

Immunity – an underestimated consumer of nutrients

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Immunity is a set of reactions to different aggressors recognised as antigens by the body. It is essential to preserve animals' health. But it is also a huge consumer of nutrients and a great disrupter of the metabolism. In some specific cases, the consequences of an immune 'over-response' for livestock can be dramatically unproductive, so it is economically interesting to use alternatives which are able to limit this nutrients loss.

Inflammation

More and more recent papers are describing the link between inflammation and immune response and the associated nutrients' cost for animals. But, in case of inflammatory triggers, we need to distinguish 'acute inflammation' and 'sub-clinical inflammation'. This article will focus on 'sub-clinical inflammation' as this phenomenon, which could be approached in a preventive way, is quite an unknown topic to improve farm profitability.

Indeed, animals are facing 'sub-clinical inflammation' at different risky periods of their lives: farrowing, weaning, high speed growth or heat stress for example.

All these factors are generating inflammation at the intestinal level and, as the gut is the main immune barrier and also the main immune organ of the organism, these factors are also generating a systemic immune response.

First, sub-clinical intestinal inflammation is characterised by an affection of gut integrity, which increases permeability of the gut barrier.

Tight junctions (proteins between epithelial cells) are contracting, causing a larger gap between cells which is commonly called 'leaky gut' phenomenon. Pathogens and antigens can thus more easily pass through those gaps and amplify the immune response. The latter immune

response is the production of cytokines (like Interleukins 8) through the activation of NF- κ B transcription factor. Interleukins are immune messengers that will activate liver cells as a systemic response. Eventually, as a consequence of this immunity activation, a decrease in feed intake can be observed.

The different steps of this immune activation are consuming a lot of energy and deviate nutrients from production. It is now well accepted that this waste of nutrient can reach between 10-30% of the maintenance needs! Immunity is really a high consumer of nutrients and in case of sub-clinical inflammation, all this 'over-activation' of the immune system is not necessarily useful and immunity can be considered as a nutrients spender.

Immunity modulation

To mitigate nutrients' waste, it would be interesting to modulate such a disproportioned immune response without, of course, inhibiting it. What could be the most pertinent components to limit the 'over-activation' of immune system in case of sub-inflammation?

Neovia R&D has screened different active ingredients and has developed a model to evaluate them in partnership with the French University of Beauvais. The aim of this 'in-vitro/in-vivo' trial was to cultivate living epithelial cells in Petri box and then to test their reaction to inflammatory challenge.

Measuring Trans-Epithelial Electric Resistance (TEER).

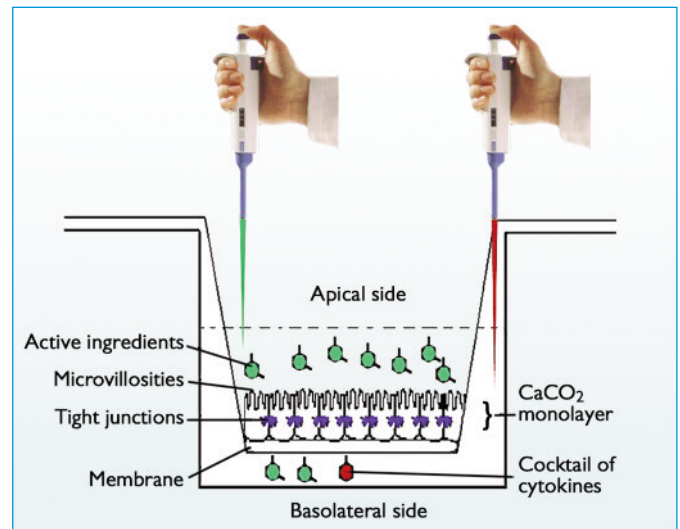
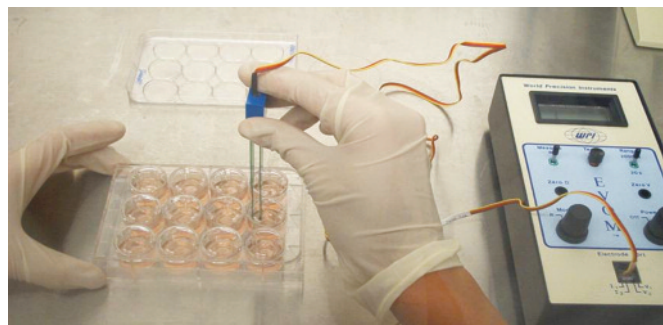


Fig. 1. Culture of epithelial cells.

Human colonic cells were thus cultivated to exactly form an epithelial barrier, with the apical side (intestinal lumen) and the basal side (lamina propria) – see Fig. 1.

These cells have then been challenged by a cytokines cocktail in order to provoke an inflammatory reaction. When inflamed, three plants extracts (sanguinarine, honokiol, magnolol), alone or in combination, have been added and two parameters have been controlled:

- Gut integrity through the Trans-Epithelial Electric Resistance (TEER) measure. TEER is the resistance of the intestinal barrier and is positively correlated with gut integrity: the higher the TEER, the better gut integrity is preserved.

Fig. 2 demonstrates that in case of inflammatory challenge, gut integrity is highly affected (positive control vs negative control) and that only a plants extracts combination (Powerjet) can restore it.

Indeed, this specific combination of three plants extracts is able to well preserve gut impermeability after an inflammatory challenge and this result is statistically significant.

On the other hand, each plant extract tested alone has no significant effect on TEER: this trial is also proving that plant extracts can be active components only when combined together.

- Immune response with Interleukins 8 (IL8) secretion at the basal side has also been evaluated in this trial. The results presented in Fig. 3 are demonstrating the positive impact of the tested vegetal combination on IL8 secretion. Indeed, plants extracts association is able to reduce the secretion of IL8 and thus the amplitude of the immune response.

This result is statistically significant and is better than for each plant extract tested independently.

On top of the demonstration of the positive impact on immunity response to inflammatory challenge, this trial is really interesting as it shows the complexity of plants

extracts action. Indeed, the two measured parameters are significantly improved by the combination of three plants extracts, whereas each plant's extract obtains only a numeric improvement. Using plant extracts to act on animal health and performance requires a precise knowledge of active components and a lot of research to ensure good results for farmers.

This two year university partnership enabled us to go further in proving the ability of a plant extracts combination to limit an 'over-activation' of the immune system in case of inflammation.

The endless question of whether

immune modulation is desirable is still current and naturally depends on the situation. As sub-clinical inflammation is an important source of nutrients' waste because of the associated immune response and decrease in feed intake, it would be interesting, in this case, to save nutrients and energy and to dedicate them to production needs.

Moreover, the tested plants extracts act on the preservation of gut integrity and avoid the 'leaky gut' phenomenon. The epithelial cells can really play their 'barrier role' and prevent pathogens from passing through. That means better nutrient absorption for animals and a better

feed efficacy due to three combined factors:

- Less nutrients' waste thanks to an immune response modulation.
- More absorbed nutrients due to a preserved intestinal integrity.
- No decrease in feed intake as a consequence of less inflammation.

Finally, by managing inflammation and its associated consequences, animals can better express their genetic potential and produce more. The return on investment is very high, especially in the current context of high raw materials' price.

In conclusion, the modulation of immunity could be an interesting way to save nutrients from useless

ends. But it must be a precise, safe and validated approach to obtain the expected results. The university trial described in this article allows us to appreciate the potential of different plants extracts on immune response after an inflammatory challenge.

Some extracts have no impact on immune response but their combination is able to significantly limit its amplitude and consequently reduce nutrients' consumption for this purpose. This scientific step is really crucial to precisely know the mode of action of this phyto-genic product and explain the improved zootechnical and economic results on the farm. ■

Fig 2. Gut integrity results – TEER measurement.

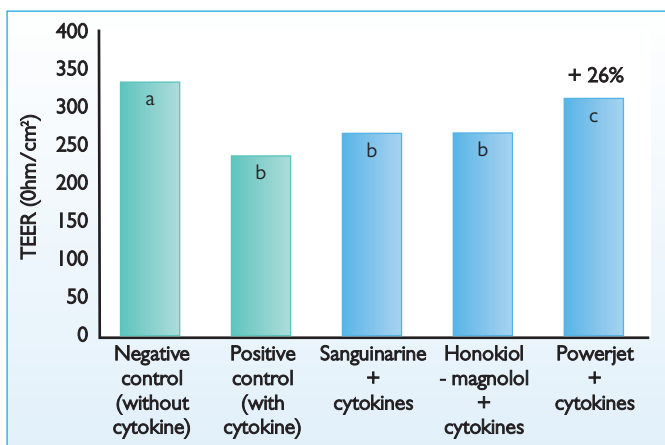


Fig 3. Immune response – IL8 secretion at the basal side.

