Essential Oils in Control of Ticks

Subjects: Agriculture, Dairy & Animal Science
Contributor: Felix Valcarcel

Ticks are forced bloodsucker ectoparasites belonging to the Order Ixodida, which comprises three families: Ixodidae (hard ticks, 720 species), Argasidae (soft ticks, 186 species), and Nuttalliellidae (1 species). Tick control is a priority in order to prevent the transmission of vector-borne diseases. The essential oil's acaricidal activity is due to the variability of its chemical composition and the relationship between these compounds. Moreover, given their low toxicities and their solubility in water these compounds can contribute to the production of milk and animal meat free from dangerous chemicals which are harmful to humans, animals, and the environment.

Keywords: ticks ; natural compounds ; efficacy

1. Introduction

Ticks are forced bloodsucker ectoparasites belonging to the Order Ixodida, which comprises three families: Ixodidae (hard ticks, 720 species), Argasidae (soft ticks, 186 species), and Nuttalliellidae (1 species) [1][2]. They are also one of the main groups of disease vectors, and tick-borne diseases (TBDs) have long been recognized as one of the major constraints to livestock development in various countries [3], particularly in the cattle industry in tropical and subtropical regions [4]. Likewise, they are the most devastating as they cause huge economic losses [5]. These losses are estimated in the billions of US dollars [4], as a consequence of higher production costs due to constant antiparasitic treatments [6] and the effects generated by the infestation: blood loss, reduced weight gain and milk production, and skin damage at the site of attachment [7].

Many commercially available chemicals are used in current tick control strategies: arsenicals, chlorinated hydrocarbons, carbamates, macrocyclic lactones [8][9], organophosphates, formamidines, pyrethroids [8][9][10][11], fluazuron, and fipronil [10][11]. They have generally been sprinkled on, poured on, or injected into animals, with high costs for farmers [10][11].

Unfortunately, the misuse, overuse, and inappropriate application of chemical acaricides led to the development and selection of resistance in the tick population [4][7][12][13][14][15]. However, apart from their high costs, these acaricides could also be potentially hazardous through contamination of ruminant milk and meat [13][16][17] and thus, may have an effect on human health [18][19], as well as contamination of the environment with residues harmful to humans and animals [15][16][18][20][21]. Due to this and the growing interest in organic farming practices, several acaricides have undergone restriction of use in the global market, such as organochlorines, organophosphates, and pyrethroids [18]. Consequently, the development of new agents and/or effective alternative strategies for their control is necessary [6][22]. Therefore, many other current strategies used for control of resistant tick populations such as biological control using pathogens or predators, pheromone-assisted control, herbal pour-on or dip preparations including green manufactured nanoparticles, and vaccination, as well as design of acaricide resistance mitigation programs based on integrated pest management control [3][23][24].

Among these alternative strategies, plant-derived products can be promising acaricidal product sources, especially essential oils [6][7][15][23][24]. The essential oil's acaricidal activity is due to the variability of its chemical composition and the relationship between these compounds [25]. Moreover, given their low toxicities and their solubility in water [25] these compounds can contribute to the production of milk and animal meat free from dangerous chemicals which are harmful to humans, animals, and the environment [13].

2. Ticks and Synthetic Acaricides

Arsenic and its derivatives were intensively used at the end of the 19th and the beginning of the 20th centuries because they had a short residual effectiveness time, were cheap, stable, and water-soluble [26]. When arsenic use decreased, due to the high toxicity of its residues, its prohibition forced the appearance of the first organochlorines: dichlorodiphenyltrichloroethane (DDT), benzene hexachloride (BHC), lindane, dieldrin, or toxaphene, which were used extensively throughout the twentieth century [27]. Initially, organochlorides were highly effective against ticks showing high residual effectiveness an ease of use, but the majority accumulated residues in the environment and animal tissues [26]. In the 1960s, organophosphates and carbamate derivatives complemented or replaced organochlorides. These new acaricides offered the advantage of being biodegradable and rapidly metabolized, although they also quickly lost their effectiveness [28]. In the 1970s formamidines appeared, such as amitraz, in an attempt to avoid the fast reduction in effectiveness of the preceding products [29]. From the 1980s, the use of acaricides with low toxicity in mammals proliferated, such as pyrethrins and some biopesticides (macrocyclic lactones: avermectins and milbemycins) [30]. The pyrethrins gave rise to the pyrethroids, synthetic analogs obtained by successive isosteric modifications [31], more stable and with less residual effect. Pyrethroids are classified as first-generation (allethrin), second-generation (tetramethrin, resmethrin, bioresmethrin, biolalethrin, and fontarin), third-generation (fenvalerate and permethrin), and the current fourth-generation, which includes cypermethrin and decamethrin, among others [32]. Finally, in the late twentieth century, mite growth regulators derived from benzoyl-phenyl urea (fluazuron, for example) began to be used [28], along with other chemical acaricides, phenylpyrazoles, such as fipronil. Spinosad is a relatively recent insecticide-acaricide produced from the fermentation of metabolites of the actinomycete bacterium *Saccharopolyspora spinosa* and a mixture of two components A and D spinosyn [33]. In both laboratory and field tests, those products were found to be equally effective against ticks and could therefore be used as an alternative [34][35]. The latest addition to the market for ectoparasiticides for pets is isoxazolines [36][37][38][39].

3. Tick Control Methods

Several methods are applied to combat ticks and tick-borne diseases [40]. At first, tick control was based on using a mixture of lard and sulfur, a combination of lard and kerosene, cottonseed oil or fish oil from kerosene mixtures, cottonseed oil and sulfur, 10% kerosene emulsion, a mixture of cottonseed oil and crude petroleum oil, or Beaumont crude oil [8][41]. Thereafter, the treatment of cattle by baths based on mineral oil and “carbolics” by Australian researchers occurred, continuing as recently as 1895 [8][42]. Currently, the main method to control ticks is the use of chemical acaricides [27][41].

Many acaricides are available on the market such as arsenicals, organochlorines, organophosphates, carbamates, formamidines, pyrethroids, macrocyclic lactones, phenylpyrazoles, benzoylphenylurea, spinosad, and isoxazolines (**Table 1**) [9][10][11][14][40][41]. The use of these acaricides reduces the tick population, as well as the diseases transmitted by ticks. However, the effectiveness of an acaricide depends on the activity of a product, as well the quality and quantity of active material sprayed or injected [40]. Moreover, inappropriate and long-term application of these acaricides, frequency of treatment, underdosing, and persistent use of a chemical group for tick control enables improvement of tolerance/resistance to the chemical and leads to the evolution of resistance in many tick species [4][14][40][41][43][44][45].

Several studies recommended an integrated strategy for the control of ticks in cattle based on the house management, slow-burning of the wastes near the walls of the animal sheds, pasture alternation and/or rotation, pasture burning, clearance of vegetation, nutritional management, rotation of acaricides, using combinations of acaricides, immunization via vaccination, improving genetic resistance in cattle, improving resistance diagnostic tests, biological control, and ethnoveterinary practices against ticks [14][41][46][47][48].

Table 1. Chemical acaricidal class, mode of action, and their mechanisms of resistance.

Acaricidal Class	First Year of Use	Mode of Action	First Report of Resistance	Mechanisms of Resistance	References
Arsenic	1893		1937		[9][41][49]

Acaricidal Class	First Year of Use	Mode of Action	First Report of Resistance	Mechanisms of Resistance	References
Organochlorines	1946	GABA-gated chloride channel antagonists Bind at the picrotoxinin site in the γ-aminobutyric acid (GABA) chloride ionophore complex.	1952	Enhanced metabolism and reduced absorption of the chemical	[14][40][41]
Organophosphates	1955	Acetylcholinesterase Inhibits the action of acetylcholinesterase	1965	Target-site insensitivity	[14][40][41]
Carbamates	1955	Inhibits the action of acetylcholinesterase	1965		[14][40][41]
Formamidines (Amitraz)	1975	Octopamine receptor α-2 agonist Overstimulates the nervous system	1981	Mutations in the octopamine/tyramine receptor Target-site insensitivity in G protein-coupled receptors Amino acid substitution in the beta-2-adrenergic-like octopamine receptor	[4][8][14][40][50]
Pyrethroids	1977	GABA-gated chloride channel antagonists Prolongs opening of sodium channels in nerve, muscle, and other excitable cells.	1989	Mutations in the voltage gated sodium channel gene	[8][40][41][51]
Macrocyclic lactones	1981	Has a toxic effect on ticks by stimulating the release and binding of GABA at nerve endings, which eventually blocks the transmittance of electrical activity in nerves and muscle cells Glutamate–gated Cl-channel Blocks nerve signals by interfering with the glutamate gated chloride (GlCl)	2001	Insensitivity of the GABA or glutamate gated chloride ion channels	[8][40][41][52]

Acaricidal Class	First Year of Use	Mode of Action	First Report of Resistance	Mechanisms of Resistance	References
Phenylpyrazoles (Fipronil)	1993	Blocks the gamma-Aminobutyric acid gated chloride ion-channel (GABA-C)	2003	Mutations in the GABA-Cl gene	[41][53][54][55]
Benzoylphenyl urea (Fluazuron)	1990	Disturbs cuticle formation Blocks the incorporation of radiola-beled N-acetylglucosamine	2010		[41][56]
Spinosad (Tetracyclic-macrolide compounds)	2001	Nicotinic acetylcholine receptors (nAChRs) γ-amino-butyric acid (GABA) receptors Hyperexcitation and disruption of an insect's nervous system			[41][57][58][59][60]
Isoxazolines	2014	Inhibits GABA-gated chloride ion channels			[36][61][62]

4. Tick Resistance

Chemical products used in traditional tick control methods are at the center of eradication and control efforts because they offer relatively rapid and effective control of tick populations. However, resistance is the result of irrational and long-term use of acaricidal drugs. In addition, they are expensive and can be harmful to the environment and dangerous for consumers if the recommended withdrawal times for foods of animal origin are not respected [63][64][65]. Resistance is broadly defined as a change in the sensitivity of the target species to a drug [66][67]. The concept of drug resistance can be defined as “the ability of a strain of parasite to survive and/or multiply despite the administration and absorption of a drug administered to doses equal to or greater than those usually recommended but within the tolerance of the subject” (World Health Organization, 1965) or “the ability of some parasites to tolerate toxic doses of a drug that would be lethal to most of their congeners” [68][69].

There are several definitions of acaricide resistance and different types of resistance were observed. In parasitology, four types of resistance were defined:

- Natural resistance or tolerance: “present in the external body-part and in all individuals of the species and does not develop as a result of acaricidal use”. This may be due to the impermeability of the cuticle or behavioral traits. It is not necessarily transmitted to their offspring [47].
- Acquired resistance: is “resistance that results from heritable decreases in sensitivity to drugs over time ” [14][40].
- Cross-Resistance: is defined as “the sharing of resistance among different acaricides with a similar mode of action” [14][40].
- Multiple resistances: is defined as “a resistance to more than one drug, even though they have different modes of action” [14][40].

The first report of tick resistance, against arsenic, was due to the indiscriminate use of this product for more than 30 years (1890–1910) to control *Rhipicephalus (Boophilus) microplus* (Wharton 1983), the main tick affecting domestic cattle over the world. There are many reports describing resistances to formamidine, amitraz, permethrin [70][71][72][73], and even to the more modern fipronil [53]. Unfortunately, there are instances of resistances to practically all the synthetic acaricides as reviewed by [14]. Although negative consequences of resistances have been partially relieved with the rotation products with different mechanisms of action, it continues to be a major problem in large territories of Africa and America [48][74][75][76][77]. This is the main threat given that most of these acaricidal groups are still applied. The development of safe and effective new acaricidal agents is therefore of great interest.

5. Natural Products

Plant products containing bioactive metabolites represent a promising alternative for the control of ticks that are susceptible and/or resistant to conventional acaricides. Studies of the effects of essential oils and plant extracts against different classes of ticks showed efficacies of 5–100% [78]. Following the line of the search for ecological alternatives for effective tick control, products derived from microorganisms or natural products were defined as biopesticides [79]. The products derived from plants are particularly attractive due to their low toxicity, scarce environmental permanence, and the complex chemistry that hinders the development of the resistances. The use of natural products for the control of ticks offers advantages but still has certain limitations. The first disadvantage is the variability of the composition of certain products, such as essential oils, and therefore their effectiveness, for which the identification and subsequent standardization of the fractions and possible effective synergies are required. Another disadvantage could be the characteristics of the product, such as photosensitivity or high volatility, which limit the residual activity depending on the form of presentation [17]. Among the advantages, its role as an alternative in the control of resistant ticks stands out, its environmental innocuousness, and the minimum impact on animal and human health that facilitates its registration and subsequent commercialization [80]. At the beginning of the 19th century, the Caucasian and Persian tribes used pyrethrum flowers as a method of control against body lice [31]. Pyrethrum or Dalmatian pyrethrum (*Tanacetum cinerariifolium* or *Chrysanthemum cinerariaefolium*) is an evergreen plant of the Asteraceae family, with insecticidal properties of low toxicity to mammals. Another plant derivative traditionally used is the neem tree (*Azadirachta indica*), belonging to the Meliaceae family that originates in the Indian subcontinent. For centuries, Indians have relied on this tree to strengthen their health and remedy dozens of diseases; in addition, it has been used to protect stored food and as a natural fertilizer and pesticide for the fields, since it intervenes in the feeding of arthropods and the hormonal processes of their development [81][82]. It is now valued throughout the world as an important source of phytochemicals for use in human health and pest control. Neem oil contains at least 100 biologically active compounds [83]. Essential oils are naturally produced by plants as secondary compounds, which are obtained for commercial use by various forms of distillation, and plant extracts are obtained through various forms of solvent extraction; some of them stand out for their pesticide, growth-regulating, and repellent or dissuasive properties [17].

6. Essential Oils in Control of Ticks

6.1. Acaricidal Activity of Essential Oils against Ticks

In recent decades, natural products and their compounds have been the most productive source for new drug development. Among them, essential oils and isolated terpenoids have shown activity against diverse stages of several species of ticks [63]. Many studies have reported the ovicidal (inhibited oviposition and inhibited hatchability), effects against all the stages of ticks [3][14][34][84][85][86][87].

The variability in the chemical composition of essential oils and the relationship between compounds play an important role in acaricidal activity. It is difficult to attribute the observed biological effects to the major chemical compounds of essential oils. These biological effects can be attributed to a synergistic action between the minority compounds and other minor or major molecules [15]. Additionally, the substances obtained from plants have a low cost, few residual effects, and a low incidence of generating resistance [15][88].

7. Mechanisms of Action of the Essential Oils and/or Their Components against Ticks

Essential oils are the most studied plant-derived compounds for tick control and prevention [9][16][18][89]. Two effects of essential oils against ticks were observed: acaricidal or repellent effects [9][16][89][90][91][92][93][94]. They cause various effects against ticks: feeding inhibition [92][95][96], inhibition of chitin synthesis [9][78][96], decrease in growth, development, or reproduction [9][78][92][93][95][97], and affect tick behavior [96].

Several studies have reported that essential oils act against ticks through three modes of action: neurotoxicity effect [16][94][96][98][99], cytotoxicity effect [94][100], and mechanical effects [96][99][101].

References

1. Klompen, J.S.H.; Black, W.C., IV; Keirans, J.E.; Oliver, J.H. Evolution of Ticks. Annu. Rev. Entomol. 1996, 41, 141–161.
2. Barker, S.C.; Murrell, A. Systematics and evolution of ticks with a list of valid genus and species names. Parasitology 2004, 129, S15–S36.
3. Djebir, S.; Ksouri, S.; Trigui, M.; Tounsi, S.; Boumaaza, A.; Hadef, Y.; Benakhla, A. Chemical Composition and Acaricidal Activity of the Essential Oils of Some Plant Species of Lamiaceae and Myrtaceae against the Vector of Tropical Bovine Theileriosis: Hyalomma scupense (syn. Hyalomma detritum). BioMed Res. Int. 2019, 2019, 1–9.
4. Alota, S.L.; Edquiban, T.R.J.; Galay, R.L.; Bernardo, J.M.G.; Sandalo, K.A.C.; Divina, B.P.; Tanaka, T. Determination of resistance status to amitraz in the cattle tick Rhipicephalus (Boophilus) microplus from Luzon, Philippines, through bioassay and molecular analysis. Exp. Appl. Acarol. 2021, 83, 399–409.
5. Abbas, A.; Abbas, R.Z.; Masood, S.; Iqbal, Z.; Khan, M.K.; Saleemi, M.K.; Raza, M.A.; Mahmood, M.S.; Khan, J.A.; Sindhu, Z.D. Acaricidal and insecticidal effects of essential oils against ectoparasites of veterinary importance. Bol. Latinoam. Caribe Plant. Med. Aromat. 2018, 17, 441–452.
6. Pazinato, R.; Volpato, A.; Baldissera, M.D.; Santos, R.C.V.; Baretta, D.; Vaucher, R.A.; Giongo, J.L.; Boligon, A.A.; Stefani, L.M.; Da Silva, A.S. In vitro effect of seven essential oils on the reproduction of the cattle tick Rhipicephalus microplus. J. Adv. Res. 2016, 7, 1029–1034.
7. Luns, D.A.R.; Martins, R.; Pombal, S.; Rodilla, J.M.L.; Githaka, N.W.; Vaz, I.D.S., Jr.; Logullo, C. Effect of essential oils against acaricide-susceptible and acaricide-resistant Rhipicephalus ticks. Exp. Appl. Acarol. 2021, 83, 597–608.
8. George, J.E.; Pound, J.M.; Davey, R.B. Chemical control of ticks on cattle and the resistance of these parasites to acaricides. Parasitology 2004, 129, S353–S366.
9. Adenubi, O.; Fasina, F.; McGaw, L.; Eloff, J.; Naidoo, V. Plant extracts to control ticks of veterinary and medical importance: A review. S. Afr. J. Bot. 2016, 105, 178–193.
10. Furtado, F.N.; Silva, V.A.R.; Pereira, J.R.G.; Kisue, A.; Coêlho, F.A.S.; Coêlho, M.D.G. Avaliação in vitro do potencial acaricida do óleo essencial de Tagetes minuta frente a Riphicephalus (Boophilus) microplus (Canestrini, 1887). Rev. Biociênc. 2013, 19, 104–110.
11. Nogueira, J.; Vinturelle, R.; Mattos, C.; Tietbohl, L.A.C.; Santos, M.G.; Vaz, J.I.D.S.; Mourão, S.C.; Rocha, L.; Folly, E. Acaricidal Properties of the Essential Oil from Zanthoxylum caribaeum against Rhipicephalus microplus. J. Med. Èntomol. 2014, 51, 971–975.
12. Habeeb, S.M.; El-Namaky, A.H.; Kamel, R.O. In vivo evaluation of-xic effects of avermectin, Citrus sinensis var. balady and C. limon on female Hyalomma dromedarii (Acari: Ixodidae). Acarologia 2009, 49, 13–22.
13. Cruz, E.M.D.O.; Costa-Junior, L.; Pinto, J.A.O.; Santos, D.; de Araujo, S.A.; Arrigoni-Blank, M.D.F.; Bacci, L.; Alves, P.; Cavalcanti, S.C.D.H.; Blank, A.F. Acaricidal activity of Lippia gracilis essential oil and its major constituents on the tick Rhipicephalus (Boophilus) microplus. Vet. Parasitol. 2013, 195, 198–202.
14. Abbas, R.Z.; Zaman, M.A.; Colwell, D.D.; Gilleard, J.; Iqbal, Z. Acaricide resistance in cattle ticks and approaches-its management: The state of play. Vet. Parasitol. 2014, 203, 6–20.
15. Castro, K.N.D.C.; Canuto, K.M.; de Brito, E.S.; Costa-Junior, L.; De Andrade, I.M.; Magalhães, J.A.; Barros, D.M.A. In vitro efficacy of essential oils with different concentrations of 1,8-cineole against Rhipicephalus (Boophilus) microplus. Rev. Bras. Parasitol. Vet. 2018, 27, 203–210.
16. Quadros, D.; Johnson, T.; Whitney, T.; Oliver, J.; Chávez, A.O. Plant-Derived Natural Compounds for Tick Pest Control in Livestock and Wildlife: Pragmatism or Utopia? Insects 2020, 11, 490.
17. George, D.R.; Finn, R.D.; Graham, K.M.; Sparagano, O.A. Present and future potential of plant-derived products to control arthropods of veterinary and medical significance. Parasites Vectors 2014, 7, 28.
18. Ellse, L.; Wall, R. The use of essential oils in veterinary ectoparasite control: A review. Med. Veter.- Èntomol. 2013, 28, 233–243.
19. Kolaczinski, J.; Curtis, C. Chronic illness as a result of low-level exposure to synthetic pyrethroid insecticides: A review of the debate. Food Chem. Toxicol. 2004, 42, 697–706.

20. Freitas, D.R.J.; Pohl, P.C.; Vaz, I.S., Jr. Caracterização da resistência para acaricidas no carrapato Boophilus microplus. Acta Sci. Vet. 2005, 33, 109–117.

21. Ramwell, C.T.; Sinclair, C.J.; Van Beinum, G.W.; Bryning, G. Management of the environmental inputs and risks of cypermethrin based sheep dips. Central. Sci. Lab. Rep. 2009, 1, 35–43.

22. Pinto, Z.T.; Carneiro, J.F.; Carriço, C.; Caetano, R.L.; Ferreira, V.D.S.B.; Mendonça, P.M.; Berenger, A.L.R.; Figueiredo, M.R. Acaricidal effects of seven Brazilian plant extracts. Rev. Colomb. Entomol. 2018, 44, 44–47.

23. Martinez-Velazquez, M.; Castillo-Herrera, G.A.; Rosario-Cruz, R.; Flores-Fernandez, J.M.; Lopez-Ramirez, J.; Hernandez-Gutierrez, R.; Lugo-Cervantes, E.D.C.; Rosario-Cruz, R. Acaricidal effect and chemical composition of essential oils extracted from Cuminum cyminum, Pimenta dioica and Ocimum basilicum against the cattle tick Rhipicephalus (Boophilus) microplus (Acari: Ixodidae). Parasitol. Res. 2010, 108, 481–487.

24. Martinez-Velazquez, M.; Rosario-Cruz, R.; Castillo-Herrera, G.; Flores-Fernandez, J.M.; Alvarez, A.H.; Lugo-Cervantes, E.; Rosario-Cruz, R. Acaricidal Effect of Essential Oils from Lippia graveolens (Lamiales: Verbenaceae), Rosmarinus officinalis (Lamiales: Lamiaceae), and Allium sativum (Liliales: Liliaceae) against Rhipicephalus (Boophilus) microplus (Acari: Ixodidae). J. Med. Èntomol. 2011, 48, 822–827.

25. Shezryna, S.; Anisah, N.; Saleh, I.; A Syamsa, R. Acaricidal activity of the essential oils from Citrus hystrix (Rutaceae) and Cymbopogon citratus (Poaceae) on the cattle tick Rhipicephalus (Boophilus) microplus larvae (Acari: Ixodidae). Trop. Biomed. 2020, 37, 433–442.

26. Drummond, R.O.; Ernst, S.E.; Trevino, J.L.; Gladney, W.J.; Graham, O.H. Boophilus annulatus and B. microplus: Laboratory Tests of Insecticides 13. J. Econ. Èntomol. 1973, 66, 130–133.

27. George, J.E. Present and Future Technologies for Tick Control. Ann. N. Y. Acad. Sci. 2006, 916, 583–588.

28. Graf, J.-F.; Gogolewski, R.; Leach-Bing, N.; Sabatini, G.A.; Molento, M.B.; Bordin, E.L.; Arantes, G.J. Tick control: An industry point of view. Parasitology 2004, 129, S427–S442.

29. Wharton, R.H. Acaricide Resistance and Alternative Methods of Tick Control. World Anim. Rev. 1983, 36, 34–41.

30. Sonenshine, D.E. Tick pheromones and their use in tick control. Annu. Rev. Èntomol. 2006, 51, 557–580.

31. Casida, J.E. Pyrethrum flowers and pyrethroid insecticides. Environ. Health Perspect. 1980, 34, 189–202.

32. ATSDR. Piretrinas y piretroides (Pyrethrins and Pyrethroids) |-xFAQ ATSDR. Available online: https://www.atsdr.cdc.gov/es/toxfaqs/es_tfacts155.html (accessed on 1 October 2019).

33. Davey, R.B.; George, J.E.; Snyder, D.E. Efficacy of a single whole-body spray treatment of spinosad, against Boophilus microplus (Acari: Ixodidae) on cattle. Vet. Parasitol. 2001, 99, 41–52.

34. Cetin, H.; Cilek, J.E.; Aydin, L.; Yanikoglu, A. Acaricidal effects of the essential oil of Origanum minutiflorum (Lamiaceae) against Rhipicephalus turanicus (Acari: Ixodidae). Vet. Parasitol. 2009, 160, 359–361.

35. Brito, L.G.; Barbieri, F.S.; Rocha, R.B.; Oliveira, M.C.S.; Ribeiro, E.S. Evaluation of the Efficacy of Acaricides Used-Control the Cattle Tick, Rhipicephalus microplus, in Dairy Herds Raised in the Brazilian Southwestern Amazon. Vet. Med. Int. 2011, 2011, 806093.

36. Shoop, W.L.; Hartline, E.J.; Gould, B.R.; Waddell, M.E.; McDowell, R.G.; Kinney, J.B.; Lahm, G.P.; Long, J.K.; Xu, M.; Wagerle, T.; et al. Discovery and mode of action of afoxolaner, a new isoxazoline parasiticide for dogs. Vet. Parasitol. 2014, 201, 179–189.

37. Weber, T.; Selzer, P.M. Isoxazolines: A Novel Chemotype Highly Effective on Ectoparasites. ChemMedChem 2016, 11, 270–276.

38. McTier, T.L.; Chubb, N.; Curtis, M.P.; Hedges, L.; Inskeep, G.A.; Knauer, C.S.; Menon, S.; Mills, B.; Pullins, A.; Zinser, E.; et al. Discovery of sarolaner: A novel, orally administered, broad-spectrum, isoxazoline ectoparasiticide for dogs. Vet. Parasitol. 2016, 222, 3–11.

39. Little, S.E. Lotilaner—A novel systemic tick and flea control product for dogs. Parasites Vectors 2017, 10, 539.

40. Abebe, D.; Kebede, A. Review on Acaricide Resistant Bovine Ticks and Alternative Solutions. Eur. J. Biol. Sci. 2018, 10, 86–94.

41. Reshma, K.R.; Prakasan, K. Synthetic Acaricides as A Promising-ol in Tick Control Program-The Present Scenario. Entomol. Appl. Sci. Lett. 2020, 7, 58–69.

42. Angus, B.M. The history of the cattle tick Boophilus microptus in Australia and achievements in its control. Int. J. Parasitol. 1996, 26, 1341–1355.

43. Harris, R.L.; George, J.E.; Ahrens, E.H.; Davey, R.B.; Bazan, H.O. Selection for Resistance to Coumaphos in a Strain of Southern Cattle Tick (Acari: Ixodidae). J. Econ. Èntomol. 1988, 81, 545–548.

44. Hemingway, J.; Field, L.; Vontas, J. An Overview of Insecticide Resistance. Science 2002, 298, 96–97.

45. Raynal, J.T.; Da Silva, A.A.B.; Sousa, T.D.J.; Bahiense, T.C.; Meyer, R.; Portela, R.W. Acaricides efficiency on Rhipicephalus (Boophilus) microplus from Bahia state North-Central region. Rev. Bras. Parasitol. Vet. 2013, 22, 71–77.

46. Muhammad, G.; Naureen, A.; Firyal, S.; Saqib, M. Tick control strategies in dairy production medicine. Pakistan. Vet. J. 2008, 28, 43–50.

47. Nath, S.; Mandal, S.; Pal, S.; Jadhao, S.; Ottalwar, N.; Sanyal, P. Impact and Management of Acaricide Resistance-Pertaining to Sustainable Control of Ticks. Int. J. Livest. Res. 2018, 8, 46.

48. Rodriguez-Vivas, R.I.; Jonsson, N.; Bhushan, C. Strategies for the control of Rhipicephalus microplus ticks in a world of conventional acaricide and macrocyclic lactone resistance. Parasitol. Res. 2017, 117, 3–29.

49. Shaw, R.D. Tick control on domestic animals. 1. A brief history of economic significance of tick infestations. Trop. Sci. 1969, 11, 113.

50. Catterall, W.A. Structural biology: A 3D view of sodium channels. Nature 2001, 409, 988–991.

51. Schnitzerling, H.J.; Nolan, J.; Hughes, S. Toxicology and metabolism of isomers of flumethrin in larvae of pyrethroid susceptible and resistant strains of the cattle tick Boophilus microplus (Acari: Ixodidae). Exp. Appl. Acarol. 1989, 6, 47–54.

52. Lovis, L.; Reggi, J.; Berggoetz, M.; Betschart, B.; Sager, H. Determination of Acaricide Resistance in Rhipicephalus (Boophilus) microplus (Acari: Ixodidae) Field Populations of Argentina, South Africa, and Australia with the Larval Tarsal Test. J. Med. Èntomol. 2013, 50, 326–335.

53. Castro-Janer, E.; Rifran, L.; Piaggio, J.; Gil, A.; Miller, R.; Schumaker, T. In vitro tests to establish LC50 and discriminating concentrations for fipronil against Rhipicephalus (Boophilus) microplus (Acari: Ixodidae) and their standardization. Vet. Parasitol. 2009, 162, 120–128.

54. Janer, E.C.; Klafke, G.; Fontes, F.; Capurro, M.; Schumaker, T. Mutations in Rhipicephalus microplus GABA gated chloride channel gene associated with fipronil resistance. Ticks Tick-borne Dis. 2019, 10, 761–765.

55. Simon-Delso, N.; Amaral-Rogers, V.; Belzunces, L.P.; Bonmatin, J.M.; Chagnon, M.; Downs, C.; Furlan, L.; Gibbons, D.W.; Giorio, C.; Girolami, V.; et al. Systemic insecticides (neonicotinoids and fipronil): Trends, uses, mode of action and metabolites. Environ. Sci. Pollut. Res. 2014, 22, 5–34.

56. Junquera, P.; Hosking, B.; Gameiro, M.; Macdonald, A. Benzoylphenyl ureas as veterinary antiparasitics. An overview and outlook with emphasis on efficacy, usage and resistance. Parasite 2019, 26, 26.

57. Sparks, T.C.; Crouse, G.D.; Durst, G. Natural products as insecti-cides: The biology, biochemistry and quantitative structure—Activity relationships of spinosyns and spinosoids. Pest. Manag. Sci. 2001, 57, 896–905.

58. Salgado, V.L. Studies on the Mode of Action of Spinosad: Insect Symptoms and Physiological Correlates. Pestic. Biochem. Physiol. 1998, 60, 91–102.

59. Snyder, D.E.; Cruthers, L.R.; Slone, R.L. Preliminary study on the acaricidal efficacy of spinosad administered orally to dogs infested with the brown dog tick, Rhipicephalus sanguineus (Latreille, 1806) (Acari: Ixodidae). Vet. Parasitol. 2009, 166, 131–135.

60. A Kirst, H. The spinosyn family of insecticides: Realizing the potential of natural products research. J. Antibiot. 2010, 63, 101–111.

61. Ozoe, Y.; Asahi, M.; Ozoe, F.; Nakahira, K.; Mita, T. The antiparasitic isoxazoline A1443 is a potent blocker of insect ligand-gated chloride channels. Biochem. Biophys. Res. Commun. 2010, 391, 744–749.

62. Gassel, M.; Wolf, C.; Noack, S.; Williams, H.; Ilg, T. The novel isoxazoline ectoparasiticide fluralaner: Selective inhibition of arthropod γ-aminobutyric acid- and l-glutamate-gated chloride channels and insecticidal/acaricidal activity. Insect Biochem. Mol. Biol. 2014, 45, 111–124.

63. Ribeiro, V.L.S.; Dos Santos, J.C.; Bordignon, S.A.; Apel, M.A.; Henriques, A.T.; Von Poser, G.L. Acaricidal properties of the essential oil from Hesperozygis ringens (Lamiaceae) on the cattle tick Riphicephalus (Boophilus) microplus. Bioresour. Technol. 2010, 101, 2506–2509.

64. De Meneghi, D.; Stachurski, F.; Adakal, H. Experiences in Tick Control by Acaricide in the Traditional Cattle Sector in Zambia and Burkina Faso: Possible Environmental and Public Health Implications. Front. Public Health 2016, 4, 239.

65. Singh, N.K.; Abhijit, N.; Harkirat, S. Detection of multi-acaricide resistance in Rhipicephalus (Boophilus) microplus (Acari: Ixodidae). Explor. Anim. Med. Res. 2019, 9, 24–28.

66. Sangster, N. Managing parasiticide resistance. Vet. Parasitol. 2001, 98, 89–109.

67. Corley, S.W.; Jonsson, N.N.; Piper, E.K.; Cutullé, C.; Stear, M.; Seddon, J. Mutation in the Rm AOR gene is associated with amitraz resistance in the cattle tick Rhipicephalus microplus. Proc. Natl. Acad. Sci. USA 2013, 110, 16772–16777.

68. Stone, B.F. The Genetics of Resistance by Ticks- Acaricides. Aust. Vet. J. 1972, 48, 345–350.

69. Benavides, E. Control de Las Pérdidas Ocasionadas Por Los Parásitos Del Ganado. Carta Fedegan 2001, 69, 52–63.

70. Nolan, J. Acaricide Resistance in the Cattle Tick Boophilus microplus, Report of Workshop Leader-FAO/UN Consultant, Porto Alegre, RS, Brazil; Food and Agriculture Organization of the United Nations Publishing Services: Rome, Italy, 1994.

71. Chen, A.C.; He, H.; Davey, R.B. Mutations in a putative octopamine receptor gene in amitraz-resistant cattle ticks. Vet. Parasitol. 2007, 148, 379–383.

72. Davey, R.B.; Miller, R.J.; George, J.E. Efficacy of amitraz applied as a dip against an amitraz-resistant strain of Rhipicephalus (Boophilus) microplus (Acari: Ixodidae) infested on cattle. Vet. Parasitol. 2008, 152, 127–135.

73. Miller, R.J.; Davey, R.B.; White, W.H.; George, J.E. A comparison of three bioassay techniques- determine amitraz susceptibility in Boophilus microplus (Acari: Ixodidae). J. Med. Entomol. 2007, 44, 283–294.

74. Mekonnen, S.; Bryson, N.R.; Fourie, L.J.; Peter, R.J.; Spickett, A.M.; Taylor, R.J.; Strydom, T.; Horak, I.G. Acaricide resistance profiles of single- and multi-host ticks from communal and commercial farming areas in the Eastern Cape and North-West Provinces of South Africa. Onderstepoort J. Vet. Res. 2002, 69, 99–105.

75. Jongejan, F.; Uilenberg, G. The global importance of ticks. Parasitology 2004, 129, S3–S14.

76. A Alonso-Díaz, M.; I Rodríguez-Vivas, R.; Fragoso-Sánchez, H.; Rosario-Cruz, R. Resistencia de la garrapata Boophilus microplus a los ixodicidas. Arch. Med. Vet. 2006, 38, 105–113.

77. Yessinou, R.E.; Akpo, Y.; Sidick, A.; Adoligbe, C.; Karim, I.Y.A.; Akogbeto, M.; Farougou, S. Evidence of multiple mechanisms of alphacypermethrin and deltamethrin resistance in ticks Rhipicephalus microplus in Benin, West Africa. Ticks Tick-Borne Dis. 2018, 9, 665–671.

78. Rosado-Aguilar, J.; Arjona-Cambranes, K.; Torres-Acosta, J.; Rodríguez-Vivas, R.; Bolio-González, M.; Ortega-Pacheco, A.; Alzina-López, A.; Gutiérrez-Ruiz, E.; Gutiérrez-Blanco, E.; Aguilar-Caballero, A. Plant products and secondary metabolites with acaricide activity against ticks. Vet. Parasitol. 2017, 238, 66–76.

79. European Commission. Encouraging Innovation in Biopesticide Development. (New Alert Issue). Science for Environment Policy. European Commission. 2008. Available online: https://ec.europa.eu/environment/integration/research/newsalert/pdf/134na5_en.pdf. (accessed on 16 June 2021).

80. Natural Tick Repellents and Pesticides|Lyme Disease CDC. 2018. Available online: https://www.cdc.gov/lyme/prev/natural-repellents.html. (accessed on 13 August 2018).

81. Schmutterer, H. Properties and Potential of Natural Pesticides from the Neem Tree, Azadirachta indica. Annu. Rev. Entomol. 1990, 35, 271–297.

82. Neem Foundation. Neem. History of Usage. 2018. Available online: https://neemfoundation.org/about-neem/history-of-usage/ (accessed on 13 June 2021).

83. Campos, E.V.R.; de Oliveira, J.L.; Pascoli, M.; de Lima, R.; Fraceto, L.F. Neem Oil and Crop Protection: From Now- the Future. Front. Plant. Sci. 2016, 7, 1494.

84. Cetin, H.; Cilek, J.; Oz, E.; Aydin, L.; Deveci, O.; Yanikoglu, A. Acaricidal activity of Satureja thymbra L. essential oil and its major components, carvacrol and γ-terpinene against adult Hyalomma marginatum (Acari: Ixodidae). Vet. Parasitol. 2010, 170, 287–290.

85. Koç, S.; Oz, E.; Aydın, L.; Cetin, H. Acaricidal activity of the essential oils from three Lamiaceae plant species on Rhipicephalus turanicus Pom. (Acari: Ixodidae). Parasitol. Res. 2012, 111, 1863–1865.

86. Gomes, G.A.; Monteiro, C.M.O.; Julião, L.D.S.; Maturano, R.; Senra, T.O.S.; Zeringóta, V.; Calmon, F.; Matos, R.; Daemon, E.; de Carvalho, M.G. Acaricidal activity of essential oil from Lippia sidoides on unengorged larvae and nymphs of Rhipicephalus sanguineus (Acari: Ixodidae) and Amblyomma cajennense (Acari: Ixodidae). Exp. Parasitol. 2014, 137, 41–45.

87. Ferreira, F.M.; Delmonte, C.C.; Novato, T.L.P.; Monteiro, C.M.O.; Daemon, E.; Vilela, F.M.P.; Amaral, M.P.H. Acaricidal activity of essential oil of Syzygium aromaticum, hydrolate and eugenol formulated or free on larvae and engorged females of Rhipicephalus microplus. Med. Vet. Ėntomol. 2017, 32, 41–47.

88. Rosado-Aguilar, J.; Aguilar-Caballero, A.J.; Rodriguez-Vivas, R.; Borges-Argaez, R.; Garcia-Vazquez, Z.; Mendez-Gonzalez, M. Acaricidal activity of extracts from Petiveria alliacea (Phytolaccaceae) against the cattle tick, Rhipicephalus (Boophilus) microplus (Acari: Ixodidae). Vet. Parasitol. 2010, 168, 299–303.

89. Benelli, G.; Pavela, R. Repellence of essential oils and selected compounds against ticks—A systematic review. Acta Trop. 2018, 179, 47–54.
90. Nerio, L.S.; Olivero-Verbel, J.; Stashenko, E. Repellent activity of essential oils: A review. Bioresour. Technol. 2010, 101, 372–378.
91. Blenau, W.; Rademacher, E.; Baumann, A. Plant essential oils and formamidines as insecticides/acaricides: What are the molecular targets? Apidologie 2011, 43, 334–347.
92. Benelli, G.; Pavela, R.; Canale, A.; Mehlhorn, H. Tick repellents and acaricides of botanical origin: A green roadmap to control tick-borne diseases? Parasitol. Res. 2016, 115, 2545–2560.
93. Elmhalli, F.; Garboui, S.S.; Borg-Karlson, A.-K.; Mozūraitis, R.; Baldauf, S.L.; Grandi, G. The repellency and toxicity effects of essential oils from the Libyan plants Salvadora persica and Rosmarinus officinalis against nymphs of Ixodes ricinus. Exp. Appl. Acarol. 2019, 77, 585–599.
94. Salman, M.; Abbas, R.Z.; Israr, M.; Abbas, A.; Mehmood, M.K.; Khan, M.K.; Sindhu, Z.U.D.; Hussain, R.; Saleemi, M.K.; Shah, S. Repellent and acaricidal activity of essential oils and their components against Rhipicephalus ticks in cattle. Vet. Parasitol. 2020, 283, 109178.
95. Kaaya, G.P. The potential for antitick plants as components of an integrated tick control strategy. Ann. N. Y. Acad. Sci. 2000, 916.
96. Goode, P.; Ellse, L.; Wall, R. Preventing tick attachment to dogs using essential oils. Ticks Tick-Borne Dis. 2018, 9, 921–926.
97. Ribeiro, V.L.S.; Avancini, C.; Gonçalves, K.; Toigo, E.; von Poser, G. Acaricidal activity of Calea serrata (Asteraceae) on Boophilus microplus and Rhipicephalus sanguineus. Vet. Parasitol. 2008, 151, 351–354.
98. Ribeiro, V.L.S.; Toigo, E.; Bordignon, S.A.; Gonçalves, K.; von Poser, G. Acaricidal properties of extracts from the aerial parts of Hypericum polyanthemum on the cattle tick Boophilus microplus. Vet. Parasitol. 2007, 147, 199–203.
99. Amer, A.M.; Amer, M.M. Efficacy and Safety of Natural Essential Oils Mixture on Tick Infestation in Dogs. Adv. Anim. Vet. Sci. 2020, 8, 398–407.
100. Powers, C.N.; Osier, J.L.; McFeeters, R.L.; Brazell, C.B.; Olsen, E.L.; Moriarity, D.M.; Satyal, P.; Setzer, W.N. Antifungal and Cytotoxic Activities of Sixty Commercially-Available Essential Oils. Molecules 2018, 23, 1549.
101. Burgess, I.F. The mode of action of dimeticone 4% lotion against head lice, Pediculus capitis. BMC Pharmacol. 2009, 9, 3.