

Lyndy J. McGaw
Muna Ali Abdalla *Editors*

Ethnoveterinary Medicine

Present and Future Concepts

 Springer

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*This book is dedicated to the memory of
Dr. Luke F. Arnot (1970–2018).
An inspirational veterinary clinician,
scientist, and educator, his energy and
uncompromising dedication to the field of
veterinary science will live on in those
countless people and animals whose lives
he influenced.*

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Lyndy J. McGaw is Associate Professor and Leader of the Phytomedicine Programme based at the Faculty of Veterinary Science, University of Pretoria. Her research focuses on investigation and development of effective and safe anthelmintic, acaricidal, anti-inflammatory, and antimicrobial remedies for use in animal and human medicine, as well as alternatives to antimicrobial feed additives.

She has published over 100 scientific papers and has contributed 14 book chapters. She serves on the editorial boards of *Frontiers in Ethnopharmacology*, *South African Journal of Botany*, *BMC Complementary and Alternative Medicine*, and *Journal of Ethnopharmacology*. She was listed as one of the top 31 cited African researchers in Pharmacology and Toxicology by Thomson Reuters in 2013 and was recently awarded “Researcher of the Year” at the Faculty of Veterinary Sciences, University of Pretoria.



Muna Ali Abdalla pursued her PhD studies in Natural Products Chemistry in the group of Prof. Hartmut Laatsch at Georg-August University of Göttingen, Germany. From February 2013 to January 2016, she worked as Alexander von Humboldt (AvH) Postdoctoral Fellow at the Institute of Chemistry, TU Berlin. From 2016, she was awarded a 3-year contract as a Senior Postdoctoral Fellow at the University of Pretoria, South Africa. She was appointed as a Phytochemist involved in collaborative projects as well as supervision of PhD students. She has published more than 30 papers in international peer-reviewed journals and discovered dozens of bioactive compounds such as abyssomicins, quinones, alkaloids, tetracyclopeptides, and phenolic compounds from microorganisms as well as several plant-derived metabolites.

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Chapter 1

Introduction



Muna Ali Abdalla and Lyndy J. McGaw

Keywords Global ethnoveterinary medicine · Documentation · Inventories · Pharmacological properties · Animal disease · Sociological aspects

1.1 Introduction

It is well documented that plant-derived secondary metabolites have been attracting the interest of researchers globally as alternative or complementary medications to synthetic agents. Research in the field of ethnoveterinary medicine is relatively neglected in comparison with research on traditional remedies for human ailments, but increasing attention is being focused on this aspect. In light of this, Chap. 2 discusses different natural products with pharmacological properties against animal diseases in addition to the effect of dietary plant natural products on animal performance. Chapter 2 indicates the promising pharmacological properties of plant-derived natural products against animal inflammatory diseases, bacterial and fungal infections as well as parasitic and viral diseases. Importantly, the authors in Chap. 3 report on 275 plant species used in different countries of the world to manage infectious ailments in animals. These medicinal plants have been used in parts of Africa such as South Africa and Uganda, as well as in other countries such as India, Pakistan, Nepal, Afghanistan, Pakistan, Brazil and Iran.

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Chapter 4 describes medicinal plants used for horses in British Columbia, Canada and Trinidad and Tobago. Different plants used to treat many horse diseases such as muscle soreness and tendon problems, injuries, coughs, colds and nosebleeds in addition to plants used as tonics are listed. Regarding the situation in Canada, products from two websites (Riva's Remedies and Greenhawk) have been used for horses in addition to ancient remedies, such as honey and cobwebs for wounds.

Chapter 5 discusses the potential of ethnoveterinary medicines for controlling parasites in goats. The authors report on plants used for both gastrointestinal parasitism and external parasitism. Conventional methods of controlling parasites and plant-derived ethnoveterinary medicaments for controlling parasites are mentioned. Additionally, indigenous plants known to have anthelmintic and acaricidal activities in South Africa are listed. In Chap. 6 ethnoveterinary practices for control of ticks in Africa are discussed extensively. The authors document information on the anti-tick ethnoveterinary practices in different parts of Africa, such as southern, East, West, Central and North Africa. Ethnoveterinary plants used against ticks in these regions are listed.

From general areas of interest in ethnoveterinary medicine, the focus of the book shifts to significant sociological issues in the second section. The authors of Chap. 7 introduce gender aspects and multiple contexts in ethnoveterinary practice and science. The cultural and ethical context of ethnoveterinary scientists and practices are considered. One of the authors (TvA) co-founded the Institute for Ethnobotany and Zoopharmacognosy (IEZ) in the Netherlands in 1995 as a private knowledge centre at a stage when there was no interest in phytotherapy research topics at universities in the Netherlands. The chapter as a whole illustrates how researchers at the IEZ work with animals and on environmental issues and how their work can contribute to Feminist Animal Studies (FAS) and Feminist Environmental Studies. It is significant in that it opens the door for new interdisciplinary collaborations, which are vital if we are to understand more about the traditions, cultures and other aspects of ethnoveterinary medicine.

The author of Chap. 8 writes from extensive experience in conducting field work in Africa and discusses difficulties in implementing practical applications of ethnoveterinary medicine in the continent. A holistic approach to medical matters and practical inputs deriving from functional interactions between traditional and Western medicine are recommended.

The third section of the book moves on to investigate in more detail ethnoveterinary medicine in various regions of the world. In Chap. 9 the authors review the use of traditional remedies for the treatment of livestock diseases in Cameroon, citing 138 plant species belonging to 110 genera and 69 families. Chapter 10 provides a summary of plants used in South African ethnoveterinary medicine. Further focus is placed on the ethnoveterinary plants as well as practices used more specifically in the control of ticks and tick-borne diseases in South Africa in Chap. 11. Traditional tick control methods in addition to the use of medicinal plants in South Africa are mentioned in this chapter. A Zimbabwean perspective of ethnoveterinary medicine is provided in Chap. 12, where interesting applications of complementary medicine and ethnoveterinary interventions in poultry care are reported. The authors also

discuss ethnoveterinary practices in cattle and goats, as well as pharmacological activity of ethnomedicinal plants. Moving further north in Africa, Chap. 13 comprises a review of ethnoveterinary medicine in the Maghreb, a fascinating area of the world. Various types of practices including preventive and curative methods are documented, as are numerous plant species commonly used in Maghreb ethnoveterinary medicine.

Crossing to other parts of the world, natural remedies for animal health in Latin America are documented in Chap. 14. The authors report 364 plant species and 61 animal species used to treat diseases of livestock and herds in Latin America. Local practices of cattle raising and ethnoveterinary medicine in Estonia are reviewed in Chap. 15. This is the first report to provide a more thorough overview of the islands Saaremaa and Muhumaa in Estonia. The authors discuss the historic ethnoveterinary medicine, different herbs, mushrooms and mosses used against cattle illnesses in addition to non-herbal treatments in the area. Chapter 16 provides an enlightening discourse on the practices and methods used by Belarusian peasants to manage livestock diseases and preserve their health along with folk concepts and beliefs. In this chapter, charm-healing and Belarusian ethnoveterinary charms are documented, and plant and non-plant remedies used to treat livestock are mentioned. The use of plants for animal health care in the Spanish inventory of traditional knowledge is discussed in Chap. 17. The authors report on different remedies traditionally used in the treatment and prevention of many diseases of domestic animals, in addition to the importance of several plants used as fodder for livestock.

1.2 Conclusion

In providing chapters of general interest as well as those focusing on ethnoveterinary medicine in certain parts of the world in this book, it is hoped that the study of ethnoveterinary medicine will increase in prominence, involving multidisciplinary teams of researchers. It is clear that there is much work still to be done in this field and many lessons to be learned from all parts of the world.

Part I
The Role of Natural Products
and Remedies in Treating Animal Diseases

Chapter 2

The Pharmacological and Nutritional Significance of Plant-Derived Natural Products: An Alternative for Animal Health



Muna Ali Abdalla and Lyndy J. McGaw

Keywords Antibiotic resistance · Animal performance · Fodder plants · Pasture · Beneficial nutrients · Nutritional supplementation

2.1 Introduction

The use of synthetic chemicals is harmful to our agricultural production systems, ecosystems and animal health. In that context there is a need for environmentally friendly practices in animal husbandry. To a great extent, grassland secondary metabolites may offer a significant approach to support livestock health (Poutaraud et al. 2017). This can be supported by evidence that grasslands and rangelands represent approximately two-thirds of global agricultural land (Leiber et al. 2014). It was reported that more than 40% of the total agricultural lands in Europe, including those in the Russian Federation, are meadows and pastures, which can be permanent or temporary grassland (FAOSTAT 2013). These agricultural lands represent around 50% of all livestock feedstuffs globally and are considered as the most important source of feed for domestic herbivores (Herrero et al. 2013). Plant natural products from permanent grasslands can contribute to limited pharmaceutical capacity and develop animal health. Due to their environmental and economic

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significance in low-cost animal feed, air and water quality, soil fertility, carbon sequestration, and flora and fauna conservation, the European Union promotes grassland maintenance (Michaud et al. 2015). Antibiotic resistance is now recognised as a major international issue across the world, and in that context the European Union has prohibited the use of antibiotics as growth promoters in farm animals since 2006 (Zeng et al. 2015). Consequently, this will increase the interest in naturally occurring plant secondary metabolites in animal diets (Acamovic and Brooker 2005).

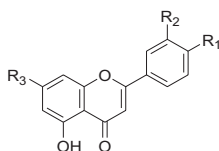
2.2 The Effect of Dietary Plant Natural Products on Animal Performance

Due to their high acceptability among consumers as natural feed additives, herbal feed additives are gaining interest as an alternative dietary strategy in animal nutrition. Plant natural products comprise groups of bioactive molecules such as flavonoids, tannins, glucosides, alkaloids, saponins, terpenoids, essential oils, amines, nonprotein amino acids and organosulfur compounds (Irchhaiya et al. 2015). A number of flavonoids have been isolated from different parts of alfalfa (Liang et al. 2011; Rafińska et al. 2017). The most important flavonoids of alfalfa (*Medicago sativa* L.) are listed in Fig. 2.1. Previous research reported that alfalfa flavonoid supplementation develops muscle oxidation stability through a lowering of thiobarbituric acid reactive substance (TBARS) values in a dose-related manner, when it was tested on growing rabbits to check their productive performances, carcass properties, meat quality and lipid oxidation. The study suggested that alfalfa supplementation is a good herbal additive to feed rabbits and has positive effects on qualitative properties of rabbit meat (Dabbou et al. 2018).

It has been reported that the promising antimicrobial activity of plant secondary metabolites is helpful in modifying the rumen microbial ecosystem to change fermentation and consequently inhibiting methane production. Essential oils, saponins and tannins are the three major plant natural products which showed greatest effectiveness in reducing methane production (Samal et al. 2016). It is important to note that the potential anthelmintic properties of particular grazing forages have gained much interest (Githiori et al. 2006).

It has also been reported that forages like *Lotus* spp., *Hedysarum* spp. (Aissa et al. 2016), *Onobrychis* spp. (Desrues et al. 2016) and *Cichorium intybus* (Peña-Espinoza et al. 2017) are rich in condensed tannins and other plant secondary metabolites. They have gained attention recently as potential candidates to control parasites in ruminant production systems if their consumption could be linked with good performance and anthelmintic impact.

In a previous study of the sheep nematode *Trichostrongylus colubriformis*, it was found that condensed tannins, extracted from *Lotus pedunculatus*, *Lotus corniculatus*, sainfoin (*Onobrychis viciifolia*) and *Hedysarum coronarium*, decreased



Flavonoid name	R ₁	R ₂	R ₃
Apigenin 7- <i>O</i> -[β -D-glucuronopyranosyl(1 \rightarrow 2)- <i>O</i> - β -D-glucuronopyranosyl]-4'- <i>O</i> - β -D-glucuronopyranoside	-OGluA	-H	-OGluA(2 \rightarrow 1) GluA
Apigenin 4'- <i>O</i> - β -D-glucuronopyranoside	-OGluA	-H	-OH
Apigenin 7- <i>O</i> -[β -D-glucuronopyranosyl(1 \rightarrow 2)- <i>O</i> - β -D-glucuronopyranoside]	-OH	-H	-OGluA(2 \rightarrow 1) GluA
Luteolin 7- <i>O</i> - β -D-glucuronopyranoside	-OH	-	-OgluA OH
Apigenin 7- <i>O</i> -[2- <i>O</i> -feruloyl- β -D-glucuronopyranosyl(1 \rightarrow 2)- <i>O</i> - β -D-glucuronopyranosyl]-4'- <i>O</i> - β -D-glucuronopyranoside	-OGluA	-H	-OGluA(2 \rightarrow 1) GluA-2- <i>O</i> -Feruloyl
Apigenin 7- <i>O</i> -{2- <i>O</i> -feruloyl-[β -D-glucuronopyranosyl(1 \rightarrow 3)]- <i>O</i> - β -D-glucuronopyranosyl(1 \rightarrow 2)- <i>O</i> - β -D-glucuronopyranoside}	-OH	-H	-OGluA(2 \rightarrow 1) GluA-[GluA(1 \rightarrow 3)]- 2- <i>O</i> -Feruloyl
Apigenin 7- <i>O</i> -{2- <i>O</i> - <i>p</i> -coumaroyl-[β -D-glucuronopyranosyl(1 \rightarrow 3)]- <i>O</i> - β -D-glucuronopyranosyl(1 \rightarrow 2)- <i>O</i> - β -D-glucuronopyranoside}	-OH	-H	-OGluA(2 \rightarrow 1) GluA-[GluA(1 \rightarrow 3)]-2- <i>O</i> - <i>p</i> -Coumaroyl
Apigenin 7- <i>O</i> - β -D-glucuronopyranoside	-OH	-H	-OgluA
Luteolin 7- <i>O</i> -[2-feruloyl- β -D-glucuronopyranosyl(1 \rightarrow 2)- <i>O</i> - β -D-glucuronopyranosyl]-4'- <i>b</i> - <i>O</i> - β -D-glucuronopyranoside	-OGluA	-	-OGluA(2 \rightarrow 1) GluA-2- <i>O</i> -Feruloyl OH

Fig. 2.1 Most important flavonoids of alfalfa (Stochmal et al. 2001)

the development of L1 larvae to L3 larvae and reduced the motility of L3 larvae when assessed by the inhibition assay of larval migration, and this might inhibit their infective capacity in vivo (Molan et al. 1999). Sheep feeding on *Hedysarum coronarium* (sulla) were found to have high performance and productivity, while carrying a substantial burden of *T. circumcincta* and *T. colubriformis* (Niezen et al. 1995), and they also had low levels of parasitism compared with sheep carrying a similar worm burden and fed on a low condensed tannin forage (*Medicago sativa*) (Robertson et al. 1995). Moreover, red deer feeding on *Cichorium intybus* showed lower lung and gastrointestinal worm burdens and high productivity, in comparison to deer grazing *Lolium perenne* (Hoskin et al. 1999). Additionally, *Cichorium intybus* showed anthelmintic effects against gastrointestinal nematode parasites in experimentally infected cattle (Peña-Espinoza et al. 2016).

2.3 Reported Plant Natural Products with Pharmacological Significance Against Animal Diseases

Plant secondary metabolites, which include a wide number of phytochemicals, are known as ingredients of the diets of humans and animals. They may have adverse effects on animals when ingested, which can be attributed to the chemistry of the molecules, the amount consumed, their concentration in the diet and the health status of the animals (Acamovic and Brooker 2005).

A number of medicinal plants and their component natural compounds have exhibited several pharmacological properties against animal diseases such as infections and inflammatory conditions. This has generated great interest and increased research regarding the use of phytochemicals and their effects in the diets of farm animals.

2.3.1 Animal Infectious Diseases

Infectious diseases of livestock are a potential threat to animal health and food safety, and their effective control is necessary for agronomic development, alleviating poverty in developing countries and in helping to improve food security (Tomley and Shirley 2009). Infectious diseases to which livestock are vulnerable are caused by pathogenic microorganisms, such as bacteria, fungi, viruses and parasites. They are classified into two major classes: endemic and exotic (Carslake et al. 2010). It is very important to note that the classification of a disease as exotic or endemic is actually a political decision to label a disease in a particular category. For example, foot-and-mouth disease (FMD) is exotic in the UK but was once endemic, and continues to be in many parts of the world (Carslake et al. 2010). Some notorious livestock diseases are endemic in many parts of the world, and pathogenic threats continue to emerge, re-emerge and persist. A number of factors such as global climate change, agronomical

practices and demography present conditions that are likely to be favourable for the expansion of arthropod-borne diseases into new geographical regions. The prevalence of zoonotic infections, which are transmissible directly or indirectly (e.g. via arthropod vectors) between animals and humans, is a huge threat to human health. A topical example of the challenge represented by zoonotic viruses is the current pandemic status of new influenza A (H1N1) (Tomley and Shirley 2009; Mehrbod et al. 2018). It is important to mention that transmission of infectious diseases has a great effect on the poultry industry and causes potentially devastating threats to both humans and wild birds (Wang et al. 2013).

2.3.1.1 Parasitic Diseases

A number of scientific research studies on the antiparasitic activity of plant natural products have focused on the medicinal significance of plant natural products. The findings have led to the identification of active compounds, such as santonin (an anthelmintic drug from *Artemisia cina*) (Athanasidou and Kyriazakis 2004). A study reported that helminths can be controlled by the use of plant natural products, particularly tannins (Williams et al. 2014a, b) such as tannin-containing legume forages such as sainfoin, *Sericea lespedeza* and some *Lotus* species (Hoste et al. 2012). Tannins might be responsible for the reduction of the worm fecundity, the ability of the host to reduce establishment of the larval population and the inhibition of the adult worm burden within the host. Some plant natural products have been found to be highly effective in controlling helminths when used as plant extracts (Athanasidou et al. 2007).

A number of natural compounds with great structural diversity exhibited remarkable activity against a wide range of target parasites such as atanine (from *Evodia rutaecarpa*, Rutaceae) (Perrett and Whitfield 1995), eugenol (a component of essential oils of clove oil, nutmeg, cinnamon, basil and bay leaf) (Asha et al. 2001), palasonin (from *Butea monosperma*, Fabaceae) (Raj and Kurup 1968), alantalone (from the roots of *Inula helenium* L. subsp. *turcoracemos*) (Azouly et al. 1986; Gökbulut and Sarer 2013), tetra-hydroharmine (from *Banisteriopsis caapi*, Malpighiaceae), ascaridole (responsible for the flavour of the Chilean tree boldo and the main component of the oil of Mexican tea (wormseed)) (Efferth et al. 2002), azadirachtin, allicin (the main active component of garlic) (Velkers et al. 2011), kaurenoic acid (from *Annona senegalensis*, Annonaceae) (Mamidou Koné et al. 2005), etc.

These molecules can act as alternative drugs for the successful control of helminth parasites (Tariq 2018). Interestingly naturally occurring mixtures of the cysteine proteinases bromelain, papain and stem bromelain, which are found in *Papaya* latex, and the pure fruit preparations exhibited anthelmintic effects against two rodent cestodes, *Hymenolepis diminuta* and *Hymenolepis microstoma* in vitro (Mansur et al. 2014).

Tick invasion, which consequently leads to tick-borne diseases, causes huge problems for animal health. Almost 850 tick species and 30 major tick-borne diseases are known (Habeck 2002). *Hyalomma lusitanicum* is one of the most

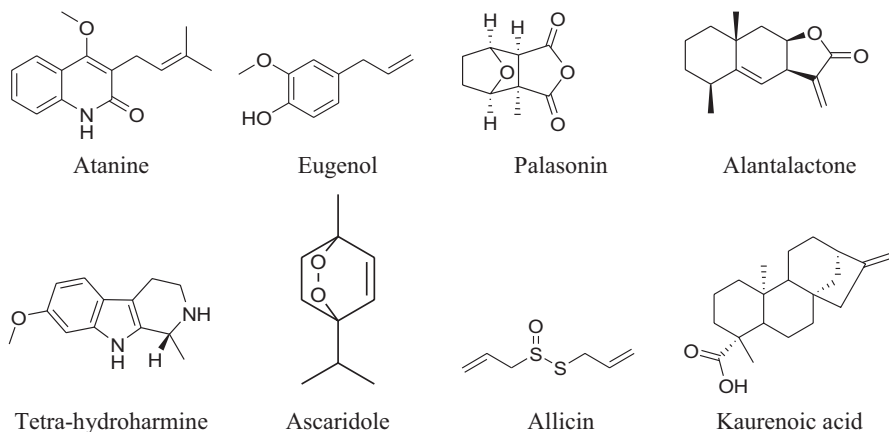


Fig. 2.2 Plant natural products with anthelmintic activity

common species. Ticks can cause skin irritation and bacterial skin infections and affect the lymphatic system, which can consequently cause anaemia, fever, weight loss, lymph node swelling, milk drop, abortions and death (Habeck 2002). The ticks are mainly controlled using synthetic chemicals, which are administered to animals or their environment. However, these chemicals have consequently increased the development of resistance in these parasites and exhibited negative effects to the environment (Adenubi et al. 2018c).

In a recent study, plant species including those belonging to the Lamiaceae, Fabaceae, Asteraceae, Piperaceae, Verbenaceae and Poaceae families were evaluated for their acaricidal activity against *Rhipicephalus (Boophilus)*, *Amblyomma*, *Dermacentor*, *Hyalomma* and *Argas* tick genera. Secondary metabolites, including thymol, carvacrol, 1,8-cineol and n-hexanal (as listed in Fig. 2.2), were found to be responsible for the acaricidal activity of the various essential oils against different species of ticks (Rosado-Aguilar et al. 2017).

In a previous review, we evaluated 66 plant species, which were reported to control ticks based on their use by rural livestock farmers. These plants may be used as a potential source of acaricidal remedies as an extract or as a source of novel acaricidal candidates (Adenubi et al. 2016). In our recent review, extracts of some species such as *Azadirachta indica*, *Gynandropsis gynandra*, *Lavandula angustifolia*, *Pelargonium roseum* and *Cymbopogon* species showed promising acaricidal and larvicidal effects with 90–100% efficacy. Plant families with the highest acaricidal effect frequency were the Lamiaceae (25%), Asteraceae and Poaceae (10% each), Piperaceae (7.5%) and Verbenaceae, Solanaceae and Amaryllidaceae (5% each). The study discussed 26 isolated active molecules including azadirachtin, carvacrol, linalool, geraniol and citronellal (Adenubi et al. 2018a). Apigenin-7-O- β -D-glycoside and isorhoifolin were isolated from the chloroform fraction of *Calpurnia aurea* ethanol leaf extract, which exhibited good acaricidal activity. Isorhoifolin was not cytotoxic and showed potent activity ($LC_{50} = 0.65$ mg/ml) (Adenubi et al. 2018b) (Fig. 2.3).

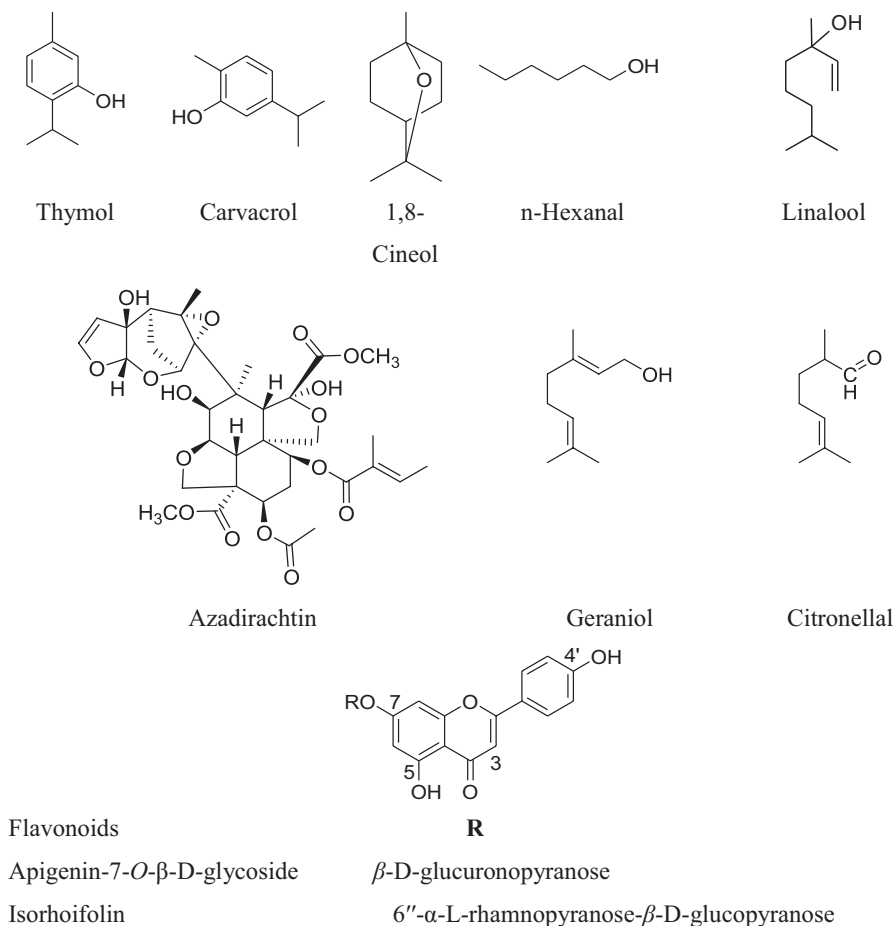


Fig. 2.3 Plant natural products with acaricidal activity against different species of ticks

2.3.1.2 Bacterial and Fungal Infections

Important animal bacterial infectious diseases are anthrax, black quarter, diarrhoea, botulism (produced by the bacterium *Clostridium botulinum*), brucellosis, tuberculosis and pleuropneumonia (Chinsemu et al. 2014).

Anthrax is an infectious disease caused by a bacterium called *Bacillus anthracis* (Mwakapeje et al. 2018). It can affect several species of birds and is particularly important in herbivores, including sheep, cattle and goats (Himsworth 2008). It was reported previously that millions of livestock died from anthrax in Russia, Iran and South Africa (Beyer and Turnbull 2009). Humans can acquire anthrax directly from anthrax-infected animals or from anthrax-contaminated animal products (World Health Organization 2008; Fasanella et al. 2014). Antibiotics exhibiting weak efficacy in combating human and animal diseases through antibiotic resis-

tance should be replaced with new drugs that can fight the burden of these microbial pathogens (National Strategy for Combating Antibiotic-Resistant Bacteria 2014; Abdalla and McGaw 2018a). Medicinal plants are known to be a highly promising source of a great number of drugs (Santos et al. 1995; Dwivedi and Wagay 2014). The discovery of antibacterial drugs from natural sources has revolutionised the treatment of many diseases in man and animals (Abdalla and Matasyoh 2014; Abdalla and McGaw 2018b). In a recent study, the extracts of nine medicinal plants showed remarkable antibacterial activity against *B. anthracis*. Interestingly the minimum inhibitory concentration values ranged from 0.02 to 0.31 mg/ml towards *B. anthracis* Sterne strain. The best MIC values were obtained with *Maesa lanceolata* (0.02 mg/ml), *Bolusanthus speciosus*, *Hypericum roeperianum*, *Morus mesozygia* (0.04 mg/ml) and *Pittosporum viridiflorum* (0.08 mg/ml). Additionally, the total antibacterial effect of the plant extracts was determined to be 92–5562 ml/g. Total activity is the extract from 1 g of the plant material that can be diluted and still inhibit activity against the microorganism. The medicinal plants *Maesa lanceolata* and *Hypericum roeperianum* delivered excellent total activity with values of 5562 and 2999 ml/g, respectively (Elisha et al. 2016).

Pathogenic fungi or mycoses have not been widely known to pose particularly high risks to global animal health. This understanding is changing due to the occurrence of various rapid declines in wildlife caused by the development of previously unknown fungi (Daszak et al. 2000; Smith et al. 2006; Fisher et al. 2012). Mycotic diseases are responsible for economic losses in the poultry industry because of direct infection or due to the production of mycotoxins (Dhama et al. 2013). Aspergillosis (mainly caused by *Aspergillus fumigatus*) is recognised as brooder's pneumonia and is known as the most pathogenic fungus affecting poultry (Arne et al. 2011). Alleviating diseases of infected animals requires long term drug administration which is a disadvantage in addition to its high cost. Plant derived antifungal molecules, particularly their application in topical therapy, might be considered as one of the attractive alternatives (Trakranrungsie 2011). Comprehensive lists of plants, extracts and isolated plant metabolites with antifungal activity have been published (Rai and Mares 2003; Rawat et al. 2008). Previous studies demonstrated that the amides and cinnamoyl derivatives, obtained from species of the family Piperaceae, could be responsible for their antimicrobial activities (Kun-anake 1998; Vasques da Silva et al. 2002).

The major constituents of *Piper betle* leaves were found to be terpenes and phenols (Bajpai et al. 2010). They showed promising antidermatophytic effects, and a 10% *P. betle* cream was formulated (Curtis 1998). Its antidermatophytic activity was effective up to 96 h after incubation compared to that of ketoconazole cream (Trakranrungsie et al. 2004). Additionally, the ointment and gel formulations containing 4% of *P. betle* extracts exhibited high antifungal activity similar to clotrimazole cream (1%), but more than tolnaftate cream (1%). The mentioned preparations decreased rash and irritation before or after UV irradiation in rabbit and guinea pig toxicity tests (Boonrattanakornki et al. 1990). On the other hand, the *P. betle* preparation was less stable and lost its activity rapidly.

2.3.1.3 Viral Diseases

Zoonotic infections feature strongly among the wide range of human diseases encountered, including anthrax, tuberculosis, plague, yellow fever and influenza, which may be transmitted from domestic animals, poultry and livestock. Additionally, climate change conditions and human behaviour and habitat will likely result in increased infections from wildlife species (Wang and Cramer 2014). Medicinal plants have been known as potential sources of antiviral agents for decades. Although it has been reported that few studies search for antiviral agents from medicinal plants, these studies have detected the presence of promising antiviral activity in plants. Almost 20–30% of plants from tropical or temperate areas were shown to have antiviral activity. It has been found that a number of molecules of different classes isolated from medicinal plants have antiviral activity (Perez 2003). The crude alcoholic extract of the seed of *Nyctanthes arbortristis* (Verbenaceae) showed antiviral activity, and the isolated iridoid glucosides, known as arbotristosides A, B and C (Fig. 2.4), were also significantly active against encephalomyocarditis virus (EMCV) and Semliki Forest virus (SFV) with an increase in average survival time of the infected animals (Rathore et al. 1990).

Foot-and-mouth disease which is caused by Aphthovirus of family Picornaviridae, and sometimes known as a fatal viral disease, affects cloven-footed animals, such as sheep, cattle, pigs, goats, llamas and deer, in addition to wild bovinds. A number of traditionally used medicinal plants in India were applied for the treatment of animal foot-and-mouth disease such as *Andrographis paniculata* (Burm.f.) Nees (kirayat) (family Acanthaceae), *Colocasia esculenta* (L.) Schott (Arvi) (family Araceae) (Panda and Dhal 2014; Mishra et al. 2015), *Cuscuta reflexa* Roxb. (Amar Bel) (family Cuscutaceae) (Malla and Chhetri 2012), *Carissa caranta* L. (Garanda) (family Apocynaceae) (Khan et al. 2012) and *Calotropis gigantea* (L.) R.Br. (Safed aak) (family Asclepiadaceae) (Rao et al. 2014).

2.3.1.4 Inflammatory Diseases

Inflammatory bowel disease (IBD) is a chronic and disrupted inflammation of the intestinal tract that is a common cause of chronic gastrointestinal upset in dogs and cats (Callahan 2018). IBD has two principal types named as ulcerative colitis (UC)

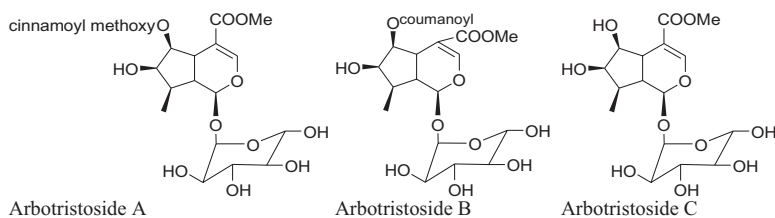


Fig. 2.4 The antiviral arbotristosides A, B and C

and Crohn's disease (CD) (Hendrickson et al. 2002). It is also associated with chronic inflammation of the intestinal tract (IT) (Shah et al. 2007). Clinical signs such as changes in appetite, vomiting, diarrhoea and weight loss are the most common inflammatory conditions caused by IBD (Goyal et al. 2014). Several plant secondary metabolites exhibited potent antioxidant activities as modulators in the expression and activity of antioxidant enzymes and as free radical scavengers. A number of plant natural molecules were proven to suppress the release of pro-inflammatory cytokines, inhibiting the activation of nuclear factor κ B (NF- κ B), which is necessary for the inflammatory response in inflammatory bowel disease (Alves de Almeida et al. 2017).

Plant secondary metabolites are a potential source of immune modulators, antioxidants and anti-inflammatory agents (Gautam and Jachak 2009; Iqbal et al. 2013; Debnath et al. 2013; Motlhatlego et al. 2018). In a previous report, 32 alkaloids were found to induce the disruption of the epithelial barrier (dextran sulphate sodium (DSS), acetic acid or mustard oil) in intestinal inflammation (TNBS) in experimental models, mainly in mice. Among these alkaloids, the effects of piperine, berberine and sinomenine on experimental colitis were discussed (Alves de Almeida et al. 2017). The alkaloid piperine (from *Piper nigrum* and *Piper longum*, Piperaceae) was known for its anti-inflammatory effects (Diwan et al. 2011). It was proven to enhance the absorption and pharmacological activity of the herbal supplement curcumin (*Curcuma longa*, Zingiberaceae). A nanoformulation encapsulating piperine and curcumin, called self-microemulsifying drug delivery system (CUR-PIP-SMEDDS), was developed. The system CUR-PIP-SMEDDS enhanced the drug stability and in vitro dissolution of curcumin at the colon site. This showed its therapeutic impact in DSS-induced colitis in mice. The system CUR-PIP-SMEDDS inhibits disease activity index (DAI), histopathological lesions, myeloperoxidase (MPO) activity, MDA content, tumour necrosis factor (TNF- α) and interleukin 6 (IL-6) levels in colonic tissues of mice (Li et al. 2015). Piperine treatment was found to ameliorate body weight loss, histological injury, diarrhoea and the expression of inflammatory mediators on DSS-induced colitis in mice. When the pregnane X receptor (PXR) was downregulated, the DSS injury was exacerbated and piperine protection against DSS colitis was inhibited (Hu et al. 2015).

A natural supplement berberine (from *Berberis*, *Hydrastis*, *Coptis* and *Phellodendron* species) (Tillhon et al. 2012) possesses potent pharmacological activity in intestinal inflammatory models (Mokhber-Dezfuli et al. 2014). Berberine was found to inhibit colonic inflammation in UC and CD experimental models and decreased release of cytokines (TNF- α , IL-1 β , IL-6, IL-12 and IL17). It was also shown to alleviate DSS-induced colitis by ameliorating intestinal barrier function and decreasing inflammation and oxidative stress (Zhang et al. 2017). It was also investigated in various clinical trials and found to reduce symptoms of many diseases such as non-alcoholic fatty liver disease (Chen et al. 2015), acute coronary syndrome inflammation (Newman and Cragg 2012) and irritable bowel syndrome (Baker et al. 2007) without any side effects.

Sinomenine activity was reported in experimental colitis (Cheng et al. 2007; Yu et al. 2013). It reduced the generation of inflammatory mediators in TNBS-induced

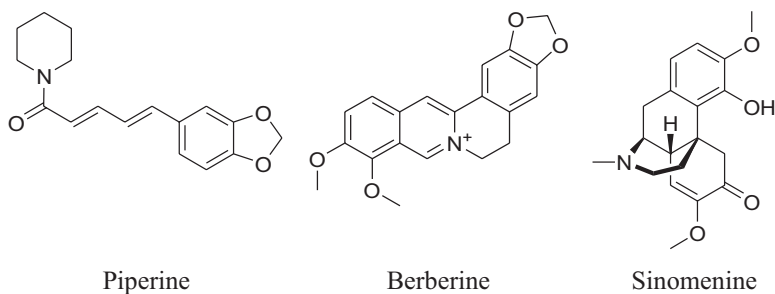


Fig. 2.5 Plant natural products with pharmacological anti-inflammatory effects

colitis in mice. It was discovered to downregulate the transcription factor c-Maf, microRNA 155 (MiR-155) and the cytokines TNF- α and IFN- γ . Sinomenine exhibited analgesic effects on neuropathic and inflammatory pain models (Gao et al. 2013) in addition to suppressive activity on colon carcinoma cell growth (Zhang et al. 2014; Liu et al. 2014) and anti-inflammatory effects (Wang and Li 2011) (Fig. 2.5).

2.4 Conclusion and Future Prospects

The growing trend of zoonotic disease emergence in the last few decades emphasises the important role that the One Health strategy plays in the aspects of investigation, control and prevention. This has established the beginning of the One Health era.

Research on plant natural product-containing fodder plants and other plant extracts is ongoing and becoming an interesting field worldwide, with a lot of potential for the control of many animal infectious diseases such as animal parasites, including ticks and helminths.

The dietary contribution of plant natural products has a huge role on animal performance and health status, so producing food with a high nutritional value and sufficient concentrations of antioxidants, vitamins and functional fatty acids is important. This can be done by expanding growth of forages rich in plant secondary metabolites. Other factors should be taken into account such as maintaining animal requirements, spatial grazing and management of pasture, as well as increasing the forage yield and quality, and providing a healthier place for livestock.

Owing to the growing trend in awareness of ethnoveterinary medicine, plant-derived natural products have been attracting the interest of scientists globally as alternatives to synthetic agents. In this regard *in vivo* studies and experiments in animal models are needed to confirm the discovered bioactivities of the extracts of medicinal plants and the isolated molecules to identify novel medicinal remedies.

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