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Herbal extracts as antiviral agents

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Introduction

The use of plants as traditional medicine against viral diseases in the production of animals have been described and practiced worldwide. The use of herbs and their extracts as antiviral agents began following World War II in Europe, and the research was later developed worldwide. Briefly in this chapter, we will discuss common herbal extracts used as antiviral agents in treating or preventing virus diseases of farm animals such as poultry, swine, and ruminants (Table 7.1).

Poultry

The poultry industry is one of the most important agricultural industries, providing food to almost 7 billion people worldwide. The demand for chicken meat has been steadily increasing and is expected to reach 131,607.3 thousand tonnes in the year 2026 (data obtained from <https://data.oecd.org/agroutput/meat-consumption.htm>). Disease causing microorganisms in the poultry industry includes various virus, bacteria and protozoa. The most challenging pathogens among these is the virus pathogen which continue to emerge through various genetic modification such as mutations, recombinations or co-evolution with vaccines (Bagust, 2008). The most destructive avian viral diseases are Newcastle disease virus (NDV), avian influenza virus (AIV), infectious bursal disease virus (IBDV), infectious bronchitis virus (IBV), egg drop syndrome avian adenovirus, and fowl pox virus. Vaccination programmes against these viruses has been applied in many countries worldwide (Marangon and Busani, 2006). However, the problems arise from backyard-reared chicken infections, which are normally not vaccinated, but still prevalent, leading to the spread of the virus that eventually causes outbreak in the community (Bagust, 2008). Modern treatments of the infected avian species are laborious and expensive. Treatments with medicinal plants have been practiced traditionally to overcome the virus infection. In this section, we will briefly discuss three major avian viruses, i.e., NDV, AIV, and IBDV, in terms of disease symptoms, some medicinal plants used for the treatment, and their mechanism of action where available.

Newcastle disease virus

Newcastle disease virus (NDV) is an avian paramyxovirus type-I (APMV-1) under the Genus *Avulavirus*, Subfamily Paramyxovirinae, Family Paramyxoviridae, and Order

TABLE 7.1 List of herbal extracts acting as antiviral agents against viral diseases of livestock.

No.	Species	Common diseases	Examples of herbs
1	Poultry	Newcastle disease	<ul style="list-style-type: none"> • aloe species • <i>Azadirachta indica</i> (neem) • <i>Commiphora swynnertonii</i> (Burt) • others
		Avian influenza	<ul style="list-style-type: none"> • <i>Camellia sinensis</i> (green tea) • <i>Eugenia jambolana</i> Lam • NAS preparation • <i>Echinacea purpurea</i> (purple coneflower) • <i>Sambucus nigra</i> L. (elderberries) • others
		Infectious bursal disease	<ul style="list-style-type: none"> • <i>Ocimum sanctum</i> and <i>Argemone mexicana</i> • combined extracts of rhizoma <i>Dryopteridis crassirhizomatis</i> and <i>Fructus mume</i> (RDCFM) • others
2	Swine	Swine flu	<ul style="list-style-type: none"> • liquorice • giloy • neem • ginger • garlic
		Porcine circovirus (PCV) related diseases	<ul style="list-style-type: none"> • sickle-leaved hare's ear
		Porcine epidemic diarrhea (PED)	<ul style="list-style-type: none"> • horny goat weed
		Porcine reproductive and respiratory syndrome (PRRS)	<ul style="list-style-type: none"> • tea seed
3	Ruminant	Foot and mouth disease (FMD)	<ul style="list-style-type: none"> • kombucha • honey
		Bovine viral diarrhea	<ul style="list-style-type: none"> • basil
		Peste des petits ruminants	<ul style="list-style-type: none"> • goat weed

Mononegavirales (Yusoff and Tan, 2001). The virus infects more than 50% of the bird order and is one of the most common viral diseases of avians. The virulence of the virus is categorized into three pathotypes: the lentogenic strain (used as vaccine strain) that causes asymptomatic infection; the mesogenic strain that causes respiratory infection with moderate mortality; and the velogenic strain that causes gastrointestinal lesions (viscerotropic) or neurological infection resulting in 100% mortality. Vaccination of NDV is practiced in the commercial poultry industry in many countries especially in South East Asia, as the virus is endemic in these countries. Nevertheless, the backyard flocks have not been vaccinated against NDV, leading to the sporadic outbreaks consecutively over the years. Several medicinal plants have been used by farmers/owners in treating diseased birds as discussed in the following sections.

Aloe species

Although various species of aloe have been used against avian diseases including NDV, scientific analysis of these aloe species in the treatment of NDV is still poor. In 2002, [Waihenya et al. \(2002\)](#) evaluated the efficacy of the *Aloe secundiflora* crude extract on experimentally NDV-infected chicken. Four-month-old chickens, free of NDV antibodies, were used. Results showed that there were no significant differences in the final mortality rates between the treated and untreated chickens. Apparently, the survival of the infected chicken depended mainly on the antibody levels, on which the aloe has no significant effect. The aloe, however, could be a potential candidate on the management rather than the treatment of NDV. [Abd-Alla et al. \(2012\)](#) used various parts of *Aloe hijazensis* against hemagglutinating viruses such as NDV, avian influenza virus type-1, and egg-drop syndrome virus (EDSV) in specific-pathogen-free (SPF) chicken embryos. They reported that the flowers and leaves of *A. hijazensis* showed relatively higher antiviral activity than other parts of the plant.

Azadirachta indica (neem)

Neem, scientifically known as *Azadirachta indica*, has been shown to demonstrate a wide variety of therapeutic effects including antimicrobial activities ([Kumar and Navaratnam, 2013](#); [Gupta et al., 2017](#)). The use of this plant in treating infections of various viruses such as poliovirus, bovine herpesvirus type-1, duck plague virus, and herpes simplex virus type-I has been reported [reviewed [Kumar and Nayaratnam, 2013](#)]. In a study by [Helmy et al. \(2007\)](#), the authors showed that neem extract from various parts of the plant exhibited antiviral activities with an IC_{50} of 4–8 $\mu\text{g}/500 \text{ EID}_{50}$ in embryonated chicken SPF eggs. However, detailed mechanisms of action were not known. In 2014, Gupta et al. investigated the immunological aspect of NDV-infected cells treated with neem leaves in vitro and in vivo. They found that neem leaf extract significantly reduced the NDV-stimulated splenocyte proliferation in mice to the level comparable to the uninfected control. This suggested that the extract demonstrated anti-NDV activity.

Commiphora swynnertonii (Burt)

Commiphora swynnertonii is a tropical tree that is widely distributed in Asia and Africa. The plant has been shown to demonstrate antifungal, antiectoparasite, and antiviral activities. [Bakari et al. \(2012\)](#) investigated the antiviral properties of this plant against NDV. Various parts of the plant were extracted using DMSO and co-incubated with NDV prior to injecting into the embryonated eggs. At concentrations of 250 and 500 $\mu\text{g}/\text{mL}$, the survivability of the embryo has greatly improved and the hemagglutinin (HA) titer of these embryonated eggs were substantially reduced. The authors further investigated the efficacy of resinous extracts against NDV in chicken ([Bakari et al., 2013](#)). The extracts, at various concentrations, were given to the chicken before the challenge (prophylactic effect) or after the challenge (therapeutic effect). Results showed significant reduction in clinical symptoms or severity as well as in antibody titers in the chicken resulting to lower mortality rate. These findings indicate that the resinous extract has strong antiviral activity against NDV in chicken.

Avian influenza virus

Avian influenza virus (AIV) belongs to the family of Orthomyxoviridae. The virus has negative, single-stranded, eight segmented RNAs encoding for at least 11 viral proteins. The virus is divided into subtypes based on the HA and neuraminidase (NA) proteins on the virus surface responsible for the attachment and release of the virus, respectively (Abdelwhab and Hafez, 2012). Birds are the natural host for all the subtypes of AIV. Reassortment of the HA and NA with other subtypes could result in catastrophic pandemics in humans such as H1N1, H2N2, and H3N2 (Abdelwhab and Hafez, 2012). The virus is classified into highly pathogenic avian influenza virus (HPAIV) and low pathogenic AIV (LPAIV) based on its pathogenicity in poultry. Vaccination against AIV has not been very successful as multiple subtypes are co-circulating (i.e., H5, H7, and H9); hence, vaccination against multiple HA subtypes are required. In addition, immune pressure leading to the increased evolution rate of the virus is also one of the factors rendering the effectiveness of the vaccine. Treatments such as M2 blocker and neuraminidase inhibitors have been used to disrupt the lifecycle of the virus during infection. Alternatively, medicinal plants could be used to overcome the infection.

Camellia sinensis (green tea)

Catechins are the major phenolic compounds in green tea that exhibit antiviral and antimicrobial activities. In 2005, Song et al. (2005) showed that the epigallocatechin gallate (EGCG), epicatechin gallate (ECG), and epigallocatechin (EGC) could inhibit various stages of AIV replication. EGCG and ECG effectively inhibit the attachment of virus by interacting with the hemagglutination protein. Kim et al. (2013) reported similar results where they showed that EGCG did not affect the binding of the protein to receptors, but inhibited the hemifusion event between virus and the cellular membrane. In addition, catechins were found to suppress the RNA synthesis by inhibiting the endonuclease activity of AIV RNA polymerase (Song et al., 2005; Kuzuhara et al., 2009). Catechins also inhibit the release of the virus by interacting with the neuraminidase protein (Song et al., 2005). The authors proposed that the 3-galloyl group of the catechin skeleton might play an important role on the antiviral activity. Lee et al. (2012b) investigated the potential of antiinfluenza virus activity of green tea by-products against AIV infection in chicken. Antiviral effects, in a dose-dependent manner, were observed when the chickens were fed with 10 g/kg of feed. Significant reduction in the number of SPF chickens that shed AIV in cecal tonsil after the virus challenge was also observed. The authors suggested that green tea byproduct extract inhibits AIV effectively in the chicken intestines.

Eugenia jambolana Lam

Eugenia jambolana is a large evergreen tree that is widely distributed throughout India, Sri Lanka-Malaya, and Australia. Various parts of the tree such as the bark and leaves have been reported to be used against chronic diarrhea, dysentery, sore throat, as well as antibacterial and antiviral infections (Sood et al., 2012). They tested the antiviral activity of the leaves and bark crude extracts on HPAIV H5N1. The extracts demonstrated 100% inhibition of cytopathic effect (CPE) of the virus on Madin–Darby Canine Kidney (MDCK) cells, further confirmed with up to 99% reduction in virus production in embryonated eggs.

NAS preparation

NAS preparation is a Chinese medicine prepared by the Yunnan eco-agricultural research institute consisting of *Hedyotis diffusa*, a common stonecrop herb, *Abrotani herba*, *Folium isatidis*, etc. (Shang et al., 2010). They infected 28-day-old chickens with H9N2 followed by a four-day treatment with different concentrations of NAS 48-hour postinfection. They showed that the chickens were free from AIV on the seventh day postinfection (five days after the first treatment), whereas the virus is still detectable in the positive control and the adamantan-amine control group nine days postinfection. This finding suggested that NAS could be a potential drug candidate to control H9N2 subtype of AIV in chickens.

Echinacea purpurea (purple coneflower)

Echinacea contains compounds such as caffeic acid derivatives, alkylamides, and polysaccharides that have been shown to exhibit antimicrobial, antioxidant and immunomodulatory activities in vitro and in vivo (Hudson, 2012). The antiviral activity of this compound against AIV in embryonated chicken eggs was investigated by Karimi et al. (2014). They found that AIV was significantly neutralized by the extract when mixed prior to inoculation into the chicken embryos. Similar results were obtained when they performed qRT-PCR of the viral gene to determine the virus titer. However, the antiviral activity was not effective when the virus has entered the cells suggesting the extract exerts its activity by inhibiting the receptor-binding activity of the virus.

Sambucus nigra L. (elderberries)

Sambucus nigra L., or commonly known as black elderberries, exhibits antimicrobial, antioxidant, antiinflammatory effect in vitro and in vivo (Krawitz et al., 2011). Elderberries are rich in phenolic acids, flavonoids, catechins, and proanthocyanidins, of which some flavonoids have been shown to significantly block influenza virions in vitro (Roschek et al., 2009). Like the findings of Echinacea, Karimi et al. (2014) found that the compound inhibited the virus penetration when the extract and virus were mixed prior to inoculation but no effect was observed after the virus has entered the cells. Molecular detection of the virus such as qRT-PCR of the viral gene showed that the virus titer was significantly reduced.

Infectious bursal disease virus (IBDV)

Infectious bursal disease virus (IBDV) is a member of the family Birnaviridae and genus *Avibirnavirus* with a nonenveloped double stranded RNA virion. Infection of the virus in three- to six-week-old chickens lead to the lymphoid depletion in the bursa of Fabricius resulting in immunosuppressive disease. The virus is categorized into three groups based on its virulence, i.e., mild strain, virulent strain (30%–60% mortality rate), and very virulent (more than 70% mortality rate). Like other poultry diseases, chickens are exposed and susceptible to IBDV infection, which causes substantial economic losses in the poultry industry. Vaccination against IBDV has been practiced worldwide. However, without proper biosecurity and effective vaccination program, the disease will still recur in the farm (Bagust, 2008). Currently, there is no effective treatment for IBDV infection. Researchers are constantly searching for medicinal plants alternatives in hope to obtain a therapeutic compound to inhibit the replication of the virus.

Ocimum sanctum* and *Argemone mexicana

Ocimum sanctum and *Argemone mexicana* extracts have been reported to exhibit antiviral activities. Varshney et al. (2013) used the leaf extracts of these plants to determine their antiviral effects in vitro and in vivo. At various concentrations, the extracts successfully reduce or inhibit the CPE of IBDV- and NDV-infected chick embryo fibroblasts (CEF). In addition, lower HA titers were also detected compared to that of the untreated control. The extracts were fed to chicken for 21 days at 250 mg/kg followed by IBDV and NDV challenge orally on day 22. Overall, the treated groups showed better protection with reduced clinical symptoms compared to untreated.

Combined extracts of *rhizoma Dryopteridis crassirhizomatis* and *Fructus mume* (RDCFM)

Rhizoma Dryopteridis crassirhizomatis (RDC) and *Fructus mume* (FM), separately, have been shown to exhibit antiviral properties previously (Lee et al., 2008; Yingsakmongkon et al., 2008). The combinatorial therapeutic effects of RDCFM on SPF chickens infected with IBDV were evaluated by Ou et al. (2013). The authors showed that the survival rate of the IBDV-challenged chicken ($10^{2.5}$ EID₅₀) increased from 66.7% to 75% when treated with various concentrations of RDCFM compared to 50% of untreated control. Quantification of IBDV using real time RT-PCR showed that the virus loads in the bursa of Fabricius were significantly lowered in the treated group compared to the untreated group, which is also correlated to the IBDV antibody level.

Other medicinal plants

Chinese herb medicine consists of dipotassium glycyrrhizinate and ligustrazine hydrochloride was found to inhibit IBDV by inhibiting virus replication and/or inactivating virus directly in CEF cells (Sun et al., 2013). Alkaloids from the fruit pulp of *Cucumis metuliferus*, at concentration above 6.25 mg/mL were also found to inhibit the CPE of the virus on CEF cells (Anyanwu et al., 2017). Root extract of *Withania somnifera* (Ashwagandha plant) were tested to determine its anti-IBDV properties. Results showed up to 99.9% decrease in virus titer when IBDV-infected CEF was treated with *W. somnifera* at 25 µg (Pant et al., 2012). In addition, the leaves of *M. oleifera* Lam (MOL), dried fruits of *Phyllanthus emblicus* Linn (PEL), roots of *Glycyrrhiza glabra* Linn (GGL), and the leaves of *E. jabolana* Lam (EJL), at various concentrations, significantly inhibit IBDV in Vero cells (Ahmad et al., 2014).

Swine

World pig meat production has nearly doubled over the last 20 years (Godfray et al., 2010). However, following such development, a wide range of diseases associated with reduced efficiency of food conversion, growth rates and significantly increased mortality rate, and continuous medication requirement in pigs have been reported in various countries. To make it worse, many established pig production systems are currently operating based on traditional farrow-to-finish systems, which involved mixing of age groups and minimal management opportunity, thus, increasing the risk of new diseases outbreaks. Among the

examples of devastating outbreaks include the porcine respiratory disease complex in the United States and several other viruses such as the influenza virus, porcine reproductive and respiratory syndrome virus (PRRSV), and coronavirus in Asian countries.

Diseases were normally controlled by the combination of vaccination programs and continuous use of antibiotics in feed or water. Unfortunately, such an approach has been unsuccessful and often leads to high production costs and endemic emergence of antibiotic resistant organisms. Traditionally, natural herbals have been used for relieving and curing many symptoms arising from viral infection including cold, flu, and other virus-related diseases (Samy et al., 2008). Though the effectiveness of these treatments is unproved, scientific research demonstrated that herbal extracts exert significant antiviral properties and could potentially be used as an alternative treatment for virus-based diseases in the farming industries.

Swine flu

Swine influenza virus (SIV) is a respiratory disease of swine caused by a type A influenza virus. Swine flu is an emerging viral infection that is a present global public health problem. In pigs, influenza infection causes fever, lethargy, sneezing, coughing, breathing difficulties, and decreased appetite (Shah and Krishnamurthy, 2013).

Liquorice

Liquorice (*Glycyrrhizaglabra*) has been widely used in traditional medicine to lower cholesterol levels, heal respiratory tract disorders, and to boost immunity level (Samy et al., 2008). Scientists have been rediscovering the health benefits of liquorice. Liquorice derives its flavor mainly from a sweet-tasting compound called anethole and glycyrrhizinic acid, an antiviral compound significantly sweeter than sugar (Singh et al., 2003). Powdered liquorice root is an effective expectorant to promote the secretions of sputum by the air passages and has been used to treat cough since ancient times. The roots of the plant contain many phenolic and active compounds particularly glycyrrhizinic acid, which exhibits antiviral, antiinflammatory, antioxidant, and immune-modulating properties (Kapil and Sharma, 1997). These properties allow it to be an important supplement for flu prevention. Animal studies have revealed that liquorice is capable of stopping virus replication (Nose et al., 1998; Curreli et al., 2005). One study found that liquorice root protects cells from the infection of influenza A virus, and in already infected cells, causing a drastic reduction in the number infected cells (Wagner and Jurcic, 2002).

Giloy (Guduchi)

Tinosporacordifolia, also called Guduchi, is a herbaceous vine of the family Menispermaceae, indigenous to the tropical areas of India, Myanmar, and Sri Lanka. Ayurvedic Medicine stated that Guduchi is able to stimulate the body's immune system by maintaining optimal levels of white blood cells such as macrophages. The plant is also used in dyspepsia and various types of fever. Traditional medicine suggested that mixing one foot long of the Giloy herb and seven leaves of Tulsi could effectively prevent infection of swine flu (Shah and Krishnamurthy, 2013). Though the recipe was not scientifically established, compound and

elemental analysis indicated that Guduchi contains various diterpene compounds, including tinosporone, tinosporic acid, syringen, berberine, giloin as well as polysaccharides, such as arabinogalactan polysaccharide (Subhose et al., 2005; Sanchez-Lamar et al., 1999). These compounds possess adaptogenic and immunomodulating properties. Studies showed that Guduchi extract could cause a significant increase in IgG antibodies in serum, along with macrophage activation (Fortunatov, 1952), besides promotions of humoral immunity and stimulation of cell mediated immunity (Winston and Maimes, 2007). The plant has immense potential for use against novel H1N1 flu since it is a potent immunostimulant.

Neem

Azadirachta indica (neem) is a tree in the mahogany family Meliaceae. Neem tree extracts has been used in the Ayurvedic tradition for thousands of years to maintain health and overall well-being. The roots, bark, gum, leaves, fruit, seed kernels, and seed oil are all used in various therapeutic preparations. Neem leaves contain a wide range of flavonoids such as quercetin as well as nimbosterol and limonoids, including azadirachtin, nimbin, and nimbidin, which are often used as antiviral agent in natural products (Choudhary et al., 2013; Sahoo, 2015). An in vitro assay indicated that dose and concentration played an important role in neem extract's antiviral property (Shah and Krishnamurthy, 2013). *A. indica* has traditionally been used as an antiviral, and animal and laboratory research has shown promising results. While researchers have still not pinpointed the exact mode of action of neem phytoconstituents, there is some evidence to show that they interfere with viral reproduction, thus minimizing the impact of viral infections (Sahoo, 2015). Thus, neem can serve as a source of promising antiviral drugs.

Ginger

Zingiber officinale (ginger, Fig. 7.1) belongs to the family Zingiberaceae. *Z. officinalis* is one of the natural remedies for swine flu prevention. Traditional medicine practitioners often used ginger to boost the body's immunity level, relief gastrointestinal illness, cure cough and flu, antinausea, antiinflammatory, and also aid digestion. The characteristic odor and



FIGURE 7.1 Ginger or known as *Zingiber officinale* is believed to enhance immune system and help in digestion and flu relieve.

flavor of the ginger root comes from the mixture of zingerone, shogaols and gingerols, and volatile oils. Ginger contains gingerol, a pungent ingredient of ginger volatile oil with sulphur-containing compounds (allicin, alliin, and ajoene), and enzymes (allinase, peroxidase, and myrosinase), which exhibited antibiotic properties (Shah and Krishnamurthy, 2013). The allicins have fibrinolytic activity that reduces platelet aggregation by inhibiting prostaglandin E2. Compounds in ginger also increase levels of antioxidant enzymes, including superoxide dismutase and glutathione peroxidase, which stimulate inflammatory reactions triggered by viral infections. Bioactive components analysis of ginger suggested that various antiinfluenza agents are presented in ginger including TNF- α , an antiinfluenza cytokine (Chopra and Nayar, 1956). Further animal trial showed similar findings, where gingerols from ginger extract is able to increase the motility of the gastrointestinal tract and have strong antimicrobial properties (Shah and Krishnamurthy, 2013).

Garlic

Alium sativum, lahsan (Hindi), or garlic (English), belongs to the family Alliaceae. *A. sativum* has been used throughout widely both for culinary and medicinal purposes (Fig. 7.2). Furthermore, garlic is a powerful natural antibiotic. Garlic has natural antiviral, antibacterial and immune-boosting properties. Traditional medicine used garlic to treat fungal, parasitic and viral infections, including influenza viruses for the past several decades (Hornung et al., 1994). Kim et al. (2005) investigated the antiviral properties of garlic toward human cytomegalovirus (HCMV) using tissue culture technique, plaque reduction and early antigen assay. A dose-dependent inhibitory effect of garlic extract (GE) was observed when GE was applied simultaneously with HCMV (Kim et al., 2005). In addition, past in vitro research also indicated antiviral effect of garlic against parainfluenza virus type 3 and human rhinovirus type 2 (Wang et al., 2006).



FIGURE 7.2 Garlic or *Alium sativum* traditionally used to treat microbial infection such as virus, bacteria, parasite and fungal.

Porcine circovirus (PCV)

Porcine circovirus is the smallest known animal virus, belonging to the genus *Circovirus* in the Circoviridae family (Chen et al., 2012). PCV2 was demonstrated to be a causative agent of porcine circovirus-associated disease (PCVAD), which includes porcine multisystemic wasting syndrome (PMWS), porcine dermatitis and nephropathy syndrome (PDNS), porcine respiratory disease complex (PRDC), congenital tremor (CT), and reproductive failure (Lv et al., 2013; Duan et al., 2014).

Sickle-leaved hare's ear

Bupleurum falcatum, also known as sickle-leaved hare's ear, is a species of flowering plant in the *Apiaceae* family. *B. falcatum* has been used in Chinese medicine for over 2000 years as a "liver tonic." *B. falcatum* is commonly prescribed by both Chinese and Japanese traditional medicine doctors for inflammatory and infectious diseases. Despite the precise mechanism of action remains unclear, *B. falcatum* has been found to possess antiinflammatory and antiviral properties (Lee et al., 2012a). Recent study by Yang et al. (2017) reported that several major triterpenoid saponins were identified in *B. falcatum* extract, including saikosaponin A (SSA) and saikosaponin D (SSD). These active components are reported to impart immunomodulatory, antiinflammatory, antibacterial, antiviral, and anticancer effects (Na-Bangchang and Karbwang, 2014). Furthermore, it has been shown that SSD could exhibit an antiproliferative effect in activated T-lymphocyte, via suppression of NF- κ B, NF-AT, and AP-1 signaling (Tundis et al., 2009). Many studies have recently focused on the use of Chinese herbal medicines to treat or prevent PCV2-induced health disorders (Sun et al., 2016). Existing data showed that *B. falcatum* could reduce PCV2-induced pathological effects, which can cause an imbalance in a variety of protein levels and cell numbers through modulating the content of immunoglobulin as well as hemoglobin (HGB) (Darwich et al., 2003; Pejsak et al., 2011; Sipos et al., 2004).

Porcine epidemic diarrhea virus (PEDV)

Porcine epidemic diarrhea virus (PEDV) is the causative agent of porcine epidemic diarrhea, dehydration, vomiting and high mortality in the piglets (Debouck et al., 1981). Most newborn piglets infected by PEDV would die and affected pigs normally exhibit severe symptoms, like massive diarrhea and dehydration, resulting in serious economic losses to the swine industry (Turgeon et al., 1980; Knowles and Reuter, 2012).

Horny goat weed

Epimedium koreanum, also known as horny goat weed or Nakai, is a genus of flowering plants in family Berberidaceae. Traditionally, *E. koreanum* has been used as an aphrodisiac, and to treat hypotensives and neurasthenia. *E. koreanum* contains a lot of flavonoids including icariin, icariside II, epimedin, epimedesides, hyperoside, qercetin, and chlorogenic acid. A recent report showed icariin in *E. koreanum* stimulates angiogenesis (Chung et al., 2008). Other researcher reported that flavonoids and icariin of *E. koreanum* Nakai improved the development of osteoblast (Zhang et al., 2008). Also, icariside II was found

to induce apoptosis in human prostate cancer cells (Lee et al., 2009). But, the antiviral effect of *E. koreanum* was not reported until recently (Cho et al., 2012). Cho et al. (2012) demonstrated that water extract of *E. koreanum* exerts a potent antiviral activity on PED virus through both in vitro and in vivo animal models. Despite the underlying mechanism of *E. koreanum* remained unknown; test result suggested that *E. koreanum* exerts antiviral effect through modulating immune responses such as macrophage and lymphocyte stimulation.

Porcine reproductive and respiratory syndrome virus (PRRSV)

PRRSV is one of the major swine pathogens. This virus has caused significant economic losses to the swine industry (Neumann et al., 2005). This single-stranded RNA virus can cause reproductive failures in pregnant sows, respiratory disorder in piglets, immune suppression, and various secondary infections (Rossow, 1998).

Tea seed

Besides being widely utilized in culinary, traditionally, Chinese communities often used tea seed extract to treat burn injuries. Previous studies demonstrated that tea seed saponins (TS), extracted from tea seeds, possess antifungal activities (Kuo et al., 2010), antiallergic (Matsuda et al., 2010), as well as antimicrobial and cardio-protective effects (Liao et al., 2009). Hayashi et al. (2000) reported that TS could inactivate human type A and B influenza virus, yet the underlying antiviral mechanisms remain unknown. A recent study investigated the inhibitory effects of TS on PRRSV and its underlying mechanisms of action using an in vitro model system (Li et al., 2015). PRRSV infection always results in persistent transmission and secondary infection. Li et al. (2015) demonstrates that TS can effectively inhibit PRRSV replication through multiple ways, including directly inactivating the virus or blocking the virus entry into the cells, and indirectly through the modulation of Poly (A)-binding protein (PABP). Such unique properties of TS might reduce the opportunity of development of drug-resistant strains.

Ruminants

Ruminants, or four-stomached animals such as cow, goat, sheep, and buffalo, differ in their digestion physiology compared to other livestock (McAnally and Phillipson, 1944). Livestock provides a huge impact on the agricultural industry as a source of protein from meat and milk in large-scale or small-scale production. However, ruminants faced a major threat due to viral infections particularly because of several factors such as stress and poor immune response. Viral infection in ruminants may affect the animal production and performance, which may contribute to low economic returns. There are several ways to overcome viral infections in ruminants such as vaccination, drugs and herbs or traditional medicine (Lin et al., 2014). Nowadays, traditional medicine becoming one of the choice as it has shown to be safer, cheaper and efficient (Jassim and Naji, 2003). In this part, common herbs that have proven to show positive effects such toward common viral diseases in ruminants such as

foot and mouth disease (FMD), bovine viral diarrhoea (BDV), and peste des petits ruminants (PPR) will be discussed.

Foot and mouth disease (FMD)

Foot and mouth disease is caused by Aphthovirus which belongs under Picornaviridae family. This disease is highly contagious and considered a fatal that affects all species of ruminants and swine (Grubman and Berry, 2004). This virus is highly infectious in nature and may be spread via aerosols, inanimate objects, and close contacts (Bayry and Kavery, 2001). The affected animals usually have blister-like lesions in the oral cavity and hoof area that lead to inappetence and lameness. Most of the affected animals show a drop in milk production, and the meat is banned from exportation. Among the herbs that can be used to prevent the disease are listed in the next sections.

Kombucha

Kombucha is a popular Chinese traditional medicine prepared from a culture of yeast and acetobacter, fermented with black tea and Chinese herbal extracts (green tea, chrysanthemum, liquorice, and *Grosvenor momordica*). This concoction has been suggested as an efficient probiotic (Greenwalt et al., 2000). It is acidic in nature, ranging between pH 2.5 to 4.6 and as FMD virus is sensitive to acidic condition or low pH, this mixture has shown to be effective in preventing FMD (Teoh et al., 2004). Based on an in vitro study in BHK21 cells, the kombucha herb can inhibit the growth of FMD virus. On the other hand, in vivo study showed it was capable of killing FMD virus with no toxicity effects on mice (Fu et al., 2014). In addition, spraying cattle in an FMD outbreak zone with kombucha protected against infection in a large-scale field trial (Fu et al., 2015).

Honey

In Kenya, an outbreak of FMD affecting 57.2% of the cattle was treated with honey, finger millet, and 97% sodium (Gakuya et al., 2011). The lesions of the ulcers and blister improved in three days following the topical application. Honey has been in use for treatment of infected wound for more than 2000 years, even before bacteria were discovered. Honey has been reported to have inhibitory effect to around 60 species of bacteria (Molan, 1992). Honey has antibacterial properties due to the production of hydrogen peroxide, which is formed and released slowly by glucose enzymes when the honey is diluted.

Bovine viral diarrhoea

Bovine viral diarrhoea (BVD) is a disease of ruminants caused by pestivirus, which is originated from the family Flaviviridae. There are two biotypes of the virus depending on the ability to cause CPE (Ridpath, 2010). Pestivirus causing BVD normally spreads by close contacts among cattle populations and also vertical transmission that means transfer of virus from cow to fetus is highly possible. The affected fetus may lead to stillbirths, abortions or persistent infection in the calf after being born. Some of the cattle may have mucosal lesion especially in the intestinal tract leading to profuse diarrhoea and anorexia and may progress to death (Thiel et al., 1996). Basil is one of the herbs that have been shown experimentally to reduce and treat BVD.

Basil

Basil, or *Ocimum basilicum* L. derived from the Lamiaceae family, is used as a cooking herb (Sartoratto et al., 2004). Despite its culinary usage, basil is used as traditional medicine of choice to treat respiratory and gastrointestinal tract disorders (Chiang et al., 2005). Basil has been demonstrated in many studies to have antiviral, antibacterial, and antifungal properties (Pozzatti et al., 2008; Suppakul et al., 2003). The effects of basil and its essential oils, known as monoterpenes, were tested against BVD virus at different time points of infection. It was demonstrated that the compound works directly on the particle of the virus based on the tremendous reduction of the virus in plaque assay (Kubica et al., 2014).

Peste des petits ruminants

Peste des petits ruminants (PPR) mainly infect small ruminants such as sheep and goat. The disease is caused by morbillivirus, an RNA virus. The manifestation of the disease is associated with gastrointestinal tract (GIT) and respiratory system. The clinical signs are ranging from pyrexia (fever), stomatitis (inflammation of the oral cavity) and respiratory symptoms including ocular and nasal discharge and GIT signs include diarrhea and ulcers (Parida et al., 2015).

Goat weed

Goat weed or *Ageratum conyzoides* Linn in the form of extract metabolites or oil have anti-inflammatory, analgesic, antipyretic, and antidepressant effects (Shekhar and Anju, 2012). It has been used in the treatment of PPR in combination with PPR vaccine and showed prominent results (Saliu et al., 2008). In addition, metabolites and extracts of goat weed dissolved in ethanol showed spasmolytic effects and protect gastric lining from ulcers.

Conclusion

The overview of the usage of traditional herbs as antiviral agents in livestock is provided in this chapter. Based on the research findings presented, in addition to being a safer and economical alternative to drugs, herbal constituents showed positive responses in animals, which suggest that it may suppress viral replication and reduce the clinical signs of viral diseases in different productive animals. Although the usage of herbs have shown profound effects in reducing viral infections, total elimination is dependent on good management practice and biosecurity of the farms.

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