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Reference Prelude VL 14
http://www.ethnovet.com/files/poster_avian_flu_ethnovet2.htm

Abstract

This paper reviews the plants that have the potential to be used in backyard poultry systems against Newcastle disease virus and avian influenza. A literature review was conducted of all plants used to treat these illnesses and symptoms associated with them. It is paramount for small-scale farmers to have ways of treating these diseases with organic methods. Specialty birds and backyard flocks have been culled worldwide, with little or no evidence that they carried any of the pathogenic strains of avian flu. This resulted in economic and genetic losses for small-scale farmers. This paper illustrates that ethnoveterinary remedies can be used for large-scale health problems. This paper addresses one of the limitations that a livestock scientist claims of EVM: that EVM has little or nothing to offer against the acute viral diseases of animals.

Family poultry and Newcastle disease in Africa: the role of ethnoveterinary medicine

Newcastle disease (ND) is especially devastating to the free-ranging flocks - it kills an average of 70-80% of unvaccinated family poultry every year. We will try to establish with this case study that ethnoveterinary medicine can play an important role in the control of the disease.

Newcastle Disease

Newcastle disease is caused by an enveloped RNA virus of the Paramyxoviridae family that is known to be able to infect at least 241 species of birds. Clinical signs vary with chickens being very sensitive to the virus and waterfowl often being asymptomatic. There are 3 pathotypes of ND: velogenic, mesogenic and lentogenic. The velogenic strain is the most virulent and there are 2 subtypes: viscerotropic and neurotropic. Viscerotropic velogenic ND is characterized by diarrhea, facial edema, nasal discharge and often, sudden death. The neurotropic velogenic strain manifests as respiratory signs (nasal discharge, coughing, sneezing) followed by neurologic signs (leg and wing paralysis, torticollis, opithotonos) and high mortality without gastro-intestinal lesions. The mesogenic strain is characterized by respiratory and neurologic signs with low mortality while the lentogenic strain manifests as mild respiratory signs. There is also an asymptomatic enteric infection where clinically normal birds have an avirulant virus replicating in the gut.

Family Poultry

Family poultry (which are small flocks of free ranging birds owned and cared for primarily by women and children) provide a critical source of food and income for people in developing countries.

Ethnoveterinary medicine for Newcastle Disease in Africa

Although a thermostable vaccine is available the majority of family poultry in Africa are not vaccinated against ND. Since there are few veterinarians working in rural Africa and family income is often limited, many farmers rely on their ancestral knowledge to control Newcastle disease. Plants used to control ND (Table 1), are usually crushed and mixed with drinking water.

Table 1: Plants used to treat Newcastle Disease in Africa

Plants(s) used	**Part(s) used**
Adansonia digitata	Fruit
Agave americana + pepper fruit & soot	Leaf
Agave sisalana	Leaf/stalk
Agave sisalana + *Aloe secundiflora* leaf, pepper fruit & oswawandhe root	Leaf
Allium sativum	Bulb
Aloe nuttii	Not specified
Aloe nuttii + *Kigelia aethiopica*, *Sesamum angolense* & soil	Not specified
Aloe secundiflora	Leaf
Aloe secundiflora + *Capsicum sp.* fruit & *Amaranthus hybridicus* leaf	Leaf
Aloe secundiflora + *Agave sisalana* leaf, pepper fruit & oswawandhe	Leaf
Aloe sp.	Leaf
Amaranthus hybridicus + *Capsicum sp.* fruit & *Aloe secundiflora* leaf	Leaf & flower
Anacardium sp.	Not specified
Anogeissus leiocarpus	Root
Apodytes dimidiate	Leaf& stalk
Azadirachta indica	Bark/leaf

Butyrospermum paradosym + *Combretum micranthum* bark & *Ficus gnaphalocarpa* bark	Bark
Capsicum annuum	Seed
Capsicum annuum + *Iboza multiflora* leaf	Fruit
Capsicum frutescens + *Lagenaria breviflora* fruit	Seed/fruit
Capsicum sp. + *Amaranthus hybridicus* Leaf/flower & *Aloe secundiflora*	Seed/fruit
Capsicum sp. + *Khaya senegalensis* bark	Seed
Cassia didymobotrya	Leaf
Cassia sieberiana	Bark
Cassia tora	Leaf/stalk
Cissus quadrangularis	Leaf/stalk
Citrus limon + *Capsicum frutescens* fruit & *Opuntia vulgaris* stem	Fruit
Combretum micranthum + *Butyrospermum paradoxum* bark & *Ficus gnaphalocarpa* bark	Bark
Diplorhynchus condylocarpon	Leaf/stalk
Euphorbia ingens	Branch
Euphorbia metabelensis	Latex
Euphorbia tirucalli	Leaf/stalk
Ficus sp.	Leaf/stalk
Ficus gnaaphalocarpa + *Combretum micranthum* bark & *Butyrospermum paradoxum* bark	Bark
Guibourtia coleosperma	Leaf/stalk
Iboza multiflora + *Capsicum annuum* fruit or *Euphorbia ingens* stem	Leaf
Inula glomerata	Leaf/stalk
Khaya senegalensis + *Capsicum sp.*	Bark
Kigelia aethiopica + *Aloe nuttii, Sesamum angolense* & soil	Not specified
Kigelia africana	Leaf/stalk
Lagenaria breviflora + *Capsicum frutescens* fruit	Fruit
Lamnea acida	Bark
Mangifera indica	Bark/leaf
Mucuna sp	Leaf
Ochna pulchra	Leaf/stalk
Parkia filicoidea	Bark
Physostigma mesoponticum	Not specified
Piper nigrum	Fruit
Sesamum angolense + *Aloe nuttii* & *Kigelia aethiopica*	Not specified
Strychnos potatorum	Leaf/stalk
Swartzia madagascariensis	Bark
Synadenium volkensii	Bark
Tephrosia vogelii	Not specified
Tylostemon sp	Not specified
Ziziphus abyssinica	Leaf/stalk

Five plants have been assessed for their activity against ND: *Aloe secundiflora*, *Azadirachta indica*, *Cassia tora*, *Euphorbia ingens* and a plant mixture containing *Capsicum frutescens*. Four species, *Adansonia digitata*, *Allium sativum*, *Combretum micranthum* and *Mangifera indica*, are antiviral, but have not been tested against ND. *Amaranthus hybridicus*, *Combretum micranthum*, *Ficus gnaphalcap*a and *Tephrosia vogelii*, are in the same genus as species with antiviral activity.

1. Plants used for Newcastle disease that have activity against this virus.
Of the five species evaluated for their activity against ND, *Aloe secundiflora*, *Azadirachta indica*, *Cassia tora* and *Euphorbia ingens* have yielded promising results; however a study on the combination of *Capsicum frutescens*, *Citrus limon* and *Opuntia vulgaris* failed to demonstrate any clinical benefit in chickens infected with Newcastle disease.
Aloe sp.

a) *Aloe secundiflora*
Aloe secundiflora decreased morbidity and mortality in experimentally infected chickens. Treatment with *A. secundiflora* at the time of infection resulted in a 21.6% decrease in mortality whereas pre-treatment for 2 weeks prior to infection resulted in a 31.6% reduction in mortality compared to untreated infected birds. Since farmers are aware of the seasonality of Newcastle disease, pre-treatment is a feasible practice. The extract used in the experiment was prepared in much the same way as villagers would and was composed of the inner gel, containing antiviral polysaccharides such as acemannan and the outer sap, containing the anthraquinone glycosides. The anthraquinone components in *Aloe* spp., (aloenin and aloin), are at least partly responsible for the anti-Newcastle disease virus activity. Enveloped viruses are sensitive to anthraquinones: influenza virus, pseudorabies virus and varicella-zoster virus, herpes simplex virus type 1, herpes simplex virus type 2 are all impaired by various anthraquinones.

b) *Cassia tora*
Cassia tora contains significant quantities of anthraquinones and has activity against Newcastle disease virus. Related species with anti-Newcastle disease virus activity include *Cassia auriculata* and *Cassia fistula*.

c) *Azadirachta indica*
Although it does possess activity against Newcastle disease virus, and foot and mouth disease virus, it is likely that *Azadirachta indica*'s anti-inflammatory and immune-stimulating properties may better explain its usefulness against ND.

d) *Euphorbia ingens*
In a small clinical trial, *Euphorbia ingens* branches were crushed and soaked in the chickens' drinking water overnight. When this water was administered at the same time as the birds were infected with Newcastle disease, mortality was decreased by 38.4%. Pretreatment with *Euphorbia ingens* decreased mortality by 100%. Other *Euphorbia* species, or their chemical constituents, possess significant antiviral activity: *E compositum*, *E. thymifolia* and *E. tirucalli* against herpes simplex viruses, *E. australis* against human cytomegalovirus, *E. compositum* against respiratory syncytial virus and influenza and *E. grantii* and *E. hirta* against poliovirus and coxsackie virus.

e) *Capsicum sp.*
Capsicum spp. are widely used to treat a variety of diseases, often in combination with other plants. Capsaicin, one of the constituents of *Capsicum*, is thought to improve resistance to disease in poultry. Various combinations with *Iboza multiflora*, *Lagenaria breviflora, Amaranthus hybridicus, Aloe secundiflora* and *Khaya senegalensis* are used to control Newcastle disease in Africa. Although the combination with *Citrus limon* and *Opuntia vulgaris* was not effective in controlling ND in a clinical trial, further study is justified.

2. Plants used for Newcastle disease that have antiviral activity against other viruses.

Four species of plants used to control ND (from Table 1) have antiviral activity against other viruses but have not been assessed for their anti-NDV properties:

Table 2: Plants used to control Newcastle disease that have antiviral activity against other viruses.

Plant (or constituents of)	Active against these viruses
Adansonia digitata	Poliovirus, HSV, SINV
Allium sativum	HSV1&2, parainfluenza-3, Vaccinia virus, VSV, HRV-2 HCMV, Murine CMV, Influenza B
Cassia didymobotrya	VSV
Combretum micranthum	HSV1, HSV-2
Mangifera indica	HSV-1, HSV-2

HCMV = human cytomegalovirus; HRV-2 = human rhinovirus type 2; HSV = herpes simplex virus;
Murine CMV = murine cytomegalovirus; SINV = Sindbis virus;
VSV = vesicular stomatitis virus

3. Plants used for Newcastle disease that are closely related (same genus) to species with antiviral activity.

Several species of plants used to control ND are closely related (same genus) to species with known antiviral activity.

Table 3: Related plants with antiviral activity.

Plant (or constituents of)	Related plant	Active against these viruses
Amaranthus hybridicus	*A. viridis*	TMV
Cassia didymobotrya, Cassia sieberiana, Cassia tora	*C. mimosoides*	HSV-1
Citrus limon	*C. junos*	Influenza A virus
Combretum micranthum	*C. hartmaniannum*	HIV
Ficus gnaphalocarpa, Ficus sp.	*F. politica, F. ovata*	HIV, HSV, poliovirus
Tephrosia vogelii	*T. madrensis, T. viridiflora, T. crassiflora*	Dengue virus

HIV = human immunodeficiency virus; HSV = herpes simplex virus; SINV = Sindbis virus; TMV = tobacco mosaic virus

4. Other properties of plant species used to control Newcastle disease.

Plants that support the immune system or provide symptomatic relief are also important. Since family poultry are almost invariably infected with the velogenic strains of Newcastle disease, the clinical signs are primarily diarrhea, respiratory distress and sudden death. Plants used for the control of Newcastle disease that exhibit anti-diarrheal properties include *Adansonia digitata*, *Mangifera indica* and *Strychnos potatorum*. *Adansonia digitata* and *Cassia didymobotrya* both have broncho-relaxant properties and *Allium sativum*, *Azadirachta indica*, *Mangifera indica*, *Piper nigrum* and *Trigonella goenum-graecum* have immune-enhancing properties. Closely related species with relevant activity include *Ziziphus abyssinica* for diarrhea, and *Aloe vera* and *Tephrosia purpurea* as immune stimulants.

5. Ecosystem health and ethnoveterinary medicine

Maintaining biodiversity will be necessary if families are to rely, even in part, on ethnoveterinary medicine to assist in the control of Newcastle disease. Ethnoveterinary medicine can play a significant role in the control of Newcastle disease in Africa. Both *Aloe secundiflora* and *Euphorbia ingens* decrease morbidity and mortality in poultry affected with this disease. Further investigation of these and the dozens of other plants used to control Newcastle disease are needed.

Evaluation of plants used to treat unspecified poultry respiratory diseases for their efficacy against AI virus.

Avian influenza poses a significant risk to both avian and human health. It has been commonplace in the media for wild birds, free-range and backyard poultry to be blamed for spreading the virus. However an investigation by the NGO GRAIN indicates that the development of industrial poultry farms in Asia and the global poultry trade should be investigated for helping to spread the virus. At the time of writing (April 2006), at least 103 people have been infected by H5N1 influenza A viruses; however human-to-human transmission is uncommon. Very limited data is available on the use of ethnoveterinary medicine for the control of avian influenza. The objective of this case study is to document the plants used for the control of unspecified respiratory disease and evaluate their effectiveness against avian influenza.
Avian influenza is caused by an enveloped RNA virus of the Orthomyxoviridae family. It is a type A influenza and is further subdivided based on membrane proteins into 15 haemagglutinin (H1 to H15) and nine neuraminidase (N1 to N9) subtypes. Wild waterfowl are the natural hosts but mammals and many species of birds can be infected.

Who's Coming Home?

Clinically, avian influenza can be classified as either low pathogenic avian influenza (LPAI) or highly pathogenic avian influenza (HPAI). Infection with LPAI is usually asymptomatic in wild waterfowl but may cause disease in domestic poultry. HPAI, usually caused by H5 or H7 subtypes, affects poultry primarily and carries with it a mortality rate approaching 100%. Since the virus replicates in both the respiratory and gastro-intestinal systems, clinical signs and viral shedding are related to these organ systems. Much of the present concern with avian influenza is its potential role in the creation of the next human influenza pandemic. When two strains of influenza (eg. avian influenza and human influenza) concurrently infect the same host, the viral genomes recombine and create a novel subtype – this process is known as antigenic shift. The last three major antigenic shifts in influenza A virus led to the human influenza pandemics of 1918 (H1 Spanish flu), 1957 (H2 Asian flu) and 1968 (H3 Hong Kong flu). A 1997 A/H5N1 outbreak in Hong Kong was controlled with depopulation.

Recent research has revealed that the H5N1 virus binds to sugars on the surface of cells in the lower lung resulting in damage to the alveoli. The molecules in question are sialic acid linked to galactose by an α-2,3 linkage and by an α-2,6 linkage. There is also binding to the alveolar macrophages – white blood cells which can trigger the inflammatory immune reaction. Researchers at the Scripps Research Institute in California claim that at least two mutations would be needed for the H5 virus to switch to the α-2,6 cell receptor on the upper airways, allowing the virus to spread by coughing and sneezing.

Resistance to adamantanes (amantadine and rimantadine) and also to oseltamivir has emerged while H5N1 vaccines are still at the developmental stage of phase 1 clinical trials. Additionally the future pandemic strain might have little cross immunogenicity to the currently tested vaccine strain. This justifies the search for medicinal plants that could be useful to treat the virus.

The following plants, usually immersed in the drinking water, are used to control clinical signs of unspecified respiratory disease in poultry globally (Table 4):
Three of these species (*Allium sativum, Andrographis paniculata* and *Nicotiana glauca*) and species of three other genera (*Citrus, Euphorbia* and *Mahonia*) have anti-influenza activity. A further seven species (*Curcuma longa*, *Eryobotrya japonica*, *Momordica charantia*, *Ocimum sanctum*, *Plantago major*, *Ricinus communis* and *Zingiber officinale*) demonstrate activity against other viruses.

Table 4: Plants used to treat unspecified respiratory disease in poultry.

Plant	Part used
Andrographis paniculata	Whole plant
Allium cepa, *Allium sativum*	Bulb
Capsicum annuum	Fruit
Citrus aurantifolia, *Citrus limetta*, *C. aurantium*	Fruit juice/peel
Coffea arabica, *Coffea robusta*	Beans
Colocasia esculata	Tuber
Curcuma longa	Rhizome
Curcuma xanthorriza, *Curcuma aeruginosa*	Not specified
Eryngium foetidum	Leaves
Eriobotrya japonica	Not specified
Euphorbia metabelensis	Latex
Heliotropium indicum	Mature leaf
Mahonia aquifolium	Root
Momordica charantia	Stem/leaf
Nicotiana tabacum, *Nicotiana glauca*	Leaf
Ocimum micranthum	Not specified
Ocimum sanctum	Leaf
Pimenta racemosa	Leaf
Piper guineense	Fruit
Piper retrofactum	Not specified
Plantago major	Not specified
Ricinus communis	Leaf
Sambucus nigra	Unspecified
Spondias pinnata	Young leaf
Tragia involucrata	Root
Trigonella foenum-graecum	Seed
Zingiber aromaticum	Not specified
Zingiber officinale	Rhizome

1. Plants used to treat unspecified poultry respiratory diseases that have activity against influenza virus.

Allium sativum, *Andrographis paniculata* and *Nicotiana glauca* exhibit activity against influenza virus either clinically or *in vitro*.

Allium sativum
Clinically garlic protects mice from influenza and its constituents are antiviral to influenza. Fresh garlic is virucidal against herpes simplex virus types 1 and 2, human rhinovirus type 2, parainfluenza-3, vaccinia virus and vesicular stomatitis virus. Garlic is immune-modulating and may combat influenza when given prior to infection.

Andrographis paniculata
Andrographis paniculata is used to prevent the spread of respiratory disease in family poultry in India. Clinical studies on *Andrographis paniculata*, either alone or in combination with *Eleutherococcus senticosis* indicate that is effective in reducing the severity of clinical signs associated with respiratory infections including colds, sinusitis and influenza in humans. *Andrographis paniculata*, or its constituents possess activity against hepatitis B, HIV and respiratory syncytial virus. *Andrographis paniculata* possesses potent immune-modulating and anti-inflammatory properties, which may account for the amelioration of clinical signs of respiratory disease observed in chickens.

Nicotiana glauca

The aqueous extract of *Nicotiana glauca* increased survival of chick embryos infected with influenza virus. *Nicotiana glauca* can be eaten by poultry without any obvious side effects. *Sambucus nigra* is immune stimulating. While plants with significant immune stimulating properties may be beneficial for less pathogenic forms of influenza, they may be contra-indicated with HPAI due to enhancement of the cytokine-mediated inflammatory response.

2. Plants used to control unspecified poultry respiratory diseases that are closely related (same genus) to plants with anti-influenza activity

Other species of the *Citrus*, *Euphorbia*, *Mahonia* and *Nicotiana* may possess activity against influenza virus (Table 5). *Citrus sp.* contains flavonoids: hesperitin from *Citrus junos* significantly inhibits influenza A virus *in vitro* and hesperidin is anti-inflammatory. *Mahonia aquifolium* is immunomodulatory, but had no activity against avian influenza *in vitro*.

Table 5: Plants used for unspecified respiratory disease that are closely related (same genus) to plants with anti-influenza activity.

Plants (or constituents of)	Closely related plants with anti-influenza activity
Citrus aurantifolia, C. limetta, C. aurantium	*Citrus junos*
Euphorbia metabelensis	*Euphorbia compositum*
Mahonia aquifolium	*Mahonia bealei*
Nicotiana tabacum	*Nicotiana glauca*

Eriobotrya japonica
ww005.upp.so-net.ne.jp/goostake/GOO/BIWAX.JPG

3. Plants used to control unspecified poultry respiratory disease that have antiviral activity.

Eight species used to control respiratory disease in poultry possess antiviral activity but their anti-influenza activity remains unknown (Table 6):

Table 6: Plants used for unspecified respiratory disease that have antiviral activity

Plant (or constituents of)	Activity against these viruses
Curcuma longa	HIV
Eriobotrya japonica	Rhinovirus
Momordica charantia	HIV, HSV1, poliovirus, HSV1, SINV, HSV
Ocimum sanctum	NDV
Plantago major	HSV2
Ricinus communis	HSV and SINV
Zingiber officinale	Rhinovirus

HIV, human immunodeficiency virus; HSV, herpes simplex virus; NDV, Newcastle disease virus; SINV, Sindbis virus.

Curcuma longa is anti-inflammatory, has vasodilator and vasoconstrictor activities and as a feed additive it improves performance in broilers. *Ocimum sanctum*'s immune supporting properties protect poultry from the immunosuppressive consequences of infectious bursal disease. *Ocimum gratissimum* is active against HIV. *Plantago major* is antiviral and immune stimulating. Several related species of *Plantago* also possess antiviral activity: *Plantago asiatica* against herpes simplex virus type 2, adenovirus and human respiratory syncytial virus and *Plantago palmata* against coxsackie virus. *Piper adauncum* is active on poliovirus.

Plantago asiatica *Eryngium foetidum*.
http://kaede.nara-edu.ac.jp/plants_of_NUE/ichiranhyou/syokubutsupage/oobako2.jpg
newcrop.hort.purdue.edu/.../images/v4-507.jpg *Mahonia aquifolium*
http://linnaeus.nrm.se/flora/di/berberida/mahon/mahoaqu7.jpg

4. Anti-inflammatory and immune-modulating plants

Curcuma xanthorrhiza has strong platelet-activating factor (PAF) receptor binding inhibitors and inflammatory activity due to germacrone and xanthorrhizol. *Tragia involucrata* and *Heliotropium indicum* have significant anti-inflammatory activity. *Eryngium foetidum*, *Ocimum sanctum*, *Pimenta racemosa* and *Zingiber officinale* are anti-inflammatory. *Andrographis paniculata, Allium sativum, Mahonia aquifolium, Momordica charantia, Ocimum sanctum, Plantago major, Trigonella foenum-graecum* and *Zingiber officinale* are all immune-modulating.

Heliotropium indicum
www.pbase.com

5. Anti-influenza plants with no or a non-poultry ethnoveterinary medicine reference

Many plants have activity against avian influenza, but documentation of their use for controlling respiratory diseases in poultry is lacking. *Crataegus crus-galli*, *Euonymus europaeus*, *Fragaria vesca*, *Ribes rubrum*, *Ribes uva-crispa*, *Solanum nigrum* and *Viburnum opulus* and several others boast activity against influenza.

An extract of *Pelargonium sidoides* showed efficacy in children with acute non-group A beta-haemolytic streptococcus tonsillopharyngitis and promotes wellness. A decoction of *L. dissectum* root was used successfully by the Washoe Indians during the 1918 influenza pandemic. *L. dissectum* (*Leptotaemia dissecta*) root possesses anti-rotavirus activity and *L. suksdorfii* is anti-HIV.

Petunia hybridia extracts retarded the multiplication speed of influenza viruses. A *Petunia nyctaginiflora* extract has activity against HSV-1.

L. dissectum roots

Pelargonium grandifolium
www.finerareprints.com/.../vanhoutte/11124.jpg

www.lomatium.com/lom-images.htm

Gardenia ternifolia is used in Cameroon as a growth-enhancer and another species *Gardenia triacantha* is used to treat bilious fever in Senegal. The preventive administration of a Gardenia-Aweto compound protected damaged lung function in a rabbit model of acute respiratory distress syndrome.

An Indonesian researcher recommends consuming *Aloe vera* and *Scutellaria* as a precaution against avian influenza. *Scutellaria* is immunomodulatory and inhibits the infectivity and replication of HIV. *Scutellaria root* added to the feed of broilers (15 g/kg of diet) increases the level of iron in the serum by 32%.

http://www.nature.org vi-va.seesaa.net/image/15_chicksandsesame.JPG

Conclusion

Ethnoveterinary medicine's role in the control of avian influenza may be twofold, depending on the presence or absence of HPAI within a poultry population. When HPAI is not present within a population, immune-enhancing plants may increase resistance to disease and prevent LPAI (if present) from mutating to HPAI. During an outbreak of HPAI, the addition of immunomodulating and anti-influenza plant extracts into the drinking water of family poultry may assist in preventing or slowing the spread of HPAI in otherwise healthy poultry and reducing environmental contamination with influenza virus. The use of these plant products do not replace sound husbandry and biosecurity measures; the effectiveness of both may be augmented as a result of improved bird resistance and/or decreased exposure to the virus. It may be that pre-treatment could be effective with AI as it is with ND in reducing the risk of AI outbreaks in family poultry and could also be used by scaling up the dosages and modifying the application process to reduce the possibility of AI occurring in the commercial poultry industry.

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