VIKELA™ NEXT GENERATION INSECTICIDE TREATED MOSQUITO NET

Innovations inspired by thinking big

African Applied Chemical

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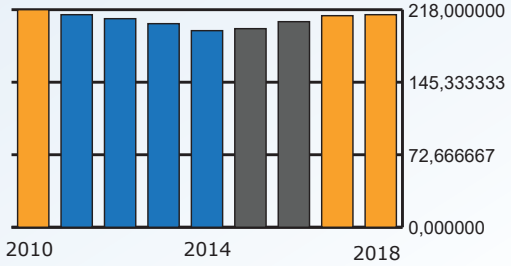
The problem

Malaria is a devastating parasitic disease that affects 250 million people worldwide. 90% of all deaths due to malaria are in sub-Saharan Africa. 74% of those deaths are in children and pregnant women. The World Health Organisation (WHO) recommends the use of Long-Lasting Insecticide-Treated nets (LLIN) as the main technique to suppress mosquito populations leading to a reduction in malaria transmission. Sleeping under an LLIN offers a physical barrier that prevents a mosquito from biting its victim. However, the mosquito will touch this insecticide-laced barrier and die. This mortality leads to a reduction in mosquito populations and ultimately in malaria

Malaria cases in Africa

Estimated number of malaria cases in Africa per year (in millions)

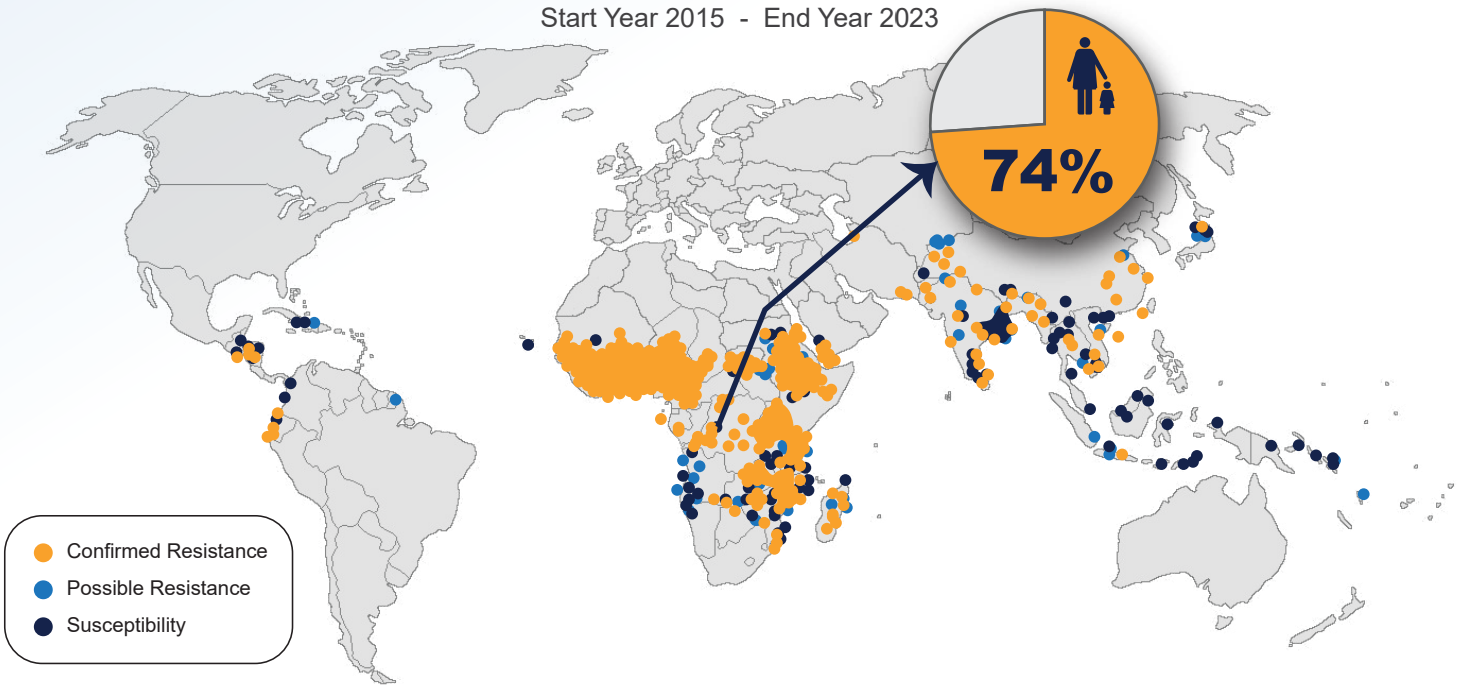


Source: World Health Organization

transmission rates The use of LLIN has been successful since their launch in the early 2000s but from 2016 onwards, malaria cases have been increasing. The problem is only one type

Resistance Heatmap

Start Year 2015 - End Year 2023



Vector Species: All vs Insecticides: All vs IRAC MoA Code: All from 2015 to 2023

https://anopheles.irmapper.com/

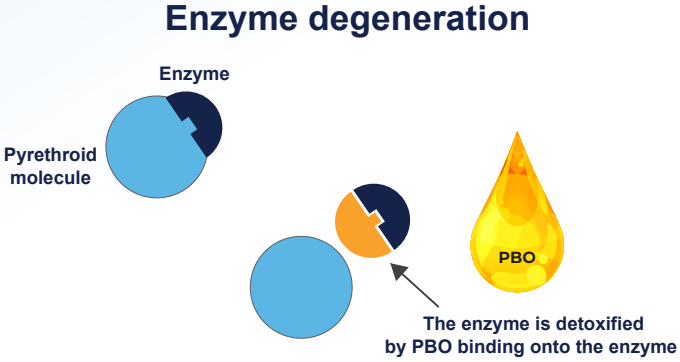
of insecticide was used to treat LLIN. This insecticide is called a pyrethroid and is commonly used in household insecticidal sprays. The insecticide has very mild toxic effects on human beings hence the widespread use of Partheroids for public health purposes.

Insecticide resistance in mosquitoes

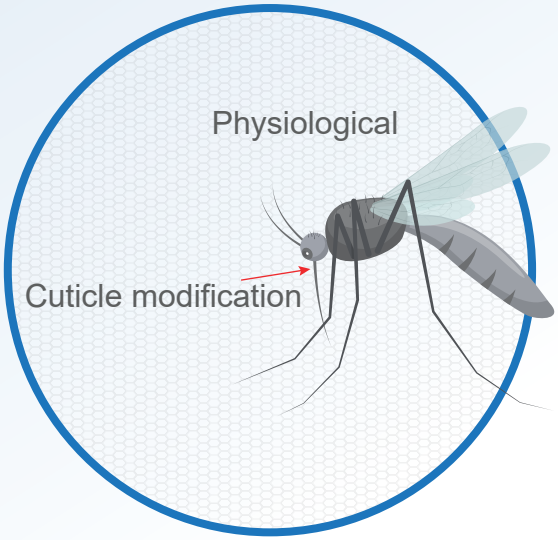
The problem with using one type of insecticide is that mosquitoes have developed resistance to the pyrethroid insecticides, and this resistance is now widespread in Africa. This is the reason why malaria cases are resurgent again. There are two main types of insecticide resistance mechanisms by mosquitoes that need to be tackled i.e. monooxygenase enzyme-mediated resistance and knockdown resistance.

Enzyme-mediated resistance

Monooxygenase enzyme sequestration resistance is a resistance mechanism in a mosquito in which the mosquito secretes monooxygenase enzymes to break down a pyrethroid insecticide into non-toxic by-products. Piperonyl Butoxide is an organic liquid that neutralizes these enzymes and prevents them from breaking down the pyrethroid insecticide. Piperonyl butoxide is not insecticidal and is completely safe for humans.



Knockdown or target site resistance is a mechanism of insecticide resistance by which the mosquito cuticle is thickened thereby preventing or delaying the penetration of the insecticide to effect its mortal action. The penetration is increased if the insecticide is delivered in solution form.



The ”next generation” (LLIN)

The mosquito vector control community believes that a “Next Generation” LLIN may be effective against insecticide-resistant mosquitoes. A “Next Generation” LLIN is defined as a product that contains a pyrethroid insecticide and a secondary active designed to increase the effectiveness of the LLIN product against pyrethroid-resistant mosquitoes. The secondary active can be a synergist and/or a novel and safe insecticide that is not used in agriculture.

The solution

AAC has developed and prototyped a technologically advanced "Next Generation" LLIN product i.e. Vikela™ II. This product utilises the proprietary Bi-Ko™ slow-release fibre technology. The LLIN incorporates a pyrethroid, Piperonyl Butoxide and Nootkatone. Nootkatone is a natural insecticide that has been shown to be very effective against mosquitoes including pyrethroid-resistant mosquitoes. Nootkatone also possesses very strong insect-repellent properties in addition to being insecticidal. This repellent quality is very important as it increases the blood-feeding inhibition in mosquitoes drastically reducing malaria transmission rates. Nootkatone is currently applied commercially as a food flavouring agent. Since it is edible it is also safe for exposure to human beings and can therefore be used on mosquito nets.

Formulation of insecticide actives

Nootkatone

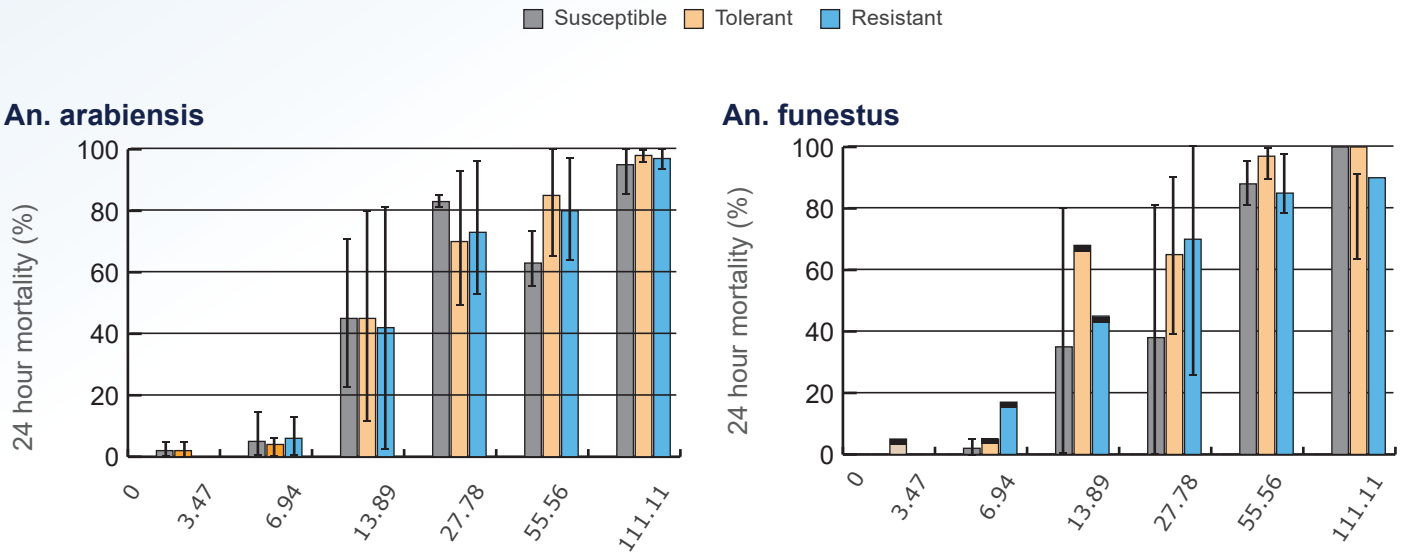
WHO Nootkatone concentration bottle assays

Using the WHO concentration assay protocol, nootkatone was evaluated for efficacy against susceptible and resistant mosquito strains. Silicon oil was substituted for Piperonyl butoxide.

Solution of Piperonyl butoxide + Nootkatone

30 minute exposure
25 non blood fed mosquitos

Performed CDC Bottle bioassy with insecticide coated bottles

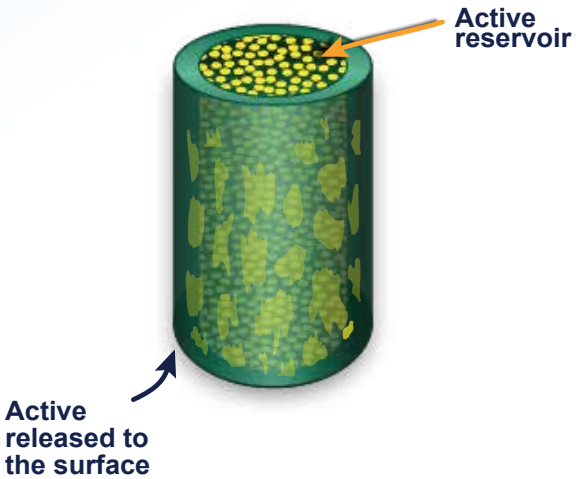


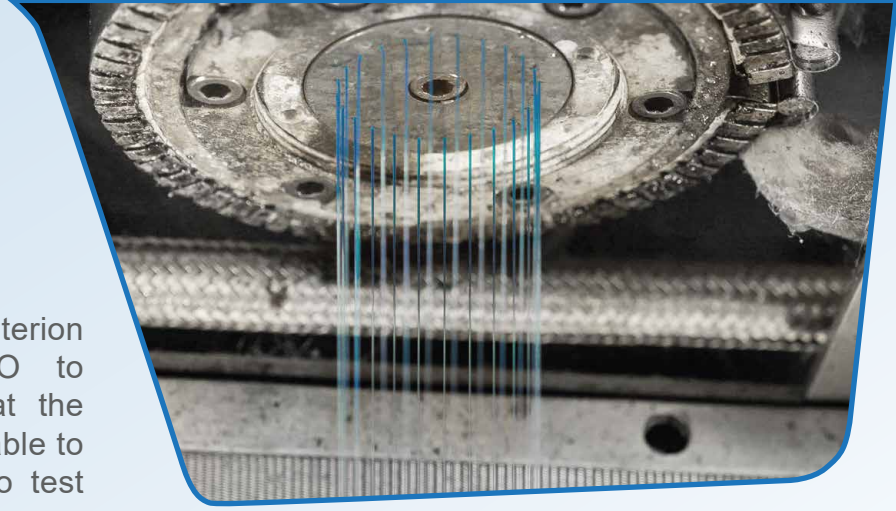
Bi-Ko™ SLOW-RELEASE TECHNOLOGY

The innovation

Disease control textiles

The most important criterion required by the WHO to register an LLIN is that the LLIN product should be able to kill 80% of the mosquito test population after 20 washes as defined by a standard testing protocol developed by the WHO. The biggest technical challenge is ensuring that the insecticide formulation incorporated into an LLIN can resist being washed off by the washing process. This challenge becomes even more difficult if the active is a liquid as in the case of the synergist Piperonyl Butoxide. The technology used in the manufacture of the proposed Vikela™ II LLIN is the proprietary Bi-Ko™ slow-release technology. This is a textile fibre specially engineered to store and slowly release non-polar organic liquids. If such a textile is washed, only the active that has been released from the internal reservoir of the fibre is washed off. The rest of the liquid active is still protected within the fibre reservoir and continually released to replenish





the surface of the fibre. This technology solves the technical challenge of infusing liquids in a textile product in such a way that they can resist multiple washes and remain active for a very long time. This feature is very important in

the case of delivering an organic liquid active such as Piperonyl Butoxide.

To solve the problem of monooxygenase enzyme resistance and knockdown resistance, AAC has devised a process of dissolving the solid insecticide actives into the Piperonyl Butoxide before incorporation into the fibre.

Delivery of the insecticide in the form of a solution in Piperonyl Butoxide greatly increases effectiveness due to increased ingestion of the insecticide by the mosquito compared to when the insecticide is in crystalline form. The Piperonyl Butoxide liquid acts as an efficient transport of insecticide into the mosquito mitigating knock-down resistance whilst at the same time preventing monooxygenase enzyme sequestration of the pyrethroid. This makes our product effective against mosquitoes with multiple resistance mechanisms. In addition, using the Bi-Ko™ slow-release technology, AAC has infused more than threefold Piperonyl Butoxide into the mosquito net fibre than the nearest competitor currently in the market. This technical fit ensures that Piperonyl Butoxide/insecticide solution formulation is slowly released for an extended period. Lastly, Vikela™ II LLIN contains the novel natural insecticide called Nootkatone as a secondary insecticide in addition to the pyrethroid and Piperonyl Butoxide. This adds another layer of effectiveness against mosquitoes.

Bi-KO™
SLOW-RELEASE TECHNOLOGY

African Applied Chemical

The company and innovation

African Applied Chemical (AAC) is a biotechnology company based at the Innovation Hub in Pretoria. AAC specialises in the manufacture of high-value products based on the proprietary Bi-Ko™ slow-release technology. The Bi-Ko™ slow-release technology was developed through collaboration with the University of Pretoria Department of Chemical Engineering, the University of Pretoria Institute for Sustainable Malaria Control (UPISMC) and the Institute for Polymer Research in Germany.

Our Partners

Contact us

info@nobuzz.co.za

www.africanappliedchemical.co.za

+27 (0) 72 663 7740

+27 (0) 12 844 1011

Lot BBFL01, Biopark Building 1606
Allan Cormack street The Innova-
tion Hub, Persequor Pretoria, 0020

Find us on: