugs are used in the meat industry. Consumers are voicing their concerns about the public health threat of antibiotic resistance in greater and greater numbers.

Over the past few years, the largest chicken producers and some of the restaurant chains they supply have become leaders in curbing routine antibiotics use. We hope that others follow suit.

In the USA, the evolution is less marked than in Europe although organic production is increasing as consumers in large US cities are demanding more natural products. The high-profile food scandals and diseases have driven the public to look for safety which they trust the FDA/USDA to ensure.

Recently, the US FDA announced that it will take concrete action on the threat of antimicrobial resistance and has outlined a proposal that would help reduce the use of some antibiotics in animal production to counter bacterial resistance to those drugs when they are prescribed for humans.

This is expected to have a ripple effect on other countries in the Asia Pacific region which usually adopt the policies of the US.

In March 2015, McDonald’s announced that it would begin using chickens that are not raised with antibiotics used to treat humans, a move likely to put pressure on competitors of the fast-food chain, which now sells more chicken than beef. The decision by McDonald’s, which is also one of the largest buyers of chicken in the United States, is likely to have a major impact on how poultry is raised and on the kinds of chicken restaurants serve.

In the Asia Pacific region, some key players have started marketing antibiotic-free chicken. For instance in the Philippines, Bounty-Agro ventures, Inc is differentiating their brand of rotisserie chicken ‘Chocks-to-Go’ as no-antibiotics-ever (NAE) Kee Song in Malaysia for a number of years has been producing antibiotic-free chicken.

Holistic approach to AGP-free poultry production

Raising chickens in an AGP-free production system is very challenging. Especially, since antibiotics have been used to cover for lapses in management. Moving to AGP-free poultry farming is not simply replacing the antibiotic.
Antibacterial effects of benzoic acid

Dissociation of benzoic acid is strongly pH dependent and in its undissociated form it exhibits various antibacterial and antifungal activities. Rahn and Conn (1944) reported that the antimicrobial effect of benzoic acid was nearly 100 times as efficient in strongly acidic solutions as in neutral ones. Its spectrum of activity includes mainly enterobacteria, Bacillus spp. and micrococcii, as well as various fungi and yeasts. Its inhibitory action on yeasts and fungi is the background for a long-term use of benzoic acid as the food preservative.

Knarreborg et al. (2002) compared the antimicrobial effects of six different organic acids (formic, propionic, butyric, lactic, benzoic and fumaric acid) in swine stomach content (pH 4.5) and in small intestinal content (pH 5.5), using a specially developed in vitro methodology. The results of this experiment showed that benzoic acid demonstrated the strongest antibacterial property.

The results of a study in broilers (Table 1) showed antibacterial properties of the benzoic acid in the broiler chicken GIT. The best performance results were noted only in early stages of growth reflecting in better feed conversion as well as bodyweight gain after its supplementation.

In the main absorption site in chickens, which is the ileum, a strong reduction in potentially pathogenic coliforms was recorded.

Selected properties and effects of essential oils

The other group of eubiotics which has been extensively evaluated is essential oils. An essential oil is a mixture of fragrant, volatile compounds, named after the aromatic characteristics of plant materials from which they can be isolated. The term ‘essential’ was adapted from the theory of ‘quinta essentia’ proposed by Paracelsus who believed that this quintessence was the effective element in a medical preparation. Because the

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growth promotant with a non-

antibiotic alternative. There is no

silver bullet. We need a holistic

approach and focus on three key

areas, namely: management,
nutrition and health.

Proper husbandry is a paramount

consideration when shifting to AGP-

free farming. Stocking density,

feeding management, ventilation

(temperature and humidity) must be

optimised to deliver the genetic

potential of the bird. In other

words, the flocks must be provided

with a comfortable environment so

that they express their full genetic

potential.

In the aspect of nutrition, the

following should be handled

adequately. For instance, stringent

quality control of raw materials

(quality and safety) must be

observed. The level of trypsin

inhibitor activity must be carefully

monitored. In a study conducted by

Palliyegu et al. (2011), they

increased the level of non-toasted

soybean to spike the trypsin

inhibitor activity.

They demonstrated that by doing

so this resulted in a marked

reduction in protein digestibility,

weight gain and feed conversion

efficiency. There was also a linear

increase in sub-clinical NE lesions in

the duodenum, jejunum and ileum,

and the caecal clostridium

perfringens counts.

Mycotoxin control is of critical

importance. Common mycotoxins

found in the feed have to be

addressed. Mycotoxins can affect

the animals either individually or

additively in the presence of more

than one mycotoxin, and may affect

various organs such as the gastro-

intestinal tract, liver, and immune

system, essentially resulting in

reduced productivity of the birds

and mortalities.

Aflatoxin, aside from being

hepatotoxic, is immunosuppressive

rendering the birds more

susceptible to infections and can

result in a poor response to

vaccination.

Optimum vitamin nutrition is also

essential. Vitamins have a small

inclusion ratio in the diet but they

have essential impact on growth,

feed efficiency and reproduction.

Table 1. Effect of benzoic acid on broiler performance and coliform
counts in the digesta (Josefiak, et. al., 2008).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Benzoic acid (0.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bodyweight gain (g)</td>
<td>2257</td>
<td>2318</td>
</tr>
<tr>
<td>Feed conversion</td>
<td>1.80</td>
<td>1.73</td>
</tr>
<tr>
<td>Coliforms (log cfu per 1g digesta)</td>
<td>4.88</td>
<td>3.36</td>
</tr>
<tr>
<td>Crop</td>
<td>6.60*</td>
<td>4.45*</td>
</tr>
<tr>
<td>Caecum</td>
<td>6.76</td>
<td>6.98</td>
</tr>
</tbody>
</table>

Biosecurity, technical performances, and antimicrobial use. There was an improvement in production results and reduction of antimicrobial use after biosecurity at the broiler farms was optimised.

However, this does not mean that statistically significant relationships were found between biosecurity, health, and production characteristics. Apart from implementing good biosecurity, maintaining the health of the flock entails a vaccination programme covering the major poultry diseases prevalent in the area of operation. Remember that antibiotics cannot kill viruses, hence, vaccination against the important viral infections is essential to achieving satisfactory flock health.

Responsible and judicious use of antibiotics still has a place in the poultry industry in the AGP-free context. Even in Europe and in South Korea, administration of antibiotics to treat diseases, under veterinary supervision, is allowed.

The advent of natural alternatives to antibacterials

Legislation and the increasing consumer pressure to stop routine use of antibiotic growth promotants have been the main drivers in the advent of eubiotics in the poultry industry.

Eubiotics contribute to health and performance of animals by ensuring optimum gastrointestinal functionality. Eubiotics are classified into four categories namely: direct-acting gut flora modulators (e.g. organic acids and essential oil compounds), probiotics, prebiotics and immune modulators.

Optimum gastrointestinal functionality is defined as a steady state where the microbiome and the intestinal tract (host) exist in symbiotic equilibrium and where the welfare and performance of the animal is not constrained by intestinal dysfunction.

Several eubiotics have been introduced in the market with differing modes of action yet having the same goal: achieving the desired ratio between the good bacteria and pathogens. Probiotics are micro-organisms that have a positive effect on the host by improving the balance of pathogenic to beneficial bacteria in the gut. Although, their use has grown over the years, there is still a lot to be learned about the gut microbiota and how their growth and multiplication can be modulated to positively influence the microbial balance.

Prebiotics are non-digestible oligosaccharides serving as substrate for probiotics and/or competing with pathogens regulating gut cell adhesion. Direct acting gut flora modulators are defined as compounds directly modulating the microbiota via growth inhibition. Examples of these are essential oil compounds and organic acids. Dietary supplementation of organic acid increases the bodyweight and improves feed conversion ratio of broilers and reduces colonisation of pathogens on the intestinal wall thus preventing damage to the intestinal wall.
Stimulation of digestive enzymes

The mechanism of hot spices activating sensory nerve fibres is through an ion channel. Platel and Srinivasan (2000) reported that the dietary consumption of the active principle of certain spices like capsaicin, piperin and curcumin, stimulated pancreatic enzyme production in rats without affecting feed intake. The stimulation, by hot spices, of endogenous enzymes is a well-known effect with the basic mechanisms recently elucidated.

Antimicrobial effect of essential oils

The antimicrobial properties of essential oils are well known and a huge amount of literature is available and the basic mechanisms for some of them were reported. Simms et al. (2003) as well as Kamel and McKay (2003) reported that two different commercial blends of essential oils and essential oil compounds could alleviate the growth depression induced by a challenge with Clostridium perfringens in broiler chickens. The exact antimicrobial mechanism of essential oils is poorly understood. However, it has been suggested that their lipophilic property and chemical structure could play a role.

Helander et al. (1998) investigated how two isomeric phenols, carvacrol and thymol, and the phenylpropanoid, cinnamaldehyde, exert their antibacterial effects on Escherichia coli O157 and Salmonella typhimurium. Both carvacrol and thymol, in a similar fashion, disintegrated the membrane of bacteria, leading to the release of membrane-associated material from the cells to the external medium. On the other hand, cinnamaldehyde failed to affect the membrane, indicating that two molecules have different mechanisms underlying antibacterial activity.

It was thus suggested that terpenoids and phenylpropanoids can penetrate the membrane of the bacteria and reach the inner part of the cell because of their lipophilicity, but it has also been proposed that structural properties, such as the presence of the functional groups, and aromaticity are responsible for the antibacterial activity. It is thought that membrane perforation or binding is the principle mode of action, leading to an increase of permeability and leakage of vital intracellular constituents, resulting in impairment of bacterial enzyme systems.

Effect of essential oil compounds in chickens

The results obtained from several studies with chickens are either significant or non-significant. A beneficial effect of EO-mediated improvement in animal production was associated with increases in antimicrobial and digestive activities. A series of trials were undertaken to investigate the effect of a specific blend of essential oil compounds on the intestinal colonisation of Clostridium perfringens. Two groups of around 30,000 birds on a diet based on wheat and soya and peas were compared. A control group received 20ppm of zinc bacitracin as a growth promoter.

For the treatment group, the zinc bacitracin was replaced by 50ppm of the blend of essential oil compounds (EOC). As shown in Fig. 2, supplementation of the EOC blend reduced the concentration of Clostridium perfringens in the ileum, caecum and colon. By day 32, the number of birds infected with Clostridium perfringens was 70% lower on the EOC group.

Effects of essential oil compounds are dose-dependent. This has been shown in trials where the effects of zero, 50ppm and 100ppm essential oil compounds blend were compared with their effects on the levels of Clostridium perfringens (Fig. 3). At the higher dose of EOC blend 100ppm, the concentration of Clostridium perfringens was 20% that of the lower dose (50ppm) and only 10% of the levels found in the control birds.

A new eubiotic concept

A novel concept recently introduced to the market is the combination of a blend of essential oil compounds and benzoic acid (CRINA POULTRY PLUS). These components have complementary mode of action, effectively moderating the proliferation of pathogenic bacteria in the bird’s gut.

This potent combination has a two-pronged approach in modulating the intestinal ecosystem. First, essential oils like piperine (pepper extract) stimulate digestive enzyme secretion to enhance digestion. The compounds of essential oils interact with receptors on the cell walls in the pancreas, increasing the secretion of the major digestive enzymes, including lipase, amylase and trypsin.

Second, some compounds of essential oils like thymol attack the cell wall of bacteria, making it more permeable to benzoic acid, facilitating its entry into the cell, altering their physiology by reducing pH inside the bacteria, causing metabolic disorders that prevent their proliferation or cause their death.

By combining essential oil compounds with organic acids, a reduction of the number of certain intestinal bacteria can be achieved, greatly reducing the growth of certain Gram-positive bacteria as Clostridium perfringens, as well as Gram-negative bacteria, such as E. coli, Salmonella and Campylobacter, without affecting the growth of beneficial bacteria such as Lactobacillus.

Essential oil compounds and benzoic acid in broilers

The combination in the appropriate proportions of a specific blend of essential oil compounds (Crina) with benzoic acid allows a more effective synergy between these compounds. Benzoic acid is a natural organic acid that is found naturally in certain berries (blueberries). This acid is used as a food preservative, mainly for its antibacterial properties against bacteria such as E. coli and salmonella, fungi and yeast. It provides a preservative effect in the feed.

The combination of essential oil compounds like thymol, eugenol and piperine stimulates the production and the secretion of digestive enzymes and inhibits the proliferation of Cl. perfringens, and thus improves zootechnical performance.

Six experimental trials carried out in different institutes in Europe and the USA, using this type of combination, showed positive results on the production performance in chicken with an increase of 44g in the final average weight of chickens and an improvement of the feed conversion rate of 0.9% in the supplemented birds from the first day of life until slaughter in comparison to the control.

A meta-analysis with all the data from the 300mg/kg eubiotic feed additive (EFA) supplemented treatments in comparison with the non-supplemented control revealed that the eubiotic product significantly improved bodyweight on day 21 (P=0.0021) and on day 42 (P<0.015).

Furthermore, the birds on the EFA 300mg/kg treatment expressed a higher average daily gain in the starter phase (day 1-21; +2.1%; P=0.0023) and over the entire experimental period (day 1-42; +1.5%; P=0.0154). Feed conversion rate was more favourable with the dietary EFA supplementation (-0.6%; P=0.0144), when compared with the control birds.

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This combination of essential oil compounds with organic acids, with its right proportions and the right doses, also has important effects on the sanitary status and the productivity of laying birds.

Reviewing the mode of action of these compounds we can use their effects to improve the digestibility in adult birds, which will result in better health, increased production and improved egg quality.

The antimicrobial effect will allow reduction of the level and the growth of Clostridium and most importantly of Enterobacteriaceae, mainly E. coli and other enterobacteria. E. coli is usually a normal saprophytic bacteria, but sometimes it becomes pathogenic, mainly in high producing birds in stress situations and in birds suffering immune depression and especially in layers close to their production peak. The use of these products in a preventive way improves the birds’ health and productive status, as observed in different production lots in field conditions.

These layers have been fed with the right combination of essential oil compounds and organic acid since they arrived in the laying farm until the peak production. Thus, in hens the addition of a combination of benzoic acid and a blend of essential oil compounds can significantly reduce mortality in the initial stage of implementation. These results can be seen from field study data shown in Fig. 4. Replacement layers raised under the same conditions were separated in three different production halls (on the same farm) at the start of their productive lives.

The birds of Group 2, which consumed the combination of benzoic acid and a blend of essential oil compounds had no high mortality nor problems of colibacillosis during the initial phase of implementation, so no antibiotic medications had to be applied, contrary to what happened in Groups 1 and 3, which were not supplemented with the eubiotic combination.

Conclusion

While antibiotics are still being freely used in most countries in Asia, the pressure to reduce the use of AGPs has been mounting, hence there is a trend towards the use of more eubiotics in poultry production. The key drivers of such pressure are changing consumer preference and legislation.

To adequately prepare the poultry producer in the event that AGPs are banned, like in South Korea and Indonesia, it has to be emphasised that it takes more than using a non-AGP alternative to shift to an AGP-free poultry production system.

Reducing reliance on antibiotics through a holistic approach is a must and this includes a focus on three key areas namely: management, nutrition and health. A high level of biosecurity has to be in place and digestibility of feed raw materials has to be optimised with the use of exogenous feed enzymes. Achieving good overall health of flocks requires a high level of biosecurity, responsible use of antibiotics and a good vaccination programme to prevent viral infections.

Eubiotics like organic acids, essential oil compounds + benzoic acid and probiotics can be used as tools to replace antibiotics and enable poultry farmers to profitably produce chicken meat and eggs.

References are available from the author on request

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