Pakistan Veterinary Journal

ISSN: 0253-8318 (PRINT), 2074-7764 (ONLINE)
DOI: 10.29261/pakvetj/2025.269

REVIEW ARTICLE

Plant-Based Therapeutics Against Bovine Respiratory Disease Complex (BRDC): Emerging Alternatives in Livestock Health Management

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ARTICLE HISTORY (25-706)

Received: July 19, 2025
Revised: September 28, 2025
Accepted: September 29, 2025
Published online: September 30, 2025

Key words:
Antimicrobial resistance
Immunomodulation
Bovine Respiratory Disease Complex (BRDC)
Herbal medicine
Phytochemicals
Veterinary phytotherapy

A B S T R A C T

Abstract
Bovine Respiratory Disease Complex (BRDC) is a major cause of morbidity and economic loss in cattle worldwide, driven by a multifactorial etiology involving viral and bacterial pathogens, environmental stress, and immunosuppression. Traditional interventions, including antibiotics and vaccines, remain the mainstay of control; however, their effectiveness is increasingly constrained by antimicrobial resistance, incomplete or short-lived protection, high costs, and management challenges. These gaps underscore the urgent need for alternative or complementary strategies. Phytochemicals from medicinal plants such as garlic (*Allium sativum*), turmeric (*Curcuma longa*), and neem (*Azadirachta indica*) demonstrate antimicrobial, antioxidant, and immunomodulatory activities, while essential oils from species like *Eucalyptus* spp. exhibit strong antimicrobial and anti-inflammatory effects. In vivo and in vitro studies suggest that such compounds can enhance respiratory health, reduce pathogen load, and strengthen immune responses in cattle. Yet, limitations related to standardization, bioavailability in ruminants, regulatory frameworks, and the lack of large-scale validation hinder their integration into veterinary practice. This review highlights these gaps in current BRDC management and provides new insights into how plant-based therapeutics, when developed as feed additives, preventive tools, or adjuncts to conventional therapies, could reduce antibiotic reliance and improve disease resilience in livestock systems.

To Cite This Article: Alkheraije KA, 2025. Plant-based therapeutics against bovine respiratory disease complex (BRDC): emerging alternatives in livestock health management. Pak Vet J, 45(3): 935-946. http://dx.doi.org/10.29261/pakvetj/2025.269

INTRODUCTION

Bovine Respiratory Disease Complex (BRDC) is a multifactorial disease that is one of the most important health challenges facing cattle globally, especially in feedlot enterprises. Also known as "shipping fever," BRDC is not an infection caused by a single pathogen but instead is the manifestation of a complex interrelationship between infectious pathogens (viral and bacterial), environmental stressors, and host immune responses (Bell *et al*., 2021). This disease is mainly responsible for targeting the respiratory system of cattle and causing pneumonia, stunted growth, reduced productivity, and death in extreme cases. The disease occurs most frequently under stress, such as weaning, transportation, and commingling, where animals are exposed to novel pathogens, altered diet, and social stress, all of which impose a cumulative effect of immunosuppression (Kumar *et al*., 2024). The occurrence of BRDC is usually preceded by primary viral infections by viruses such as those caused by *bovine herpesvirus*-1 (BHV-1), bovine viral diarrhea virus (BVDV), *Parainfluenza virus* type 3 (PI3), or bovine respiratory syncytial virus (BRSV). These infections compromise the mucosal barriers of the upper respiratory tract, providing it with a favorable environment for secondary bacterial pathogens to proliferate (Werid *et al*., 2024). The most common bacterial pathogens are *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni*, and *Mycoplasma bovis*. Both viral injury and bacterial invasion interact to result in inflammation, lung tissue damage, and gas exchange impairment, clinically manifested as coughing, discharge from the nose, fever, lethargy, and reduced feed intake (Cengiz *et al*., 2021). The disease is also augmented by non-contagious factors such as poor ventilation, harsh climatic conditions, and stress resulting from handling or overcrowding. The conditions not only increase the susceptibility of animals to infection but also augment the severity of the symptoms. BRDC is thus a classic example of a disease complex wherein multiple interacting variables contribute to morbidity and mortality in herds of livestock. The economic effect of BRDC on the world's livestock industry is considerable (Ferrulli, 2023). It is considered to be the prime cause of morbidity and mortality of feedlot cattle and is accountable for as much as 70–80% of all illnesses and nearly 50% of mortality in certain operations (Smithyman, 2025). The costs of BRDC are multifaceted and include direct costs as a result of death, treatment, and reduced productivity, and indirect costs such as reduced carcass quality, reduced feed efficiency, increased time to market weight, and increased labor requirements (Corbin & Griffin, 2006).

BRDC is typically expensive to cure, and it involves diagnostic procedures, veterinary checks, and repeated courses of antimicrobial medication and supportive therapy (Neal, 2024). Additionally, the recurring signs in some herds may lead to chronic respiratory disease in the animal, ruining its performance and market value forever. Apart from these economic constraints, BRDC also impacts the welfare of the animals, putting them through suffering, pain, and reduced quality of life (Sundman *et al*., 2024).

On an industrial level globally, BRDC lowers global productivity of dairy and beef production and hence food security and sustainability (Tona, 2021). With high throughput and high turnover in intensive production systems in the interest of profitability, the existence of BRDC will interfere with production calendars, lower the return on investment, and require additional utilization of input resources per unit output. This is especially problematic in third-world nations where veterinary clinics and access to immediate medical treatment are generally limited. In addition, the disease has significant trade implications too (Majiwa, 2023). Nations suffering from frequent incidence or weak control policies risk losing barriers to trade or diminished access to market, particularly in the face of increased global consideration of animal welfare and antimicrobial resistance. It is thus not only a veterinary but a strategic livestock economic imperative to successfully control BRDC (Koyun *et al*., 2023). Antibiotics have long been the backbone of BRDC therapy, both being used for treatment and, in certain instances, for metaphylactic or prophylactic use. Nevertheless, the use of traditional antibiotics is beset by a variety of challenges and problems that undermine their long-term effectiveness and sustainability (Bell *et al*., 2021).

The first of these important concerns is the concern for antimicrobial resistance (AMR). Overuse and misuse of antibiotics in animal agriculture have been the reasons for developing resistant bacterial strains, rendering many of the favorite drugs useless or even redundant (Samad *et al*., 2025). This is a dual threat: not just are animal infections harder to treat, but resistant bacteria can be passed directly from animals to humans by contact, cross-contamination, or through the food chain, which is the origin of the global public health problem of AMR (Neal, 2024). In addition, livestock antibiotic use is increasingly coming under scrutiny from consumers and regulators. Restrictions or complete bans on routine antibiotic use for disease prevention or growth promotion have been put into place by many nations (Bishoyi *et al*., 2024; Younas *et al*., 2025). Consumer demand for "antibiotic-free" dairy and meat products is also growing, providing market incentives to minimize antibiotic use in production systems (Zhao *et al*., 2024). There are also biological restraints to take into account. Antibiotics can usually most easily attack bacterial pathogens, but can't combat the viral aspects of BRDC, which tend to drive the disease process forward. Therefore, even when bacterial infections are successfully treated, animals may not fully recover and may have prolonged disease (Abebe & Birhanu, 2023).

In addition, antibiotic therapy is logistically challenging and expensive. Treatments of large herds entail considerable labor, and such delays in diagnosis or in initiating treatment may detract from therapeutic effectiveness. Frequent treatment also tends to destabilize the normal gut microbiota of cattle and may jeopardize digestion, nutrient utilization, and immunity. As such, given these constraints, it is apparent that although antibiotics are critical to the control of disease, they are not a cure-all (McDonnell *et al*., 2024). This review highlights the plant-based medicinal alternatives to treat BRDC.

Understanding BRDC: BVDV is another significant viral contributor to BRDC, which has a systemic immunosuppressive effect. While mainly linked to enteric disease, BVDV also targets the respiratory system and decreases host immunity through leukocyte depletion, neutrophil dysfunction, and prevention of cytokine signaling (Zhang *et al*., 2023; Frucchi *et al*., 2024). It can directly infect lymphoid tissues and cause lymphopenia, hence predisposing the host to secondary infections. Chronic infected (CI) animals are other significant reservoirs of BVDV, which persistently release the virus and transmit it to susceptible cattle. Recurrent infections from the virus may lead to chronic respiratory diseases, particularly when accompanied by secondary bacterial infections (Bell *et al*., 2021) (Table 1).

Environmental and Stress-Related Factors: Beyond infectious agents, environmental and management stressors play a central role in BRDC. Transportation stress from prolonged travel, overcrowding, and commingling elevates cortisol, suppresses immunity, and heightens susceptibility. Sudden shifts in temperature, humidity, or wind chill further compromise mucosal defenses (Vogel *et al*., 2024). The disease typically develops through a sequence of viral infection or stress, bacterial colonization, immune suppression, and progressive respiratory injury, with severity depending on the timing and interaction of these events (Bell *et al*., 2021). Viral agents such as BVDV and BHV-1 directly impair innate and adaptive immunity by reducing the number and function of neutrophils, macrophages, and lymphocytes (Amjad *et al*., 2025). Corticosteroid release during stress further weakens immune defenses by suppressing cytokine production, phagocytosis, and inflammation (Xu *et al*., 2025). This "window of opportunity" allows opportunistic bacteria to invade and proliferate, often as co-infections that intensify tissue damage, complicate diagnosis, and increase mortality (Gaudino, 2022).

Once upper airway defenses are breached, bacteria colonize the lungs, eliciting a strong inflammatory response characterized by cytokine release (IL-1, IL-6, TNF-α) and neutrophil accumulation. While protective, this response causes collateral tissue injury through reactive oxygen species, enzymes, and neutrophil

Table 1: Etiology and Pathogen Roles in BRDC

Pathogen	Type	Role in BRDC	Mechanism of Pathogenesis	Host Interaction and Persistence	References
BVDV (Bovine Viral Diarrhea Virus)	Virus	Major viral contributor with systemic immunosuppressive effects	Leukocyte depletion, neutrophil dysfunction, impaired cytokine signaling, lymphopenia; infects lymphoid tissue	Chronic infected (CI) animals serve as reservoirs	(Bell *et al.*, 2021)
PI3 (Parainfluenza-3 Virus)	Virus	Less virulent, but compromises mucosal immunity	Weakens mucosal barriers, increasing susceptibility to bacterial colonization	Acts synergistically with bacterial pathogens	(Werid *et al.*, 2024)
BoHV-1 (Bovine Herpesvirus-1)	Virus	Causes infection bovine rhinotracheitis (IBR); immunosuppressive	Infect upper respiratory tract, induces apoptosis of immune cells, impairs mucociliary clearance	Establishes latency in sensory ganglia; reactivation under stress	(Jiang *et al.*, 2024)
BRSV (Bovine Respiratory Syncytial virus)	Virus	Common in calves; causes severe lower respiratory infection	Induces bronchiolitis syncytia formation, impairs pulmonary macrophages	Promotes secondary bacterial infections	(Werid *et al.*, 2024)
M. haemolytica	Bacterium	Primary bacterial pathogen; major cause of fibrinous pneumonia	Produces leukotoxins (kill immune cells), endotoxins, proteases; forms biofilms	Becomes pathogenic under stress/immunosuppression	(Abbas *et al.*, 2023)
P. multocida	Bacterium	Secondary invader; causes acute and chronic pneumonia	Possesses capsules, adhesins, outer membrane proteins; immune evasion; stress or viral infections trigger pathogenicity	Normally a commensal organism in upper respiratory tract	(Piorunek *et al.*, 2023)
H. somni	Bacterium	Opportunistic agent; systemic and respiratory infections	Causes endothelial damage, vasculitis, intracellular survival; contributes to mixed infections and persistent inflammation	Associated with treatment failure and complications	(Yaman, 2023)
M. bovis	Bacterium	Causes chronic pneumonia, otitis, arthritis	Adheres to ciliated epithelium; modulates immune response; avoids immune detection	Persists intracellularly; difficult to eradicate	(Wiseman *et al.*, 2024; Iqbal *et al.*, 2024a)
Trueperella pyogenes	Bacterium	Secondary invader in chronic lung lesions	Produces pyolysin, promotes abscess formation and tissue necrosis	Found in necrotic lung areas and mixed infections	(Magossi *et al.*, 2025)
Ureaplasma spp.	Bacterium	Opportunistic; causes mild respiratory issues	Adhere to epithelial cells; may exacerbate co-infections	Colonizes mucosal surfaces; rarely pathogenic alone	(Ozcan and Tutuncu, 2025)

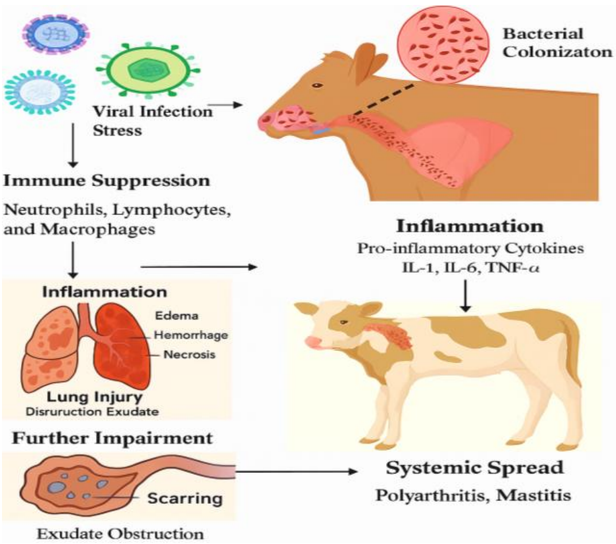

Fig. 1: Pathogenesis of BRDC.

extracellular traps. *M. haemolytica* leukotoxins exacerbate damage, leading to necrosis, fibrin deposition, consolidation, edema, and impaired gas exchange. Chronic cases may result in fibrosis, scarring, and reduced productivity. Some pathogens, such as *M. bovis*, can disseminate to deeper tissues, causing polyarthritis, otitis media, and mastitis, particularly in dairy calves (Zeitoun *et al.*, 2024), leading to persistent health issues and financial losses (Ireland-Hughes, 2025).

Management Strategies: Vaccination remains a cornerstone of BRDC prevention, aiming to protect against key viral pathogens such as BHV-1, BVDV, BRSV, and PI3, as well as bacterial agents like *M. haemolytica* and *P. multocida* (Mahmoud & Allam, 2013). Two main vaccine types are used: Modified Live Vaccines (MLVs), which provide robust and long-lasting immunity but require careful handling and are unsuitable for some groups, and Killed (Inactivated) Vaccines, which are safer but require multiple doses and adjuvants (Chae, 2021; Mehwish & Muzamail, 2023). Intranasal vaccines are increasingly applied in calves, providing rapid local protection (Qammar-uz-Zaman *et al.*, 2023). The timing of immunization is critical, as maternal antibodies can interfere with early vaccination (Chase, 2022). Preconditioning programs, where calves are vaccinated prior to weaning or shipment, are increasingly practiced to reduce risk during high-stress periods (Browning, 2023) (Fig. 2).

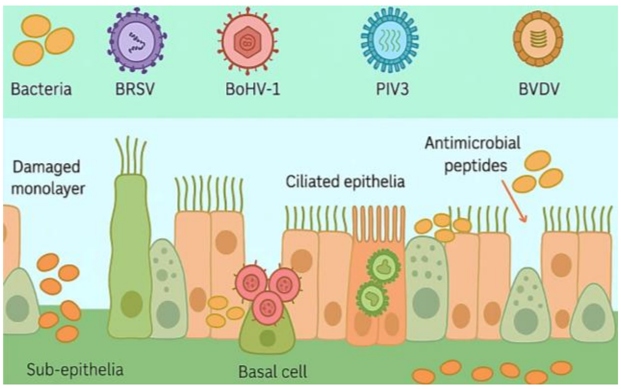

Fig. 2: Bacterial and Viral agents of BRDC.

Despite vaccination, antibiotics remain widely used for treatment and metaphylaxis. When administered promptly, they reduce disease severity and mortality (Ishaque *et al.*, 2025). Commonly used classes include macrolides, tetracyclines, cephalosporins, and, in severe cases, fluoroquinolones, though resistance is rising (Crosby *et al.*, 2018; LaPlante *et al.*, 2022). Metaphylactic administration at feedlot entry is effective but criticized for accelerating antimicrobial resistance (Baptiste & Pokludová, 2020). Supportive measures such as anti-inflammatories, fluid therapy, and optimized nutrition (vitamins A, C, E, and trace minerals) improve recovery, while environmental management (ventilation, dust control, shelter) helps reduce respiratory stress (Calder *et al*., 2020).

Biosecurity is another essential component, including quarantine of new arrivals, "all-in, all-out" herd management, sanitation, stress minimization, and record-keeping for early detection (Bell *et al*., 2021). Nevertheless, global antimicrobial resistance poses a major challenge. Multidrug-resistant *M. haemolytica*, *P. multocida*, and *M. bovis* strains are increasingly reported, limiting treatment options and threatening both animal and public health (Belwal *et al*., 2023). Stewardship programs emphasizing prudent use, improved diagnostics, and reliance on preventive strategies are therefore being promoted (Yaman, 2023).

Still, vaccination efficacy is variable. Antigenic heterogeneity, maternal antibody interference, improper administration, and incomplete pathogen coverage all contribute to failures (Cengiz *et al*., 2021). Moreover, financial and logistical barriers—vaccine cost, cold chain requirements, lack of veterinary infrastructure, and coordination difficulties—restrict effective implementation, particularly for smallholders in resource-limited settings. These shortcomings highlight the urgent need for complementary, cost-effective, and sustainable alternatives for BRDC management.

Plant-based Therapeutics: A New Alternative: Phytotherapy or plant therapeutics refers to prevention, management, or therapy of animal diseases with medicinal plants and bioactive phytoconstituents. Phytotherapy is becoming widely recognized as an environmentally friendly, efficient, and secure alternative to synthetic medication in veterinary practice, particularly in the therapy of infectious diseases such as Bovine Respiratory Disease Complex (BRDC). The approach utilizes the antimicrobial, anti-inflammatory, antioxidant, and immunomodulatory activity of plant compounds to enhance animal health. Phytotherapy includes diverse plant preparations like herbal extracts, essential oils, powder to tinctures. The latter can be conveniently supplied by feed additives, water supplements, or topicals and can be conveniently administered in diverse animal production systems. therapeutic activity of plants like *Azadirachta indica* (neem), *Curcuma longa* (turmeric), and *Eucalyptus spp*. has been established to control BRDC-associated pathogens like *P. multocida*, *M. haemolytica*, and *M. bovis* (Callaway *et al*., 2021).

One of the benefits of phytopharmaceuticals over chemical drugs is that they provide less opportunity for the accumulation of antimicrobial resistance (AMR), which is becoming a worldwide issue in human and animal health. Unlike antibiotics, phytochemicals often have multiple targets in microbes, which limits the space for pathogen adaptation. In addition, herbal remedies are biodegradable and provide less residue on animal products and the environment. This makes them more attractive under organic and residue-free animal production systems. Besides, phytotherapies are not likely to cause side effects, are inexpensive, and can be localized, stimulating rural economies and sustainable agriculture (Nazli and Zahra, 2024). As demand for antibiotic-free meat and milk continues to grow, phytotherapy is one industry that has enormous potential to move in the direction of more sustainable and holistic animal health. Increased research, standardization, and regulation are, however, required for larger acceptance and mainstreaming in veterinary practice. Phytochemicals are bioactive chemical compounds in plants that occur naturally. Unlike essential nutrients, such compounds are not required for minimal human or animal existence but exert considerable biological effects. Phytochemicals play a significant role in animal health based on their extensive range of therapeutic actions. They may be applied directly by supplements or indirectly by functional feeds (Beigh, 2024).

Bioactive Compounds in Medicinal Plants: Herbs are rich in bioactive molecules with a wide range of pharmacological activities, such as antimicrobial, anti-inflammatory, antioxidant, and immunomodulatory activity. These features make them potential candidates for the management of complex diseases like Bovine Respiratory Disease Complex (BRDC) which is a multidimensional disease in cattle caused by a combination of bacterial and viral agents like *M. haemolytica*, *P. multocida*, *H. somni*, and *M. bovis*. The rise of antimicrobial resistance, along with antibiotic residues in animal products, has necessitated interest in using plant derivatives for the control of BRDC (Ferrulli, 2023).

Phytochemicals with Antimicrobial and Anti-inflammatory Properties: One of the most extensively studied groups of phytochemicals includes flavonoids, alkaloids, tannins, terpenoids, saponins, and phenolic acids. These bioactive compounds, naturally present in a wide range of medicinal herbs, have shown strong potential in blocking respiratory pathogens and modulating inflammation in both in vitro and in vivo studies. Flavonoids such as quercetin and luteolin, abundant in *Camellia sinensis* (green tea) and *Eucalyptus* spp., exhibit multiple antimicrobial mechanisms. They inhibit bacterial enzymes, disrupt microbial cell membranes, and interfere with nucleic acid synthesis. Additionally, they can inhibit DNA gyrase, β-lactamases, and efflux pumps, thereby impairing bacterial survival. In viral infections, flavonoids block viral entry and RNA synthesis. Their anti-inflammatory effects are mediated through modulation of cytokine production and suppression of the NF-κB pathway. Saponins are known to block viral fusion with host cell membranes, limiting viral spread (Alghirani *et al*., 2022).

Alkaloids, particularly berberine from *Berberis vulgaris*, display potent antibacterial activity against *Pasteurella* and *Mycoplasma* species. Berberine interferes with bacterial DNA synthesis, inhibits prostaglandin-mediated inflammation, and acts as an efflux pump inhibitor, thereby resensitizing resistant bacteria such as *P. multocida* to antibiotics (De Rubis, 2023). Tannins from plants like *Terminalia chebula* and *Punica granatum* exert antimicrobial effects by binding and cross-linking microbial proteins and enzymes. This interaction impairs microbial adhesion, enzyme activity, and nutrient utilization, reducing pathogen colonization. Terpenoids and essential oils, including thymol and carvacrol from *Thymus vulgaris* and *Origanum vulgare*, disrupt bacterial cell membranes, impair energy metabolism, and exert anti-inflammatory actions by suppressing prostaglandin and leukotriene synthesis. Beyond direct antimicrobial effects, many of these phytochemicals also possess antioxidant properties, which help protect host tissues from oxidative stress and secondary damage during respiratory infections.

Mechanisms of Action against BRDC Pathogens: Phytochemicals suppress BRDC pathogens through different mechanisms. They first disrupt bacterial cell membrane and cell wall composition, causing cell death and cell integrity loss. This is most effective against gram-negative bacteria like M. haemolytica and P. multocida. They secondarily chelate critical bacterial enzymes and inhibit DNA/RNA synthesis, thereby suppressing pathogen multiplication. This maintains the integrity of lung tissue and amplifies immune resilience. By targeting both pathogens and host defenses at the same time, these compounds provide a synergetic and sustainable solution to synthetic antibiotics in BRDC management (Fig. 3).

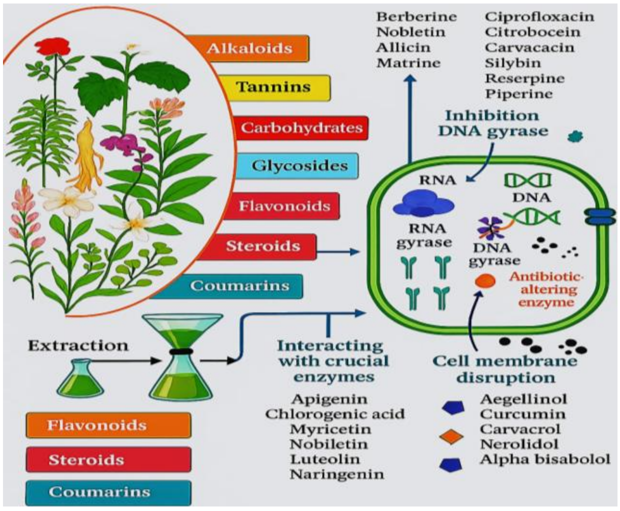

Fig. 3: Antibacterial mechanism of plant-derived compounds.

Chief Medicinal Plants Utilized in BRDC Management

***Eucalyptus spp*:** Eucalyptus spp. The essential oils of Eucalyptus species, particularly *Eucalyptus globulus*, are rich in bioactive compounds such as eucalyptol (1,8-cineole), pinene, and limonene, which exhibit antimicrobial, antioxidant, and anti-inflammatory properties. Eucalyptus oil disrupts microbial cell membranes, suppresses quorum sensing, and downregulates pro-inflammatory cytokines like TNF-α and IL-1β, thereby reducing respiratory pathogen load. In vitro, it significantly inhibited *Pasteurella multocida* and *Mycoplasma bovis*. In cattle trials, inhalation of aerosolized oil reduced coughing, respiratory rate, and nasal discharge, while improving lung function. Native to Australia, Eucalyptus comprises over 700 species, widely valued for medicinal use (Cock, 2011). *E. globulus* is of particular veterinary interest as a potent expectorant, antiseptic, and anti-inflammatory agent in respiratory diseases. It lowers mucus viscosity, facilitates expulsion, and inhibits *M. haemolytica* and *P. multocida*, major BRDC pathogens. By inhibiting prostaglandin synthesis and leukocyte migration, it limits lung tissue damage. Eucalyptus is used in aerosol products to relieve bronchial congestion and, when incorporated into feed or dried leaves, helps maintain respiratory health in calves during weaning or transport. It has also shown preventive benefits against respiratory outbreaks in cold or wet weather, making it a valuable adjunct for BRDC control (Rajamanickam *et al*., 2019).

***Azadirachta indica* (Neem):** Neem (*Azadirachta indica*) is a medicinal tree with a long history of traditional use and a broad spectrum of pharmacological activities. The major bioactive compounds include limonoids (azadirachtin, nimbin, nimbidin, salannin, and gedunin) and flavonoids such as quercetin. These phytoconstituents contribute to neem's antimicrobial, antiviral, antiparasitic, antioxidant, and immunomodulatory properties. Azadirachtin is considered the most potent limonoid, with insecticidal and antimicrobial activity (Jumba, 2014). Nimbin, nimbidin, and salannin are triterpenoids responsible for anti-inflammatory and antibacterial effects, while gedunin has demonstrated antiviral and immune-enhancing activity.

Neem extracts exert antimicrobial effects primarily by disrupting microbial membranes and interfering with nucleic acid synthesis. Bark and leaf preparations have shown inhibitory action against bacterial pathogens and enveloped viruses including *Bovine Herpesvirus-1* (BHV-1), *Bovine Coronavirus* (BCoV), and *Parainfluenza-3 virus* (BPIV-3). In vitro studies indicate that neem bark extract (NBE) can achieve >2 log10 reduction in coronavirus infectivity and completely inhibit BHV-1 replication at safe, non-cytotoxic concentrations (<0.87 mg/mL) (Pulido-Huertas *et al*., 2024). In vivo, dietary supplementation with neem leaf powder (≈250 mg/kg BW) has been associated with enhanced immune status, elevated antioxidant enzyme activity, improved hematological parameters, and reduced incidence of diarrhea in calves, without adverse effects (Ghareeb *et al*., 2010). Immunostimulatory activity is reflected in increased lymphocyte proliferation, enhanced phagocytosis, and cytokine upregulation (Pulido-Huertas *et al*., 2024).

Thymbra spicata L. also demonstrates significant antiviral potential, with in vitro activity against several BRDC-associated viruses such as *Bovine Respiratory Syncytial Virus* (BRSV), BPIV-3, *Bovine Viral Diarrhea Virus* (BVDV), and BHV-1 (Toker & Yeşilbağ, 2022). The bioactivity is linked to phenolic and terpenoid compounds, which disrupt viral membrane integrity and suppress virulence mechanisms. Although most evidence is currently derived from in vitro assays, the strong inhibitory effects and low toxicity profiles support the potential application of both neem and *T. spicata* in BRDC management. Taken together, the broad-spectrum antimicrobial, antiviral, and immunomodulatory actions of neem and related phytotherapeutics highlight their promise as adjuncts or alternatives to conventional interventions in livestock respiratory disease control, particularly in resource-limited settings where access to vaccines and antibiotics may be constrained.

***Curcuma longa* (Turmeric):** Turmeric (*Curcuma longa*) is a rhizomatous plant of the ginger family, widely recognized in Ayurveda and traditional Chinese medicine for its therapeutic properties. Its principal bioactive compound, curcumin, constitutes about 2–5% of turmeric and is complemented by minor curcuminoids (demethoxycurcumin and bisdemethoxycurcumin) and essential oils such as turmerone (Clarence *et al*., 2022; Leigh-de Rapper, 2023). Curcumin is a polyphenolic alkaloid with broad-spectrum anti-inflammatory, antioxidant, and antimicrobial activities. It suppresses inflammation by downregulating NF-κB signaling, inhibiting COX-2, and reducing the production of pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6 (Clarence *et al*., 2022). Curcumin also decreases neutrophil migration into lung tissue, thereby limiting collateral damage during bacterial pneumonia. Its antioxidant properties involve scavenging free radicals and enhancing endogenous antioxidant defenses such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), preventing oxidative stress–induced lung injury (Ali *et al*., 2022). Antimicrobial activity is exerted through inhibition of bacterial quorum sensing, prevention of biofilm formation, and direct suppression of respiratory pathogens including *Mannheimia haemolytica*, *Histophilus somni*, and *Mycoplasma bovis* (Clarence *et al*., 2022).

In vitro studies confirm curcumin's ability to block bacterial adhesion to host tissues and inhibit microbial proliferation. In vivo studies in calves show that oral curcumin supplementation reduces lung lesions, lowers oxidative stress biomarkers, and improves growth performance during recovery from BRDC. Treated animals exhibited reduced lung inflammation, better feed intake, and higher weight gain compared to controls (Clarence et al., 2022). Inflammation is a hallmark of BRDC pathogenesis, particularly during bacterial pneumonia, where excessive cytokine production damages lung tissue and prolongs disease. Curcumin and related plant metabolites (e.g., boswellic acid, resveratrol, apigenin) effectively modulate but do not abolish inflammatory responses. By suppressing overactivation of NF-κB and cytokine cascades while enhancing immune competence, curcumin helps strike a balance between pathogen clearance and tissue protection (Hong et al., 2022; Bejenaru et al., 2024; Tahir et al., 2024).

Overall, the safety, efficacy, and multifactorial mechanisms of curcumin position it as a strong candidate for integration into phytotherapeutic strategies for BRDC management. Its immunomodulatory and antioxidant actions are especially relevant for young or stressed calves, in which immune suppression and oxidative lung injury are common.

***Allium sativum* (Garlic):** Garlic (Allium sativum) produces allicin and other sulfur compounds with broad antimicrobial and immunostimulatory activity. Its bioactive constituents inhibit microbial growth by disrupting metabolic pathways, cell wall integrity, and viral envelope stability, while also enhancing phagocytosis and regulating cytokine production. In vitro, garlic extract inhibited *Pasteurella multocida* and *Mannheimia haemolytica*, with MIC values ranging from 2–16 µg/mL, and in calves, supplementation reduced nasal carriage, pneumonia incidence, and clinical respiratory distress, improved lung scores, and increased survival. These effects are mainly attributed to organosulfur compounds: allicin (enzymatically formed from alliin on crushing), ajoene, diallyl sulfides, and S-allyl cysteine, all possessing antimicrobial and antioxidant activity (Abd El-Ghany, 2024; de Almeida Campos *et al*., 2023). Garlic also showed antiviral activity against BHV-1 and BVDV, likely through allicin-mediated inhibition of viral replication. Supplementation further enhanced antioxidant enzymes (SOD, CAT, glutathione peroxidase), total antioxidant capacity, and immunoglobulin levels (IgA, IgM, IgG) in ruminants (Abd El-Ghany, 2024; Zeedan & Abdalhamed, 2021) (Table 2).

***Ocimum sanctum* (Holy Basil or Tulsi):** *Ocimum sanctum,* or tulsi, is yet another herb utilized since antiquity in the therapeutic treatment of respiratory diseases. Eugenol, ursolic acid, and carvacrol are the major active compounds.

Tulsi is an adaptogen and antimicrobial substance which helps animals tolerate stress and suppress the growth of respiratory pathogens. It is also an immune function modulator and cortisol regulator. In vitro studies prove tulsi extract to suppress bacterial growth and biofilm formation of BRDC pathogens. In vivo studies in transport-stressed calves given tulsi extract (an inducer of BRDC) proved lower respiratory symptoms, decreased pathogen load, and increased weight gain over control animals (Varghese *et al*., 2023).

***Glycyrrhiza glabra* (Licorice):** Licorice contains glycyrrhizin and flavonoids that confer antimicrobial, antiviral, and anti-inflammatory properties. Glycyrrhizin inhibits replication of respiratory viruses and modulates immune response through inhibition of cytokine storms and prostaglandin synthesis. It also gives mucosal protection to the respiratory tract. Licorice extract was also reported to have antiviral properties against Bovine Respiratory Syncytial Virus in vitro. Animals suffering from mild respiratory disease treated with herbal products incorporating licorice in a field trial recovered earlier, coughed less, and experienced lower fever compared to control animals. *Glycyrrhiza glabra* (licorice) saponins are surfactants that have the ability to disrupt the bacterial membranes. They have anti-inflammatory activity by inhibiting prostaglandin and leukotriene production. *Glycyrrhiza glabra* (licorice) saponins are surfactants that can lyse bacterial membranes. They also enhance mucosal immunity and suppress the overproduction of cytokines, which is significant in controlling BRDC-induced inflammation (Thirumeignanam, 2010; Alghirani *et al*., 2022; Hong *et al*., 2022). Phenolic acids such as caffeic acid and gallic acid are highly antioxidant and antimicrobial in nature. They are free radical scavengers, inhibitors of microbial enzymes, and inhibitors of inflammatory signal pathways (Leigh-de Rapper, 2023; Maggini *et al*., 2024; Nedeljković *et al*., 2024).

***Zingiber officinale* (Ginger):** Ginger contains active gingerol and shogaol compounds that are said to be antimicrobial and anti-inflammatory. Ginger inhibits prostaglandin and leukotriene synthesis and also affects T-cell function. It is also antimicrobial against gram-negative and gram-positive bacteria, including BRDC pathogens. Ginger extract suppresses *P. multocida* and *H. somni* in vitro. Ginger powder supplementation in the animal model reduced the score of lung inflammation and appetite and behavior scores of infected calves (Tomanić *et al*., 2022). Ginger root also has antioxidant, anti-inflammatory, and carminative properties. Active Compounds are Gingerol, shogaol, and zingerone (Virmani & Pathak, 2022). Activates macrophage and cytokine balance. Used to stimulate growth, guard against infection, and promote immune condition of calves and weaning animals.

Nigella sativa **(Black Seed):** *Nigella sativa* seeds are rich in thymoquinone, which possesses antimicrobial, antioxidant, and immunomodulatory properties. Thymoquinone exhibits antimicrobial activity by interfering with bacterial membrane potential and redox homeostasis. It also inhibits the critical inflammatory mediators TNF-α and IL-6. In vitro assays confirmed its inhibitory effect against BRDCs-related bacteria. In a clinical trial, oral administration of black seed oil to calves exhibited improved respiratory scores, improved feed intake, and improved blood antioxidant levels (Majdalawieh & Fayyad, 2015).

Routes of Administration and Formulations

Herbal Extracts: Herbal extracts are prepared by solubilizing bioactive plant material constituents (roots, leaves, bark, or seeds) with solvents (water, ethanol, or methanol). They can be concentrated or standardized to yield equal potency. They are usually given orally by being added to drinking water or feed or intranasally in aerosol form for direct action in the respiratory pathway. Drinking water with aqueous neem (*Azadirachta indica*) leaf extract was given to decrease symptoms of respiratory infections. Varies among various plant and animal species, usually between 10 to 50 mL per day per animal for fluid extracts (Pulido-Huertas *et al*., 2024).

Essential Oils: Essential oils are volatile oils, highly concentrated liquids that are obtained by steam distillation or cold pressing from aromatic plants like Thymus vulgaris, *Eucalyptus* globulus, and Origanum vulgare (Ullah, 2024). They have active ingredients like thymol, eucalyptol, and carvacrol, which are recognized for their antimicrobial and anti-inflammatory activities. Essential oils may be administered via aerosol sprays or nebulization, orally, or by topical preparations. In the management of BRDC, nebulization is especially useful in the delivery of volatile compounds directly into the lung tissue. Inhalation of *Eucalyptus* oil has been used to relieve respiratory signs in calves. 0.5–2 mL inhaled in water, depending on the weight and the severity of the disease in the animal. Much smaller doses are administered orally (0.05–0.1 mL/kg body weight) because of the potency. Essential oils are volatile, perfumery oils obtained from the leaves, flowers, stems, bark, and roots of plants. They are highly concentrated bioactive terpenes and phenolic compounds. Peppermint oil, Utilized for carminative and analgesic effects. Essential oils have been utilized in veterinary use as natural growth promoters, respiratory therapeutics, and antimicrobials (Leigh-de Rapper, 2023). Their addition to feed or water systems aids in the prevention of disease as well as in performance improvement. Their advantages are rapidly backed by empirical studies and are the backbone for their application in veterinary protocols (Mohammed *et al*., 2024). One of the most striking benefits of plant therapeutics is their antimicrobial spectrum of action. Several plant constituents have been found to inhibit pathogenic bacterial, fungal, viral, and protozoal growth, representing a phytogenic alternative to antibiotics (Wang *et al*., 2024). Numerous essential oils and phytochemicals act on bacterial cell walls, perturb membrane integrity, or interfere with enzymatic activity (Leigh-de Rapper, 2023). This antimicrobial activity is especially useful against respiratory pathogens of BRDC and gastroenteritis in calves (Ferrulli, 2023).

Feed Additives: Phytogenic feed additives involve the inclusion of powdered plant material, dried herbs, or encapsulation of bioactive compounds in the diet of animals. It ensures prolonged consumption and long-term preventive action, especially in stressful conditions that are recognized to cause BRDC, such as weaning or transport. Garlic powder (Allium sativum) or turmeric powder (*Curcuma longa*) added in feed has shown to have beneficial effects in promoting respiratory health and immune function. Usually 0.5% to 2% of the feed weight, depending on the plant type and formulation (Choudhary *et al*., 2022).

Dietary Supplements and Boluses: Supplements are also formulated as plant extract and vitamin blends in the form of oral boluses, pellets, or capsules. They are particularly handy in clinical treatment schemes or for when dosing must be controlled. A bolus of *Nigella sativa* and *Glycyrrhiza glabra* extracts has been used in the treatment of bovine respiratory infections. Usually one bolus per day for 3–5 days depending on the strength of the preparation and clinical situation (Wahab *et al*., 2022; Pazla *et al*., 2024).

Synergistic Effects and Integration with Traditional Therapies

Synergistic Action of Plant Compounds and Antibiotics: Medicinal plants are rich in diverse bioactive compounds that act through mechanisms such as microbial membrane disruption, virulence factor inhibition, immune modulation, and anti-inflammatory activity (Iqbal *et al*., 2024b). When combined with antibiotics, these phytoconstituents can enhance drug efficacy, particularly against resistant microorganisms. For example, flavonoids like quercetin and *Terminalia chebula* tannins increase bacterial sensitivity to antibiotics by altering cell wall permeability. Essential oils from *Thymus vulgaris* (thyme) and *Origanum vulgare* (oregano) display synergistic antimicrobial effects with tetracycline and ampicillin, significantly lowering the MICs required to inhibit BRDC pathogens such as *P. multocida* and *M. haemolytica*. This synergy optimizes therapeutic efficiency, reduces antibiotic dosage, and helps slow antimicrobial resistance (AMR). Lipophilic compounds in these oils integrate into bacterial membranes, increasing permeability, leading to leakage of intracellular materials and eventual cell lysis. This mechanism is particularly effective against Gram-positive bacteria but also impacts certain Gram-negative

Table 2: Mechanism of action of the bioactive agents against target pathogens

Bioactive Agent(s)	Source Plants	Formulation Type	Primary Mechanism(s)	Target Spectrum	Expected Outcomes	References
Allicin, Ajoene	Garlic (*Allium sativum*)	Oral extract, aerosol	Enzyme inhibition, biofilm disruption, immune modulation	BRDC bacteria	↓ Lung lesions, ↑ antibiotic synergy, ↑ immunity	(Abd El-Ghany, 2024; de Almeida Campos *et al*., 2023)
Curcumin + Piperine	Turmeric (*Curcuma longa*), Black pepper	Nanoemulsion/ combined	NF-κB inhibition, antioxidant, ↑ bioavailability	Broad BRDC pathogens	↓ Pulmonary inflammation, ↑ efficacy	(Clarence *et al*., 2022; Heidari *et al*., 2023)
Thymol, Carvacrol	Thyme, Oregano	Feed additive, microencapsulated	Membrane disruption, quorum sensing inhibition	BRDC bacteria (*M. bovis, H. somni, M. haemolytica*)	↓ Colonization, ↓ bacterial load	(Tomanić *et al*., 2022; Nedeljković *et al*., 2024)
Eucalyptol, Essential Oil Blends	*Eucalyptus globulus*, mixed oils	Inhalant, nebulizer	Mucolytic, antiseptic, anti-inflammatory	Respiratory bacteria & viruses	↑ Respiratory function, ↓ clinical signs	(Cock, 2011; Rajamanickam *et al*., 2019; Leigh-de Rapper, 2023)
Eugenol, Cinnamaldehyde	Clove, Cinnamon	Nebulized, aerosol	Prostaglandin inhibition, wall disruption, antioxidant	*P. multocida*, other BRDC bacteria	↓ Clinical signs, ↓ survival of bacteria	(Maggini *et al*., 2024; Shu *et al*., 2024)
Polyphenols (Quercetin, esveratrol, Green tea catechins)	Onion, Apple, Grapes, Green tea	Injectable, oral drench, feed inclusion	Antioxidant, immunoregulatory, antiviral	BRDC viruses + bacteria	↓ Oxidative stress, ↑ tissue repair, ↑ resistance	(Hong *et al*., 2022; Bejenaru *et al*., 2024; Ugoeze & Odeku, 2025)
Alkaloids (Berberine, Andrographolide)	*Berberis vulgaris*, *Andrographis paniculata*	Capsules, syrup	DNA synthesis inhibition, immune modulation	*M. bovis*, viral BRDC pathogens	↓ Inflammation, controlled viremia	(De Rubis, 2023; Jiang *et al*., 2021)
Saponins, Tannins	Yucca, Chestnut, Acacia	Feed additives	Surfactant action, protein binding	Mixed bacterial & viral infections	↓ Lung edema, inhibited viral replication	(Alghirani *et al*., 2022; Thirumeignanam, 2010)
Beta glucans, Ginsenosides, Isoflavones	Mushrooms, Ginseng, Soy	Oral supplements/fermented feed	Immune cell activation, vaccine responsiveness, mucosal immunity	Broad bacterial & viral pathogens	↑ Resistance, ↑ vaccine efficacy, improved growth	(Luo *et al*., 2018; Van Steenwijk *et al*., 2021; You *et al*., 2022)
Other agents (Azadirachtin, Citral, Zingerone, Artemisinin, Aloe-emodin, Neem oil)	Neem, Lemongrass, Ginger, *Artemisia annua*, Aloe	Nasal spray, feed, injectable, topical	Vector repellent, mucolytic, antiviral, tissue regeneration	Mixed pathogens, external vectors	↓ Co-infections, ↓ respiratory distress, mucosal healing	(Jumba, 2014; Singh *et al*., 2021; Virmani & Pathak, 2022)

BRDC pathogens due to the amphipathic nature of the phytochemicals. Oregano oil, for instance, disrupts *M. haemolytica* membranes, inducing rapid bactericidal activity without resistance development (Matté *et al*., 2023).

Oregano, a Mediterranean herb rich in carvacrol and thymol, disrupts bacterial membranes, inhibits COX enzymes and NF-κB, and is widely used in cattle and poultry feed as a respiratory protector and growth promoter (Nedeljković *et al*., 2024; Cui *et al*., 2024). Thyme, a close relative of oregano, contains thymol, carvacrol, and linalool, providing bronchodilatory and mucolytic effects while suppressing *M. bovis* and *S. aureus*. It is administered in feed or vapor form to alleviate BRDC-associated congestion (Nedeljković *et al*., 2024). Other promising botanicals include neem (*Azadirachta indica*), whose bark and leaf extracts inhibit bacterial pathogens and exhibit antiviral activity against enveloped viruses like BHV-1, BCoV, and BPIV-3, and *Thymbra spicata L.*, which shows broad-spectrum antiviral effects in vitro against BRDC-associated viruses such as BRSV, BPIV-3, BVDV, and BoHV (Pulido-Huertas *et al*., 2024). These findings highlight the potential of phytotherapeutics in controlling both primary viral pathogens and secondary bacterial invaders in BRDC (Table 2).

Decreased Antibiotic Use and Resistance Prevention: One of the major advantages of plant therapeutics in conjunction with conventional therapy is the potential to reduce antibiotic dependence. By stimulating the immune system and modulating inflammation, phytochemicals can reduce the severity of disease and healing time, and therefore the duration and dosage of antibiotic therapy. For example, supplementation with *Azadirachta indica* (neem) or *Curcuma longa* (turmeric) during an outbreak of respiratory disease in cattle has been shown to reduce clinical signs and improve recovery, allowing lower doses or shorter treatment periods with antibiotics. This approach not only reduces the likelihood of the development of resistance but also reduces the likelihood of antibiotic residues entering the food chain (Pulido-Huertas *et al*., 2024).

Combined Efficacy and Safety: The mixture of plant drugs with man-made drugs has also proved to be very safe for animals. Most of the medicinal plants utilized in the management of BRDC, such as *Glycyrrhiza glabra* (licorice) and *Nigella sativa* (black seed), are less toxic when administered at therapeutic doses. Further, their antioxidant and anti-inflammatory constituent neutralizes the adverse effects of man-made drugs, such as gastrointestinal upset or liver load, hence improving the health of animals. But appropriate selection and standardization of plant chemicals have to be carried out so that they can be compatible with veterinary drugs. Certain phytochemicals can interfere with drug absorption or metabolism if either dosed or formulated inappropriately (Emerald, 2024).

Limitations and Challenges: The most important limitation to the effective use of plant therapeutics in veterinary medicine is the lack of standardization. Unlike synthetic drugs with defined molecular structures and concentrations, herbal extracts vary widely in their chemical composition depending on factors such as plant species, geographic origin, soil type, harvest time, and extraction method. This variability affects product consistency, efficacy, and safety. For example, allicin in garlic or curcumin in turmeric can fluctuate between batches, leading to inconsistent dosing and unpredictable outcomes (Abd El-Ghany, 2024). Compounding this issue, many commercial preparations do not report full phytochemical profiles, and contamination with pesticides, heavy metals, or mycotoxins (e.g., aflatoxin) poses additional risks. Without strict control of cultivation and processing, herbal products may become as problematic as the conditions they are intended to treat. Addressing this requires adherence to Good Agricultural and Collection Practices (GACP) and Good Manufacturing Practices (GMP), coupled with routine use of analytical tools such as HPLC, GC-MS, and FTIR to verify active constituents and ensure product consistency (Lees *et al*., 2024).

Another challenge is poor bioavailability. Even when phytochemicals survive ruminal metabolism, their gastrointestinal absorption is often limited by molecular size, polarity, and solubility. Allicin, for instance, is unstable and rapidly metabolized, requiring special formulations to preserve activity. Likewise, saponins, tannins, and flavonoids may bind dietary proteins or minerals, reducing systemic uptake (Thirumeignanam, 2010). Limited pharmacokinetic data in ruminants further complicates determination of effective dosing, onset of action, and withdrawal periods—key to therapeutic safety. Progress depends on detailed pharmacokinetic studies, including plasma concentration–time profiles, tissue distribution, and bioequivalence trials (Ozma *et al*., 2023). Regulatory gaps further hinder adoption. Whereas synthetic drugs undergo rigorous testing for efficacy, safety, and pharmacokinetics, most herbal products are marketed as feed additives or nutraceuticals and face minimal oversight. In many countries, veterinary phytomedicines lack clarity on approved active ingredients, label claims, residue limits, or cross-border standards, discouraging their use despite promising evidence (Mtewa *et al*., 2021). Safety concerns also remain. Although generally less toxic than synthetic chemicals, some phytoconstituents can cause adverse effects at high doses or when combined with other drugs. For example, excessive garlic can trigger hemolytic anemia in ruminants, saponins may induce bloat, and essential oils can interfere with hepatic drug metabolism. Without comprehensive toxicological data, risks of inadvertent toxicity or treatment failure persist. Standardized safety testing for residues, interactions, and toxic thresholds is therefore essential (Ramdani *et al*., 2023).

Finally, evidence from large-scale, randomized livestock trials remains scarce. Most studies are limited to in vitro experiments or small-scale in vivo trials with short durations, small sample sizes, and limited endpoints. Few assess outcomes relevant to production, such as lung lesion scores, mortality, growth, or long-term immunity under field conditions (Staudacher *et al*., 2017). This lack of robust evidence constrains decision-making by veterinarians, producers, and regulators. Progress requires coordinated, multi-institutional research involving academia, industry, and livestock producers, with standardized trial protocols, multi-site testing across regions, and comparative studies against antibiotics and vaccines. Cost-benefit analyses are also necessary to establish economic justification (Donner, 2010).

Integration into Livestock Health Management: Plant therapeutics are not meant to fully replace antibiotics and vaccines but to complement them. When used together, they can reduce the need for high-dose antimicrobials or extend intervals between vaccine doses, contributing to antibiotic stewardship and improved herd immunity (Rashid *et al*., 2024). Some phytochemicals show synergism with conventional antibiotics; for example, essential oils such as thymol and carvacrol disrupt bacterial membranes, thereby enhancing the penetration and efficacy of beta-lactams and macrolides (Nedeljković *et al*., 2024; Raikwar *et al*., 2024; Tomanić *et al*., 2022). Curcumin has been shown to suppress resistance gene expression and potentiate the effect of co-administered drugs. During BRDC outbreaks, herbal therapies can provide supportive treatment by reducing lung inflammation and oxidative stress (e.g., neem, turmeric), stimulating immune responses (e.g., echinacea, garlic), and preventing bacterial secondary infections. By integrating these therapeutics into treatment regimens, veterinarians can lower antibiotic use while improving overall outcomes. Plant compounds may also act as vaccine adjuvants. Quillaja saponaria saponins and Aloe vera polysaccharides, for example, enhance antigen-specific immune responses (Luo *et al*., 2024; Zhao *et al*., 2024).

Feed supplementation remains the most practical delivery system for herbal therapeutics in livestock. This method ensures steady intake, reduces stress associated with injections, and fits seamlessly into feeding routines. Dried powders or extracts of garlic, turmeric, neem, ginger, and oregano can be incorporated into concentrate feeds or total mixed rations. Such additives improve gut health, optimize nutrient use, enhance immunity, reduce microbial load in the respiratory tract, and support growth performance. Garlic extract, for instance, has been linked to higher weight gain and reduced respiratory disease in calves, while microencapsulated essential oils provide antimicrobial action and improve rumen fermentation. Seasonal premixes of multiple phytocompounds can also be tailored to production stages, such as calf starters, transition cow diets, or finishing rations, with veterinarian and nutritionist oversight to ensure balance and effectiveness (Alem, 2024; Phupaboon *et al*., 2024).

Beyond treatment, phytotherapeutics can play a preventive role by reducing disease susceptibility and boosting resilience to infections like BRDC. Routine supplementation with immunomodulators such as echinacea, garlic, and turmeric strengthens immunity during stressors like weaning, transport, weather fluctuations, and group mixing. This can lower morbidity, enhance vaccine responses, and improve herd immunity. Since BRDC peaks in transitional seasons (fall, spring), targeted use of botanicals like eucalyptus or licorice can prevent early respiratory disease in high-risk groups such as recently arrived feedlot calves (Nabi *et al*., 2023). Additionally, many botanicals contribute to environmental sanitation: neem sprays reduce insect vectors in bedding, while eucalyptus or thyme oil foggers lower airborne microbial loads in housing systems. Such measures align with One Health principles, supporting animal health, farm biosecurity, and environmental safety (Githaiga, 2021).

Effective integration of phytotherapeutics in livestock health depends on stakeholder education and engagement (Nazir *et al.*, 2024). Farmers and veterinarians must be trained to recognize quality products, apply them correctly, and monitor outcomes. A knowledge gap persists between ethnoveterinary traditions and evidence-based science, and bridging it requires accessible extension services, farmer field schools, demonstration farms, and online platforms. These platforms can share comparative trials, success stories, and standardized protocols to build confidence and promote adoption. The wider acceptance of plant-based medicines by veterinarians will ultimately depend on solid evidence of safety and efficacy, well-defined usage and withdrawal guidelines, and broad availability of standardized, quality-controlled products (Hellec *et al.*, 2021).

Conclusions: Bovine Respiratory Disease Complex (BRDC) remains a major threat to cattle health and productivity due to its multifactorial nature and limited control with current antibiotics and vaccines. Evidence from both in vitro and in vivo studies shows that medicinal plants such as eucalyptus, garlic, turmeric, and neem provide antimicrobial, antioxidant, anti-inflammatory, and immunomodulatory benefits, supporting their use as complementary therapies. Practical application is most feasible through feed supplementation, preventive health schemes, and integration alongside conventional treatments, where they can lower antibiotic dependence and improve herd resilience. However, key challenges, such as variability in phytochemical content, poor bioavailability in ruminants, regulatory gaps, and the scarcity of large-scale clinical trials, must be addressed before widespread adoption. Advancing standardization, developing validated formulations, and generating robust clinical evidence under commercial production systems are essential next steps. With these measures, plant-based therapeutics can realistically serve as adjuncts to conventional strategies, strengthening antibiotic stewardship and promoting sustainable livestock health management.

Acknowledgments: The Researcher would like to thank The Deanship of Graduate Studies and Scientific Research at Qassim University for financial support (QU-APC2025).

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