Development of eco-friendly natural formulation for management of resistant tick infesting animals and humans

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Abstract
Almost all livestock species are suffering from tick infestations. Ticks are voracious blood suckers, causing significant blood loss in livestock resulting low productivity in terms of weight gain and milk yield, increased mortality and low-quality hides. Ticks also serve as the major vector of economically important diseases like babesiosis, theileriosis and anaplasmosis. The use of synthetic acaricides of different classes is the backbone of tick management programme. But indiscriminate application of these chemicals has led to the development of resistance against commonly used synthetic acaricides.

It is become a challenging task to manage tick infestations using existing resources. The present study was undertaken to develop green nano formulation for mitigation of the resistant problem. The characterized green nano-formulation may be a suitable alternative to minimize the excessive use of chemical acaricides. The use of synthetic acaricides of different classes is the backbone of tick management programme. But the indiscriminate application of these chemicals has led to the development of resistance against commonly used synthetic acaricides.

Keywords: Natural formulation, Ticks, multiacaricides, resistance etc.

1. Introduction
Ticks are obligate blood-feeding ectoparasites of mammals, birds and reptiles, distributed worldwide and are of major medical and veterinary importance. The association between ticks and disease was first demonstrated when Smith and Kilbourne proved in 1893 that Texas cattle fever was caused by a protozoan transmitted by an infected tick. Ticks are the most potent and versatile vector of pathogenic microorganisms and are second to mosquito as vector of a number of human pathogens, like viruses, bacteria, rickettsia, spirochetes, etc, and the most important vector of pathogens affecting livestock worldwide [1]. In humans, tick infestations typically involve few specimens and the greatest risk for people bitten by a tick lies in infection due to a tick-borne pathogen. So, tick control has become a challenge to researchers exploring a sustainable way to mitigate the problem of tick infestations. In spite of some drawbacks of use of chemicals for tick management, acaricides are still remaining a primary tool in tick management platform. Currently, there are 104 acaricides comprising five chemical groups and 22 different active ingredients registered for use [1].

1.1 Resistance to Chemical compounds
In India, due to the indiscriminate and repeated application of chemical acaricides, ticks have already developed resistance to commonly used OP and SP compounds. Based on questionnaire survey made by reported the possibility of development of large scale acaricidal resistance in ticks infesting livestock animals in India [2]. This estimation has been proved by many reports recently published showing high level of deltamethrin, cypermethrin, diazinon and amitraz resistance in tick species collected from different agroclimatic regions of the country [3-7]. Similarly, slow emergence of tick populations resistant to amitraz and macrocyclic lactones has also been reported [4,8]. For determination of frequency distribution of gene conferring resistance in Indian cattle ticks against pyrethroids (deltamethrin, cypermethrin), efforts are underway to develop genotyping tool [5]. Further, the application of commonly used acaricides for tick management is not working in surveyed area as reported by a number of farmers and animal owners. The other tick control strategy needs to be explored for the control of resistant tick population in different parts of the country.

1.2 Need of eco-friendly natural formulation
As Indian R. microplus population has developed resistance to multiple acaricides identification of new molecules having different mode of action alone or in synergy in the presence of additives/
inhibitors is one of the key researchable areas [9,5,10,11,3,4,8]. One of the parameters i.e., assessment of tissue or cellular level changes induced by synthetic or natural formulations is considered as an important tool for better understanding on the effect of the molecule on morpho-physiology and biology of ticks [12].

To develop a sustainable tick management strategy in the present complicated scenario, attempts have been made to identify plants with strong antitick activity with success [13-16]. Earlier, by an extensive screening of plant parts having insecticidal property, Ageratum conyzoides Linn. (Family: Asteraceae), a common annual herbaceous weed has been selected for further exploitation. A number of medicinal properties of this weed have been reported earlier viz. as analgesic, antioxidative, hepatoprotective, blood booster, antioxidant and for the treatment of high blood pressure, fever, diabetes, pneumonia, wounds and burn, microbial infections, arthrosis, headache, inflammation, dyspnea, pain, asthma, spasms, gynecological diseases, leprosy and numerous infectious and skin diseases [17-21]. It is reported that the multi-function activities of the plants are possibly be due to Synergism of phyto-constituents present in the extracts [22].

In our earlier study, the ethanolic extract of the plant was found 76.7-90% efficacious against acaricides-resistant field ticks and its active fraction and sub-fraction contained 6,7-dimethoxy-2,2-dimethyl-2H-1-benzopyran (Precocene II, ageratocromene) as the major chemical component [23]. Indian cattle ticks have already developed resistance to most of the chemicals marketed today and this situation is further complicated due to development of multi-caricide resistant ticks [3,4,5,24]. So, to tackle the situation, a multi-institutional programme was funded in NAIP and significant lead was obtained [25]. Chemical characterization of solvent guided extracts identified few compounds in Acorus calamus, Ricinus communis and Semecarpus anacardium [26,27,5].

Acaricidal activity of plants viz., Leucas aspera, Cassia alata, Jatropha carica, Cassia fistula were reported [28-31]. Two characterized phyto-formulations have been developed and tested in multi-locational field trial. In a recent study, the identified extract was chromatographically fractionated and altogether 41 compounds were identified based on GC/MS/MS analysis [32]. Major compounds were checked for their antitick activity and promising acaricidal compounds were identified. The lead molecule induced cellular changes in the different stages of ovary were also worked out and drug induced expression changes of targeted GPCRs was observed [32].

2. Conclusion
The impact of Ticks will continue to increase in many parts of the world including India. Long-term use of hazardous chemical acaricides is leading to the development of many societal and environmental issues. Amongst the different components of integrated tick management system, continuous monitoring of resistance using robust tools, development of vaccine against ticks and formulation of eco-friendly phytoacaricides are showing a lot of promise in future.

Conflict of Interest
The author declares no conflict of interest.

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