Acaricidal potential of various plant natural products: A review

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Abstract

The present review article describes anti-tick efficacy of various plant natural products, that is, plant extracts, pure bioorganic compounds, essential oils (EOs), and its components. This review indicates rising problem of resistance to chemical acaricides in ticks and environmental toxicity due to its residual effects. Both EOs and pure molecules show synergistic effects. These act as strong herbal repellents and reduce tick bite exposure and transmission of pathogens. Repellents can be used topically or in impregnated clothing to avoid tick bites. These plant origin acaricides showed significant mortality in ticks, these were proved eco-friendly, biodegradable and have no side effect to the environment. Furthermore, acaricide-resistant strains of the cattle tick can be controlled by using *Metarhizium anisopliae* fungus found on field and farmyard livestock. The present review suggests the use of herbal preparations to replace the highly toxic chemical acaricides for the control of the population of cattle ticks. For more effective control of tick population, integrated tick management must be used by the farmers, dairy owners, veterinarians, and clinicians.

Key words: Essential oils, plant natural products, repellents, tick-borne pathogens, ticks

INTRODUCTION

Ticks are blood-sucking external parasites which transmit wide ranges of diseases pathogen in livestock and wild animals.[1] These are most important vectors of major human diseases and transmit pathogens among multiple hosts in the both tropical and subtropical and even in temperate countries. These are small-sized animals serve as vectors of zoonotic disease pathogens of diverse groups, that is, viruses, rickettsiae, and spirochete, bacteria, fungi, protozoa, and filarial nematodes. They massively invade livestock and human population in tropical and subtropical areas around the world. These largely affect dairy and agriculture production, particularly in poor countries throughout the world. These cause great economic losses to livestock and adversely affect livestock hosts in several ways. They maintain very high reproductive rate and their all life stages essentially rely on blood feeding are of considerable medical and veterinary importance. Ticks remain attached to body surface of hosts for continuous blood sucking in large numbers. They make host animals anemic, weaker, and results in heavy weight loss.

Ticks economically impact cattle production by reducing weight gain and milk production. These also put major impact on public health, hence, there is immense need to identify novel molecules to repel and kill larvae and adults of various species of ticks. There are few methods used for controlling ticks. Among them, different synthetic acaricides were applied for controlling the ticks last 4–5 decades, but all these have shown high anti-tick activity in beginning and killed large population of ticks. But now, these become serious problem both for environment, livestock, and health. There is a rising resistance found in ticks against chemical formulations.[2] Therefore, it is highly needful to develop new strategies to replace the existing synthetic acaricides by developing herbal formulations. So far, researches have been done so many plant species have been evaluated for their antifeedant and acaricidal activity against ticks.[3] Besides, laboratory owned control of ticks traditional methods are also used for the management of arthropods mainly ticks those who invade livestock herds. In many parts of world, ethnopractices are used by various ethnic tribes for integrated tick control and management.[3]

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Mongolian nomadic people possess traditional knowledge of wild plants that grow in their areas of habitation. Many of these are forage plants in nature and are consumed by livestock. However, these plants are known to have medicinal and/or toxic properties against ticks [Figure 1 and Table 1].[4]

These plant natural products have been used throughout the world by people against several diseases which affect both livestock and human health.[4] Moreover, few plant species *Cissus quadrangularis*, *Lippia javanica, Psydrax livida,* and *Aloe* sp. showed acaricidal properties between 14% and 30% efficacy.[5] Acetone extracts of *Tulbaghia violacea* show repellant activity against ticks *Rhipicephalus appendiculatus* larvae at 5% w/v concentration.[6] Acetone extracts *Schkuhria pinnata* (whole plant) and *Senna italica* subsp. arachoides (roots, leaves, and fruits) and ethanol extract *Calpurnia aurea* (leaves and flowers) and *S. pinnata* and *Cleome gynandra* (leaves) showed 80–90% mortality in *Rhipicephalus turanicus* at a concentration of 200 mg/ml [Table 1 and Figure 1].[7]

Similarly, acetone extract from *Tagetes minuta* and *Tithonia diversifolia* was found active against *R. appendiculatus*.[8] Ethiopian plants species, that is, *C. aurea* and *Ricinus communis* showed strong anti-tick activity. Its methanolic extracts have shown more than 90%

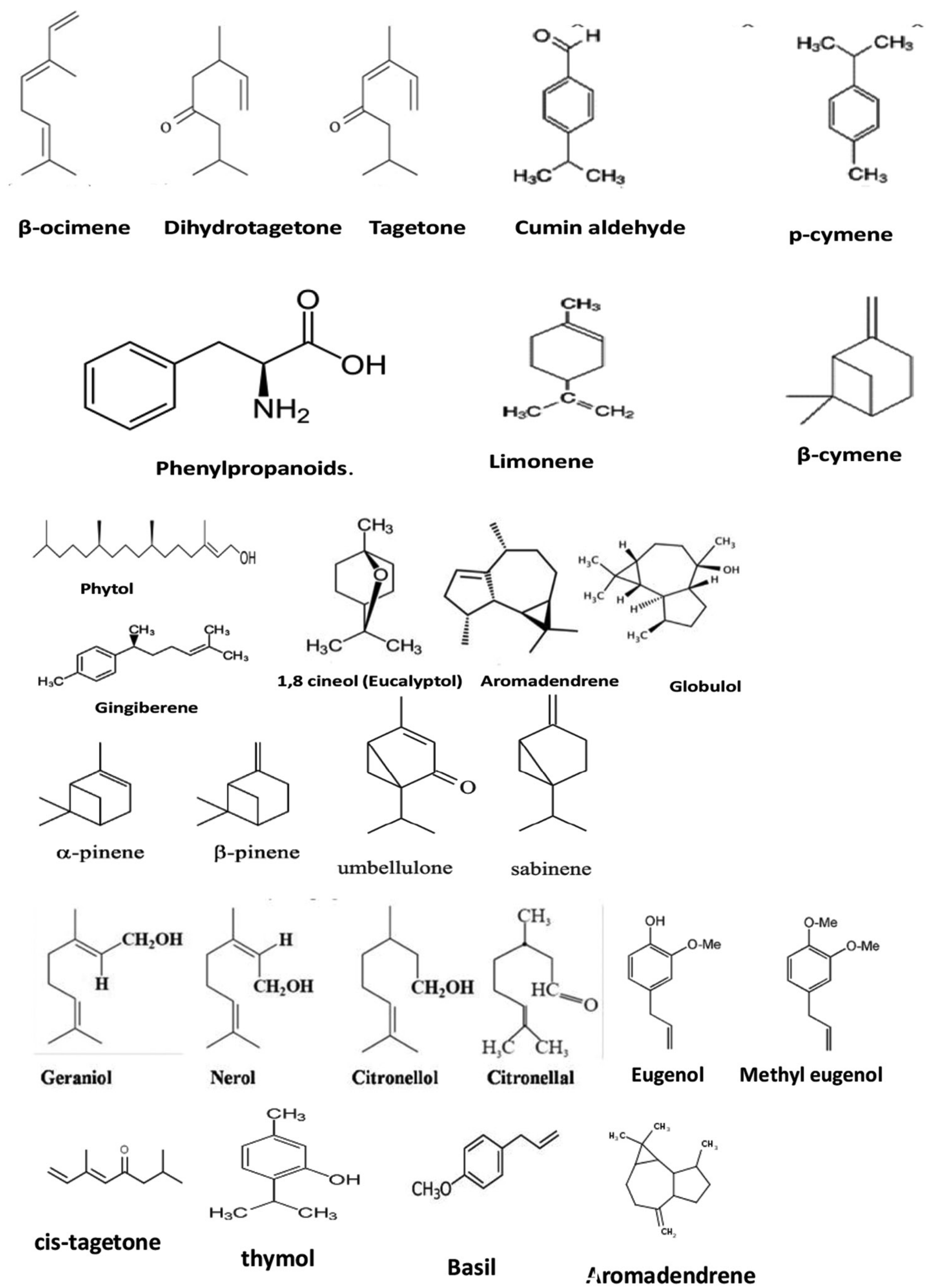

Figure 1: Various anti-tick bio-organic constituents isolated from various plant species

Table 1: Acaricidal potential of plant natural products: A review

S. No.	Plant species	Plant product/ extract	Effect against ticks or pathogen	Reference
1.	*Colchicum autumnale*	Aqueous and acetone extract	*Hyalomma* spp.	Norouzi *et al.*, 2021[29]
2.	*C. aurea*	Hydroethanolic extracts	*R. turanicus*	Fouche *et al.*, 2019[7]
3.	*Allium sativum*	DCM extract/DCM	*Hyalomma rufipes*	Nchu *et al.*, 2016[32]
4.	*Rotheca glabrum*	Methanol, acetone and DCM	*R. appendiculatus*	Mawela *et al.*, 2019[33]
5.	*Matricaria glabrum*	Flowers ethanol extracts	*Rhipicephalus annulatus*	Pirali-Kheirabadi and Razzaghi-Abyaneh, 2007[36]
6.	*S. italica* subsp. *arachoides*	Ethanol extract of roots, leaves, and fruits	*R. turanicus*	Fouche *et al.*, 2017[7]
7.	*Monsonia angustifolia*	Ethanol extract	*R. turanicus*	Fouche *et al.*, 2017[7]
8.	*Schkuhria pinnata*, *S. italica* subsp.	Ethanol extract	*R. turanicus*	Fouche *et al.*, 2017[7]
9.	*Cleome gynandra*, *C. aurea*	Acetone and ethanol extracts	*R. turanicus*	Fouche *et al.*, 2017[7]
10.	*T. minuta*	Ethanol and aqueous extract	*R. appendiculatus*	Wanzala *et al.*, 2104[8]
11.	*Nicotiana tabacum*	Methanol and N-hexane leaf extracts	*Rhipicephalus sanguineus*	Oyagbemi *et al.*, 2019[30]
		EO		
12.	*Cymbopogon winterianus and Syzygium aromaticum*	EO	*R.* (*Boophilus*) *microplus*	De Mello *et al.*, 2014[45]
13.	*Cuminum. cyminum*, *P. dioica and O. basilicum*	EO	*R.* (*Boophilus*) *microplus*	Martinez-Velazque *et al.*, 2010[45]
14	*O. gratissimum*	EO	*R. microplus*	Lima *et al.*, 2017[10]
15.	*Piper amalago*, *Piper mikanianum*, and *Piper xylosteoides*	EO	Larvae of cattle tick *R. microplus*	de Ferraz *et al.*, 2010
16.	*T. minuta*, *Tagetes erecta*, *Tagetes patula*, and *Tagetes tenuifolia*	EO	Larvae of all ticks	Salehi *et al.*, 2018[50]
17.	Allspice berries (*P. dioica*) and basil leaves (*O. basilicum*)	EO	*R.* (*Boophilus*) *microplus* tick larvae	Martinez-Velazquez *et al.*, 2010[46]
18.	*O. gratissimum species*	EO	*R.* (*Boophilus*) *microplus*	Hüe *et al.*, 2014[11]
19.	*C. cyminum*, *P. dioica* and *O. basilicum*	EO	*R. microplus* larvae. *C. cyminum* and *P. dioica*	Martinez-Velazquez *et al.*, 2010[49]
		Integrated tick management		
20.	Phyto-formulations chemical acaricides.	Tri-terpenes, pigments, phytosterols	*R. microplus*	Lazcano-Díaz *et al.*, 2019[65]

(*Contd...*)

Table 1: (*Continued*)

S. No.	Plant species	Plant product/ extract	Effect against ticks or pathogen	Reference
21.	*M. anisopliae* (TIS-BR03)	Cypermethrin and chlorpyriphos.	Fungus *M. anisopliae*	Webster *et al.,* 2014[68]
22.	Control by protease inhibitor serine protease inhibitors (SPIs or serpins)	Regulation of inflammation, blood clotting, wound healing, vasoconstriction.	*R.* (*Boophilus*) *microplus*	Blisnick *et al.,* 2017[71]
		Epigenetic control		
23.	*Anaplasma phagocytophilum*	Histones and HMEs	*Ixodes scapularis*	Cabezas-Cruz *et al.,* 2016[74]
24.	*Babesia bovis*	Histones and HMEs	(*Boophilus*) *microplus*	Bastos *et al.,* 2009[76]
		Use of vaccines		
25.	OspC bindsto Salp15	Commercialize anti-parasitic vaccines	Tick saliva antigen raise antibodies and provide protection against infection	Grabowski and Hill, 2017[77]
		Ecological and cultural control		
26.	Restoration of ecology and environment, clean cultivation	Re-emergence of tick-borne zoonotic diseases	Control tick population in field as well as in urban sites	Inci *et al.,* 2016[79]

C. aurea: *Calpurnia aurea*, *S. italica*: *Senna italic*, *T. minuta*: *Tagetes minuta*, *C. cyminum*: *Cuminum cyminum*, *P. dioica*: *Pimenta dioica*, *O. basilicum*: *Ocimum basilicum*, *O. gratissimum*: *Ocimum gratissimum*, *O. basilicum*: *Ocimum basilicum*, *M anisopliae*: *Metarhizium anisopliae*, *R. turanicus*: *Rhipicephalus turanicus*, *R. appendiculatus*: *Rhipicephalus appendiculatus*, *R.* (*Boophilus*) *microplus*: *Rhipicephalus* (*Boophilus*) *microplus*, *R. microplus*: *Rhipicephalus microplus*, HMEs: Histone-modifying enzymes, EO: Essential oil, DCM: Dichloromethane

mortality against *Rhipicephalus decoloratus* at 100 mg/ml concentration.[9] Zerokeet®, a polyherbal commercial plant product, shows significant control against field tick *Rhipicephalus microplus* at 1:2 dilutions.[10] Both acetone and ethanol extracts of *Vernonia amygdalina*, *C. aurea*, *Schinus molle*, *R. communis*, *Croton macrostachyus*, and *Nicotiana tabacum*, against *Rhipicephalus* (*Boophilus*) *decoloratus* and *Rhipicephalus pulchellus* using an *in vitro* adult immersion test.[7,9] Butox® Vet one of the commercial polyherbal product, Zerokeet® showed an efficacy (E%) of 41.8–75.4% [Figure 1 and Table 1].[10]

Besides, extracts plant essential oils (Eos) were also found active against ticks. Among them, few EOs isolated from *Ocimum gratissimum* and *Ocimum* species[11] and its major constituents were found active several species of ticks, that is, *R. microplus* and *R.* (*Boophilus*) *microplus*.[12] It is a well-known fact that ticks are major transmitters of pathogens and severely affect cattle health, and cause massive production loss in tropical and subtropical regions. Hence, there is a need to eliminate the population of various tick species using low toxic environmentally safer and easily available acaricides. These ethnobotanicals can be used for making highly effective low-cost anti-tick formulation if suitable blended with conventional methods. The present review is focused on ticks importance and their control.[13] This article explains plant origin active ingredients as acaricides to replace highly toxic chemicals [Figure 1 and Table 1].

ANTI-TICK PLANT NATURAL PRODUCTS

After mosquitoes, ticks are more dangerous vectors of deadly diseases, which spread epidemics or pandemics in the increasing world population of humans and animals. Among them, ticks transmit more pathogen species than any other group of blood-feeding arthropods worldwide. However, for control of tick population, both repellents and acaricides of botanical origin have been used. Various research groups have screened and evaluated different botanicals from so many plant species. These have shown diverse effects and great potential as tick repellent and control agents.[14] Ticks are important vectors for the transmission of pathogens including viruses. The viruses carried by ticks also known as tick-borne viruses, contain a large group of viruses with diverse genetic properties, and are concluded in two orders, nine families, and at least 12 genera [Figure 1 and Table 1].[15]

At present, tick control methods primarily rely on the application of chemical acaricides, which results in the development of resistance among tick populations and environmental contamination. To combat the acaricide-resistant tick infestations on animals, attention should be paid to develop eco-friendly phytoacaricides.[10] Hence, many plant-based anti-tick commercially available products and newly developed phytoformulations are used against resistant tick *R.* (*Boophilus*) *microplus and R.* (*Boophilus*) *microplus*.[17] *Hyalomma* species of ticks spread *Theileria annulata* infection in animals mainly multi-host species, hence, its management is very challenging.[18] However, for controlling ticks and pathogen, cystatins found in the salivary glands and/or the midgut, which assist in blood digestion and the expression of pharmacologically potent salivary proteins for blood feeding are tried to inhibit. Cystatins, mainly Hlcyst-1 or Om-cystatin 2, are involved in regulating blood digestion. Inhibition of these proteins using plant formulations might obstruct tick embryogenesis [Figure 1 and Table 1].[19]

Ticks as blood-feeding ectoparasites spread vast array of pathogens, including bacteria, viruses, protozoa, and helminthes.[20] Due to global climate changes, development of modern molecular tools and exposure of various chemicals new tick-borne microorganisms are emerging which impose great challenge as because of their high zoonotic potential [Figure 1].[21] To control them, plant origin repellents can be used to repel ticks from blood feeding and thereby do prevention of tick-borne diseases. Till the date, many plant-derived molecules, which act as repellents are used. These significantly reduce tick bites and the potential transmission of pathogens.[22] Repellents are also used topically or in impregnated clothing. Few commercialized skin repellents which are used against arthropods are 3-(N-acetyl-N-butyl) aminopropionic acid ethyl ester (IR3535), icaridine, permethrin, and EOs.[22] N,N-diethyl-meta-toluamide (DEET), IR3535, picaridin or KBR 3023, and para-menthanediol are used to repel ticks.[23] Products based on natural compounds, for example, eugenol.[24] Newer, synthetic repellents exist such as IR3535 which, as well as being less toxic, also exhibits greater efficacy against ticks. Some repellents are used on the skin, while others, like permethrin, which is actually an insecticide, may be applied to clothing [Figure 1 and Table 1].[25] Little nanoherbal acaricidal formulation can be used for successful control of ectoparasites *R.* (*Boophilus*) *microplus* ticks.[26] However, for significant reduction in tick population, management of tick vector populations is highly essential. It could be possible using synthetic or botanical acaricides and use of vaccines. Awareness and educating people may provide good results to control of cattle ticks [Figure 1].[27] People should be encouraged to use eco-friendly control and management of tick vectors.[28]

PLANT EXTRACTS

Hyalomma species spread protozoan, bacterial, rickettsial, and viral diseases and cause huge economic loss to the livestock owners.[29] For control of *Hyalomma* species, *Colchicum autumnale* (autumn crocus) extract was found effective.[29] Few African plant species such as *C. aurea* (stems) showed 75.0% mortality in ticks, while *S. pinnata* (whole plant) showed 67.0% and *Aloe rupestris* (leaves) 66.6% mortality. Both methanol and N-hexane leaf extracts of *N. tabacum* exhibited observable acaricidal property against the larvae and adult *Rhipicephalus sanguineus* of dog [Figure 1 and Table 1].[30]

Few African plants such as *Ficus sycomorus* (bark and stems) 86.7% and *S. italica* subsp. arachoides (roots, leaves, and fruits) aqueous and hydroethanolic extracts showed 83.3% efficacy against *R. turanicus*.[31] Dichloromethane (DCM) extract of garlic (*Allium sativum* Linn.) bulbs showed very strong repellent activity against the hard tick, *Hyalomma rufipes* (Acari: *Ixodidae*).[32] *Rotheca glabrum* methanol, acetone, and DCM plant extracts showed repellent activity against adults of *R. appendiculatus*.[33] This effect may be due to the presence of secondary metabolites [Figure 1 and Table 1].[34] Plant-based insect repellents containing IR3535, picaridin, or oil of lemon eucalyptus (p-menthane-3, 8-diol or PMD) would offer better topical protection act as important topical barriers of personal protection from arthropod-borne infectious diseases.[35] *Chamomile* (*Matricaria chamomile*) flowers' extract was found effective against the survival and egg laying of the cattle fever tick (Acari: *Ixodidae*) *Rhipicephalus annulatus.*[36] *Azadirachta indica*, *Gynandropsis gynandra*, *Lavandula angustifolia*, *Pelargonium roseum,* and *Cymbopogon* spp. had good acaricidal and larvicidal effects with 90–100% efficacy against cattle tick *R.* (*Boophilus*) *microplus* [Figure 1 and Table 1].[37]

Besides, biological researches ethnobotanical traditional methods are also practiced by human tribes. These traditional formulations have shown enormous potential for integrated tick control and management of ticks and improvement in livestock production. These have shown toxic, repellent, antifeedant, and oviposition inhibition ability against several tick species. These ethnobotanical substances are potentially useful in developing sustainable, efficient, and effective anti-tick agents suitable for rural livestock farmers.[3] Both *Allium sativum* and *Cannabis sativa* extracts showed anti-tick activities against *Rhipicephalus* (Boophilus) *microplus* [38]. Both plant species showed lethal effect on egg laying, egg hatching and total larval mortality at very low dose.[38] The crude methanolic extract of *Datura stramonium*, *A. indica,* and *Calotropis procera* leaves, *A. sativum* cloves, and *Carica papaya* seed extracts have shown very acaricidal effects against *R.* (*Boophilus*) *microplus*.[39] Similarly, *C. procera*, the apple of Sodom, and *Taraxacum officinale*, the common dandelion, showed acaricidal potential against *R. microplus* larvae and adults *in vitro*.[40] *Acmella oleracea* showed strong acaricidal activity *in vitro* against *R. microplus*).[41] More specifically, plant species which have shown significant mortality in ticks can be used to develop herbal acaricides to control *R. microplus* infestations.

Hydroethanolic extracts of *Randia aculeata* seed and shell showed very high larvicidal activity against *R. microplus* (100 and 91% mortality, respectively) at a concentration of 100 mg/mL. *R. aculeata* (seed and shell), *Moringa oleifera,* and *C. papaya* treatments showed 85, 75, 66, and 55%, mortality in adults at the same concentration (100 mg/mL). Hydroethanolic extracts prepared from *R. aculeata* seeds significantly reduced the index of egg laying and increased the percentage inhibition of oviposition of female ticks at a concentration of 100 mg/mL.[42] A water-based formulation of a commercially available botanical acaricide (Essentria® IC3) was found effective against an acaricide-resistant strain of *R. microplus* 6.25% was 100% lethal against unfed larvae, and 94% mortality in engorged female ticks.[43] Polyherbal formulations mainly kill ectoparasites will be prove more beneficial for veterinary use [Figure 1 and Table 1].[44] Such formulations will certainly assist in dairy farm productivity, reducing economic losses, and curtailing the overuse of synthetic chemical acaricides.[40]

Besides above methods, toxic sugar baits are used for mass killing of ticks in the field.[45] For this purpose, bait boxes of 5 × 7 inch boxes are used to attract mice (and, to a lesser extent, chipmunks, and voles), which are most responsible for spreading Lyme and other tick-borne pathogens. Two main ingredients i.e. an insecticide that kills ticks and baits that attracts mice are used in such operations. As a rodent moves through the box, a wick containing a low-dose insecticide brushes its backside. Ticks that attach to the animal die after exposure to the insecticide. The rodents themselves are unharmed. The boxes are installed (usually at the interface between a landscaped yard and wooded areas) and replaced at two specific intervals timed to disrupt the ticks' life cycle at crucial stages across the season. Such poison baits successfully kill nymphs and tiny sized tick larvae after taking blood meals by them.[45] Besides this, plant EOs, vaccination, and biological control methods are also used to manage populations of *Rhipicephalus* ticks.[46]

EOS

For the control of field population of ticks, both EOs and their components have been used. Both EOs and its active components have shown very high acaricidal activity against *Rhipicephalus* ticks in cattle. More specifically, Zingiber officinalis and Eucalyptus globulus against *Rhipicephalus* bursa EOs showed high acaricidal and repellent activity against R. bursa hard.[47] Similar acaricidal activity is reported in *T. minuta, T. diversifolia, Juniperus procera*, *Solanecio mannii*, *Senna didymobotrya, Lantana camara, Securidaca longepedunculata*, and *Hoslundia opposita* against brown ear tick *R. appendiculatus. T. diversifolia* oil contains α-pinene (63.64%), β-pinene (15.00%), isocaryophyllene (7.62%), nerolidol (3.70%), 1-tridecanol (1.75%), limonene (1.52%), sabinene (1.00%), and cis-tagetone (1.95%). These components protect farmyard cattle against infestations with *R. appendiculatus*.[7] This acaricidal activity was time and dose dependent. *Cymbopogon winterianus* and *Syzygium aromaticum* EOs showed acaricidal properties against the cattle tick, *R.* (*Boophilus*) *microplus*.[48] EOs extracted from *Cuminum cyminum, Pimenta dioica,* and *Ocimum basilicum* showed acaricidal activity against the cattle tick *R.* (*Boophilus*) *microplus* (Acari: *Ixodidae*) [Table 1 and Figure 1].

EOs extracted from cumin seeds (*C. cyminum*), allspice berries (*P. dioica*), and basil leaves (*O. basilicum*) were found effective against 10-day-old *R.* (*Boophilus*) *microplus* tick larvae.[49] Similarly, EOs of *Ocimum* species showed acaricidal activity against *R.* (*Boophilus*) *microplus* larvae. This activity was due to the presence of thymol as major constituents.[10] EOs extracted from *O. gratissimum* L. (three samples), *Ocimum urticaefolium* Roth., and *Ocimum canum* Sims. were found highly effective against 14- to 21-day-old *R. microplus* tick larvae [Table 1 and Figure 1].[11]

Similarly, EOs extracted from resin and heartwood of five endemic conifers of New Caledonia (*Araucaria columnaris, Agathis moorei*, *Agathis ovata*, *Callitris sulcata*, and *Neocallitropsis pancheri)* showed very strong acaricidal activity 14–21-day-old larvae of cattle tick *R.* (*Boophilus*) *microplus*.[50] This anti-tick activity was due to the presence of high level of sesquiterpene hydrocarbons and oxygenated sesquiterpenes mainly of aromadendrene (23.1%) and bicyclogermacrene (16.0%).[50] EOs isolated from *Piper mikanianum, Piper xylosteoides. P. mikanianum, and P. xylosteoides* contain phenylpropanoids (67.89% and 48.53%, respectively), whereas *Piper amalago* is rich in monoterpene and sesquiterpene hydrocarbons (84.95%).[51] The main volatile compounds identified in *Piper* EOs are monoterpenes hydrocarbons, oxygenated monoterpenoids, sesquiterpene hydrocarbons, oxygenated sesquiterpenoids, and large amounts of phenylpropanoids.[52] These showed strong acaricidal activity.[51, 52] Essential oil from *Tagetes* (marigold) species cis-tagetone, 1-tridecanol, and limonene showed both repellent and acaricidal [Table 1 and Figure 1].[53,54]

BIOLOGICAL CONTROL

Besides, the use of plant natural products used for control of tick population, entomopathogenic microbes such as fungi and bacteria are employed to kill ticks.[55] A number of biological control programs have been launched using natural enemies of ticks and microbial pathogens. Biological agents mainly tick predators are employed as a part of integrated pest management (IPM) for reducing tick population on livestock.[27] However, encapsulated conidia of entomopathogenic fungus *Metarhizium brunneum* exhibited significantly higher tick control.[56] *Metarhizium anisopliae* isolated from paddocks of cattle farms showed strong acaricidal effects against two populations of the cattle tick *R. microplus*.[57]

Besides this, Beauveria bassiana control various life stages of cattle tick Rhipicephalus microplus [Table 1].[58]

Ticks as main ectoparasite make severe loss to world economy as it directly affects meat, milk, and leather production, hence, its control is very essential.[59] Use of entomopathogenic fungal *M. anisopliae* kill host-seeking ticks or ticks on rodents and suppress *Ixodes scapularis* abundance in residential areas and reduce human tick bites. *M. anisopliae* fungus also more effectively controls tick infestation in pasture grazing cattle.[60] This fungus showed 100% control in lone star tick, *Amblyomma americanum* (L.) [Table 1].[61] Few wood ant species are also natural enemies of ticks and feed on tick larvae.[62] Similarly, *Bacillus thuringiensis*, *Beauveria bassiana,* and *M. anisopliae* are widely employed agents to control *Acarid* species, *Dermanyssus gallinae* and *Psoroptes* sp. [Table 1].[63]

INTEGRATED TICK MANAGEMENT (ITM)

For fast and effective control of tick population, ITM approaches are proved best options. These include conventional and recent methods of tick control. ITM consists of the systematic combination of at least two control technologies which could kill acaricide-resistant ticks. It assists in prevention of tick invasion in dairy cattle.[64] Hence, there is a need to develop alternative approaches, that is, cleanliness of farmyards, removing thick grass beds, use of animal husbandry practices, synergized pesticides, rotation of acaricides, pesticide mixture formulations, and manual removal of ticks. Other methods such as release of sterile male hybrids, environmental management, growing anti-tick plant canopies, and pasture management, and essential routine vaccination of farm animals could be employed.[65] Today, there are two important problems rising resistance against synthetic acaricides in tick populations and second poisoning of environment. Therefore, alternative tick control methods must be opted in form anti-tick herbal products, plant extracts, and essential oil components and bio-pesticides might represent a promising source of new acaricides.[66]

These methods can easily replace chemical acaricides might be proved highly useful in controlling population of various species of ticks[67] and will reduce the risk of contracting tick-transmitted diseases [Table 1].[68] However, development of phytoformulations using a mixture of various components/ingredients will be safer. Among other eco-friendly methods, employment of fungus *M. anisopliae* (TIS-BR03) to kill field population of acaricide-resistant strain of the cattle tick *R. microplus* was proved much better.[69] Use of biopesticides assists both in prevention of transmission of tick-borne diseases and environmental protection.[70] Further, identification of genes of interest with differential genomic expression may explore gene ontology, it will assist in exploration of "response to parasite" in the form of various transcripts which could be used for tick control by doing their putative inhibition [Table 1].[71]

There is a need for the development of eco-friendly pesticide alternatives (e.g., EcoSMART) and IPM techniques to reduce the hazardous impacts of pesticides.[72] In addition, the use of appropriate and safe usage with precautions in pesticide handling could minimize human exposure to pesticides and their potential adverse effects on the environment.[73] Few cultural practices such as removal of invasive vegetation, that is, *Amur honeysuckle*, *Lonicera maackii* Ruprecht (Dipsacales: Caprifoliaceae) and common buckthorn, *Rhamnus cathartica* Linnaeus (Rosales: Rhamnaceae) and deployments of permethrin-treated cotton nesting materials (tick tubes) especially target the white-footed mouse (*Peromyscus leucopus* Rafinesque) (Rodentia: Cricetidae). Killing of host mouse also significantly encounters tick larval population by 61%.[74] Similarly, a novel topical combination of fipronil, amitraz, and (S)-methoprene causes detachment of ticks in treated dogs.[75] The high repellency rate and the lethal efficacy of CERTIFECT(®) resulted in significantly fewer live attached ticks, consequently reducing blood intake and fluid exchanges.[76] A similar combination of imidacloprid 10% and permethrin 50% showed higher efficacy than fipronil 10% and methoprene 9% against immature larval stages.[77]

CONTROL BY PROTEASE INHIBITOR

R. (*Boophilus*) *microplus* possesses serine protease inhibitors (SPIs or serpins) a group of complex proteins secreted into their saliva during blood feeding to evade the host's hemostatic system.[78] These SPIs serine protease inhibitors modulate diverse and essential proteases involved in different physiological processes, that is, regulation of inflammation, blood clotting, wound healing, vasoconstriction, and the modulation of host defense mechanisms. These molecules represent highly suitable and attractive targets for the development of effective tick control strategies.[78] *Ixodes scapularis* tick serine proteinase inhibitor (serpin) is a large superfamily of structurally related, and functionally diverse proteins which control essential proteolytic pathways in many tick species [Table 1].[79]

EPIGENETIC CONTROL

Ticks live in diverse environments and transmit numerous pathogens among multiple hosts. Due to their long and unique life cycles, these arthropods likely evolved robust epigenetic mechanisms that provide sustainable responses and buffers against extreme environmental conditions.[79] Epigenetic regulation of tick biological processes is an essential element of the infection by *Anaplasma phagocytophilum*. However, few exogenous factors such as histones and histone modifying enzymes may use for the development of anti-tick drugs. Such drugs will more successfully control tick vector *I. scapularis*.[80] Further, genome sequence can assist in exploration of such histone genes, to inactivate or modify its activity.[81] Similarly, RNA interference and gene silencing of a putative immunophilin gene in the cattle tick *R.* (*Boophilus*) *microplus* can control larval population of ticks [Table 1].[82]

USE OF VACCINES

For effective control of tick population, vaccines produced against few novel antigens explored and identified. Vaccines generated against these novel assemblies of antigens may more effectively check pathogen transmission.[83] There is a need to develop commercialize anti-parasitic vaccines. Such vaccines will prohibit transmission of zoonotic parasites and could be effectively pathogen multiplication [Table 1].[84] Immunization with an immunogenic peptide of tick protein P0 greatly reduced survival of ticks.[85] P0 is a synthetic 20 amino acid peptide vaccine found highly effective against *R. sanguineus* infestations. This vaccine shows a significant diminution in the number of engorged females recovered, in the weight of females, and the weight of egg masses in cattle tick *R. Boophilus microplus.* The number of eggs hatched was also significantly reduced for the vaccinated group, with an overall effectivity for the antigen pP0 of 96%.[86]

A recombinant antigen Bm86 shows mode of immunity against *R. microplus* and *R. annulatus*. However, Bm86-based vaccine significantly decreased the exposition of bovines to babesiosis and anaplasmosis (Almazan *et al*., 2018).[87] Vaccination controlled 99.9% and 91.4% of the ticks in 8 weeks and 5.5 months after the initial vaccination, respectively. Enhanced use of such anti-tick vaccine is an important tool for the integrated eradication of the cattle fever tick, *R.* (*Boophilus*) *annulatus*.[88] There are transmission blocking vaccines which effectively and more sustainably control tick population. These also target pathogen reservoirs and disrupt enzootic cycles.[89]

ECOLOGICAL AND CULTURAL CONTROL

By controlling environmental and ecological changes re-emergence of tick-borne zoonotic diseases cab be controlled (TBDs).[90] *Rhipicephalus* species and its interactions with their host species depend on exposure and climatic conditions remain throughout the year. *Rhipicephalus* species are well established and ecologically adapted and maintaining its successful coexistence within human dwellings. Its population distribution and density depend on socioeconomic and environmental factors and the global climate predominantly in tropical and subtropical conditions. Tick interactions with their host species are influenced by ecological factors. If these are restored, tick population will decline because of decline in host population.[90] It will reduce vector presence and risk of infection in exposed populations.[91] More specifically, tick densities are strongly influenced by population density fluctuations in vertebrate host species and wildlife management.[92]

CONCLUSION

Ticks are major vectors of livestock and human pathogens. These have high medical and veterinary importance. Synthetic acaricides were used to kill large population of ticks in various parts of the world. These chemicals prove highly harmful to man and his environment. However, a serious problem of acaricidal resistance is developed due to repetitive exposure of chemical acaricides. There is felt an immense need of biodegradable acaricides of plant origin. These plant material-based phytoformulations displayed good acaricidal and repellent efficacy against natural population of ticks and put no adverse effect on environment and host body. Majority of these plants are holistic in action, economically affordable, user-friendly, easily adaptable and accessible, and environmentally friendly. These can be used to develop community-driven tick control interventions according to local conditions and specific to different livestock communities. Few microbes such as *B. thuringiensis*, *B. bassiana,* and *M. anisopliae* are the most widely employed as tick controlling agents. These reduce egg laying and hatchability in ticks. However, its feasibility in-field application and the effectiveness of the administration alone or combined with conventional and alternative herbal formulations must be tested in multiple-choice assays to know their efficacy level against ticks.

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CONFLICTS OF INTEREST

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