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ORIGINAL PAPER

Comparison of the tick repellent efficacy of chemical and biological products originating from Europe and the USA

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Abstract The present paper investigates the efficacy of common anti-tick repellents in Europe and in the USA. There were tested *Ixodes ricinus*, *Dermacentor reticulatus,* and *Rhipcephalus sanguineus* when they are placed onto hands and clothes of male and female humans being treated with common tick repellents. It was seen that DEET needed high concentrations to repel ticks, while essential oils are mostly inefficient. On the other hand saltidin = icaridin, p-menthan-diol and IR 3535 showed long-lasting effects, which in the case of combinations of saltidin and *Vitex* extracts were even increased.

Introduction

Ticks are able to transmit agents of severe diseases to humans and animals with a considerable zoonotic potential (Nentwig 2003; Aspöck and Dobler 2008; Eckert et al. 2008; Mehlhorn et al. 1993, 1995). If there is no transovarial transmission (as e.g., in the case of FSME viruses), larvae or nymphs become infected during their blood meals and may transmit the agents of diseases during the next blood meal to another host. In some cases (as in *Babesia* infections) the ticks stay infected for their whole life. While endangered horses, camels, sheep, and goats might be protected by repeated "dippings" into water containing acaricidal compounds (all 4 to 6 weeks) or while dogs are safely protected for 4–6 weeks by application of one of the numerous available pour-on medicaments, the protection of humans poses much more problems. This is due to the fact, that no one wishes to be covered permanently by acaricides for such a long period, because of the bad smell of most compounds, because of fears from the potential side effects along the skin (such as reddening, itching), or because the daily showers would diminish the concentration of the repellent on the skin. Therefore short-term repellents have been developed to bring protection from attacking ticks during rather short periods of working, walking, or playing in natural surroundings. Of course the first repellents have been based on natural extracts from plants, since the latter had developed ingredients that should protect them from feeding of insects and/or acaridal species. Already the Greek Herodotus and the Roman Plinius reported the use of strong smelling substances on the skin amongst the ancient populations around the Mediterranean Sea (Büchel 1970). Over the last two thousand centuries—and even increasingly nowadays—more and more plant extracts, in particular essential oils, have been described to offer repellent effects against insects, ticks, and mites (literature c.f. Büchel 1970; Nentwig 2003; Mehlhorn et al. 2005, Mehlhorn and Mehlhorn 2009; Kumar et al. 1995; Marchio 1996; Mwangi et al. 1995; Solberg et al. 1995, Amer and Mehlhorn 2006). Among the isolated substances, the following were found often at high concentrations: citronellol, geraniol, cineoles, monoterpenoids, cyclopantenes, azadirachtin etc. (Büchel 1970; Cockcroft et al. 1998; Mumcuoglu et al. 1996; Thorsell 1998; Marazanye et al. 1988; Watanabe et al. 1995; Sharma et al. 1993, 2001; Schreck et al. 1995). However, in many cases, it turned out

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that the essential oils alone—especially in high concentrations—may introduce phototoxic and allergenic reactions or even lead to olfactory and skin reactions (see Barnard 1999; Faulde 2001; Semmler et al. 2009).

These unwanted and often serious effects and the incomplete protection offered by essential oils initiated the development of chemical repellent products, which, however, always had a better efficacy against mosquitoes than against ticks. One of the most common is DEET (N,N-diethyl-m-toluamide), which was described already in the year 1954 (McCabe et al. 1954). Other early chemical repellents are dimethylphthalate, ethylhexanediol=Rutgers 612, indalone=3,4dihydro-2,2-dimethyl-4-oxo-2Hpyran-6-caboxylate-n-bytylester, DEPA=N,N-diethylphenyl acetamide, Merck 3,535=N-acetyl-N-butyl aminoproprionic acid ethyl ester (see Nentwig 2003), p-menthan-3,8-diol, which is included also in the naturally obtained Citronella oil and which is described in China under the name "Quwenling", may also be produced during chemical synthesis. One of the most recent chemically designed products is 1-piperidine carboxylic acid known under different names (KBR 3,023, Bayrepel, picaridin, icaridin, recently renamed saltidin), which is on the way to replace (at least on the mosquito scene) the good old, but gluing, bad smelling, and plastic dissolving DEET.

Since in temperate zones in Europe and USA ticks are much more important than mosquitoes due to their potential transmission of agents of severe diseases, it is important to protect humans from tick bites (Lane and Crosskey 1993; Aspöck and Dobler 2008, Turberg and Hansen 2008; Mehlhorn 2008; Mehlhorn and Mehlhorn 2009; WHO 1987).

Therefore the present study deals with the efficacy of several common products being based either on biological, on chemical compounds, or on a mixture of both.

Material and methods

1. Ticks

   The developmental stages of the tick species *Ixodes ricinus*, *Rhipicephalus sanguineus,* and *Dermacentor reticulatus* originated from outdoor catches (*I. ricinus*, *D. reticulatus* in the surroundings of Berlin and Düsseldorf, Germany) or from tick cultivation (*R. sanguineus*) at the Berlin Institute of Veterinary Parasitology. Prior to use they were kept under favorite conditions in the institute. Prior to the test their motility was tested when breathing warm air into the glass vessel, within which they had been stored under humidity.
2. Products

   The different products used in the tests were bought in pharmacies and/or relevant shops. According to the label all products had been produced 1 year at the maximum before the tests.
3. Test period and persons

   Own test series were done during the years 2008–2010 always involving four to eight persons including females and males, who washed their hands thouroughful before the start of the test.
4. Tests on clothes

   The tests on the clothes of the test persons were done on leather shoes and wool and/or cotton trousers, and all showed similar results.
5. Test design according to Mehlhorn and colleagues

   a). The upper side of a hand of a test person was sprayed with one of the products until the skin appeared wet.

   b) The sprayed hand of a test person was waved until the surface of the hand had become dry.

   c) After 1–5 or 6 h, one adult tick or nymph (of the species *I. ricinus*, *D. reticulatus* and/or *R. sanguineus)* was placed onto the treated skin of the hand of each test person (up to eight persons per test). This was repeated with five tick specimens of the tick species used.

   d) After 10 s the hand was brought into an upright position, so that the ticks had to decide to crawl upwards or to let fall themselves down from the skin.

   e) It was noted how long they stayed on the treated skin before they fall down.

   f) Their staying on the skin longer than 1 min and their crawling further upwards was noted as the end of the protection period.

   g) These tests were also done with ticks placed onto leather and onto clothes of persons wearing wool or cotton trousers.
6. Cited tests: Test design of "Stiftung Warentest" (Test 5/2008; p. 82–85; this is an institution which tests all types of products available on the German market)

   a) Skin was treated according to the label of the product.

   b) A plate of copper (diameter 3 cm) was glued at the center of the treated skin (leg).

   c) The treated leg was kept in an upright position and a circle of 13 cm in diameter was drawn around the center of the copper plate.

   d) One, 2, 3, 4, 5, or 6 h after the treatment of the skin, two nymphs and/or adults of *I. ricinus* ticks were placed onto the metal plate.

   e) It was observed whether the ticks dropped down from the copper plate when leaving it or whether they ran at least 5 cm onto the treated skin.

   f) Dropping down was noted as positive test result, no dropping down during the test period was noted as end of the protection period.

Table 1 Test results of the present study when placing ticks on treated skin and/or shoes, trousers

Name of the product	Active ingredient	Period of protection against		
		Ixodes	*Rhipicephalus*	*Dermacentor*
Tea tree (*Melaleuca alternifolia*)	3% Oil of *Melaleuca alternifolia* (cineol, terpinem)	none	none	none
Great Outdoors (USA)	29.55% DEET	5 h (mean)	n.d.	n.d.
Bug Mace (USA)	Catnip oil, lemongrass, citronella oil, caranja oil	1–2 h	n.d.	n.d.
Natrapel Plus (USA)	Citronella oil, geraniol	1–2 h	n.d.	2–3 h
OFF Clean feel (USA)	Picaridin (low concentration)	2–3 h	n.d.	n.d.
OFF Smoothand dry (USA)	15% DEET	5 h (mean)	n.d.	n.d.
Autan Active	20% Icaridin=saltidin	5 h (mean)	4.5 h (mean)	5 h (mean)
Picksan Tickstop on hands	p-Menthan-3,8-diol, *Vitex* extract	5–6 h (mean)	5 h (mean)	5 h (mean)
Picksan Tickstop on trousers	p-Menthan-3,8-diol, *Vitex* extract	5–6 h (mean)	5 h (mean)	5 h (mean)
BZZZStop on hands	Ethyl-butyl-acetyl-amino-proprionate	n.d.	4 h	5–6 h
BZZZStop on trousers	Ethyl-butyl-acetyl-amino-proprionate	n.d.	3–4 h	3 h
· Viticks Cool on hands	5,8% Icaridin, *Vitex* extract	6 h (mean)	6 h (mean)	6 h (mean)
· Viticks Cool on trousers	5,8% Icaridin, *Vitex* extract	6 h (mean)	6 h (mean)	6 h (mean)
· Viticks Cool Plus on hands	5,8% Icaridin, geraniol, *Vitex* extract	6 h (mean)	6 h (mean)	6 h (mean)
· Viticks Cool Plus on trousers	5,8% Icaridin, geraniol, *Vitex* extract	6 h (mean)	6 h (mean)	6 h (mean)
Controls on untreated hands/ trousers	None, water	Ticks remained and crawled upwards	Ticks remained and crawled upwards	Ticks remained and crawled upwards

Experimental design see Material and methods

n.d. test not done

Results

The results of the tests of the present study are summarized in Table 1. It can be seen that tea tree oil has absolutely no effects. Some effects are seen if combinations of essential oils were used at rather high concentrations (e.g., products Bug Mace, Natrapel Plus), DEET products had a repellent effect, if they are used at high concentrations. Icaridin alone needs also high concentrations. However, in case of addition of a small amount of the patented *Vitex agnus castus* extract into the product, icaridin showed also a long repellent effect even at a concentration of only 5.8%. In case of an icaridin/*Vitex* treatment the duration of the repellent effects is identical when the product is sprayed either on the naked skin or on shoes and/or trousers consisting of wool or cotton/synthetics (e.g., Viticks products, Table 1). In case of treatments using products containing ethyl-butyl-acetyl-amino-proprionate the treated trousers (wool) repel less long as in the case when these products are sprayed onto skin. These results were mostly very similar when nymphs or adult females of the ticks were used. However, considering the length of the

Table 2 Comparison of the efficacy against ticks of some chemical compounds (according to Nentwig 2003 and the present study)

Compounds	Efficacy better than DEET	Authors
A13-35765 A13-37220 (both are piperidine derivates)	Similar better	Perich et al. 1995 Perich et al. 1995
Icaridin, saltidin (1-piperidine-carboxylic acid, 2–2 hydroxyethyl, 1-methylester)	Better	Nentwig 2003, Dautel 2001, present study
CIC-4 (lactone)	Less good	Perich et al. 1995
DEPA (N,N-diethyl-phenyl-acetamide)	Similar	Kumar et al. 1992
p-Menthane-3,8-diol	Better	Present study, test of Stiftung Warentest
Merck 3,535 (3-N-acetyl-N-butyl amino proprionic ethyl ester)	Better	Present study
Oil of *Ocimum suave*	Similar	Mwangi et al. 1995
Extract of seeds of *Vitex agnus castus*	Better	Mehlhorn et al. 2005, present study

Table 3 Efficacy against *Ixodes ricinus* ticks of some products as tested 2008 by Stiftung Warentest (Germany)—please note the experimental design in Material and methods

Name of the product	Active ingredients	Period of protection
Azaron before	Icaridin	1.5 h (mean)
ContraZeck	Lauric acid	2 h (mean)
Smellwell Biozeck	Citrodiol	2 h (mean)
Braeco-Zeckenabwehr	Oil of *Lavendula* plant	some minutes
AntiBrumm Naturel	p-Menthan-3,8-diol	3 h (mean)
AntiBrumm forte	Diethyl-toluamid (DEET)	2 h (mean)
Autan Active	Icaridin	2.5 h (mean)
BZZZStop	Ethyl-butyl-acetylamino-proprionate	1.5 h (mean)
Nobite Sensitive	Icaridin	1 h (mean)
Anti-Mosquizan	p-menthan-3,8-diol	3 h (mean)
Zanzarin Bio-Lotion	Caprin acid, cocos oil	2 h (mean)
Hansaplast Anti-Insekten-Spray	Ethyl-butyl-acetylamino-proprionate	2 h (mean)

protection period there were slight variations in each product. But these variations were independent from the sex of the test person.

Discussion

At times, when Nentwig (2003) summarized the situation of the available repellents against the different groups of arthropods, DEET (N,N-diethyl-m-toluamid) was the basic bench mark with respect to repellency against mosquitoes and ticks. Since DEET is a very old compound being officially available since 1954 (while already used in the Korea War) and since it has several disadvantages (e.g., gluing, destroying plastic, bad smelling) many trials had been done to replace it by other chemical products, especially in the case of repellency against ticks (Table 2). In nature, ticks and mosquitoes occur in the same biotopes and the specimens of both groups transmit often agents of severe diseases (e.g., viruses, bacteria, parasites), which threaten the life of humans and animals even in moderate climatic zones. In the latter zones, the ticks have a significantly higher importance as vectors than mosquitoes. Therefore any new developed product has to cover both groups. Thus these products must protect humans as well from bites from mosquitoes as from blood sucking ticks. The Tables 1 and 2 show that several compounds act better than DEET, if the latter is not used in extremely high concentrations, which would increase unwanted effects (at least in user friendliness and skin feeling). When looking at the effects on mosquitoes and ticks, the compound icaridin (now saltidin) has best repellent effects. However, if it is used alone there are higher dosages needed in order to repel ticks for a longer period, too. The repellency against mosquitoes lasts often up to 8 h even in lower concentrations. If icaridin is used in compositions with a patented *Vitex agnus castus* extract, even lower dosages bring about long-lasting repellency effects against ticks (e.g., product Viticks Cool).

Our results when testing the repellent effects of essential oils were confirmed by the results obtained by the German Waretesting Agency "Stiftung Warentest" (2008). In this publication it was shown that essential oils alone offer practically no protection against ticks (Table 3). However, this publication also shows that repellent tests using other test methods (see Material and methods) may bring variations in the results. Differences may also be based on the concentrations of the active compounds in the products and on the formulation of the product, since some of the additives may cover the evaporation of the active repellent ingredients.

When evaluating the efficacy of the different compounds against ticks the following statements can be drawn from the results listed in Tables 1, 2, and 3.

1. Essential oils alone have nearly no or only short-lasting repellent effects on ticks.
2. DEET and icaridin need high concentrations to repel ticks for long.
3. 3,8-p-Menthan-diol (PMD) alone has in some formulations (Table 3) lower effects against ticks as are produced by DEET or icaridin alone.

Table 4 Summary of LD50 and skin absorption of some important repellent compounds (listed according to Nentwig 2003)

Repellent	LD50 (rat, mg/kg)		Absorption model (%)	
	Oral	Dermal		
Ethyl hexane diol	1,400	5,000	12	Human
DEET	3,300	5,000	30	Human
Icaridin	4,743	>5,000	5	Human

4. If icaridin and 3,8-p-menthan-diol are mixed each with the patented *Vitex agnus castus* extract, a period of up to 6 h of protection may be reached against ticks.
5. Both combinations—icaridin plus *Vitex*, PMD plus *Vitex*—keep their activity, when they are sprayed onto clothes shoes and trousers (this is absolutely needed, since ticks start their hitchhiking from the tips of grass), while ethyl-butyl-acetyl-amino-proprionate is less active on trousers. DEET (even in spray products) cannot bring onto shoes and trousers, it would destroy them.

For users, DEET has some considerable disadvantages (as it was seen in our tests and reported by several users):

1. Only very high concentrations are active against ticks.
2. This brings a bad smelling and an increased feeling of gluing on the skin.
3. DEET destroys plastic.
4. DEET is absorbed in higher rates (up to 30%, Combemale et al. 1992), while icaridin is only absorbed at 5% (Bayer official dossier, Table 4).

Conclusions

Results of testing the repellent activity of compounds against ticks may vary with respect to the length of protection depending on:

1. the mode of testing,
2. the formulation of the product,
3. the concentration of the active ingredient,
4. the developmental stage of the tick species,
5. the fitness of the developmental stage,
6. the tick species tested,
7. the amount of the product that is brought onto the skin or clothes.

However, all tests clearly showed that:

1. Essential oils alone have no or only low repellent activities.
2. DEET acts only in very high concentrations against ticks, which then bring increasing disadvantages.
3. 3,8-p-Menthan-diol and icaridin alone need rather high concentrations in the product to bring about a long lasting effect.
4. However, if both (PMD and icaridin) are used in combination with the extract of *Vitex agnus castus* a long lasting repellent effect can be reached by low concentrations, which offer a rather acceptable smelling.
5. These latter combinations (e.g., in the products Viticks Cool, Picksan) can be sprayed as well on naked skin as on shoes and clothes (which is essential to avoid the attacks of the ticks from the soil), while DEET in any formulation or in body milks and "crèmes" containing any other active compounds would leave dirty spots on shoes and/or clothes.

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