Grape polyphenols in animal nutrition: more resilience to oxidative stress

1. Introduction

Modern animal production has achieved higher levels of efficiency thanks to genetic improvement, nutritional optimization and intensive management, but this advance also implies an **increased metabolic demand** and an increased generation of reactive oxygen species (ROS) in high-activity tissues such as liver, intestine, muscle and reproductive system.

Although ROS are part of normal cell physiology, when they exceed the antioxidant capacity of the body, a redox imbalance or **oxidative stress** is generated, a silent factor that can compromise cell function, metabolic efficiency, immune response, quality of the final product and production consistency.

2. Grape polyphenols: an antioxidant strategy with multimodal action

Polyphenols are bioactive compounds present in different plant sources. Among them, polyphenols from **grape** (*Vitis vinifera*) **extract** have garnered growing interest due to their high antioxidant capacity and their role in modulating cellular pathways related to oxidative stress and inflammation.

Unlike other more specific antioxidants, such as vitamin E or selenium, grape polyphenols have a broader mode of action. Vitamin E acts primarily as a chain-breaking lipid antioxidant, protecting membranes and lipoproteins from the propagationof lipid peroxidation. Selenium, on the other hand, exerts its function through selenoproteins such as glutathione peroxidase (GPx) or thioredoxin reductase (TrxR), which are involved in the detoxification of peroxides and the maintenance of intracellular redox homeostasis. In contrast, grape polyphenols combine direct antioxidant action with broader cellular regulatory mechanisms.

One of their main mechanisms is the **direct neutralization of reactive species**, due to their ability to donate electrons or hydrogen atoms and stabilize free radicals by forming reactive adducts. This activity contributes to reducing the propagation of oxidative reactions in cell membranes, circulating lipids and metabolically active tissues.

In addition, grape polyphenols can act by **chelating transition metals**, such as iron and copper. These metals participate in pro-oxidant reactions, such as the Fenton reaction, which favor the generation of highly reactive hydroxyl radicals. By limiting the availability of these metal catalysts, polyphenols help reduce ROS formation early in the oxidative process.

Another key aspect is their ability to **modulate redox signaling pathways**. Among them, the **Nrf2/ARE** pathway stands out, considered one of the main cellular systems of endogenous antioxidant response. The activation of Nrf2 favors the expression of antioxidant and detoxifying enzymes, such as superoxide dismutase, catalase, glutathione peroxidase, heme oxygenase-1 and enzymes related to glutathione metabolism. In this way, polyphenols not only act as exogenous antioxidants, but can also contribute to strengthening the animal's own antioxidant capacity.

In parallel, grape polyphenols can **modulate pathways involved in inflammation and radical production**, such as **NF-κB, iNOS and NADPH oxidase**. This action is especially relevant because, under commercial conditions, oxidative stress rarely appears in isolation: it is usually associated with intestinal inflammation, heat stress, dysbiosis, tissue damage or high metabolic demand. Therefore, reducing oxidative stress "at source" can be as important as neutralizing the radicals once they have been formed.

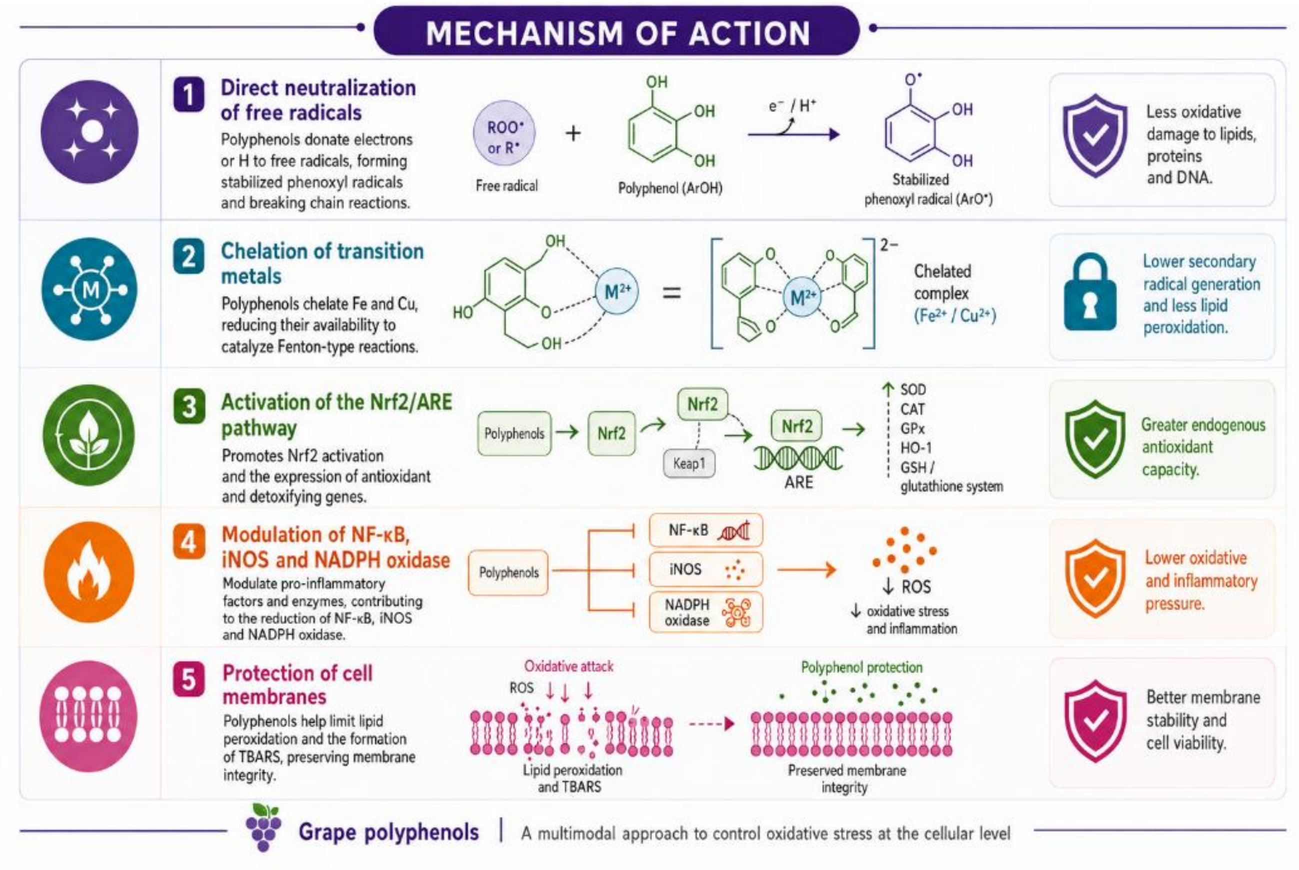

Figure 1. Mechanisms of antioxidant action of grape polyphenols.

3. Cellular evidence: protection against oxidative challenge

The *in vitro* evaluation of nutritional additives allows us to accurately study their effects on cell viability, membrane oxidation and response to oxidizing agents. In this context, Olivares-Ferretti et al. evaluated the antioxidant effect of a molecule based on grape extract (**ENTAN)** in two **cell lines**: LMH, derived from hepatocytes of *Gallus gallus*, and CHSE-214, derived from salmonid embryos. The objective was to determine the ability of ENTAN to protect terrestrial and aquatic cells against oxidative stress induced by hydrogen peroxide.

The results showed that, under exposure to 0.1 mM hydrogen peroxide, the product allowed cell viability to recover to levels comparable to the control in both cell lines. The study also showed a reduction in the formation of TBARS, biomarkers of lipid peroxidation and indicators of cellular oxidative damage, from values close to 5 µM MDA/mg protein to approximately 2.5 µM MDA/mg protein when the product was used at concentrations of 0.05 or 0.5 g/L.

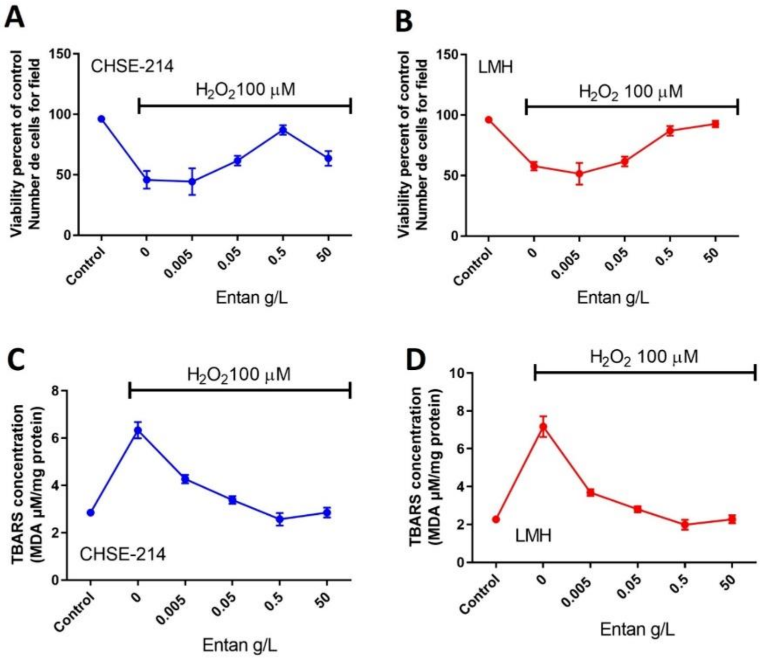

Figure 2. Antioxidant effect.
(A) Quantification of the number of CHSE-214 cells after 24 h of culture with 0.1 mM H_2O_2 in the presence of ENTAN at concentrations of 0 to 50 g/L. (B) Quantification of the number of LMH cells after 24 h of culture with 0.1 mM of H_2O_2 in the presence of ENTAN at concentrations of 0 to 50 g/L. (C) Quantification of TBARS in CHSE-214 cells after 24 h of culture with 0.1 mM of H_2O_2 in the presence of ENTAN at concentrations from 0 to 50 g/L. (D) Quantification of TBARS in LMH cells after 24 h of culture with 0.1 mM H_2O_2 in the presence of ENTAN at concentrations from 0 to 50 g/L. The graphs represent 3 independent experiments, with three replicates each. Each dot represents the mean ± SEM. ***Source:*** *Olivares-Ferretti et al. (2024).* *https://doi.org/10.1016/j.ejbt.2024.07.001*

This point is especially relevant from a production perspective. Lipid peroxidation of membranes compromises cell fluidity, integrity, and functionality. If a nutritional strategy is able to reduce membrane oxidation and preserve cell viability under oxidative challenge, it can contribute to maintaining the functionality of key tissues in animals subjected to high metabolic demand.

In the same study, the authors concluded that the reduction in cell mortality induced by oxidative stress suggests a protective mechanism based on the antioxidant effect of the compound. In addition, they observed that the presence of the molecule limited the increase in TBARS induced by increasing concentrations of hydrogen peroxide, indicating lower lipid oxidation and better membrane quality under metabolic stress conditions.

4. Productive impact of improved redox homeostasis

The value of grape polyphenols lies not only in reducing oxidation markers, but also in helping translate this cellular protection into **greater productive stability**. By contributing to the maintenance of redox homeostasis, they help preserve the functionality of key tissues and organs involved in performance, reproduction, and end-product quality, especially in intensive systems subjected to metabolic, environmental, or inflammatory challenges.

5. Applications in poultry farming

In **layers**, persistent egg production implies a high metabolic demand, especially at the hepatic and reproductive level. In addition, the yolk contains lipids susceptible to oxidation, particularly when diets rich in unsaturated fatty acids are used. In this context, polyphenols can help preserve the oxidative stability of the egg during storage, reduce lipid peroxidation and contribute to greater consistency of internal quality.

In **breeders**, the redox balance is decisive for fertility, fertile egg quality, embryonic viability and chick robustness. Gametes and the early embryo are highly sensitive to oxidative damage. Therefore, antioxidant support through grape polyphenols can be an interesting strategy in older flocks, periods of heat stress or situations with variability in fertility and hatching.

In **broilers**, their application can be targeted at phases of high metabolic pressure, heat stress, intestinal challenges or diets with increased oxidative risk. In these cases, redox modulation can help preserve feed efficiency, tissue integrity and flock uniformity.

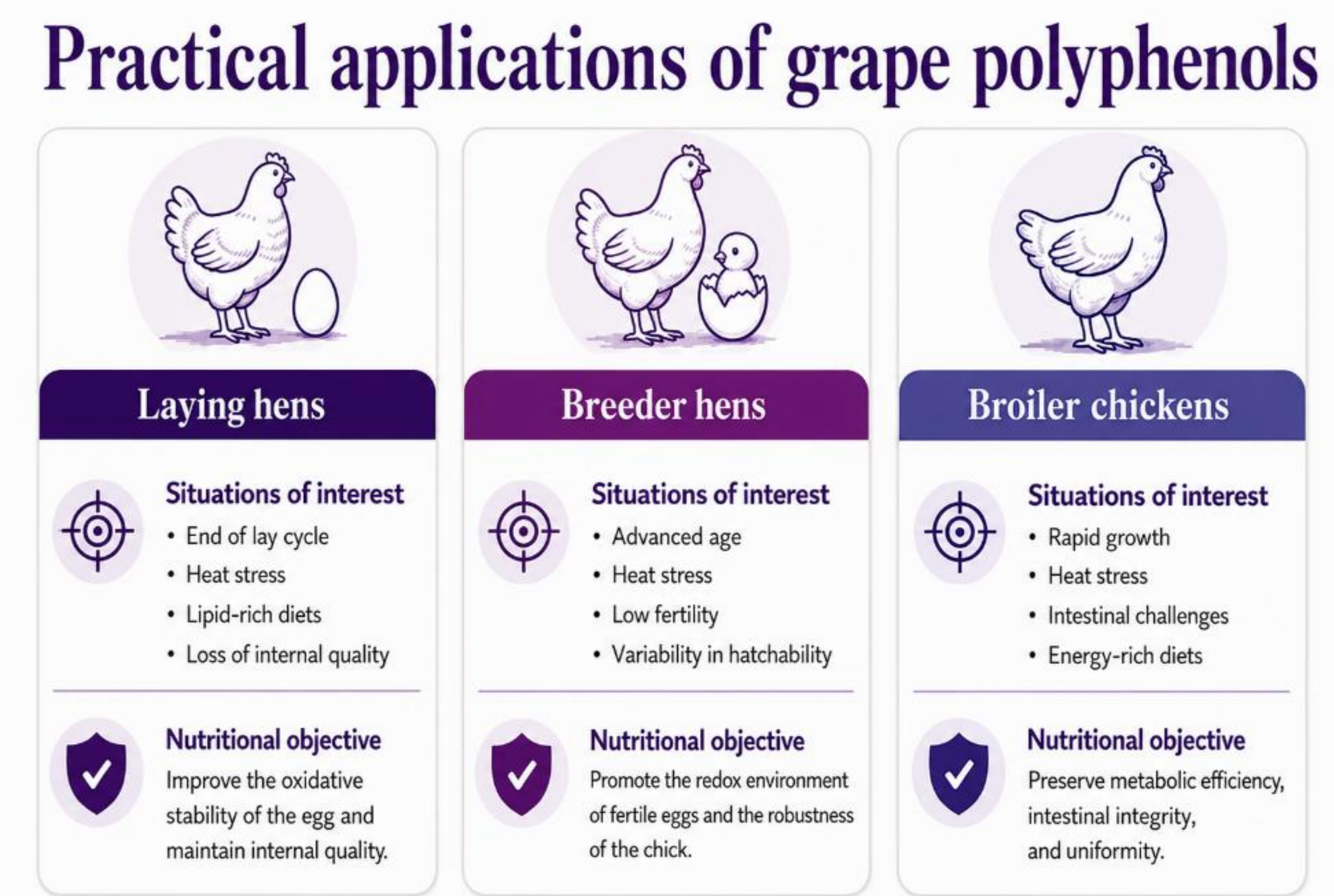

Figure 3. Practical applications of grape polyphenols in poultry farming.

6. Applications in pigs

In **breeding sows**, gestation, farrowing and lactation are phases of high metabolic demand. Oxidative stress has been linked to lower reproductive performance, greater variability in birth weight, poorer litter uniformity and lower piglet vitality. A polyphenol-based antioxidant strategy can help maintain redox balance during these critical phases, supporting placental functionality, metabolic response, and lactation quality.

In **growing-finishing pigs**, rapid growth, high-energy diets, and stressors associated with management can increase ROS generation. In addition, lipid oxidation directly influences the stability and shelf life of the meat. In this regard, grape polyphenols can contribute both to metabolic efficiency and to the preservation of meat quality under commercial conditions.

Article

Practical applications of grape polyphenols

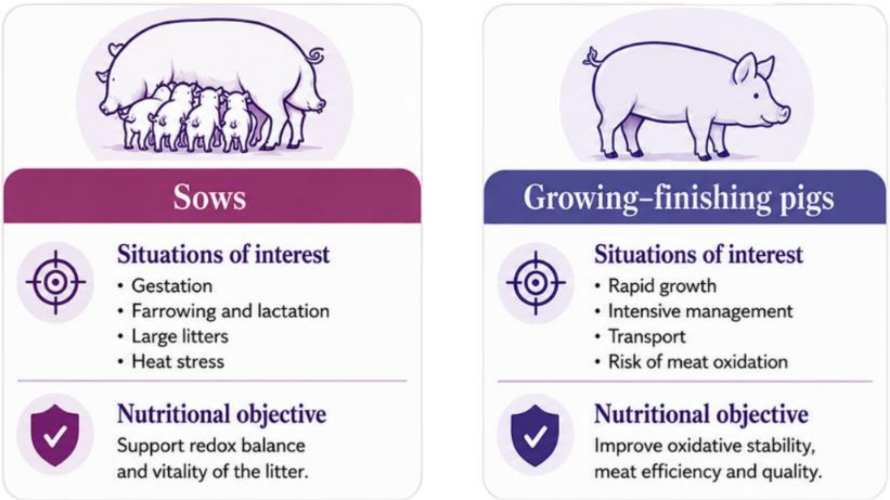

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Figure 4. Practical applications of grape polyphenols in pigs.

7. Conclusion

In conclusion, grape extract polyphenols are a valuable nutritional tool of interest for modern animal production due to their multimodal action on redox balance. This approach makes it possible to address oxidative stress as a factor linked to metabolism, reproduction, end-product quality and production efficiency, contributing to preserving cell function and improving resilience under challenging conditions.

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