

Mosquito repellent effectiveness: A placebo controlled trial comparing 95% DEET, Avon Skin So Soft, and a “special mixture” containing eucalyptus oil

The introduction of the West Nile virus in Canada is changing the way we look at mosquitoes. Which repellent is most effective?

ABSTRACT:

Background: The introduction of West Nile virus in Canada is changing the perception that mosquitoes are nothing more than nuisance pests. Interest is increasing in ways to protect against mosquitoes. One of the commonest is the use of insect repellents.

Methods: Tests were undertaken to determine the effectiveness of three mosquito repellents: 95% DEET, Avon Skin So Soft bath oil, and a “special mixture” of substances thought to have insect repellent qualities. The repellents were compared with each other and against a placebo in eight separate test sessions. During each session, the three repellents and placebo were tested simultaneously. Each session lasted between 90 and 120 minutes. After every session, the repellents were thoroughly washed from the test site and a minimum of 72 hours elapsed between tests. There were four test sites: the author’s right arm, left arm, right leg, and left leg. All test

sites were of similar surface area. Both mosquito bites and landings were counted as events. Measures were taken to ensure that events were not counted twice.

Results: A total of 74 events occurred. The event distribution was as follows: placebo—40 events; special mixture—28 events; Avon Skin So Soft—6 events; DEET—0 events.

Conclusions: When tested against a placebo, both DEET ($P < .0001$, $NNT=1$) and Avon Skin So Soft ($P = .0001$, $NNT=1$) were found to provide significantly better protection, while the special mixture did not ($P = .30$). When tested against the special mixture, both DEET ($P < .0001$, $NNT=1$) and Avon Skin So Soft ($P = .0048$, $NNT=2$) were found to provide better protection. When DEET and Avon Skin So Soft were compared with each other, Avon Skin So Soft was found to be 85% as effective as DEET ($P = .046$, $NNT=7$).

Background

In Canada, mosquitoes are mainly considered to be nuisance pests—their bites causing a pruritic irritation that itches for a day or two and then subsides. Until recently, there were no short- or long-term sequelae from such bites, aside from the rare case of cellulitis or scarring. However, the recent spread of the West Nile virus has increased concerns about mosquito-transmitted disease. Health Canada states that even though “the risk of illness from West Nile virus is low, and the risk of serious health effects is even lower... it is important to know the symptoms of illness related to infection and how to minimize your risk, especially if virus activity is reported in an area near you.”¹

On a global basis mosquito-transmitted disease is responsible for a significant amount of morbidity and mortality. It is estimated that more than 700 million people become ill each year from mosquito-transmitted disease, and that 3 million people die from malaria, including one child every 30

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seconds.² In response, numerous measures have been used to protect people from mosquitoes. On an international level, attempts have been made to create genetically modified mosquitoes that are resistant to malaria,³ and to produce vaccines against yellow fever, Japanese B encephalitis, dengue, and West Nile virus.⁴ On a municipal level, many communities spray insecticide. On an individual level, people adopt numerous personal protective measures to reduce the risk of mosquito bites.⁵ These measures include:

- Avoiding perfumed cosmetics
- Avoiding mosquito habitat during peak mosquito feeding times
- Remaining in completely enclosed, well-screened, or air-conditioned areas
- Sleeping under permethrin-impregnated mosquito nets
- Wearing loose-fitting, light-colored clothing
- Using mosquito repellents

In Canada, permethrin is not registered for use on clothing and permethrin-impregnated mosquito nets are not available.⁵ And remaining in completely enclosed, well-screened, or air-conditioned areas is simply unacceptable for the outdoor enthusiast. Of the various insect repellents available, those containing DEET have become the gold standard. Many consumers, however, are reluctant to use DEET. Some view it as an "artificial chemical" and are concerned that it may have unwanted or unknown side effects on them. Indeed, DEET is a plasticizer, capable of dissolving watch crystals, the frames of glasses, and some synthetic fabrics.⁶ In addition, many DEET products have an unpleasant odor and leave skin feeling dry. As a result, "natural products," often derived from mineral oil or plant-based essential oils, have been gaining popularity as alternatives to DEET. Avon Skin So Soft bath oil and eucalyptus

oil are two such alternatives.

Methods

This study compared the effectiveness of three different insect repellents: 95% DEET, Avon Skin So Soft (ASSS), and a "special mixture" (Spec) of substances thought to have insect repellent qualities (note that the highest concentration of DEET now available in Canada is 30%). The special mixture consisted of 15 mL of 100% eucalyptus oil, 250 mL white vinegar (5% acetic acid), 250 mL ASSS, and

500 mL tap water. The three repellents were compared with each other and against a placebo.

Four test sites were used: the author's right arm, left arm, right leg, and left leg. Each arm was exposed from the proximal deltoid to the end of the digits; each leg was exposed from the distal fifth of the thigh to the proximal medial malleolus. The exposed surface area of each arm was 2125 cm² and of each leg was 2080 cm². The surface area difference between upper and lower limbs was negligible: the surface area of each limb was within a 1% variance of the mean surface area of 2102.5 cm².

Each repellent was systematically rotated between the upper and lower test sites on one side of the body. Specifically, DEET and the placebo were applied only to the left limbs.

When the left arm received DEET, the left leg received placebo. On the subsequent test, the application sites were reversed so that the left arm received placebo and the left leg received DEET. Similarly, ASSS and Spec were applied only to the right limbs. Each repellent was applied as a liquid. After every test, the repellents were thoroughly washed from the test sites and a minimum of 72 hours elapsed before the next session.

There were a total of eight separate sessions. The three repellents and

Avon Skin So Soft was 85% as effective as DEET.

placebo were all tested simultaneously. Each test session lasted between 90 and 120 minutes. All sessions were conducted under field conditions in the Bella Coola Valley area of British Columbia, where the predominant species of mosquito is *Culex pipiens*. The tests all took place in the late afternoon or early evening during the fall of 2002.

An event was judged to have occurred if a pruritic papule appeared on the test limb within 12 hours of the test period. An event was also judged to have occurred if a mosquito landed on the test limb and was destroyed. The site of each mosquito landing was marked with an ink pen so that if a pruritic papule later appeared it would not be counted as a second event.

Results

A total of 74 events occurred. The event distribution was as follows: placebo test sites—40 events; special mixture test sites—28 events; Avon Skin So Soft test sites—6 events; DEET test sites—0 events. This is not a random distribution ($P < .0001$). Further, there was no difference between the event distribution for each repellent when upper and lower limbs were compared: placebo: 19, 21 ($P > .05$); Spec: 14, 14 ($P > .05$); ASSS: 4, 2 ($P > .05$); DEET: 0, 0 ($P > .05$).

Comparing each repellent against the placebo, it was found that both DEET and ASSS (40 vs 0, $P < .0001$; 40 vs 6, $P = .0001$) provided significantly better protection than placebo, but that Spec did not (40 vs 28, $P = .30$) (Figure). The use of DEET, ASSS, and Spec resulted in a 100%, 85%, and 30% reduction in event occurrence, respectively, and the number needed to treat to prevent one event was 1.00 (=1) for DEET and 1.17 (~1) for ASSS (Table 1).

Comparing the repellents with each other, it was found that both DEET and ASSS protected better than Spec, and that DEET protected better than ASSS (Table 2), which was 85% as effective as DEET.

Conclusions

On any given day, numerous confounding variables affect mosquito bite frequency. These include the ambient temperature, wind speed, and humidity; the species of mosquito, the mosquitoes' level of hunger, and the density of the mosquito population; and the test subject's age, sex, activity level, and biochemical attractiveness to the mosquito.⁶ In this study, measures were taken to minimize or eliminate these variables. For instance, the potential effect of variations in test subject age, sex, activity level, and biochemical attractiveness to the mos-

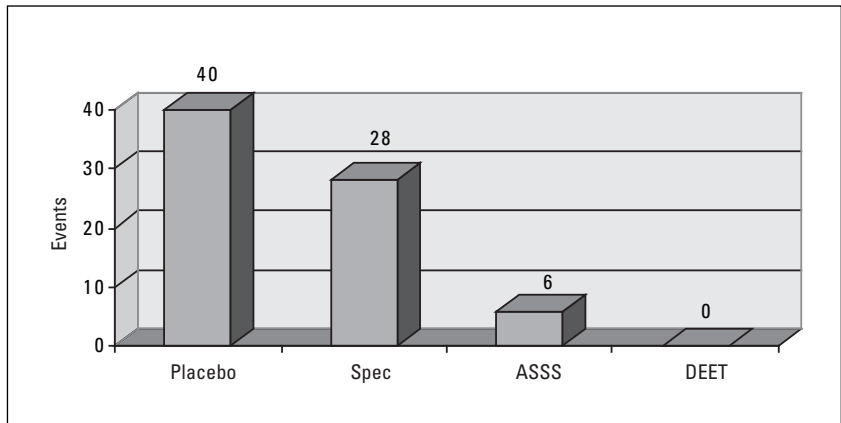


Figure. Number of events after repellents were applied.

quitoes were eliminated by using a single test subject. Further, the effect of variations in ambient temperature, wind speed, and humidity, as well as variations in mosquito species, hunger, and density were minimized by testing all four body sites, all three insect repellents, and the placebo simultaneously.

The systematic rotation of each insect repellent between the upper and lower test sites was designed to mini-

mize any potential bite frequency variation between upper and lower limbs, and to negate the potential effect of the 1% surface area difference between the arm and leg mean surface area. In fact, analyses of the results show that there was no difference in bite frequency between upper and lower limbs ($P > .05$). This is significant in that future studies of similar design will not need to rotate test limbs.

This study was carefully designed

Table 1. Effectiveness of repellents compared with placebo.

	Event distribution	P-value	Absolute risk reduction	Number needed to treat
Placebo vs DEET	40 vs 0	$P < .0001$	100%	1.00 (=1)
Placebo vs ASSS	40 vs 6	$P = .0001$	85%	1.17 (~1)
Placebo vs Spec	40 vs 28	$P = .30$ (ns)	30%	*

* Not statistically different from placebo

Table 2. Effectiveness of repellents compared with each other.

	Event distribution	P-value	Absolute risk reduction	Number needed to treat
DEET vs Spec	0 vs 28	$P < .0001$	70%	1.43 (~1)
ASSS vs Spec	6 vs 28	$P = .0048$	55%	1.82 (~2)
DEET vs ASSS	0 vs 6	$P = .046$	15%	6.67 (~7)

to eliminate any potentially confounding effects of previously applied repellent. After every session, the test site was thoroughly washed and a minimum of 72 hours was allowed to elapse before the next testing. A 72-hour interval was chosen based on the pharmacodynamics of DEET and the fact that after five half-lives, the active effect of any substance is negligible.⁷ Ninety-five percent DEET is effective for 10 hours,^{1,5,8,9} so if any repellent remained on the test area despite thorough washing, a minimum of seven half-lives would have passed before the next testing. Thus, the 72-hour period should have been more than enough to nullify any potential effect from residual repellent.

The finding that DEET was the most effective repellent is consistent with the literature.⁶⁻¹⁵ The finding of an 85% ASSS:DEET effectiveness ratio is similar to that reported by Magnon and colleagues,¹¹ and supports the claim that ASSS may be used as a mosquito repellent where there is no significant risk of infection by mosquito-transmitted disease. The finding that ASSS provided longer protection than was reported by other researchers^{6,12} may be due to a number of variables, such as differences in study design or the use of different mosquito species. Further, other studies of ASSS have involved testing periods of many hours.^{11,13} As repellent efficacy tends to decrease with time, this study's shorter test sessions may account for the increased effectiveness of ASSS.

The results suggesting that the special mixture was no better than placebo may reflect this study's lack of statistical power. Alternatively, the active ingredients in Spec may have been too dilute: Spec contained relatively small amounts of eucalyptus oil, modest amounts of ASSS, modest amounts of vinegar, and large amounts of water. A more concentrat-

ed form of Spec might have been more effective. Indeed, a literature search revealed that eucalyptus oil is an effective repellent and its effectiveness is proportional to its concentration.^{9,14,15}

Overall, the results indicate that both DEET and ASSS protect better than Spec or placebo, and that DEET protects better than ASSS. These results suggest that ASSS may be used as an alternative to DEET in areas where mosquitoes are nuisance pests and mosquito repellents are needed solely to promote comfort. However, the use of any product less effective than DEET should be avoided in areas where mosquito-transmitted disease results in significant morbidity or mortality.

Competing interests

None declared.

Acknowledgments

The research for this project was conducted while the author was a UBC Family Practice resident. An earlier version of this paper won the PAIRO award, one of two awards given annually by the Professional Association of Internes and Residents of Ontario, in 2003.

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Safety assessments and Health Canada recommendations regarding DEET

DEET (N, N-diethyl-m-toluamide) is the most widely used insect repellent in the world. Since its first use in 1956, billions of applications have been made to human skin. It is currently used by about one-third of the US population. Studies sponsored by S.C. Johnson & Son conclude that the risk of adverse reactions from label-directed use is low.^{1,2}

Adverse reactions to DEET

From 1993 to 1997, poison control centres in the US received notice of 20 764 exposures to DEET.³ Most of these exposures occurred in infants and children—a group that experienced lower rates of adverse effects than teens and adults. Thirty percent of the exposures were symptomatic and most involved irritative symptoms from non-label-directed use. Adverse reactions were related to the route of exposure, with the highest rates being associated with ocular exposure, followed by inhalation, multiple exposure routes, dermal application, and ingestion.³ In total, neurotoxicity has been reported in 26 to 40 individuals, including at least 3 and potentially 5 case fatalities.^{1,3} Two deaths have been reported following dermal exposure: one in a 26-year-old male and one in a 34-year-old female.³ Although the concentration of DEET is known to determine the duration of effectiveness (ranging from 2 hours for 5% DEET to 9.5 hours for 100% DEET), there is no clear relationship between the concentration of DEET and the presence or severity of adverse reactions.^{1,3} Most of the severe reactions to DEET have been idiosyncratic or have resulted from non-label-directed use.

What Health Canada says

In April 2002, Health Canada's Pest Management Regulatory Agency (PMRA) released a "Re-evaluation Decision Document"⁴ based on a comprehensive review of the data surrounding DEET and findings from the agency's research into the effects of daily DEET application over a 3-month period. Because the research was conducted on rodents, the standard 100-fold margin of exposure (MOE) was used to calculate levels of safe human exposure: a 10-fold MOE to allow for extrapolation between species and a further 10-fold MOE to allow for variability within the human population.

The PMRA document states that DEET is a noncarcinogenic, nonmutagenic, nonteratogenic insect repellent that does not accumulate within tissue. DEET is metabolised by the liver and excreted by the kidneys. Hepatic cytochrome P-450 induction occurs significantly less with dermal exposure than with oral exposure.

DEET may have both acute and chronic toxic effects. The acute toxicity of DEET can be manifested by gastrointestinal or neurological symptoms. In humans, these symptoms can include nausea, vomiting, headache, ataxia, tremor, and seizures. Chronic toxicity can be manifested in children by failure to thrive or less than expected weight gain.

Multigenerational dosing has been found to cause epididymides and testicular degeneration in hamsters, but neither effect has been found in rats or rabbits. The potential for multigenerational dosing toxicity in humans is unknown.

These and other findings led Health Canada to redefine the safety limits for DEET and make the following recommendations and regulatory amendments:

- Retail sales of sunscreens containing DEET are not permitted because of incompatible application instructions: sunscreens should be applied liberally and frequently whereas repellents containing DEET should be applied sparingly and infrequently.
- Retail sales of products that contain more than 30% DEET are not permitted.

A straightforward and practical summary of Health Canada's recommendations⁵ is available at www.hc-sc.gc.ca/pmra-arla/english/pdf/pnotes/deet-e.pdf.

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Ways to prevent mosquito bites

In Canada, mosquitoes are mainly nuisance pests—their bites cause an itchy bump that may last for a day or two and then goes away. However, the recent spread of the West Nile (WN) virus has increased our awareness of mosquito-transmitted disease. Though alarming, Health Canada states, "The risk of being bitten by a WN virus-infected mosquito is low, as is the risk of serious health effects from the virus for normally healthy people. Very few mosquitoes—less than 1%—are likely to be infected... even if the mosquito is infected, less than 1% of people who get bitten and become infected will experience serious health effects." So in Canada, mosquitoes are still mainly a nuisance pest, rather than a major public health concern.

However, you can reduce your risk of mosquito bites. You can:

- Avoid perfumed cosmetics.
- Avoid areas with mosquitoes during dawn and dusk.
- Remain in completely enclosed, well-screened, or air-conditioned areas.
- Wear loose-fitting, light-colored clothing.
- Use insect repellents.

Regarding insect repellents, Avon Skin So Soft (ASSS) may be used as a mosquito repellent. However, as DEET protects better than ASSS, we do not advocate the use of ASSS in areas where there is a significant risk of infection by mosquito-transmitted disease. Allergic reactions can occur with anything applied to the skin, regardless of its source—natural or synthetic.

A recent study in the *British Columbia Medical Journal* provides unbiased evidence that over a 2-hour period:

- A 95% DEET preparation was 100% effective at preventing mosquito bites.
- Avon Skin So Soft was 85% effective at preventing mosquito bites.

Since the research was conducted, retail law has changed and concentrations of DEET higher than 30% are not permitted in Canada. However, Health Canada has found that 30% DEET provides more than 6 hours of protection, which is sufficient in most cases.

Health Canada's general recommendations

- Apply repellents containing DEET sparingly.
- Wash treated skin with soap and water when returning indoors or when protection is no longer needed.
- Do not get in eyes, do not use on open wounds, and do not use near food.
- Do not breathe spray mist. Use only in well-ventilated areas.

Age-specific recommendations:

- Children under 6 months of age: do not use DEET. Use non-chemical, physical control methods instead (i.e., mosquito nets on strollers and the above measures).
- Children aged 6 months to 2 years old: limit use of 10% DEET (or less) to one application per day. Do not apply to the face or hands.
- Children between 2 and 12 years old: limit use of 10% DEET (or less) to three applications per day. Do not apply to the face or hands.
- Individuals older than 12 years old: limit use of 30% DEET (or less) to three applications per day.