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REVIEW ARTICLE

Prevention of ND Using Herbal Adjuvanted Vaccines

Ahmed I. Alajaji[1*] and Abdulaziz M. Almuzaini[1]

[1]Department of Veterinary Preventive Medicine, College of Veterinary Medicine, Qassim University, Buraydah, 51452, Saudi Arabia
*Corresponding author: ajajy@qu.edu.sa

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A B S T R A C T

Newcastle Disease (ND) is caused by the avian paramyxovirus serotype 1 (APMV-1) that still poses a threat to the health and production of poultry, particularly in areas with low biosecurity and high poultry densities. High transmission, economic cost, and genetic diversity of the virus question the traditional mode of control mechanisms, such as vaccination. To prevent infection, the current vaccines used, live attenuated and inactivated, are significantly compromised due to erratic storage, cross-interference of maternal antibodies, and genetic non-alignment of the circulating strains. New studies underline the possibilities that phytochemicals, as active compounds of medicinal plants, can be active immune-stimulants and vaccine adjuvants to ensure better vaccine efficiency. *Ocimum sanctum, Curcuma longa, Allium sativum,* and *Tinospora cordifolia* herbs have demonstrated substantial antiviral, antioxidant, and immune-enhancing medicinal attributes, to produce more antibody titres, enhanced cell-mediated immunity, and decreased viral replication. These herbs provide their action by activating innate and adaptive immunity, fighting free radicals, and modulating cytokines. Enhanced bioavailability and targeted delivery through nano-encapsulation, chitosan nanoparticles, and liposomes solve problems of stability and absorption by enhancing the bioavailability and targeted delivery of the phytochemicals. When administered via water or as vaccine adjuvants, these phytochemicals provide a sustainable, natural, and economical advantage of prevention of ND, especially for small-scale poultry farmers operating in low-resource sectors. Nevertheless, the inconsistency of plant bioactive contents, challenges in standardization and regulatory hurdles hinder their widespread adoption. Phytotherapy, together with enhanced vaccination and biosecurity, is a synergistic solution in controlling ND. It is also recommended in future studies to streamLine the phytochemical formulations and delivery systems as they relate to organic poultry production objectives in terms of effectiveness and safety with respect to the global poultry industry.

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INTRODUCTION

Newcastle disease (ND) is to date one of the most economically relevant and transmissible viral poultry diseases in the world (Rehan *et al.*, 2019; Li *et al,* 2023). The disease is caused by avian paramyxovirus serotype 1 (APMV-1) (Pedersen *et al.*, 2016; Hu *et al.,* 2023). It is differentiated into several degrees of pathogenicity, from mild respiratory infection to an acute fatal type with neurological and gastrointestinal signs. Recently, the signs of the disease outbreak in Asia (Pakistan, India, Indonesia, and China), Africa (Nigeria, Egypt, and South Africa), and Latin America (Colombia and Mexico) proved that ND is an ongoing threat, especially in areas with high-density poultry production and weak biosecurity practices (Pierson and Diamond, 2020). The virus is easily transmitted to birds either by direct contact with infected birds, contaminated feeds, water, humans, dogs, carcasses, infected eggs, vehicles, and even equipment, and even through airborne transmission to short distances, as given in Fig. 1 (Staley *et al.*, 2018). Fig. 1 illustrates these diverse modes of transmission, emphasizing the complexity of viral spread and the need for comprehensive control strategies that combine biosecurity, vaccination, and complementary measures including phytochemicals. The presence of wild birds, which are mainly pigeons and cormorants, complicates control as they act as reservoirs for the disease. The development of new virulent strains, including sub-genotype VII.2 in Asia and Africa, has also questioned the effective use of vaccines, since some field isolates have genetic differences from those of normal vaccine strains (Patel *et al.*, 2024). The economic consequences are very serious because of the loss due to high mortality (up to 100% in unvaccinated flocks), reduced egg production, trade limitations, and control management costs. Nevertheless, in light of such challenges, constant monitoring, fast diagnostics (e.g., RT-PCR, genetic sequencing), and flexible vaccination solutions are essential for slowing down global transmission of ND (Dimitrov *et al.*, 2017). Nevertheless, there are several key issues that are unsolved. The spread of genetically varied and hyper-virulent strains is an ongoing threat to vaccine effectiveness that has led to recurrent outbreaks despite routine vaccinations. Handling of vaccines, cold chain, and lack of proper administration practices in rural and resource-constrained regions also lead to a decrease in the anticipated level of protection. The laxity of biosecurity, the use of wild birds as natural reservoirs, and poor farm management practices provide more loopholes through which the viruses can persist and be reintroduced to the flocks. All these challenges emphasize the fact that, to have a sustainable ND control, it is not possible to rely only on traditional vaccination and requires additional measures to supplement the poultry health management.

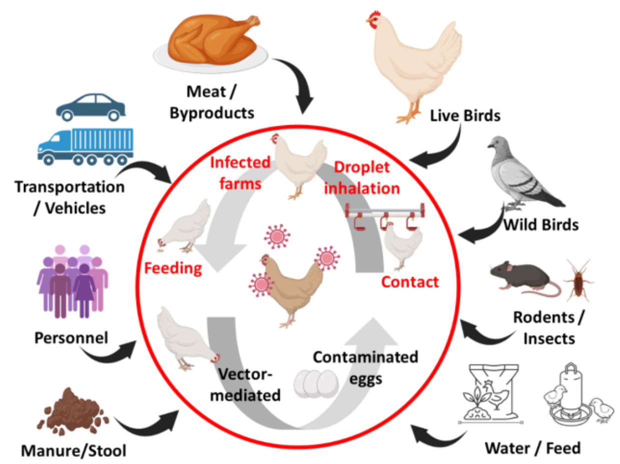

Fig. 1: Modes of transmission for Newcastle disease.

A blend of strong biosecurity practices, a combination of vaccination and good farm management practices, comprises the cornerstone of the prevention of ND (Mohamed, 2019). Vaccination is the most common option, but live attenuated vaccines (e.g. La Sota, B1, and VG/GA strain) and inactivated vaccines are the best methods used to trigger immunity (Minor, 2015). Live vaccines induce high levels of mucosal and cellular immunity with minimal respiratory side effects but induce shorter-term humoral immunity, whereas inactivated vaccines induce longer-term humoral immunity that requires the use of adjuvants and subsequent doses (Lavelle and Ward, 2022). There are, however, factors that curtail the effectiveness of a vaccine; these include: the wrong storage of a vaccine, poor administration, cross-reactivity with maternal antibodies in chicks, and antigenic incompatibility with the vaccine and field strains being circulated (Endale *et al.*, 2022). Also, low-resource settings may experience difficulties in performing mass vaccination campaigns, besides logistic issues like cold chain breakdowns and irregularities. More than the vaccination process, biosecurity plans including restricted access to the farms, foot baths, decontamination of vehicles, and rodent/pest control are also necessary to prevent the introduction of the virus. Rapid culling, restriction of movement, and disinfection of premises are important in outbreak situations to contain the disease (Tao *et al.*, 2021). In the absence of such, recurrent outbreaks underline the need to work on better vaccine formulations (e.g. recombinant vector vaccines) and the implementation of complementary measures. The evidence shows that with the shortcomings of currently made vaccines and with the rising health background on antibiotic resistance and chemical residues in poultry, more concern about the use of phytogenic supplements (plants) as adjuvants to boost immune response is gathering attention (Jiang *et al.*, 2021). Immune modulation, antiviral, and antioxidant effects of several herbs used in medicines, like *Ocimum sanctum* (Tulsi), *Azadirachta indica*, *Echinacea purpurea*, *Allium sativum* (garlic), and *Curcuma longa,* have been shown in poultry species. An example would be that Tulsi leaf extract enhances antibody titers to ND vaccines, and garlic and turmeric enhance macrophage activity and lower oxidative stress (Rizwan *et al.*, 2022). The general botanicals can be given as a feed, in the water, or used as an extract together with vaccines in the hope of enhancing the effectiveness of vaccines, lowering viral shedding, and stress-induced immunosuppression. Besides, the phyto-therapy will be a viable, economical, and sustainable option to small-scale farmers in developing nations where high-quality vaccines and veterinary care are not as accessible (Obahiagbon and Ogwu, 2023). The nano-encapsulated herbal extracts and synergies with vaccines hold the potential to transform the control of ND as the future area of research in processing it. Through the addition of phytotherapy to traditional vaccines, the poultry industry has an opportunity to not only be better protected against ND, but using the same means, it may also decrease its use of artificial drugs in compliance with global trends of organic and all-natural poultry farming (Enioutina *et al.*, 2017).

Review Methodology: This review utilizes Google Scholar (www.scholar.google.com) as the primary source collector. Other secondary websites include the use of Scopus (www.scopus.com), PubMed (pubmed.ncbi.nlm.nih.gov), ResearchGate (www.researchgate.net), and ScienceDirect (www.sciencedirect.com). The keywords used for Google Scholar, ScienceDirect, PubMed, and ResearchGate were Prevention of ND, AND, Using Herbals, AND, Adjuvant, which showed results and were used as the basis for making the table.

Structure of the ND virus: ND, which belongs to the *Avulavirus* genus and family*, Paramyxoviridae,* is a viral disease by the name ND virus (NDV) (Haddas, 2023). Being an enveloped virus, NDV has a spherical morphology with dimensions of between 100 to 500 nanometers (Nath *et al.*, 2020). It has a structure that consists of internal and surface components that are important in its infectivity and replication, as shown in Fig. 2. The structural organization of NDV, including its nucleoprotein, fusion protein, and hemagglutinin-neuraminidase, underlies both its pathogenicity and its potential as a vaccine target. Notably, the F protein cleavage site is a key determinant of virulence, and many phytochemicals are thought to interfere at this step, either by inhibiting protease activity or by preventing receptor binding. This structural insight provides a mechanistic rationale for why certain phytochemicals act as antiviral agents. The genome is single-stranded, negative-sense, non-segmented RNA genome about 15 kilobases in length, and encodes six structural proteins, organized as follows: Nucleoprotein (NP), phosphoprotein (P), matrix protein (M), fusion protein (F), hemagglutinin-neuraminidase (HN), and large polymerase protein (L). All these proteins are conserved among the paramyxoviruses and work together to coordinate the replication cycle and interactions with the host of NDV (Suarez *et al.*, 2020). The viral RNA genome is encapsulated by the nucleoprotein to give a ribonucleoprotein complex (RNP), the template of transcription and replication. Coupled to this complex is the phosphoprotein that serves as a cofactor to the viral polymerase, in assisting the synthesis of the RNA, and the L protein, which is a large polymerase enzyme that mediates the process of RNA-dependent RNA replication and transcription. The RNP is enclosed in the matrix protein, which seeks to connect the inner core and envelope of the lipid bilayer, contributing to the important function of virion assembly and budding (Weidmann *et al.*, 2021).

The viral envelope is embedded with fusion (F) or hemagglutinin-neuraminidase (HN) glycoproteins, which extend outward toward the surface and are essential in the recognition and entry of the host cell. The HN protein also recognizes sialic acid-containing receptors in the host cell surface, causing the onset of the infection, and has a neuraminidase activity that provides viral release (Burzyńska *et al.*, 2021). The F protein, as an inactive preprotoype (F0), must be cleaved by host proteases into two parts (F1 and F2). This protein cleavage is a determinant of the NDV virulence, since strains with high pathogenicity have F proteins that become cleaved by common host proteases, permitting systemic infection. When the receptors bind, the F protein causes fusion between the viral envelope with the host cell membrane, allowing the RNP complex to enter the cytoplasm. Viral genome does not insert into the host genome; instead, all replications are carried out in the cytoplasm, where viral polymerase produces protein-coding mRNAs and new copies of the genome to form progeny virions (Willemsen and Zwart, 2019). These new synthesized pieces attach themselves to the membrane of the host cell through binding of the matrix protein and the cytoplasmic ends of the glycoproteins, resulting in a budding arrangement that detaches as new infectious particles.

One main characteristic of NDV is its genetic diversity, and there are three pathotypes classified according to their virulence: lentogenic (little), mesogenic (moderate), and velogenic (high) (Zhang *et al.*, 2016). The virulence differences are associated with the differences in the place of F protein cleavage and other areas of the genome. This diversity in the genes has some consequences for vaccine preparation and epidemiological control. Selective replication of NDV in cancer cells and immune-stimulating properties have enabled it to be utilized as both a vaccine vector and as an oncolytic agent (Absalón *et al.*, 2019). In general, the structural complexity of NDV provides evidence that the virus can be used extensively as a pathogen and as a possible therapeutic agent. Its structure takes the form of a highly optimized system of host interaction, replication, and immune modulation based on avian evolution and selective pressures of vaccination and biosecurity (Sun *et al.*, 2024).

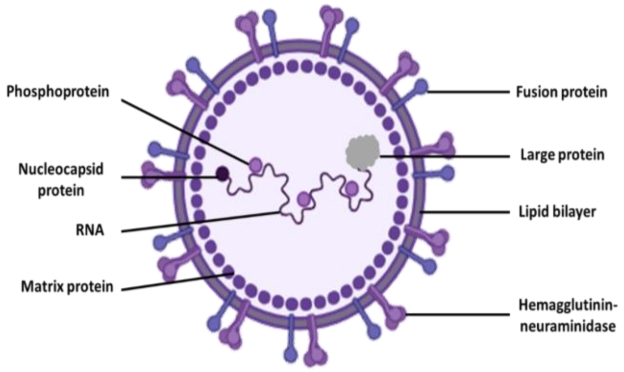

Fig. 2: Structure of Newcastle Disease virus.

Mechanisms of immune stimulation of herbs: ND is affecting poultry health and results from the virulent NDV (Abdisa and Tagesu, 2017). Herbal immunostimulants are an effective, natural approach to improving immunity against ND, through the regulation of both innate and adaptive immune responses. The first line of defense is advanced by many herbs, including Echinacea, Astragalus, and Ginseng, which activate macrophages and natural killer (NK) cells (Wink, 2015). They also facilitate the secretion of the pro-inflammatory cytokines (IFN-2, IL-2, TNF-α) that play a vital role in controlling viral replication early in the infection. There is also the possibility of using herbs such as *Andrographis paniculata* and *Tinospora cordifolia* IFN-2 that boost the level of interferons, thereby preventing the replication of NDV (Senthilkumar *et al.*, 2021).

The humoral immunity is enhanced by producing more antibodies (IgG, IgM), and herbs such as Aloe vera, neem, and Turmeric enhance the antibodies after vaccination, which include hemagglutination inhibition (HI) antibodies that neutralize NDV (Camargo and Luz, 2018). Herbs like Ashwagandha and *Moringa oleifera* increase cell-mediated immunity (CMI), which is required to clear viral infections by activating/stimulating the CD4+, CD8+ T-cell response to clear the virus. In addition, antioxidant herbs, such as Garlic, Ginger, and Turmeric, have been studied in curbing oxidative stress that NDV inflicts on the body in order to minimize tissue damage and confer an effect on the overall body's immunity (Bahgat *et al.*, 2025). Viral replication inhibition may occur directly by some bioactive compounds such as quercetin.

Herbs are also known to boost the gut-associated lymphoid tissue (GALT), boosting mucosal immunity by stimulating the production of IgA, which is critical as NDV infections can occur through the GI tract. Some herbs, including Astragalus polysaccharides and Ginseng saponins, are natural adjuvants that enhance the efficacy of ND vaccines, optimize lymphocyte production. Using it as a supplement either in the feed of poultry or as drinking water can enhance the immunity of the flocks and minimize losses caused by NDV and synthetic drug adoption (Adedokun and Olojede, 2019). Herbal immunostimulants offer sustainable multi-target interventions in the control of ND in poultry.

Phytochemicals are natural products of biologically active substances present in plants and used in the protection of plants against diseases, pests, and environmental stresses (Xiao and Bai, 2019). An extensive selection of phytogenic plants and active compounds has been considered as having a potential effect on the prevention of ND. These are extracts of *Allium cepa, Glycyrrhiza glabra, Azadirachta indica, Justicia adhatoda*, and others, and have been tested in both in vitro and in vivo experiments (summarized in Table 1). Together, these studies underscore the variety of phytochemicals (flavonoids, alkaloids, saponins, organosulfur compounds) and their modes of action, such as viral replication, cytokine responses, and antibody titers. It is interesting to note that certain plant extracts like onion essential oil and neem-garlic blends exhibit nearly 100 percent protection in vaccinated flocks, indicating that phytochemicals may contribute substantially to commercial vaccines. Nonetheless, the difference in experimental models and dosing highlights the role of standardization in a trusted field application. Although they are not vital substances in the body, such as vitamins or minerals, the compounds have been discovered to have substantial health benefits in animals, including poultry. Phytochemicals have also been looked into in the last few years as alternatives to antibiotics, vaccine supplements, and immune boosters in poultry farming, especially in the fight against viral ailments such as the ND (Lillehoj *et al.*, 2018). Such naturally occurring compounds of edible plants exert their effect via numerous processes; either directly against viruses, modulation of the immune system, performing antioxidative tasks, or positively affecting gut health, and, as such, can be used as effective approaches regarding sustainable health management of our poultry.

It is possible to divide phytochemicals according to some classes existing within their chemical structure and their role (Campos-Vega and Oomah, 2013). Some of the most researched phenolic compounds are flavonoids, such as quercetin, together with polyphenols, with curcumin being the most notorious, because of their antioxidant, anti-inflammatory, and immune-stimulating effects (Mutha *et al.*, 2021). Turmeric, green tea, and citrus fruits contain flavonoids that have the capability of neutralizing harmful free radicals and enhancing the response to vaccines. Polyphenols are found in grapes, pomegranates, and berries and help promote health in the gut as well as increase antibodies (Maniglia *et al.*, 2021). Other significant classes, the terpenoids, contain such compounds as limonene and ginsenosides that have antimicrobial and immune-stimulating properties. Alkaloids, including berberine extracted from *Tinospora cordifolia* and piperine extracted from black pepper, are also widely appreciated for stimulating the immune cells and suppressing the viral replication (Pradhan *et al.*, 2022). Organosulfur compounds such as allicin in garlic are hyper-antibacterial and antiviral, whereas carotenoids such as beta-carotene in carrots are super antioxidants and enhance health (Mandal *et al.*, 2019).

ND has posed threats to poultry health and productivity in many parts of the world, and there is a great need for the use of new practices to enhance immunity and disease resistance on a sustainable basis (Abdisa and Tagesu, 2017). Medicinal plants have been attracting interest in phytochemicals as natural immune stimulants because they can alter immune responses, diminish oxidative stress, and have a direct anti-viral efficacy. The role of such bioactive compounds as flavonoids, alkaloids, polyphenols, terpenoids, and saponins in the stimulation of innate and adaptive immune functions in poultry means that they can be excellent adjuvants to conventional ND vaccines (Brindha, 2016).

Phytochemical Immune Stimulating Mechanisms: Phytochemicals strengthen immunity by exerting various effects in various parts of the immune system (Brindha, 2016). The first line of defense, which is innate immunity, is enhanced using such herbs as *Echinacea purpurea*, *Astragalus membranaceus*, and *Panax ginseng*, all of which trigger macrophages, natural killer (NK) cells, and dendritic cells (Chen *et al.*, 2019). The effect of these herbs is that they induce the production of pro-inflammatory cytokines, which include interferon-gamma (IFN-g), interleukin-2 (IL-2), and tumor necrosis factor-alpha (TNF-a), and these cytokines play an important role in early viral destruction. An example is that *Andrographis paniculata* (Kalmegh), the andrographolides present in this plant promote IFN production and restrict the generation of the NDV (Nie *et al.*, 2017; Anam *et al.*, 2021). Similarly, *Tinospora cordifolia (Guduchi)* increases the level of interferon, giving a non-specific antivirus treatment.

Phytochemicals present in Aloe vera, *Azadirachta indica* (neem), and *Curcuma longa* (turmeric) support humoral immunity, which produces antibodies (Chauhan *et al.*, 2022). These compounds augment the elicitation of neutralizing antibodies, especially to hemagglutination inhibition (HI) antibodies, so essential in the neutralization of NDV. It has been found that administration of turmeric and garlic *(Allium sativum)* increases antibody titers after vaccination, which enhances vaccination (Alagawany *et al.*, 2016). Herbs that boost cell-mediated immunity (CMI), which is needed against intracellular pathogens such as NDV, include *Withania somnifera* (Ashwagandha) and *Moringa oleifera*. These plants boost the multiplication of CD4+ and CD8+ T-cells, which have an important role in eradicating the virus-infected cells. Additionally, phytochemicals like quercetin (found in onions and apples) exhibit direct antiviral properties by inhibiting viral entry and replication. NDV typically causes tissues to be destroyed via oxidative processes and immune suppression. Oxidative damage is more alleviated with antioxidant herbs such as garlic, ginger *(Zingiber officinale),* and turmeric that scavenge free radicals and increase endogenous antioxidant enzymes (e.g., superoxide dismutase and glutathione peroxidase) (Ajanaku *et al.*, 2022). Not only does it decrease damage to tissues, but it also helps to increase immune resiliency as a whole.

Important Phytochemicals and Their Immunomodulatory Potentials: Medicinal plant phytochemicals have elicited much popularity in the management of poultry, especially because of their outstanding antiviral, antioxidant, coupled with immunomodulatory capabilities (Boukhatem and Setzer, 2020). Of these bioactive components, flavonoids, alkaloids, polyphenols, saponins, and organosulfur compounds are unique in boosting immune reactions, fighting viral infectious diseases, such as ND, and overall resilience in the flock. Quercetin and rutin (contained in *Ocimum sanctum* (Tulsi) and *Ginkgo biloba*) are types of flavonoids that are imperative in enhancing the immunity of the poultry (Oliveira *et al.*, 2016). These agents stimulate the production of antibodies, especially immunoglobulin G (IgG) and IgM, which play a crucial role in neutralizing the pathogens. Also, flavonoids have high anti-inflammatory activity that is achieved through the regulation of cytokine expression, thus minimizing tissue destruction in the course of infection (Chanput *et al.*, 2016). They have a special significance in their direct antiviral effects in that they disrupt the viral fusion and viral replication processes, and thus are effective against RNA viruses, such as avian paramyxovirus-1 (APMV-1), the agent that causes ND. Other compounds known as alkaloids: berberine in the *Tinospora cordifolia* and piperine in black pepper *(Piper nigrum)* have vital roles they play in innate immunity; this is because they stimulate macrophages and natural killer (NK) cells that are needed to detect and eliminate a pathogen at the very early stages (Ashokkumar *et al.*, 2021). These compounds also trigger the release of interferons (IFNs), a type of critical signaling molecules that prevent the spreading of viruses and improve the immune system's activities to defeat infections (Anjum *et al.*, 2020). Alkaloids enhance cellular and humoral immunity and thereby assist poultry in launching a strong immune response against NDV and other pathogens (Bernardo *et al.*, 2015). Polyphenols: Polyphenols, which include turmeric (curcumin), grape seed (resveratrol), etc., boost immune response, antibody production, and oxidative stress. Infections with NDV normally result in an overproduction of free radicals, causing unwanted cell damage and might impair immune response (Subbaiah *et al.*, 2015). This is overcome by their action as a reactive oxygen species (ROS) scavenger and by an increase in expression of endogenous antioxidant enzymes using curcumin and resveratrol to ensure tissue protection and enhance recovery of the infected birds. Among other advanced types of phytochemicals, the saponins are natural vaccine-enhancing adjuvants (Wang, 2021). The saponins in ginseng (*Panax ginseng*) and *Astragalus membranaceus,* the saponins enhance the ingestion of antigens by antigen-presenting cells (APCs) and then activate lymphocyte replication, thus further amplifying and enhancing immune responses. This is because they are effective in strengthening both the Th1 and Th2 immune pathways, and thus they are highly useful in ND vaccination programs that require a combination of balanced immunity as a defense against the disease (Kollmann *et al.*, 2020). In addition, organic sulfur-containing oleaginous compounds such as allicin (a compound obtained from garlic *(Allium sativum)*) have tremendous immunomodulatory and direct antiviral properties. Allicin boosts the phagocytic capabilities of macrophages and cytotoxic potential of NK cells, which play a pivotal role in virus-infected cells (Sultan *et al.*, 2020). It also improves viral load by interfering with viral envelope proteins and viral replication enzymes.

The use of these phytochemicals in poultry using feed additives, water supplements, or adjuvants in vaccines is an effective and long-term measure to boost immunity and minimize the use of synthetic medicines (Al-Mnaser *et al.*, 2022). They are particularly irreplaceable against ND and other poultry diseases because of multi-modal action, ability to stimulate immunity, decrease oxidative stress, and even have direct antiviral effects. Nevertheless, the issue related to variability of bioactive contents, ideal dosing, as well as bioavailability has to be resolved using an advanced delivery mechanism like nano-encapsulation (Abdisa and Tagesu, 2017). As studies advance, phytochemicals are destined to have a more crucial part in enhancing the health of poultry, efficacy of vaccines, and sustainable food production as a whole (Lillehoj *et al.*, 2018).

Role of Delivery agents for transport of herbals: Phytochemicals have enormous potential in poultry health management, especially in the treatment of ND, although their usefulness is frequently restricted by restrictions in bioavailability, stability, and selective delivery (Lillehoj *et al.*, 2018). In order to get the maximum effect, innovative delivery systems are under evaluation to improve absorption, bioactive compound protection, and exact delivery of immune-relevant tissues (McGlynn and McClellan, 2017). One of them is nano-encapsulation, which has shown promise. This technology consists of encapsulating phytochemicals in nanoscale carriers called liposomes, polymeric nanoparticles, or solid lipid nanoparticles (SLNs), preventing the early degradation of the compounds and facilitating their intake (Singh *et al.*, 2019; Fatima *et al.*, 2024). As an example, the liposomal encapsulation of hydrophobic compounds such as curcumin is still very effective and could increase intestinal absorption and distribution in the body by many folds. On the same note, chitosan nanoparticles, which are traced back to shellfish, have good mucoadhesion characteristics, thus suitable to deliver herbal extracts orally to get to gut-associated lymphoid tissue (GALT), which is an essential locus of mucosal immunity against NDV (Mohammed *et al.*, 2017). Also, the volatility of compounds, such as garlic oils, is addressed because SLNs provide stability and steady release in the gastrointestinal tract and increase their therapeutic duration. The primary reason why nano-encapsulation systems have been chosen is that they can address the most unbreakable obstacles to phytochemical efficacy. Numerous herbal extracts, including flavonoids, alkaloids, and essential oils are insoluble in water and this significantly decreases the uptake and bioavailability of these compounds in the intestines when taken in a crude state. Nano-encapsulation is not only more soluble, but also provides better control and delayed release, to keep therapeutic levels in the body longer. Besides, such nano-carriers prevent enzyme degradation of the sensitive compounds in the gastrointestinal tract, as well as oxidation of the active components during storage, resulting in the delivery of the highest active component to the immune-relevant sites. This is especially critical in poultry because the rapid transit of feed and fluctuating pH of the gut frequently leads to lower bioactive contact time of conventional forms. Besides that, surface-modified nanoparticles (as the surface is covered with chitosan) are preferentially adhered to mucosal tissues, allowing a highly specific stimulation of gut-associated lymphoid tissue, which is at the heart of the response to ND virus.

An alternative approach with potential includes a combination of phytochemicals with immunization (Luo *et al.*, 2023). Commercial vaccines already contain adjuvants of plant origin (e.g., saponins of *Quillaja saponaria*) to promote higher body antibodies. The herbal micro-particles loaded with muco-adhesive herbal ingredients such as extracts of *Ocimum sanctum*, when used simultaneously with live ND vaccines, could augment respiratory tract immunity, which is the key port of entry of NDV (Gaur *et al.*, 2020). These synergistic vaccinations not only enhance the effectiveness of immunization but also reduce the content of viral shedding and transmission between flocks. To have easy use of phyto-therapy on the farm, they can be supplied in the form of water-soluble extracts or can be added to nutrition (Plaskova and MLcek, 2023). Bioactive enhancing compounds, such as immune boosting herbs (e.g. Echinacea or neem) can be in liquid formulation which is added to the drinking water (ensuring even coverage of the flock), and microencapsulated herbal powders (e.g. turmeric or garlic) added to the food protect the bioactive ingredient against gastric destruction and enhancement of delivery of the bioactive to the immune system (Isbill *et al.*, 2020). Even with these improvements, the extensive use of phytochemical interventions faces a number of challenges. Plant bioactive contents are also variable, requiring quality control and standardization of the herbal doses in order to guarantee a similar efficiency (de Sousa Brito *et al.*, 2020). Besides, commercial herbal-vaccine combinations involve strict safety and efficacy trials by regulators, an Expensive and laborious process. Also, proper education of the farmer is an important aspect in ensuring that they will not over- or underdose (Dewi *et al.*, 2022). Future prospectively, addressing the current limitations, further research on engendering the most advanced systems of delivery, including nano-emulsions and target-directed nanoparticle carriers, has very big potential. Overcoming these obstacles, the phytochemicals may become the basis of sustainable poultry health management, helping to diminish the use of antibiotics and being in line with the global trend of organic production (Mnisi *et al.*, 2022). Such a combination of these natural compounds with modern delivery technology not only contributes to their immunomodulatory effects but also creates a pathway of healthier and more effective ND control in poultry production all around the world (Zhuravel *et al.*).

Integration with vaccines: Combining phytochemicals with commercially available Newcastle disease (ND) vaccines has both potential and challenges. Phytochemicals, including flavonoids, alkaloids, saponins, and organosulfur compounds, have beneficial effects as natural adjuvants that promote antigen uptake, stimulate humoral and cellular immunity, and reduce viral shedding, oxidative stress, and gut health to amplify vaccine effectiveness and flock resilience on the benefit side. These strategies also take into account consumer trends in the production of antibiotic-free and sustainable poultry. Nevertheless, their use is complicated by a number of risks: inconsistent results due to variability of phytochemical content, the potential to interfere with the stability of antigens or standard adjuvants, toxicity at high concentrations, or variable uptake in relation to administration time. Further, the problems of bioavailability, shelf-life of the product, and compatibility with other types of vaccines are to be solved before the use in the field. Regulatory hurdles to herbal adjuvants include ensuring the standardization of extracts, reliable quality control procedures, provisional evidence of safe and effective use, and compliance with Good Manufacturing Practice (GMP) standards, and lack of patentability can discourage investment by the private sector. Thus, despite the undoubted potential of phyto-chemistry-vaccine combinations to improve ND control, their effective translation to practice will necessitate uniform extraction and delivery protocols, stringent safety and efficacy evaluations, and active government involvement to warrant consistency in performance and trust among the farmers**.**

Limitations: Although phytochemicals and herbal immune-stimulatory effects show great hope as far as ND is concerned, there are various limitations, which limit their wide usage (Danquah *et al.*, 2022). The concentration of bioactive compounds within medicinal plants, not being consistent, depending on different factors (geography, cultivation, and processing), is also of great concern. Such variability makes standardization difficult, and impossible to predict the dosage, which may be under- or overdose, particularly with small or low-skilled farms (Pham *et al.*, 2020). The inconsistency of bioactive compound content does not only restrict its use in the field but also poses serious difficulties in experimental research. As an example, the immunology result may be different when two studies are conducted on the same plant species, but the plants are cultivated in different soil, climate, or harvesting conditions. This kind of inconsistency is detrimental to reproducibility of results, difficult to use in meta-analyses and undermines the development of consistent dose-response relationships. In the practical sense, this variability can be seen as uncertainty to farmers, where a batch of herbal supplement made in a certain geographic area could be very protective and another batch made in a different place could have poor concentration, resulting in a lack of consistency in disease resistance. In the absence of stringent standardization, it is close to impossible to develop commercial products of a reliable nature or to assure the policymakers and veterinarians of their effectiveness in the long run. Furthermore, such variability can lead to misinterpretation of efficacy in the case of vaccine-adjuvant studies, because varying levels of herbs may conceal or exaggerate the real synergistic response between herbs and Newcastle disease vaccines. Moreover, the bioavailability and stability of most phytochemicals are poor, and some compounds are broken down in the gastrointestinal tract or the environment prior to their therapeutic action. Though technologies such as nano-encapsulation and chitosan nanoparticles make this better, this is still not accessible to poor poultry farmers yet, since it is expensive (Chadha, 2021). Also, regulatory hurdles are present to integrate herbal products with commercial vaccines or feeds. The processes of approval involve lengthy tests of safety, efficacy, and quality control, which not only use a lot of resources but also take time. The unavailability of international standard protocols on the usage of herbal-vaccine combinations is further compounded because it cannot be readily incorporated into the standard poultry health care practices. Farmers and veterinarians also lack awareness and technical knowledge for the application of phyto-therapy (Ruston *et al.*, 2016). Benefits can be lost or result in unwanted effects when dosage, preparation, and administration are misunderstood or misused. Lastly, though a number of studies argue about the immunomodulatory effects of some herbs, there is still a lack of in vivo information in poultry models, and it is not well reproduced across strains and conditions (Kadiyska *et al.*, 2023). Therefore, even though phytochemicals have such multidimensional potential, it is necessary to engage with all these limitations once, by conducting research, farmer education, regulatory changes, and technological advances (Wink, 2022).

Future Research Directions: Despite the promising immune-stimulant and adjuvant properties exhibited by phytochemicals against Newcastle Disease (ND), there are still gaps that need to be filled before they can be used extensively in the field. Standardization and quality control (e.g., controlled cultivation systems, validated extraction methods, and chemical fingerprinting techniques, e.g., HPLC, LC-MS, NMR) should be addressed in future studies to reduce fluctuations in bioactive compounds content. Dose optimization experiments are required to establish the safe and effective range of concentrations in various poultry species, ages, and production systems. Moreover, extensive in vivo challenge experiments should be performed across a variety of environmental and management conditions to confirm laboratory results and determine practical usefulness. The second priority is the creation of innovative delivery systems that will improve bioavailability and stability. Nano-encapsulation, liposomal carriers, and muco-adhesive nanoparticles are promising but need to be optimized to achieve cost-efficiency and scalability in small- and medium-scale farms. Systematic compatibility tests are also needed when combining phytochemicals with licensed commercial vaccines, not only to maximize synergistic immune response but also to exclude interference or toxicity. Future work should include long-term safety studies and residue monitoring to ensure food safety and adherence. Lastly, farmer awareness, training, and extension will be critical in translating to field conditions. They should be formulated as practical preparations (e.g., water-soluble extracts, feed additives, or premixes) that can be easily used in low-resource environments. Practical trials on commercial and backyard farms would offer assurance of effectiveness, minimize the application of antibiotics as well, and conform to consumer needs of natural production of poultry products. Overall, these research directions will play a crucial role in turning the experimental potential of the phytochemical-vaccine strategies into a trustworthy instrument for controlling NDs sustainably.

Conclusions: ND is a major threat to the poultry markets around the world because of its high mortality rate, economic impacts, and boundaries of applicable control strategies. Although traditional vaccination and biosecurity are the first line of defense, their effectiveness is compromised by the genetic changes in the NDV and deficiencies in operation, such as mishandling of the vaccines or a break in the cold chain. Phyto-therapy can be a potential auxiliary measure in this situation because it is a multi-target approach to immune-stimulation as a natural supplement to vaccination and infection. Evidence shows that phytochemicals (including flavonoids, polyphenols, alkaloids, saponins, and organosulfur compounds) in certain herbs such as Tulsi, turmeric, garlic, neem, and ginseng exhibit definite immune-enhancing and antioxidant, as well as antiviral properties. These are innate and adaptive immunity stimulators, antibody promoters, and lower oxidative stress, which play a vital role in viral infection. Moreover, the phytochemical absorbability and stability are optimized by delivery system innovation, specifically using nano-encapsulation and mucoadhesive nanoparticles that can considerably increase the therapeutic potential of phytochemicals. Inclusion of these compounds in the poultry feed, drinking water, or vaccines provides a more affordable, sustainable, and easily accessible option, especially in resource-poor environments. Nonetheless, to take full advantage of phytochemicals in the management of ND, issues concerned with standardization, dosage, education of farmers, and regulation compliance should be resolved. The main area of future research would be the optimization of compositions, proving the synergy between the vaccine and herbal combination, and scaling the delivery technologies. Summing up, this synergy of phytotherapeutic and conventional ND management has the potential to provide a humane, green, and effective solution to sustainable poultry production, which will minimize the use of antibiotics and healthier and less susceptible flocks all over the world.

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Table 1: Chemicals of herbal origin used for immunostimulation to control Newcastle Disease virus as adjuvant, synergist, or exclusive in multiple experimental types

Sr. No	Plant	Active Compounds	Type of Trial	Type of ND vaccine	Dose Rates	Proposed Mechanisms of Action	Results	References
1.	*Iresine herbstii*	Phenolics, alkaloids, and Flavonoids	*In ovo*	La Sota	300 µg/mL + 0.2mL 4HA; 400 µg/mL + 0.2mL 4HA; 500 µg/mL + 0.2mL 600 µg/mL + 0.2mL	The ethanolic extract and acetonic extract of the plant inhibit the multiplication of NDV In ovo by arresting viral infectivity, lowering hemagglutination titers, and causing death of the embryo. The high content of phenolic and flavonoid compounds makes them have antioxidant properties, immunostimulatory activity, and inhibition of viral replication, which represents evidence of their inhibitory but not virucidal mechanism against the ND virus.	Complete NDV inhibition along with embryo survival and hemagglutination titers in the ethanolic and acetonic extracts was observed.	(Andleeb *et al.*, 2020)
2.	*Allium Cepa*	Essential oils	In vivo	MEFLUVAC-H9ND-16, LaSota strain	0.5 mL (MEFLUVAC-H9ND-16, s/c, Day 1), Day 9 and Day 15 (LaSota strain, drinking water, volume not specified), 0.2mL (Challenge virus, 10^6. EID_{50}, intranasal, Day 36), 1kg (each of onion bulb, green bulb, green stalk for ACEO extraction).	Has been shown to have an antiviral effect on NDV by reducing its viral replication and shedding by modulating inflammation and boosting the immune response. NDV inhibition of attachment, cell replication, and pathogenesis occurs through bioactive substances of flavonoids and sulfur compounds, which enhance long-term defense and defenses after viral infection.	It contains a vaccine that minimizes clinical manifestations, viral shedding, death, boosts immunity, and provides protection was up to 100%.	(Lebdah *et al.*, 2022)
3.	*Nicotiana benthamiana*	Viruses are like particles of Plant origin	In vivo	Plant-produced ND-Like Particle (ND VLP) Vaccine	5µL of plant-produced ND VLPs (titrated at 1024 HAU or 10 log_2) Diluted in 1× PBS Mixed with 20% [v/v] Emulsigen®-P adjuvant Plus 1% [v/v] enrofloxacin for antimicrobial support	The vaccine is based on the display of the NDV Fusion (F) and Hemagglutinin-Neuraminidase (HN) proteins in Nicotiana benthamiana, which will be organized into virus-like particles that resemble the surface of the virus. With the use of adjuvants in chickens, these VLPs provoke the immune system into manufacturing certain antibodies that can offer protection without infection.	Plant-derived vaccination of chickens with adjuvant induced the development of potent NDV-specific antibodies and strong virus-neutralization.	(Smith *et al.*, 2023)
4.	*Glycyrrhiza glabra*	Soyasaponin I Glycyrrhizin Liquorice Rutin Vicenin 2 Licuroside	In vivo	Potential of root extract (licorice)	0.5g/L of powdered root extract (Licorice Extract, LE) in drinking water	Licorice root extract acts to regulate the response of the immune system by inhibiting the expression of IFN-γ and TLR-3, decreasing the oxidative stress, and inhibiting replication of viruses by interacting with a variety of bioactive compounds to target viral proteins such as RNA polymerase and fusion glycoprotein.	The licorice extract lowered the death rate triggered by NDV, shedding and damage in tissues, replenishing the immune balance, and antioxidant enzymes.	(Haleem *et al.*, 2024)
5.	phytogenic plants, *Vernonia amygdalina*, *Cucumis melo*, *Azadirachta indica*	Flavonoids Saponins Tannins Steroids Phenolic acids Alkaloids Glycosides Sesquiterpene lactones Polyphenols Flavonoids Tocopherols Phytosterols Carotenoids Fatty acids Azadirachtin Nimbin & Nimbidin Gedunin Salannin Flavonoids & Tannins	In vivo	phytogenic extracts like bitter leaf (Vernonia amygdalina) and Christmas melon (Cucumis melo), as natural treatments for ND in indigenous chickens.	---------	Both bitter leaf and Christmas melon have bioactive compounds, saponins, flavonoids, and phenols, which enhance immunity, stabilize gut microflora, stimulate digestive enzyme production, and act as antimicrobials in birds, making them resistant to ND and enhancing resistance and recovery of birds through physiologic resilience and pathogen inhibition.	46.46% used bitter leaf; 42.42% used Christmas melon; all of them helped improve ND symptoms such as paralysis, neck twisting, and circling.	(Irivboje *et al.*, 2021)
6.	Neem (*Azadirac*	Azadirachtin Nimbin	In vitro	The antiviral	100% Undiluted	Neem compounds interfere with the viral envelope of NDV,	100 percent concentration	(Hasan and Ahad,

	hta indica) Garlic (*Allium sativum*) Ginger (*Zingiber officinale*)	Nimbidin Nimbolide Gedunin Salannin Sodium nimbidate Epicatechin Catechin Allicin Alliin Ajoene Diallyl sulfide Diallyl disulfide Diallyl trisulfide S-allyl cysteine Ginger (Zingiber officinale) Gingerol Shogaol Zingerone Paradol Bisabolene Zingiberene Zingiberol		effects of medicinal plant extracts, neem, garlic, and ginger	(1:1 with virus)0.2mL per egg. Most effective for viral inactivation 75% 3 parts extract: 1 part PBS 0.2 mL per egg Moderate efficacy 50% Equal extract and PBS 0.2 mL per egg, Reduced antiviral activity 33% 1 part extract: 2 parts PBS 0.2mL per egg	prevent cell attachment as well, and increase immunity. Allicin of garlic inhibits viral enzymes, increases oxidative stress, and interrupts replication. Ginger phenolics penetrate viral membranes and remove inflammation. They all act pre-infection and neutralize virus particles in vitro and are dose dependent, with the strongest effects at undiluted concentrates, and the lowest at post-autoclaving.	of neem bark extract was found ineffective against NDV in the cell culture medium, and its activity level was dose-based and heat-sensitive; garlic and ginger revealed less strong dose and heat-sensitive action.	2024)
7.	*Cyperus rotundus L.*	Methyltartronic acid 2Hydroxypropanoicacid(Lactic acid) Hydroxyura 1Hydrazin-2-propanol Allantoic acid Isopropyl alcohol	In vitro	Iraqi attenuated AMHA1 strain	10 MOI 5 MOI 3 MOI	The NDV-alkaloid combination leads to the killing of abnormal cells based on apoptotic induction, induction of p53, destabilization of the glycolysis pathway, and inhibition of angiogenesis. The effect of NDV is to alter the tumor cell membrane, making them easier to target with immune cells, whereas the alkaloid components of Cyperus rotundus are cytotoxic, inducing cell cycle arrest and DNA disruption. Collectively, they work synergistically without harming normal cells and attacking abnormal growths in the digestive tracts.	The combination of NDV and the alkaloid of Cyperus rotundus increased the abnormal cell death, high synergy, and low normal cell toxicity.	Al-Shammari *et al.* 2021)
8.	*Curuma longa (*Turmeric*)* *Coriadrum sativum (*Corianer *Allium sativm (Garlic) Andograps paniclata (Nilavembu) Trigonella fonumgraecum (Fenugreek)*	Alkaloids Flavonoids Saponins Tannins (including hydrolysable tannins) Terpenoids Glycosides (including cardiac glycosides) Phenols Volatile oils Amino acids and proteins Carbohydrates	*In ovo*	Antiviral effect of an ethanolic herbal mixture	500mg/mL 250mg/mL 50mg/mL 200µL per egg 100%, 50%, 33.33%, 0% (mortality rates depending on group) HA titers: 2048, 1024, 0 (depending on treatment group)	The mechanism of action of the herbal extract probably prevents replication of the NDV due to the protease inhibitory action of the extract, inhibition of the cleavage of the viral glycoprotein (haemagglutinin-neuraminidase, fusion protein), and its attachment or entry into the virus. Flavonoids, alkaloids, terpenoids, among other phytochemicals, have the potential to interfere with viral enzymes, lower oxidant stress, and enhance immune response, thus triggering low titers of the virus in ovo.	This was reported to be a potent antiviral agent against NDV, as the herbal extract at 50 mg/ mL killed the virus titre and embryo mortality.	(Priya *et al.*, 2022)
9.	*Justicia adhatoda*	Bromhexine Flavonoids Alkaloids Phenolic compounds Tannins Coumarins	In vitro In ovo	LaSota strain	300µg/mL 400µg/mL 500µg/mL 600µg/mL	Phytochemicals in *Justicia adhatoda* have antiviral effects and involve scavenging of free radicals, prevention of viral replication, and adsorption to proteins in NDV. Strong interactions are supported by molecular docking, as less virus penetration and destruction of cells occur, resulting in an increase in the survival of embryos and antiviral protection.	The 400 0g/mL methanolic *Justicia adhatoda* extract reduced embryo mortality up to zero percent, the best antioxidant activity, and established high antiviral potential in NDV, hence	(Andleeb *et al.*, 2024)

						establishing its therapeutic potential.	
10.	Neem (*Azadirachta indica*) Scent Leaf (*Ocimum sanctum*)	Azadirachtin Eugenol	In vivo	Gumboro vaccine Lasota vaccine	Neem Leaf Meal (NLM): 3% Scent Leaf Meal (SLM): 3% Neem + Scent Leaf Blend: 2% NLM + 2% SLM	Neem (azadirachtin) and scent leaf (eugenol) boost the immunity through stimulation of antibody production, an increase in lymphocyte count, and a drop in viral load. The effect of these compounds is enhanced gut health, improvement of liver functionality, and normalization of haematological and biochemical parameters as natural antiviral protection to broiler chickens.	The Neem and scent leaf foods enhanced immunity, promoted growth, contributed to good blood condition, and gave natural defense against poultry viral diseases.	(Omidiwura *et al.*, 2023)

REFERENCES

Abdisa T and Tagesu T, 2017. Review on Newcastle disease of poultry and its public health importance. J Vet Sci Technol 8(3):441.

Absalón AE, Cortés-Espinosa DV, Lucio E *et al.*, 2019. Epidemiology, control, and prevention of Newcastle disease in endemic regions: Latin America. Trop Anim Health Prod 51(5):1033-1048.

Adedokun SA and Olojede OC, 2019. Optimizing gastrointestinal integrity in poultry: the role of nutrients and feed additives. Front Vet Sci 5:348.

Ajanaku CO, Ademosun OT, Atohengbe PO *et al.*, 2022. Functional bioactive compounds in ginger, turmeric, and garlic. Front Nutri 9:1012023.

Alagawany M, Ashour EA and Reda FM, 2016. Effect of dietary supplementation of garlic (Allium sativum) and turmeric (Curcuma longa) on growth performance, carcass traits, blood profile and oxidative status in growing rabbits. Ann Anim Sci 16(2):489-505.

Al-Mnaser A, Dakheel M, Alkandari F *et al.*, 2022. Polyphenolic phytochemicals as natural feed additives to control bacterial pathogens in the chicken gut. Arch Microbiol 204(5):253.

Anam S, Rahman SU, Ali S, *et al.*, 2021. Comparative growth kinetic study of Newcastle disease virus, infectious bursal disease virus and avian influenza virus in chicken embryo fibroblast and DF-1 cell lines. Pol J Vet Sci: 287-292.

Andleeb R, Ashraf A, Muzammil S *et al.*, 2020. Analysis of bioactive composites and antiviral activity of Iresine herbstii extracts against Newcastle disease virus In ovo. Saudi J Biol Sci 27(1):335-340.

Andleeb R, Zafar N, Ijaz MU *et al.*, 2024. In-vitro, in-vivo and in-silico exploration of different extracts of Justica adhatoda against Newcastle viral disease. J King Saud Uni Sci 36(5):103163.

Anjum FR, Anam S, ur Rahman S, *et al.*, 2020. Anti-chicken type I IFN countermeasures by major avian RNA viruses. Virus Res, 286:198061.

Ashokkumar K, Murugan M, Dhanya MK *et al.*, 2021. Phytochemistry and therapeutic potential of black pepper [Piper nigrum (L.)] essential oil and piperine: A review. Clini Phytosci 7(1):52.

Bahgat SW, Lebda MA, Taha NM *et al.*, 2025. Enhancing immune response in broiler chicks against Newcastle disease virus using lemongrass and geranium oils: A comprehensive study on biochemical and antioxidant effects: Effects of LO and GO on NDV Response in Broilers. J App Poult Res 34(2):100528.

Bernardo AR, da Rocha JDB, de Lima MEF *et al.*, 2015. Modulating effect of the piperine, the main alkaloid from Piper nigrum Linn., on murine B lymphocyte function. Brazilian J Vet Med 37(3):209-216.

Boukhatem MN and Setzer WN, 2020. Aromatic herbs, medicinal plant-derived essential oils, and phytochemical extracts as potential therapies for coronaviruses: future perspectives. Plants 9(6):800.

Brindha P, 2016. Role of phytochemicals as immunomodulatory agents: A review. International J Green Pharm (IJGP) 10(1):1-18.

Burzyńska P, Sobala ŁF, Mikołajczyk K *et al.*, 2021. Sialic acids as receptors for pathogens. Biomol 11(6):831.

Camargo ZP and Luz ECR, 2018. Humoral immunity, Paracoccidioidomycosis. CRC Press.pp:187-202

Campos-Vega R and Oomah BD, 2013. Chemistry and classification of phytochemicals. Handbook of plant food phytochemicals. John Wiley & Sons, Ltd. pp:5-48.

Chadha S, 2021. Recent advances in nano-encapsulation technologies for controlled release of biostimulants and antimicrobial agents. Adva nano-ferti nano-pesti agri :29-55.

Chanput W, Krueyos N and Ritthiruangdej P, 2016. Anti-oxidative assays as markers for anti-inflammatory activity of flavonoids. Int Immunopharm 40:170-175.

Chauhan NS, Singh MR, Sharma V *et al.*, 2022. Traditional Indian knowledge of immunity from plants, Plants and Phytomolecules for Immunomodulation: Recent Trends and Advances. Springer.pp:251-283

Chen Y, Bi L, Luo H *et al.*, 2019. Water extract of ginseng and astragalus regulates macrophage polarization and synergistically enhances DDP's anticancer effect. J Ethnopharm 232:11-20.

Danquah CA, Minkah PAB, Agana TA *et al.*, 2022. The phytochemistry and pharmacology of Tulbaghia, Allium, Crinum and Cyrtanthus:'talented'taxa from the Amaryllidaceae. Molecule 27(14):4475.

de Sousa Brito L, Pereira AN, Campos EÍA *et al.*, 2020. Identification and quantification bioactive compounds on liquid extract of Capsicum chinense jacq. biquinho variety: Standardization and quality control is frontier to acceptance of herbal products on market. Pharma Maga 16(69)

Dewi YA, Yulianti A, Hanifah VW *et al.*, 2022. Farmers' knowledge and practice regarding good agricultural practices (GAP) on safe pesticide usage in Indonesia. Heliyon 8(1)

Dimitrov KM, Afonso CL, Yu Q *et al.*, 2017. Newcastle disease vaccines—A solved problem or a continuous challenge? Vet Microbiol 206:126-136.

Endale H, Aliye S and Mathewos M, 2022. Vaccine epidemiology, evaluation, and constraints of vaccine effectiveness-A review. Vet Vaccin 1(1):100004.

Enioutina EY, Teng L, Fateeva TV *et al.*, 2017. Phytotherapy as an alternative to conventional antimicrobials: combating microbial resistance. Exp Review Clini Pharm 10(11):1203-1214.

Fatima A, Zaheer T, Pal K, *et al.*, 2024. Zinc oxide nanoparticles significant role in poultry and novel toxicological mechanisms. Biolog Trace Elem Res, 202(1): 268-290.

Gaur N, Mishra S, Srivastava S *et al.*, 2020. Naturapolyceutics-Emerging Science & Technology in Drug Delivery System. Int J Pharma Res (09752366)

Haddas R, 2023. Newcastle disease virus, Infectious Diseases. Springer.pp:427-440

Haleem MIA, Gaballa MMS, El-Far AH *et al.*, 2024. Mitigating impact of Glycyrrhiza glabra on virulent Newcastle disease virus challenge in chickens: clinical studies, histopathological alterations and molecular docking. Vet Res Commu 48(6):3823-3845.

Hasan MM and Ahad A, 2024. Antiviral efficacy of Neem, Garlic, and Ginger extracts on Newcastle Disease Virus in Poultry: Impact of concentration and heat treatment. Asian J Res Ani Vet Sci 7(4):429-437.

Hu E, Li Z, Li T., *et al.*, (2023). A novel microbial and hepatic biotransformation-integrated network pharmacology strategy explores the therapeutic mechanisms of bioactive herbal products in neurological diseases: the effects of Astragaloside IV on intracerebral hemorrhage as an example. Chin Med 18(1):40. doi: 10.1186/s13020-023-00745-5.

Irivboje OA, Olufayo OO and Irivboje YI, 2021. A survey on phytogenic extracts commonly used in the control of Newcastle disease in indigenous chickens raised in Yewa South local government area of Nigeria. Nigerian J Ani Sci 23(1):86-94.

Isbill J, Kandiah J and Kružliaková N, 2020. Opportunities for health promotion: highlighting herbs and spices to improve immune support and well-being. Integrative Medicine: A Clini J 19(5):30.

Jiang L, Zhang G, Li Y *et al.*, 2021. Potential application of plant-based functional foods in the development of immune boosters. Front Pharm12:637782.

Kadiyska T, Tourtourikov I, Dabchev K *et al.*, 2023. Herbs and plants in immunomodulation. Int J Funct Nutri 4(1):1-11.

Kollmann TR, Marchant A and Way SS, 2020. Vaccination strategies to enhance immunity in neonates. Sci 368(6491):612-615.

Lavelle EC and Ward RW, 2022. Mucosal vaccines—fortifying the frontiers. Nature Revi Immuno 22(4):236-250.

Lebdah M, Tantawy L, Elgamal AM *et al.*, 2022. The natural antiviral and immune stimulant effects of Allium cepa essential oil onion extract against virulent Newcastle disease virus. Saudi J Biol Sci 29(2):1239-1245.

Li H, Zhou Y, Liao L, *et al.*, (2023). Pharmacokinetics effects of chuanxiong rhizoma on warfarin in pseudo germ-free rats. Front Pharmacol 13:1022567.

Lillehoj H, Liu Y, Calsamiglia S *et al.*, 2018. Phytochemicals as antibiotic alternatives to promote growth and enhance host health. Vet Res 49(1):76.

Luo L, Lin C, Wang P *et al.*, 2023. Combined use of immune checkpoint inhibitors and phytochemicals as a novel therapeutic strategy against cancer. J Cancer 14(12):2315.

Mandal SK, Das A, Dey S *et al.*, 2019. Bioactivities of Allicin and related organosulfur compounds from garlic: Overview of the literature since 2010. Egyptian J Chem 62:1-11.

Maniglia BC, Rebelatto EA, Andrade KS *et al.*, 2021. Polyphenols, Food Bioactives and Health. Springer.pp:1-39

McGlynn EA and McClellan M, 2017. Strategies for assessing delivery system innovations. Health Affair 36(3):408-416.

Minor PD, 2015. Live attenuated vaccines: Historical successes and current challenges. Virology 479:379-392.

Mnisi CM, MLambo V, Gila A *et al.*, 2022. Antioxidant and antimicrobial properties of selected phytogenics for sustainable poultry production. App Sci 13(1):99.

Mohamed RS, 2019. Role of Biosecurity in Reducing risk of Newcastle Disease.

Mohammed MA, Syeda JTM, Wasan KM *et al.*, 2017. An overview of chitosan nanoparticles and its application in non-parenteral drug delivery. Pharma 9(4):53.

Mugo Moses H, Investigating the Immunomodulatory effects of medicinal plants in HIV treatment. Res Output J Public Health Med 5(2):23-30

Mutha RE, Tatiya AU and Surana SJ, 2021. Flavonoids as natural phenolic compounds and their role in therapeutics: An overview. Future J Pharma Sci 7(1):25.

Nath B, Sharma K, Ahire K *et al.*, 2020. Structure analysis of the nucleoprotein of Newcastle disease virus: An insight towards its multimeric form in solution. Int J Biol Macromol 151:402-411.

Nie X, Chen S-R, Wang K *et al.*, 2017. Attenuation of innate immunity by andrographolide derivatives through NF-κB signaling pathway. Scient Report 7(1):4738.

Obahiagbon EG and Ogwu MC, 2023. The nexus of business, sustainability, and herbal medicine, Herbal Medicine Phytochemistry: Applications and Trends. Springer.pp:1-42

Oliveira VM, Carraro E, Auler ME *et al.*, 2016. Quercetin and rutin as potential agents antifungal against Cryptococcus spp. Brazil J Biol 76(04):1029-1034.

Omidiwura BRO, Agboola AF, Asipa WA *et al.*, 2023. Antiviral efficacies of neem (Azadirachta indica J.) and scent (Ocimum sanctum L.) leaf meals against Newcastle and infectious bursal disease in broiler chickens. J Anim Sci Vet Med 8(6):258-269.

Patel SS, Chauhan HC, Sharma KK *et al.*, 2024. Genetic evolution of Newcastle Disease Virus sub-genotype VII. 2 isolates, diagnosed from vaccinated poultry farms of Gujarat, India. Gene 930:148859.

Pedersen K, Marks DR, Afonso CL *et al.*, 2016. Identification of avian paramyxovirus serotype-1 in wild birds in the USA. J Wildlife Dis 52(3):657-662.

Pham LL, Watford SM, Pradeep P *et al.*, 2020. Variability in in vivo studies: Defining the upper limit of performance for predictions of systemic effect levels. Comp Toxicol 15:100126.

Pierson TC and Diamond MS, 2020. The continued threat of emerging flaviviruses. Nature Microbiol 5(6):796-812.

Plaskova A and MLcek J, 2023. New insights of the application of water or ethanol-water plant extract rich in active compounds in food. Front Nutri 10:1118761.

Pradhan Y, Alim H, Patel N *et al.*, 2022. Piper longum (Long Pepper or Pipli) and Tinospora cordifolia (Giloy or Heart-Leaved Moonseed), Herbs, Shrubs, and Trees of Potential Medi Beneft. CRC Press. pp:217-234

Priya MS, Murthy T and Vijayanand T, 2022. Antiviral effect of herbal mixture (garlic, nilavembu, turmeric, coriander, and fenugreek) against Newcastle disease virus In ovo. J App Poult Res 31(1):100229.

Rehan M, Aslam A, Khan MR *et al.*, 2019. Potential economic impact of Newcastle disease virus isolated from wild birds on commercial poultry industry of Pakistan: A review. Host virus 6(1):1-15.

Rizwan HM, Khan MK, Mughal MAS *et al.*, 2022. A new insight in immunomodulatory impact of botanicals in treating avian coccidiosis. J Para Dis 46(4):1164-1175.

Ruston A, Shortall O, Green M *et al.*, 2016. Challenges facing the farm animal veterinary profession in England: a qualitative study of veterinarians' perceptions and responses. Preven Vet Med 127:84-93.

Senthilkumar N, Sumathi R and Babu DS, 2021. Prospection of antiviral compounds from forest plants under ongoing SARS-COV-2 pandemic. Annal Phytomed-an Int J:S195-S208.

Singh M, Devi S, Rana VS *et al.*, 2019. Delivery of phytochemicals by liposome cargos: Recent progress, challenges and opportunities. J Microencapsul 36(3):215-235.

Smith T, O'Kennedy MM, Ross CS *et al.*, 2023. The production of Newcastle disease virus-like particles in Nicotiana benthamiana as potential vaccines. Front Plant Sci 14:1130910.

Staley M, Hill GE, Josefson CC *et al.*, 2018. Bacterial pathogen emergence requires more than direct contact with a novel passerine host. Infec Immunol 86(3):10-1128.

Suarez DL, Miller PJ, Koch G *et al.*, 2020. Newcastle disease, other avian paramyxoviruses, and avian metapneumovirus infections. Dis Poul:109-166.

Subbaiah KCV, Valluru L, Rajendra W *et al.*, 2015. Newcastle disease virus (NDV) induces protein oxidation and nitration in brain and liver of chicken: Ameliorative effect of vitamin E. Int J Biochem Cell Biol 64:97-106.

Sultan SA, Khawaji MH, Alsughayyir J *et al.*, 2020. Antileukemic activity of sulfoxide nutraceutical allicin against THP-1 cells is associated with premature phosphatidylserine exposure in human erythrocytes. Saudi J Biol Sci 27(12):3376-3384.

Sun L, Liang C, Qin S *et al.*, 2024. Exploring the interplay of T cell receptor-V gene copy numbers and major histocompatibility complex selection pressure in avian species: Insights into immune system evolution and reproductive investment. Avian Res 15:100204.

Tao Y, Probert WJM, Shea K *et al.*, 2021. Causes of delayed outbreak responses and their impacts on epidemic spread. J o Royal Soci Interface 18(176):20200933.

Wang P, 2021. Natural and synthetic saponins as vaccine adjuvants. Vaccines 9(3):222.

Weidmann CA, Mustoe AM, Jariwala PB *et al.*, 2021. Analysis of RNA–protein networks with RNP-MaP defines functional hubs on RNA. Nature Biotec 39(3):347-356.

Willemsen A and Zwart MP, 2019. On the stability of sequences inserted into viral genomes. Virus Evol 5(2):vez045.

Wink M, 2015. Modes of action of herbal medicines and plant secondary metabolites. Medicines 2(3):251-286.

Wink M, 2022. Current understanding of modes of action of multicomponent bioactive phytochemicals: potential for nutraceuticals and antimicrobials. Ann Rev Food Sci Tech 13(1):337-359.

Xiao J and Bai W, 2019. Bioactive phytochemicals. Criti revi food sci nutri 59(6):827-829.

Zhang P, Xie G, Liu X *et al.*, 2016. High genetic diversity of Newcastle disease virus in wild and domestic birds in Northeastern China from 2013 to 2015 reveals potential epidemic trends. App Enviro Microbiol 82(5):1530-1536.

Zhuravel NA, Miftakhutdinov AV and Zhuravel VV, Identification and risk assessment in determining the effectiveness of production veterinary and sanitary control in poultry farmspp:012180.