

a fórmula



# ICARIDINA

Repelente efetivo contra o  
*Aedes aegypti*, indicado  
para crianças e gestantes



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# ICARIDINA

Repelente efetivo recomendado pela OMS contra o *Aedes aegypti*

## DESCRIÇÃO

**Icaridina** ou KBR 3023 (1-piperidinecarboxylic acid, 2-(2-hydroxyethyl)-1-methylpropylester) é um repelente derivado da pimenta, indicado pela OMS, eficaz contra mosquitos, moscas e carraças, inodora, sem deixar uma textura pegajosa ou untuosa, nem danifica o material têxtil, com baixa probabilidade de causar irritação cutânea.

## MECANISMO DE AÇÃO

A ação ocorre pelo “efeito de nuvem”, após a aplicação em que o KBR 3023 evapora formando uma proteção de aproximadamente 4 cm em volta da pele que repele o inseto, com seu uso recomendado por cima dos tecidos das roupas (não recomendado seu uso por baixo) ou apenas na pele exposta. Em concentração a 10%, a **Icaridina** confere proteção por um período de três a cinco horas, e a 20% algumas referências informam de oito a dez horas. Sua ação é comparável à concentrações de 15-50% de DEET, sem necessitar de reaplicações em intervalos menores de tempo como este último. Pesquisadores informam que em caso do produto repelente ser utilizado em associação com outro, como o filtro solar, recomenda-se o uso deste antes do repelente, com intervalo mínimo de 15 minutos para que o filtro seja absorvido pela pele, e só então aplicar a **Icaridina**.

## INDICAÇÕES

- ✓ Crianças a partir de 2 anos de idade;
- ✓ Gestantes.

## DOSE USUAL

Recomendação tópica de 10 a 50% de **Icaridina**, 3 vezes ao dia em **crianças** (acima de 2 anos) e não ultrapassar de 3 a 4 vezes ao dia em **adultos**, com intervalo de aplicação variando entre 3 a 10 horas.

## SUGESTÕES DE FÓRMULAS

**Icaridina**..... 20%  
Loção hidratante qsp..... 80g

**Modo de uso:** aplicar nos locais expostos a picadas de insetos, 3 vezes ao dia.

**Indicação:** repelente de insetos indicado para gestantes.

**Icaridina**..... 25%  
Loção qsp..... 60ml

**Modo de uso:** aplicar nos locais expostos a picadas de insetos, 3 vezes ao dia.

**Indicação:** repelente em crianças a partir de 2 anos.

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# ICARIDINA

## ESTUDO CLÍNICO

### Repelentes de insetos: recomendações para uso em crianças

**Objetivo:** Apresentar uma revisão bibliográfica sobre o uso de repelentes de insetos em crianças, com ênfase especial na proteção contra mosquitos. Fontes de dados: Realizou-se uma pesquisa bibliográfica nas bases de dados Pubmed e Lilacs, cujos artigos incluíam produtos comercialmente disponíveis no Brasil. Foram selecionados artigos publicados nos últimos dez anos em língua inglesa ou portuguesa, referentes a crianças, obtidos com as seguintes palavras-chave: “insect repellents”, “children”, “mosquitoes”, “N,N-diethyl-metatoluamida (DEET)”. Síntese dos dados: Entre os repelentes tópicos, DEET, icaridina e óleo natural de eucalipto-limão apresentam, em concentrações adequadas, perfil de segurança favorável e são eficazes na prevenção de picadas de mosquitos em crianças e adultos. Em geral, são indicados para crianças acima de dois anos de idade. Medidas físicas são fundamentais para proteger lactentes jovens, especialmente menores de seis meses, com destaque para o uso de telas com permetrina.

**Conclusões:** Os mosquitos são vetores de doenças infectoparasitárias que acometem, anualmente, milhões de pessoas no mundo e causam milhares de mortes. O combate aos mosquitos inclui medidas ambientais e de proteção individual. O uso de repelentes tópicos para proteção individual da criança exige cuidados específicos e conhecimento quanto ao produto ideal para cada idade, especialmente quando consideradas sua eficácia e segurança.

**Tabela 1 – Repelentes disponíveis comercialmente no Brasil, concentrações e tempo de ação estimado**

Princípio ativo	Produto (fabricante) e formas de apresentação	Concentração (%)*	Idade permitida*	Tempo de ação estimado*
DEET	Autan (Johnson Ceras) aerossol, loção, <i>spray</i>	6-9	>2 anos	Até 2 horas
	OFF (Johnson Ceras) loção, <i>spray</i>	6-9	>2 anos	Até 2 horas
	OFF kids (Johnson Ceras) loção	6-9	>2 anos	Até 2 horas
	OFF (Johnson Ceras) aerossol	14	>12 anos	Até 6 horas
	Super Repelex (Reckitt Benckis) <i>spray</i> , loção	14,5	>12 anos	Até 6 horas
	Super Repelex kids gel (Reckitt Benckis)	11,05		
Icaridina	Super Repelex kids gel (Reckitt Benckis)	7,34	>2 anos	Até 4 horas
	Exopis adulto (Osler) gel, <i>spray</i>	50	> 12 anos	Até 5 horas
	Exopis Extreme (Osler) <i>spray</i>	25	>10 anos	Até 10 horas
IR3535	Exopis infantil (Osler) <i>spray</i>	25	> 2 anos	Até 10 horas
	Loção antimosquito (Johnson & Johnson)	**	> 6 meses	Até 4 horas
Óleo de citronela	Citromim <i>spray</i> (Weleda)	1,2	>2 anos	Até 2 horas

Icaridina confere proteção por um período de até 10 horas.

### Prevention with repellent in children.

Use of topical insect repellent is an important component in prophylaxis of arthropod bite vector borne diseases. Topical insect repellent are used in a three part management regimen, along with impregnated clothing and mosquito netting. Parental training for efficacious and secure use of repellents for their children is essential part of a successful strategy to combat Lyme borreliosis, dengue fever, Chikungunya, West Nile virus infection and malaria, amongst children, according to local epidemiological risks. Rational repellent prescription for a child must take into account age, active substance concentration, topical substance tolerance, nature and surface of the skin to protect, number of daily applications, and the length of use in a benefit-risk ratio assessment perspective. The 4 currently repellents recommended by Whopes (Who) for their long lasting efficacy and patient tolerance are: 1) Citriodiol (PMD), 2) DEET,



3) Icaridine (KB3023), and 4) IR3535. In field trials the minimum required concentration of each four of these agents to be effective for 3 hours against most arthropods is 20% (in cream, roll-on or spray vehicle). Described side effects of these agents are mild, being limited to local irritative dermatitis and allergy. The risk of severe side effects has been related to DEET misused and neurotoxicity. The international recommendations concerning utilization of topical repellent amongst children for prophylaxis of arthropod borne diseases is concerning short term usage (several weeks). But the use of repellent is sub chronic or chronic amongst the majority of children living in subtropical regions where these vector borne diseases are endemic. And toxicity of topical repellent when used sub-chronically and chronically is not well studied in pediatric age groups. Taking into account these considerations, the current recommendations of the French Group of Tropical Paediatrics are to teach the parents of children who live in arthropod vector disease endemic regions to use topical insect repellent on their children with the recommended age related frequency in the following way: the use of topical repellent in infants above 6 months, once daily. Only in exceptional circumstances of severe arthropod exposure risk, their brief use in nursing infants as young as 2 months is acceptable, however with never more than 1 application daily. From ages 1 to 12 years, 2 applications daily may be safely used; 3 applications daily after 12 years old through adulthood.

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#### **Repellent efficacy of DEET, Icaridin, and EBAAP against *Ixodes ricinus* and *Ixodes scapularis* nymphs (Acari, Ixodidae)**

Repellent efficacy of 10% EBAAP (3-[N-butyl-N-acetyl]-aminopropionic acid, ethyl ester) and 10% Icaridin ((2-(2-hydroxyethyl)-1-piperidinecarboxylic acid 1-methylpropyl ester)) were evaluated against 20% DEET (N,N-diethyl-3-methylbenzamide) in human subject trials against ticks. Responses of host-seeking nymphs of the European castor bean tick (*Ixodes ricinus* L.; Acari: Ixodidae) and the North American blacklegged tick (*I. scapularis* Say; Acari: Ixodidae) were compared. Tests were carried out according to the US-EPA standard protocol with ethanolic solutions of the active ingredients of repellents being applied to the forearm of 10 volunteers. The upward movement of ticks was monitored until repellent failure taking up to 12.5 h. Application of 20% DEET resulted in median complete protection times (CPT; Kaplan-Meier median) between 4 and 4.5 h, while 10% EBAAP yielded CPTs of 3.5-4h. No significant differences were found between the efficacies of two repellents nor between the two species tested. The median of the CPT of a 10% Icaridin solution was 5h in nymphs of *I. scapularis*, but 8h in those of *I. ricinus* (P<0.01). Based on these studies, EBAAP and Icaridin are efficacious alternatives to DEET in their repellent activity against nymphs of the two *Ixodes* ticks with Icaridin demonstrating particularly promising results against *I. ricinus*. Future research should investigate whether similar results occur when adult *Ixodes* ticks or other tick species are tested.

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#### **Length of tick repellency depends on formulation of the repellent compound (Icaridin=Saltidin®): tests on *Ixodes persulcatus* and *Ixodes ricinus* placed on hands and clothes**

The present study had the aim to test the repellent potential of the compound icaridin = Saltidin® against the tick species *Ixodes ricinus* and *Ixodes persulcatus* using different formulations of the compound. Tests were done on backs of impregnated human hands, on impregnated linen cloth and versus impregnated dog hair. It was found that 1. *Ixodes persulcatus*-the common Eastern European, Russian *Ixodes* species is significantly sensitive to icaridin = Saltidin® as *I. ricinus* protecting for the test period of 5 h. This is an important finding, since *I. persulcatus* is the vector of agents of the severe Eastern meningoencephalitis; 2. that this repellent compound acts similarly on both *I. ricinus* and *I. persulcatus*, when sprayed either on naked skin or on cloths; 3. that there are only slight differences in duration of the repellency when using different formulations containing icaridin = Saltidin®; 4. that icaridin = Saltidin® sprayed on dog hair has identical repellent effects like those seen on human skin and cloths; thus, this compound can also be used to protect animals such as dogs, cats, horses; and 5. that the icaridin = Saltidin® did not induce a bad sensation on skin, nor bad smells; furthermore, it was not sticky and did not leave residuals neither on clothes nor on dog's hair.



### Catastrophic effect of *Aedes Aegypti*: An insect borne virus from Togaviridae family

Chikungunya fever is a viral disease transmitted to humans by the bite of infected mosquitoes. The virus is a member of the genus Alphavirus, in the family Togaviridae. Chikungunya fever is a viral disease transmitted to humans by the bite of infected mosquitoes. Steps to prevent infection with chikungunya virus include use of insect repellent, protective clothing, and staying in areas with screens. Chikungunya virus is indigenous to tropical Africa and Asia, where it is transmitted to humans by the bite of infected mosquitoes, usually of the genus *Aedes*. The most effective means of prevention are protection against contact with the disease-carrying mosquitoes and mosquito control. These include using insect repellents with substances like DEET (N,N-Diethyl-meta-toluamide; also known as N,N'-Diethyl-3-methylbenzamide or NNDB), icaridin (also known as picaridin and KBR3023, hydroxyethyl isobutyl piperidine carboxylate), PMD (p-menthane-3,8-diol, a substance derived from the lemon eucalyptus tree), or IR3535 (ethyl 3-[acetyl(butyl)amino]propanoate). Wearing bite-proof long sleeves and trousers (pants) also offers protection. In addition, garments can be treated with pyrethroids, a class of insecticides that often has repellent properties.

### Preventing mosquito and tick bites: A Canadian update

The present practice point provides updated guidance on personal protective measures to safely and effectively prevent mosquito and tick bites in Canada. Means of avoidance as well as physical and chemical barriers are described. Current information regarding insect and tick repellents and recommendations for their use are provided, along with instructions for removing ticks. Guidance on using insecticide for additional chemical protection is offered. There are only five registered 'active ingredients' in the many different repellents available in Canada (including creams, lotions, gels, solutions, pump sprays and aerosols). (1) The active ingredient in most products is a chemical known as DEET (N,N-diethyl-metatoluamide), while other chemical repellents are icaridin (hydroxy-ethyl isobutyl piperidine carboxylate, also known as picaridin) and biopesticides, which are derivatives of natural materials. The main biopesticides are oil of lemon eucalyptus and its synthetic equivalent, p-menthane 3,8-diol (PMD), (5) 2% soybean oil and citronella oil. Although there is no evidence that DEET-free repellents are safer, many parents prefer them. Icaridin/picaridin has levels of efficacy similar to DEET in preventing mosquito and tick bites. Although it is widely used in Europe and in the United States, this repellent was only licensed in Canada in 2012. Icaridin is considered to be the repellent of first choice by the Public Health Agency of Canada's Canadian Advisory Committee on Tropical Medicine and Travel for travellers six months to 12 years of age. Products containing up to 20% icaridin (9) are considered to be safe and efficacious. However, in 2013, only Avon products (Avon Products Inc, USA) containing icaridin were readily available in Canada (Table 2). Natural repellents are not necessarily safer than DEET or icaridin. People who are sensitive to plant oils may develop dermatitis or eye irritation. Repellents that contain PMD should be considered the next choice after icaridin or DEET. Soybean- and citronella oil-based repellents may not protect against tick bites.

### Repellent and deterrent effects of SS220, Picaridin, and Deet suppress human blood feeding by *Aedes aegypti*, *Anopheles stephensi*, and *Phlebotomus papatasi*

A series of behavioral tests with *Aedes aegypti* (L.), *Anopheles stephensi* Liston, mosquitoes, and the sand fly *Phlebotomus papatasi* Scopoli in the presence of Deet, SS220, and Picaridin topically applied to the skin of human volunteers showed that the insects were deterred from feeding on and repelled from surfaces emanating the compounds. When offered a 12- or 24-cm<sup>2</sup> area of skin, one-half treated with compound and one-half untreated, the insects fed almost exclusively on untreated skin. The sand flies and mosquitoes did not at any time physically contact chemically treated surfaces. When treated and untreated skin areas were covered with cloth, insects contacted, landed, and bit only through cloth covering untreated skin. These observations provided evidence that the compounds deterred feeding and repelled insects from treated surfaces primarily as a result of olfactory sensing. When cloth, one-half untreated and one-half treated with chemical, was placed over untreated skin, insects only touched and specifically bit through the untreated cloth. This showed that the activity of the chemicals does not involve a chemical x skin interaction. In the presence of any of the three chemicals, no matter how they were presented to the insects, overall population biting activity was reduced by about one-half relative to controls. This reduction showed a true repellent effect for the compounds. Results clearly showed that Deet, SS220, and Picaridin exert repellent and deterrent effects upon the behavior of mosquitoes and sand flies. Heretofore, the combined behavioral effects of these compounds upon mosquito and sand fly behavior were unknown. Moreover, protection afforded by Deet, SS220, and Picaridin against the feeding of these three disease vectors on humans is mechanistically a consequence of the two chemical effects



## Expert Review of the Evidence Base for Arthropod Bite Avoidance

Repellents for Topical Use - *Major Findings:* *N,N*-diethyl-3-methylbenzamide (deet), (2-(2-hydroxyethyl)-piperidinecarboxylic acid 1-methyl ester (icaridin), *p*-methane 3, 8-diol (PMD), and ethyl butylacetyl aminopropionate (IR3535)-based repellents all provide protection against biting arthropods, but volatile oils and other natural products are less reliable. On the strength of available evidence, the first-line choice for those visiting areas where malaria or other arthropodborne diseases are endemic remains formulations with higher concentrations (20–50%) of deet. Higher concentration icaridin and PMD preparations are the most useful alternatives to deet where they are available. Icaridin and PMD are reasonable alternatives to deet for those visiting areas where arthropodborne diseases are endemic, whereas IR3535 has shown reduced efficacy against *Anopheles* mosquitoes and should not be advised for malaria endemic areas. When advising a formulation, the concentration of AI and the expected application rate of AI should always be considered because these will greatly influence longevity of the applied dose. There are, for instance, some icaridin formulations containing suboptimal concentrations. Apart from the repellent choice, the following factors will determine the duration of any repellent product.

**Table 1** Summary of evidence base for topically applied repellents

Aspect of bite avoidance	Strength of evidence*	Quality of evidence†	Comments
<b>Deet</b>			
Dermal application to avoid mosquitoes	A	I	Deet provides shorter protection against <i>Anopheles</i> sp. mosquitoes than <i>Culex</i> mosquitoes. Reapplication times will vary to maintain optimal effectiveness.
Dermal application to avoid ticks	B	I	Laboratory and field tests showed deet provides minimal protection, recent test showed adequate protection.
Application of deet to wristbands	E	I	Wristbands provide no protection for uncovered and untreated human skin.
<b>Icaridin</b>			
Dermal application to avoid mosquitoes	A	I	Icaridin provided good protection against <i>Anopheles</i> sp. mosquitoes in Africa and Asia, also effective against <i>Culex</i> mosquitoes.
Dermal application of icaridin to humans to avoid ticks	B	I	Laboratory test showed icaridin provides protection for 1 h. Recent test showed adequate protection.
<b>IR3535</b>			
Dermal application to avoid mosquitoes	B	II	Based on limited field studies for mosquitoes. Not recommended in malaria endemic areas.
Dermal application to avoid sand flies	B	II	Based on one laboratory study.
<b>PMD</b>			
Dermal application to avoid mosquitoes	A	I	Can be highly recommended as an alternative repellent to deet at concentrations of >20% as a repellent for use in disease endemic areas. (Some evidence of efficacy against ticks.)
<b>Citronella</b>	C	III	Not recommended for use when engaging in vigorous activities, in disease endemic areas or areas with high densities of mosquitoes.
<b>Neem</b>	D	III	More studies should be conducted before it is recommended as a repellent.
<b>Essential oils</b>	D	III	Essential oils require careful formulation to be effective, and safety data suggest skin irritation is a factor.

\*A = good evidence to support use; B = moderate evidence to support use; C = poor evidence to support use; D = moderate evidence to support a recommendation against use; E = good evidence to support a recommendation against use.  
 †I = evidence from one or more properly randomized, controlled trials; II = evidence from one or more well-designed clinical trials without randomization, from case-controlled analysis of cohort study; III = consensus evidence, evidence from one authority or reports of expert committees, single case studies.

## Evaluation of biological and chemical insect repellents and their potential adverse effects

These low or reduced repellent effects of plant oils or of plant extracts were the reason that intense research started early in the last century leading to the finding of several chemical compounds such as dimethyl phthalate (phthalic acid dimethyl ester), indalone, ethyl hexane diol (Rutger 612), Merck 3535 (IR 3535), *N,N*-diethyl phenylacetamide (DEET), and KBR (= Bayrepel, Icaridin, picaridin, Saltidin) among others. Especially the latter two chemical compounds are used today worldwide in a very broad range of formulations and dosages. Among the few remaining notified repellents now, some are synthetic compounds (DEET, paramenthan diol, Icaridin) and others are of plant origin (e.g., lavender, geraniol). Fragrances like oils of lilac, rosewood, sandalwood, and extract of *Vitex agnus castus* had not been listed as notified ingredients, although some of them may bring about protection as repellents if they were applied in higher concentrations. In order to clarify this question, plant-derived compounds notified and not anymore allowed were brought onto hands of volunteers at concentrations of 0.25 or 1 % before being exposed to hungry *Aedes aegypti* mosquitoes, and their effects were compared to those of two synthetic repellents (DEET, Saltidin = Icaridin). The synthetic products Icaridin and DEET at a concentration of 10 % showed full protection within three test minutes starting 10 or 30 min after the spraying of the product onto the skin at the upper side of the hands of each test person. Comparing plant extracts and synthetic compounds (DEET, Icaridin = Saltidin), it was found in all cases that high concentrations of at least 20 % will achieve relevant repellency independently whether the compounds are plant-derived or synthetic chemicals. However, only a few plant-derived compounds showed sufficient and long-lasting repellency. Furthermore, these efficacies depended on the mosquito species. When comparing laboratory strains of *A. aegypti*, *Culex quinquefasciatus*, and *Anopheles stephensi*, it turned out that *A. aegypti* was the most aggressive species and was considerably less long repelled by plant extracts as well as by DEET or Icaridin/ Saltidin than *A. stephensi* or *C. quinquefasciatus*.



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