Capsicum for ruminants: Old player, new game

Plant extracts (PE) are naturally occurring bioactive plant-protective substances. Their antibacterial, anti-fungal, and anti-mould properties have been exploited for years in both human medicine (1) and in the food industry (2). More recently, their antimicrobial properties have prompted research efforts in animal nutrition with the initial objective of replacing antibiotic growth promoters (AGP) and later on to create stand-alone feeding technologies.

This article will first summarise the recent findings in monogastric species, then present the new paradigm driving the development of PE-based technologies, and finally will briefly review research and present new trends and opportunities in calves and ruminants species.

Much of the research investigating the effects of PE on farm animal performance has been conducted using monogastric species. Individually or as blends, various PE – including cinnamaldehyde (from cinnamon), thymol and carvacrol (from thyme or oregano), garlic, curcuma (from turmeric), eugenol (from cloves), and capsaicin (from capsicum, chilli peppers) – mitigate oxidative stress (3), prevent disease symptoms (4-12) and improve vaccination responses (13) by enhancing immunity and improve gut health during normal and disease conditions (4, 6, 14, 15) in both poultry and swine.

Enhanced energy metabolism

Notably, the doses fed to animals are far below the bactericidal dose for these PE (16). Therefore, although these molecules were originally selected for their antibacterial properties, the mode of action may not be direct killing of pathogens but via altered host gene expression associated with anti-inflammatory processes as well as innate and adaptive immune responses linked to improved performance (5, 6, 14, 15, 17). Interestingly, this mode of action is analogous to the one hypothesised for AGP (18).

As a consequence of their effects on the host, PE streamlines energy utilisation by enhancing energy metabolism (19, 20) and by decreasing the energy requirement for maintenance, which includes immune responses (3). The changes in energy partitioning lead to an increase in the flow of nutrients toward production and thereby result in a consistent improvement in production efficiency (21).

Recent research goes even further and indicates that the effects of PE (eugenol in this case) are mediated by the host: The host responding to PE shapes its gut ecosystem (22). Taken together, these findings suggest the need for a change in the current paradigm around the mode of action of PE in improving animal performance.

Indeed, the initial efforts driving research and product development for PE were based on their antimicrobial properties, which favours the selection of products with potent killing ability (e.g. thymol) over other molecules (e.g. capsicum). Alternatively, the selection of products should perhaps be driven by their capacity to prompt immune or metabolic responses from the host which can be evaluated by their pleiotropic effect on gene expression (17, 23) (see Figure 1 for illustration).
The original interest in PE was based on their antimicrobial activity, with bacteria as a target. Now, based on observed responses in animals, the paradigm needs to be revised to consider the other actions of PE with the host as a target.

Historical perspective
In calves and ruminants, the research activities on PE were less abundant, but the historical perspective is relatively similar to what has occurred in monogastric species. As such, new findings in ruminants and calves are leading scientists in a similar direction with more interest on other properties of PE separate from their antimicrobial effects.

Research evaluating the effects of PE on calf performance is limited. However, a blend of cinnamaldehyde, carvacrol and capsicum (CCC) has increased both dry matter intake and growth in calves (24, 25) coincident with two additional observations (25).

Firstly, CCC stimulated butyrate production in the rumen (25). Since ruminal butyrate is the critical initiator of the development and differentiation of rumen papillae and consequent rumen function, supplementation with CCC apparently optimised the rumen environment and this might have been the cause of increased feed intake.

Secondly, CCC increased the blood concentration of leukocytes (25). Although the implications of this response are unclear since animals were free from disease, it shows that PE influences the immune system of calves and may improve disease resistance. This was also shown with a PE administered individually (oregano), which was as effective as neomycin in treating E. coli-induced calf scours (26).

Anti-bacterial properties
Although scarce, the effects of PE on growth, development, and immunity are certainly promising and warrant further investigation using disease challenge and more mechanistic experimental models. Particularly now considering that the response of calves to PE seems very close to what has been observed in monogastric animals.

As for monogastrics, research on PE for ruminants was first aimed at investigating the antibacterial properties of PE as potential modifiers of rumen fermentation to optimise rumen function and subsequent production efficiency using the mode of action of monensin as a model (27, 28).

Consistently with improved rumen fermentation, decreasing the acetate-propionate ratio (Figure 2) and enhancing nitrogen utilisation (29-32). These effects on rumen fermentation were then confirmed in various animal models for cinnamaldehyde (33), eugenol (34), anethole (35) and thymol (33), as well as a blend of cinnamaldehyde and eugenol (CE) (34, 36).
CE – increased dry matter intake and milk production (39, 40) – and with ECC under high ambient temperatures – increased milk production and feed efficiency (41). Clearly, these research findings support the improvement of the performance of ruminant animals with PE.

**Altered rumen function**
Although the enhanced production has been attributed to altered rumen function (33, 34), the exact mode of action of PE in ruminants is still unclear. Several observations suggest that PE might also affect the host itself and not only the rumen ecosystem. For example, the improved performance of beef cattle with ECC was observed together with fewer rumen lesions indicating improved rumen health (38).

Although this could be mediated by more ruminal butyrate being produced (25), it could also be due to the effect of CO on feeding behaviour (and rumen pH) (42). Also, CCC – a blend used for monogastrics and calves – improved the feed efficiency in feedlot cattle (43). This, combined with the immune responses observed in calves, suggests that PE can affect the host response and not only rumen fermentation.

In the light of this discussion, capsicum oleoresin (CO, composed of capsaicin and dihydrocapsaicin), is an intriguing PE. Metabolic effects of CO have been reported in rodent species (44). In addition, CO affects gut integrity in rodents (45), poultry (9), and swine (14). Moreover, at low doses CO has elicited improvements in production performance of swine (10, 14, 15) and poultry (9).

In ruminants, CO was initially overlooked during the development of PE technologies because its effects on rumen fermentation *in vitro* were modest (32) and were not observed in animal models (35). Interestingly, however, performance studies in ruminants with blends including CO have shown consistent improvements in production efficiency.

**Increased dry matter intake**
For example, although both CE and ECC increased milk production in dairy cows, CE was associated with increased dry matter intake (39) whereas ECC improved efficiency (41). Notably, the only difference between the two PE blends is CO. In addition, feeding behaviour of beef cattle was improved with CO (42) coincident with increased growth efficiency (37, 38).

Because of the immune response and the increase in milk fat yield and serum beta hydroxybutyrate (46), it was hypothesised that CO influences both the immune system and nutrient metabolism. Indeed, direct post-ruminal infusion of CO altered the immune profile and milk production of dairy cows (48).

Finally, an *in vivo* analysis of rumen stability demonstrated that the active ingredients of CO have between 20 and 40% stability in the rumen (49), indicating that a significant amount leaves the rumen intact to elicit effects elsewhere. These findings not only open the doors to new applications of capsicum for ruminants, they point to modes of action distinct from antimicrobial activity and altered rumen function.

**Conclusion**
The interest in PE was originally based on their natural anti-bacterial activity and therefore their potential to replace AGP or to modify the function of the rumen. The interest in PE was originally based on their natural anti-bacterial activity and therefore their potential to replace AGP or to modify the function of the rumen. The interest in PE was originally based on their natural anti-bacterial activity and therefore their potential to replace AGP or to modify the function of the rumen.