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Review Article

Ethnoveterinary perspectives and promising future

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ABSTRACT

In this review, we have discussed the recent potential effects of plants and their derivatives in treating diseases of veterinary importance in livestock. The therapeutic value of these natural products depends upon their bioactive metabolites that are developed and isolated from crude plants, thus produced a selective action on the body. The crises of drug resistance in most pathogenic bacteria and parasites that cause economic loss in animals necessitate developing new sources for drugs to overcome therapeutic failure. We summarized the different antibacterial and antiparasitic plants with their bioactive compounds that have widely used in animals. Finally, the environmental friendly feed additives that may be used as alternatives to an antibiotic growth promoter for broiler chickens were illustrated.

1. Introduction

In almost all countries, plants have been used broadly all over history for treatment and prevention of different diseases and infections in human and domestic animals. Nowadays, these traditional remedies are encouraged in veterinary medicine due to their promising therapeutic efficacy minimal side effects of chemotherapeutic agents and decreasing of drug residues in animal products that consumed by human [1]. Perspective and future approaches to ethnopharmacology research are developed parallel with the advances in laboratory and clinical sciences especially phytochemistry and pharmacology [2]. Researchers should have an apparent vision for those new trends to achieve practical and applicable resonance approaches and as in all disciplines adherence to internationally recognized for the ecological factors, ethical and economic issues and the appropriate use of plants [3]. Human ethnopharmacology has become an information science depends upon professional researches that reported on published literature [4]. An accurate methodological approach in ethnopharmacology invariably requires the use of a database that ideally serves two main functions: storage of data, and facilitation of analysis, such as quantification and comparisons.

In this review, we discussed the basic requirements and standards to verify ethnoveterinary information. Future uses of such information both in the experimental research and applied missions emphasized the various tasks of such data generated in herbal field studies [5]. Systematic pharmacovigilance is necessary to augment consistent pharmaco-toxicological information on the safety for the development of right plans for safe effective use [6].

There is an increasing substantiation to explain that synergistic and/or side-effects counteracting combinations of local herbs. Herbal medicine as an alternative remedy has already developed and is likely to play the more significant role. The scientific and local names of mostly used herbs are essentially requested as they may apply to more than one scientific species, which may or may not be closely related. For example, there are a number of plant species of “Chamomile,” including *Anthemis nobilis* L., *Matricaria chamomilla* L., *Matricaria discoidea* DC, *Cotula matricarioides* (Less.) Bong and *Tanacetum annuum* Pursh. On the contrary, a scientific species may be famous by a number of local plants and classified in folk medicine as they do not correspond to the same botanical category [5,7].

The use of separated bioactive alternatives is a talented approach, which has established the high efficacy with little doses than parent crude herb. Nowadays, natural organic drugs as strychnine, atropine, turpentine oil, cater oil and ephedrine were previously discovered and achieved significant success in veterinary medicine [8]. Garlic, is an extensive example of botanical, which is gaining acceptance as an alternative to patentable chemical drugs. The medical uses of garlic all over the ages in prevention and treatment of diseases in human and domestic animals had potential benefits. Garlic achieved an intentional success for control of hypertension and hypercholesterolemia besides its use as a food additive [9]. Garlic was in use at the beginning of recorded history and was found in Egyptian pyramids and ancient Greek temples. In many cultures, garlic was administered to provide strength and increase work capacity for manual workers [10]. The interest of garlic advantages has been developed in all culture as the efficacy of garlic is obtained from all experimental trials [11]. The different

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Table 1
Summary of different actions and their mechanism of garlic extract (*Allium sativum* L).

Actions	Mechanism of Actions	References
Anticoccidial	Decreases *Eimeria vermiformis* oocysts output in mice	[14]
	Prophylactic effect against hepatic coccidiosis in rabbits	[15]
Amebicidal	Inhibition of *Acanthamoeba castellanii* life cycle	[16]
Antipseudomonas	Inhibition biofilm coated *Pseudomonas aeruginosa* bacteria that leads to failure of antibacterial treatment and humoral immunity	[17]
Antibacterial	Significantly inhibits the growth and division of oral pathogens	[18]
	Food preservatives so prevent food poisoning crises	[19–21]
Antioxidant	Potent antioxidant activity	[22,23]
	Antagonizes β-hexosaminidase enzyme release so it has a potent antiallergic effect	[24]
Antileishmaniasis	Immunostimulant via activation the efficacy of macrophages to engulf the intracellular protozoan Leishmania	[25,26]
Antischistosomiasis	Potent broad spectrum against all stages of Schistosoma life cycle	[27–29]
Hepatoprotective	Increases all the hepatic biomarkers antioxidant enzymes concerned with oxidative stresses	[30]
Antithrombus	Inhibition of prostaglandin synthesis through cyclooxygenase pathway and prevents platelets aggregations in blood vessels or lungs	[31]
Antifungal	Inhibition of saprophytic fungal growth that induced external mycosis	[32]
	Inhibition of metabolism process of *Candida albicans* by NADH oxidation and glutathione depletion, and increased reactive oxygen species (ROS)	[33]
Insecticide	Potent natural larvicidal activities against the filarial mosquito *Culex quinquefasciatus*	[34,35]
Anticancer	Suppress the growth of human breast cancer cells *in vitro* through several mechanisms the activation of metabolizing enzymes, the suppression of DNA, antioxidant activity, and stop cell division	[36–39]
Aquacultures	Highly efficacious in most infectious fish diseases	[40]
	Immunostimulant and antiprotozoal activities in different aquacultures	[41]

pharmacological actions of garlic with possible mechanisms of action and exploring garlic's potential for disease prevention and treatment in human and domestic animals are summarized in Table 1. Previous literature that concerned with ethnoveterinary medicine were conducted in certain regions or countries [12,13] and they focused on their traditional and local uses. Consequently, the nature of plant species, bioactive metabolites, weather, cultivation method and animal diseases will be different from the Far East to the Middle East. Moreover, the knowledge on the environment-friendly feed additives that may be used as alternatives to an antibiotic growth promoter for broiler chickens are intermittent. Consequently, the aim of this review is to correlate the ethnoveterinary uses with their secondary bioactive metabolites content. Moreover, we select global plant species that exist all over the world especially Arabian countries and used alternatively to chemicals.

2. Antibacterial activity of some plant extracts against pathogenic bacterial strains

Although many new antibiotics have produced in the recent decades, bacterial resistance to these chemotherapeutic agents has increased. Generally, bacteria have the inherited ability to transmit and acquire resistance to antibacterials, which are developed to infectious diseases in human and domestic animals [42].

Additionally, weak immunity in host cells and the ability of bacteria to develop biofilm-associated drug resistance have further increased the number of life-threatening infections [43]. Thus; bacterial infections remain a major causative agent of death, even today. The use of several antibacterial agents at higher doses may cause toxicity. This has prompted researchers to explore alternative new key molecules against bacterial strains.

There is an efficient support that many of the health-promoting activities of phytochemicals also intercede through their capacity to augment the host's defense against microbial infections [44]. The efficiency of essential oils varies from one to another as well as against different target bacteria depending on their cell membrane and cell wall structure (Gram-positive and Gram-negative bacteria) [45]. The cell wall of Gram-negative bacteria is more resistant to the toxic effects of essential oils than Gram-positive bacteria [46]. The structure of the Gram-positive bacterial cell wall allows hydrophobic molecules to easily penetrate the cells [47].

The antibacterial effects of a large number of plant extracts and oils have been evaluated and reviewed [48,49], and the mechanisms that facilitate the bioactive compounds of herbs to combat bacteria have been discussed [50]. Different antibacterial extracts and oils with their mechanisms and susceptible bacterial species are illustrated in Table 2.

The results show that these mechanisms differ significantly depending on the essential oil components [51]. Essential oils exhibit extremely good antimicrobial effects against bacteria, yeasts, fungi, and viruses [52]. Accordingly, it was assumed that the essential oils may have antimicrobial activity by modulating bacterial and fungal targets involved in the cytoplasm and cell wall metabolism [53].

It is affirmed by several researchers that especially monoterpenes will increase cytoplasmic membrane fluidity and permeability, disturb the order of membrane implanted proteins, inhibit cell respiration, and alter ion transport pathways [54,55]. However, the assessment of different results in the literature is frequently complicated because of the use of different local plant species, diverse techniques, bacterial strains, and incubation period [56].

3. Plants with antiparasitic activity in animals

The crises of drug resistance in parasites that cause different diseases in animals necessitate developing new sources of drug to overcome failure therapy. Such parasites cover a broad phylogenetic range and include protozoa, helminths and arthropods. In order to achieve effective parasite control in the future, the identification and diagnosis of resistance will be essential [77]. Many new natural products have revealed antiparasitic properties of potent efficacy and selectivity, as will be shown in this review for plant-derived bioactive secondary metabolites [78]. Parasitic infestations reduced productivity in livestock, particularly in poor worldwide. Phytomedicine has been used traditionally to treat parasitism and improve the performance of livestock. Scientific validation of the anti-parasitic effects and possible side-effects of plant products in animals is necessary prior to their approval for parasite control [79].

A variety of methods has been explored to validate the anthelmintic

Table 2
Summary of different antibacterial extracts and oils with their mechanisms and susceptible bacterial species.

Plant	Scientific name	Mechanism of action on bacteria	Susceptible bacteria	References
Extracts				
Cumin seeds	*Cuminia cyminum* J.F.Gmel.	Damage to the cell membranes and loose of intracellular organelles	*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus pumilus*	[57]
Ginger rhizome	*Zingiber officinale* Roscoe	Inhibits bacterial multiplication	*Pseudomonas aeruginosa*	[58]
Clove flowers	*Syzygium aromaticum* (L.) Merr. & L.M.Perry	Enhanced membrane permeability and oxidative stress of bacteria	*Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli*	[59,60]
Pomegranate peel	*Punica granatum* L.	Interferes with bacterial protein secretions	*Listeria monocytogenes, Staphylococcus aureus, Escherichia coli and Yersinia enterocolitica*	[61,62]
Thyme leaves	*Thymus vulgaris* L.	Cell wall lysis of bacteria	*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus*	[63,64]
Oils				
Coriander seeds	*Coriandrum sativum* L.	Damage of cell membrane, leads to cell death	*Staphylococcus aureus, Escherichia coli, Salmonella typhi, Klebsiella pneumonia, Proteus mirabilis,*	[65,66]
Black cumin	*Nigella sativa* L.	Anti-biofilm activity	*Bacillus cereus, Bacillus subtilis, Staphylococcus aureus, and Pseudomonas aeruginosa*	[67,68]
Fennel seeds	*Foeniculum vulgare* Mill.	Leakage of electrolytes, the losses of cellular contents	*Pseudomonas syringae, Bacillus subtilis, Escherichia coli, Staphylococcus sp., and Aeromicrobium erythreum*	[69–71]
Rosemary leaves	*Rosmarinus officinalis* L.	*Anti-R-plasmid activity* Elimination of R-plasmids	*Staphylococcus aureus and Escherichia coli*	[72]
Caraway seeds	*Carum carvi* L.	Inhibition of *S. aureus* growth		
Peppermint leaves	*Mentha piperita* L.	Change cell morphology Forming elongated filamentous forms	*Salmonella enteritidis, Escherichia coli, methicillin-resistant Staphylococcus aureus (MRSA)*	[73]
Savory leaves	*Satureja montana* L.	Affected cell membrane of bacteria and induced depletion of the intracellular ATP	*Escherichia coli and Listeria monocytogenes.*	[53]
Chamomile dried flowers	*Matricaria chamomilla* L.	Alterations of bacterial Morphology	*Bacillus cereus, and Staphylococcus aureus*	[74]
Carrot umbels	*Daucus carota* L.	Cell Membrane/Protein Synthesis Inhibition	*Campylobacter jejuni Vibrio, Aeromonas hydrophila*	[75,76]

properties of such plant remedies, both *in vivo* and *in vitro*.

The main advantages of using *in vitro* assays to test for the anti-parasitic activities of essential oils and extracts from plants are the low expenses and rapid results which permits screening of large numbers of samples [80].

It has been suggested that consumption of some plants may be associated with an enhanced immune response of the host towards the parasites, as a result of nutrient supplementation and thus improved nutrition [81]. It is known that high dietary protein intake in animals can enhance the immune response of ruminants towards parasites [82].

In vivo studies are more applicable and reliable than *in vitro* studies, although large-scale screening of plant extracts is more expensive. The *in vivo* methods normally have parasitized hosts being treated with known doses of extracts compared with untreated controls and standard anthelmintic drug [83].

However, in most cases the active material has to be extracted from the plant and *in vitro* conditions and concentrations used are not always comparable to those *in vivo*, and thus often the results can differ in the two assays [84].

A concerted effort on isolation, development, and validation of the effects of these herbal remedies will have to be undertaken before their wider acceptance (Table 3).

4. Common plants used for growth promoters in broiler chickens

Among the livestock divisions, poultry production systems are intensively reared with developments in nutrition and disease control strategy, genetic selection, and management along with the demand for poultry products as well as crises of virulent pathogens [104]. Prohibition of antibiotic uses as growth promoters in broiler chicken diets has resulted in increased use of natural additives in broiler feeds over the current years [105].

Therefore, antibiotic growth promoters were disparaged by consumer associations as well as by scientists, e.g. the use of most antibiotic growth promoters was banned by the European Union [106]. Consequently, the animal feed manufacturers are exposed to increasing consumer pressure to reduce the use of antibiotic growth promoters as a feed additive and find alternatives to antibiotic growth promoters in poultry diets. Veterinarians particularly look for herbs that can affect growth performance, immune response, or killing of pathogenic bacteria [107].

Such products have several advantages over frequently used marketable antibacterials since they are residue-free and distinguished as safe alternatives in the food industry [108]. Feed agencies are approving new formulations of natural feed additives that are the products of modern science [109]. This new era of botanical growth enhancers includes combinations of herbs and extracts as garlic and thyme that have many different bio-active ingredients such as alkaloids, flavonoids, glycosides, saponins, and tannins are mainly synergistic. Therefore, the expected effects are modulating the appetite and intestinal microflora, stimulate the enzyme activity and immune system [110]. Because of possible synergism between constituents, it remains indistinct which components of the herb may stimulate the endogenous digestive enzymes or act as antimicrobial agent. There are experimental data showing the *in vitro* antimicrobial effects with respective MIC-values and spectrum of activity [111].

Optimal combinations of various alternatives coupled with good husbandry will be the key to get maximum performance and maintain animal productivity, with the crucial goal of limiting of antibiotic use [112].

There is a need to put and then to meet standards for the replacement of antibiotic compounds in poultry by natural in the assessment of product and monitoring of performance requires information in poultry [113].

Table 3
Summary of different antiparasitic plants with their bioactive compounds and uses.

Plant	Scientific name	Secondary bioactive metabolites	Uses	References
Nematodes				
Garlic bulb	*Allium sativum* L.	thiosulfinates, such as allicin	*Haemonchus contortus* in goats sheep	[85] [86]
Walnut Leaves& peels	*Juglans regia* L.	naphthoquinone	nematodes	[87]
Chicory forage	*Cichorium intybus* L.	terpenoids or phenolic compounds coumarins	lungworm in deers *Ostertagia ostertagi* in cattle GIT nematode in lambs	[88] [89] [90]
Wormseed	*Chenopodium ambrosioides* L.	ascaridole	*Haemonchus contortus* in goats	[91]
Coccidiosis				
Garlic bulb	*Allium sativum* L.	allicin	*Eimeria ninakohlyakimovae* in goats hepatic coccidiosis in rabbits	[85] [92]
Pine bark	*Pinus radiata* D.Don	Tannins	*E. tenella*, *E. maxima*, and *E. acervulina*	[93]
Green tea	*Camellia sinensis* (L.) Kuntze	polyphenolic compounds	inactivate the enzymes for coccidian sporulation	[94]
Barberry root bark	*Berberis lycium* Royle	isoquinoline alkaloid berberine	inhibition of the sporozoites of *E. tenella* in chickens via induction of oxidative stress.	[95]
Guar bean	*Cyamopsis tetragonoloba* L. Taub	Saponins which could lyse oocysts	suppression of coccidiosis in chickens	[96]
Olive tree	*Olea europaea* L.	Maslinic acid	increases the anticoccidial index	[97]
Grape seed	*Vitis vinifera* L.	Proanthocyanidin	diminishes coccidiosis via downregulation of oxidative stress.	[98]
Turmeric rhizome	*Curcuma longa* L.	Curcumin (diferuloylmethane)	destroyed sporozoites of *E. tenella* and diminished gut damage in poultry	[99] [100]
Coneflowers	*Echinacea purpurea* (L.) Moench	Flavonoid echinolone chicoric acid,	elicit humoral immune response against coccidial infection in chickens	[101]
Emblic fruits	*Phyllanthus emblica* L.	Tannins		[102]
Aloe leaves	*Aloe vera* (L.) Burm.f.	acemann sugars anthraquinones,	*Aloe vera*-supplemented group showed significantly fewer intestinal lesions	[103]

Table 4
Summary of growth promoters in chickens with their bioactive compounds and uses.

Plant	Scientific name	Secondary bioactive metabolites	Actions	References
Aloe leaves	*Aloe vera* (L.) Burm.f.	Acemann	growth promoter, immune-modulator	[107,114]
Turmeric rhizome	*Curcuma longa* L.	Curcumin	Increases the feed utilization	[115]
Thyme leaves & flowers Star anise seeds	*Thymus vulgaris* L. *Illicium verum* Hook. f.	Essential oils	Improves the absorption and digestion in the small intestine	[116] [117]
Moringa leaves	*Moringa oleifera* Lam.	Proteins 9% Polyphenols	Protein supplement and economically uses in broiler production	[118]
Black cumin seeds	*Nigella sativa* L.	Thymoquinone	Immunostimulant, hepatoprotective,	[119]
Onion bulb	*Allium cepa* L.	Organic sulphur compounds, flavonoids and phenolic acids	Improves the role of microflora in digestion	[120,121]
Cinnamon bark	*Cinnamomum cassia* (Nees & T.Nees) J.Presl	Cinnamaldehyde, eugenol and carvacrol	Potent growth promoter in broilers diet	[122,123]
Grape seed	*Vitis vinifera* L.	Catechins tetrameric proanthocyanidins	Hypolipidemic, antioxidant and antibacterial	[124]
Olive leaf Pomegranate peel Ginger rhizome	*Olea europaea* L. *Punica granatum* L. *Zingiber officinale* Roscoe	Oleuropein Proanthocyanidin Ginerol and shagaol	Modifies lipid metabolic patterns and microflora counts Improves the feed conversion ratio and meat quality	[125] [126] [127,128]
Rosemary leaves	*Rosmarinus officinalis* L.	Oil	High antioxidant capacity	[129]

The herbal growth promoters that are widely used in chickens with their bioactive compounds are shown in Table 4.

5. Toxicological aspects of plant uses

Since safety continues to be the main concern with the use of herbs, an appropriate inspection becomes essential to validate the safety of herbal medicines and to protect public health from hazardous use [130]. Although some herbs have promising potential activity, many of them are not assessed and monitored to evaluate their use. This makes knowledge of their probable adverse effects scarce. This necessitates the responsibility of official organizations to register novel marketed herbal products and product license should be obtained [131]. The intercalating concern among pharmacology and toxicology is significant as therapeutic efficacy occurs at a lower dose, where overdosing can provoke toxicity. However, toxic plants may contain active compounds with useful biological activities. It is essential to be aware of the toxic potential plants of veterinary significance to avoid toxicity crisis and mortality in livestock [132].

Plant toxicity for the human is significantly linked to the use of toxic doses in medicine, with many cases, including fatal cases, presumed to occur without diagnosis or documentation [133]. Contamination of human foodstuffs with toxic plants and accidental exposure to plant toxins are reported in many countries. In addition, animals may be grazed on harmful wild herbs especially in desert areas.

Finally, interactions between natural products and drugs are an essential issue especially with drugs with a narrow safety margin [134]. The herbal-drug interactions are mainly due to modulating of detoxifying enzymes as cytochrome P450 families and/or drug transport mechanisms [135].

6. Conclusions

Veterinarians often have little instructions on the mechanisms of actions of herbal medicines in the animal tissues and organs. Many of them are also inadequately informed about the new products and how they are being used so sufficient training is now necessary. Further strategies should be developed to determine the scientific and practical basis for the selection the most effective separated bioactive compounds from ethnoveterinary medicine literature. In many occurrences, herbal remedies have been identified for the treatment of a definite animal, but clinical trials mostly should be required for their use in other species.

This review indicates that the herbal natural feed additives may be used as alternatives to an antibiotic growth promoter for broiler chickens, as they increased broiler performance under environmentally friendly conditions. Further researches are encouraged to determine the therapeutic doses, mechanisms of action, possible interactions with other chemicals of herbal alternatives and above all on consumer's preferences and prospects.

Competing interests

The author declares no competing interests.

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