

USE OF NATURAL ANTIMICROBIAL PHYTOCHEMICALS IN IN POULTRY AND LIVESTOCK PRODUCTION; A COMPREHENSIVE REVIEW

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ABSTRACT: Antimicrobial resistance (AMR) in poultry production is a serious global issue that has threatened public safety and animal health. The careless use of antibiotics in poultry feed and health management has accelerated the development of resistant bacterial strains, reduced the effectiveness of traditional medicines and posed the risk of the prevalence of resistant diseases via the food chain. Therefore, phytochemicals derived from edible beverages, herbs, spices, and medicinal plants have drawn attention as viable substitutes in this regard. Phytochemicals include a variety of bioactive compounds (alkaloids, flavonoids, terpenoids, saponins, tannins, and essential oils) that have antimicrobial, antioxidant, and immunomodulation effects. These compounds work by breaking down the membranes or cell walls of bacteria, preventing the creation of proteins and nucleic acids, interfering with quorum sensing, and improving host immunity. In addition to lowering the microbial burden, phytochemicals have also been reported to enhance growth, gut health, and meat quality, making them excellent options for replacing antibiotics in animal feed. Moreover, using phytochemicals in combination with traditional medications may help restore the effectiveness of antibiotics against resistant bacteria. Yet, there are still issues with their safety, extraction procedures, bioavailability, dose rates, ideal dosage conditions, and standardization. Therefore, this review article discusses the potential of phytochemicals derived from food and medications to reduce microbial resistance in poultry, along with the need for further studies to explore economical, environmentally friendly, and scientifically supported bioactive compounds to address the antimicrobial resistance and food-related public health safety issues to promote sustainable poultry production.

Keywords: Antibiotics, Antimicrobial resistance, Alternative antibiotics, Phytochemicals, Animal Production.

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INTRODUCTION

Microorganisms, including bacteria, fungi produce secondary metabolites called antibiotics, which have been used to either kill or suppress the growth of microorganisms. Antibiotics are structurally divided into several classes, including β -lactams, quinolones, fluoroquinolones, macrolides, aminoglycosides, and tetracycline (Coates *et al.*, 2011). Since the discovery of penicillin, antibiotics have been used to successfully treat infectious diseases as well as to promote growth in the aquaculture, agricultural, fisheries, and animal husbandry

(Roca *et al.*, 2015). Over the past several decades, the world's meat production has increased which has caused a rise in use of antibiotics and it is expected that global use of antibiotics will exceed 110,000 tonnes by 2030 (Van Boeckel *et al.*, 2015). Veterinary medications include around twice as many antibiotics as human medications. Though, antibiotics are wisely used to treat infectious illnesses, however, misuse of antibiotics have increased the number of leftover drugs in food and the environment, which can cause antibiotic-resistant bacteria to proliferate and appear quickly (Ben *et al.*, 2019). Therefore research in recent decades are focused to

address the antimicrobial resistance (AMR) due to the continuous escalation of the problem that is jeopardizing the food safety, the environment, and veterinary and human medicine, even though their use may contribute to its development (Kasimanickam *et al.*, 2021). Globally, antimicrobial resistance (AMR) presents serious obstacles to the production of poultry and animals (Stoica C *et al.*, 2021). The misuse of antibiotics as growth promoters and for disease prevention rather than treatment has led to the emergence of antibiotic-resistant bacterial strains in animal and poultry production. Commonly used antibiotics cause these less effective against resistant microorganisms, making it more difficult to treat animal infections which may lead to increased morbidity, death, decreased feed efficiency, and productivity losses causing farmers heavy financial losses. Furthermore, there is a significant risk to public health since resistant germs can spread from animals to people through the food chain, direct contact, or the environment. AMR in animal production systems also makes it more difficult to guarantee food safety and export quality, particularly in countries where agriculture and animal production is a major source of economic growth. The viability of the livestock industries, global food security, and animal health and welfare are all at risk due to this increasing resistance.

According to research, antibiotic-resistant bacterial diseases claim the lives of 700,000 people each year, and by 2050, that number might rise to 10 million (O'Neill 2016). The rise of bacteria resistant to antibiotics, particularly those that are multidrug resistant, has become a major issue in the food business, public health, animal husbandry, and medical treatment (Monger *et al.*, 2021). Additionally, the development of bacteria resistant to several medications outpaces the research and development of new antibiotics, which restricts the use of antibiotics to prevent and treat infectious diseases. Research and development into the new antibiotics will cost a lot of money. To avoid antibiotic abuse/overuse, it is crucial to comprehend the effects of antibiotic usage and residues in food animals.

When antibiotics are used improperly in animal production the resistant bacteria can develop and contaminate meat, milk, eggs and other animal products significantly threatens both food safety and public health. These resistant pathogens can enter the human population through the consumption of contaminated food or direct contact with animals, leading to infections that are increasingly difficult to treat. This undermines the effectiveness of antibiotics, prolongs illnesses, increases healthcare costs, and raises the risk of severe complications or death, especially in vulnerable populations. Additionally, AMR jeopardizes the safety of contemporary medical operations that rely on potent antibiotics, including surgeries, cancer treatments, and organ transplants. From a food safety perspective, AMR

limits the ability to control bacterial contamination in the food chain, raising concerns about public health, trade restrictions, and consumer trust. Addressing AMR is therefore essential not only to protect human health but also to ensure the integrity, safety, and sustainability of global food systems.

The effectiveness of contemporary medicine, food security, and public health are all at risk due to the rising worldwide threat of AMR. Once-treatable illnesses like sepsis, pneumonia, and TB are becoming costlier and harder to treat as bacteria develop antibiotic resistance, which raises death rates. If AMR is not immediately addressed, it is predicted to result in up to 10 million fatalities per year by 2050. International travel, trade, and the pervasive abuse of antibiotics in human healthcare, veterinary medicine, and agriculture all contribute to the global spread of resistant infections. The issue is made worse in low- and middle-income nations by the availability of over-the-counter antibiotics, inadequate regulatory frameworks, and a lack of surveillance. Additionally, AMR threaten the effectiveness of medical operations that rely on efficient antibiotics for infection control, such as cancer therapies and surgery. Furthermore, there is a significant risk to global food safety and economic stability due to its effects on livestock and food production. To tackle AMR, a concerted international effort is required, utilizing a One Health approach that integrates environmental, animal, and human health initiatives. Therefore the intent of this review article is to discuss the impact of excessive usage of antibiotics on animal and public health due to the emergence of AMR and exploring the alternative options to tackle this serious issue with special emphasis on exploring the potential phytochemicals..

Antibiotics emergence over time: The term "antibiotics" refers to naturally occurring substances produced by a range of microorganisms, such as bacteria and fungi, that can kill and inhibit the growth of other microorganisms (Table 1 and 2). The term "antimicrobial," which refers to natural, semi-synthetic, and synthetic substances that can inhibit microbe growth and induce apoptosis, has supplanted the term "antibiotics" due to the production of semi-synthetic derivatives (Kourkouta L *et al.*, 2018). Numerous novel antimicrobial agents with diverse modes of action have been identified over time, and it is commonly known that the existing arsenal offers total defense against practically all infections (Antoniadis *et al.*, 2000). Antimicrobials are often used medications these days, not only in medicine but also in agriculture, fish farming, cattle farming, and as growth-protective or growth-enhancing agents (Sarmah *et al.*, 2006). It is crucial to note that chemotherapeutic medications that target bacteria and are made from living things are referred to as antibiotics, whilst laboratory-produced synthetic medications are known as antimicrobials

(Patrikis *et al.*, 2011). Broadly Antibiotics are classified into two main groups, bacteriostatic and bactericidal.

Without a question, one of the most significant pharmacological discoveries of the 20th century was the discovery of antibiotics. These potent weapons assisted humanity in his never-ending fight against microbial diseases and helped to manage a wide range of illnesses. Scientists had to create new antibacterial medications because, very quickly, many community-acquired infections, such as *Staphylococcus aureus*, *Enterococcus fecium*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and some *Enterobacter* species, had shown remarkable resistance to the newly discovered antibiotics (Ruddaraju LK *et al.*, 2019). Unfortunately, the FDA found that although the number of new antibiotics approved has dropped by 56% in the last three decades, the number of multidrug-resistant (MDR) bacteria is continuously rising, while the intense efforts to create new antibiotics are rapidly declining. The FDA also declared that we are approaching a true health crisis (Conly *et al.*, 2005). However, research on the antibacterial properties of plant-based and natural medicines has shown impressive potency against several bacterial infections without significant side effects when compared to antibiotics, and interest in medicinal plants has grown (Mohamed *et al.*, 2020).

In order to provide sustainable alternatives to synthetic antibiotics in the production of poultry and cattle, this research aims to critically assess the possible use of natural antimicrobial resistance (AMR) phytochemicals in diets and medications. In order to manage microbial infections and improve animal health, the review aims to investigate the efficacy, mechanisms of action, safety, and useful uses of chemicals produced from plants. It also seeks to draw attention to how phytochemicals might improve food safety, slow the emergence of antibiotic resistance, and aid in the transition to animal husbandry systems devoid of antibiotics. The study will also highlight research gaps, regulatory obstacles, and future potential for the incorporation of phytochemicals into contemporary animal production techniques by synthesizing recent scientific information.

A-Mechanisms of bacterial resistance to antibiotics:

Bacteria develop antibiotic resistance because of a self-defense mechanism that develops naturally to become resistant to hazardous situations. Antibiotics are frequently categorized based on their inhibitory methods, which include inducing alternative metabolic pathways, inhibiting the synthesis of proteins and nucleic acids, disrupting the cytoplasmic membrane, and inhibiting the creation of cell walls (Culp *et al.*, 2020; Kapoor *et al.*, 2017). Lincosamides, macrolides, cephalosporins, penicillins, β -lactamase inhibitors, and other bactericidal medications that stop cell wall construction can affect

gram-positive bacteria. Gram-negative bacteria can be impacted by aminoglycosides, polymyxins, and quinolones, which mainly impede protein synthesis to provide bactericidal effects. The development of metabolic bypass, changes to drug target sites, modification of membrane permeability, and antibiotic efflux pump systems are some of the methods by which bacteria can become resistant to antibiotics (Lin *et al.*, 2015).

B-Modification of antibiotic target sites:

The modification of drug target sites is one self-resistance strategy under the selection pressure of antibiotics (Reygaert *et al.*, 2018). The β -lactam antibiotics and penicillin-binding proteins (PBPs), which are essential for the synthesis of peptidoglycan, have structural similarities (Sauvage *et al.*, 2008). An active site of PBPs is permanently acylated by the structural analogues' cephalosporin and penicillin, which inhibit bacterial growth (Zapun *et al.*, 2008). Due to their overproduction of low-affinity PBPs for β -lactam antibiotics, *Streptomyces* species and *Streptococcus pneumoniae* exhibit substantial penicillin resistance (Beceiro *et al.*, 2013; Blair *et al.*, 2015; Watts *et al.*, 2017). Vancomycin and teicoplanin are examples of glycopeptides that attach to peptidoglycan precursors (D-Ala-D-Ala) and prevent transpeptidation and transglycosylation of cell walls (Kang *et al.*, 2015). The affinity for the glycopeptide is significantly reduced when the peptidoglycan precursor is changed from D-Ala-D-Ala to D-Ala-D-Lac or D-Ala-D-Ser (Peterson *et al.*, 2018). Resistance to antibiotics that target the bacterial ribosome can result from erythromycin ribosome methylase (*erm*), which methylates ribosomal subunits (Reygaert *et al.*, 2018). For instance, methylation of ribosomal subunits caused resistance to streptogramin B (MLSB), lincosamide, and macrolide (Lioy *et al.*, 2014; Roberts *et al.*, 2004). The structural alterations in DNA gyrase and topoisomerase IV (GryA or ParC) that result in a decreased capacity to bind to the DNA gyrase-DNA complex are the source of resistance to quinolones and fluoroquinolones that target these enzymes (Hawkey *et al.*, 2003; Hooper *et al.*, 2016; Redgrave *et al.*, 2014).

Enzymatic degradation of antibiotics:

The capacity of hydrolase-type enzymes to cleave substrates such β -lactams, aminoglycosides, phenicols, and macrolides can lead to antibiotic resistance in bacteria. β -lactamases may typically hydrolyse β -lactam antibiotics, including carbapenems, monobactams, clavams, cephalosporins, and penicillins. Moreover, extended-spectrum β -lactamases (ESBLs) can impart resistance to most β -lactam antibiotics, including oxyimino-cephalosporins (Livermore *et al.*, 2008). In recent years, the emergence and spread of bacteria that generate carbapenemase, such as Enterobacteriaceae and *Klebsiella pneumoniae*, have become a global health issue due to high rates of

morbidity and mortality (Pitout *et al.*, 2015). Steric blockage of antibiotic target sites can lead to antibiotic resistance. Antibiotic-modifying enzymes like transferases can create antibiotic resistance by incorporating functional groups (acyl, phosphate, nucleotidyl, and ribitoyl) into aminoglycosides, chloramphenicol, streptogramins, and fluoroquinolones (Ramirez *et al.*, 2010; Robicsek *et al.*, 2006). Furthermore, the infection's rifamycin resistance is directly linked to the rifamycin phosphotransferases (Spanogiannopoulos *et al.*, 2014). The leading beef-producing countries include Brazil, Canada, the United States, Argentina, the European Union, and Australia. The cattle and dairy industries utilise a variety of antibiotics, including tetracyclines, aminoglycosides, β -lactams, chloramphenicol, fluoroquinolones, glycolipids, ionophores, macrolides, quinolones, streptogramins, and sulfonamides (Zalewska *et al.*, 2021). In North America, cattle have frequently been treated with sulfamethoxazole, ceftiofur, tylosin, and chlortetracycline (Aust *et al.*, 2008). In Europe, lincosamides and macrolides are often used to treat a variety of infectious cattle illnesses. Tetracyclines, in particular, are frequently used to treat skin, gastrointestinal, and respiratory conditions in cattle. *Salmonella* species, *Staphylococcus aureus*, *Streptococcus* species, *Escherichia coli*, *Pasteurella multocida*, and *Mannheimia hemolytica* are the main infectious illness causes in cattle (Andrés-Lasheras *et al.*, 2022; Awosile BB *et al.*, 2018). The use of antibiotics in cattle has expanded along with the consumption of beef, leading to a significant problem with antibiotic resistance. Furthermore, the use of cow dung as soil fertilizer greatly aids in the spread of antibiotic resistant genes (ARGs) and bacteria resistant to antibiotics (Chen *et al.*, 2019; Sachi *et al.*, 2019). Numerous transferable genes that give resistance to MLSB, tetracyclines, and sulfonamides are present in the microbial population of calves who have received antibiotic treatment (Alexander *et al.*, 2011; Chen *et al.*, 2008). The overuse of ceftiofur in cattle contributes significantly to the spread of multidrug-resistant bacteria and ARGs (Chambers *et al.*, 2015). A major issue may arise from the possible spread of ARGs from cattle to meat and humans.

Antibiotics used in poultry and livestock production:

The Asia-Pacific area consumes a lot of chicken, and the worldwide poultry industry has grown. In 2019, the United States of America produced the most poultry (19,710,000 tonnes), followed by China, Brazil, and the European Union. The United States and the European Union have recently limited the use of antibiotics in meat and poultry products. However, to prevent illness and promote chicken development, antibiotics must be used. In poultry, virginiamycin, bacitracin, salinomycin, and tilmicosin are the most often used antibiotics. Avian

pathogenic *E. coli* (APEC), *Salmonella Pullorum*, *S. Gallinarum*, *Pasteurella multocida*, *Avibacterium paragallinarum*, *Gallibacterium anatis*, *Ornitobacterium rhinotracheale*, *Bordetella avium*, *Clostridium perfringens*, *Mycoplasma spp.*, *Erysipelothrix rhusiopathiae*, and *Riemerella anatipestifer* are among the infectious poultry diseases that have been treated with these antibiotics (Porter *et al.*, 1998). Antibiotic-resistant bacteria have unavoidably emerged as a result of the widespread use of antibiotics to prevent sickness and promote growth (Fletcher *et al.*, 2015). Specifically, APEC has become resistant to tetracycline, ampicillin, and amoxicillin (Nhung *et al.*, 2017). Furthermore, phenotypic resistance to ceftiofur, amoxicillin, gentamicin, enrofloxacin, and co-trimoxazole was markedly elevated in *O. rhinotracheale*. Tetracyclines, which are still present in meat, were the antibiotics used in food animals in 37% of Europe and 71% of the US (Ronquillo *et al.*, 2017; Idowu *et al.*, 2010). Humans are in danger from the residual antibiotics that are tainted in chicken eggs (Amador *et al.*, 2019). Furthermore, ciprofloxacin-resistant bacteria were highly prevalent in poultry. Poultry has been found to possess genes that are resistant to tetracyclines, quinolones, sulfonamides, and chloramphenicol (Economou *et al.*, 2015).

Phytochemicals and antimicrobial resistance (AMR)

in poultry: Interest in plant-derived phytochemicals as natural substitutes for traditional antibiotics has increased due to growing concerns about antimicrobial resistance (AMR) in chicken production. Because of their antibacterial, antioxidant, and immunomodulatory qualities, phytochemicals hold promising role as feed additives to improve the gut health by reducing pathogen load without antimicrobial resistance (See Table 3). Some of the important plant based bio-active compound and their role to combat the antimicrobial resistance in poultry and animal production is discussed below:

A. Phenolic compounds and essential oils: Carvacrol, thymol, and cinnamonaldehyde are found in essential oils made from *Origanum vulgare*, *Thymus vulgaris*, and *Cinnamomum spp.*. These bioactive compounds are capable to damage cell membranes of bacteria, preventing quorum sensing, and inhibit efflux pumps. These processes prevent the process of resistance development in pathogens such as *Escherichia coli* and *Salmonella enterica*. Research on broilers has revealed that oregano and supplements of cinnamon can oil improve the production performance and reduces the colonization of pathogens resistant to drugs.

Table 1: Commonly used antibiotics groups in the livestock and poultry

Antibiotic group	Mechanism of action	Indications/ Contraindications	Salt name	Trade name	Recommended dose
Penicillin's (Bactericidal)	Cell wall inhibition Inhibit the last step of cell wall synthesis PBPs Autolysins	Narrow spectrum: anaerobic, many gram-positive, few gram-negative	Procaine Penicillin + Benzyl Penicillin NS	Penicill 40 (star)	LA: 1ml/50kg SA: 1ml/25kg
		Broad Spectrum: many gram-positive and gram-negative	Procaine penicillin + Benzyl penicillin + Streptomycin NS	Pen biotic (Nawan)	LA: 5g/animal SA: 1g/animal
		Local & systemic acute infections, eyes, ear, skin infection, IMM Amoxicillin: C&F UTI	Amoxicillin BS	Amoxivet (ICI) Amovet LA (Nawan)	H: 11-22mg/kg IM Bid R: 11-22mg/kg IM Bid
		Ineffective: Mycobacteria, Mycoplasma, Protozoa, Viruses, fungi	Ampicillin Trihydrate BS	Ampicillin – 20%	H: 11-22mg/kg IM Bid R: 11-22mg/kg IM Bid
		Pregnancy safe (except: streptomycin, clavulanic acid)			
Cephalosporin (Bactericidal)	Cell wall synthesis inhibitor	Do not use in bone, cartilage, CSF, cornea, bronchial secretions 1 st Generation: gram positive, Staphylococcus, dermatitis, surgical prophylaxis	1 st G: Cephadrine, Cephalexin, Cefazoline NS	Velosef (Bristol M.S)	R: 1.1-2.2 mg/kg IM IV H: 2.2-5 mg/kg IV IM H: 25-50mg/kg IM
		2 nd Generation: Both positive & negative	2 nd G: Cefamandole, Cefachlor BS		
		3 rd Generation: Gram-negative, less Gram-positive Positive	3 rd G: Ceftiofur, Ceftriazone, Cefotaxime BS	Cefur RTU (Nawan) Oxidil (Sami)	
		4 th Generation: Broad Spectrum Infections of soft tissue, osteomyelitis, and arthritis.	4 th G: Cefipime BS		
Aminoglycosides (Bactericidal)	Inhibit Protein synthesis by irreversibly binding to 30s Ribosome, resulting in formation of abnormal protein.	3 rd G cross BBB- meningitis Effective against rapidly multiplying bacteria, eyes, ears	Gentamycin BS	Gentawan-10 (Nawan)	R: 3-6mg/kg BID IM H: 3-6mg/kg BID IM
		Intrauterine treatment of Endometritis, IMM for treating Mastitis	Streptomycin NS		
		Pregnancy unsafe	Tobramycin BS		
Quinolones/	Inhibit	Effective against Gram-negative and several	Enrofloxacin	Encure 20	R: 0.5 ml/40 kg

Fluoroquinolones (Bacteriocidal)	Topoisomerases 2 and Topoisomerase 4 resulting in reduced supercoiling, reduced DNA pair	Gram positive aerobes including <i>E.Coli</i> , <i>Salmonella</i> , <i>Klebsiella</i> , <i>Enterobacter</i> , and <i>Proteus</i> Active against deep-seated infections, intracellular pathogens e.g, <i>Brucella spp</i> Respiratory, Intestinal, Urinary, Skin infections, Arthritis, Meningio-encephalitis and osteomyelitis Not recommended in younger age as it causes erosion of growing cartilages (reversible arthropathy)	Norfloxacin Ciprofloxacin	(Nawan) Norfloxin 10% (Star) Cipoxin (Selmor)	H: not used R: 1 ml/10 kg LA = 1 ml/20 kg SA = 1 ml/10 kg
Pregnancy unsafe					

Table 2: Classification of bactericidal antibiotics

Antibiotic group	Mechanism of action	Indications/ Contraindications	Salt name	Trade name	Recommended dose
Sulfonamides (Bacteriostatic)	Sulfonamides are analogues of para-aminobenzoic acid (PABA) and competitively inhibit the formation of dihydropteroate synthetase, resulting in blockage of several enzymes necessary for the formation of RNA, protein synthesis, and folic acid	Effective in early stages of acute infection. Actinobacillosis, colibacillosis, mastitis, metritis, pododermatitis, coccidiosis, toxoplasmosis and respiratory infections. Effective against <i>Nocardia</i> , <i>Actinomyces spp</i> , some protozoan infections like <i>Toxoplasmosis</i> and <i>Coccidia</i> <i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Salmonella</i> , <i>Pasteurella</i> , <i>E.Coli</i> .	Sulfadimidine Sodium (Sulfamethazine) BS Trimethoprim + Sulfadiazine (Potentiated Sulfonamides BS	Dimadin (Nawan) Tribrissen (GSK)	1ml/15 kg
Tetracyclines (Bacteriostatic)	Reversible binding to the bacterial 30S ribosomal subunit and t RNA acceptor site thus preventing ribosomal translation.	Pregnancy unsafe Effective against Mycoplasma, Chlamydiosis, Heart water, Anaplasmosis, Actinomycosis, Nocardiosis, Fatal diarrhea in foals (Horses) Causes nephrotoxicity when administered at highly recommended doses. Calcium chelation is the major side effects It can affect growing bone and teeth formation (because of the straining of teeth) in young animals, and some hepatotoxicity may occur at large doses	Oxytetracycline BS Oxytetracycline LA BS Doxycycline BS	Oxy S (Selmore) Oxtra LA	H: 5mg/Kg IV R: 5-10mg/kg IM or IV 1 ml/10 kg
Phenicols (Bacteriostatic)	Inhibition of microbial protein synthesis by binding to 50S	Pregnancy unsafe Efficacy against many <i>Salmonella</i> spps, gram-positive, gram gram-negative. Used to treat both local and systemic	Chloramphenicol BS	Chlorobiotic (Star)	H: 3- 25ml/animal

	subunit of the 70S ribosome	infections.			
		Upper respiratory tract infections, urinary tract infections, enteritis, and bacterial conjunctivitis	Florfenicol BS	Naflor (nawan)	R: not used H: not used R: 1 ml/15 kg
		Florfenicol is approved in Bovine respiratory disease in cattle.			
		Prohibited food-producing animals in many countries because it may cause blood dyscrasias, non-regenerative anemia, and irreversible aplastic anemia in humans.			
Macrolides (Bacteriostatic)	Interfere with protein synthesis by reversibly binding to 50S subunit of ribosome	Effective in rapidly dividing bacteria and <i>Mycoplasma</i>	Tylosin NS	Tylomac – 20% (Star)	R: 10-20mg/kg
		General indications include URT infection, bronchopneumonia, bacterial enteritis, metritis, UTI, arthritis			
		Tylosin is contraindicated in horses, can cause fatal diarrhea			
Lincosamides (Bacteriostatic)	Bind exclusively to 50S sub-unit of bacterial ribosome and suppress protein synthesis.	Upper respiratory tract infections, skin infections, <i>Streptococcus</i> and <i>Staphylococcus</i>	Lincomycin HCl NS	Lincomycin (UpJohn)	R: 10mg/kg IM BID

Table 3: Phytochemicals, Their Antibacterial Activities, and Target Sites: Some Literature Evidence

Phytochemical	Bacteria	Target site	Mode of action	Author
Carvacrol/oregano	<i>E. coli</i>	Survival mechanism and multi-drug efflux system	Missense mutation in <i>cadC</i> and <i>marR</i>	Al-Mnaser and Woodward (2020)
Thymol/carvacrol	<i>E. coli</i>	Heat and oxidative stress responses and iron transportation	Increased expression of membrane genes (<i>pspD</i> and <i>pspG</i>), heat responses genes (<i>ibpB</i>), oxidative stress responses genes (<i>grxA</i> and <i>soxS</i>) and iron transport gene (<i>feoA</i>)	Yuan et al., (2018)
Carvacrol	<i>E. coli</i>	Redox sensor system and multi-drug efflux system	Missense mutation in <i>soxR</i> and frameshift in <i>marR</i>	Chueca et al., (2018)
Carvacrol/oregano	<i>Salmonella</i>	Stress response	Influence on the <i>rpoS</i> gene	Cariri et al., (2019)
Carvacrol	<i>Salmonella</i>	Oxidative stress response	Single nucleotide modification in the transcriptional regulators (<i>yfhP</i> and <i>soxR</i>)	Berdejo et al., (2020)
Thymol	<i>E. coli</i>	Multi-drug efflux system	Non-sense mutation in <i>acrR</i> gene encoding for the AcrAB repressor	Al-Kandari et al., (2019)
Thymol	<i>Salmonella</i>	Thermal stress response	Upregulation in the expression of the chaperones (GroEl and DnaK)	Di Pasqua et al., (2010)
Thymol/carvacrol	<i>Salmonella</i>	Virulence genes	Downregulation in the expression of the main virulence genes (<i>hilA</i> , <i>prgH</i> , <i>invA</i> , <i>sipA</i> , <i>sipC</i> , <i>sipD</i> , <i>sopB</i> , <i>sopE2</i>)	Giovagnoni et al., (2020)
Carvacrol	<i>Campylobacter</i>	Motility systems	Downregulation in the expression of genes encoding for motility systems (<i>flaA</i> , <i>flaB</i> and <i>flgA</i>)	Wagle et al., (2019)

B. Flavonoids: Through processes like DNA gyrase inhibition, interruption of protein synthesis, and interference with bacterial signaling pathways, flavonoids like quercetin, catechins, and luteolin have broad-spectrum antibacterial activity. Quercetin has demonstrated potential in the treatment of *Campylobacter jejuni* and *E. coli* in particular. Additionally, it cooperates with conventional antibiotics to postpone the development of resistance and lower the required therapeutic dosage.

C. Alkaloids: It has been demonstrated that alkaloids like capsaicin (found in chili peppers) and berberine (found in *Berberis* spp.) inhibit bacterial efflux pumps, which are essential resistance mechanisms in Gram-negative bacteria. Berberine has been demonstrated to lower the incidence of necrotic enteritis and the growth of *Clostridium perfringens* in chicken diets, hence lowering the requirement for antibiotic intervention.

D. Tanning agents and saponins: Condensed tannins from chestnut and quebracho extracts, as well as saponins from *Yucca schidigera* and *Quillaja saponaria*, have antibacterial and anti-quorum sensing properties. They selectively reduce dangerous bacteria while preserving a healthy microbiota, prevent bacterial adherence to the gut mucosa, and suppress the formation of toxins. This aids in re-establishing the equilibrium of gut microbes and increases their resistance to illnesses that are resistant to antibiotics.

To increase the production of food animals, natural bioactive components called phytochemicals, such as tannins and essential oils, are added to animal feed (Lillehoj *et al.*, 2018). The use of phytochemicals as natural growth enhancers in the ruminant and poultry industries has increased recently (Lee *et al.*, 2011). Specifically, commercial chicken farms employ phytochemicals to avoid sickness and promote growth. According to the European Medicines Authority (EMA) and the European Food Safety Authority (EFSA), phytochemicals can effectively stimulate chicken development. For instance, by stimulating the growth of chicken spleen cells, cinnamonaldehyde (2E)-3-phenylprop-2-enal, which is derived from cinnamon (*Cinnamomum cassia*), enhanced chicken immunity (Lee *et al.*, 2011). Furthermore, in *E. acervuline*-infected birds, *Curcuma longa* (turmeric), *Capsicum annuum* and *C. frutescens* (hot pepper), and *Lentinus edodes* (shiitake mushroom) improved serum antibody titers against profilin, decreased fecal oocyst shedding, and caused weight gain (Liu *et al.*, 2014). When given to pigs with *E. coli*, capsaicin oleoresin, garlic botanical, or turmeric oleoresin enhanced the pigs' intestinal health and reduced the negative effects of the bacteria. Additionally, phytochemicals improved the pig's physiological defense system and reduced the activation of the immunological

response (Oh *et al.*, 2015). By raising neutrophils and lowering lymphocytes, capsaicin oleoresin in beef cattle feed enhanced milk production and immunological markers (Dono *et al.*, 2014). Nevertheless, there are still safety concerns with using phytochemicals as substitutes in animals. Therefore there is dire need to conduct research on the best practices to extract and safe doze evaluation of these phytochemicals to address the AMR in animal production (See Table 4).

Effect of different phytochemicals to address amr in poultry and animal production: The Centers for Disease Control and Prevention (CDC) estimates that 48 million people suffer from foodborne infections each year. Gram-negative bacteria generating ESBLs, Common foodborne pathogens include *Salmonella* spp., *Staphylococcus* spp., *Enterococcus* spp., *Campylobacter* spp., *Bacillus cereus*, pathogenic *Escherichia coli*, and others can cause fever, diarrhea, vomiting, and other symptoms. In severe situations, they can even be lethal (Gadde *et al.*, 2017). Infectious disorders that are challenging to treat are caused by food-borne bacteria that develop antibiotic resistance through horizontal or vertical gene transfer. In the past a range of herbs and plant were being used to address the food born illness and these medicinal plant also showed significance importance to address the the problems created by a range of pathogens, and to combat AMR problem. In this section some important medicinal plants and their effect to combat AMR is discussed

A-Honey antibiotic resistance: The study's leader, Susan M. Meschwitz, Ph.D., stated that "the unique property of honey lies in its ability to fight infection on multiple levels, making it more difficult for bacteria to develop resistance." As a result, it uses a range of weapons that actively destroy bacterial cells, including hydrogen peroxide, acidity, osmotic impact, high sugar content, and polyphenols. Because honey contains a lot of sugar, it has an osmotic action that pulls water out of the bacterial cells, dehydrating and killing them.

Furthermore, honey prevents the growth of biofilms, or colonies of slimy bacteria that cause illness, according to several studies, she noted. Additionally, honey may interfere with quorum sensing, which reduces bacterial pathogenicity and makes the germs more vulnerable to traditional antibiotics, according to Meschwitz. The process by which bacteria interact with one another, known as quorum sensing, may have a role in the development of biofilms. The release of toxins is also regulated by this communication system in some bacteria, which impacts the pathogenicity, or capacity to cause disease, of the bacterium.

Another benefit of honey, according to Meschwitz of Salve Regina University in Newport, Rhode Island, is that it doesn't interfere with the vital processes that bacteria use to develop, in contrast to

traditional antibiotics. Conventional antibiotics are based on this kind of targeting, which has the drawback of making germs more resistant to the medications.

Table 4: Best Practices for Extraction and Application of Phytochemicals to Combat Antimicrobial Resistance in Poultry and Livestock Production.

Step	Best Practices	Details / Examples
Extraction Methods	Solvent extraction	Ethanol and water-based solvents for alkaloids, flavonoids, tannins.
	Cold pressing/ Steam distillation	Used to extract essential oils like carvacrol, thymol, and eugenol.
	Green technologies	These are robust, faster, eco-friendly, and give high yield. E.g. microwave and Ultrasound assisted extraction .
Standardization and Quality Control	Supercritical CO ₂ extraction	Advanced techniques to get high-purity extracts (without residues).
	Analytical methods	GC-MS, HPLC, to quantize the bioactive compounds.
	Storage considerations	Protect from light and heat to maintain quality of sensitive compounds.
	Consistency checks	Assure uniform concentration of phytochemical across batches.
Application Forms	Feed inclusion	Make premix first or directly add in the diets.
	Water supplementation	May be added in water especially during disease outbreaks or stressful conditions for fast action.
	Micro or nanoencapsulation	Helps controlled release in GIT, protects heat-sensitive compounds, and masks flavors,
	Blended phytochemicals	For synergistic effect e.g., carvacrol + thymol + cinnamaldehyde.
On-Farm Use	Stage-specific strategies	Higher doses in starter and grower phases for gut improvement and pathogens control.
	Dosage management	Correct levels.
	Monitoring	Monitor performance, resistance profiles and gut health to optimize formulations.
	Integrated health program	Combine with good management practices, vaccination, and strict biosecurity .

According to her, honey works because it contains a lot of antioxidants called polyphenols. These consist of many flavonoids, phenolic acids, caffeic acid, p-coumaric acid, and ellagic acid. "The presence of honey phenolics has been linked in multiple studies to the antioxidant and non-peroxide antimicrobial properties of honey," she continued. According to Meschwitz, honey's broad-spectrum antibacterial, antifungal, and antiviral qualities have been validated by several laboratories and a small number of clinical investigations.

According to her, her research also discovered that honey has antimicrobial and antioxidant qualities. "To determine the amount of antioxidant activity in honey, we have conducted standard antioxidant tests," she said. We have discovered and isolated the different polyphenol components that are antioxidants. We have been evaluating honey's antibacterial properties against a variety of pathogens, including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *E. coli*.

B-Natural antibiotic effect of turmeric: Commercially accessible antibiotics have been added to chicken feed over the past ten years to help combat dangerous exogenous bacteria (Casewell *et al.*, 2003). These antibiotics aid in addressing the morbidity and mortality

problems associated with raising chickens, but they may also have an impact on public health by creating drug-resistant microorganisms (Cabuk *et al.*, 2006). According to reports, European nations have outright prohibited the use of antibiotics in chicken diets since January 2006 (Cabuk *et al.*, 2006). Industries must discover necessary alternatives to provide chicken feed in order to avoid using antibiotics (Aggarwal *et al.*, 2009). Various bioactive products are tested in diets without antibiotics to maximize the health quality of poultry (Casewell *et al.*, 2003; Aggarwal *et al.*, 2009). A particular bioactive substance known as curcumin, a polyphenolic phytochemical with antibacterial, anti-inflammatory, anti-cancer, and antioxidant qualities, is produced by turmeric (Al-Sultan, 2003; AMA G. 2011). According to recent findings, turmeric may be an effective alternative to antibiotics in chicken feed (Casewell *et al.*, 2003). Turmeric rhizome powder has been shown to reduce the morbidity and mortality of grill chickens when added to the poultry diet (Zhongze *et al.*, 2009). Additionally, it has been demonstrated that adding turmeric to chicken feed has no negative health consequences (Casewell *et al.*, 2003).

C-Effect of turmeric on the health status of broiler chickens: Turmeric supplementation may be an efficient way to regulate the haematological parameters of grill chickens (Kermanshahi *et al.*, 2006). Studies on the metabolism of fat in male chickens have demonstrated that hormone-sensitive lipase (HSL) consistently stimulates activity and contributes to the rise in blood levels of high-density lipoprotein (HDL) (Kurkure *et al.*). Turmeric also helps regulate blood serum levels of total cholesterol, total triglycerides, and very low-density lipoprotein (VLDL). (Sawale *et al.*, 2009). Turmeric's role in controlling the serum lipid profile has also been documented. Turmeric is an effective dietary supplement that helps to maintain the function of the liver by stimulating bile output and flow. Alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) in the blood of grilled chickens are likewise regulated by turmeric. Turmeric's immunomodulatory properties significantly strengthen the immune system, giving it immediate, natural antimicrobial protection against invasive invaders (Sawale *et al.*, 2009). To stop the development of inflammation-induced disease in poultry, turmeric can precisely control inflammation (Ben *et al.*, 2019; Roberts, 2004). Turmeric is also well-known for its cellular healing mechanism, which aids in the restoration of lymphocytes in lymphoid organs (WHO, 1987). Turmeric's natural and harmless photobiotic qualities are already well established. The World Health Organization (WHO) has declared that turmeric is the safest dietary item to include in the diets of both humans and animals (Bora *et al.*, 2011). The adverse effects of small doses of turmeric meals on poultry diets have not yet been reported in any literature, which is also important to mention.

D-Phytochemical and Antimicrobial Activity of Medicago sativa (Alfalfa): Since the dawn of human civilisation, several plants have been utilized to cure and manage a variety of illnesses. Finding a novel antimicrobial chemical with few side effects is one of the most crucial stages in microbiological research since bacterial resistance to antibiotics is a prevalent issue in the medical field. Because *Medicago sativa* contains biologically active chemicals and is used in both animal feeding and traditional medicine, it appears to have a significant antibacterial ability. Therefore, the purpose of this work is to identify several phytochemical components and examine the antibacterial efficacy of *Medicago sativa* aqueous and solvent extracts on a few therapeutically significant animal diseases. *Medicago sativa* hot and cold aqueous extracts and successive solvent extracts (acetone, ether, ethanol, and chloroform) were evaluated for their antimicrobial activity using agar well diffusion against many medically significant pathogens isolated from animal and poultry farms, such as *Salmonella typhimurium*, *Pseudomonas aerogenes*,

Staphylococcus aureus, *Escherichia coli*, *Streptococcus pyogenes*, *Salmonella aerogenes*, *Enterococcus*, *Bacillus cereus*, *Klebsiella pneumoniae*, and *Candida albicans*. The hot aqueous extract works best against *Staphylococcus aureus*, while the ether extract showed no discernible antibacterial or antifungal action against any of the microorganisms tested, except for *Enterococcus*. The cold aqueous extract demonstrated significant antibacterial activity against *B. cereus*, *S. typhimurium*, *K. pneumoniae*, *P. aerogenes*, and *E. coli*. But the only extract that had a strong antifungal action against *Candida albicans* was ethanol extract. Additionally, the phytochemical composition of the ethanol extract was identified; the findings of the chemical tests clarify that the extracts of *M. sativa* contain components such as flavonoids, tannins, alkaloids, saponins, and glycosides. Therefore, it can be said that *M. sativa* extract has exceptional antimicrobial activity against microbial infections and that more research is needed before it can be used as a substitute for chemical antimicrobial medications. Researchers have examined the antibacterial activity of saponins extracted from *M. sativa* against a variety of therapeutically significant yeasts as well as Gram-positive and negative bacteria. The saponin extracts were shown to have increasing antibacterial activity. Xiao-kang and Pinarosa reported that lucerne extract had superior antibacterial activity against *P. aeruginosa* and *S. dysgalactiae*, whereas its antibacterial activities against *E. coli* and *S. aureus* were mediocre (Livermore 2008; Pitout 2015). Activity was particularly strong against Gram-positive bacteria (*B. cereus*; Kapoor 2017). However, six distinct *M. sativa* extracts were used in this study to evaluate antibacterial activity. The Agar Well Diffusion Method was used to screen for antibacterial activity in the preliminary phase. The inhibitory activity was assessed by the clear zone's diameter. Most effective against *S. aureus*, the cold aqueous extract demonstrated strong antibacterial activity against *Salmonella typhimurium*, *B. cereus*, *K. pneumoniae*, *ps. aerogenes*, and *E. coli*, followed by ethanol, acetone, chloroform, and ether extracts. The ether extract did not exhibit any significant antibacterial or anti-fungal activity against any of the microorganisms tested, except for *Enterococcus*.

E-Natural antibiotic effect of tannin: Tannic acid belongs to a polyphenolic category as it is a phenolic acid. Because of its special antiviral and antibacterial qualities, it has been extensively researched in the biomedical field of study. According to reports, tannic acid exhibits activity against the human immunodeficiency virus (HIV), Papilloma viruses, noroviruses, Herpes simplex virus types 1 and 2, and both Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Pseudomonas*

aeruginosa, *Yersinia enterocolitica*, and *Listeria innocua*. Natural substances are now the foundation of material science, and this movement is known as "from nature to nature". However, the qualities of biopolymers may be improved by modifying them with both organic and inorganic additions. Like phenolic acid, tannic acid belongs to the polyphenolic group and can be extracted from natural sources, such as components of plant extracts or pure compounds. Because of its special qualities, tannic acid has been the subject of several investigations on its use as an addition to biopolymer materials. It has antibacterial and antiviral characteristics, but it also has intriguing biological qualities, such as promoting wound healing, tissue regeneration, and cell proliferation. Various biopolymers, collagens, and polysaccharides including chitosan, agarose, and starch are supplemented with tannic acid (Kaczmarek B *et al.*, 2020).

F-Natural antibiotic effect of Cinnamon: Cinnamon bark has been used as a spice, culinary flavouring, and seasoning since ancient times. Diabetes, tumours, diarrhoea, fever, toothache, nausea, chill, flatulence, amenorrhoea, headache, cough, cardiovascular diseases, eye inflammation, foul breath, dyspnoea, leukorrhoea, frigidity, vaginitis, impotence, neuralgia, and many other ailments are also treated with it in traditional medicine (Figure). Botanically, cinnamon is a tropical tree whose inner bark is primarily used as a spice. It is a member of the Lauraceae family and has about 250 species, four of which are important to the global economy and traded: Chinese cinnamon (*Cinnamomum cassia* or *Cinnamomum aromaticum*), Indonesian cinnamon (*Cinnamomum burmannii*), Vietnamese cinnamon (*Cinnamomum loureiroi*), and Ceylon cinnamon (*Cinnamomum verum* or *Cinnamomum zeylanicum*) from India and Sri Lanka (Ribeiro-Santos *et al.*, 2017).

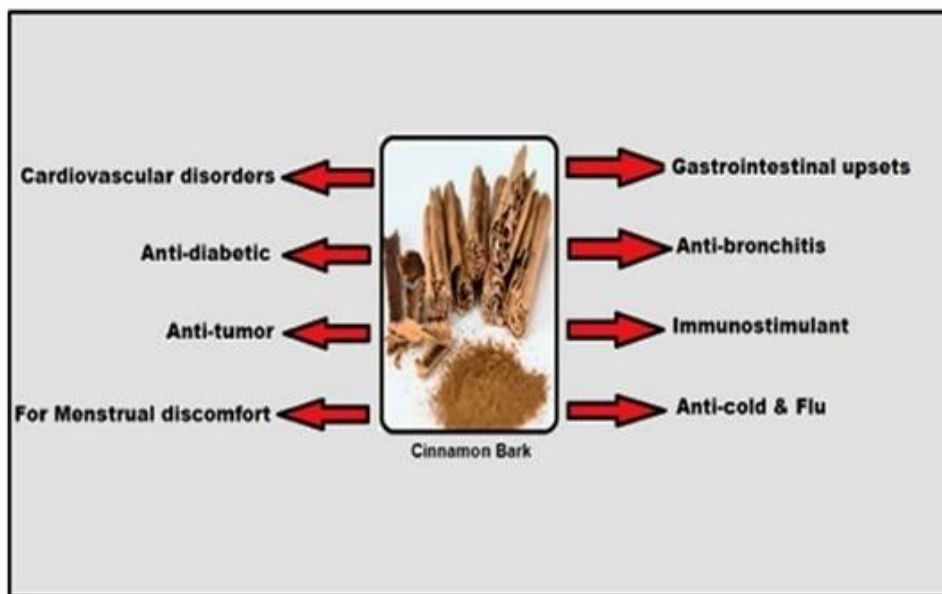


Figure 1: Some applications of cinnamon bark in traditional medicine

Researchers were able to examine the antibacterial properties of spices like cinnamon bark, which have thousands of years of therapeutic history, thanks to the resurgence of interest in medicinal plants. Numerous scientific investigations have revealed the potent antibacterial properties of cinnamon bark. According to a published study, the essential oils of *Cinnamomum cassia* (bark) demonstrated a noteworthy inhibitory effect against the three MDR-pathogens like *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. Additionally, it was noted that streptomycin and that essential oil significantly inhibited each other (El Atki *et al.*, 2019). According to reports, eugenol and cinnamon aldehyde isolated from the essential oils of *Cinnamomum verum* have strong antibacterial properties against *Paenibacillus larvae*, the

causal agent of a major bacterial illness that affects honeybee brood globally.

G-Garlic as a natural antimicrobial resistance phytochemical: *Salmonella* may colonise practically every portion of the digestive system, and chickens are a natural host for the bacteria. Early colonisation frequently happens at the hatchery, during transit, or on the farm through vertical transfer or environmental exposure (El-Desoukey *et al.*, 2015; Avato *et al.*, 2006). During grow-out, infected birds can subsequently transmit *Salmonella* horizontally; this transmission is frequently linked to stressful situations like feed withdrawal before slaughter (Amararadjou *et al.*, 2019). Meat can get infected with *Salmonella* when carcasses are exposed to faeces during slaughter and evisceration. During processing, additional

carcasses frequently get cross-contaminated, posing a danger to public health (Ramirez *et al.*, 1997). Currently, pre- and post-harvest measures are used to control Salmonella in chicken. Preventing transmission and colonisation is the goal of pre-harvest biosafety measures include disinfecting eggs and the hatchery environment, as well as controlling vectors and fomite (El-Desoukey *et al.*, 2015; Biswas *et al.*, 2019). However, the efficiency of these procedures is limited due to the widespread presence of Salmonella serovars. Although antibiotics have been used to reduce intestinal burden and shedding, they are linked to bacterial infections developing resistance to antibiotics (Foley *et al.*, 2011; Kumar *et al.*, 2019) (Grossi *et al.*, 2023). Because of this, using antibiotics on cattle has become a serious public health issue, necessitating the development of safer alternatives. Commercial poultry products are disinfected with per acetic acid (PAA) after harvest (Upadhyay *et al.*, 2019). However, when consumers' choice for natural alternatives grows, their acceptance of PAA declines. Recent research has shown that phytochemicals are a new antibiotic substitute that may be used both before and after harvest. They can alter the pathogenicity of bacteria and destroy them by rupturing their cell wall and membrane (Kim *et al.*, 2013). It has been demonstrated that adding some phytochemicals to a chicken's diet can enhance its innate immune response, encourage development, and have positive effects on gut health (Lillehoj *et al.*, 2018; Castillo *et al.*, 2014). Furthermore, several studies have looked at how well phytochemicals work as antimicrobial coatings and washes against *Campylobacter jejuni* (Yang *et al.*, 2018). Since ancient times, garlic (*Allium sativum*) has been a staple in diets all across the world. Its medicinal benefits, however, go beyond taste and include antiviral, antifungal, anti-inflammatory, and anti-cancer properties. For millennia, garlic has also been used to cure bacterial illnesses. The bacteria *Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus* are susceptible to crude garlic extract. It has been determined that the main components of garlic's antibacterial activity are the organo-sulphur compound sallicin, ajoene, and various aliphatic sulphides. These compounds are also present in garlic oil and have been shown to have antibacterial activity against *Salmonella typhimurium*, *Listeria monocytogenes*, *Shigella* species, *Vibrio* species, *Yersinia enterocolitica*, *Pseudomonas aeruginosa* (Tsao *et al.*, 2001), *Klebsiella pneumoniae* (Tsao *et al.*, 2001), *Campylobacter jejuni* (Mnayer *et al.*, 2014), *Helicobacter pylori*, *Staphylococcus aureus* (Jain, 1993), *Bacillus cereus*, *E. coli* (O'Gara *et al.*, 2000) (Mnayer *et al.*, 2014). *Shigella* species and *Vibrio* species. The World Health Organisation (WHO) reports that over 30,000 antimicrobial chemicals have been identified from plants, and over 1340 species have been shown to have specific antibacterial activity. Plants can produce secondary metabolites that serve a variety of purposes for the plant,

including defence against pests, environmental adaptation, and giving the plant a particular flavour and aroma. From a chemical perspective, these substances fall into three groups known for their biological activity: alkaloids, phenolics, and terpenoids (Belcher *et al.*, 2020). Although phytochemicals have great antibacterial potential as antibiotic substitutes in animal production, a number of restrictions prevent their widespread and regular use. Although promising, the use of phytochemicals as natural antibiotic substitutes in the production of poultry and cattle is constrained by several significant issues. Variability in plant component composition, which can vary depending on plant species, harvest time, extraction techniques, and environmental factors, is one significant drawback. This discrepancy impedes the standardization of dosages for practical use and makes it challenging to guarantee consistent effectiveness. Many phytochemicals are also chemically unstable and susceptible to oxidation, heat, light, and pH changes, which can cause them to degrade during feed preparation or storage and eventually lessen their efficacy. Palatability is still another major issue; many phytochemicals have strong smells or harsh flavors that might reduce feed intake, particularly in poultry, and perhaps jeopardize development.

Phytochemicals must be successfully incorporated into cattle and poultry production systems using an all-encompassing, evidence-based strategy. Creating standardized formulations that guarantee constant phytochemical concentration, stability, and bioavailability is part of this. To ensure targeted administration and efficacy, advanced technologies like emulsification, nanotechnology, and microencapsulation can assist in safeguarding active chemicals throughout feed processing and digestion. Furthermore, current veterinarian protocols or feeding plans should include phytochemicals with explicit instructions on how to employ them at various periods of production, including growth, reproduction, and disease outbreaks. To increase farmers' understanding and trust in the use of plant-based alternatives, integration should also incorporate training initiatives, extension services, and demonstration trials at the farm level. The absence of clear and uniform regulations is one of the main obstacles to the use of phytochemicals in animal agriculture, especially in nations like Pakistan. Authorities like the Drug Regulatory Authority of Pakistan (DRAP) or the Ministry of National Food Security and Research must create regulatory frameworks to assess the safety, effectiveness, and residual levels of goods based on phytochemicals to solve this. Clear guidelines must be set for production quality control, withdrawal periods, acceptable residual limits in meat, milk, and eggs, and labelling. Without such rules, export compliance becomes challenging, and industry and farmer trust is maintained at a low level. Additionally, harmonization with international

organizations such as the European Food Safety Authority (EFSA) or U.S. Food and Drug Administration (FDA) will boost worldwide credibility and guarantee compliance for international commerce. One important factor influencing farmer adoption is economic feasibility. Products made from phytochemicals need to be affordable, simple to use, and work on par with conventional antibiotics. To guarantee effectiveness at lower concentrations without side effects, dose schedules must be optimized. Using native medicinal herbs in local production might drastically save costs and promote involvement in rural areas. Adoption can also be accelerated by farmer education initiatives supported by government subsidies or trial projects, as well as veterinary assistance. To create workable, scalable, and reasonably priced solutions that satisfy both productivity and public health objectives, public-private collaborations, including academic institutions, feed businesses, and regulatory bodies, can be extremely important. Thus, plants can represent an almost unlimited source of bioactive compounds, and their use as antimicrobial agents can be exploited in different ways, considering that natural antimicrobial agents can act alone or in different combinations (Table 5).

Standardizing phytochemicals in poultry and animal feed to ensure safety, consistency, and efficacy:

Though there has been a lot of interest in using phytochemicals as natural antibiotic replacements in animal feed, their safety and effectiveness need to be rigorously standardized before considering in poultry and animals feed. Unlike manufactured drugs, phytochemicals are derived from a range of plant sources, and their composition might vary depending on harvest time, extraction methods, and climatic conditions. It is essential to develop procedures that guarantee feed formulations include constant amounts of bioactive substances due to this inherent variability.

The selection of raw materials is the initial step in standardisation. The concentration of active compounds like flavonoids, alkaloids, terpenoids, and saponins is greatly influenced by the dates of harvest, the cultivation methods, and the region of origin. Variability may be reduced at its source through the use of good agriculture and collection practices (GACP). Then, in order to maintain phytochemical activity while eliminating undesirable impurities, extraction and processing techniques need to be adjusted. Advanced techniques like HPLC, GC-MS, and LC-MS are essential tools for measuring and characterising active chemicals to ensure that only batches that satisfy specific quality criteria are used for feed manufacture. An essential component of standardisation is safety evaluation as phytochemicals can have negative effects despite being natural. Extensive toxicological testing is required on target animals because certain substances, such as

alkaloids, may become harmful at increasing concentrations. Pharmacognosy, feed science, toxicology, and regulatory frameworks should be used in an extensive strategy to standardize phytochemicals compounds for safe and trustworthy usage in animal feed. Since a plants chemical composition may change due to genetics, location, and harvesting season, therefore, the first step is to accurately characterize the botanical source. Reproducibility needs the development of criteria for plant species, plant parts, and chemical markers. Chromatographic fingerprinting and the quantification of marker molecules might help overwhelm the momentous hindrances of inconsistent phytochemical composition (Hashemi and Davoodi, 2011).

Safety assessment is critical after the mixture is standardized. Toxicological and tolerance studies in target animals are part of this, especially when extracts hold new bioactive chemicals. Under Regulation (EC) No. 1831/2003, the European Food Safety Authority (EFSA) offers comprehensive recommendations, emphasizing the need of toxicological evaluation and residues investigations when consumer exposure is feasible (EFSA FEEDAP Panel, 2010). Furthermore, repeated-dose oral toxicity studies (TG 407 and TG 408) are commonly recognized as international standards for guaranteeing the safety of feed additives (OECD, 2008). Evaluation of efficacy, which necessitates standardized and carefully planned in vivo trials, is equally crucial. According to Windisch et al. (2008), gains in growth performance, feed efficiency, and immunological response can only be confirmed by carefully monitored animal trials, even though numerous phytochemicals have antimicrobial and antioxidant activities in vitro. Additionally, at least two independent efficacy studies per claim for each target species are advised per the new EFSA guidance (2024).

In vivo studies may be used to identify safe dose ranges that maximise growth promotion, immunological modulation, and antibacterial advantages while minimising side effects. Guidelines for safety research, including genotoxicity, mutagenicity, and tolerance testing, are established by international regulatory frameworks, such as those published by the U.S. Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA).

Moreover, efficacy must be confirmed in controlled field and experimental settings. Phytochemicals should be regularly used to demonstrate measurable advantages such enhanced feed conversion ratio, decreased pathogen load, or better gut health. Long-term trials, dose-response studies, and meta-analyses are utilised to determine appropriate dosage ranges. The bioavailability and reproducibility of results are influenced by standardised formulations, encapsulating technology, and synergistic combinations of several phytochemicals.

Table 5: Some common plants, their active phytochemicals compounds and antimicrobial activity.

Common and Scientific name	Class	Compound	Resistance against	Activity
<i>Anemone pulsatilla</i> (Pasque-flower)	glycoside ranunculin, Triterpenoid saponins, Flavonoids, Sterols & Phenolic compounds	Anemonins	Bacteria	
<i>Achillea millefolium</i> (Yarrow)	Sesquiterpene lactones, Alkaloids, Tannins, Flavonoids, Phenolic compounds	Apigenin, Caffeic acid, Luteolin, Quercetin, Chamazulene, Borneol, Thujone, Achillolide (A and B), Parthenolide, Cineole, Camphor, Rutin, Chlorogenic acid, Achilleine	Broad spectrum	
<i>Acorus calamus</i> (Sweet flag, calamus)	Terpenoid, Flavonoids, Alkaloids, Tannins, Glycosides, essential oils,	Gallic acid, Acorenone, Calamenene, Shyobunine, Ferulic acid, Calamenol, Eugenol, Calamene	Broad spectrum	
<i>Aegle marmelos</i> (Bael tree)	Terpenoid	Essential oil	Fungous	
<i>Agrostemma githago</i> (Cockles)	Polysaccharides, Omega-3 Fatty Acids, Proteins & Peptide, Sterols, Polysaccharides	EPA, DHA, phytosterols, Glycosaminoglycans	Broad spectrum	
<i>Allium Citrus sinensis</i> (Orange peel)	Terpenoid, Flavonoids, vitamin C, carotenoids, essential oils, pectin, coumarins,	limonene, naringin, ascorbic acid, linalool, hesperidin, pinene, limonoids, citral, myrcene,	Broad spectrum	
<i>Allium sativum</i> (Garlic)	Sulfoxides, Sulfated, terpenoids	Allicin, ajoene	General	
<i>Aloe barbadensis</i> , <i>Aloe vera</i> (Aloe)	Complex mixture	Latex	<i>Corynebacterium</i> , <i>Salmonella</i> , <i>Streptococcus</i> <i>E. coli</i> , <i>M. tuberculosis</i> , <i>S. aureus</i> , <i>Ascaris</i> <i>Propionibacterium</i> <i>acnes</i> , Bacteria, fungi	
<i>Aloysia triphylla</i> (Lemon verbena)	Terpenoid	Essential oil		
<i>Anacardium pulsatilla</i> (Cashews)	Polyphenols	Salicylic acids		
<i>Anethum graveolens</i> (Dill)	Terpenoid	Essential oil		
<i>Arctium lappa</i> (Burdock)	Polyacetylenes, tannins, terpenoids, Inulin, lignans polyphenols phytosterols, tannins, essential oils,	arctiin, arctigenin, chlorogenic, Chlorogenic acid, ferulic and caffeic, acids	Broad spectrum	
<i>Arnica montana</i> (Mountain tobacco)	Lactones	Helanins	General	
<i>Artemisia dracunculus</i> (Tarragon)	Terpenoid, Polyphenols	Caffeic acids, tannins	Viruses, helminths	
<i>Barosma setulina</i> (Buch)	Terpenoid	Essential oil	General	
<i>Berberis vulgaris</i> (Barberry)	Alkaloid	Berberine	Bacteria, protozoa	
<i>Betel pepper</i> (Betel pepper)	Essential oils	Catechols, eugenol	General	
<i>Calendula officinalis</i> (Marigold)	Triterpenoid, Carotenoids, Essential oil, Flavonoids, Phenolic acids, Coumarins	Faradiol monoesters, Cardinol, Carryophyline oxide, T Muurolol, Taraxasterol, Lutine, B-Carotein, Zeaxanthin, Oleanolic acid derivatives	Broad spectrum	
<i>Camellia sinensis</i> (Green tea)	Flavonoids	catechins	General,	<i>Shigella</i> , <i>Vibrio</i> , <i>S. mutans</i> , <i>Viruses</i>
<i>Cannabis sativa</i> (Hemp)	Organic acid	β -Resercyclic acid	Bacteria and viruses	

<i>Capsicum annuum</i> (Chili peppers, paprika)	Terpenoid	Capsaicin	Bacteria
<i>Carica papaya</i> (Papaya)	Mix of terpenoids, organic acids, alkaloids	Latex	General
<i>Carum carvi</i> (Caraway)	Coumarins, Essential oil, Flavonoids, Phenolic acids, Sterols & Tannins	Chlorogenic acid, Caffeic acid, Oleic acid, linoleic acid, Kaempferol, Quercetin, Apigenin, Ferulic acid, β -sitosterol	Broad spectrum (Bacteria, fungi, viruses)
<i>Cassia angustifolia</i> (Senna)	Anthraquinone	Rhein	<i>S. aureus</i>
<i>Centella asiatica</i> (gotu kola)	Terpenoid	Asiatocosides	<i>Mycobacterium leprae</i>
<i>Cinchona</i> sp. (Quinine)	Alkaloid	Quinine	<i>Plasmodium</i> spp.
<i>Cinnamomum verum</i> (Ceylon cinnamon)	Terpenoids, tannins	Essential oils, others	General
<i>Citrus paradise</i> (Grapefruit peel)	Terpenoid, Limonoids, Pectins, phrnols, Essential oils, Flavonoids	Hesperidin, Naringenin, Quercetin, D-limonene, β -pinene, Naringin, Ferulic acid, Galacturonic acid, 6', 7'-Dihydroxybergamottin, polymers, Bergamottin, Caffeic acid, Limonin, Nomilin	Broad Spectrum, Improve gut health
<i>Coriandrum sativum</i> (Coriander, cilantro)	Coumarins, Essential oil, Flavonoids, Phenolic acids, Sterols & Tannins	β -sitosterol, Linalool Camphor, γ -terpinene, α -pinene, Caffeic acid, Ferulic acid, Chlorogenic acid, Quercetin, Apigenin, Rutin, Umbelliferone, Scopoletin	Broad spectrum
<i>Curcuma longa</i> (Turmeric)	Terpenoids	Curcumin, Turmeric oil	Bacteria, protozoa
<i>Dioica allspice</i> (Allspice)	Essential oil	Eugenol	General
<i>Echinaceae angustifolia, E. purpurea</i> (Echinacea)	Alkamides, Phenols, Flavonoids, volatile oils, Glycoproteins	Dodeca-2E,4E,8Z,10E/Z-tetraenoic acid isobutylamides, Cichoric acid, Chlorogenic acid, Quercetin, Germacrene D, kaempferol, caryophyllene	Broad spectrum
<i>Erythroxylum coca</i> (Dough)	Alkaloid	Cocaine	Bacteria
<i>Eucalyptus globulus</i> (Eucalyptus)	Polyphenol, Terpenoid	Tannin	Bacteria, viruses
<i>Euphorbia pulcherrima</i> (The poinsettia)	Triterpenoids, Diterpenoids, Phenol, Sterols, Latex constituents,	Jatrophone-type diterpenes, Euphorbol esters, β -amyirin, Rutin, Cycloartenol	Broad spectrum
<i>Euphorbia tirucalli</i> (Aveloz)	Triterpenoids, Phenol, Sterols, Latex constituents, Diterpenes	Lupeol, Campesterol, β -sitosterol, quercetin, Phorbol esters, kaempferol	Broad spectrum
<i>Faba bean</i> (fava bean)	Thionin	Ingenol esters, Tirucallol, Euphol, Cycloartenol, β -amyirin, Lupeol, Campesterol, β -sitosterol, quercetin, Phorbol esters, kaempferol	Bacteria
<i>Gallium odoratum</i> (Woodruff)	Coumarin, Flavonoids, Phenolic acids, Iridoids, Tannins	Fabian	General
<i>Garcinia hanburyi</i> (Gamboge)	Resin, Xanthones, phenolic	Chlorogenic acid, Kaempferol, Quercetin, Apigenin, Deacetylasperulosidic acid, Asperuloside	General
<i>Gaultheria procumbens</i> (Wintergreen)	Polyphenols	Gambogic acid, Iso-morellin, Morellin, Guttiferone, Hydroxycitric acid, Garcinol	General
<i>Glorious gorgeous</i> (Glory lily)	Alkaloid	Tannins	General
		Colchicine	General

<i>Glycyrrhiza glabra</i> (Licorice)	Phenolic alcohol	Glabrol	<i>S. aureus</i> , <i>M. tuberculosis</i>
<i>Humulus lupulus</i> (Whoops)	Phenolic acids, terpenoids	Lupulonehumulone	General
<i>Hydrangea arborescens</i> (Smooth hydrangea, seven barks)	Coumarins, Glycosides, Flavonoids, Saponins, Phenolic acid	Umbelliferone, Scopoletin, Quercetin, Rutin, Kaempferol, Hydrangin, Loganin derivatives, Triterpenoid, Chlorogenic acid, Caffeic acid	General
<i>Hydrastis canadensis</i> (Goldenseal)	Alkaloids	Berberine, hydrastine	Bacteria, <i>Giardia duodenale</i> , trypanosomes, Plasmodia
<i>Hypericum perforatum</i> (St. John's wort)	Anthraquinone	Hypericin, others	General
<i>Hyssopus officinalis</i> (Hyssopi)	Terpenoids	β -pinene, Pinocamphone, 1, Isopinocampone, Diosmin, Apigenin, Quercetin, Rosmarinic acid, Caffeic acid, Hydrolysable tannins, 8-cineole, Luteolin, Limonene	Brod spectrum
<i>Jatropha gossypifolia</i> (Tua-Tua)	Tannins, Flavonoids, Saponins, Diterpenoids, Lignans	Phorbol esters, Apigenin, Isovitexin, Vitexin, Orientin	General and Broad-spectrum
<i>Juglans regia</i> (Walnut)	Juglone	Naphthoquinone	<i>S. aureus</i> , <i>M. tuberculosis</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>Klebsiella</i> , <i>Candida</i> , <i>Aspergillus</i> , <i>Fusarium</i> , <i>Leishmania</i> , <i>Trypanosoma</i> , HSV-1, HCV
<i>Lantana chamber L.</i> (Lantana)	Essential oils, Iridoid glycosides, Flavonoids, Triterpenoids, Phenolic	caryophyllene, quercetin, apigenin, germacrene-D, luteolin, lantadene (A and B) α -humulene	General
<i>Larrea tridentata</i> (Chaparral)	Lignans	Nordihydroguaiaretic acid	Skin bacteria
<i>Laurus nobilis</i> (Bay)	Terpenoids	Essential oils	Bacteria, fungi
<i>Lawsonia inermis</i> (Henn)	Phenolic	Gallic acid	<i>S. aureus</i>
<i>Linum usitatissimum</i> (Flaxseed)	Lignans, phenolics, Terpenoids, saponins	Secoisolariciresinol diglucoside, Alpha-linolenic acid, rhamnogalacturonans, Ferulic acid, p-coumaric acid, kaempferol, β -sitosterol, eyc	Bacteria, Parasites, Viruses, Fungi
<i>Lophophora williamsii</i> (Peyote)	Alkaloid	Mescaline	General
<i>Mahonia aquifolia</i> (Oregon harrows)	Alkaloid	Berberine	<i>Plasmodium</i> , Trypanosomes, general
<i>Malus sylvestris</i> (Apple)	Flavonoid derivatives	Phloretin	General
<i>Matricaria chamomilla</i> (Chamomile)	Phenolic acid	Anthemic acid	<i>Mycobacterium tuberculosis</i> , <i>S. aureus</i> , <i>Salmonella typhi</i>
<i>Medicago sativa</i> (Alfalfa)	Saponins, Coumarins, Flavonoids, Phenolic acids, Alkaloids, Phytoestrogens	apigenin, quercetin, luteolin,	Gram-positive organisms

<i>Melissa officinalis</i> (Lemon balm)	Polyphenols	Tannins	Viruses
<i>Mountain saturation</i> (Savory)	Terpenoid	Carvacrol	General
<i>Myristica fragrans</i> (Poppy, nutmeg)	Alkaloids, Flavonoids, Fatty oils	Phenolic acids	General
<i>Ocimum basilicum</i> (Basil)	Terpenoids	Essential oils	<i>Salmonella</i>
<i>Olea europaea</i> (Olive oil)	Aldehydes	Hexanal	General
Onion)	Sulfoxides	Allicin	Bacteria, <i>Candida</i>
<i>Onobrychis viciifolia</i> (Sainfoin)	Polyphenols	Tannins	Ruminal bacteria
<i>Panax notoginseng</i> (Ginseng)	Saponin		<i>E. coli</i> , <i>Sporothrix schenckii</i> , <i>Staphylococcus</i> , General
<i>Papaver somniferum</i> (Poppy)	Alkaloids and others	Opium	Protozoa, Bacteria, fungi
<i>Peganum harmala</i> (Harmel, rue)	β -carboline alkaloids, Quinazoline alkaloids, Flavonoids, Phenols, tannins	Harmaline, Quercetin, Tetrahydroharmine, Peganine, Kaempferol, Deoxyvasicine, Harmalol, Harmine	
<i>Peppermint</i> (Peppermint)	Terpenoid	Menthol	General
<i>Petalostemum</i> (Purple prairie clover)	Flavonoids	Petalostemumol	Bacteria, fungi
<i>Piper nigrum</i> (Black pepper)	Alkaloid	Piperine	Fungi, <i>E. coli</i>
<i>Podocarpus nagi</i> (Tree bard)	Flavonoids, Lactones	Totarol, Nagilactone	<i>Lactobacillus</i> <i>P. acnes</i> , other gram-positive bacteria, Fungous
<i>Polygonum aviculare</i> (Prostrate knotweed)	Triterpenoids, Flavonoids, Alkaloid, Phenol, Tannins, Stilbenes	Quercetin, Caffeic acid, p-coumaric acid, Avicularin, ferulic acid, Hyperoside, Myricetin	General
<i>Prosopis juliflora</i> (Mesquite)	Triterpenoids, Saponins, Flavonoids, Alkaloid, Polysaccharides, Fibers Phenol, Tannins,	Quercetin, Juliflorine, Julifloricine, Gallic acid, Caffeic acid, Ferulic acid, proanthocyanidins, Luteolin, Kaempferol	General
<i>Quercus rubra</i> (Oak)	Polyphenols	Tannins	General
<i>Rabdosia trichocarpa</i> (Japanese herb)	Terpenes	Trichorabdol A	<i>Helicobacter pylori</i>
<i>Ranunculus bulbosus</i> (Buttercup)	Lactones	Protoanemonin	General
<i>Rauvolfia serpentina</i> (Rauvolfia, chandra)	Alkaloid	Reserpines	General
<i>Rhamnus purshiana</i> (Cascara Sagrada)	Polyphenols	Tannins	Viruses, bacteria, fungi
<i>Ricinus communis</i> (Castor bean)	Ricin, Ricinine, Flavonoids, Phenolics, Steroids, Terpenoids, Flavonoids, Phenols	Stigmasterol, β -sitosterol, Lupeol, Linoleic acid, Oleic acid, Gallic acid, Quercetin, Caffeic acid, Stearic acid, Palmitic aci	General
<i>Rivea corymbosa</i> (Snake plant)	Organic acids, Flavonoids, Phenolic compounds, Terpenoids, Steroidal saponins	Quercetin, Ferulic acid, Caffeic acid, Malic acid, citric acid, Kaempferol	General
<i>Rosmarinus officinalis</i>	Terpenoid	Essential oil,	General

(Rosemary)			
<i>Rumex crispus</i> (Yellow dock)	Anthraquinones, Flavonoids, Phenolic acids, Saponins, Terpenoids, Tannins.	Emodin, Chrysophanol, Quercetin, Kaempferol, Caffeic acid, Catechins, proanthocyanidins, Gallic acid, Ferulic acid, Rutin, Physcion	<i>E. coli</i> , <i>Salmonella</i> , <i>Staphylococcus</i>
<i>Rustic armor</i> (Horseradish)	Terpenoids		General
<i>Salix alba</i> (Willow)	Phenolic glucosides, Polyphenols, Terpenoid	Salicin, Tannins, Essential oil	General
<i>Santolina chamae cyparissus</i> (Lavender-cotton)	Essential oils, Sesquiterpene lactones, Flavonoids, Phenolic acids, Tannins	Santolinolide, Limonene, Camphor, Borneol, Caffeic acid, 1,8-cineole, β -pinene, Apigenin, Luteolin, Chlorogenic acid	Gram-positive bacteria, <i>Candida</i>
<i>Sassafras albidum</i> (Sassafras)	Coumarins, Essential oils, Flavonoids, Phenolic acids, Tannins	Safrole,	Helminths
<i>Sesamum indicum L.</i> (Sesame)	Lignans, Tocopherols, Phytosterols, flavonoids	Sesamin, Sesamol, Sesamol, Sesaminol.	Bacteria, Fungi, Viruses (Influenza and herpes simplex virus)
<i>Schinus terebinthifolius</i> (Brazilian pepper tree)	Terpenoids	Terebinthone	General
<i>Solanum tuberosum</i> (Potato)	Glycoalkaloids, Phenolic, Flavonoids, Anthocyanins	Cyanidin, pelargonidin, Quercetin, kaempferol, rutin	Bacteria, Parasites, fungi
<i>Syzygium aromaticum</i> (Cloves)	Terpenoid	Eugenol	General
<i>Tabebuia impetiginosa</i> (Pau D'arco)	Terpenoids	Sesquiterpenes	Fungous
<i>Tanacetum vulgare</i> (Tansy)	Terpenoid	Essential oils	Helminths, bacteria
<i>Taraxacum officinale</i> (Dandelions)	Sesquiterpene lactones, Flavonoids, Phenolic acids, Triterpenes, Inulin	luteolin, taraxinic acid, taraxasterol, chlorogenic acid, taraxerol, β -amyrin, caffeic acid, apigenin	<i>Broad spectrum, especially C. albicans, Saccharomyces cerevisiae</i>
<i>Thevetia peruviana</i> (Lucky nut, yellow)	Cardiac glycosides, Flavonoids, Alkaloids, Saponins	Thevetin A and B, neriifolin, peruvoside, thevetoxin, Kaempferol, Thevetidine, Perruvine, Neriifolin, Quercetin, Steroidal saponins, Apigenin, Rutin	Broad spectrum especially effective against Plasmodium
<i>Thymus vulgaris</i> (Thyme)	Terpenoid, Phenolic alcohol, Polyphenols, Flavones	Caffeic acid, Thymol, Tannins	Viruses, bacteria, fungi
<i>Tussilago farfara</i> (Coltsfoot)	Alkaloids, Phenolic acids, Mucilage, Flavonoids, Triterpenoids, Sterols, Volatile oils	Senkirkine, Quercetin, Kaempfero, Taraxasterol, β -sitosterol, Caffeic acid, Chlorogenic acid	General
<i>Vaccinium spp.</i> (Blueberries)	Monosaccharides	fructo	<i>E. coli</i>
<i>Vaccinium spp.</i> (Cranberries)	Monosaccharides	Fructo	Bacteria
<i>Valeriana officinalis</i> (Valerian)	Terpenoid	Essential oil	General
<i>Vinca minor</i> (Periwinkle)	Alkaloid	Reserpines	General
<i>Withania somniferum</i> (Ashwagandha)	Lactones	Withaferin A	Bacteria, fungi

Table 6: Antibacterial Activity of some Plants and their Important Extracts

Scientific name (common name)	Plant part used	Type of extracts	Pharmacologically active phytoconstituents	Antibacterial activity against
Allium sativum (garlic)	Cloves	Juice	-	Cryptosporidium sp.
Acacia nilotica, Tetradenia riparia	Bark, flower	Acetone	-	S. aureus, Streptococcus uberis, S. agalactiae, K. pneumoniae, E. coli, P. aeruginosa, P. mirabilis
Aloe vera, Curcuma longa	-	Aqueous, ethanol, and ethyl acetate	-	E. coli, S. aureus, P. aeruginosa
Combretum molle (velvet leaved Combretum), Xanthium strumarium (Cocklebur)	Stem, bark, leaves	95% ethanol	-	S. aureus and Streptococcus agalactiae
Cinnamon cassia	-	-	-	S. aureus, S. epidermidis, S. hyicus, S. xylosus, E. coli
Bunium persicum, Oryza sativa, Triticum aestivum	Bulb, seeds, fruits	Methanolic	Alkaloids	S. aureus, E. coli, K. pneumoniae
Dalbergia retusa, Crescential alata, P. guajava, Vitex mollis	Leaves	Methanolic	-	Methicillin-resistant S. aureus
Evernia prunastri (plum lichen), Artemisia absinthium (Absinthe wormwood), Lavandula angustifolia (Lavender)	-	96% Ethanol	-	S. aureus, S. xylosus, S. intermedius, S. chromogenes, S. hyicus, Vibrio fluvialis, Serratia liquefaciens, E. coli, Lactococcus lactis, Enterobacter intermedius, Bacillus cereus, Yersinia ruckeri, Aeromonas hydrophila, Kytococcus sedentarius
Holarrhena antidysenterica	Bark	Ethanolic	-	E. coli
Neoglaziovia variegata	Leaves	Hexane and ethanolic	-	Rhipicephalus (Boophilus) microplus
Psidium guajava (guava), T. foenum-graecum (fenugreek)	Leaves, seeds	Methanol	-	S. aureus, Escherichia coli, Pseudomonas aeruginosa, Salmonella sp.
Panicum turgidum (Thummam)	-	Aqueous	-	Streptococcus pyogens, Candida albicans
Senna macranthera	Roots	Dichloromethane	Emodine, physione, and chrysophanol	Staphylococcus aureus
Salvadora persica, Colophospermum mopane, Dichrostachys cinerea	Leaves, bark, roots	Methanolic	-	S. aureus, E. coli
Thalictrum minus	Roots	Dichloromethane and methanol (1:1)	Benzylisoquinoline alkaloids (5'-hydroxythalidasine, thalrugosaminine, O-methylthiadiberine)	Staphylococcus xylosus, S. lentus, S. epidermidis, E. coli, Enterococcus faecalis, E. coli

Furthermore, testing for compatibility and stability guarantees that phytochemicals continue to work during feed processing and storage. The stability of these additives during pelleting, feed uniformity, and compatibility with other feed additives must all be assessed. In commercial production systems, disregarding stability and interactions can result in uneven responses and decreased repeatability, as shown by Wallace et al. (2010).

Putting post-market monitoring (nutriviigilance) into practice may helpful to find long-term performance problems and uncommon side effects, guaranteeing ongoing safety and effectiveness in field settings. Such type of monitoring is essential for the long-term use of phytochemical bioactive compounds in animal and poultry production and is comparable to pharmacovigilance in human medicine. Botanical standardization, post-market surveillance, proven safety testing, controlled effectiveness studies, and stability evaluation can together be combined to make phytochemicals a reliable natural substitute as alternative antimicrobial and production boosters in animal and poultry production.

Conclusion: In conclusion, the risk of antibiotic resistance has been a global problem in the food system. Antibiotics are known as effective therapeutic agents for the treatment of bacterial infectious diseases of humans and food-producing animals. However, as the double-edged sword of antibiotics, the possible leftover of residual antibiotics and the potential reservoir of ARGs through the food chain from farm to table are high-priority health issues. Residual antibiotics in animals can affect the evolution of antibiotic resistance in foodborne pathogens. Furthermore, the transfer of ARGs can accelerate the emergence and spread of antibiotic-resistant pathogens. The use of antibiotics in farming animals should not be underestimated in terms of food safety and public health. Therefore, other than the regulations that passively restrict the use of antibiotics in farm animals, the discovery and development of effective prevention, control, and treatment strategies are needed to reduce the risk of residual antibiotics and ARGs. With increasing problems of antimicrobial resistance (AMR) in animal husbandry, quick solutions are needed to control the persistence and emergence of drug-resistant microbial pathogens. Medicinal plant resources such as probiotics, prebiotics, symbiotics, enzymes, phytochemical, and antimicrobial peptides have shown great antimicrobial potential in recent years and are looked upon as potential alternatives to conventional veterinary antibiotics. The study of these medicinal plant products has confirmed their putative role in targeting the pathogenicity of microbes.

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