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Review

Plant extracts to control ticks of veterinary and medical importance: A review

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ABSTRACT

Farmers in developing countries are faced with many diseases that limit the productivity of their animals, many of these are caused by tick infestations. Years of use and overuse of available chemical ectoparasiticides have resulted in the large scale development of resistance in these parasites as well as negative environmental impacts. To reduce these impacts, much focus has been placed on the search for alternative, environmentally friendly parasite control strategies with lower chance of the development of resistance. Many rural farmers have used plants to control ticks. In some cases the traditional use has been confirmed, in other cases, only the traditional use has been documented. A review of published scientific articles was conducted for medicinal plants with *in vitro* acaricidal or tick-repellent activities against immature and adult stages of ticks. Veterinary databases (All Databases, CAB Abstracts and Global Health, Medline, Pubmed, Web of Science, BIOSIS Citation Index, Science Direct, Current Content Connect and Google Scholar) were used. The search words included “acaricidal”, “tick-repellent”, “medicinal plants”, “phytomedicine” and “anti-tick assays”. More than 200 plant species from several countries globally have tick-repellent or acaricidal properties using *in vitro* assays. The different extractions and plant parts used as well as the efficacy where available is listed. Species including *Azadirachta indica*, *Gynandropsis gynandra*, *Lavendula augustifolia*, *Pelargonium roseum* and *Cymbopogon* spp. had good acaricidal and larvicidal effects with 90–100% efficacy, comparable to those of currently used acaricides. A number of active compounds such as azadirachtin, carvacrol, linalool, geraniol and citronellal have been isolated. Based on their wide use by rural livestock farmers, plant-based compounds may be a good source of effective acaricidal preparations either as an extract or as a source of new acaricidal compounds. The focus may have to be on acaricidal rather than on repellent activities to facilitate control of ticks.

Contents

1. Introduction

In the tropics and sub-tropics, small-scale and emerging farmers own approximately 40% of the national livestock herds/flocks (Keyyu

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et al., 2003). These farmers are faced with many constraints that limit the productivity of their animals. The prevalence of ticks and tick-borne diseases particularly in the wet seasons (Keyyu et al., 2003) is an important restraint. Ticks, which are haematophagous ectoparasites, have a wide range of hosts and geographic diversity. They transmit protozoan, bacterial, rickettsial and viral diseases and are among the most important vectors of diseases which can be severely debilitating or fatal to livestock, humans and companion animals (Walker et al., 2003; Jongejan and Uilenberg, 2004).

Ixodid ticks such as *Amblyomma variegatum* Fabriscius, *Rhipicephalus appendiculatus* Neumann and *Rhipicephalus* (*Boophilus*) *microplus* (Canestrini, 1888) in particular are among the most economically important parasites in the tropics and subtropics (Bram, 1983). Tick-borne protozoan diseases such as theilerioses and babesiosis and rickettsial diseases such as anaplasmoses and cowdriosis are the most common diseases of small and large ruminants affecting the livelihoods of farming communities in Africa, Asia and Latin America (Jongejan and Uilenberg, 2004). In addition to transmitting diseases, heavy infestations of ticks can cause a reduction in live weight, anaemia and losses in milk production in domestic animals, while tick bites themselves result in damage to hides (Rajput et al., 2006).

Due to severity of the diseases transmitted by ticks a substantial proportion of the annual input costs by many livestock keepers go into the management and control of ticks and tick-borne diseases (Kaaya and Hassan, 2000). While the true economic losses are not easily quantifiable, losses were estimated at US$720 million, US$100 million and US$1 billion per year for Africa, Australia and South America respectively (Horn, 1987; Cobon and Willadsen, 1990; Kaaya and Hassan, 2000; Minjauw and McLeod, 2003). When losses per disease are looked at, *Theileria* control in eastern, central and southern Africa was estimated at US$168 million annually, while the annual cost of tropical theileriosis management in India was estimated at US$384.3 million. The *Theileria* parasite has also been implicated as the cause of annual production losses in excess of US$200 million in small scale and traditional farming communities of Kenya and Tanzania (Mukhebi et al., 1992; Kivaria, 2006). While less substantial than *Theileria*, losses from heartwater were estimated at US$6 million *per annum* in Zimbabwe over a 10-year period from the cost of acaricides, milk losses and treatment costs (Coetzer et al., 1994). Based on this information, it is evident that ticks and the diseases they transmit are a major constraint to the improvement of the livestock industry, particularly in developing countries, where they contribute to food insecurity. Due to financial devastation caused by ticks and tick-borne diseases, animals infected are often treated by the farmer with either an allopathic or herbal remedy.

Current control programmes are largely based on the use of commercially available chemicals such as the arsenicals, chlorinated hydrocarbons, organophosphates, carbamates, formamidines, pyrethroids, macrocyclic lactones, and more recently the insect growth regulators (George et al., 2004). Arsenicals were effectively used globally to control ticks for 30 to 40 years prior to the development of resistance in *Boophilus* ticks (George et al., 2004). While these products were inexpensive, stable and water-soluble, they were characterized by short residual effects of less than one or two days and were also environmentally destructive (Drummond, 1960). The arsenicals were eventually replaced by the chlorinated hydrocarbons between 1945 and 1955. The chlorinated hydrocarbons were characterized by a long residual effect and were very effective. Unfortunately these molecules were very stable and persisted in the environment and tissues of treated livestock for fairly long periods (Connell et al., 1999). The product also had a major knock-on effect on predators higher in the food chain prompting their eventual withdrawal (Spickett, 1998). Organophosphates, an esteric compound of phosphoric acid synthesis, supplemented organochlorines in the 1955–70s. In contrast to the organochlorines, they were characterized by a shorter residual effect, lower environmental persistence but substantially higher acute toxicity in livestock and by 1963, resistance was reported (Wharton, 1967).

Formamidines, chlordimeform, clenpyrin and chloromethiuron, are members of a small group of chemicals that are effective against ticks (George et al., 2004). Chlordimeform was introduced in Australia as an additive to organophosphates in dipping vats to restore their efficacy on organophosphate-resistant tick strains (Nolan, 1981). It was later withdrawn from the market because of evidence of carcinogenicity (Ware, 2000). Results of successful tests of amitraz for the control of *R.* (*B.*) *microplus* on cattle in Australia with an experimental formulation (BTS 27 419) were reported in 1971 (Palmer et al., 1971). Subsequent trials with commercial amitraz formulations in Australia (Roy-Smith, 1975) and in the United States of America (George et al., 1998) proved the efficacy of the acaricide against *R.* (*B.*) *microplus*. A series of trials executed over a five-year period in South Africa proved the effectiveness of amitraz for the control of *B. decoloratus*, *R. appendiculatus*, *R. evertsi* and *A. hebraeum* (Stanford et al., 1981).

Macrocyclic lactones are acaricides with potent insecticidal activity which were first described in 1978 (Burg et al., 1979). Two classes of macrocyclic lactones with acaricidal activity are the avermectins (ivermectin, eprinomectin), which are derivatives of the actinomycete *Streptomyces avermitilis* and the milbemycins, derived from fermentation products of *Streptomyces hygroscopicus aureolacrimosus* (Lasota and Dybas, 1991). Macrocyclic lactone acaricides are efficacious, but their high cost limits their use (Kemp et al., 1999). Fipronil, a phenylpyrazole compound; fluazuron, a benzoyl phenyl urea; spinosad represents new pesticides, but because of the persistence of residues in fat, it is necessary to withhold treated cattle from human consumption for up to six weeks after use (Bull et al., 1996).

The issues mentioned above have motivated the search for alternative parasite control strategies that are potentially environmentally friendly with fewer negative consequences to the animal being treated. Principal among these alternatives are the plant-based treatment protocols as the healing effect of plants has been explored for thousands of years (Chopra, 2003; Wang and Li, 2005). Other proposals for the full development of medicinal plants as tick repellents/acaricides has been advocated (Gassner et al., 1997) as plants inherently have a number of protective mechanisms to combat predator and pathogen attacks. These include repellency through production of hairs and volatile compounds such as cis-Jasmone (Birkett et al., 2000), 1, 8-cineole (Klocke et al., 1987); and production of chemicals with arthropocidal activities such as I-menthone from *Mentha piperita* L. (Croteau and Winters, 1982; Silva-Aguayo, 2006). These phytochemicals act in different ways, such as counteraction of growth regulatory hormones, inhibition of egg development, disruption of mating and sexual communication, and inhibition of chitin formation (Katoch et al., 2007; Chagas et al., 2012). A number of plant-derived novel antiparasitic drugs have already made significant contributions to human and animal health such as quinine, the oldest antimalarial drug, obtained from the South American plant, *Cinchona officinalis* L., and artemisinin from *Artemisia annua* L. (Ronald and Acton, 1987).

Pyrethrum derived from the dried flower heads of *Chrysanthemum cinerariifolium* (Trev.) Vis and *Chrysanthemum coccineum* has been used for centuries as an insecticide and lice remedy in the Middle East (Casida, 1980). More importantly, pyrethrum provided the backbone for the synthesis of more potent synthetic pyrethroids. The 1st generation pyrethroids (bioallethrin, tetramethrin, resmethrin and bioresmethrin) developed in the 1960s, following the elucidation of the structures of pyrethrin I and II, its main pesticidal components (Isman and Machial, 2006). The third generation of this class of chemicals, permethrin and fenvalerate, were the first of these products available for control of ticks on cattle (Davey and Ahrens, 1984; Ware, 2000). Cypermethrin and deltamethrin are examples of fourth generation cyano-substituted pyrethroids that are effective acaricides (Stubbs et al., 1982; Kunz and Kemp, 1994; Aguirre et al., 2000). Pyrethroids now constitute the majority of commercial household insecticides and their activity is often enhanced by addition of the synergist piperonyl butoxide, a known inhibitor of key microsomal cytochrome