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Dietary Antigens and its Effect on Livestock

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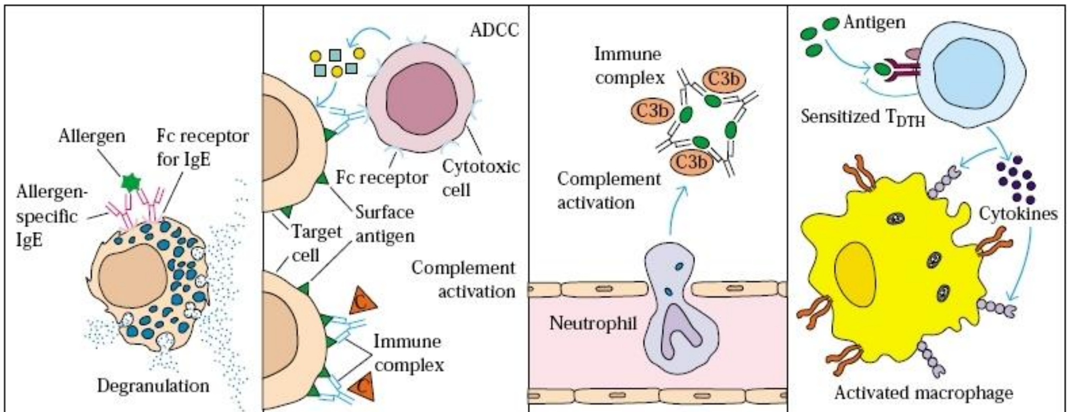
Research in several species indicates that an animal's immune system response to antigens is a major cause of reduced growth rates and feed efficiency. There is also an emerging body of evidence to indicate that dietary antigens may serve as an antigenic stimulus eliciting an immune response. Soybean meal (SBM) is the most commonly used protein source in the animal feed industry. As the main source of vegetable protein, soybean plays an important role in the world of animal feed and food production. It is a major source of both vegetable proteins for humans and animals and of edible oil. However, it contains many kinds of anti-nutritional factors, such as trypsin inhibitor, lectin, α-amylase inhibiting factor, goitrin, soybean antigen and so on. The existence of these anti-nutritional factors affects the nutritional value, utilization and digestibility of soybean protein, causing digestive and metabolic diseases of animals as well as reduced performance traits. The allergenicity of soybean proteins was first noted in humans by Duke (1934). The identified dietary antigenic proteins in soybean meal (SBM) are soybean hydrophobic protein and soybean hull protein, soybean vacuolar protein, glycinin, and conglycinin.

Any feed ingredient or feed stuff or any component/nutrient of feed ingredient having a role in raising antibodies or causing allergic reactions in the animal on ingestion. These antigenic proteins can also be explained as macromolecular proteins or glycoprotein which are present in plant raw material which are capable of inducing immune response when consume by animals. Continuous exposure to these proteins may cause an increase chances that the immune response of the animals may develop into an acute or chronic hypersensitivity. Antigenic concentration in raw soya bean is about 610mg/g protein.

Among all these, the α-conglycinin, and β-conglycinin are said to be most potent Ags, because of their thermal stability of soybean antigen, the general heat treatment cannot inactivate. They are known to trigger specific and non-specific immune response in several farm animals, but especially in a large proportion of pre-ruminant calves and nursery pigs and mice. β-conglycinin activity is the best predictor for measuring the quality of protein from soybeans. B-conglycinin is more resistant to the proteolytic enzymes in the digestive processes than other proteins in soybeans. Pre ruminant animals are more susceptible compared to ruminants b/c antigenic activity is removed inside the rumen.

Fig.1. Types of hypersensitivity reactions and their mechanism of action



Type I	Type II	Type III	Type IV
IgE-Mediated Hypersensitivity	IgG-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces crosslinking of IgE bound to mast cells and basophils with release of vasoactive mediators	Ab directed against cell surface antigens meditates cell destruction via complement activation or ADCC	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils	Sensitized T_H1 cells release cytokines that activate macrophages or T_C cells which mediate direct cellular damage

Effect in preruminant calves and pigs

The feeding of soya bean products in some pre-ruminant calves were linked with intolerance, reduction in digesta transit time, vomiting and diarrhoea, failure of immunodefence mechanism of the gut due to low secretion of immunoglobulins such IgA and IgM against soya bean antigens. Further, these Ags also depress the digestibility, especially this effect more profund with β-conglycinin and rapid loss of weight. The presence of β-conglycinin in soya bean meal has more potent depressive effect on protein digestibility than trypsin inhibitor. Researchers showed that calves fed raw soybean and soybean antigens had variety of specific antibody titers and were significantly higher than the group fed whole milk.. researches showed that fermentation in the rumen of weaned calves appeared to be efficient in inactivating most of the potentially harmful dietary constituents.

The allergenicity of soybean protein apparently is greater, if pigs are exposed to soybean meal during the nursing phase mainly by damaging the villi in the small intestine, which will result in poor protein absorption, poor growth rate (post weaning performance). The hypersensitivity response occurs within 3-4 days after adequate exposure to soy proteins and recovery occurs after 7-10 days. During this period of hypersensitivity, pigs experience decreased growth performance and are more susceptible to enteric diseases. After they develop oral tolerance, their growth performance will return to normal and they may demonstrate some compensatory gain. Histologically the intestinal morphology appears normal at 56 days post-exposure. Researchers have speculated that the damage to the intestine is due to formation of complexes between systemic IgG antibodies and residual soybean meal antigens plus complement activation. The majority of the physiological and morphological changes observed in the intestine during a dietary hypersensitivity reaction can be associated with an accelerated turnover rate of enterocytes resulting in increased numbers of immature enterocytes lining the villi Enteropathic changes may occur even in the complete absence of microbial involvement, and because proliferation of E. coli is commonly observed subsequent to such changes, it has been suggested that E coli is an opportunist rather than a primary pathogen. This response may have a cascading effect within the small intestine and affect pig performance in the first few weeks following weaning. However, the mechanism by which this occurs is obscure, perhaps low preweaning feed intake, which commonly occurs when weaning at 3 wk or less, results in a transient hypersensitivity to dietary antigens, which may, in turn, lead to an increase in mitotic rate in enterocytes. The effect of this increase is an elongation of the crypts. As the rate of migration of the enterocytes up the villi increases, the enterocytes are shed from the top of the villi at a greater rate; therefore, the number of mature enterocytes decreases. Because these cells have absorptive ability and high sucrose activities in their brush borders, a reduction in the number of mature cells will result in lower enzyme activity and absorptive capacity. These changes are associated with increased enterocyte turnover and malabsorption, which increases the susceptibility of the intestine to pathogenic bacteria such as E. coli.

Mechanism of immune response

The majority of dietary protein is digested into small particles that cannot stimulate an immune response. A small portion of these antigens are absorbed unaltered (0.002%) and can be detected in circulating blood IgG titres specific for soybean proteins can be detected in pigs exposed to soybean meal. The rise in soy-specific antibodies is correlated with a decline in circulating soy proteins. Using I^{125}-labeled-soy it has been shown that the decline in circulating soy antigens is a result of decreased absorption of the antigen rather than increased clearance. This decreased absorption is accomplished by the immune system and is termed oral tolerance. The exact mechanisms involved with the establishment of oral tolerance are still unknown. It has been speculated that IgA continues to be secreted, binds the antigen to the intestinal mucosa, prevents further absorption, and allows breakdown from digestive enzyme activity. Intraepithelial lymphocytes may play a primary role in the development of tolerance due to their suppressor cell activities.

Hypersensitivity management in piglets

As stated earlier, pigs do not need to be primed to experience a transient hypersensitivity response to soybean meal after weaning. Basically, pigs will develop the hypersensitivity at the point in their life when they are exposed to adequate levels of antigenic soy proteins. To minimize the negative impact of this response, it is important to choose the optimum time for piglets to acquire this hypersensitivity and develop oral tolerance. Most researchers agree that the ideal time to establish oral tolerance in piglets is before weaning. Studies have indicated that a total of 400-600 g (0.9-1.3lb) of high protein creep feed intake is necessary during lactation to induce oral tolerance in piglets while nursing the sow. It is difficult to get pigs to consume this amount, particularly as the trend toward earlier weaning ages intensifies. Using oral or parental adjuvant may enhance the immune system's ability to develop tolerance with low pre-wean intakes. As pigs get older, they absorb fewer antigens, perhaps because their digestive function is improved and their mucosal immune system is more mature. Feeding pigs a complex starter diet during the first week post-weaning has been determined to be the most cost-effective time to induce a hypersensitivity reaction and develop tolerance. Complex starter diets that use alternative protein sources such as plasma protein and milk products reduce the amount of soybean meal in the ration, which diminishes the clinical disease associated with transient hypersensitivity. Another way to manage soybean-meal hypersensitivity would be to decrease the antigenicity of the soy proteins by additional processing. Further processing of soybean meal decreases the hypersensitivity response, improves digestibility and growth performance. Skin-fold thickness tests can be used as an indicator for the antigenicity of soybean meal products. This simple test may be useful to determine the immunological quality of soybean meal products.

Strategies to reduce Antigenic effect:

The antigenicity of soybean meal can reduced by different methods complete elimination of SBM from the ration of the animals, treatment with hot ethanol, protease treatment, twin screw extrusion techniques and fermentation of soyabean meal. Treatment with hot ethanol found to remove all immunologically active antigens found to be effective in both calves and piglets. Also removes oligosaccharides such as stachyose, raffinose, which are not digested by pre-ruminants and nursery pigs are removed successfully. Recent developments in feed enzyme technologies suggest that protease treatment of soyabean may be an alternate means of reducing the antigenic challenge of soyabean meal. Two proteases enzymes are available in which alkaline protease hydrolyses polypeptides nonspecifically whereas acid protease preferably hydrolyses high molecular weight polypeptides. Experiments in piglets showed that acid proteases are better effective in reducing the antigenicity of the soya proteins though bot shown to decrease the antigenic concentration. Twin screw extrusion method of soyabean processing has been developed that reduces the soybean antigens to 0.001 of the original activity.

Fermented Soybean Meal (FSBM)

Partial cooking and fermentation using 0.3% Aspergillus oryzae has found to decrease the antigenic protein content of the soyabean meal as well as it has an added advantage to increase the digestibility by enhancing the enzyme activity in the gut and their by improving the weight gain compared to groups supplemented with untreated soyabean meal. Dried SBM was soaked with distilled water for 60 min. The hydrated SBM was then cooked in a steam tank at 60-70 °C for 1h. Then, the cooked SBM was cooled to room temperature for 1 h, inoculated with 0.3% Aspergillus oryzae, mixed, and fermented in a bed-packed incubator for 48 h. The nutrient composition of fermented soya has found superior when compared to roasted soya. Fermentation reduced the level of trypsin inhibitor in FSBM compared to SBM (2.6 mg/g vs. 0.0 mg/g) in addition to reduction in antigenic proteins.

Scanning electron micrographs of piglet small intestine

A) unweaned piglet 26 days of age **B) piglets fed soya (5 days after weaning)**