

Synergisms of phytogenic feed additives and antibiotic growth promoters

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Intensive livestock production has brought about many challenges for both man and animals. Along with discussions on housing conditions and stocking densities, man has become more conscious of exploring the maximum genetic potential of agricultural livestock irrespective of the physiological and other stresses they are confronted with.

Animals need to withstand these odds and maintain high productivity. This challenge certainly demands specific and novel agents that can help animals withstand difficult times and maintain high levels of productivity.

For decades, sub-therapeutic doses of antibiotics have been used to reduce challenges (diseases) for increasing or maintaining performance. The key target of using antibiotic growth promoters (AGPs) is to increase nutrient digestibility by suppressing bacterial growth in the gut (by interfering with the synthesis of DNA, RNA and proteins).

Besides antibacterial effects, AGPs play a central role in suppressing inflammation that is signalled by the release of catabolic hormones and leads to significant reduction in muscle mass.

| | E. coli | S. enteritidis | C. perfringens |
|----------------------|---------|----------------|----------------|
| PFA extract (300ppm) | 3.0 | 1.5 | 2.5 |
| Colistin (120ppm) | 2.0 | NA | NA |
| Avilamycin (40ppm) | 4.0 | 1.5 | 3.0 |
| PFA + Avilamycin | 15 | 7.5 | 11 |
| PFA + Colistin | 20 | NA | NA |

NA: Not Assayed *Inhibition value = Total inhibition diameter – diameter of the disk/2

Table 1. Inhibitory effects represented by inhibition values* of PFA extracts used in a commercial product and antibiotics on some bacterial species.

Although hundreds of studies were conducted to explore the mode of action of AGPs, little information was gathered about how they work in the gastrointestinal tract.

Almost a decade ago, the use of natural growth promoters (NGPs) in animal feed was a growing trend.

Phytogenic feed additives (PFAs) are a group within the NGP family known for their biological effects.

They show potent antimicrobial, antiviral, antioxidative and anti-inflammatory effects. The functional components within PFAs are, among others, essential oils which have been known to exert different positive effects in the body (such as antiseptic, antispasmodic, carminative, cholagogue, diaphoretic, expectorant, stimulant, stomachic and tonic effects).

Several studies have shown that PFAs

increase digestibility of protein, energy, amino acids and even minerals through their capabilities in modulating gut micro flora, gut morphology and relief from intestinal inflammation, thus improving animal performance and hence profitability.

The World Health Organization (WHO) published several reports concerning health complications which might occur from consuming meat of animals fed AGPs.

The development of antibiotic resistant bacteria is the number one concern of human health.

Moreover, food safety and bacterial resistance issues made the decision to ban AGPs an obvious one for several countries. However, the use of these agents is still allowed in a large number of countries.

To achieve profitable livestock production

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Fig. 1. Effect of PFA with or without AGP on the body weight of Ross broiler chickens.

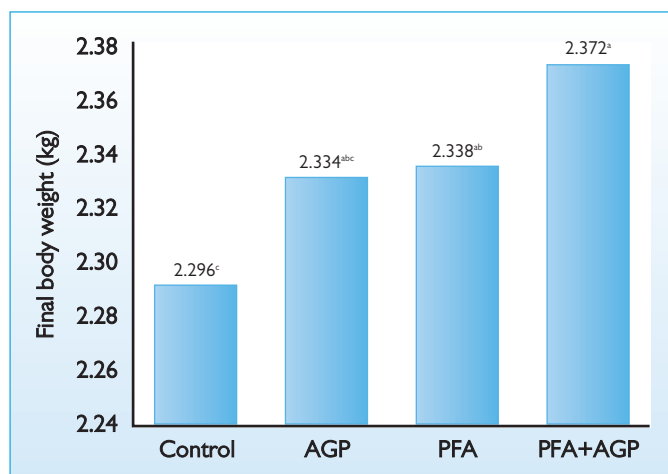
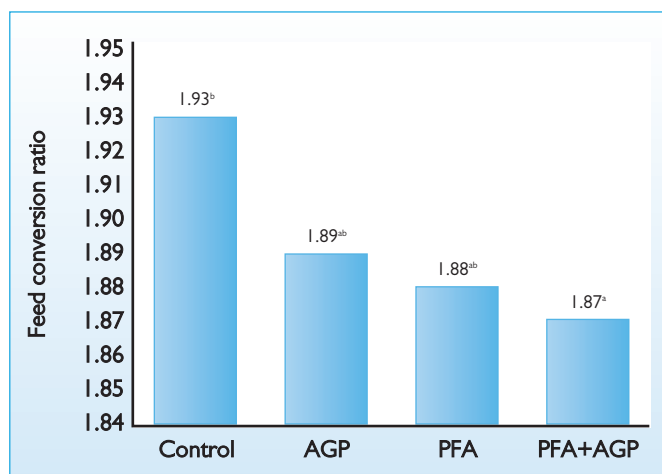


Fig. 2. Effect of PFA with or without AGP on feed conversion ratio in Ross broiler chickens



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in any country, two strategies can be implemented depending on the production context of the particular country – the use of PFAs as alternatives to AGPs or a combination of both elements to maximise benefits.

The first strategy works very well in European countries and those that have prohibited the use of AGPs in feed.

To implement the second strategy, an important question that arises is: Can we expect a synergistic action between AGPs and PFAs?

Theoretically, both agents share some very important characteristics at the level of efficacy; therefore, there might be an additive effect when they are combined.

In vitro

A bacterial inhibition assay (in vitro) was performed to assess the antibacterial effect of a PFA extract alone, with antibiotics (Colistin and Avilamycin) and a mixture of both (PFA+AGP).

Results obtained revealed that the PFA exhibited strong inhibitory effects when used alone. Interestingly, when the PFA was combined with antibiotics, the effect was by far greater (5-7 fold). These data give a strong indication of synergisms between PFAs and antibiotics (Table 1).

Regarding the mechanism of action, as to how PFA suppress or kill bacteria, several studies have proven that by disrupting the bacterial cell membrane, PFAs can inhibit bacterial growth. Recent data by Biomin also indicated that PFAs play a very important role in phagocytosis.

In vivo

An in vivo study was conducted to ascertain whether the response in animals would be in line with the in vitro findings. For this purpose, 1800 one-day-old Ross 308 broiler chicks were allocated in four treatments (450 birds/treatment) with nine replicates per treatment (50 birds/replicate) as follows:

| Parameter | Control | Chlor-tetracycline (CTC) | Digestarom | Digestarom + CTC |
|-----------------------|--------------------|--------------------------|--------------------|--------------------|
| No. of animals | 30 x 10 | 30 x 10 | 30 x 10 | 30 x 10 |
| Trial duration (days) | 35 | 35 | 35 | 35 |
| Final weight (g) | 1487 ^b | 1502 ^b | 1524 ^a | 1541 ^a |
| Daily gain (g) | 41.13 ^a | 41.58 ^b | 42.20 ^a | 42.70 ^a |
| Daily feed intake (g) | 71.00 | 71.08 | 71.08 | 71.10 |
| Feed conversion ratio | 1.73 ^b | 1.71 ^b | 1.68 ^a | 1.67 ^a |
| Mortality (%) | 1.33 | 0.67 | 0.99 | 0.67 |

Means with different superscripts differ significantly at P<0.01

Table 2. Effect of PFA with or without AGP on zootechnical parameters in Hubbard broiler chickens.

- Control group (no supplementation)
- AGP group (supplemented with Bacitracin 10%, 500g/t).
- PFA group (supplemented with Digestarom P.E.P. MGE, 100g/t (commercial phytogetic product based on oregano oil, anise oil and citrus peel oil).
- AGP + PFA group (supplemented with Bacitracin 500 g/t + PFA 100 g/t).

Results obtained revealed that AGP supplementation resulted in a numerical improvement in final body weight over the control group.

The PFA group showed significantly higher body weight than the control group. Interestingly, the AGP+PFA group showed the highest body weight (Fig. 1).

A similar trend was seen with feed conversion ratio (FCR) where a numerical improvement was obtained when the AGP and PFA were used together. The concomitant supplementation of the PFA and AGP showed significant improvement in FCR over the negative control group.

In a similar study at the Institute of Agricultural Sciences, Ho Chi Minh City, Vietnam, 1200 Hubbard broiler chickens were randomly allotted to four treatments (300 birds per treatment) with 10 replicates per treatment (30 birds/replicate).

The chickens were reared for 35 days. A clear-cut synergistic effect was observed in

almost all zootechnical parameters with the combination of PFA (Digestarom Poultry at a dosage of 150g/t of feed) and AGP (chlortetracycline, CTC 200g/t of feed). However, the PFA alone also depicted significantly higher zootechnical performance than the control (Table 2).

Perspective

In view of the aforementioned studies and discussion, it is obvious that there is an additive value when PFAs are combined with AGPs. The tested hypothesis revealed a strong synergism which is supported by the antibacterial effects assessed in vitro.

It is worth mentioning that PFAs were recently found to exert their anti-inflammatory effect which positively affects productive performance by down-regulating the expression of the inflammatory genes and up-regulating the cyto-protective genes.

There is reason to believe that the mechanism of action of AGPs and PFAs is quite different although they exhibit similar efficacies. Therefore, the biological responses triggered by the combination of AGPs and PFAs should be further explored.

References are available on request.