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Coccidiosis Control Through Phytochemical Modulation of Immunity

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Introduction:

Avian coccidiosis is a major enteric parasitic disease of poultry caused by protozoa of the genus Eimeria, belonging to the phylum Apicomplexa and the family Eimeriidae. Multiple Eimeria species infect different regions of the intestinal tract, resulting in severe disease manifestations (Gerhold, 2023). The predominant species reported in South India include *E. tenella, E. necatrix, E. acervulina, E. maxima, E. mitis, E. brunetti,* and *E. praecox*, with E*. tenella* and *E. necatrix* being the most pathogenic. The life cycle of Eimeria is complex, encompassing both intracellular and extracellular developmental stages that elicit strong inflammatory responses in the host. These responses cause extensive intestinal tissue damage, which is often accompanied by oxidative stress, lipid peroxidation, enteric haemorrhages, reduced growth performance (ill thrift), and heightened vulnerability to secondary infections, particularly those caused by Clostridium spp. In severe infections, high flock-level mortality can occur, resulting in substantial economic losses to the poultry industry (El-Shall *et al*., 2022).

Key words: Coccidiosis, Phytochemicals, Immune Modulation, CCO.

Economic Loss:

Coccidiosis accounts for a significant portion of economic losses in poultry production, with an estimated 95.61% of total losses attributed to this disease. In the commercial layer industry alone, approximately 3.53% of the economic loss is incurred, primarily due to expenses related to chemoprophylaxis, treatment of infected birds, and decreased productivity. According to A.K. Bera *et al*., 2010, the total financial loss attributed to coccidiosis was estimated at around Rs. 1.14 billion during the 2003–04 fiscal year.

Challenges in Conventional Control Methods:

Vaccines and various anti-coccidial drugs have long been used to prevent and control avian coccidiosis. These include amprolium, clopidol, folic acid antagonists, halofuginone hydrobromide,

robenidine, diclazuril, and ionophores such as monensin, salinomycin, lasalocid, narasin, maduramicin, and nicarbazin (Gerhold *et al.,* 2024). However, several limitations have been reported with conventional methods, including the development of drug resistance and the presence of chemical residues in poultry products raising concerns among consumers. These drawbacks have steered research towards natural, safe, and effective alternatives, such as phytochemicals, saponins, and enzymes. Phytochemicals are non-nutritive, bioactive compounds produced by plants that provide protective or health-promoting effects. These include antioxidants such as carotenoids and polyphenols (e.g., flavonoids), which help neutralize harmful free radicals in the body. As natural alternatives to synthetic anti-coccidial drugs, phytochemicals are particularly appealing because they align with the demand for chemical-free and herbal-based poultry production.

The anti-coccidial effects of herbal extracts are primarily attributed to their ability to reduce oocyst output by impairing the invasion, replication, and development of *Eimeria* Sp. in the intestinal tissues of chickens. Phenolic compounds in these extracts can disrupt cytoplasmic membranes, leading to coccidial cell death. Additionally, these compounds can reduce intestinal lipid peroxidation, promote epithelial repair, and decrease *Eimeria*-induced intestinal permeability by enhancing epithelial turnover (El-Shall *et al*., 2021). An ideal phytochemical should support intestinal health at low concentrations by modulating the host's physiological mechanisms such as regulating inflammation, enhancing immune responses, providing antioxidant protection, and maintaining gut barrier integrity. These actions help mitigate pathogen-induced damage and support growth performance during infections (Lillehoj *et al*., 2018 and Hotea *et al*., 2022). While single phytochemicals targeting one mechanism can be beneficial, greater effectiveness may be achieved through combinations of multiple phytochemicals. Such combinations can provide synergistic effects by acting through diverse pathways (Seidavi *et al*., 2022; Al-Mnaser *et al*., 2022 and Park *et al*., 2025).

Affective to Control Coccidiosis:

Globally, over 300,000 species of flowering plants have been documented, yet less than 1% have been investigated for their potential against protozoan diseases, including avian coccidiosis. Among those studied, 68 plant species and their phytochemicals have demonstrated promising anticoccidial activity through various in vitro and in vivo models targeting Eimeria spp. (T Muthamilselvan *et al*., 2016). Notable examples include artemisinin from *Artemisia annua*, tannins from *Pinus radiata* and *Agrimonia officinalis*, allicin and propyl thiosulfinate from *Allium sativum*, polyacetylene from *Bidens pilosa*, berberine from *Berberis lyceum*, n-3 fatty acids from *Linum usitatissimum*, flavonoids from *Ageratum conyzoides,* vernoside from *Vernonia amygdalina* and papain from *Carica papaya.*

Several essential oils have also exhibited significant efficacy, including carvacrol, thymol, and γ-terpinene from Origanum compactum; β-thujone, 1,8-cineole, and p-cymene from *Artemisia absinthium*;

cineole, α-pinene, and bornyl acetate from *Rosmarinus officinalis*; eugenol and eugenyl acetate from *Syzygium aromaticum*; terpinen-4-ol and γ-terpinene from *Melaleuca alternifolia*; limonene and linalool from *Citrus sinensis*; and thymol and p-cymene from *Thymus vulgaris*. Other active compounds include curcumin (diferuloylmethane) from *Curcuma longa*; maslinic acid from *Olea europaea*, arabinoxylans from *Triticum aestivum*, cinnamaldehyde from *Cinnamomum cassia*, acemannan from Aloevera, lectins from *Fraxinea fraxinea*, chicoric acid from *Echinacea purpurea* and various phenolic compounds from *Prunus salicina*. These findings highlight the diverse phytochemical arsenal present in medicinal plants, offering a promising natural alternative to synthetic anticoccidials in poultry health management.

Essential oils in control of Coccidia:

Essential oils are valuable natural resources rich in diverse phytochemicals. Both in vitro and in vivo studies have demonstrated their potential as feed additives for controlling coccidiosis in poultry. Bioactive compounds in essential oils from *Origanum compactum*, *Artemisia absinthium*, *Rosmarinus officinalis, Anredera cordifolia*, *Morinda citrifolia*, *Malvaviscus arboreus*, *Syzygium aromaticum*, *Melaleuca alternifolia*, *Citrus sinensis*, and *Thymus vulgaris* have shown efficacy against Eimeria Sp., targeting oocysts and sporozoites (Muthamilselvan *et al.*, 2016). Many laboratories have already conducted in vitro tests on 25 phytochemicals, evaluating their effects on intestinal epithelial cells, macrophages, and muscle cells, with a focus on cytotoxicity, inflammation, tight junction proteins (TJPs), and growth. Clove, oregano, and cinnamon essential oils showed significant benefits in reducing inflammation and enhancing intestinal integrity (Mark *et al*., 2023 and Park *et al*., 2025). A combination of these three cinnamon, clove, and oregano essential oils (CCO), mixed equally (1:1:1), has been shown to synergistically improve intestinal health and mitigate growth suppression in broilers infected with Eimeria maxima (Park *et al*., 2025).

Action of CCO on chicken intestinal epithelial cells, macrophages, and muscle cells:

Inkyung Park *et al*., 2025, conducted in vitro tests on intestinal epithelial cells, chicken macrophage cells (CMCs), and muscle cells, focusing on cytokine expression levels, TJPs, and muscle growth. They studied intestinal inflammatory responses, TJPs, and antioxidant enzymes in young broilers infected with E. maxima and concluded that combinations of phytochemicals, effectively screened through in vitro models representing host-mediated responses, can alleviate coccidiosis and improve growth performance. Specifically, CCO inhibited cytokine production induced by inflammatory responses in CMCs and increased TJP expression in intestinal epithelial cells. Therefore, the phytochemical mixture selected through in vitro screening can be used as a dietary supplement to effectively mitigate intestinal damage in broilers infected with Eimeria spp., helping to maintain growth and demonstrating its potential as an in-feed coccidiostat (Inkyung Park *et al*., 2025).

Discussion on Key Compounds-

1. *Origanum vulgare* 2. Cinnamon essential oil 3. Clove essential oil.

Description:

Essential oils represent promising natural alternatives for controlling avian coccidiosis, with oregano, cinnamon, and clove oils being among the most studied for their anticoccidial activity. *Origanum vulgare* (oregano oil) contains phenolic compounds such as thymol and carvacrol, which interact with the cytoplasmic membrane by altering its cation permeability. This disruption dissipates ion gradients, impairs essential processes, and leads to leakage of cellular constituents, water imbalance, collapse of membrane potential, inhibition of ATP synthesis, and ultimately, cell death (Sidiropoulou *et al*., 2020 and Nahad A. El-Shall *et al*., 2021). Cinnamon essential oil, derived from the bark of Cinnamomum Sp., is rich in cinnamaldehyde, eugenol (5–10%), and camphor (50–60%). These active compounds reduce oocyst numbers and shedding in a dose-dependent manner, while phenolic constituents such as carvacrol contribute to membrane destruction, further inhibiting parasite survival (Ultee *et al*., 2002, Remmal *et al*., 2011, Sharifi-Rad *et al*., 2021, Nahad A and El-Shall *et al*., 2021). Similarly, *Syzygium aromaticum* (clove) oil contains eugenol, caryophyllene, and tannins, which prevent Eimeria oocyst development, act as antioxidants, and help reduce intestinal lesions, thereby improving body weight gain, feed conversion ratio, and overall zootechnical performance in poultry (Cox *et al*., 2000; Nahad A. El-Shall *et al*., 2021). Despite these benefits, challenges remain. The advantages of essential oils include their role in overcoming antimicrobial resistance, reducing the risk of antibiotic residues in meat animals, enhancing consumer trust, and offering a cost-effective approach. However, their limitations include lower potency compared to synthetic immunomodulators, variable or low bioavailability, complex extraction and standardization procedures, and potential toxicity if overdosed due to the lack of fully established dosing guidelines. Overall, oregano, cinnamon, and clove essential oils provide a valuable phytochemical-based strategy to mitigate coccidiosis in poultry, though further research is required to optimize their efficacy and safety in practical field applications.

Challenges and Opportunities:

While the efficacy of phytochemicals in coccidiosis control is well documented, several challenges persist, particularly regarding product variability and lack of standardization. The composition and potency of phytogenic products often fluctuate depending on the quality of the plant source, environmental conditions, and extraction methods used. Ensuring consistent quality and establishing standardized dosing protocols are essential to fully realize the potential benefits of phytochemicals in poultry production systems. Although tannins and saponins have demonstrated encouraging results, they should not be regarded as complete solutions. Instead, a comprehensive and integrated approach that combines phytochemicals with sound management practices including strict biosecurity, vaccination, and balanced nutrition is required to achieve optimal control of coccidiosis and ensure sustainable poultry production.

Conclusion:

Phytochemicals, particularly tannins and saponins, represent a promising natural strategy for managing coccidiosis in poultry. Their antimicrobial, antioxidant, and immunomodulatory properties not only reduce Eimeria infections but also support gut health and enhance immune responses. As the poultry industry transitions toward sustainable alternatives to chemical drugs, phytochemicals offer a viable option that aligns with consumer expectations and environmental priorities. With further research, standardization, and field validation, they could become a core component of integrated control strategies, thereby reducing reliance on conventional anticoccidials. Importantly, phytochemicals may serve as effective alternatives to antimicrobials, especially in light of the growing concerns over antimicrobial resistance and the negative consequences of routine sub-therapeutic drug use on productivity and the environment.

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