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Review Article

# Concise Review on Herbal Medicine Effects on Combating Newcastle Disease Virus as a Threat to the Poultry Industry

**Kamyar Ahmadi [1], Mahdieh Farzanehpour [1], Ehsan Malekara [2], Seyed Mojtaba Aghaie Tabaeezavareh [3], Hadi Esmaeili Gouvarchin Ghaleh [1], Majid Mirzaei Nodooshan [1*]**

[1] Applied Virology Research Center, Biomedicine Technologies Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran
[2] Applied Microbiology Research Center, Biomedicine Technologies Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran
[3] Center for Science and Technology of Biology, Faculty of Basic Sciences, Imam Hossein Comprehensive University, Tehran, Iran

**Corresponding Author:** Majid Mirzaei Nodooshan, MSc, Applied Virology Research Center, Biomedicine Technologies Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran. Tel: +98-9120687556, E-mail: majid.mirzaei.n.67@gmail.com

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**Abstract**
Many domestic and wild avian species are afflicted with Newcastle disease virus (NDV), an infectious bird illness. It is a zoonotic illness with a broad geographic prevalence. The avian paramyxovirus serotype 1 virus, together with viruses of the other eight serotypes (avian paramyxovirus 1–9), has been classified as belonging to the genus Avulavirus, subfamily paramyxovirinae, and family paramyxoviridae. Most of Asia, Africa, and certain North and South American nations have endemic outbreaks of the dangerous NDV virus in chickens. The clinical symptoms of Paramyxovirus, a virus with a global distribution that affects chickens of all ages, vary greatly depending on the viral strain, species and age of the bird, treatment, concomitant diseases, and pre-existing immunity. Respiratory aerosols, exposure to faeces and other excretions from diseased birds, recently introduced birds, selling and giving away ill birds, and contact with contaminated feed, water, equipment, cannibalism, and clothes are all ways that NDV is spread. The clinical manifestations of the illness include rales, tremors, paralyzed wings and legs, twisted necks, circling, colonic spasms, and total paralysis. When a human is exposed to high levels of the virus, Newcastle disease virus may result in conjunctivitis. Since the dawn of civilization, natural remedies derived from plants, animals, microorganisms, and marine sources have been used to cure a variety of illnesses. The basis for contemporary drug research is information from our predecessors. This review aims to provide a succinct overview of the effects of herbal medicines in treating the Newcastle disease virus.

**Keywords:** Newcastle Disease Virus, Paramyxovirus, Pathogenicity, Zoonosis, Herbal Medicine
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## Introduction

As long as humans have existed, medicine has existed. Ancient writings from China, India, and North Africa provide evidence of the use of natural ingredients as medicine.[1] A Sumerian clay tablet containing written treatments for several illnesses that dates back 4000 years is considered to be the first known medical record. Examples of such treatments include the use of mandrake for pain alleviation and garlic for heart and circulation problems. The development of contemporary medicine today is based on scientific research and scientists' observational efforts.[2] However, a large part of this information was developed by our predecessors' old wisdom. For both infectious and non-communicable disorders, plants have a long history of usage as traditional remedies. Since the development of contemporary drug discovery methodologies, medicinal plants have been researched as a source of new therapeutic compounds.[3] Plants produce a variety of structurally diverse and frequently complex secondary metabolites that serve a variety of purposes. These compounds have evolved for a specific biological purpose within plants, and they frequently display biologically relevant privileged molecular scaffolds, which makes them a good candidate for use as a drug discovery resource.[4] The literature on the antiviral action of plants and their components is extensive, suggesting that plants may be a source of new antiviral medicines. Additionally, several natural compounds have been shown to have anticancer properties that might be utilized to prevent or cure malignancies brought on by viral infections like HCV and HIV.[5] Globally, viral infections place a heavy economic and health cost. This is demonstrated by the advent of the Coronavirus Disease 2019 (COVID-19) pandemic, which is the biggest pandemic since the 1918 influenza epidemic and has resulted in >180 million infections and 4 million fatalities.[6] To prevent and control upcoming worldwide pandemics, it is essential to comprehend the viral danger. Novel, powerful antivirals are

required, especially in light of the emergence of new viruses and the emergence of antiviral medication resistance. The greatest domestic animal stock in the world, measured by the number of animals, is poultry.[7] Backyard flocks make up a large percentage of poultry production, especially in developing nations, and poultry production as a whole. Villagers farm chicken in these nations to provide for their families' food needs and as extra sources of revenue. Low biosecurity standards and a higher risk of infectious illnesses like Newcastle disease virus or zoonosis like Highly Pathogenic Avian Influenza (HPAI) are implied by backyard production practices.[8] Many domestic and wild avian species are afflicted by the infectious sickness known as Newcastle disease virus, which can also infect people. Avian Paramyxovirus-1, a single strand non-segmented negative sense RNA virus that causes NDV, is a serious viral illness that affects poultry. One of the most significant poultry illnesses in the world is the Newcastle disease virus, a viral illness brought on by avian paramyxovirus serotype 1 (APMV1).[9] In contrast to Europe, where outbreaks of NDV throughout poultry are infrequent, the disease continues to be an epizootic in Asia, Africa, Central America, and South America. About 66 percent of the population in developing nations consumes a diet that is inadequate in animal proteins. Newcastle disease virus is a serious danger to the chicken industry and a disease with a significant economic impact. The rate of death and morbidity in a flock varies depending on the variance in NDV strains reduction in egg production and pathotyping of NDV using reverse transcriptase polymerase chain reaction (RT-PCR) and restriction enzyme analysis.[10] The presence of velogenic NDV was determined by viral isolation, serological diagnostics such as the hemagglutination inhibition (HI) test, ELISA, and molecular diagnostics like real-time PCR.[11] The meat quality of chicken may be impacted by NDV's economic relevance. The amount of eggs available is growing at a pace of around 4% each year. Because it is affordable and contains high-quality protein, meat is a highly significant source of protein in the diets of people in the majority of developing nations.[12] The illness is spread via infected bird droppings and secretions from the mouth, nose, and eyes. Direct contact with the secretions of sick birds; mostly through ingestion (through the feces or oral route) and inhalation, fomites: feed, water, tools, settings, people's clothing, boots, bags, egg trays/crates, etc. Faeces, like those found in contaminated eggshells, help an agent survive longer. Incubation, clinical stages, and a brief time during convalescence are when the virus is shed. The NCD virus can be mechanically transmitted by dogs, fleas, rodents, insects, and other animals (Figure 1).

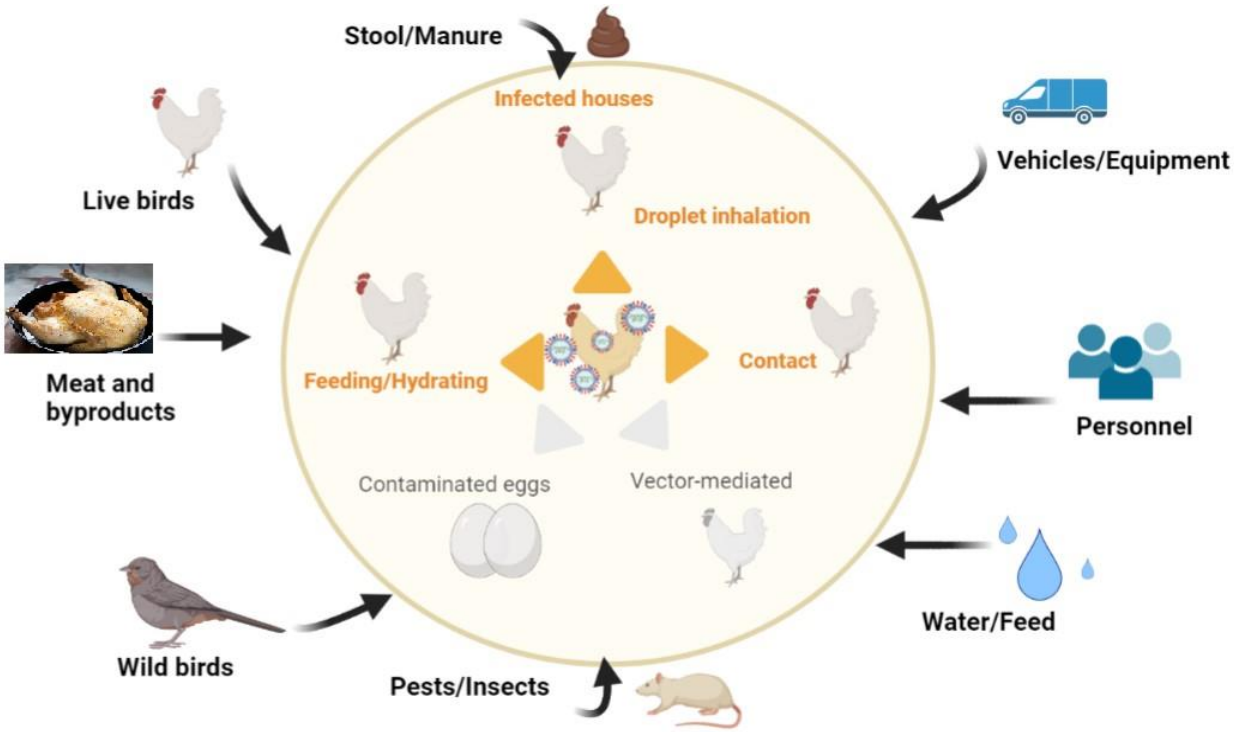


**Figure 1.** Transmission Routes of Newcastle Virus.

The primary method of transmission of the illness is direct contact between healthy birds and bodily excretions of diseased birds. From an infected flock to a healthy one, virus-bearing material can also be transferred via shoes and clothing. Therefore, possible transmission pathways include contact between birds as well as the transit of contaminated

goods such as manure, equipment, feed, and water. The virus can endure for several weeks on materials like bird excrement and feathers in a warm, humid atmosphere. Direct contact with the bodily fluids of sick birds, particularly their faeces, and aerosol contact are the two main ways the disease is transmitted.[9] The goal of this review is to provide a brief overview of the effectiveness of herbal remedies in treating Newcastle disease.

## Structure and Genomic Organization of NDV

There are no segmented, encapsulated RNA viruses with helical capsid symmetry among the members of the Paramyxoviridae family. Its single-stranded, negatively polar genome is assembled into capsids in the cytoplasm.[13] As a result, a modified cell membrane envelope budding from the cell surface. Newcastle disease virus particles are big, pleomorphic, and range in size from 150 to 400 nm.[14] The molecular weight of the NDV's negative sense single-strand RNA genome ranges from 5.2 to 5.7 × 10 (6) Daltons. Genome length ranges from 15,186 nucleotides for class II genotype I-IV early isolates to 15,192 nucleotides for class II genotype V-VIII late isolates to 15,198 nucleotides for class I.[15] Fusion (F) protein and hemagglutinin-neuraminidase (HN) protein, two viral glycoproteins with an outer surface length of 8–12 nm, make up the vision's envelope, which was obtained from the host cell's plasma membrane. The HN protein attaches the virion to the host cell receptor, while the fusion (F) protein works to fuse the viral envelope with the host cell membrane. The two primary immunogenic proteins in a virion are F and HN.[16] The helical nucleocapsid of the vision's center constantly serves as a template for the production of RNA. Nucleocapsid (NP) proteins that are firmly attached to the genomic RNA make up the core. They also have big polymerase (L) and phosphoprotein (P) proteins linked to them. The matrix protein, also known as the M protein, lies between the viral envelope and nucleocapsid core. The assembly of the viral particles is propelled by this protein (Figure 2).[17]

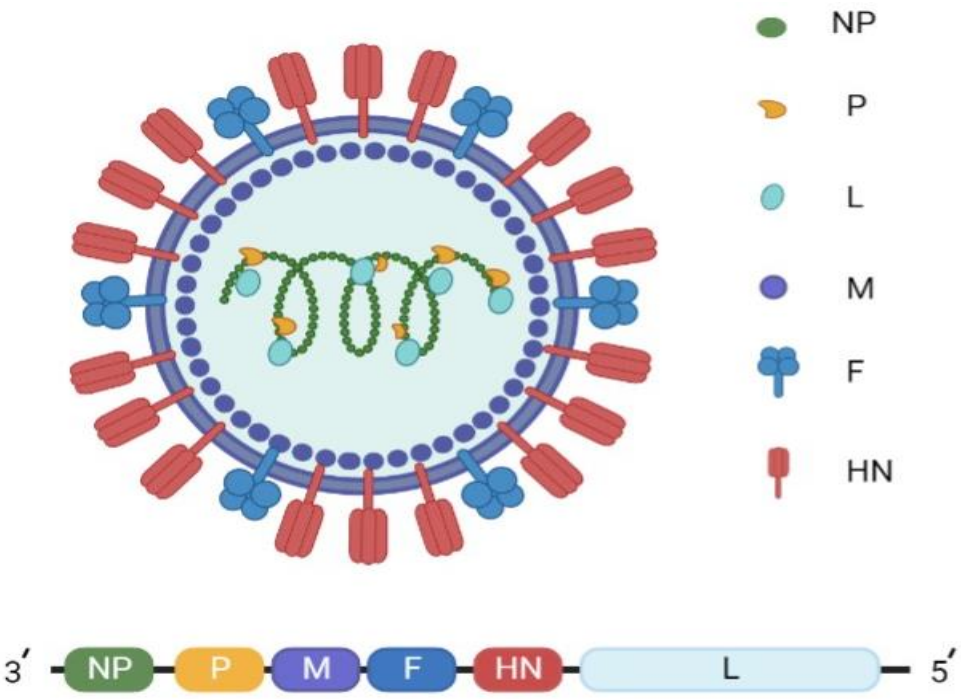


**Figure 2.** Structure of NDV. The six main viral proteins include nucleoprotein (NP), phosphoprotein (P), matrix protein (M), fusion protein (F), hemagglutinin-neuraminidase (HN), and large polymerase protein (L). ssRNA: single-stranded RNA.

## Epidemiology, Pathogenicity and Clinical Signs

There are several domestic and wild bird species of Newcastle disease virus host. Turkeys rarely show serious symptoms of illness, although chickens are more vulnerable to it.[18] The susceptibility varies among game birds (pheasants, partridges, quail, and guinea fowl) and parrots (order Psittaciformes); cockatiels are vulnerable. Waterfowl and wild birds (order Anseriformes) may have subclinical viral infection; certain isolates from particular genotypes have led to epiornitics in these species. An illness linked to APMV-1 has been seen in young cormorants (Phalacrocorax spp.). Pigeons (order Columbiformes) are known to be vulnerable, and disease has been reported in ostriches (order Struthioniformes). Except for cases of acute sickness in wild ospreys (Pandion haliaetus), white-tailed sea eagles (Haliaeetus albicilla), bearded vultures (Gypaetus barbatus), and several species of falcons, raptors are often resistant to NDV.[19] Gulls (order Charadriiformes), chickens (order

Strigiformes), and pelicans are some other birds that have been linked to NDV (order Pelecaniformes). The vulnerability of passerine birds (order Passeriformes) varies; some species exhibit no symptoms yet still excrete NDV, whilst others may have severe sickness. Crows and ravens (genus Corvus) have been reported to have died. Penguins (order Sphenisciformes) have been known to develop acute NDV.[20] The rates of morbidity and mortality vary depending on the virus strain and the species. Conjunctivitis, sub-conjunctival haemorrhage, severe lachrymation, oedema of the eyelids, and unilateral or bilateral reddening are symptoms of infection in humans. The host has a significant impact on the pathogenicity of NDV strains. Even with strains that are fatal for hens, ducks can become sick and have little to no clinical symptoms.[21] Although dosage, delivery method, age of the bird, and environmental factors can have an impact, the viral strain that causes NDV in chickens is mostly responsible for its pathogenicity. In general, a chicken's susceptibility to the illness increases with age. Young chickens may die suddenly in the wild from virulent viruses without having significant clinical symptoms, whereas older birds may have a longer illness with recognizable clinical symptoms.[22] The susceptibility of hens to the illness does not appear to be significantly influenced by breed or genetic stock. From moderate to severe, the condition might vary. Exotic Newcastle disease virus (ENDV), a severe and extremely infectious variation of the illness, kills so many birds quickly and without warning. Numerous variables, including the virus/pathotype, host species, age of the animal, co-infection with other organisms, environmental stress, and immunological state, influence the clinical symptoms seen in birds infected with NDV.[23] The diagnosis of NDV cannot be made with just the use of clinical indicators. The aggressiveness of the virus strain, level of immunization immunity, environmental factors, and flock health all affect morbidity and mortality. The three most virulent avian paramyxovirus (APMV-1) pathotype' clinical symptoms are listed below: Lentogenic strains: Typically linked to moderate respiratory illness characterized by coughing, gasping, sneezing, and rales.[24] Severe symptoms may develop if there are additional co-infectious agents present. Mortality is quite low. Mesogenic strains: in some animals, they can result in acute respiratory illness and neurologic symptoms. The mortality rate is typically modest (less than 10%). Severe symptoms may develop if there are other circulating co-infectious agents.[25] Most frequently, velogenic strains induce a fatal severe sickness in hens; the main symptoms are respiratory and/or nervous. Lethargy, inappetence, ruffled feathers, oedema, and injection of conjunctiva are a few of the initial clinical symptoms, however they can vary. Birds may have dyspnea, head and neck swelling, cyanotic coloring, and greenish or white watery diarrhoea as the illness worsens.[26]

## Herbal Medicine of Newcastle Disease Virus

Because they have been linked to the treatment of several infectious and non-infectious ailments, medicinal plants are seen as a supplementary method of containing this virus, especially in underdeveloped nations. Plant-derived alkaloids, flavonoids, saponins, and tannins have been considered new antiviral drugs.[27]

## In vitro Antiviral Activity of Medicinal Plants

Hardy Azadirachta indica, sometimes known as the neem tree, is a member of the Meliaceae family and is widely distributed throughout South Asia and certain regions of Africa. The advantages of numerous components of A. indica, including its leaves, flowers, root, bark, and fruit, are covered in literature from Ayurvedic times.[28] A. indica has a wide variety of chemically and structurally varied physiologically active chemicals. However, it appears that its antiviral properties are restricted to certain viruses, including fowl pox, smallpox, and polio, as examined by virus inhibition assays. It has been reported that different parts of A. indica contain more than 140 different compounds, which are used to treat bacterial and fungal diseases.[29] For the NDV Kamarvo strain, VERO cells are employed as the culture, while embrocated eggs are used for the NDV Lasota strain in nine to eleven-day-old chicks. The findings demonstrated that metabolic neem leaf extracts had antiviral activity in VERO cells without any detectable host cytotoxicity, as did neem seed extracts in hexane and chloroform.[30] Although information is few and restricted to laboratory methods, sweet wormwood, commonly known as *Artemisia annua* L., shows modest antiviral action against NDV. The components of *A. annua* were extracted using decoction techniques, and the compounds' ability to suppress NDV was examined in chicken embryos. The outcomes showed that these extracts prevented NDV from proliferating in chicken embryos.[31] The African baobab tree is also known as *Adansonia digitata*. Using 175 specific antibody-negative embrocated chicken eggs infected with a field strain of NDV, the antiviral activity of methanolic extracts of this tree's bark was investigated. In order to assess mortality using both a negative and positive control with high concentrations of extract or virus, respectively, eight graded concentrations were created after 24 hours of exposure to NDV and then incubated for 12 hours at 37 ºC. The outcomes showed that 200 and 250 mg/ml doses of baobab root bark extracts have antiviral activity against NDV.[32] An experiment was used to examine the effectiveness of aqueous seed extract from *Moringa oleifera* against NDV. Increasing extract concentration increased embryo survival in a direct proportion. An increase in extract concentration was directly correlated with viral death against NDV and inversely correlated with antibody formation.[33] Chromones, flavonoids, anthrones, and anthraquinones are among the

physiologically active substances found in Aloe hijazensis' leaves and roots. Antiviral action has been discovered in Barbaloin (Aloe) and emodin (Rheum, Polygonum). Using specific pathogen-free (SPE) chicken embryos, Aloe hijazensis leaves, flowers, roots, and flower peduncles were tested against NDV. It was shown that flower and leaf extracts showed higher antiviral activity against NDV than those from the plant's other components.[34]

### In vivo Antiviral Activity of Medicinal Plants

According to anecdotal evidence, NDV and other chicken illnesses have been treated using aloe species in Kenya, Tanzania, and Uganda to lessen their symptoms. To test the effectiveness of aloe species against NDV in rural poultry across multiple Tanzanian villages, two duplicate studies were conducted.[35] Four-month-old local hens devoid of NDV antibodies were employed, and half of them received aloe extract treatment after contracting NDV. In both treated and untreated birds, body weight, antibody levels, clinical symptoms, and death were tracked. In comparison to untreated hens, the results demonstrated that aloe treatment reduced the severity of clinical symptoms and the death rate during the acute phase of infection. Additionally, there was no aloe impact on antibody levels that was significant ($p$ >0.05) and that could be attributable to the survival of hens. The results of this investigation showed that Aloe secundiflora could be a contender for treating NDV in hens.[36] Alkaloidal components found in the fruit extract of Cucumis metuliferus have been proven to have antiviral activities when tested on NDV-infected chicks. Birds with NDV infection (a control group vs a group given C. metuliferus injections) were inspected for illness symptoms, infected organs were analyzed histopatologically, and the birds' death dates were recorded. The outcomes showed that this plant's alkaloids were able to counteract the virus's harmful effects on chicks. Extract was injected intraperitoneal to alleviate the clinical symptoms; 600 mg/kg was more effective than 400 mg/kg.[37] In experiments on chickens, Anthocleista nobilis ethanol extracts were utilized to cure NDV. Following NDV infection, research found that these extracts' biochemical values for chicken birds dropped under the normal range, providing a strong signal for NDV therapy.[38]

### Boosting Immunity

The immune system and belly fat deposition in broiler chicken were examined using polysavone, an extract of Medicago sativa (alfalfa). At five and six weeks old, this extract lowered belly fat deposition but had no statistically significant ($p$ >0.05) impact on body weight, feed intake, or feed gain ratio. In comparison to the control group, the extract increased the weights of the thymus, spleen, and bursa at ages four and five weeks, all of which were associated with an increase in immunological activity without impairing the performance of broiler chickens.[39] It has been demonstrated that tannins included in the aqueous extract from Melissa officinalis leaves may prevent NDV infection in chick cell culture and eggs as well as stop NDV-induced haemagglutination.[40] Momordica cochinchinensis seed extracts have been utilized to assess any effects the plant may have on hens' NDV immunological responses. The trial findings showed that after receiving the NDV vaccination, the humoral immune response was boosted, but the cellular immunological response did not change significantly ($p$ >0.05). No negative consequences on the hens' ability to grow during the trial.[41]

### Conclusion

NDV, a disease that affects the chicken business economically, may be effectively treated with a variety of medicinal herbs that have great antiviral and immune-boosting properties. These botanicals might replace commonly used, synthetic medications, which have a number of risks, such as drug resistance in endemic pathogen populations and drug residues in poultry meat. It could be possible to use less chemical prophylactics in chicken husbandry by doing this. It is advised that active product(s) from these plants should be extracted and commercialized for use in feed in order to support the scientific validation of medicinal plants for immunity-boosting and therapeutic actions in poultry birds.

### Authors' Contributions

All authors contributed equally to this study.

### Ethical Approval

The study was approved by the Institutional Review Board of, Baqiyatallah University of Medical Sciences (IR.BMSU.BLC.1400.011).

### Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

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