

REVIEWING THE ROLE OF FUNCTIONAL INGREDIENTS IN IMPROVING IMMUNE HEALTH AND DISEASE MANAGEMENT IN BREEDING ANIMALS: CURRENT PERSPECTIVES AND EMERGING TRENDS

Raluca Aniela Irimia (Gheorghe), Dana Tăpăloagă, Cosmin Șonea*, Oana Mărgărita Ghimpețeanu, Maria Rodica Gurău, Paul-Rodian Tăpăloagă

University of Agronomic Sciences and Veterinary Medicine of Bucharest, 59 Marasti Blvd, District 1, Bucharest, Romania

Corresponding author email*: cosmin_sn@yahoo.com

Abstract

This review delves into recent advancements in livestock research, focusing on genetic diversity, disease resistance, and immune function. Through an in-depth analysis of various studies, this review elucidates the intricate interplay of genetic factors influencing disease susceptibility and resilience in livestock populations. Investigations highlight the efficacy of functional ingredients, such as plant extracts and marine-derived compounds, in enhancing immune health and disease resistance in breeding animals. Additionally, the review examines the molecular mechanisms underlying the immunomodulatory effects of specific ingredients, shedding light on signaling pathways and gene expression profiles involved in bolstering immune function. Furthermore, the review explores emerging trends in livestock nutrition, including the utilization of fruit processing by-products to improve animal health and performance. Insights into the role of prebiotics in modulating gut microbiota and mitigating diet-related maladies provide valuable perspectives for enhancing livestock welfare and productivity. By synthesizing these findings, this review underscores the critical importance of genetic selection, dietary interventions, and immunomodulatory strategies in promoting the health and resilience of livestock populations.

Keywords: disease resistance, immune function, functional ingredients, gut microbiota

1. INTRODUCTION

The immune function and disease resistance in breeding animals are paramount for ensuring their health, welfare, and productivity. Genetic and genomic techniques have been pivotal in elucidating the intricate mechanisms underlying disease resistance, interpreting data, and leveraging research outcomes to breed animals with enhanced resistance [1]. For instance, studies have revealed the influence of genetic diversity among cattle breeds on susceptibility to diseases like bovine tuberculosis, underscoring the genetic underpinnings of disease resistance [2,3]. Moreover, innate immune genes, such as Toll-like receptors, play a pivotal role in cattle immune systems, further highlighting the genetic basis of disease resistance [4].

Selective breeding for disease resistance has gained prominence in aquaculture breeding programs, particularly in species such as Atlantic salmon and rainbow trout, thus emphasizing the criticality of genetic evaluation for disease resistance in aquaculture species [5]. Furthermore, understanding the genetic footprints of cattle breeds has been instrumental in elucidating their disease resistance and genetic contributions, thereby accentuating the necessity to consider breed characteristics in disease resistance strategies [6,7]. Notably, genetic variations in specific genes like SLC11A1 and TLR2 have been associated with resistance to bovine tuberculosis and other diseases in cattle,

offering insights for selective breeding of disease-tolerant animals [8,9,10]

The identification of major quantitative trait loci related to innate mechanisms has furnished invaluable insights into the genetic foundation of disease resistance in rainbow trout, paving the way for discerning the genes responsible for resistance to specific diseases [11]. Additionally, the advent of precise genome editing holds promise in augmenting animal disease resistance, production efficiency, and welfare, thereby underscoring the role of advanced genetic technologies in enhancing disease resistance [12]. Furthermore, the evaluation of genetic variations and selection of animals based on resistance genes are imperative for the implementation of disease resistance breeding programs in small ruminant breeds, such as goats and sheep [13].

The immune system and genetic markers distinguishing between resistant and susceptible genotypes for specific diseases, such as Johne's disease, have been extensively studied in red deer, thus highlighting the influence of host genotype on disease susceptibility [14]. Moreover, the advent and dissemination of DNA-based diagnostics have significantly impacted animal breeding, health, and population management, underscoring the indispensability of genetic testing in disease management and breeding programs [15].

Functional ingredients play a pivotal role in enhancing immune health and disease resistance in breeding animals. These ingredients, derived from various sources, exhibit

promising potential in improving animal health and welfare. The use of functional ingredients in animal nutrition has garnered significant attention owing to their immunomodulatory effects and their ability to enhance disease resistance [16,17]. Additionally, the identification of potential biomarkers through advanced analytical techniques, such as mid-infrared spectrometry, offers avenues to discern the immunomodulatory effects of functional ingredients [18].

Furthermore, genetic studies have underscored the significance of functional ingredients in disease resistance, with a focus on the immunogenetics of small ruminant lentiviral infections and the selection of animals based on resistance genes for disease management [19,20]. The genetic diversity and innate immune genes among different cattle breeds have been associated with variations in disease resistance, thus accentuating the potential of genetic selection for improved disease resistance [1].

In addition to genetic factors, the immune response of animals to pathogens and parasites has been scrutinized concerning functional ingredients. For instance, the resistance of sheep to nematode infections has been correlated with variations in specific genes and immune responses, thereby shedding light on the potential role of functional ingredients in enhancing disease resistance [21,22]. Moreover, the utilization of functional ingredients in aquaculture has exhibited promise in augmenting disease resistance in fish species, with studies focusing on immune responses and genetic parameters associated with enhanced disease resistance [23]. The potential of functional ingredients in bolstering the immune responses of animals has also been probed in reptilian species, furnishing insights into the role of photoperiod and melatonin in modulating immune responses [24].

The aim of this comprehensive review article is to provide a thorough examination of the interplay between immune function, genetic factors, and the utilization of functional ingredients in enhancing disease resistance in breeding animals.

2. OVERVIEW OF IMMUNE FUNCTION IN BREEDING ANIMALS

The immune system of breeding animals encompasses pivotal constituents crucial for maintaining their health and bolstering disease resistance. Constituting a multifaceted network of cells, tissues, and organs, the immune system orchestrates a coordinated defence mechanism against pathogens and exogenous agents. Numerous investigations have illuminated the diverse facets of the immune system in breeding animals, offering invaluable insights into their genetic, cellular, and molecular underpinnings. Genetic inquiries have underscored the significance of immune-related genes and

their pivotal role in conferring disease resistance in breeding animals. Specifically, research has elucidated the crucial involvement of certain genes, notably major histocompatibility complex (MHC) genes, in orchestrating immune responses and fortifying resistance to diseases across vertebrates. Furthermore, the delineation of quantitative trait loci (QTL) associated with innate immune mechanisms has yielded profound insights into the genetic architecture underpinning disease resistance, thereby paving avenues for identifying pivotal genes governing resistance. The cellular and molecular constituents of the immune system in breeding animals have been subjected to extensive scrutiny in scientific discourse. Investigations have meticulously examined T lymphocyte subpopulations, including CD4+ and CD8+ T cells, and their genetic regulatory mechanisms in swine, thus underscoring the criticality of specific immune cell subsets in engendering disease resistance. Additionally, inquiries into the roles of distinct immune cells, such as leukocytes, in responding to environmental and breeding-related stimuli have furnished insights into the modulation of immune responses in breeding male ground squirrels. The immune system of breeding animals is further susceptible to seasonal and environmental influences. Empirical findings have delineated how seasonal variations can exert profound effects on immune responses and parasite impact on hosts, with individuals in peak condition exhibiting heightened immune reactivity during breeding periods. Moreover, investigations into the ramifications of shifting climatic conditions and burgeoning population densities have shed light on their interplay with immune function in Turkish native cattle breeds, thereby accentuating the imperative of adopting preemptive measures against potential risks. Disease resistance and immune function are intricately interwoven facets of the immune system in breeding animals. Studies have underscored the pivotal role of maintaining a harmonious immune responsiveness in breeding endeavors to ameliorate animal health, thus underscoring the necessity of integrating immune function as a cardinal consideration in breeding initiatives. Furthermore, the identification of immune-related genes and their allelic variations among disparate breeds has furnished profound insights into the genetic foundations of disease resistance and immune function in animals.

The ramifications of compromised immune function on animal health and productivity are intricate and have been extensively scrutinized. The immune system assumes a pivotal role in safeguarding animals against diseases and upholding their overall well-being. When immune function falters, it precipitates significant repercussions for animal health and productivity across diverse domains. Firstly, compromised immune function heightens susceptibility to infectious diseases, rendering animals more vulnerable to infections and ailments.

Empirical evidence has elucidated that animals with attenuated immune systems are at an elevated risk of contracting diseases, culminating in deleterious effects on their health and welfare [25,26]. Secondly, compromised immune function exerts adverse effects on animal productivity. Studies have underscored that animals grappling with compromised immune systems may encounter diminished growth rates, attenuated feed efficiency, and impaired reproductive performance, ultimately undermining overall productivity [27,28,29]. Thirdly, animals with compromised immune function may manifest signs of discomfort, subdued activity, and altered behavior, thereby impinging upon their welfare. The ramifications of compromised immune function on animal welfare have emerged as a burgeoning concern, given its potential to impinge upon the overall quality of life for the animals [30,31]. Moreover, environmental stressors such as heat stress can compromise immune function in animals, precipitating diminished productivity and health maladies. Seasonal vicissitudes and extreme meteorological conditions can further exacerbate the implications of compromised immune function on animal health and productivity [31,32]. Additionally, compromised immune function can precipitate metabolic stress, oxidative stress, and impaired nutrient absorption, thereby exerting profound impacts on animal health and productivity. Studies have underscored the intricate interplay between immune function, nutritional status, and metabolic processes in animals [33,34]. Furthermore, animals with compromised immune function may evince heightened susceptibility to the deleterious effects of toxins and pollutants, exacerbating health ailments and impeding productivity. The implications of compromised immune function vis-à-vis exposure to environmental contaminants constitute an emerging area of concern [35,36].

3. FUNCTIONAL INGREDIENTS AND THEIR MECHANISMS OF ACTION

Functional ingredients in animal nutrition encompass bioactive compounds, nutrients, or substances derived from various sources that confer additional health benefits beyond fundamental nutrition. They are integrated into animal diets to bolster immune function, advance overall health, and heighten disease resistance. Illustrative examples of frequently employed functional ingredients in animal nutrition include:

1. Plant Feedstuffs: Plant-derived ingredients like oilseeds, legumes, and cereal grains serve as functional ingredients in animal nutrition, providing protein, energy, and essential nutrients. Additionally, they may contain bioactive compounds that augment animal health and well-being.
2. Algal Proteins: Algal proteins are increasingly utilized as functional ingredients in animal nutrition, offering a sustainable and nutrient-rich reservoir of amino acids, vitamins, and minerals. Their incorporation contributes to enhanced animal health and performance [37].
3. Soybean Molasses: Employed as a functional feed ingredient, soybean molasses acts as a pelleting aid and imparts nutritional benefits, thus enhancing the overall quality of animal feed [38].
4. Insect and Fish By-Products: By-products sourced from insects and fish are harnessed as sustainable alternatives to traditional animal proteins in animal nutrition. These by-products furnish essential nutrients such as protein, fatty acids, and minerals, thereby fortifying animal health and well-being [39].
5. Fucoxanthin: Fucoxanthin, a functional ingredient with potential medicinal and nutritional attributes, is utilized in animal nutrition to confer antioxidant and anti-inflammatory properties, thereby augmenting health and disease resistance [40].
6. Fruit and Vegetable Co-Products: Residues generated from fruit and vegetable processing serve as functional feed ingredients in animal nutrition. These co-products confer nutritional value and contribute to enhanced animal performance [41].
7. Plant Proteins: Proteins derived from plants are integrated into animal nutrition as functional ingredients, providing essential amino acids and augmenting the overall protein content of animal diets [42].

These examples underscore the diverse repertoire of functional ingredients employed in animal nutrition to fortify immune health, bolster disease resistance, and improve the overall animal welfare.

4. EFFECTS OF FUNCTIONAL INGREDIENTS ON IMMUNE FUNCTION AND DISEASE RESISTANCE

The investigation into the impact of functional ingredients on immune parameters, encompassing cytokine production, antibody response, and phagocytic activity, has undergone extensive scrutiny within the scientific community. Studies have delved into the immunomodulatory effects of diverse functional ingredients, unraveling their potential in fortifying host defense mechanisms. Notably, research endeavors have elucidated the influence of vitamin A supplementation on immune responses and clinical outcomes, underscoring its role in bolstering antibody production and lymphocyte proliferation [43,44].

Furthermore, examinations into the immunomodulatory ramifications of various nutritional combinations have shed light on their effects on cytokine production and immune competence [45]. Additionally, investigations probing into the influence of functional ingredients on gut health and immunity have unveiled the modulation of immune responses through dietary components, elucidating intricate interactions therein [46].

Moreover, the exploration of specific functional ingredients, such as soybean products, has delineated their potential in modulating gut microbiota and immunity in aquatic animals, offering insights into the dynamic interplay between functional ingredients and immune function [47]. Complementary research has delved into the effects of antioxidant and non-antioxidant vitamin supplementation on immune function, emphasizing their impact on both innate and adaptive immune responses [48]. Additionally, investigations into the potential of food ingredients, including pro- and prebiotics, β -glucans, and fungal immunomodulatory proteins, have underscored their capacity for immune stimulation and allergic disease mitigation [49].

In the realm of animal nutrition, inquiries have probed the effects of diverse oil sources on immune function, shedding light on their influence on cytokine production and immune competence in broiler chicks [50]. Functional ingredients assume a pivotal role in averting and alleviating specific diseases prevalent among breeding animals. These ingredients, sourced from diverse origins, have been scrutinized for their potential in enhancing immune function, fostering overall health, and mitigating the incidence or severity of diseases in animals. Numerous investigations have explored the impact of functional ingredients on disease prevention and mitigation, illuminating their potential contributions to animal health and welfare.

For instance, research endeavors have elucidated the molecular mechanisms and health roles of functional ingredients, such as anthocyanins and polyphenols found in blueberries, in preventing chronic diseases in humans, thereby hinting at their potential application in animal nutrition [51]. Additionally, the review of functional components and medicinal properties of food has underscored their potential in reducing the risk of chronic degenerative diseases and promoting overall well-being [52].

Furthermore, investigations into the therapeutic potential of functional ingredients, including organopolysulfides and quercetin sourced from barley grass, have been conducted to prevent chronic diseases in humans, with implications for their application in animal health and disease prevention [53]. Additionally, examinations into the role of functional ingredients in mitigating micronutrient deficiency have provided insights into their potential application in animal nutrition to address nutritional inadequacies [54].

Moreover, discussions revolving around the management of parasites, prions, and pathogens in the global feed industry have underscored the importance of implementing biosafety and biosecurity measures to curb the spread of animal diseases through feed ingredients [55]. Additionally, explorations into the potential utilization of fruit processing by-products in the aquafeed industry have emerged as a viable strategy for enhancing intestinal microbial balance, digestibility, and local intestinal immunity in aquaculture settings [56].

5. FACTORS INFLUENCING THE EFFICACY OF FUNCTIONAL INGREDIENTS

Numerous factors contribute to the effectiveness of functional ingredients in bolstering immune function and disease resistance, encompassing aspects such as dosage, formulation, and duration of supplementation. These parameters wield substantial influence over the impact of functional ingredients on animal health and well-being. A plethora of investigations have delved into these factors, furnishing invaluable insights into their potential ramifications on immune function and disease resistance. For instance, Jagim et al. (2019) scrutinized various determinants, including physiological rationale, clinical evidence, cost-efficiency, raw material availability, patent status, and sensory attributes, shaping the development of multi-ingredient pre-workout supplements (MIPS), elucidating their potential efficacy [57]. Additionally, Haroyan et al. (2018) delved into the impact of treatment strength, baseline disease severity, delivery route, and sample size on the efficacy of curcumin, either alone or in combination with boswellic acid, in mitigating osteoarthritis [58].

Moreover, investigations into fucoxanthin have addressed aspects such as bioavailability, metabolism, safety profile, and strategies for enhancing bioavailability, shedding light on factors underpinning its efficacy [40]. Similarly, Gencoglu et al. (2020) explored the influence of dosage and supplementation duration on the efficacy of undenaturated type II collagen (UC-II) in preserving joint health, offering insights into its optimal usage [59].

Furthermore, the efficacy of prebiotics as functional food ingredients in averting diet-related diseases has been scrutinized in the context of formulation and supplementation duration, delineating factors that sway their effectiveness [60]. Likewise, Sirri et al. (2018) investigated the impact of dosage and supplementation duration on the effectiveness of curcumin, alone or in combination with vitamin E, selenium, or plant extracts, in enhancing pig health [61].

Additionally, the intricate interactions between functional ingredients and other dietary or environmental components significantly influence their effectiveness in augmenting animal health and performance.

Factors like diet composition, genetic background, and environmental conditions exert notable influence over the efficacy of functional ingredients. For instance, Glencross et al. (2007) underscored the pivotal role of ingredient digestibility, palatability, and nutrient utilization in evaluating aquaculture feeds, accentuating the intricate interplay between feed components and their impact on fish health and performance [62]. Similarly, Xue et al. (2014) delved into the additivity of apparent and standardized ileal digestibility of amino acids in diets containing multiple protein sources fed to growing pigs, elucidating potential interactions between dietary proteins and their effects on nutrient utilization [63]. These investigations yield critical insights into the potential interactions between functional ingredients and other dietary or environmental constituents, offering a holistic understanding of factors influencing animal health and performance.

6. CHALLENGES AND FUTURE DIRECTIONS

Enhancing immune health and disease resistance in breeding animals through the utilization of functional ingredients encounters various challenges and constraints. These encompass the imperative to refine formulations, identify novel ingredients, and unravel the underlying mechanisms of action. Herein lie potential avenues for future exploration:

1. **Optimization of Formulations:** The refinement of formulations is imperative to ensure the stability, bioavailability, and effectiveness of functional ingredients within animal diets. This necessitates the exploration of innovative delivery systems, encapsulation methodologies, and synergistic amalgamations of ingredients to potentiate their bioactive attributes and functional prowess [64].
2. **Discovery of Novel Ingredients:** There exists a pressing need to unearth and assess novel functional ingredients harboring inherent immunomodulatory and disease-resistant qualities. Such endeavors may entail the screening of diverse natural reservoirs, encompassing plant extracts, marine-derived compounds, and bioactive peptides, to unveil hitherto undiscovered bioactive agents with favorable impacts on animal health [65].
3. **Elucidation of Mechanisms of Action:** Future investigations should pivot towards elucidating the intricate mechanisms of action underlying the immunomodulatory and disease-resistant attributes of functional ingredients. This may entail delving into molecular and cellular realms to unravel the signaling cascades, gene expression dynamics, and metabolic responses

entwined with the immunomodulatory effects of specific ingredients [53].

4. **Gut Microbiota Interaction:** Delving into the interplay between functional ingredients and the gut microbiota assumes paramount importance in comprehending their influence on immune health. Explorations in this sphere hold promise in elucidating the prebiotic and probiotic properties of functional ingredients, along with their role in sculpting the gut microbiome to bolster immune function [65].
5. **Environmental Implications:** The assessment of the environmental footprint engendered by functional ingredients and their integration into animal production constitutes a pivotal frontier for forthcoming research. This entails a comprehensive evaluation of sustainability metrics, ecological ramifications, and ethical considerations entailed in the production and deployment of functional ingredients in animal feed formulations [66].
6. **Integration of Traditional Medicine:** Exploring the untapped potential of traditional medicine and herbal remedies as reservoirs of functional ingredients for animal health heralds as a burgeoning realm of interest. Endeavors in this domain proffer insights into the utilization of traditional medicinal flora and their bioactive constituents in fortifying immune function among breeding animals [67, 68, 69, 70].

7. CONCLUSIONS

In conclusion, the utilization of functional ingredients holds immense promise for enhancing immune health and disease resistance in breeding animals. However, this endeavor is not without its challenges and complexities. Through this review, we have elucidated various factors influencing the efficacy of functional ingredients, ranging from formulation optimization to the exploration of novel ingredients and understanding their mechanisms of action. Moreover, we have underscored the importance of investigating the interaction between functional ingredients and gut microbiota, assessing environmental impacts, and tapping into the potential of traditional medicine. As we navigate these frontiers, it becomes evident that a multidisciplinary approach, encompassing molecular biology, nutrition science, and environmental studies, is imperative to unlock the full potential of functional ingredients in promoting animal health and welfare. By addressing these challenges and advancing our understanding of functional ingredients, we pave the way for the development of innovative strategies to bolster immune function and disease resistance in breeding animals, thereby contributing to the sustainability and resilience of animal agriculture.

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