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LYSOFORTE® EXTEND legacy explained by a dual approach of surface chemistry and nutrigenomic activity

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SUMMARY

LYSOFORTE® EXTEND (LEX) is a unique nutrient absorption enhancer that contains a synergistic mix of three active ingredients (lysolecithins, glyceryl monooleate and a synthetic emulsifier) in a specific patented ration, that facilitate lipid emulsification, hydrolysis and absorption (via surface chemistry).

Recent research reveals, that LEX not only improves lipid digestion but also facilitates the digestion and absorption of other nutrients such as proteins[1,2].

The latter can be partly explained by surface chemistry (via removing part of the lipid matrix) but there is more: the lyosphospolipids (LPL) fraction potentially improves intestinal morphology via cell signalling pathways (nutrigenomic action), which results in an increased absorption surface area and also more nutrient transporters in the upper intestines[3,4].

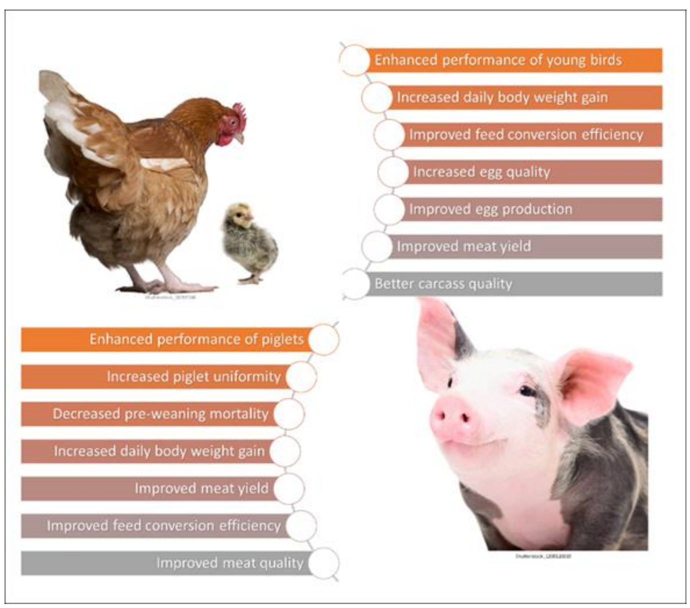
Both surface chemistry and nutrigenomic activities do directly result in financial gains as feed efficiency is increased for several nutrients. The latter is an incentive for a more cost effective (re)formulation of the diets.

Keywords: LYSOFORTE EXTEND, surface chemistry, lipids, nutrigenomics,nutrient digestion and absorption

LYSOFORTE EXTEND Legacy

LEX provides value to the poultry and swine industry either applied 'on top' of the existing diet or in reformulation. It substantially supports growth performance and feed efficiency as well as providing a multitude of additional benefits across all stages of production. Previous research has highlighted that LEX directly enhances all phases of lipid digestion and fatty acid absorption through a multi-level, synergistic mode of action. However, there are indications it affects more pathways influencing the digestion processes and absorption of other essential nutrients also such as amino acids, which have not been fully explored and unravelled yet. The main positive already identified effects of LEX in poultry and swine production are captured in Figure 1.

Figure 1. Benefits of LEX in poultry and swine.



References[5,6,7,8]

While improving animal performance, there is a significant feed cost saving when LEX is applied with its nutritional matrix in reformulation, which is now mostly done based on energy inclusion. However, the "one million dollar" question is to which extent can we also reformulate the diets on digestible amino acids as there are various scientific data showing LEX also can improve protein digestibility[1,2]. In order to elaborate on this and to finetune the matrix to get the full potential out of the diet reformulation, it is crucial to gain more scientific proof of the exact process behind the mechanism how LEX positively impacts protein and other nutrients digestion and absorption. However, some aspecst need to be considered here such as:

(1) When taking into account the ratio of LEX inclusion versus the amount of dietary lipid content of pig and poultry diets, it becomes clear that the amount of fats that can be emulsified by LEX, remains rather limited due to the low reatio of LEX over crude fat (for example, 1:200[9]).

(2) If only surface chemistry would be the mode of action, then the more LEX you would supply, the more impact on lipid digestion one would expect. However, when adding more LEX to the animal diets, there is a plateau phase that is being reached[2]. Hence, there must be another mechanism that comes into play.

(3) It is generally accepted that LEX increases the degradation of the dietary fat matrix, allowing digestive enzymes to better access their specific substrates and subsequently degrade[1,2,10]. This way LEX improves the efficiency of exogenous enzymes and thus acts synergistically to increase nutrient release in the intestinal tract but this does not directly imply those nutrients will also be better absorbed[19]. How LEX in addition can also specifically contribute to more nutrient absorption, needs to be explored more in depth.

(4) Several studies showed that the addition of LEX into the feed affected intestinal morphology and transcriptome profiles of enterocytes[11,12]. The latter can not be explained by surface chemistry. Hence, other factors and mechanisms come into play.

Modes of action of LYSOFORTE EXTEND

1. IMPROVEMENT OF THE SURFACE CHEMISTRY

First lysolecithins, in synergy with a synthetic emulsifier, enhance the emulsification step of the digestion of the fat matrix by formation of smaller emulsified triglyceride droplets. Subsequently, there is a larger water/oil interface for the lipase digestive enzyme to act resulting in the hydrolysis of the triglycerides into two free fatty acids (FFA) and one 2-monoglyceride (2-MG) molecule increasing the quantity of FFA available for absorption. However, crucial here is to determine the most efficient ratio of inclusion of both active compounds, as synthetic emulsifiers are larger molecules that can also impair the hydrolysis step by steric hindrance. Next, through the inclusion of Glyceryl monooleates (GMO), the initiation, formation, and stabilization of aggregates of 2-MG and FFA, so-called 'mixed micelles', is stimulated, a crucial step to ensure optimal uptake of the FFA into the enterocytes[13].

2. NUTRIGENOMIC ACTIVITIES

Throughout the past years, multiple insights have been published on the benefits of lyoclecithins, which can not be exclusively explained by improving the surface chemistry alone. Here nutrigenomic actions come into play. Nutrigenomics elucidate how the components of a particular diet may affect the expression of genes and thereby can impact cellular pathways in the intestinal tract.

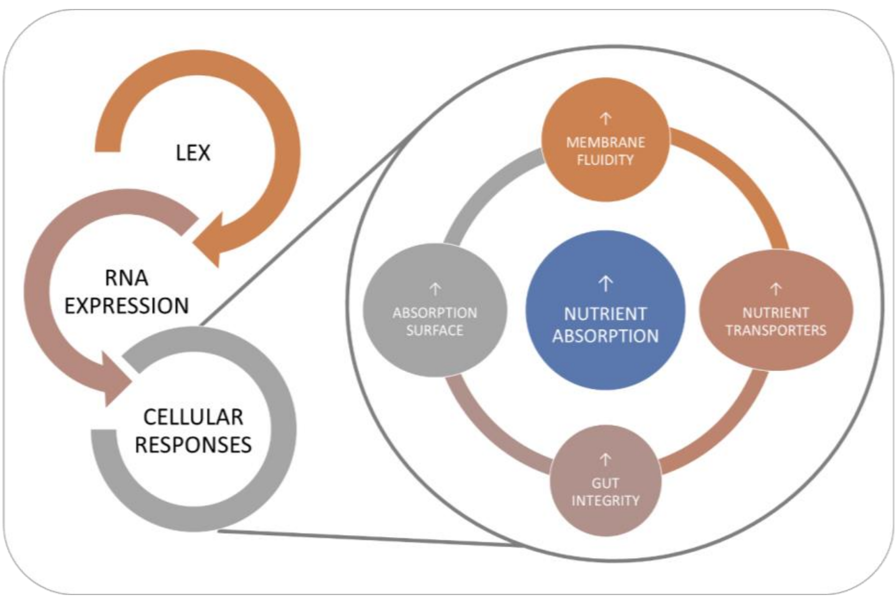
The bioactive compounds in lysolecithins are considered to be the lysophospholipid (LPL) fractions. When studying the mode of action of these LPLs more into depth, it has become more evident that the different LPL types present in the lysolecithins within LEX, such as LPC (Lysophosphatidylcholine), LPI (Lysophosphatidylinositol), LPE (Lysophosphatidylethanolamine) and LPA (Lysophosphatidic acid) can indeed trigger cell signaling pathways ands thereby mediate the effects observed at intestinal tract levels.

In this context, LEX has been proven to:

(1) Alter intestinal membrane fluidity and protein channel formation, increasing absorption of nutrients across the enterocyte membrane[3,4,10].
(2) Stimulate gene expression related to collagen deposition, which enhances villi length, gut integrity, and strength[11].
(3) Increase intestinal absorption surface area by proliferation and differentiating pathways[14].

The latter events can be, most probably explained by the nutrogenomic approach (see Figure 2). Furthermore, these improvements in gut structure and function could explain the better utilization of the available dietary nutrients, including energy[10,15,16,17] and protein[Error! Bookmark not defined.,15,18], which subsequently may drive the improvements in performance efficiency and carcass yield as reported by Li *et al*. (2022[14]).

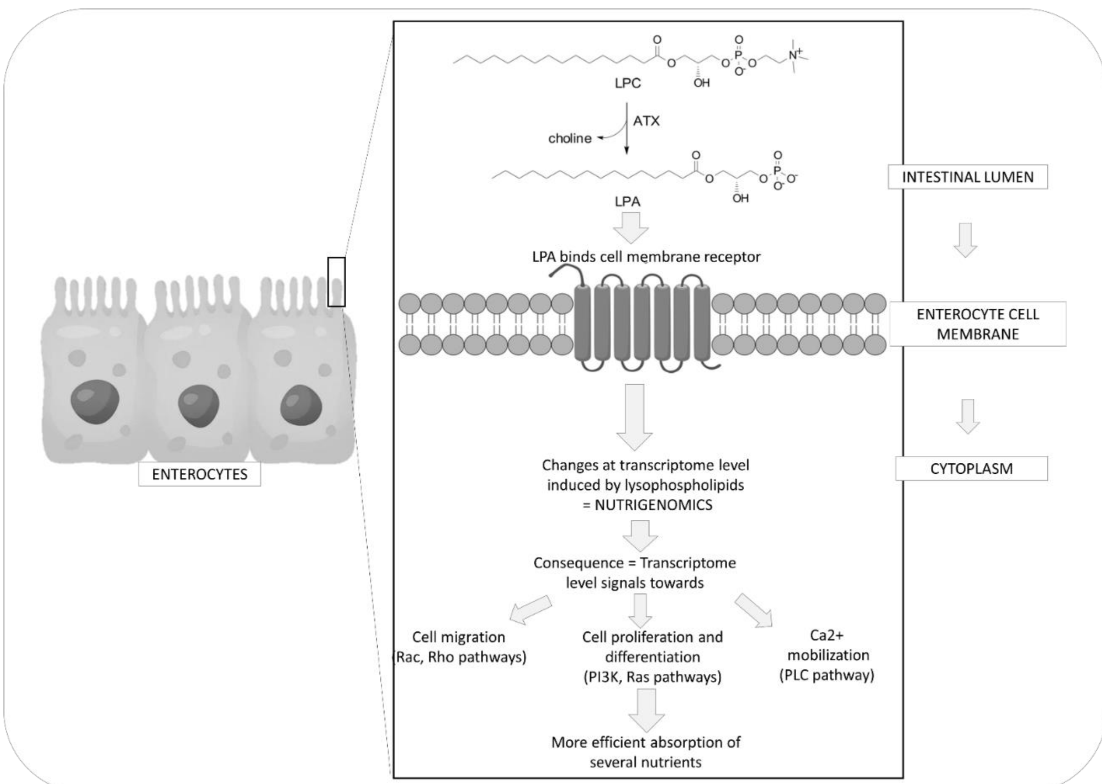
Figure 2. Nutrigenomic impact of LEX in the intestinal tract.



What remains a matter for debate (and further study) is to which extent each type of PL and LPL intervene at intestinal transcriptome level. Lysolecithins, either in LEX or other lysolecithin-only-based-solutions, contain a mixture of PL and LPL but can differ in composition (ratio & type of PL and LPL) depending on the conditions and source of the lecithin used for its production. As global leader in biosurfactants, KEMIN has invested strongly in the characterization of the PL and LPL content of various commercial lysolecithin sources available in the market. Based on this thought leadership and developed expertise, in combination with extensive studies on the MOA of LEX *in vitro* (proliferation and differentiation of cells) and *in vivo* (amino acid availability and reformulation studies), more evidence has been found distinguishing LEX from other solutions.

But what scientific proof actually exists on the nutrient absorption effects of the different LPL fractions? There is evidence yet on the nutrigenomic pathways triggered by LPC, but also LPA, in enterocytes. Pathways triggered are depicted in Figure 3. Interestingly, LPC has the ability to improve intestinal morphology, nutrient digestion and absorption[19,7,2]. Nutautaite *et al*. (2021[20]) documented significant improvement in intestinal villus height. LPC addition reduced the crypt depth, increased the jejunal villi height, and improved the ratio of villi height to crypt depth in the jejuna and duodena of chicken. Very interestingly, LPC upregulates the expression of AA and cholesterol transporter genes in enterocytes and increasing the fat digestibility and the intake of cholesterol and amino acids[21]. In addition, Zhang *et al* (2022[3]) showed recently that LPL significantly increases the ileal digestibility of AA, including Ile, Thr, Phe, His, Arg, Tyr, Glu, Pro, Gly, Ala. Also, the gene expression of amino acid transporters was significantly elevated via LPL supplementation. Even more, LPL significantly increased the gene expression of growth hormone and insulin-like growth factor 1. The latter fact can be a crucial additional effect of LEX, but more research would be necessary to further explore this mode of action. Also, the potential of LPA, LPE and LPI as other fractions being present in LEX needs to be explored more into depth.

Figure 3. Schematic presentation of the potential nutrigenomic impact of LPL on the intestinal tract.



Conclusion

LEX is an unique nutritional solution with triple effect on lipid emulsification, hydrolysis and absorption. However, besides this surface chemistry action, one can not ignore that the specifically-designed combination of its active ingredients, can also exert an impact on digestion and absorption of other nutrients, such as proteins and carbohydrates. One pathway to explain this additional benefit is that degrading the lipid matrix increases the access of enzymes totheir specific substrates, allowing for a more optimal interaction and enhanced enzyme efficacy. However, step by step, it becomes more clear that LEX also seems to exert a direct action on the intestinal tract by triggering proliferation, differentiation and upregulation of nutrient transporters. In this context, nutrigenomics shows a new way of working with nutrition can explain how LPL fractions interfere the genetic expression in enterocytes resulting in cellular responses that are beneficial for the nutrient absorption in the animal. The MOA work focusing on nutrigenomics can thereby be directly translated into an increased ROI.

Modern fast-growing production animals have high energy and amino acid requirements and meeting these requirements leads to improved feed efficiency, but also increases diet costs, especially when the prices of oils and protein meals remain volatile. Increasing the utilization of dietary energy and other nutrients with the right nutritional solutions, allows nutritionists to formulate diets to lower basal nutrient levels and lower feed costs. Future research with LEX should focus on finetuning its current self-regulating nutritional matrix for energy, including also for digestible amino acids when applied in a reformulation, resulting in even more significant feed cost savings.

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