



Review Article

Alternative Medicines Targeting Newcastle Disease in Poultry: A Review

Farhana Amin*, Tahira Kamal, Bilal Javid, Khadija Yasmeen and Muhammad Naeem Riaz

National Institute for Genomics and Advanced Biotechnology (NIGAB), National Agricultural Research Center Islamabad (NARC), 44000, Pakistan

*For correspondence: farhana.phdbt35@iiu.edu.pk

Received 01 February 2024; Accepted 18 March 2024; Published 16 April 2024

Abstract

The poultry sector secures an important position in the livestock industry providing major sources of protein; however, is always at the risk of many viral diseases including Newcastle disease (ND), causing substantial economic losses. This disease affects both commercial and backyard poultry, with the latter contributing significantly to rural livelihoods. The virulence of NDV is attributed to various factors, including the virus's genetic diversity, posing challenges to vaccination strategies. Vaccines in practice exhibit limitations leading to sporadic outbreaks and do not offer complete cure. Additionally, imported vaccines may not match field strains, highlighting the need for alternative approaches, such as natural medicines, to enhance ND control strategies in Pakistan and other affected regions. Medicinal plants are the gift of nature to fulfill food and therapeutic needs. Medicinal plants are being used for centuries against different diseases. With advancement in modern medicine these natural sources get overlooked. Conventionally many plants are being used for treating diseases in domestic poultry. Many plants have been tested from 2016–2024 against viral diseases. The objective of this study is to give an overview of alternative medicines being used by different countries to mitigate the loss caused by ND. © 2024 Friends Science Publishers

Keywords: Poultry growth; Newcastle disease; Economic challenges; Vaccine limitations; Alternative medicines

Introduction

In the year 2023, the livestock sector played a substantial role in the agricultural landscape, contributing 62.68 % to the value added in agriculture and comprising 14.36% of the country's GDP. Within the livestock industry, the poultry sector holds strategic importance, creating employment opportunities for over 1.5 million individuals in Pakistan. Over the past decade, this sector has experienced remarkable expansion, marked by a significant investment exceeding Rs 1,056 billion and maintaining a remarkable annual growth rate of 7.3%. Pakistan has now ascended to the eleventh position globally in poultry production, indicating substantial potential for future development and advancement Pakistan Economic Survey (2022–2023).

Despite the rapid growth of the poultry sector in Pakistan, the industry consistently challenges the forthcoming threat of viral diseases. Among these, Newcastle disease (ND) stands out as one of the most destructive viral infections affecting poultry worldwide (Mottet and Tempio 2017). ND is a highly contagious and acute disease in birds, caused by the Newcastle disease virus (NDV). It exhibits high morbidity and mortality rates, affecting a diverse range of avian species. Additionally, it is a minor zoonosis, with infected individuals experiencing conjunctivitis. The disease was initially reported in

Indonesia in 1926, and since then, the world has witnessed at least four pandemics. Each outbreak is marked by the emergence of new genotypes (Ganar *et al.* 2014) (OIE 2009) causing huge economic losses to the poultry industry.

ND leads to weight loss, respiratory discomfort, and reduced egg production in poultry. This disease is widespread in developing countries, posing a significant impact on the poultry industry (Absalón *et al.* 2019). The mortality and morbidity rates in a chicken flock exhibit significant variation, ranging from 90% to 100% in inadequately vaccinated birds. Well-vaccinated layers also experience declines in egg production due to the ND. The prevalence of ND in developing countries poses a substantial challenge to the poultry industry (Bessell *et al.* 2020). This highly contagious disease continues to be a prominent threat to poultry globally, resulting in significant economic losses for both commercial and backyard poultry sectors in developed and developing countries (Khatun *et al.* 2022).

Back yard poultry

The current count of domestic poultry stands at 94.04 million, surpassing the figures recorded in both 2020 and 2021. In contrast, the population of commercial poultry is significantly higher at 1,792.46 million (Pakistan Economic

Survey 2022–2023). For generations, rural households have kept poultry in their backyard, with indigenous chickens playing a crucial role in the livelihoods of both poor urban and rural communities. However, the growing commercialization of indigenous chicken farming in developing nations, such as India, has led to a rise in the occurrence of infectious diseases like ND. The ND continues to impact many backyard chicken flocks in the domestic poultry community, despite vaccination efforts. This is particularly prevalent as these chickens are typically maintained in multi-age group flocks within a free-range system. Notably, there is a growing awareness and demand for organic farm products in recent times (Mekala *et al.* 2018). In the Asian context, Pakistan is considered endemic for ND infections in poultry. Both commercial and backyard flocks can harbor the infection, with all viruses isolates from these sectors belonging to genotype VII. Interestingly, backyard flocks may not exhibit apparent ND symptoms, although the virus isolated from them carries a characteristic motif in the F-protein associated with virulence. The transmission of virulent NDV into backyard flocks is suspected to occur through frequent contact with commercial poultry. Subsequently, the virus adapts within the backyard flocks, even though these flocks do not manifest the typical ND disease. This scenario underscores the complex dynamics of NDV in both commercial and backyard poultry sector (Munir *et al.* 2012). In Nepal, ND was identified as the cause of 90% mortality in backyard flocks in 1992 (Alexander 2001). In Iran's Bushehr province, a seroprevalence of 40% unvaccinated backyard chickens for NDV antibodies were identified (Saadat *et al.* 2014).

Virulence of NDV

The NDV belongs to the avian paramyxovirus type-I (APMV-1) within the Avulavirus genus, Paramyxovirinae subfamily, Paramyxoviridae family, and Mononegavirales order (Rima *et al.* 2019). The causative agent NDV is characterized as an enveloped virus with a negative-sense, single-stranded RNA genome that is approximately 15 kb in length. The genome is responsible for the synthesis of six major structural proteins, which are encoded in the 5 to 3 directions. These proteins comprise a large RNA-dependent RNA polymerase (L), Hemagglutinin-Neuraminidase (HN), Fusion protein (F), Matrix protein (M), Phosphoprotein (P), and Nucleoprotein (NP) (Kattenbelt *et al.* 2006; Dortmans *et al.* 2011).

The virulence of the virus is classified into three pathotypes: the lentogenic strain, utilized as a vaccine strain, induces asymptomatic infection the mesogenic strain leads to respiratory infection with moderate mortality and the velogenic strain causes gastrointestinal lesions (viscerotropic) or neurological infection, resulting in a 100% mortality rate. The primary determinant of NDV isolates' virulence is the sequence at the F cleavage site within

positions 112–116 (Paldurai *et al.* 2014).

The variation in cleavage sites serves as a key determinant of the distinct virulence characteristics observed in lentogenic, mesogenic, and velogenic strains. In the process of virus replication, inactive precursor F glycoproteins, designated as F₀, are generated within NDV particles. To attain infectivity, these virus particles necessitate the cleavage of F₀ into two segments: F₁ and F₂ polypeptides. The cleavage efficiency of the F₀ glycoprotein is directly linked to the *in vivo* virulence of the viruses (Leeuw *et al.* 2003).

The hypothesis suggests that the F₀ glycoproteins in highly pathogenic and can be cleaved by various proteases present in numerous tissues and organs. Infections with these virulent viruses lead to widespread dissemination throughout the chicken or embryo, causing damage to various tissues and organs. In contrast, low-virulence ND viruses are susceptible only to trypsin-like proteases, limiting infection to specific cell types in the chicken or embryo. At the molecular level, the amino acid sequence at specific glycoprotein sites is responsible for the pathogenicity of ND. The virus exhibits a broad host range, capable of infecting approximately 241 species across 27 orders, out of the total 50 orders of birds (Doan 2022).

Vaccination and their limitations

In Pakistan, regular and thorough vaccination is a common practice in the poultry industry to prevent the occurrence of diseases. Nevertheless, the ND remains prevalent in poultry, including both commercial broiler and layer operations (Farooq *et al.* 2014). During the 2011–2012 periods in the Punjab province of Pakistan, ND led to the deaths of 45 million broiler chickens, resulting in a significant economic loss of 6 billion PKR. In Pakistan, there has been a shift in NDV isolates, with sub-genotype VIIi viruses replacing the previously common genotype XIIIa isolates observed from 2009–2011. Since 2012, sub-genotype VIIi has become the predominant sub-genotype, indicating the emergence of a fifth panzootic (Munir *et al.* 2016).

Currently, live attenuated vaccines, such as the La Sota or Mukteswar strain, followed by the administration of Mukteswar or Komarov strain, are in practice. While these vaccines provide immunity to day-old chicks, they do not fully control the disease, leading to sporadic outbreaks. Because of the incompatibility of field and vaccine strains, inadequate vaccination methods, and the occurrence of novel genotypes under strong immunological pressure, vaccination failures have raised doubts about the effectiveness of these vaccines (Miller *et al.* 2007). The genomic diversity of NDV increases the possibility of diagnostic failures, resulting in unidentified infections (Umar 2017).

In Pakistan, imported vaccines are being used for poultry diseases rather making indigenous vaccines. These substandard imported vaccinations are not effective in

controlling the disease because of incompatibility with field strains. The idea of biosecurity is exclusive to certain larger farms. The role that wild birds play in the spread of disease is unknown to the general public. Despite the widespread use of both live and inactivated ND vaccines, the rising frequency of outbreaks and high prevalence of the disease demonstrate that these immunization approaches are ineffective in controlling the disease. But these vaccines are produced with technology based on embryonated eggs, which have several drawbacks, including low yields, labor-intensiveness, potential for biohazard, and frequent impurities (Pandey *et al.* 2010).

Genotype VII of NDV is still common in domestic poultry in Asia, and it was discovered that these strains are the same as those that were isolated in the 1990s (Shabbir *et al.* 2013). According to reports, co-infections between NDV and H7N3 are occurring in flocks of poultry; the rate of co-infections between NDV and H7N3 is highest, followed by NDV. Therefore, identifying the common strain and preparing vaccines are essential for maximizing the effectiveness of vaccinations (Channa *et al.* 2020).

The development of a different strategy is desperately needed in order to prevent such vaccination failure. The World Health Organization (WHO) estimates that over 75% of people worldwide use natural medicines, mostly from different backgrounds. The formulations for pharmaceutical medications that protect against different viral diseases, such as the influenza virus and NDV, have been standardized by various countries. Even though synthetic chemical components are utilized extensively in current products, it is still important to consider the effectiveness of herbal products that have the fewest negative effects (Yasmin *et al.* 2020).

Alternative approach

In order to avoid problems such as vaccination failure and disease spread, there is need to explore alternative sources of medicines which are cheap, nontoxic can help to reduce the drug resistance and drug residues problem. The most reliable alternative medicines include the use of medicinal plants against ND. Medicinal plants are the gift of nature and from a long time ago these botanical treasures have acted as natural pharmacy for human and animal health care system. Numerous medicinal plants are being used for treating ND which is discussed below.

Research demonstrates the effect of *Phyllanthus amarus* against ND. The screening of bioactive constituents was done by using n-hexane. The phytochemical constituents of *Phyllanthus amarus* leaf was administered to two groups of birds one was given by prophylactic approach and the other group was treated as therapeutic. Symptoms of bodyweight alterations and % mortality was recorded. Results showed that Prophylactic approach gives lower % mortality than therapeutic approach It was concluded that n-hexane bioactive constituents of *P. amarus* present

substantial antiviral effect against ND virus in broiler chickens and that prophylactic administration at 500 mg/L might be a safer approach in utilization of the leaf extract against ND (Faeji *et al.* 2019).

In a study *Iresine herbstii* from Amaranthaceae family was used to analyze anti NDV activity. Phytochemical analysis including TPC, TFC and HPLC was performed to evaluate the bioactive constituents of *Iresine herbstii*. Four different solvents were used for extraction of bioactive compounds from which ethanolic extract of *Iresine herbstii* showed variety of phytoconstituents. TPC was present in higher concentration in acetone extract than ethanolic extract. Similarly, TFC was present in higher concentration in ethanolic extract. HPLC confirmed the presence of therapeutically important phytoconstituents. *In ovo* administration of acetone extract at 300 µg/mL showed no mortality and 100% protection, similarly ethanolic extract of *Iresine herbstii* at dose 400 µg/mL give 100% protection against NDV which was induced by using live virus showed no mortality. At dose 600 mg/mL of plant extract causes toxicity. Phytochemical analysis demonstrates the presence of important bioactive constituents which are responsible for the observed antiviral effect against NDV (Andleeb *et al.* 2020).

An *in ovo* study report that methanolic extract of *Boswellia dalzielii* stem bark extract and their fractions were used to treat ND to analyze cytotoxicity, prophylactic, therapeutic and neutralization activities, whereas the fractions were employed to analyze cytotoxicity and neutralization potential. The plant extract at the dose of 50 mg/mL possesses more pronounced antiviral potential against ND and gave 100% protection whereas 100 mg/mL dose proves to be toxic to the embryo, furthermore the extract showed maximum protection than the fractions. Qualitative analysis of bioactive constituents showed the presence of polyphenols, steroids and saponins which are responsible for anti-NDV effect (Ohemu *et al.* 2020).

A study was conducted to assess the antiviral potential of *Glycyrrhiza glabra* leaves for treating ND through *in ovo* assay. Bioactive formulations were administered to 9-day old chick embryos and ND was induced by using velogenic pathotype to all treated groups except control group followed by candling to check embryo survival. Results showed 100% mortality in negative control group after administration of velogenic strain. Whereas % protection of treatment group was significantly higher at dose of 300 µg/mL and effect was dose dependent. In the same way no viruses were found in HA titer, the plant extracts in treated group (Ashraf *et al.* 2017).

Scutellaria baicalensis belongs to family *Lamiaceae* used in conventional therapies. This study was designed to evaluate the potential of *Scutellaria baicalensis* against NDV *in vitro* by employing ND induced embryonic fibroblasts followed by fluorescence-activated cells. Plant therapeutic effect against ND and cell toxicity was analyzed. The *Scutellaria baicalensis* at the dose of 1×2^{-2} mg/mL

was not toxic to cells and strongly inhibited ND and ultimately reduced the prevalence of ND. This plant can be used as a potential candidate for developing drugs against NDV (Jia *et al.* 2016). Different concentrations of *Scutellaria baicalensis* showed varying levels of blocking, neutralizing and inhibition rate. The minimal concentration 1×2^{-2} mg/mL of *Scutellaria baicalensis* presented 100% blocking rate, 100.41% neutralization rate while inhibition rate was 103.70% (Jia *et al.* 2016).

Tribulus terrestris belongs to the family Zygophyllaceae was used to treat ND. The alcoholic extract was subjected to phytochemical analysis which confirms the presence of therapeutically important bioactive compounds. Furthermore, these extracts were used to analyze *In vivo* anti NDV effect *in vero* cell culture followed by HA titer. Different doses from 20–80 μ L/mL were mixed with Lasota strain of the NDV and applied to cell lines. Standard conditions were maintained for cell lines. Results showed that pretreatment of *T. terrestris* give more pronounced antiviral effect in vero cell line at the dose below 80 μ L/mL and this plant has ability to control NDV as preventive measure (Malik *et al.* 2018).

This study was performed to investigate the invitro anti NDV potential of alcoholic bioactive formulation of *Polyalthia longifolia* against vero cell lines and to analyze the potential procedure involve in action. Cell toxicity, mechanism of virus infection and quantification of viral RNA was established. A non-lethal dose of *Polyalthia longifolia* leaves extract restrict replication of virus at initial stages of virus attack. The test plant conclusively showed promising potential against NDV at the initial stages like invasion and budding stage making *Polyalthia longifolia* a promising candidate for antiviral drug development (Yadav *et al.* 2020).

A study was carried out to analyze the effect of *Nigella sativa* (6%), curcumin (1%), and Oregano sol was administered to live chicks with a positive and negative control group. After administration a pronounced betterment in immunity of birds were observed. in the same way an enhanced expression of cytokine genes upregulate immunostimulation action, ultimately reduce NDV pathogenesis. When chicks were given Oregano sol®, there was a greater evident reduction in viral shedding and an improvement in their immune responses (Zain *et al.* 2024).

A study reported the application of herbal medicines against ND in backyard poultry. The effected birds were administered consortium of *Phyllanthus amarus*, *Cuminum cyminum* seeds and *Allium cepa* pulp mixed with jaggery. The birds were also provided with *C. cyminum* water solution 1 g/100 mL. Results showed herbal remedy proved very effective to recover the effected birds within 3–5 days. Results confirmed the potential of medicinal plants in for control of ND in backyard poultry (Mekala *et al.* 2018).

A research study describes the phytochemical analysis and immunomodulatory effect of *Nilavembu Kudineer*

Chooranam (NKC) by using sixty day-old unsexed country chicken. Chickens were divided into six groups each group have 10 chickens. The groups were treated as positive, negative and treated groups. The three treated group were provided with Nilavembu Kudineer Chooranam (NKC) @ 0.5, 1.0 and 2.0 mL/kg of body weight for five consecutive days before vaccination. Results showed that pretreated group (1.0 mL/kg) presented enhanced titer in comparison with vaccine control. These findings showed that NKC at the dose of 1.0 mL/kg for 5 days in drinking water prior to vaccination enhance the immune response in backyard chicken.

A study reported that alcoholic extract of different flowers was used to analyze the antiviral activity against NDV by employing *in ovo* method. HA titer revealed the antiviral effect of *Rosa damascena* Miller, *Achillea millefolium*, *Woodfordia fruticosa* Kurtz and *Bombax ceiba* L. contrary to NDV. The phytoconstituents including alkaloids, ethers and terpenoids detected through GCMS might be active compounds in treating NDV (Nazir *et al.* 2021).

The bioactive compounds from the two Tanzanian *Artabotrys* species, *A. monteiroae* and *A. modestus* (*Annonaceae*) were screened for their antiviral activities against NDV *in ovo* (in the egg). For ND assay, the allantoic fluids from the specimens were further harvested to determine viral infection. The tested compounds also exhibited *in ovo* antiviral activity against NDV, showing viral titer reduction at a range of 1:128–1:256 in the hemagglutination test, indicating 16- and 8-times viral load decline compared with untreated embryo (positive control; 1:2048). Further studies to determine the mode of action and toxicity of the potent compounds need to be undertaken towards the development of such antiviral agents (Nyandoro 2017).

Research was conducted in which methanolic extracts of the leaves and fruit of *Aegle marmelos* (Bael) were employed for analyzing qualitative and quantitative phytochemical constituents and their antiviral efficacy NDV. The fruit extract of *A. marmelos* showed considerable antioxidant activity which reflect the presence of significant quantity of polyphenoles in leaves and fruit extract. Enhanced doses (90 μ g/mL) of laves and fruits of *Aegle marmelos* proved very effective against NDV. *In silico* analysis also give better affinity of compounds with HN protein by satisfying required condition therefore it was established that bioactive compounds of *Aegle marmelos* have potential to be used as alternative medicine for treating NDV (Andleeb *et al.* 2021).

Two different extracts and an isolated compound from *Andrographis paniculata* were employed against NDV through *in ovo* assay by using ribavirin as negative control. NDV2K35 mesogenic strain was used for inducing disease. Results showed that there was 100% survival rate and no virus was observed in HA titer furthermore RTPCR confirmed these results. This study revealed the anti NDV

Table 1: Medicinal plants used to treat ND in poultry

Plant Name	Strain	Plant part	Dose of administration	Trial	References
<i>Curcuma longa</i> , <i>Coriander sativum</i> , <i>Allium sativum</i> , <i>Andrographis paniculata</i> , and <i>Trigonella foenum graecum</i>	(NDV) Genotype XIII,	Whole plant	500 mg/mL	<i>In ovo</i>	(Priya et al. 2022)
<i>Anemarrhena rhizome</i> , <i>Astragalus root</i> and <i>Flos chrysanthemi indic</i>	NDV (F48E9 strain)	Root Root Root	8 mg/kg	DF-1 fibroblast cell line	(Wang et al. 2016)
<i>Folium isatidis</i> <i>Forsythia suspense</i> <i>Houttuynia cordata</i> Thunb, <i>Scutellaria baicalensis</i> Georgi <i>Lonicerae japonicae</i> Flos.	NDV strain	stem leaf root stem leaf	15.6 mg/mL	chick embryo fibroblast	(Lv et al. 2019)
<i>Radix scutellariae</i> <i>Herba agastaches</i> <i>Flos chrysanthemi indic</i>	(BHK-21), (HeLa) chicken DF-1 fibroblast cell.	Root Over ground Flower	80 mg/mL	Chicken	(Wang et al. 2016)
<i>Phyllanthus amarus</i> <i>Glycyrrhiza glabra</i> <i>Iresine herbstii</i>	wild NDV (Kudu strain) Lasota strain	Leaf leaf	500 mg/L 300 µg/mL	Chicken	(Faeji et al. 2019) (Ashraf et al. 2017) (Andleeb et al. 2020)
<i>Aegle marmelos</i> <i>Andrographis paniculata</i> <i>Andrographis paniculata</i>	HN of NDV NDV2K35 mesogenic NDV2K35 mesogenic	Leaf fruit Leaves leaves	300-400 mg/mL 90 µg/mL 2.5 µg/mL 1-5 µg/mL	<i>In ovo</i> <i>In ovo</i> <i>In vivo</i> fibroblast cell	(Andleeb et al. 2021) (Nagajothi et al. 2020) (Nagajothi et al. 2023)
<i>Scutellaria baicalensis</i>	La Sota strain IV	Whole plant	1 × 2 ⁻² mg/mL	embryonic fibroblasts cells	(Jayaraman et al. 2014)
<i>Tribulus terrestris</i> <i>Polyalthia longifolia</i> <i>Nigella sativa</i> (6%), curcumin (1%), and Orego sol	La Sota Strain NDV/Hisar/2015 vNDV strain	Whole plant leaves seeds	20-80 µL/mL 10 µg/mL 6% 1%	vero cell lines vero cell lines chickens	Malik et al. 2018 (Yadav et al. 2020) (Zain Eldeen et al. 2024)
<i>Phyllanthus amarus</i> , <i>Cuminum cyminum</i> seeds and <i>Allium cepa</i> pulp	-	Whole plant Seed pulp	1 g/100 mL	chickens	(Mekala et al. 2018)
<i>Nilavembu Kudineer Chooranam (NKC)</i>	(D58 strain)	-	1.0 mL/kg	chicken	(Kavinilava et al. 2017)

potential of aqueous extract of *A. paniculata*, andrographolide compound through column chromatography (Nagajothi et al. 2020).

In another study antiviral activity of *A. paniculata* against mesogenic strain of NDV was analyzed by using chicken embryo fibroblast cells. These extracts were applied at the dose of 1–5 µg/mL. The test samples showed anti NDV activity in the cell lines. Aqueous extract and andrographolide standard exhibited antiviral activity at all doses and was compared with standard antiviral drug ribavirin. Alcoholic bioactive constituents were not effective in complete inhibition of NDV which was confirmed by HA titer and expression of F gene (Nagajothi et al. 2023).

In a study 25 different medicinal plants were employed against ND to test their antiviral effect in fibroblast cell lines. The medicinal plants were tested individually and in mixture form. Among them a group including *Anemarrhena rhizome*, *Astragalus root* and *Flos chrysanthemi indic* in equal concentration and another group of herbs including *Radix scutellariae*: *Herba agastaches*: *Rhizoma anemarrhenae* were in (1:1:2) ratio showed significant antiviral effect against ND. Additionally, they are also employed *in vivo* to analyze their effect in live chickens. Results showed that IgY titers were enhanced in plant extract treated group with less morbidity rate and 63% protection in NDV-infected chicken (Wang et al. 2016).

In this study anti NDV efficacy of natural herbs was analyzed by using chick embryos. Bioactive formulations were administered along with NDV strain Herts 33 and kept on incubation followed by HA test and RTPCR. These *Moringa peregrine*, *Acacia cyanophylla*, *Eucalyptus*

camaldulensis, and *Pistacia atlantica* presented no embryo death and HA titer and efficiently reduced viral replication. Comparatively, *Ceratonia siliqua* and *E. camaldulensis* was not very effective against ND (Al-Hadid 2016).

In another study the efficacy of mixture of different herbs against NDV were tested. A consortium was prepared by using different plants including *Folium isatidis*, *Forsythia suspense*, *Houttuynia cordata* Thun, *Scutellaria baicalensis* Georgi and *Lonicerae japonicae* Flos. The formula was used both *in vitro* in chick embryo fibroblast and *in vivo* to analyze the expression of interferon-induced transmembrane protein 3 (IFITM3) and Interferons (IFNs) in NDV-induced chickens. Results showed that mixture of herbs gives considerable anti NDV activity *in vitro* and enhanced IFITM3 expression to restrict the viral reproduction in NDV induced chickens. However, individually these plants couldn't exert antiviral activity but their formula showed dose dependent effect. The formula used enhanced the expression of IFNs post infection and their antibodies to boost the immune system (Lv et al. 2019).

In a recent study a combination of medicinal plants including *Curcuma longa*, *Coriander sativum*, *Allium sativum*, *A. paniculata*, and *Trigonella foenum graecum* were inoculated in embryonated chicken eggs to evaluate their synergistic anti NDV effect. The finding of this study elaborated that alcoholic extract showed considerable reduction in virus titers and treated group did not show observable viruses. The extract at the dose of 500 µg/mL showed 0% mortality. Phytochemical analysis revealed the occurrence of alkaloids, flavonoids, saponins, tannins and terpenoids etc. which reported to have antiviral efficacy. This

study focused on the use of alternative medicine in order to mitigate drug resistance, drug residue and other associated infections. Additionally *in vivo* studies are required to confirm these herbs against ND (Priya *et al.* 2022).

Conclusion

Ethno-veterinary medicines presented promising antiviral efficacy against NDV. The varying nature of bioactive phytoconstituents showed synergistic effect in mitigating ND. Numerous research studies demonstrate the anti NDV effect of bioactive compounds by inhibiting the NDV replication and reduction in the symptoms associated with infection. Additionally, the utilization of botanical remedies corresponds to growth trend of natural and sustainable pharmaceutical substitutes in animal healthcare. Harnessing plants' therapeutic properties resolves issues with drug resistance and residual effects in poultry products while also providing a more affordable alternative and lowering reliance on synthetic medications. Domestically, many plants including *Coriander sativum*, *Allium sativum* and *Allium cepa*, *Curcuma longa* and *Aloe vera* are being used for treating ailments in livestock and poultry. In this review 28 different plants are used individually and in combination against NDV which presented novel antiviral activities and pronounced improvement in immunity (Table 1). Furthermore, these phytochemical constituents were administered in three different ways such as *in ovo*, *in vitro* and *in vivo*. It is suggested that supplementation of alternative sources of medicines is required to combat the vaccination failure and drug resistance. It is a need of the time to explore more botanical treasures and there is need to isolate lead compounds exhibiting antiviral properties from medicinal plant. These bio drugs can be used in poultry feed which could be serve as an immune booster to avoid lethal diseases. Incorporating traditional knowledge with modern scientific approaches can pave the way for the development of effective herbal remedies for NDV. In conclusion as research in this field progresses, the integration of medicinal plants into veterinary practices may offer a sustainable and natural solution for combating NDV.

Acknowledgements

The first author FA acknowledged TK, BJ and MNR for providing technical support for writing this review.

Author Contributions

FA presented the main idea and write original article. TK, BJ and MNR help in providing technical support, editing and reviewing the paper.

Conflicts of Interest

All authors declare no conflicts of interest.

Data Availability

Data will be available on demand

Ethics Approval

Not applicable in this paper

References

- Absalón A, DV Cortés-Espinosa, E Lucio, P Miller, C Afonso (2019). Epidemiology, control, and prevention of Newcastle disease in endemic regions: Latin America. *Trop Anim Health Prod Trop Anim Health Prod* 51:1033–1048
- Alexander DJ (2001). Newcastle disease. *Brit Poult Sci* 42:5–22
- Al-Hadid KJ (2016). Evaluation of antiviral activity of different medicinal plants against Newcastle disease virus. *Amer J Agric Biol Sci* 11:157–163
- Andleeb R, MU Ijaz, A Rafique, A Ashraf, N Bano, N Zafar, F Tasleem, RA Marc, OL Pop, HT Ahmedah (2021). Biological activities of methanolic extract of aegle marmelos against HN protein of newcastle disease virus. *Agronomy* 11:1784
- Andleeb R, A Ashraf, S Muzammil, S Naz, F Asad, T Ali, R Rafi, KA Al-Ghanim, F Al-Misned, Z Ahmed (2020). Analysis of bioactive composites and antiviral activity of Iresine herbstii extracts against Newcastle disease virus *in ovo*. *Saud J Biol Sci* 27:335–340
- Ashraf A, MM Ashraf, A Rafiqe, B Aslam, S Galani, S Zafar, F Asad, RD Ashghar, S Akram, H Ahmed (2017). *In vivo* antiviral potential of Glycyrrhiza glabra extract against Newcastle disease virus. *J Pharm Sci* 30:1–6
- Bessell PR, R Woolley, S Stevenson, L Al-Riyami, P Opondo, L Lai, N Gammon (2020). An analysis of the impact of Newcastle disease vaccination and husbandry practice on smallholder chicken productivity in Uganda. *Prev Vet Med* 177:104975
- Channa AA, NH Kalhor, ZA Nizamani, AH Mangi, J Soomro (2020). Prevalence of Newcastle disease virus and avian influenza virus (H7N3) in poultry at Karachi. *RADS J Biol Res Appl Sci* 11:9–14
- Doan PTK (2022). Transcriptome profiling of infected chickens with newly emerged genotype VI I Newcastle disease virus strains. *Ph.D. Dissertation*, pp:1–162. The University of Adelaide, Australia
- Dortmans JC, G Koch, PJ Rottier, BP Peeters (2011). Virulence of Newcastle disease virus: What is known so far? *Vet Res* 42:1–11
- Faeji C, M Oladunmoye, I Adebayo, T Adebolu (2019). Antiviral effect of *Phyllanthus amarus* leaf extract against newcastle disease virus in broilers. *Asian Plant Res J* 2:1–9
- Farooq, M, U Saliha, M Munir, QM Khan (2014). Biological and genotypic characterization of the Newcastle disease virus isolated from disease outbreaks in commercial poultry farms in northern Punjab, Pakistan. *Viol Rep* 3:30–39
- Ganar K, M Das, S Sinha, S Kumar (2014). Newcastle disease virus: Current status and our understanding. *Virus Res* 184:71–81
- Jayaraman P, E Sivaprakasam, V Rajesh, KMP Arumugam (2014). Comparative analysis of antioxidant activity and phytochemical potential of *Cassia absus* Linn., *Cassia auriculata* Linn. and *Cassia fistula* Linn. *Ind J Drugs Dis* 3:1–7
- Jia Y, R Xu R, Y Hu, T Zhu, T Ma, H Wu, L Hu (2016). Anti-NDV activity of baicalin from a traditional Chinese medicine *in vitro*. *J Vet Med Sci* 78:819–824
- Kattenbelt JA, MP Stevens, AR Gould (2006). Sequence variation in the Newcastle disease virus genome. *Vir Res* 116:168–184
- Kavinilava R, P Mekala, M Raja, MA Eswaran, G Thirumalaisamy (2017). Exploration of immunomodulatory effect of nilavembu kudineer chooranam against newcastle disease virus in backyard chicken. *J Pharmacol Phytochem* 6:749–751
- Khatun A, MZ Ali, M Morshed (2022). Prevalence and risk factors of newcastle disease in chickens of live bird markets, commercial poultry farms and backyard in selected areas of Bangladesh. *J Adv Vet Res* 12:6–10

- Leeuw OSD, L Hartog, G Koch, BP Peeters (2003). Effect of fusion protein cleavage site mutations on virulence of Newcastle disease virus: Non-virulent cleavage site mutants revert to virulence after one passage in chicken brain. *J Gen Vir* 84:475–484
- Lv W, C Liu, Y Zeng, Y Li, W Chen, D Shi, S Guo (2019). Explore the potential effect of natural herbals to resist Newcastle disease virus. *Poul Sci* 98:1993–1999
- Malik A, MD Mehmood, H Anwar, U Sultan (2018). *In-vivo* antiviral potential of crude extracts derived from *Tribulus terrestris* against newcastle disease virus. *J Drug Deliv Therap* 8:149–154
- Mekala P, V Vadivoo, K Sukumar (2018). Incidence of Newcastle disease in desi chicken and its control through ethno veterinary medicines. *J Pharm Phytochem* 7:1418–1419
- Miller PJ, DJ King, CL Afonso, DL Suarez (2007). Antigenic differences among Newcastle disease virus strains of different genotypes used in vaccine formulation affect viral shedding after a virulent challenge. *Vaccine* 25:7238–7246
- Mottet A, G Tempio (2017). Global poultry production: Current state and future outlook and challenges. *World Poult Sci J* 73:245–256
- Munir M, M Chowdhury, Z Ahmed (2016). Emergence of new sub-genotypes of Newcastle disease virus in Pakistan. *J Avian Res* 2:170
- Munir M, M Abbas, MT Khan, S Zohari, M Berg (2012). Genomic and biological characterization of a velogenic Newcastle disease virus isolated from a healthy backyard poultry flock in 2010. *Vir J* 9:46
- Nagajothi S, P Mekala, A Raja, M Raja, PS Kumar, G Thirumalaisamy (2023). Antiviral activity of *Andrographis paniculata* against NDV2K35 strain of Newcastle disease virus in chicken embryo fibroblast cells. *Pharm Innov J* 12:1461–1469
- Nagajothi S, P Mekala, A Raja, M Raja, PS Kumar (2020). *In ovo* antiviral activity of *Andrographis paniculata* against NDV2K35 strain of Newcastle disease virus. *J Pharm Phytochem* 9:2023–2029
- Nazir I, M Rabbani, AA Sheikh, MI Riaz, S Raza, Q Ul-Ain, AY Shaheen, A Kokab (2021). Evaluation of *in ovo* antiviral activities of medicinal flowers against Newcastle disease virus and avian influenza virus. *Intl J Agric Biol* 26:185–192
- Nyandoro SS (2017). *In ovo* antiviral activity of the constituents of *Artabotrys monteiroae* and *Artabotrys modestus* against infectious bursal disease and newcastle disease viruses. *Intl J Biol Chem Sci* 11:3075–3085
- Ohemu TL, A Ahmed, TE Alemika, SC Chollom, TP Yakubu, DG Dafam, NJ Damos (2020). *In-ovo* biological activity of *Boswellia dalzielii* stem bark extract and fractions against Newcastle disease virus. *J Pharmacogn Phytother* 12:62–70
- OIE (2009). Chapter 2.3.14. Newcastle disease. In: *OIE Terrestrial Manual 2009: Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*, pp:576–589. World Organisation for Animal Health, Paris, France
- Pakistan Economic Survey (2022–2023). Finance Division, Government of Pakistan, Islamabad-Pakistan
- Paldurai A, SH Kim, B Nayak, S Xiao, H Shive, PL Collins, SK Samal (2014). Evaluation of the contributions of individual viral genes to newcastle disease virus virulence and pathogenesis. *Virol J* 88:8579–8596
- Pandey A, N Singh, S Sambhara, SK Mittal (2010). Egg-independent vaccine strategies for highly pathogenic H5N1 influenza viruses. *Hum Vacci* 6:178–188
- Priya MS, TRGK Murthy, T Vijayanand (2022). Antiviral effect of herbal mixture (garlic, nilavembu, turmeric, coriander, and fenugreek) against Newcastle disease virus *in ovo*. *J Appl Poult Res* 31:100229
- Rima B, A Balkema-Buschmann, WG Dundon, P Duprex, A Easton, R Fouchier, R Rota (2019). ICTV virus taxonomy profile: Paramyxoviridae. *J Gen Vir* 100:1593–1594
- Saadat Y, SA Ghafouri, F Tehrani, AG Langeroudi (2014). An active serological survey of antibodies to newcastle disease and avian influenza (H9N2) viruses in the unvaccinated backyard poultry in Bushehr province, Iran, 2012–2013. *Asian Pac J Trop Biomed* 4:213–216
- Shabbir MZ, M Abbas, T Yaqub, N Mukhtar, A Subhani, H Habib, MU Sohail, M Munir (2013). Genetic analysis of Newcastle disease virus from Punjab, Pakistan. *Vir Gen* 46:309–315
- Umar S (2017). Emergence of new sub-genotypes of Newcastle disease virus in Pakistan. *World Poult Sci J* 73:567–580
- Wang M, Y Yu, K Brad, W Xie, XY Zhang (2016). The screening and evaluation of herbs and identification of herbal combinations with anti-viral effects on Newcastle disease virus. *Brit Poult Sci* 57:34–43
- Yadav P, S Choudhury, S Barua, N Khandelwal, N Kumar, A Shukla, SK Garg (2020). *Polyalthia longifolia* leaves methanolic extract targets entry and budding of viruses-*an in vitro* experimental study against paramyxoviruses. *J Ethnopharmacol* 248:1–26
- Yasmin A, S Chia, Q Looi, A Omar, M Noordin, A Ideris (2020). Herbal extracts as antiviral agents. *Feed addit* 2020:115–132
- Zain Eldeen A, AM Younes, KM El-bayoumi, A Bazid, MM Effat, NMAI Eissa, M Salman, M AboElkhair (2024). Influence of some herbals on immunostimulation of cellular immunity in experimentally ndv-vaccinated chicks. *Egypt J Vet Sci* 55:1165–1174