Chapter 27

Phytochemicals as Promising Defense against Infectious Bursal Disease

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ABSTRACT

Infectious Bursal Disease (IBD), is a highly contagious disease caused by the infectious bursal disease virus (IBDV) that affects young chicks and causes large financial losses for the poultry industry. The illness suppresses the immune system and makes birds more vulnerable to secondary infections by attacking the bursa of Fabricius, an organ that is essential for the formation of B cells. The advent of new virus strains and vaccine failures present problems with the use of vaccination and other traditional control methods. Phytochemicals present a viable path for IBD management. Phytochemicals are naturally occurring bioactive substances that have a variety of biological roles in plants, such as immune-stimulating and antiviral qualities. Many phytochemicals have shown antiviral action against IBD in both in vitro and in vivo investigations, including curcumin, resveratrol, epigallocatechin gallate (EGCG), quercetin, and silymarin. These substances work by reducing oxidative stress and inflammation, inhibiting the growth of viruses, and altering immunological responses, among other methods. The incorporation of phytochemicals into disease management methods has the potential to improve the well-being and efficiency of chicken farms while decreasing dependence on artificial pesticides and antibiotics.

KEYWORDS		
Phytochemicals, Infectious bursal disease, Antiviral, Poultry, Immunity,	Received: 17-May-2024 Revised: 12-Jul-2024 Accepted: 12-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Gumboro disease, also known as Infectious bursal disease (IBD), is caused by a highly contagious virus infectious bursal disease virus (IBDV) that mainly affects young chicks, especially those between the ages of 3 and 6 weeks (Wagari, 2021). The bursa of Fabricius, an important organ in the immune system in handling B cell development, is the target of the IBDV, which causes the disease. IBDV is spread by water, contaminated feed, and microbes in addition to direct interaction with infected birds (Yuan et al., 2020) In addition, contaminated equipment, insects, and wild birds can transfer the virus, accelerating its spread among chicken flocks. IBD's rapid propagation and negative impacts on chick health and productivity make it a danger to the chicken farming industry. The virus strain (vvIBDV), the birds' age, and their immunological status all affect the clinical symptoms of IBD (Eladl et al., 2020). Dehydration, diarrhea, depression, ruffled feathers, and an inability to eat or drink are typical signs. Birds that are severely impacted may display immunosuppression, bursal atrophy, heightened vulnerability to subsequent infections, and higher mortality rates.

IBD pandemics have a significant financial impact on the chicken economy. Reduced egg production, slower development rates, higher treatment expenses, and bird death are all consequences of the condition. IBD outbreaks can also cause trade and export disruptions, which can cost chicken farmers and the larger agriculture industry financially (Yadav et al., 2020). For veterinary professionals and poultry farmers, containing and controlling IBD epidemics presents several difficulties. IBD outbreaks remain because of vaccine failures, and the introduction of novel virus strains. Viral antigenic diversity, incorrect storage, and mishandled administration can all reduce the effectiveness of vaccinations. Novel techniques, such as the consumption of phytochemicals and other natural substances, are being investigated as possible additions to or substitutes for traditional techniques (Jha and Sit, 2022). Preserving the health and viability of poultry farms requires a thorough understanding of how IBD affects poultry farming and the investigation of innovative solutions. Phytochemicals are naturally occurring bioactive molecules found in plants that have a variety of positive effects on human health but are not necessary for the growth or development of the plant. Plants produce these substances as a component of their defensive mechanisms against infections, UV rays, and herbivores, among other environmental stresses. Phytochemicals provide foods made from plants with their distinctive tastes, colors, and fragrances (Onuh and Pathak, 2024). They are frequently found in grains, fruits, legumes, vegetables, nuts, and seeds. A wide range of chemical groups, each with distinct characteristics and biological functions, make up phytochemicals. Among the most well-known categories of phytochemicals are the following: Flavonoids are comprised of isoflavones, anthocyanins, flavonols, flavones, flavanones, and flavan-3-ols (catechins) (Ullah et al., 2020). Phenolic Acids are comprised of ferulic acid, ellagic acid, and caffeic acid among others (Valanciene et al., 2020). Beta-carotene, lutein zeaxanthin, and lycopene are examples of carotenoids (Huang et al., 2021). Alkaloids are comprised of morphine, nicotine, and caffeine (Manna et al., 2020). Terpenoids are comprised of diterpenes, triterpenes, monoterpenes, and sesquiterpenes. Sulfides and Thiols are comprised of Garlic and onions contain allyl sulfides. Polyphenols are comprised of lignans and stilbenes (like resveratrol) (Hazafa et al., 2022). Various biological actions are displayed by these substances, such as immunomodulatory, antiviral, antibacterial, antioxidant, and anti-inflammatory properties (Sobhani et al., 2021). Research has been done on the antimicrobial qualities of phytochemicals, and many of the substances have been shown to have inhibitory effects on fungi, viruses, bacteria, and parasites. These substances can target invasion, adhesion, and replication of the production of virulence factors, among other stages of the microbial life cycle. Phytochemicals can modulate immunity, which can strengthen the host's defenses against infectious pathogens (Behl et al., 2021). Phytochemicals can strengthen the body's resistance against invasive pathogens by inducing both adaptive and innate immune processes. This can lower the risk of infection and assist in the healing process. This chapter will examine the potential of phytochemicals in the fight against infectious diseases, emphasizing their modes of action, effectiveness against certain pathogens, and uses in the prevention and management of disease.

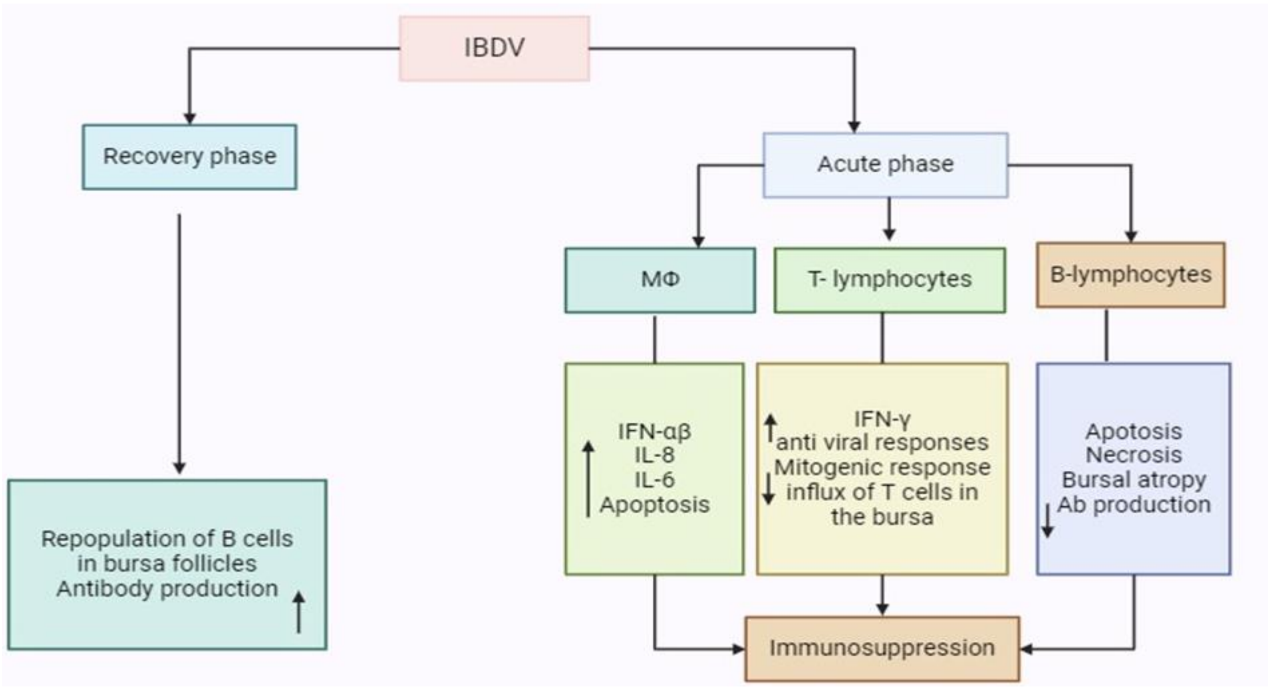

Fig. 1: Immunosuppressive and pathogenic aspects of IBDV (Retrieved from Biorender).

Phytochemicals with Potential Anti-IBD Activity

A variety of phytochemicals have been thoroughly investigated for their possible ability to improve immunity and prevent viruses.

Quercetin

A flavonoid called quercetin can be found in a variety of grains, fruits, and vegetables (Batiha et al., 2020). It shows strong antiviral properties against a variety of viruses, including coronaviruses and influenza, which are respiratory viruses. Quercetin works by preventing the growth of viruses, altering the signaling pathways of host cells, and boosting immune responses by encouraging the synthesis of chemokines and cytokines (Shorobi et al., 2023).

Over the past 20 years, flavonoids and their potential chemo-preventive bioactivities have gained a lot of attention, especially because of their antiviral properties in viral infectious illnesses (Sharma et al., 2021). Flavonoids are now being researched against a range of viruses with DNA and RNA. They show a range of physiological effects in humans, such as antibacterial, antioxidant, antiviral, cytotoxic, anti-inflammatory, and anti-allergic properties (Al-Kahtani et al., 2022). Flavonoids are substances that strengthen the humoral immune system of broilers by promoting the synthesis of IgM and IgG antibodies. By stimulating macrophages, flavonoids promote the manufacture of cytokines, including interferon. They inhibit infectious IBDV in broilers especially well by reducing bursal lesions and viral protein expression. These characteristics of flavonoids have led numerous researchers to propose their potential application in the management of IBDV (Shehata et al., 2022).

Epigallocatechin Gallate (EGCG)

A catechin called EGCG can be found in green tea along with various types of tea. It has antiviral qualities against many viruses, such as the herpes simplex virus (HSV), HIV, and influenza. By inducing immune cell activation and boosting cytokine production, EGCG suppresses viral attachment and penetration into host cells, interferes with viral replication, and boosts immunological responses (Zhao et al., 2021). Research shows that EGCG has the ability to prevent the IBDV from replicating in vitro. By inhibiting the virus's capacity to enter and multiply within host cells, it lowers the viral load and stops the infection from spreading infections (Yasmin et al., 2020).

Curcumin

Turmeric, a spice that is frequently used in Asian cooking, is the source of the polyphenol curcumin. It shows antiviral action against several viruses, such as HIV, hepatitis viruses, and influenza. Curcumin has immunomodulatory effects by controlling the production of cytokines and the activity of immune cells. It also inhibits the replication of viruses and modifies host cell signaling pathways associated with viral infection (Makuch et al., 2021). Curcumin's anti-inflammatory properties help in lowering inflammation caused by IBDV. It also possesses antioxidant qualities which help in reducing oxidative stress and absorbing free radicals, both of which may increase viral damage (Hartady et al., 2021).

Resveratrol

A stilbenoid called resveratrol can be found in berries, red wine, and grapes. It has antiviral qualities against a range of viruses, such as herpesviruses and respiratory viruses. By interfering with the production of viral proteins and modifying the host cell's response to viral infection, resveratrol prevents the spread of viruses. Resveratrol also has immunomodulatory effects by lowering inflammation and improving immune cell function (Alesci et al., 2022). The anti-inflammatory properties of resveratrol help in reducing inflammation caused by IBDV. Because of its antioxidant properties, host cells are protected from viral pathogen-induced damage and oxidative stress (Shehata et al., 2022).

Silymarin

A flavonolignan called silymarin is extracted from milk thistle seed. It shows antiviral action against influenza, HIV, and hepatitis viruses. By preventing viral entry into host cells, interacting with the development of viral proteins, and boosting host immune responses to viral infection, silymarin prevents the spread of viruses (Palit et al., 2021). There have been few research specifically examining silymarin's benefits against IBDV, its broad-spectrum antiviral characteristics and immunomodulatory actions point to possible uses in chicken farming to reduce IBDV infection.

Mechanism of Action

Many modes of action displayed by phytochemicals may contribute to their potential effectiveness in treating IBD. Some phytochemicals prevent viruses from replicating by focusing on important proteins and viral enzymes involved in the virus life cycle. Flavonoids such as EGCG and quercetin reduce the activity of the viral RNA polymerase, which in effect suppresses the reproduction of the IBDV virus (Wu et al., 2023). Phytochemicals can stop viruses from attaching to surfaces and entering host cells by inhibiting viral binding sites or interacting with viral entry pathways by inhibiting viral binding sites or interacting with viral entry pathways. Curcumin has been shown to prevent IBDV from attaching itself to cell surface receptors, preventing the virus from entering host cells. Phytochemicals may induce innate immune responses by stimulating immune cells including dendritic, natural killer (NK), and macrophage cells (Gasmi et al., 2023). These immune cells are essential for recognizing and getting rid of viral infections. Certain compounds, such as resveratrol and curcumin, increase the cytotoxic activity of NK cells and both the phagocytic function of macrophages targeting infected cells. Phytochemicals can modify the synthesis of pro- and anti-inflammatory cytokines to control immunological responses to viral infection (Baranwal et al., 2021). Quercetin inhibits the synthesis of pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) but stimulates the synthesis of anti-inflammatory cytokines like interleukin-10 (IL-10). Some phytochemicals influence T helper cell (Th) actions, facilitating a balanced Th1/Th2 immunological response (Gandhi et al., 2020). Sufficient Th1/Th2 balance is necessary for antiviral immunity to be effective. EGCG causes a Th1/Th2 imbalance to be shifted in favor of a Th1-dominated action, which may strengthen the immune system against IBDV. Viral infection-induced oxidative stress can be reduced by phytochemicals having antioxidant qualities. These substances defend host cells from oxidative damage brought on by viral replication by absorbing reactive oxygen species (ROS) and preventing lipid peroxidation. Quercetin and EGCG are flavonoids with strong antioxidant activity that may help reduce oxidative stress brought on by IBDV infection (Hartady et al., 2021). By lowering excessive inflammatory responses brought on by a viral infection, phytochemicals may reduce tissue damage and diseases linked to inflammation. Curcumin and resveratrol are examples of compounds that have anti-inflammatory properties because they prevent the synthesis of mediators that promote inflammation, such as leukotrienes and prostaglandins. Phytochemicals possess the ability to fight against IBDV infection and reduce its harmful consequences by focusing on multiple stages of the viral life cycle and adjusting the immunological responses of the host (Faisal et al., 2023).

Efficacy of Phytochemicals against IBD

Several research have been carried out both in vitro and in vivo to assess the phytochemicals' effectiveness against the IBDV. Several phytochemicals have been shown to have antiviral action against IBDV in vitro investigations utilizing cell culture models (Jumaa et al., 2021). Usually, these investigations involve the infection of vulnerable cell lines (such as DF-1 cells or chicken embryo fibroblasts) with IBDV and the evaluation of cytopathic effects and viral replication in the light of phytochemical treatments (Rekha et al., 2014). To assess the inhibitory impact of phytochemicals on IBDV replication, antiviral techniques like quantitative PCR tests, virus yield reduction assays, and plaque reduction assays are frequently employed. Viral RNA levels, viral titer, viral protein expression, and infected cells injected with phytochemicals are only a few of the characteristics that these investigations examine. Phytochemicals like curcumin, quercetin, EGCG, and resveratrol have been shown in vitro to reduce IBDV proliferation and lower viral infectivity in cell culture models (Mehrotra, 2020).

Studies on animals, specifically chickens, have been carried out in vivo to assess the effectiveness of phytochemicals in combating IBDV infection. These trials usually entail giving oral, intramuscular, or dietary phytochemical therapies to chickens that have been infected with IBDV. Several clinical criteria are evaluated by in vivo efficacy trials, such as death rates, bursal weight-to-body weight ratios, histological alterations in the bursa of Fabricius, bursal lesion evaluations, and serum antibody titers (Ray et al., 2021). These metrics shed light on how phytochemicals affect host immune responses and IBDV development. In vivo, research might investigate the immunomodulatory influence of phytochemicals on the human immune system in addition to their antiviral action. These studies evaluate the reaction of immune cell populations, lymphocyte proliferation, and cytokine production to phytochemical treatments. Phytochemical therapies can lessen bursal lesions, boost immunological responses, and lessen IBDV-induced mortality in infected hens, according to in vivo investigations (Guo et al., 2022). Inhibiting viral attachment, entrance, protein synthesis, and replication as well as modifying host immunological responses to viral infection are some of the ways phytochemicals can carry out their antiviral actions. Overall, the results of research conducted in vivo and in vitro provide validity to the possible use of phytochemicals as all-natural remedies for the management and prevention of IBD.

Challenges and Limitations

Although phytochemicals appear to have potential as therapies or preventatives for IBD, several limitations and restrictions must be considered. A large number of phytochemicals are poorly absorbed and used by the body due to their low bioavailability (Shahidi and Pan, 2022). The efficiency of phytochemicals in vivo can be decreased by factors that impact their bioavailability, such as limited tissue distribution, fast metabolism, and low solubility. It can be difficult to determine the best phytochemical dosage and delivery system (Ahmad et al., 2021). Dosing regimens can become complex due to factors including individual variability in absorption rates, variations in the phytochemical content of plant sources, and the requirement for sustained release formulations. Although different phytochemical combinations can have synergistic benefits, it can be difficult to determine the best ratios and combinations of different components. The particular phytochemicals involved, their quantities, the target pathogen, and the host immune response can all affect synergistic interactions. Chronic use of phytochemical therapies carries a danger of developing virus resistance. The effectiveness of treatment may be diminished if viruses become resistant to the antiviral effects of phytochemicals due to changes that they have developed in response to their presence. Phytochemicals can interact or cause negative effects with other drugs or food ingredients (Pham et al., 2020). To assess the safety properties of phytochemicals at dosages for therapy and identify any possible side effects, toxicity studies are required. Obtaining regulatory approval to use phytochemicals as therapies or preventatives for IBD might be difficult. Phytochemicals are frequently categorized as herbal treatments or dietary supplements, which may need different regulation processes than traditional pharmaceutical pharmaceuticals. Accessibility to phytochemical-based goods may be restricted by the cost of obtaining and manufacturing them, especially in environments with limited resources (Díaz-Puertas et al., 2023). Furthermore, there may be differences in the accessibility of standardized phytochemical formulations that are consistently high-quality and effective. The absence of defined techniques for phytochemical characterization, extraction, and quality control can lead to variations in the efficacy and content of products derived from phytochemicals (Fonmboh et al., 2020). To assess the safety, effectiveness, and best usage of phytochemicals for the prevention and treatment of IBD, extensive preclinical and clinical research are required.

Future Perspective

The development of standardized phytochemical formulations with constant quality, potency, and purity should be the main goal of future studies. Standardization guarantees the consistency and dependability of goods derived from phytochemicals, allowing for easier comparisons between research and enhancing the safety and effectiveness profiles of these products (Gupta et al., 2021).

Systematic dose-response studies are required to determine the best phytochemical dosage schedules. This involves assuming out the lowest effective dose needed to maintain antiviral effectiveness while reducing toxicity or unfavorable effects. To help with dosage optimization, pharmacokinetic studies can shed light on the distribution, metabolism, excretion, and absorption of phytochemicals. It is essential to research the synergistic effects of mixing various plants or phytochemicals with traditional antiviral medicines. Combination medicines have the potential to overcome viral resistance, improve antiviral activity, and lower the risk of side effects related to high dosages of individual drugs (Shyr et al., 2021). Assays for synergy screening and in vivo, research can assist in identifying combinations that show promise for additional assessment. It is necessary to further clarify how phytochemicals work against IBDV. Mechanistic research can shed light on the molecular targets and pathways that explain the immunomodulatory and antiviral properties of phytochemicals, which can help develop more specialized treatments and practical approaches to drug manufacturing. Testing the results from preclinical investigations and field trials requires clinical studies in populations of chickens (Van de Wall et al., 2023). These investigations can evaluate how well phytochemicals work to stop IBD outbreaks, lessen viral shedding, and enhance clinical results in birds with the disease. Studies of long-term surveillance can also assess the long-term viability of phytochemical-based therapies and the possibility of the development of viral resistance. To assess the financial viability of using phytochemical-based therapies in chicken farming techniques, a cost-effectiveness analysis ought to be carried out (Manickam et al., 2021). This involves estimating the expenses related to the manufacture, formulation, and distribution of phytochemicals as well as the possible financial benefits from lower rates of illness, death, and antibiotic use. It is necessary to establish or modify regulatory frameworks for the licensing and registration of medicines based on phytochemicals for use in veterinary medicine. In addition to addressing regulatory issues with product classification, registration procedures, and global harmonization, this entails developing guidelines for quality control, labeling, product safety, and marketing authorization. The possible role of phytochemicals as useful instruments for IBD treatment and prevention can be realized by solving these research priorities, which will enhance the welfare and health of chickens as well as promote sustainable agricultural methods.

Conclusion

In conclusion, investigation into phytochemicals as all-natural treatments for IBD offers a bright future for the chicken industry. Phytochemicals have been shown to have immunomodulatory and antiviral properties, making them an effective means for managing illness. The potential advantages of phytochemicals as affordable and environmentally friendly substitutes for antibiotics exceed these drawbacks. Phytochemical-based therapies can change disease control procedures in the chicken sector by enhancing animal welfare and decreasing dependency on synthetic pesticides. However, more research and cooperation are required to solve issues like bioavailability, dosage optimization, and regulatory approval. There is potential for improving the productivity, sustainability, and health of chicken production systems through the incorporation of phytochemicals into controlling disease measurements.

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