

Letter

Efficacy of the main repellents available in the Brazilian market against *Aedes aegypti* bites under concentrations applied to pediatric populations

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Dear Editor:

Mosquitoes are the most important vectors of infectious diseases in the world, and currently in Brazil, there are endemic areas of viruses such as dengue, zika, chikungunya, and yellow fever, besides malaria and leishmaniasis, which require public health actions, such as control of breeding sites and use of insecticides and repellents¹.

Insect repellents are aimed at avoiding bites, and their efficacy depends, in addition to the concentration of the active components, on elements related to the insect and the user, such as sweat, temperature, eczema, or areas with higher insect density. They can be applied topically on the skin, clothing, or on mosquito nets. Its adoption as a prevention strategy promoted reduction in malaria-associated mortality in China and Africa, as well as cutaneous leishmaniasis infection in South America and the Middle East²⁻⁴. However, children are restricted to certain products or concentrations, according to age, making them susceptible to illness⁵.

N,N-Diethyl-3-methylbenzamide (DEET) at a concentration of 30-50% is the best known repellent substance; however, its administration is limited by toxicity and skin irritation, contraindicating it in children younger than 10 years. Lower concentrations (10-30%) are, however, present in pediatric products⁶.

Icaridin at a concentration of 20-25% is a compound derived from piperidine, found in black pepper (*Piper nigrum*). It is highly effective, with a low rate of sensitization and is safe to use in children older than 2 years of age; however, studies have not been conducted in pregnant women⁵⁻⁷.

Insect repellents with IR3535® at a concentration of 10-20% has synthetic origins, and is considered safe to use from 6 months of age⁵⁻⁷.

Ethical considerations

This study aimed to evaluate the efficacy of the main pediatric repellents marketed in Brazil against *Aedes aegypti* (Table 1). The project was approved by the institution's ethics committee and proceeded between February and April 2017 (CEP 135/08).

The experiment was carried out by 5 healthy adults who exposed their forearms to 30 healthy adult females *A. aegypti* (Rockefeller strain) retained on transparent plastic beds treated with 5% glucose solution and submitted for fasting blood feeding for 24 hours⁸. The mosquito breeding laboratory included temperature, humidity, and illumination control to standardize the experimental conditions, being maintained by the *Department of Parasitology, Instituto de Biociências, Universidade Estadual Paulista* (IBB-UNESP), Botucatu-SP.

The time (in seconds) of the exposure to the first mosquito bite in each forearm without products and with bilateral combinations of the main Brazilian commercial repellents with pediatric indications was measured. Each experiment, therefore, resulted in three measures⁸.

The forearms were exposed to groups of 30 mosquitoes for a period of 60 s. If no bites occurred, the forearm was removed from the cage for 540 s (9 min) and then, reintroduced. For the standardization of the exposed areas, the hands of the volunteers were protected by latex gloves. If no bites occurred, the study was interrupted in 10,800 s (3h). Mosquitoes were replaced if necessary (in cases of death, flight, or loss of vitality)⁸. Data normality was assessed using the Shapiro-Wilk test⁹. Bilateral comparative analysis was performed using a generalized linear model of mixed effects and two-tailed p values <0.05 were considered significant. Multiple comparisons were corrected by the Sidak procedure.

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TABLE 1: Times until the first bite in the forearms with the different products tested (n = 90).

Product	Time to first bite: mean (SD) in seconds
IR3535 30%	10,400 (1,041) ^{a,b,c}
Icaridin 25%	8,871 (2,531) ^{a,b,c}
IR3535 12.5% + botanical extracts*	7,553 (2,809) ^a
DEET 7.1%	6,447 (2,134) ^a
Nude forearm	23 (11)

SD: standard deviation; **IR3535:** insect repellent with IR3535®; **DEET:** N,N-Diethyl-3-methylbenzamide. ^ap<0.05 from nude forearm. ^bp<0.05 from IR3535 12.5%. ^cp<0.05 from DEET 7.1%. *Clove, citronella, cinnamon, nutmeg and bergamot.

Thirty contralateral experiments (90 measurements) were recorded. There were no systemic adverse effects in the volunteers¹⁰.

The mean times to the bites in the forearms was greater for 30% IR3535 and 25 % icaridin (**Table 1**).

An ideal insect repellent has not yet been developed and its characteristics would involve the absence of toxicity, irritations, absorption, and odor; biodegradability; lack of effect on the ozone layer; insecticide properties; safety during childhood and pregnancy; a broad spectrum; and resistance to sweat, wind, water, and temperature¹¹.

Botanical extracts, such as clove, bergamot, andiroba, citronella, neem, and eucalyptus, are being explored as potential repellents for children and pregnant women, nevertheless having less efficacy than industrial ones^{8,12}.

In our study, high concentrations of IR3535, as well as icaridin, resulted in more favorable repellent performance against *A. aegypti* bites than DEET and IR3535 at low concentrations associated with botanical extracts.

The variability of the volunteers' measurements reinforces the individual susceptibility to *A. aegypti* bites and subsidizes the need for comparative studies with paired analysis of the data for more consistent conclusions, as well as explaining the superior global performances of all repellents in certain subjects.

The results obtained in controlled experimental studies should not be extrapolated to clinical situations. The concentration of mosquitoes used (5 mosquitoes/liter of air), and the voracity promoted are higher than those found in nature. On the other hand, the hierarchy of protection time identified in the laboratory tends to remain between products in open clinical trials.

Likewise, periodic reapplication of less efficient repellents is a safe strategy to maintain protection¹¹. For example, DEET at a concentration of 7.1% is recommended to be reapplied every 2 hours, which can compensate for protection as efficiently as icaridin or 30% IR3535 in a single application.

Finally, repellents should be understood as measures of individual protection, with the potential to reduce disease indicators if used correctly, and in adequate quantities. Efficient public policies, however, should not be based only on repellents, but on restricting the reproduction of vectors.

In conclusion, 25% icaridin spray and 30% IR3535 resulted in better performance among pediatric repellents tested against *A. aegypti* bites.

Conflict of interest

The authors declare that there is no conflict of interest.

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