ABSTRACT

In recent years the topic of food safety in relation to products of poultry origin mainly concentrated on Salmonella contamination. This paper will concentrate on the results of an experiment in which the shedding pattern of Salmonella enteritidis after oral challenge of broilers fed Flavomycin® were compared with a zero-control group. In addition to this the effects of inclusion of this product in broiler feed on the level of Salmonella contamination in the slaughterhouse under USA-field conditions and the possible synergetic effect of Flavomycin® in broiler diets with the general use of Salmonella vaccines in broiler breeders will be discussed. The position of Flavomycin® in the current discussion on the use of antimicrobial growth promoters will also be reviewed.

It is concluded that the use of Flavomycin® clearly reduced the spread of Salmonella in broilers in an infectious environment without creating a risk for an increase in antibiotic resistance.

1. INTRODUCTION

The demand for poultry products is strongly influenced by the consumers’ concern for healthy and safe food. The topic of food safety mainly concentrates on Salmonella contamination, but in recent years there are public concerns that the use of antibiotic feed additives in animals may give rise to bacterial resistance to human therapeutic drugs, especially those antibiotics that are closely related to human drugs (1 and 16).

The poultry industry implements an array of measures to prevent the infection by Salmonella and to reduce the level of contamination in all stages of the production.

Recently new data were published on the reducing effect on Salmonella shedding of inclusion of the feed additive flavophospholipol in broiler diets. This product may give an additional stimulation to the animals’ natural protection against Salmonella colonisation by the intestinal microflora. The intestinal microflora has the ability to protect the animal against infection in a contaminated environment. This phenomenon is known as Competitive Exclusion and was first described by Nurmi en Rantala (10). The underlying mode of action(s) is (are) still not fully understood. Most probably it is a combination of several factors, among which:

- Production of agents by certain beneficial organisms that have a negative influence on the growth capacity of other harmful or at least unwanted organisms (2 and 4). Recently van der Wielen et al (15) concluded that volatile fatty acids (in the undissociated form) are responsible for the reduction in numbers of Enterobacteriaceae in the ceca of broiler chickens during growth;
- Competition for substrate;
- Competition for attachment sites;
- Immunomodulation.

As the routes for Salmonella infection are numerous, it is essential to realise that the efficacy of a Salmonella Control Program does not solely depend on the implementation of one measure exclusively. Simultaneous implementation of a adequate monitoring program, in case of observed contamination followed by corrective measures, adequate biosecurity and vaccination of broiler breeders is essential. Another important, sometimes neglected phenomenon is the birds’ own natural intestinal microflora that can provide protection against Salmonella infections.
2. MATERIALS AND METHODS

2.1. The study on the reducing effect on Salmonella shedding of inclusion of flavophospholipol in broiler diets.
In the European Union a new registration procedure, known as the Fifth Amendment of the Feed Additive Directive (70/524/EEC) requires, among other data, the submission of information on the possible effect of feed additives on the excretion of food-borne pathogenic bacteria like Salmonella and Campylobacter. This study was conducted to satisfy the new EU requirement for the commercial product Flavomycin® and was recently published by Bolder et al. (3). For the complete experimental design the original publication is available on request. The experimental design can be summarised as follows. Commercial broiler chickens were orally challenged on Day 11 and 12 with $10^8$ cfu Salmonella enteritidis of a chicken field isolate. Samples during the experimental period up to the fifth week consisted of a mixture of fecal and cecal material. In the sixth week on the day of slaughter the animals were killed and the ceca were removed and sampled.

2.2. The USA field study
Under field conditions broiler rations containing Flavomycin® were compared to rations containing other antimicrobial growth promoters. Intestinal samples were collected at the slaughterhouse and these were analysed for the numbers of Salmonella. A part of this work is published by Schleifer et al. (13).

2.3. Product characteristics of flavophospholipol
Flavophospholipol (Flavomycin®), belonging to the antibiotic-class of the phosphoglycolipids, is licensed as a digestive enhancing antibiotic by the regulatory authorities in the EU, the USA and most countries worldwide. Due to it’s limited efficacy against human bacteria and it’s poor pharmaceutical properties it is not related to any antibiotic currently in use or under development for the treatment of human or animal diseases. In May 1999 it was described by the EC Scientific Steering Committee on Antibiotic Resistance from the Directorate XXIV as posing “no known risk” to humans or animals with regard to resistance.

The very limited direct antibacterial activity is restricted to the gram-positives. The enzyme glycosyltransferase, that plays an essential role in the synthesis of the cell wall of this group, can not distinguish between Flavomycin® and the natural compound. This results in an instable cell wall, leading to the death of this cell. In gram-negatives glycosyltransferase plays no role, due to the different cell wall structure. However when a plasmid bridge (pylus) is formed it’s biosynthesis is disrupted in a similar way, leading to the death of the donor-cell. This plasmid bridge plays an essential role during the transfer of genetic information on antibiotic-resistance from one bacterium to another. In this way Flavomycin prevents this genetic transfer and actually reduces the number of resistance carrying bacteria. This reducing effect of Flavomycin® on plasmid-bound antibiotic resistance has already been described since the early 70’s (5, 6, 7, 9 and 14). Of more recent date is the publication of Riedl et al (12).

3. RESULTS

3.1. The study on the reducing effect on Salmonella shedding of inclusion of flavophospholipol in broiler diets.
The results of this study are summarised in figure 1 and 2.
In this study Flavomycin® reduced significantly (P<0.05) the level of Salmonella-shedding at slaughter age. Less broilers in the Flavomycin®-group were Salmonella-positive after the initial oral infection at day 12 and 13 and mean fecal Salmonella cfu counts were significantly (P<0.05) lower in the Flavomycin®-group than those in the control group. These results confirm earlier studies in broilers (8). In this study an effect to the same extent was found on Clostridium perfringens shedding. The level and incidence of Campylobacter was not affected. Studies in pigs and calves (5 and 6) show identical results on the level of Salmonella-shedding.

3.2. The USA field study

The results of this study are summarised in table 1.

<table>
<thead>
<tr>
<th>Integrator</th>
<th>Positive control</th>
<th>Flavomycin®-group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integrator A</td>
<td>50 %</td>
<td>18 %</td>
</tr>
<tr>
<td>Integrator B</td>
<td>45 %</td>
<td>21 %</td>
</tr>
<tr>
<td>Integrator C</td>
<td>11 %</td>
<td>5 %</td>
</tr>
<tr>
<td>Integrator D</td>
<td>81 %</td>
<td>15 %</td>
</tr>
</tbody>
</table>

These data correspond with several millions of broilers processed every week, covering all major production regions in USA. The only difference between the positive control and the Flavomycin®-group is the used antimicrobial growth promoter. These data confirm the results of Bolder et al. under field conditions.

3.3. The possible synergistic effect of Flavomycin® in broiler diets with the general use of Salmonella vaccines in broiler breeders.

It is possible to combine the use of Salmonella vaccines at breeder level with the use of Flavomycin® in broiler diets. This concept will combine the benefits of both (11). The offspring of vaccinated breeders will start uninfected and will be protected by maternally derived antibodies during the first weeks. An existing infection pressure on a broiler farm will be countered by the inclusion of Flavomycin® in the feed. This mechanism will act as a barrier against infection by the time the protection by the maternal antibodies is absent.

It is known that due to the Competitive Exclusion of the normal intestinal flora the infectious dose necessary for a Salmonella infection decreases with increasing age. As Flavomycin® will not affect the equilibrium in the intestinal flora, the natural defence of the Competitive Exclusion mechanism will be an additional barrier against Salmonella-infection of the broilers. In figure 3 an idea is given how these protective mechanisms can be used in combination and can provide a useful concept for further development.

4. DISCUSSION / CONCLUSIONS

The above mentioned data clearly indicate that inclusion of Flavomycin® in broiler diets is an efficacious instrument to reduce the level of Salmonella-infections in broiler production in an infectious environment. The impact thereof is underlined by the experience that all benefits in earlier stages of the production may be lost, due to the vulnerability of broilers to Salmonella-infection. The effect of Flavomycin® is most pronounced at slaughter age and processing. These are the stages in broiler production that come nearest to the consuming moment and are therefore of utmost importance.

Combination of the use of Salmonella vaccines at breeder level and the inclusion of Flavomycin® in broiler diets could be a synergistic beneficial instrument in a Salmonella Control Program in addition to an adequate monitoring program, in case of observed contamination followed by corrective measures, and adequate biosecurity.
However Salmonella is only one aspect of Food Safety. Another aspect is the level of antibiotic resistant organisms in animal production as this may be a risk that could influence the efficacy of human antibiotic treatments. Flavomycin® is supported by sufficient scientific evidence that it does not increase the level of antibiotic resistant organisms in animal production. In fact a reducing effect is more likely.

5. REFERENCES