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Review article

A review on *Hyalomma* species infestations on human and animals and progress on management strategies

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ABSTRACT

The *Hyalomma* species of ticks have gained additional attention due to their role in the transmission of *Theileria annulata* infection in animals and the Crimean-Congo Haemorrhagic Fever (CCHF) virus in humans. Apart from these, many other pathogens viz., other species of *Theileria*, a few species of *Babesia, Rickettsia* and viruses are either maintained or transmitted by this tick species. The medium to large size species with longer proboscis has inflicted additional burden on the overall impact of tick infestations. Being a multi-host species, management of the species is very challenging. Presently, the traditional method of tick management using chemical acaricides is found insufficient and unsustainable. Henceforth, the overall burden of tick infestations and tick-borne diseases are increasing gradually. After the successful development of vaccines against cattle tick, *Rhipicephalus microplus*, the anti-*Hyalomma* vaccine is considered a feasible and sustainable management option. In the recent past research on herbal acaricides and its possible application for tick control seems promising. Other eco-friendly methods are still under experimental stage. The present review is focused on impact of *Hyalomma* species infestation on human and animal health with special emphasis on progress on its sustainable management.

1. Introduction

Globally, ticks and tick-borne diseases (TTBDs) are the major hurdles to enhance livestock productivity with the threshold being much higher in developing countries. The cumulative global losses incurred for the management of TTBDs are estimated at the tune of US $ 22–30 billion per annum (Minjauw and Mc Leod, 2003; Lew-Tabor and Rodriguez-Valle, 2016). The direct effect of tick infestations on hosts includes pyemia, toxicosis and paralysis which cause a cumulative projected loss of about US $ 500 million annually (Minjauw and Mc Leod, 2003; Chhillar et al., 2014). In addition, production losses due to tick infestations with respect to growth and milk production were estimated as 8.9 ml of milk and 1 g live weight gain per engorging female tick per day, respectively (Jonsson et al., 2001). Recently, due to climate change and other risk factors, TTBDs have risen insidiously, triggering heightened attention about their impact on human health. In concurrence to this, the Centre for Disease Control and Prevention (CDC) reported nearly doubling of TTBDs cases over 13 years (Rosenberg et al., 2018).

The ixodid tick species of the genus *Hyalomma* have major medical and veterinary significance in terms of health and economic impediment in the tropical and subtropical regions (Bakheit et al., 2012). The natural distribution of *Hyalomma* species is limited to Asian, African and European continents (Sands et al., 2017). Out of the 27 valid species of *Hyalomma* (Guglielmone et al., 2010), five species are widely distributed and recorded in all the three continents, seven species are restricted in Asia, five in Africa, nine in Asia-Africa and one in Africa-Europe. About 50% of the species can infest and transmit pathogens, most significantly, the Crimean Congo Haemorrhagic Fever (CCHF) virus in humans (Verma et al., 2011; Hornok and Horváth, 2012; Aktas et al., 2014; Gargili et al., 2017) and *Theileria annulata* in cattle (Robinson, 1982; Dumanli, 1989). Apart from that, *Hyalomma* species are also known for the maintenance and transmission of many other viruses, bacteria and protozoan pathogens to animals and humans.

Repeated applications of chemical acaricides are the backbone of tick management having limited efficacy (Chema, 1990; Pegram et al., 1991, 1993; Meneghi et al., 2016). The approach based on acaricide application suffers from many drawbacks such as repetition of applications, environmental pollution, acaricide residues in livestock products, selection of resistant ticks, non-availability of new generation acaricides in near future and high cost of development of new generation acaricides (de la

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Fuente and Kocan, 2006). It has been estimated that the cost of discovering and developing a novel product is around the US $ 100 million, with an average time requirement is 10 years (Graf et al., 2004). These issues enforced the scientific community to develop and introduce alternatives to acaricides that are consistent with the principles of sustainable TTBDs management (Willadsen, 2006; de la Fuente and Kocan, 2006; Merino et al., 2011; Ghosh et al., 2013). The alternative approaches are strategic use of effective acaricides; adoption of the resistance monitoring system for identification of zone-specific effective acaricides; biological control; use of phytoformulation; vaccines. The present review is focussed on direct and indirect impact *Hyalomma* ticks and its possible management strategies.

2. Impact of *Hyalomma* tick on human beings

Many species of *Hyalomma* are recorded from human and considered as zooanthrophilic, occasionally feed on a human. Apart from many unreported cases of human- *Hyalomma* association, some cases are well documented viz., *H. marginatum* (Keirans and Durden, 2001) and *H. truncatum* (Apanaskevich and Horak, 2008; Mathison et al., 2015).

Table 1. Zoonotic pathogens of public health importance transmitted and/or maintained by *Hyalomma* species.

Pathogens	*Hyalomma* species	Countries where pathogens detected in *Hyalomma* tick
Crimean-Congo Haemorrhagic Fever (CCHF) virus	*H. marginatum* (Jameson et al., 2012; Gargili et al., 2017; Duscher et al., 2018) *H. anatolicum* (Tajeri and Razmi, 2011; Gargili et al., 2017) *H. asiaticum* (Teng and Jiang, 1991) *H. dromedarii* (Hoogstraal et al., 1981) *H. rufipes* (Hornok and Horváth, 2012; Gargili et al., 2017) *H. truncatum* (Linthicumlt and Logan, 1994; Gargili et al., 2017) *H. turanicum* (Gargili et al., 2017) *H. impeltatum* (Bakheit et al., 2012)	Africa, Asia and Europe. like Crimea, Astrakhan, Rostov, Uzbekistan, Kazakhstan, Tajikistan, Democratic Republic of the Congo, Uganda, Mauritania, Iraq, the United Arab Emirates, Saudi Arabia, Pakistan, Iran, Bulgaria, Turkey, Russia, Spain and India (Whitehouse, 2004; Aradaib et al., 2010; Patel et al., 2011; Estrada-Peña et al., 2012; Messina et al., 2015; Akuffo et al., 2016; Al-Abri et al., 2017; Dowall et al., 2017; Negredo et al., 2017)
Dhori virus	*H. marginatum H. dromedarii* (Hoogstraal et al., 1981; Labuda and Nuttall, 2004; Lledó et al., 2020); *H. impeltatum* and *H. schulzei* (Al-Khalifa et al., 2007)	Egypt (Williams et al., 1973), Saudi Arabia (Al-Khalifa et al., 2007), Portugal, Russia (Lledó et al., 2020)
Kadam virus	*H. dromedarii* and *H. anatolicum* (Wood et al., 1982; Al-Khalifa et al., 2007)	Kenya, Uganda (Wood et al., 1982), Saudi Arabia (Wood et al., 1982; Al-Khalifa et al., 2007)
Sindbis virus	*H. dromedarii* and *H. impeltatum* (Al-Khalifa et al., 2007)	Saudi Arabia (Al-Khalifa et al., 2007)
Chick Ross virus	*H. dromedarii* (Al-Khalifa et al., 2007)	Saudi Arabia (Al-Khalifa et al., 2007)
Thogoto virus	*Hyalomma* spp. (Labuda and Nuttall, 2004; Mueller and Lormeau, 2018), *H. dromedarii, H. rufipes* (Kazimírová et al., 2017), *H. nitidum* (Lledó et al., 2020)	Egypt, Nigeria (Mueller and Lormeau, 2018), Central African Republic (Lledó et al., 2020)
West Nile virus	*H. marginatum* (L'Vov et al., 2002; Formosinho and Santos-Silva, 2006; Oehme et al., 2017)	Russia, Portugal (L'Vov et al., 2002; Formosinho and Santos-Silva, 2006)
Bhanja virus	*H. marginatum, H. detritum, H. dromedarii, H. truncatum and H. asiaticum* (Hubalek, 2009)	Central and southern Europe (Hubalek, 2009)
Venezuelan equine encephalitis virus	*H. truncatum* (Linthicumlt and Logan, 1994)	Experimental transmission study (Linthicumlt and Logan, 1994)
Rift Valley Fever virus	*H. truncatum* (Nchu and Rand, 2013)	Experimental transmission study (Linthicum et al., 1989), Africa (Nchu and Rand, 2013)
Anaplasma phagocytophilum	*H. aegyptium* (Pastiu et al., 2012)	Romania (Pastiu et al., 2012)
Ehrlichia canis	*H. aegyptium* (Pastiu et al., 2012)	Romania (Pastiu et al., 2012)
Coxiella burnetii	*H. aegyptium* (Pastiu et al., 2012) *H. dromedarii* (Rehácek and Brezina, 1968) *H. scupense* (Goddard, 2012) *H. truncatum* (Capponi et al., 1970)	Experimental transmission study (Rehácek and Brezina, 1968; Siroký et al., 2010), Senegal (Capponi et al., 1970), Romania (Pastiu et al., 2012)
Rickettsia aeschlimannii	*H. aegyptium* (Bitam et al., 2009), *H. dromedarii* (Demoncheaux et al., 2012), *H. marginatum, H. scupense, H. truncatum, H. rufipes, H. ditritum, H. impeltatum, H. exavatum* (Beati et al., 1997; Demoncheaux et al., 2012; Kumsa et al., 2015; Duscher et al., 2018)	Africa (Morocco, Zimbabwe, Niger, Mali, Algeria, Senegal, Ethiopia, Chad, Egypt, Sudan, Tunisia), Europe (Russia, Italy, France, Croatia, Portugal, Greece, Spain, Georgia, Germany, Turkey, Austria (Bitam et al., 2009; Demoncheaux et al., 2012; Duscher et al., 2018)
R. sibirica	*H. asiaticum, H. excavatum, H. truncatum, H. turanicum, H. marginatum* (Parola et al., 2001; Psaroulaki et al., 2005; de Sousa et al., 2006; Kleinerman et al., 2013; Keskin and Bursali, 2016)	Mongolia, Niger, Greece, Cyprus, Israel and Turkey (Parola et al., 2001; Psaroulaki et al., 2005; de Sousa et al., 2006; Kleinerman et al., 2013; Keskin and Bursali, 2016)
R. conorii	*H. albiparmatum* (Heisch et al., 1962), *H. rufipes, H. truncatum* (Mathison et al., 2015)	Kenya (Heisch et al., 1962)
R. rickettsii	*H. dromedarii* (Mohamed, 2000)	——
R. africae	*H. impeltatum* (Parola et al., 2013), *H. dromedarii* (Kernif et al., 2012), *H. aegyptium* (Gargili et al., 2012) *H. marginatum* (Wallménius et al., 2014)	Algeria, Egypt, Turkey, Italy, Greece (Abdel-Shafy et al., 2012; Kernif et al., 2012; Gargili et al., 2012; Wallménius et al., 2014)
Borrelia turcica	*Hyalomma aegyptium* (Kalmar et al., 2015)	Romania (Kalmar et al., 2015)

Many times tick bites are unrecognized but it may cause itching, pain, inflammation, redness and swelling at the site of the bite. *Hyalomma* species are also been involved in otoacariasis and tick paralysis in humans, for example, *H. brevipunctata, H. marginatum, H. isaaci* and other species of *Hyalomma* were recovered from patients having facial nerve paralysis, ear pain, swelling and inflammation around the ear (Edussuriya and Weilgama, 2003; Dilrukshi et al., 2004; Gurbuz et al., 2010; Doğan et al., 2012).

After mosquitoes, ticks are considered as the second most important arthropod vector in the transmission of pathogenic agents. In human, *Hyalomma* ticks act as vector of CCHF virus (Turell, 2007). Worldwide, *CCHFV* has been reported in 15 species of *Hyalomma* viz., *H. aegyptium, H. anatolicum, H. asiaticum, H. dromedarii, H. excavatum, H. impeltatum, H. impressum, H. lusitanicum, H. marginatum, H. nitidum, H. rufipes, H. schulzei, H. scupense, H. truncatum* and *H. turanicum* along with other ticks species through PCR/RT-PCR identification and/or by inoculation tick extract in mice (Gargili et al., 2017). At least eight species of *Hyalomma* such as *H. marginatum, H. dromedarii, H. rufipes, H. anatolicum, H. asiaticum, H. truncatum, H. turanicum* and *H. impeltatum* were recognized as potential vector competence for acquiring, maintenance and transmission of *CCHFV* (Bakheit et al., 2012; Mourya et al., 2012; Gargili et al., 2017; Deka, 2018; Spengler and Estrada-Peña, 2018). The CCHF is an acute, often fatal hemorrhagic fever (VHF) and the reported case fatality rate is 3 % to >30% (Ergonul, 2006; Yadav et al., 2016; Al-Abri et al., 2017; Gargili et al., 2017). The disease is endemic in Africa, Asia, Eastern Europe, and the Middle East and few sporadic outbreaks were also recorded in Kosovo, Albania, Iran, and Turkey. Recently, the westward expansion of the virus in Europe has been observed through detection of *CCHFV* in ticks and autochthonous human cases in Spain (Estrada-Peña et al., 2012; Negredo et al., 2017; Oteo and Palomar, 2018). During the last one decade, most of the outbreaks were reported from Pakistan, Iran, Sudan, India and Bulgaria (Whitehouse, 2004; Aradaib et al., 2010; Patel et al., 2011; Messina et al., 2015; Akuffo et al., 2016; Al-Abri et al., 2017; Dowall et al., 2017). Apart from *CCHFV*, other zoonotic important viruses and bacteria were also recorded sporadically in *Hyalomma* ticks in limited geographical areas (Table 1). But, further studies are to be done to define the vector competence and relationship between the geographic distributions of these ticks and pathogens. In Saudi Arabia, Al-Khalifa et al. (2007) reported various zoonotic viruses from different *Hyalomma* species like Sindbis in *H. dromedarii* and *H. impeltatum*; Chick Ross in *H. dromedarii*; Kadam in *H. dromedarii* and *H. anatolicum* and Dhori in *H. impeltatum* and *H. schulzei* but transmission potential of these species has not been confirmed. Bhanja virus, a member of family *Phenuiviridae* (Order: *Bunyavirales*) is transmitted to vertebrates through biting arthropods including ticks (Matsuno et al., 2013). It was first isolated from *Hemaphysalis intermedia* and later from different species of *Hyalomma* (Table 1) responsible for causing sporadic cases of febrile illness and encephalitis in humans (Vesenjak-Hirjan et al., 1980; Hubalek, 2009). Seroprevalence of Kadam virus in human and recognition of virus in *H. dromedarii* may be correlated but with a precaution that both the events are reported at two different geographical locations (Wood et al., 1982). Further, the Thogoto and Dhori viruses (family: *Orthomyxoviridae)* cause severe illness and even death in humans. Primarily, it is a 'tick--borne virus' but aerosol transmission could also possible in humans (Peng et al., 2017). Dhori viruses may cause a disease similar to avian influenza (H5N1) in humans (Li et al., 2008). The West Nile virus is mainly transmitted through mosquitoes and cause mild to severe disease with the involvement of brain (encephalitis) but the virus was also isolated from tick, *H. marginatum* collected from animals and birds (L'Vov et al., 2002; Oehme et al., 2017) and vector capacity of *H. marginatum* was established experimentally (Formosinho and Santos-Silva, 2006). Similarly, Venezuelan equine encephalitis virus (family: *Togaviridae*) is responsible for causing serious disease in horses and humans. The mosquitoes are the principal vector but experimental transmission of the virus through *H. truncatum* was also reported (Linthicumlt and Logan, 1994).

Tick-borne rickettsioses are recognized as emerging/reemerging zoonotic infections worldwide. *Rickettsia aeschlimannii* was first isolated from *H. marginatum* and characterized as spotted fever group rickettsia (Beati et al., 1997), later, it was detected in many other *Hyalomma* species. Other rickettsias of spotted fever group such as *R. sibirica, R. conorii, R. rickettsii* and *R. africae* were also isolated from various species of *Hyalomma* but the vector capacity of these species has not been confirmed (Nicholson et al., 2009). Similarly, *Coxiella burnetii, Anaplasma phagocytophilum* and *Ehrlichia* organisms were detected in *Hyalomma* but its vector competency has not yet been established. A spirochetes bacteria, *Borrelia turcica*, a reptile-associated borreliae, has been identified in *H. aegyptium* and tortoise which may be zoonotic though its pathogenicity is unknown (Kalmar et al., 2015).

3. Impact of *Hyalomma* ticks on animals

Hyalomma ticks are medium to large in size and have long mouthparts through which the species cause tissue damage and predispose conditions for myiasis and tick pyaemia. Though *Hyalomma* may cause significant impact through its painful bite, sucking of the large volume of blood leading to anaemia, tick worry and annoyance affecting the productivity of the animals but these parameters are rarely quantified. According to Balashov (1972), *H. asiaticium* may take about 8.856 ml of blood for repletion. Sajid et al. (2007) assessed the direct effect of *Hyalomma* ticks on animal productivity and reported an average daily increase of 1.15 L in milk yield per animal with 1.31 % more fat in acaricide-treated animals compared to *Hyalomma* infested animals. Moreover, the salivary toxin may cause dermatitis, paralysis and lameness viz., bites of *H. asiaticum* and *H. truncatum* cause lameness to lambs (Azizi and Yakhchali, 2006) and sweating sickness in animals (Jongejan and Uilenberg, 2004).

Besides these, *Hyalomma* ticks are transmitting and/or maintaining a number of bacterial, viral and protozoan pathogens (Bakheit et al., 2012). The major haemoparasitic pathogens causing babesiosis, theileriosis, and anaplasmosis in cattle are transmitted by the tick species and the economic impact of the diseases in the cattle production system is very high (Minjauw and Mc Leod, 2003; Jongejan and Uilenberg, 2004). Although *Hyalomma* species are not normally involved in the transmission of major pathogenic species of *Babesia* viz., *B. bigemina, B. bovis, B. divergens* and *B. major* but recently few genetically distinct *Babesia* like *Babesia* U sp., *Babesia* sp. Kashi 1 and 2, *Babesia* sp. Kayseri 1, *Babesia* sp. CS58, *Babesia* sp. Hy, *B. beliceri* and *B. ocultans* are recorded from *Hyalomma* spp. (Table 2). The equine piroplasmosis, an economically significant disease of equines, caused by *B. caballi* and *T. equi* are also transmitted by *Hyalomma* (*H. truncatum, H. anatolicum*). Similarly, different species of *Theileria viz.*, *T. annulata, T. lestoquardi, T. ovis, T. equi* and *T. camelensis* are also transmitted by *Hyalomma* spp. (Geevarghese and Dhanda, 1987; Lewis et al., 2005; Li et al., 2010). These haemoprozoans have mild to severe impact on animal productivity. Apart from haemoprotozoans, *Hyalomma* ticks are also maintained and/or transmit zoonotic rickettsial pathogens viz., *R. aeschlimannii, C. burnetii, R. conorii, R. sibirica, R. africae, A. phagocytophilum, A. marginale, A. ovis, A. central* and *Ehrlichia canis* to animals (Losos, 1986; Aubry and Geale, 2011; Bakheit et al., 2012; Goddard, 2012) (Table 2) but the tick species of the genus does not denote its active involvement in the transmission and/or maintenance of these pathogens in natural cycles. For most of these rickettsial pathogens, animals act as symptomless carrier/reservoir but some of the pathogens cause mild to severe diseases like Q-fever in ruminants caused by *C. burnetii*, granuloctic Anaplasmosis in livestock by *A. phagocytophilum*, Erythrocytic Anaplasmosis in ruminants by *A. marginale* and *A. ovis* and Canine Ehrlichiosis by *E. canis* in animals.

Almost all the viruses discussed under the heading 2 (Impact of *Hyalomma* tick on Human beings) are zoonotic, maintained in ticks and non-human vertebrate animals. Many other viruses have been isolated from the *Hyalomma* spp. infesting animals viz., Kadam, Chick Ross, Sindbis and Wanowrie viruses (Williams et al., 1973; Al-Khalifa et al.,

Table 2. List of pathogens of veterinary importance transmitted and/or maintained by *Hyalomma* species.

Hyalomma spp.	Pathogens list I[#]	Pathogens list II[##]
H. aegyptium	*Theileria annulata* (Ray, 1950) *Hepatozoon kisrae* (Paperna et al., 2002) *Hemolivia mauritanica* (Paperna, 2006) *Coxiella burnetii* (Siroký et al., 2010)	*Anaplasma phagocytophilum* and *Ehrlichia canis* (Pastiu et al., 2012) *Borrelia turcica* Sp. Nov. (Güner et al., 2004) *Borrelia burgdorferi* s.l. and *Rickettsia* spp. (Kar et al., 2011) *T. lestoquardi* (Vashishta et al., 1987)
H. anatolicum	*Theileria annulata* (Dhar et al., 1982; Lewis et al., 2005; Ica et al., 2007; Li et al., 2010) *T. equi* (Bhattacharyulu et al., 1975; Li et al., 2010), *T. lestoquardi* (Uilenberg, 1997; Kirvar et al., 1998; El-Azazy et al., 2001; Khalid and ElHussein, 2010), *T. ovis* (Li et al., 2010)	*Babesia* spp. (Guan et al., 2009), *Babesia* U spp. (Luo et al., 2003), *B. beliceri* (Chaudhuri et al., 1975), Karyana and Kundal viruses (Yadav et al., 2019)
H. dromedarii	*T. annulata* (Samish and Pipono, 1978; Ica et al., 2007) *T. camelensis* (Hoogstraal et al., 1981)	*C. burnetii* (Hoogstraal et al., 1981)
H. excavatum	*T. lestoquardi* (Hashemi-Fesharaki, 1997) *A. marginale* and *A. centrale* (Shkap et al., 2009)	*T. annulata* (Abdel-Shafy and Zayed, 2002; Aktas et al., 2004)
H. impeltatum	*B. ocultans* (Dipeolu &Amoo, 1984) *T. lestoquardi* (El-Azazy et al., 2001)	
H. imperessum	*B. ocultans* (Dipeolu and Amoo, 1984)	
H. lusitanicum		*A. phagocytophilum* (Kumsa et al., 2015)
H. marginatum	*B. ocultans* (Dipeolu and Amoo, 1984), *T. annulata* (Aktas et al., 2004; Samish and Pipono, 1978; Estrada-Pena et al., 2004)	*Babesia* sp. Kashi 1 and 2, *Babesia* sp. Kayseri 1, *Babesia* sp. CS58, *Babesia* sp. Hy (Aktas et al., 2014)
H. rufipes	*B. ocultans* (Gray and De Vos, 1981; Dipeolu and Amoo, 1984)	
H. scupense	*T. annulata* (Samish and Pipono, 1978; Aktas et al., 2004; Ica et al., 2007)	*C. burnetii* (Goddard, 2012)
H. truncatum	*B. ocultans* (Dipeolu and Amoo, 1984) *B. caballi* (Blouin and de Waal, 1989) Rift Valley Fever virus (Nchu and Rand, 2013) Venezuelan equine encephalitis Virus (Linthicumlt and Logan, 1994)	*C. burnetii* (Hoogstraal et al., 1981) Bhanja, Dugbe and Jos viruses (Hoogstraal et al., 1981)

Note: [#]Pathogens detected in *Hyalomma* tick and transmission potentials have been confirmed. [##]Pathogens detected in *Hyalomma* tick but transmission potentials have been not confirmed.

2007), but the potentiality of the tick species as an efficient biological vector has not been established.

Overall the direct and indirect impact of *Hyalomma* ticks on human and animal health is considerably high. An estimated control cost of US$ 239.5 million alone due to bovine tropical theileriosis (Minjauw and Mc Leod, 2003) has been projected for India. Moreover, control cost of ticks through chemicals and its consequences in the society posing serious challenges before the scientific community to develop country-specific strategies.

4. Management of *Hyalomma* species

4.1. Mechanical/Physical intervention

As a traditional practice, the animals are groomed to dislodge ticks from the body and are then killed mechanically through crushing, burning or dipping in insecticides/oils. This approach has many limitations especially for multi-host ticks where the collection of feeding larvae and/or nymphs from animals is very difficult. In addition to this, larvae and nymphs have weak host specificity (Nava and Guglielmone, 2013; Espinaze et al., 2015) can feed on rodents, birds etc. and are transmitting deadly pathogens to humans. The hand-picking and mechanical killing of ticks without taking proper biosafety precautions is not advisable.

4.2. Use of chemicals

Out of the existing tick management platforms, use of chemical acaricides form the backbone of the programme due to easy availability and application. The commonly available acaricides are organophosphates (OP) (chlorfenvinphos, chlorpyrifos, coumaphos and diazinon), synthetic pyrethroids (SP) (cypermethrin, deltamethrin, flumethrin, permethrin), amidines (amitraz) and phenylpyrazole (fipronil) etc. After the introduction of injectable/parenteral endectocides, macrocyclic lactones (ML), avermectin (Ivermectin, Doramectin) and milbemycin (Moxidectin) compounds, the use of MLs is increased significantly for the management of endo and ectoparasites. Consequent to the indiscriminate usage of acaricides, resistant tick populations have been developed and established (FAO, 2004; Li et al., 2004; Jonsson and Hope, 2007; Perez-Cogollo et al., 2010; Fernandez-Salas et al., 2012; Shyma et al., 2012; Kumar et al., 2014; Singh and Rath, 2014; Jyoti et al., 2016; Nandi et al., 2018). Both *Hyalomma* and *Rhipicephalus* species are simultaneously infesting same animals, but due to the change in life cycle pattern (multi-hosts) of former species, the resistance development was reportedly less in comparison to Rhipicephalids (Wharton and Roulston, 1970; Sangwan et al., 1993; Shyma et al., 2012; Singh et al., 2013; Nandi et al., 2015; Jyoti et al., 2015). In a comprehensive study, Shyma et al. (2012) reported level-I resistance to deltamethrin [Resistance factor (RF) = 1.79–4.62] in nine isolates and to cypermethrin in 10 isolates while resistance to diazinon was detected in six isolates out of 20 isolates collected from three agro-climatic regions of India. Singh et al. (2015) recorded cypermethrin and amitraz resistance while Gaur et al. (2016) recorded resistance to deltamethrin and diazinon in isolates collected from Punjab and Rajasthan states. Kumar et al. (2016) studied acaricide resistance in isolates collected from 10 districts of Rajasthan against deltamethrin, cypermethrin, diazinon through adult immersion test (AIT) and larval packet test (LPT) and concluded that *Hyalomma* ticks are developing resistance where intensive crossbred cattle

Table 3. List of plants evaluated for acaricidal/repellent properties against *Hyalomma* species.

Name of plant	Part of plant and solvent used	Ticks species	In-vitro efficacy	References
Artemisia herba alba Asso (Asteraceae)	Diethyl ether (DE), ethyl acetate (EA), hexane, and ethanol extracts of aerial parts	*H. dromedarii*	Against larvae LC_{50} = 0.0296 μg/μl (DE), 0.0022 μg/μl (EA), 0.369 μg/μl (hexane) and 0.018 μg/μl (ethanol)	Abdel-Shafy et al., 2007
A. herba alba (Asteraceae)	aerial parts	*H. aegyptium*	LC_{50} = 1.105 (eggs), 0.755 (larvae) and 0.0079 μL/mL (nymphs)	Laghzaoui et al., 2018
A. monosperma Del. (Tarragon)	Diethyl ether (DE), ethyl acetate (EA), hexane, and ethanol extracts of aerial parts	*H. dromedarii*	Against larvae LC_{50} = 0.0952 μg/μl (DE), 0.0636 μg/μl (EA), 0.0437 μg/μl (hexane) and 0.252 μg/μl (ethanol)	Abdel-Shafy et al., 2007
Azadirachta indica (Meliaceae)	NeemAzal F (Commercial product prepared from seed)	*H. excavatum*	Significant decrease in eggs hatching rate; LC_{50} = 1.0 % (newly hatched larvae), 0.5 % (unfed larvae) and unfed adults (1.6–3.2 %)	Abdel-Shafy and Zayed, 2002
A. indica A Juss (Meliaceae)	Neem oil and azadirachtin essential oil formulation	*H. dromedarii*	Significant effect on larva feeding, molting of nymph and molt ability at 2.5 μg/mL azadirachtin; Against adult contact LC50 is > 40.7 μg cm^{-2} and against larvae dipping LC_{50} = 5.0 μg/mL	Al-Rajhy et al., 2003
Calotropis procera (Asclepiadaceae)	A cardiac glycosidal (cardenolide) extract	*H. dromedarii*	Against larvae contact LC_{50} = 9.63 μg/cm^2 and dipping LC_{50} = 1.096 μg/mL	Al-Rajhy et al., 2003
Cymbopogon winterianus	Ethanolic extracts of leaves	*H. anatolicum*	Against larvae LC_{50} (leaves extracts) = 0.14 %	Singh et al., 2014
Digitalis purpurea L. (Scrophulariaceae)	A cardiac glycosidal (digitoxin) extract	*H. dromedarii*	Against larvae contact LC_{50} = 4.08 μg/cm^2 and dipping LC_{50} = 0.410 μg/mL.	Al-Rajhy et al., 2003
Eucalyptus camaldulensis Dehnh (river red gum)	Essential oil from leaves and flowering tops through hydrodistillation	*H. scupense*	100 % inhibition of reproduction of female at 6.250 μl/ml; Against larvae LC_{50} = 0.207 μl/ml, LC_{90} = 1.653 μl/ml and LC_{95} = 2.978 μl/ml)	Djebir et al. (2019)
E. globulus Labill (blue gum)	Essential oil from leaves and flowering tops through hydrodistillation	*H. scupense*	100 % inhibition of the reproduction in female at 6.250 μl/ml; Against larvae LC_{50} = 0.155 μl/ml, LC_{90} = 2.387 μl/ml and LC_{95} = 5.183 μl/ml	Djebir et al. (2019)
E. globoidea	dichloromethane extract of plant	*H. rufipes*	Significant repellent effects against adults (30–40 % of extract up to 120 min)	Magano et al. (2011)
Euphorbia aegyptiaca (Euphorbiaceae)	Diethyl ether (DE), ethyl acetate (EA), hexane, and ethanol extracts of aerial parts	*H. dromedarii*	Against larvae LC_{50} = 0.2595 μg/μl (DE), 1.511 μg/μl (EA), 0.763 μg/μl (hexane) and 0.6117 μg/μl (ethanol).	Abdel-Shafy et al. (2007)
Francoeuria crispa (Asteraceae)	Diethyl ether (DE), ethyl acetate (EA), hexane, and ethanol extracts of aerial parts	*H. dromedarii*	Against larvae LC_{50} = 1.069 μg/μl (DE), 0.455 μg/μl (EA), 0.849 μg/μl (hexane) and 0.656 μg/μl (ethanol).	Abdel-Shafy et al. (2007)
Geranium macrorrhizum (Geraniaceae)	Essential oils through hydrodistillation of arial part	*H. lusitanicum*	Against larvae LC_{50} = 1.37 mg/ml and LC_{90} = 2.87 mg/mL	Navarro-Rocha et al., 2018
Guierase negalensis (Combrataceae)	Leaves, Petroleum ether PE) and ethanolic extracts (EE)	*H. anatolicum*	100% failure of egg hatching: both PE and EE at 15%; IC_{50} for inhibition of hatchability: PE = 1.71 % and EE = 0.508 %; LC_{50} and LC_{99} (against larvae): PE = 2.08 and 14.09 % and EE = 0.787 and 11.054 %; 100 % inhibition of egg-laying of female: PE and EE = 15 %	Osman et al. (2014)
Haplophyllum tuberculatum (Rutaceae)	Essential oils from aerial parts	*H. dromedarii*	Against larvae LC_{50} = 0.5 %	Abdel-Shafy et al. (2007)

(*continued on next page*)

Table 3 (*continued*)

Name of plant	Part of plant and solvent used	Ticks species	In-vitro efficacy	References
Lavandula stoechas L. (lavender)	Essential oil from leaves and flowering tops through hydrodistillation	*H. scupense*	100 % inhibition of reproduction at 3.125 μl/ml; Against larvae LC_{50} = 0.253 μl/ml, LC_{90} = 2.212 μl/ml, and LC_{95} = 4.092 μl/ml	Djebir et al. (2019)
Mesembryanthemus forsskale (Aizoaceae)	Diethyl ether (DE), ethyl acetate (EA), hexane, and ethanol extracts of aerial parts	*H. dromedarii*	Against larvae LC_{50} = 0.611 μg/μl (DE), 1.646 μg/μl (EA), 0.294 μg/μl (hexane) and 0.380 μg/μl (ethanol).	Abdel-Shafy et al. (2007)
Nicotiana tabacum	Ethyl-acetate extract of plant	*H. rufipes*	Significant repellent effects on adult tick (40% v/w of extract for the first 40 min).	Magano et al. (2011)
Origanum floribundum Munby (oregano)	Essential oil from leaves and flowering tops through hydrodistillation	*H. scupense*	100 % inhibition of reproduction at 3.125 μl/ml; Against larvae LC_{50} = 0.131 μl/ml, LC_{90} = 0.982 μl/ml, and LC_{95} = 1.740 μl/ml	Djebir et al. (2019)
Reaumuria hirtella (Tamaricaceae)	Diethyl ether (DE), ethyl acetate (EA), hexane, and ethanol extracts of aerial parts	*H. dromedarii*	Against larvae LC_{50} = 124.68 μg/μl (DE), 16.417 μg/μl (EA), 8.382 μg/μl (hexane) and 23676.62 μg/μl (ethanol).	Abdel-Shafy et al. (2007)
Rosmarinus officinalis L. (rosemary)	Essential oil from leaves and flowering tops through hydrodistillation	*H. scupense*	100 % inhibition of reproduction at 0.781 μl/ml; Against larvae LC_{50} = 0.108 μl/ml, LC_{90} = 0.495 μl/ml, and LC_{95} = 0.761 μl/ml	Djebir et al. (2019)
SaturejathymbraL. (Lamiaceae)	Volatile essential oil collected from arial part of plant at flowering stage through hydrodistillation	*H. marginatum*	100 % adult tick mortality in 3 h at 40 μl/L	Cetin et al. (2010)
Senna italica subsp. arachoides (Fabaceae)	Ethyl acetate extract of root	*H. rufipes*	Against adult LC_{50} = 8.66 % (w/v) in 24 h and 3.59 % (w/v) in 48 h	Magano et al. (2008)
Tagetes minuta L. (Asteraceae)	Essential oil from aerial parts and flowers	*H. rufipes*	Repellent EC_{50} for male ticks = 0.072 mL/mL and for female = 0.070 mL/mL; Significant number of nymphs (60%) delayed in moulting	Nchu et al. (2012)
Thymus capitatus L. (thyme)	Essential oil from leaves and flowering tops through hydrodistillation	*H. scupense*	100 % inhibit the reproduction in femaleat 1.562 μl/ml; Against larvae LC_{50} = 0.058 μl/ml, LC_{90} = 0.358 μl/ml, and LC_{95} = 0.600 μl/ml	Djebir et al. (2019)
Vitex negundo	Ethanolic extracts of leaves and roots	*H. anatolicum*	Against larvae LC_{50} (root extract) = 1.27 % and (leaves extract) = 0.011 %	Singh et al. (2014)
Withania somnifera	Ethanolic extracts of leaves	*H. anatolicum*	Against larvae LC_{50} (ethanolic extracts) = 10.12 %	Singh et al. (2014)

population are reared and SP and OP compounds are used for the management of tick populations.

4.3. Biological control

Naturally, ticks have relatively few enemies, but the use of predators, parasites and pathogens viz., bacteria, fungi, spiders, ants, beetles, rodents, birds and other living organisms have been documented to limit tick populations. Amongst the 96 commercially active ingredients listed against pests based on microorganisms, 33 and 36 active ingredients are bacteria and fungi, respectively, and eight are entomopathogenic nematodes (Samish et al., 2004). The pathogenic effect of active ingredients of bacteria against ticks has been reported. For example, Brown et al. (1970) observed the pathogenic effect of *Proteus mirabilis*, a gram-negative bacterium on *Dermacentor andersoni*. Further, Hendry & Rechav (1981) reported a detrimental effect of *R. decoloratus* extracts containing bacteria (*Proteus* spp., *Klebsiella pneumoniae, Pseudomonas* spp., *P. mirabilis* and *Staphylococcus* spp.) on *H. marginatum* and on other ticks. Hassanain et al. (1997) studied the efficacy of spraying three commercial varieties of *Bacillus thuringiensis* (*B. thuringiensis kurstaki, B. thuringiensis israelensis* and *B. thuringiensis thuringiensis*) against adults of *H. dromedarii*. Among the three varieties, the LC50 of *B. thuringiensis kurstaki* (1200–2344 mg/ml) was most pathogenic against *H. dromedarii*. The eggs of both the tick species were highly susceptible to the bacterial infection. Researchers so far reported 20 natural fungal species, of which, the efficacy of *Beauveria* and *Metarhizium* species against ticks is well documented (Abdigoudarzi et al., 2009). Under the laboratory conditions, it was reported that *R. microplus* and *H. excavatum* larvae are more susceptible to 12 fungal strains than *R. sanguineus* larvae. However, engorged *R. microplus* and *R. sanguineus* females were more susceptible to entomopathogenic fungi in comparison to *H. excavatum* females (Gindin et al., 2003). Further, 100% susceptibility of eggs to fungi were also reported (Gorshkova, 1966; Monteiro et al., 1998; Kaaya, 2000). Elham et al. (2013) studied the effect of *Scopulariopsis brevicaulis* fungal spore suspension and culture filtrate on larvae, nymphs and adults of *H. anatolicum* and high mortality of larvae and reduced biotic potential of the adults was reported. Sun et al. (2011) collected 13 species of entomopathogenic fungi from different areas in China and reported <90%

efficacy of *B. bassiana* (B.bAT01, B.bAT17) and *M. anisopliae* strains against *H. anatolicum*.

El-Sadawy and Habeeb (1998) studied the effect of five strains of entomopathogenic nematode (EPNs); *Steinernema* spp. on *H. dromedarii* engorged nymphs and reported strain S1 has a lethal effect after 7-day post infestation. Similarly, the lethal effect of IS-5 strain of *Heterorhabditis indicus* was reported on both engorged nymphs and unfed adults of *H. excavatum* at a concentration of 250 nematodes/cm^2 within 2–3 days (Samish et al., 1999, 2000). El-Sadawy et al. (2008) studied two families of EPNs; Heterorhabditidae and Steinernematidae against *H. dromedarii* and higher efficacy of *Heterorhabditid* strains (12–92%) than *Steinernematid* strains (4–88 %) were recorded. Although promising results were reported in *in vitro* conditions, the *in vivo* efficacy data is almost non-existing. There is a need to have research collaboration between laboratories involved in the exploration of biocontrol agent and tick experts to establish the *in vivo* efficacy of the biocontrol agent as a part of the integrated tick management (ITM).

4.4. Phytoformulation

Literature reveals about 356 species of plants belonging to 105 families have been evaluated against 31 tick species worldwide. In most of the cases *R. microplus* was used as model parasite in in-vitro model and the subject has been reviewed time to time (Benelli et al., 2016; Wanzala, 2017; Nwanade et al., 2020). Due to the vastness of the subject and the focused area of the present review, the results obtained by different groups is tabulated in Table 3. As observed in the case of *R. microplus*, a number of solvent guided extracts and essential oils were extracted from aerial parts of different plants and very high level of antitick activity up to 100% was recorded. In general, plant-derived products are having many advantages over the chemical acaricides such as low mammalian toxicity, short environmental persistence and complex chemistry that limit the development of resistance against them (George et al., 2014). But, along with advantages, plant products are also having drawbacks such as variable efficacy, chemically less-stable and limited residual activity, often due to photosensitivity or high volatility (George et al., 2014).

Although there has been a considerable progress in the recent past in natural product development research, most of the findings were restricted to *in-vitro* studies. The effects of geographical and climatic variations on the chemical constituents within the same plant species and identification of activity-based marker compound for quality assurance are the two key important impediments in large scale development of a natural formulation for the management of ticks. In our recent multi-centered studies we observed a very wide variation of 10–90% in antitick activity of the same plant extracts prepared from 177 accessions collected from 17 states of India. The variations in antitick activity has recently been attributed to the variation in key compounds present in the extracts (Ghosh unpublished data). One more hurdle is expensive toxicology testing for new products which may have limited intellectual property (IP) protection. Other challenges include the economical supply of plant product, biased perception regarding chemical acaricides vis-à-vis phytoformulation, quality protection after exposing to sunlight.

4.5. Immunization of hosts

Acquired resistance in ticks is expressed as reduced engorgement weight, increased duration of feeding, decreased number and viability of ova, blockage of moulting and death of feeding ticks (Wikel, 1996). During 1979, Allen and Humphreys conducted a preliminary experiment of immunization of cattle and guinea pigs using extracts of the gut and internal organs of *D. andersoni* and recorded protective efficacy against homologous challenge infestations (Allen and Humphreys, 1979). Thereafter, several researchers started working on the development of an anti-tick vaccine. However, in most of the cases, *R. microplus* was used as model parasite and consequently, majority of publications are dealt with *R. microplus* alone and the subject has been reviewed time to time. On the other hand, limited information is available against the multi-host tick, *H. anatolicum* (Willadsen, 2004; de la Fuente et al., 2007; Parizi et al., 2012; Lew-Tabor and Rodriguez-Valle, 2016; de la Fuente, 2018; Manjunathachar et al., 2014).

Earlier, Gill et al. (1986) reported the involvement of salivary proteins of *H. anatolicum* in hypersensitivity reaction as an indicator of resistance against homologous challenge in rabbits. Subsequently, several workers reported comparatively higher adaptive immunity in laboratory animals than in natural hosts (Ribeiro, 1989). Momin et al. (1991) and Singh et al. (1991) reported significantly adverse effect on ticks fed on animals repeatedly infested with *H. anatolicum* and reconfirmed the earlier observations of Gill et al. (1986). Ghosh et al. (1998) immunized rabbits with extracts of larvae and nymphs and a significant reduction in the engorgement percentage, engorgement weight and egg masses in ticks fed on immunized animals compared to ticks fed on a control group of animals was recorded. A significant reduction of nymphs (91.3%) and adults (79.7%) fed on calves immunized with 39 kDa larval antigen (Ghosh et al., 1999) while, 84.2%, 61.4% and 58.7% rejection of larvae, nymphs and adults, respectively, in ticks fed on animals immunized with 39 kDa nymphal antigen (Sharma et al., 2001) was reported. Further, the protective efficacy of cocktails of three polypeptides of 100, 59.4 and 37 kDa isolated from larvae of *H. anatolicum* was assessed in calves and significant protection of 70.6 %, 54.5 % and 61.9 % against the homologous challenge of larvae, nymphs and adults, respectively, was recorded (Das et al., 2000). Subsequently, Das et al. (2003) used a mixture of 106.8 and 68 kDa antigens isolated from midgut extract of *H. anatolicum* and reported 74.4 % and 52.2 % decrease of nymphs and adults, respectively, after challenge infestations on cattle. In the same year, Singh and Ghosh (2003) isolated 34 and 29 kDa glycoprotein from unfed larvae of *H. anatolicum* and *R. microplus*, respectively, and reported the direct effect of immunization (DT %) of 69 % and 52 % against larvae and adults of *H. anatolicum* and 60 % against *R. microplus* adults. Hakim et al. (2011) evaluated three major glycoproteins (97, 66 and 40 kDa) purified from *H. dromedarii* adults and larvae and demonstrated 63–67 % reduction in egg hatchability of ticks fed on immunized animals in comparison to ticks fed on control animals.

Successively, transmission-blocking potentiality of antigens was studied viz., Das et al. (2005) used 37 kDa larval antigen of *H. anatolicum* and recorded reduced level of *T. annulata* infection in ticks fed on immunized calves compared to control groups. The results were substantiated through staining of salivary glands of challenged ticks, polymerase chain reaction (PCR) amplification of *T. annulata* specific 721 bp gene segment (30 kDa major merozoite surface antigen gene) and *in vitro* infectivity study on bovine mononuclear cells. Overall they concluded that a partial reduction in the growth rate of *T. annulata* in ticks is possible by immunization of hosts with 37 kDa larval antigen.

Though a lot of work has been done with native antigens but most significant results were obtained after the discovery of Bm86 molecules from *R. microplus* and development and commercialization of Bm86-based vaccines as TickGARD/Gavac against *R. microplus* infestations on cattle (Willadsen et al., 1989; de la Fuente et al., 2007). On the similar line, protective efficacy of homologue of Bm86 gene in *Hyalomma* species was studied. For example; de Vos et al. (2001) identified a homologue of Bm86 in *H. anatolicum* and reported 50 % protection against *H. anatolicum* by limited immunization trial. Subsequently, Ebrahimi et al. (2012) successfully established the presence of cross-reactive epitopes between Bm86 and HAO3 antigens of *H. anatolicum*. Said et al. (2012a) cloned and characterized the Hd86 antigen from *H. scupense*, an ortholog of the Bm86 gene and reported very low intra-specific diversity in amino acid sequences of Hd86 of different isolates of *H. scupense* of Tunisia and a 59.1 % protection against the nymphal stage of *H. scupense* and no protection against adults was reported (Galai et al., 2012). To explain the variation in results, Said et al. (2013) determined the expression profile of Hd86 in different stages and demonstrated a significant reduction ($p < 0.001$) in the number of transcripts level during the feeding period and particularly after moulting to adults (12.78 and

9.25 fold in unfed males and unfed females) respectively. Lower Hd86 mRNA levels in adult ticks may result in lower protein levels in immunized animals. Concurrently, Said et al. (2012b) studied Bm86 ortholog in four different *Hyalomma* species, viz., *H. marginatum* (Hm86), *H. excavatum* (He86), *H. dromedarii* (Hdr86) and *H. scupense* (Hd86-A1) and suggested that Hd86-A1 vaccine candidate might be more appropriate to target *Hyalomma* tick species in contrast to Bm86 commercial vaccines. Kopp et al. (2010) raised series of monoclonal antibodies against synthetic peptides of BD86, a Bm86 homologue of *R. decoloratus* and detected strong signal of one of the antibodies (mAbs 12.1) in immunohistochemical analyses with the gut of four species of ticks including *H. anatolicum*. But no further progress was reported to exploit the observation. Further, Haa86, a Bm86 homologue of *H. anatolicum* was generated and tested against homologous challenge infestations. The protective efficacy was variable from 47- 60% against larvae and 40–80% against adults (Azhahianambi et al., 2009a, 2009b; Jeyabal et al., 2010; Kumar et al., 2012a). Recently five antigens namely; Subolesin (SUB), Calreticulin (CRT), Cathepsin-L like cysteine protease (CathL), Ferritin 2 (FER2) and Tropomyosin (TPM) ortholog of *H. anatolicum* were selected based on their established role in tick physiology and metabolism in different tick species. A very low level of variation of 0.6–2.4 %, 0.3–1.8 %, 0.3 to 6.4, 0.1–0.6% and 0.1–1.3 % in the deduced amino acid sequences of various field isolates of *H. anatolicum* was observed in SUB, CRT, CathL, FER2 and TPM genes, respectively. Similarly, the amino acid sequence identity for the same genes in other ticks species was 77.4–99.3 %, 85.1–99.7 %, 57.5–89.5 %, 80.1–90.9 % and 98.8–99.9 % against reference *H. anatolicum* IVRI II strain (Kumar et al., 2017; Manjunathachar et al., 2019).

Following transcriptomic analysis of SUB, CRT, CathL, FER2 and TPM genes revealed that amongst all the life stages except in eggs and frustrated females, the differences in fold change in expression (FCE) of SUB gene was not significant ($p > 0.05$). In eggs and in frustrated females (tick released on animal but not allowed them to feed for 24 h), relative expression of SUB gene was significantly ($p < 0.05$) higher than in engorged larvae, nymphs, females and in unfed males. The differences in FCE of CRT gene were not significant ($p > 0.05$) in all the life stages except in fed males and in between engorged larvae and females. The FCE of CathL gene was ($p < 0.001$) highest in frustrated females followed by unfed females than in all other stages while differences in FCE were not significant ($p > 0.05$) among all the other stages except in between eggs and larvae. Similarly, in FER2, only statistically significant ($p < 0.01$) low FCE was recorded in eggs. Unlike FER2, the FCE of TPM gene was significantly ($p < 0.001$) higher in fed larvae, nymphs, females, males and in the unfed adult stage ($P < 0.01$) (Kumar et al., 2017; Manjunathachar et al., 2019). The functional properties of the genes were studied by RNA interference (RNAi) technology and following immunization of animals with recombinant proteins, SUB, TPM, FER2, CRT and CathL, 65.4%, 63.7%, 51.7 %, 41.3% and 30.2%, respectively, protection against larvae was observed. However, against adults, the TPM and FER2 proteins were more effective (Kumar et al., 2017; Manjunathachar et al., 2019). The results of different immunization studies clearly indicated that the majority of the experiments were conducted using the homologous challenge system and the protective efficacy of the antigens was variable. Further, it is emphasized that a multi-antigenic vaccine involving multi-targets is the suitable option for getting significant cross-protection against heterologous challenge (Schetters and Jansen, 2015, PCT/EP2014/056248).

In an attempt to develop cross-protective vaccine, Rodriguez-Valle et al. (2012) immunized cattle and camels with rBm86-based vaccine and challenged with *H. dromedarii* and *A. cajennense* ticks and recorded partial efficacy against former tick and no effect against later tick species. Similarly, cross-protective efficacy of Gavac™ was assessed against *H. anatolicum*, Indian isolate and 25 % efficacy was recorded (Kumar et al., 2012b). The cross-protective efficacy of rHaa86, SUB, CRT and CathL was also tested against *R. microplus* but the results were not much encouraging and revealed that the species-specific vaccine is more efficacious (Kumar et al., 2017). Ideally, a cross-protective anti-tick vaccine is an appropriate strategy towards simultaneous control of multi-tick species but for region-specific management of the vector of animal and human pathogens, a vaccine against *H. anatolicum* has a distinct position in tropical and sub-tropical countries including India.

5. Integrated control strategies

As an alternative to acaricides, a number of methods including the maintenance of hosts naturally resistant to ticks, pheromone-impregnated decoys for attracting and killing ticks, biological control using natural enemies, resistance monitoring and strategic application of effective acaricides, natural anti-tick formulation and vaccines are in use (Hanifah et al., 2011; Silva et al., 2009; Madzimure et al., 2011; Merino et al., 2011; Willadsen, 2006; de la Fuente and Kocan, 2006; Ghosh and Nagar, 2014; Kumar et al., 2020). Vaccine-controlled field trials in combination with acaricide treatment demonstrated that an integrated approach resulted in significant management of tick infestations while reducing the use of acaricides (de la Fuente et al., 2007; de la Fuente and Kocan, 2003). These trials proved that management of ticks by vaccination has an added advantage in terms of cost-effectiveness, safety and for preventing the selection of drug-resistant ticks (de la Fuente et al., 2007; Rodriguez-Valle et al., 2004). Cost-effective analysis of the vaccine in the integrated tick management system revealed a 60% reduction in the number of acaricidal treatments, increased milk production capabilities and a preventive effect on the transmission of babesiosis in vaccinated herds resulted in savings of US$ 23.4 /animal/year (de la Fuente et al., 1998). At present, there is no vaccine available against *Hyalomma* tick and dependency on acaricides is increasing. Henceforth, to reduce the dependency on acaricides and management of ticks in a sustainable manner following strategies can be taken:

1. Regular monitoring of resistance using bioassay, biochemical and molecular assays.
2. Formulation of region-specific tick management strategies on the basis of resistance data.
3. Use of characterized phytoformulations;
4. Rearing of local poultry birds, voracious feeder of tick stages, along with animals;
5. Pasture spelling/burning, wherever possible;
6. Prevention of invasion of wild animals into pasture areas.

Though, implementation and monitoring of ITM is a difficult task in most of the countries. It is necessary to implement ITM at the policy level regions/sector-wise and in a phased manner to increase the level of acceptability of the technology at farmer level.

6. Future prospects

Literature reveals the acaricide resistant status in *Hyalomma* species is comparatively less in comparison to *R. microplus* and most of the SP and amidine compounds are still working against the species. This is because of the multi-host life cycle of the vector and exposure to different chemicals is comparatively less in comparison to one host tick. However, since co-infestation is the common features in many tropical and sub-tropical countries, the species will definitely develop resistance against a wide range of chemicals in the coming years. A vaccine against *H. anatolicum* can be an effective sustainable measure along with strategic use of natural formulations. Significant lead has been reported but due to severe shortage of funding opportunities in tick vaccine research

globally, the work is not progressing in ladder manner. There is an urgent need to increase funding support for research on one health concept in which vaccine against *Hyalomma* spp. forms a focused area of research. The different groups working on tick vaccine globally should come together in a consortium mode to develop suitable immunoprophylactic measures to mitigate the burning problem of ticks and tick-borne diseases.

Declarations

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

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Additional information

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