Review Article:

Mode of actions of some phytoconstituents of medicinal plants in controlling animal microbial disease

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Abstract:
Since ancient times, medicinal plants have been utilized to cure and prevent a wide range of animal and human illnesses. Nowadays, the use of therapeutic herbs is increasing in utilization of medicinal plants. The growing resistance of bacteria to antibiotics has made humans more worried about finding other ways to cure infections. Phytoconstituents have the potential to act as antimicrobial drugs against sensitive and resistant pathogens by various modes of action. Phytobiotics are naturally occurring bioactive compounds derived from plants that are secondary metabolites such as essential oils, phenolics, flavonoids, tannins, alkaloids, organosulfur, and saponins. These compounds are produced by herbal plants and have antimicrobial and growth-promoting properties that can help treat a variety of animal diseases. Plant extracts possess several advantages over synthetic drugs as most of them have no residual effects, due to its applicability in human medicine so they could be added to animals' food to prevent and treat various animal health disorders in addition to their possible nutritional characteristics. However, additional investigation is necessary to have a greater awareness of the phytochemicals' mechanisms of action. In this regard, this review summarizes several effects of some biologically active plants and their phytoconstituents on some infectious microbial diseases in animal. It also summarizes the efficiency, modes of action, and some applications of medicinal plants active phytochemicals to solve the antibiotic resistance problem. Regarding these facts, it could be concluded that medicinal plants resemble a furious source of active constituents that possess antimicrobial potential.

Keywords:
phytoconstituents, phenolics, flavonoids, tannins, terpenes, alkaloids, essential oils and polypeptides

Introduction:

Infectious microbial diseases in livestock are becoming a global health problem facing the veterinary sciences [1]. The current trend worldwide is involvement of folklore medicine with primary health care systems[2]. In this regard, medicinal plants have been and are still the major sources of medicine worldwide [3]. Active phytoconstituents are increasingly being used as alternatives for synthetic chemicals in the treatment and development of live stocks due to their powerful properties and exceptional bioactivity [4]. Ethnoveterinary medicine is based on traditional knowledge, skills, methods, and uses for treating diseases and keeping animals healthy. Ethnoveterinary medication is becoming more popular in underdeveloped nations because it is easy to find, prepare, and provide, and it is often free or very cheap [5]. It could be very important for animal productivity as well as earning a living, and it often becomes the main technique for farmers to care for their animals [6]. Dietary phytochemicals and medicinal plants are helpful and suitable substitutes to synthetic drugs according to their economic value, efficiency, non-resistance, renewability, and eco-friendly[7]. They are naturally originated molecules possessing configurational diversity which impact, stress or stimulation to resident microbiota, thus, they could be a tool for prevention of many illnesses such as metabolic, inflammatory, infectious diseases and cancer [8]. However, the antioxidant activity of the phytoconstituents prevents the loss in the livestock industry through stimulating animals' fertility and protecting against diseases[1]. Bioactive plant constituents that are included as feeding additives, possess a wide range of impacts on the animals, from health promotors and important for animal breeding to poisonous or even fatal [9]. Bioactive plants and plant compounds like phenolics, flavonoids, alkaloids, saponins and terpenoids could be helpful and economically valuable, environmentally safe and possess valuable medicinal properties like reduction or prevention of the incidence of cancers, cardiovascular diseases, neurodegenerative diseases, acting as antimicrobial drugs and many other values [10]. There is increasing interest in the livestock industry for reducing or eliminating feeding antibiotics as growth promotors due to the developing antibiotic-resistant microbes in order to find safer and effective alternatives of natural origin like the phytochemicals produces by medicinal plants [11]. According to the FAO, lacking drugs for treating illnesses and infections leads to about 35% loss in the breeding industry in several developing countries due to bad animal health. There are two main causes for the legislative changes regarding using antibiotic growth promoters. One of them is trying to withstand against developing of microbial resistance while the other is the consumer demands for eliminating usage of non-plant xenobiotics from animal's

feed. Accordingly, phytomedicines could be helpful for managing diseases and mortality of animals especially in rural areas[12]. Phytotherapy has been used for centuries, regardless the curative properties of the used plants were assured or not. Unluckily, there is little research about medicinal plants used in ethnoveterinary fields regarding their active constituents, mode of action, and applicability. Therefore, there is still a need for intensifying phytochemical, physiological, and phytopharmacological studies regarding these plant species [13]. Zoonosis is an infectious disease which could be transferred between animals and humans. Around 61% pathogenic microbes are known to influence humans as zoonotic [14]. where most of the dangerous infectious diseases are of zoonotic origin[15] and around 75% have originated from wild animals [16]. The transmission of these pathogens occurs thorough close contact with infected animals, inhaling, ingesting, or contamination of mucous membranes and damaged skin [17]. The sources of zoonotic pathogenic microbes in foodborne illnesses arise from rare cooked meat, seafood in addition to unpasteurized milk, dairies and vegetables [18]. In veterinary medicine, both humans and animals have Staphylococcus aureus on their skin and mucous membranes. Additionally, it has been reported to cause mastitis in dairy animals and manifests in hens and farmed rabbits [19]. Staphylococcus hyicus have been recognized to cause osteomyelitis to turkeys and exudative epidermitis to pigs [18]. Staphylococci could be cured using antibiotics; however, emerging of methicillin-resistant Staphylococcus aureus (MRSA) [20] has enforced the search for drugs of natural origin to substitutes the antibiotics like phytochemicals.

In this regard, I will summarize several effects of some biologically active plants and their phytoconstituents on some animal health, with special attention to animal diseases.

The mode of action of medicinal plants and their active components:

A wide variety of secondary metabolites are produced by plants, including phenolics, flavonoids, tannins, terpenes, alkaloids, essential oils and polypeptides, which they act as protective substances against biotic and abiotic stressors. These metabolites are not only vital for plant survival but also have therapeutic importance for human and animals [21,22]. The broad existence of such phytocompounds has illustrated their beneficial advantages as antioxidant, antibacterial, antiviral, and antifungal agents [23] and have exhibited the ability to overcome the increased antibiotic resistance in microbial pathogens [24].

Plants possess impressive impacts as stimulators of rumen fermentation and affecting microflora for increasing productivity and improving health[25]. Azadirahta indica, Hobrrhena antidysentrica, Barberis aristata, Embelia

ribes, Acorus calamus, Artemisia annua and Artemisia absinthium exhibited high anticoccidial potential as they are used for treatment of the infectious disease Coccidiosis that infect the digestive tract of poultry [26]. Many plants secondary active constituents exhibited broad antimicrobial potential against many pathogenic intestinal bacteria [27]. For instance, essential oils are used for controlling colonization and proliferation of Clostridium perfringens in the broilers gut [28] inhibiting Salmonella typhimurium and E.coli growth in pigs [9] or preventing infection with Bacillus anthracis in mice [29]. Some phytochemicals like Trans-cinnamaldehyde in Cinnamomum verum, linolenic acid in Linum usitatissimum and extract of Terminalia chebula possess the ability to diminish E. coli levels in the mammary gland [30]. Other components have anti-inflammatory effects like cynatratoside-C from Cynanchum atratum is capable of deactivating NF-**κ**B complex, inhibiting TLR4 expression, and decreasing IL-1**β**, IL-6, and TNF-**α** production [31]. The caffeic acid is capable of attenuating the production of proinflammatory cytokines through diminishing the p65 phosphorylation in the NF-**κ**B route and the I**κ**B**α** degradation [32]. Persicaria pensylvanica crude extracts exhibit bactericidal activity against S. aureus that causes contagious mastitis in dairy cows with economic withdraw of about two billion dollars per year in the United States and mastitis elimination using antimicrobial therapy still difficult according to its capability of forming a biofilm, becoming a small colony variant, or gaining antimicrobial resistance. Antimicrobial phytochemical compounds of P. pensylvanica may act as substitutes to synthetic drugs for treatment of Staphylococcal infections in human and animals [33]. Vitex mollis, Psidium guajava, Dalbergia retusa, and Crescential alata leaves extracts were found to act as potential antibiotics that possess antioxidant capabilities for inhibition of all the tested MRSA isolated from cattle's and rabbits [34]. Oregano extract was found to be efficient in treating E. coli O27, the most frequent serotype, which causes large losses in broiler farms [35]. Among the phytoconstituents possesses antioxidant activity, antimicrobial activity and stimulates immune response are terpenoids including monoterpenes (fruits and spices), diterpenes (berries), triterpenes (olive oil), tetraterpenes (colored fruits and vegetables), sesquiterpenes (essential oils of plants), and phenolics including various subclasses like flavonoids (from tea and grapes) [36,37]. These phytoconstituents with amphipathic or hydrophobic structure, could exhibit impact on the interaction with microbial membranes, regarding permeability and micro viscosity [38]. The mode of action of these phytocompounds was interpreted on basis of their influence on binding-receptors, enzymes, ion-exchange channels, transporters, and biological pathways [39,40] as illustrated in Table 1.

Table 1: Examples of useful phytochemicals and how they work against target strains of bacteria.

Chemical Class	Phytochemicals	Sources	Targeted pathogens	Mechanism of action	Reference
Alkaloids	Berberine	Berberi's species	Escherichia coli	Cell division/Protein/DNA synthesis inhibition	[43]
	Conessine	Holarrhena antidysenterica	Pseudomonas aeruginosa	Efflux pump inhibition (EPI)	[44]
	Reserpine	Rauwolfia serpentina	Staphylococcus sp., Streptococcus sp.	(EPI)	[45]
	Tomatidine	Solanaceous plants	Listeria, Bacillus and Staphylococcus spp.	ATP synthase inhibitor	[46]a steroidal alkaloid from solanaceous plants, possesses potent antibacterial activity against S. aureus small-colony variants (SCVs
Organosulfur	Allicin	Allium sativum	S. epidermidis, P. aeruginosa,	Sulfhydryl-dependent enzyme inhibitor, DNA/ protein synthesis inhibitor	[47]
	Ajoene	A. sativum	Campylobacter jejuni, Staphylococcus sp., E. coli	Sulfhydryl-dependent enzyme inhibitor	[48]
	Sulforaphane	Diplotaxis harra	E. coli	Membrane destruction, ATP synthase and DNA/ protein synthesis inhibitor	[49]
Phenolics	Kaempferol	Alpinia calcarata	Methicillin-resistant S. aureus	(EPI)	[50]
	Resveratrol	Vitis vinifera	C. jejuni	(EPI)	[51]
	Taxifolin	A. cepa	Enterococcus faecalis	Beta-Ketoacyl acyl carrier protein synthase inhibitor	[52]

Coumarins	Aegelinol	Ferulago campestris	Enterobacter aerogenes, Salmonella enterica serovar Typhi, E. cloacae, S. aureus	DNA gyrase inhibitor (GR)	[53]
	Osthole	Prangos hulusii	Bacillus subtilis, S. aureus, Klebsiella pneumoniae,	DNA (GR)	[54]
Terpenoids	Carvacrol	Thymus capitatus	E. coli, Enterobacter aerogenes, S. aureus, P. aeruginosa	Cell membrane disruption (CMD)	[55]
	Cinnamaldehyde	Essential oils	E. coli and S. aureus	(CMD)	[56]and the underlying mechanism were evaluated. Antibacterial activity was determined based on the diameter of inhibition zone (DIZ
	Eugenol	Essential oils	Methicillin-resistant S. aureus	(CMD)	[57]

Medicinal plants have antibacterial capabilities through several ways, such as destroying bacterial cell walls, reducing enzyme function, and altering immunological responses. For example, essential oil constituents like citral and linalool from plants such as Cymbopogon citratus and Lavandula angustifolia have been shown to damage the cytoplasmic and outer membranes of Gram-negative bacteria, leading to bacterial inactivation. Furthermore, compounds like berberine from Berberis vulgaris have been reported to hinder the action of **β**-lactamase enzymes, thereby enhancing the effectiveness of antibiotics against resistant bacterial strains41. Some of the commercially available plants and/or plant components that possess antimicrobial activities are listed in Table 2 [42].

Table 2: List of some plants and their components that possess antimicrobial activity [42]

Common name	Scientific name	phytochemicals	Biological Activity
Barberry	Berberis vulgaris	Berberine	Antibacterial, antiprotozoal
Black pepper	Piper nigrum	Piperine	Antifungal, antibacterial against Lactobacillus, Micrococcus, E. coli and E. faecalis
Cascara sagrada	Rhamnus purshiana	Tannins	Antibacterial, antifungal, and antiviral
Chamomile	Matricaria chamomilla	Anthemic acid	M. tuberculosis, S. typhimurium, S. aureus
Eucalyptus	Eucalyptus globulus	Tannin	Antibacterial and antiviral
Goldenseal	Hydrastis canadensis	Berberine, hydrastine	Antibacterial, active against Giardia duodenale, Trypanosomes
Licorice	Glycyrrhiza glabra	Glabrol	Antibacterial, active against S. aureus, M. tuberculosis
Onion	Allium cepa	Allicin	Antibacterial, antifungal (active against Candida spp.)
Grape	Mahonia aquifolia	Berberine	Active against Plasmodium, Trypanosomes
Thyme	Thymus vulgaris	Caffeic acid, Thymol, Tannins	Antibacterial, antifungal, and antiviral

The mode of action of phenolics and flavonoids as antimicrobials:

Phenolics are plant secondary metabolites having hydroxyl groups linked to aromatic rings and included in defense mechanisms against UV radiation or pathogenic infections[58]. They are broadly distributed in plants [59]. These compounds play a crucial role as antimicrobial drugs against antibiotic-resistant pathogens by different mechanisms, for instance, there are plenty of phenolics in bilberry, cranberry, and blueberry, like anthocyanidins, flavone, luteolin, flavanols, myricetin, quercetin and epigallocatechin-3-gallate [59,60] ,in addition to others like galangin, puerarin, and ursolic acid are efficient as antimicrobial drugs [61]. 3-p-Trans-coumaroyl-2hydroxyquinic acid expressed antioxidant and antimicrobial activities against S. aureus where it contains 2-hydroxyquinic acid moiety and p-coumaric acid, but the active moiety or group responsible for antibacterial activity is unclear [62]. p-Coumaric acid expresses antibacterial potential against E. coli through destructing cell membranes and attaching its DNA genome leading to cells malfunctions [63]. Flavonoids, including quercetin and kaempferol, are antioxidants that shield plants from oxidative stress due to environmental causes. They also play a role in signaling and defense against pathogens [64]. Flavonoids, as a class of phenolics, possess the ability to kill or inhibit bacterial cells through different routes, including disruption

of membranes and inhibition of nucleic acid synthesis (inhibition of dihydrofolate reductase, helicase, and gyrase/topoisomerase), as well as inhibition of bacterial virulence, for instance, toxins and quorum sensing, that destroy the formation of biofilms [65]. They could also inhibit the cell envelope synthesis, which involves the inhibition of fatty acids and peptidoglycans synthesis (inhibiting Alanine–Alanine dipeptide synthesis, inhibiting the peptidoglycans cross-linking) [66]. Flavonoids may also block efflux pumps, potentially reversing antimicrobial resistance [67]. Moreover, inhibiting NADH-cytochrome c reductase in the respiratory chain so inhibiting ATP [66].

The mode of action of peptides as antimicrobials:

Antimicrobial polypeptides are small proteins made by various living organisms that help fight off harmful microbes and are important for health and food safety. They can act as natural alternatives to antibiotics and include types like, defensins, thionine, lactoferricin, lactoferrampin, lactoglobulins derived peptides, casein-derived peptides, and lysozyme-derived peptides [68–70]. These peptides have different structures and are mostly positively charged, while plants produce unique defense proteins to protect against microbes, which are different from traditional antibiotics, as they are gene-coded[71,72]. Antimicrobial peptides attach to negatively charged bacterial membranes, overcoming barriers like lipopolysaccharides in Gram-negative bacteria and acidic polysaccharides in Gram-positive bacteria, allowing them to disrupt membranes and reach the cytoplasmic layer [73]. These peptides can also boost the immune response by activating immune cells and influencing how the body recognizes harmful microbes and their components[74]. Antiviral peptides (AVPs) are crucial therapeutic agents because of rising virus resistance and the limited effectiveness of traditional medications [75]. Antiviral peptides inhibit viruses at different stages of their cycle through a variety of ways [76]. Certain AVPs can deactivate the virus by incorporating it into the viral envelope and cell membrane, which can destabilize the viral membrane or stop infection and likewise, they have the ability to attach to viral glycoproteins, which prevents the viruses from attaching to the surface of the host cell [77]. However, some (like heparan for the herpes simplex virus) attach to host cell receptors, blocking the virus's ability to attach to its target receptor and deactivating it. Some, like influenza viruses, stop viral attachment and stop the virus cell's membranes from fusing[78,79]. RNA and DNA can be AVPs' target sites[80] ,moreover, as in the cases of the Junin virus (JV), HIV-1, and HSV-2, their objective is to damage the viral envelope, causing it to become unstable[81]. Modifying or disrupting cell signaling pathways, such as BMAP-18 (bovine myeloid antimicrobial

peptide-18), which can deactivate the Zika virus (ZIKV) by interfering with interferon type 1 signaling, is another method of virus inhibition [82,83]. A possible treatment for fungal infections may be antifungal peptides (AFPs). The majority of AFPs work by targeting particular targets and using membrane-associated mechanisms. Ergosterol is the primary membrane sterol in fungal membranes, along with PI concentration and sphingolipid composition. High selectivity and prevention of treatment resistance are made possible by definite targets such glucosylceramides, mannosyldiinositol phosphorylceramide, or a fungal protein target[84,85].

The mode of action of essential oils as antimicrobials:

Essential oils have garnered significant attention for their potent antimicrobial properties, offering a natural alternate to synthetic preservers and antibiotics. Their mode of action is multifaceted, targeting various cellular components and processes in microorganisms. Essential oils with compounds like terpenes can damage microbial membranes, increase their permeability and cause leakage of important cell materials, especially in E. coli under acidic conditions. Thymus capitatus oil can destroy cell walls in various bacteria, including MRSA, leading to loss of essential cell contents and increased effectiveness against resistant strains. These oils can also block the production of peptidoglycan, a key part of bacterial cell walls, which weakens the bacteria and can lead to their death, especially when combined with antibiotics like penicillin G [41,86].

These oils can also block DNA synthesis, crucial for bacteria to grow and multiply. For instance, Thymus capitatus essential oil was shown to prevent DNA replication in E. coli and MRSA, stopping their growth. Additionally, essential oils can hinder important enzymes needed for bacteria to survive. They can bind to these enzymes, disrupting their function, and making bacteria more vulnerable to antibiotics like **β**-lactam, as shown in studies with **α**-terpinyl acetate and citral [86]. Essential oils can stop the growth of biofilms, which are tough groups of germs that resist treatments. They can break down the protective layer of biofilms, helping to fight infections, especially in hospitals, with Thymus pallescens oil being effective against certain bacteria at low amounts [87]. These oils can also boost the effectiveness of regular antibiotics by working on different parts of the germs at once. When combined, they can make antibiotics work better against resistant germs, offering a possible way to tackle the issue of antibiotic resistance [88.] Essential oils have antioxidant properties that help reduce stress in microbial cells, enhancing their ability to act as natural preservatives in food. Oils like rosemary, thyme, and tea tree are effective due to their strong antioxidant

activity [89]. These oils can also fight airborne germs by releasing volatile compounds that disrupt microbial cell membranes, showing effectiveness against harmful bacteria like E. coli and Pseudomonas aeruginosa when used in gaseous form [90]. Essential oils can fight many germs like bacteria and fungi, making it hard for them to resist. Garlic and rose oils are especially effective against spoilage microbes, with specific amounts needed to stop their growth [89,91]. Using nanomaterials and mixing essential oils with other substances can boost their effectiveness. For example, combining thyme and rose oils improves their antioxidant and antimicrobial benefits [88,89,91].

The essentials oils from medicinal plants like basil, citrus, lemon grass, oregano, rosemary and thyme expressed antifungal potential against large number of pathogenic fungi [92]. Garlic and clove expressed the potential of inhibiting Candida acutus, C. albicans, C. apicola, C. catenulata, Rhodotorula rubra and Trignopsis variabilis [93]. Isothiocyanate isolated from onion and garlic plants have the ability to deactivate the extracellular enzymes by breaking of di-sulphide bond [94]. Oregano and thyme essential oils are capable of inhibiting fungal pathogens according to the presence of the phenolics like carvacrol and thymol that might disrupt fungal cell membranes [95]. Clove and cinnamon are efficient against Aspergillus parasiticus and Fusarium moniliforme [96]. Essential oils have the ability to penetrate and damage the fungal cell wall, cytoplasmic and mitochondrial membranes by changing the electron transport chain in mitochondria and destroying lipids, proteins, and nucleic acids within the cell [97]. The essential oils could be able to decrease the membrane potential, affecting Ca+2 ions channels, decreasing the pH and influencing the proton pump and ATP levels. The changes of membranes fluidity led to leaking of radicals, cytochrome C, Ca+2 ions and proteins resulting in cell death by apoptosis and necrosis [98,99].

Recently, plant extracts and their biological activity have gained the interest of researchers as phytoconstituents possess antiviral potential through various modes of action. They could attach to certain sites on virion surface and prevent target cell recognition by virus [100,101]. Different modes of action were identified where such phytoconstituents capable of blocking targets on the host cell surface, the penetration into the cell and the synthesis of viral nucleic acids. They might also be capable of inhibiting viral proteins synthesis and post translational processing. Another action is assembling daughter virions, or releasing the viral daughter particles from host cell[102]. Melissa officinalis contains the essential oils citral and citronellal that are capable of inhibiting Herpes simplex virus type 2 (HSV-2) [103]. Herpes simplex virus type 1 (HSV-1) replication can be inhibited by the in-vitro incubation of various essential

oils. essential oils extracted from Artemisia arborescens could strongly suppress the (HSV-1), that causes common viral infections in humans. Essential oils have been used as antivirals in animals [104] and could be used as alternatives to the synthesized antiviral drugs [105,106].

The mode of action of alkaloids as antimicrobials:

Alkaloids have antibacterial activity against bacteria, fungus, and other pathogens, making them ideal candidates for the creation of natural antimicrobial drugs [107,108]. Their mode of action could be through DNA intercalation, targeting RNA polymerase, gyrase, topoisomerase, the inhibition of cell division [109]. Another investigation found that its antibacterial activities are associated with the inhibiting of the cell division protein FtsZ [43]. Ungermane is an iso-quinoline alkaloid found in the methanolic extract of Pancratium illyricum L., that possess antibacterial potential. It could increase DNA cleavage through attacking and inhibiting the bacterial topoisomerase IA [110]. Alkaloids can boost the immune system by activating stress resistance pathways and lowering harmful substances in the body, helping to fight infections like MRSA. They show potential for use in treatments [111]. These compounds can also disrupt how bacteria move and form protective layers, making it harder for them to infect the host. Specific alkaloids, like piperine, can improve the effectiveness of antibiotics by helping them penetrate bacterial layers, making them useful in treating infections related to biofilms [112]. Alkaloids can block bacterial efflux pumps, which helps keep antibiotics inside the bacteria, making them more effective against drug-resistant strains like E. coli. This can lower the amount of antibiotics needed to fight infections [113]. Some alkaloids also target harmful factors in bacteria and help the immune system, reducing inflammation and aiding in healing. For example, 6-ethoxysanguinarine can lessen the effects of toxins in MRSA and help wounds heal faster. These properties of alkaloids make them promising options for treating tough infections, as they can both fight bacteria and support the body's healing processes [114]. The chemical structure of alkaloids affects their ability to fight bacteria, with changes like methylation improving their strength and effectiveness. Isoquinoline alkaloids show better activity than their simpler forms, and modifications can enhance their interaction with bacterial membranes [115]. Alkaloids can work together with traditional antibiotics to make them more effective against resistant bacteria. They help antibiotics penetrate biofilms and make bacteria more vulnerable, as seen with piperine improving the action of ciprofloxacin and azithromycin [112]. Using alkaloids alongside antibiotics could be a smart way to tackle drug-resistant infections, potentially reducing the need for higher doses

or longer treatments. This approach highlights the importance of understanding how alkaloids can enhance antibiotic therapy [113]. Alkaloids are safe for use in medicine due to their low toxicity to human cells and their ability to target harmful microbes specifically, making them good candidates for new antimicrobial drugs[116]. They work effectively against bacteria by disrupting their cell membranes, blocking harmful processes, and reducing their ability to cause disease, which is important for fighting drug-resistant bacteria. Compounds like oroidin and 6-ethoxysanguinarine show strong antibacterial effects while being safe for human cells, highlighting their potential in developing effective treatments with fewer side effects [114].

The mode of action of tannins compounds as antimicrobials:

Tannins are water-soluble phenolics abundantly dispersed in plants with the capacity to precipitate proteins [117]. Tannins could be divided to condensed and hydrolysable [118]. Hydrolysable tannins are numerous esters with d-glucose, whereas condensed tannins, such as proanthocyanidins, have building units of flavonoid monomers. There is increasing interest in using tannins for enhancing nutrition and animal health, especially for ruminants like cattle [119]. Tannins are capable of reducing the risk of livestock illnesses and transmission of zoonotic pathogenic microbes[120]. Tannic acid is a natural phytoconstituent possessing unique antimicrobial properties as antiviral and antibacterial effect. Activity against viruses like Influenzas A, Papilloma, noroviruses, and human immunodeficiency virus. It expressed broad antibacterial spectrum for instance, S. aureus, E. coli, S. pyogenes, E. faecalis, P. aeruginosa, Yersinia enterocolitica, L. innocua [121]. Tannic acid express activity against viruses through inhibiting receptors binding, stopping viruses' attachment to the various types of surfaces and inhibiting proteins attachment to cells that are important for the metabolism [122]. Tannic acid could inhibit the bacterial attachment [123]. The absence of bacterial cohesion to the surface leads to bacterial cell death. Also, tannic acid inhibits sugar and amino acid usage by bacteria for limiting bacterial growth [124]. The antibacterial mechanism of action of tannins is attributed to their ability for passing the bacterial cell wall and interfering the cell metabolism leading to destruction. Tannins demonstrated fast activity in Gram-positive bacteria, but slow activity in Gram-negative bacteria, which are more toxic and cause specific diseases, due to the presence of a bilayer membrane. Tannic acid has been tested against several species of bacteria including S. aureus and E. coli [122].

The mode of action of saponins compounds as antimicrobials:

Saponins are a group of plant active phytoconstituents. They include glycosylated

steroids, triterpenoids, and steroid alkaloids. Such saponins possess the capability of modifying rumen fermentation and enhancing animal production [125]. They found to be present in the plants Yucca schidigera, Quillaja saponaria, Acacia auriculiformins, Sapindus saponaria, Sesbania sesban and Medicago sativa[126]. Saponins are used in folkloric treatments to treat animal diseases. They are a category of high molecular-weight glycosides that may react with a triterpene to produce triterpene saponins or with a steroid to form steroid saponins [127]. They could be monodesmosidic like Spirostanol, bidesmosidic like furostanol or tridesmosidic like lucerne [128]. Saponins present in seeds, roots and bulbs of different plants [117]. Saponins' ability to combat microorganisms depends on how they interact with their sterol moiety[127]. Saponins has strong antifungal and antibacterial properties against infections such as Candida, Trichophyton species and methicillin-resistant Staphylococcus aureus and other multidrug-resistant pathogens. Additionally, because saponins can alter host immune responses and disrupt lipid membranes, they demonstrate potential in defending against viral diseases [129].

The mode of action of organosulfur compounds as antimicrobials:

Sulfur-containing substances like allicin, ajoene, dialkenyl, dialkyl sulphides, S-allylcysteine, and isothiocyanates have a broad antibacterial broad spectrum [23]. Allicin (diallyl thiosulfinate) present in garlic (Allium sativum), a species in the family Alliaceae that exhibited antibacterial activity against Staphylococcus epidermidis, P. aeruginosa, Streptococcus agalactiae and MRSA [47]. The mode of allicin action as antimicrobial drug attributed to its ability to inhibit sulfhydryl-dependent enzymes like alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase [130]. The antibacterial activity of garlic organosulfur compounds possesses the ability to form disulfide bonds with the free sulfhydryl groups enzymes rendering them inactive leading to bacterial death. They could also interact with and disrupt the bacterial cell membrane leading to leakage of cell content and finally death. They are interfering with protein production, DNA replication and gene expression [131]. Furthermore, allicin found to inhibit DNA and protein synthesis in addition to its ability to target RNA [132]. Ajoene is another organosulfur compound present in garlic that possess broad-spectrum antimicrobial activities It is similar to allicin in antibacterial mechanism of action [48]. Allyl isothiocyanates, is an organosulfur compound present in Armoracia rusticana and Eutrema japonicum and exhibits antibacterial activity against E. coli, S. pyogenes and S. aureus [133]. Several modes of action were recorded where the vapors of this compound could damage cell wall integrity leading to leakage of cellular

metabolites [134]. It was proposed that these substances might cause the deactivation of important intracellular enzymes by oxidative destruction of disulfide bonds. It could also result in cell membranes pores leading to leakage of the intracellular components [132].

Conclusion:

Medicinal plants are considerably important regarding the needs for intensive and largescale production of animals and for preventing and controlling of their diseases. Locally available herbs contain a significant number of functional phytochemicals like flavonoids, polyphenols, alkaloids, saponins, polypeptides, tannins, anthraquinones and terpenes. The current review discusses these active phytoconstituents in the form of crude extracts or pure active compounds have which bioactivities like immunostimulatory, antimicrobial, antiviral, antiparasitic, appetizers and growth promotors. The review also discusses how each herbal plant had a unique, dose-dependent mechanism of action for a particular disease. Moreover, the toxicological safety research of medicinal plants needs to be more studied. The application technology of medicinal plants, including extraction, drug duration, and delivery routes, also requires more study. Understanding the mechanisms of medicinal plants action regarding animal diseases is very limited and further research needed to know these mechanisms. Last but not least, the usage of medicinal plants and their active phytoconstituents could be a safe, effective and suitable alternative to synthetic drugs and antibiotics.

Recommendations:

The global increase in antibiotic-resistant microbes resembles a great danger to successful treatment of microbial infections. There is a need for developing novel strategies aiding in combating antibiotic resistance. Phytochemicals that are distinguished by their various chemical configuration and modes of actions are crucial therapeutics for exploring bioactive phytoconstituents. However, continued research should be done for understanding the modes of action and also pharmacodynamic and pharmacokinetic properties of these constituents.

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