Chemical Actives to Eliminate Mosquitoes

SITARAM DIXIT
Senior Manager – Fragrance Applications, International Flavours & Fragrances India Ltd.
Floral Deck Plaza, 3rd Floor, B. Wing, Mumbai 400 093
E-mail: sitaram.dixit@iff.com

INTRODUCTION

In the 21st century world, Malaria is still the biggest killer of people and mosquitoes are the primary transmitters of Malaria parasite to humans. There are a number of diseases borne by mosquitoes namely malaria, filaria, dengue, brain fever and yellow fever. Mosquito borne diseases are prevalent in more than 100 countries, infecting 300-500-mn people and causing about 1-mn deaths every year. Mosquitoes in jungle areas in parts of Africa & South America cause yellow fever.

In India, more than 40-mn people suffer from mosquito diseases annually. Over 2-mn cases of malaria alone are reported a year. Malaria, filaria, and dengue are the most prevalent diseases spread by mosquitoes. Even more astonishing is the fact that India spends $100-mn on malaria. In spite of spending so much, the diseases continue to explode from time to time. The reason is that these mosquitoes develop resistance to medicines and chemicals. Hence, fighting mosquitoes and the diseases spread by them is a continuous process.

Eradication of mosquitoes is the only way to protect humanity. The mosquito-borne diseases are no more downmarket diseases, since you find them in boardroom, in the lifts, in the cars, in the theatres, in the golf clubs, etc. However, let us not forget that mosquitoes and mosquito-borne diseases are the result of low hygiene and sanitation in the downmarket areas and poor insect control in the upmarket areas.

MALARIA & DENGUE

Four species of parasites cause malaria in man. They are *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium ovale*. The most dangerous of these is the *plasmodium falciparum* that can cause cerebral malaria. This species afflicts about one-tenth of total malaria victims and might even prove fatal. The parasite enters the body by the bite of the female anopheles mosquito, which is the only mosquito type that transmits human malaria. You cannot catch malaria directly from another human being — the infecting parasite has to pass through a mosquito first. Even if a mosquito that has bitten a malarial patient bites you, the transmitted malaria parasite has an incubation period in mosquitoes, just as it has in human beings.

Dengue is an acute flu-like fever caused by virus and spread through the bite of an infected *Aedes Aegypti* mosquito. The mosquito gets the virus by biting an infected person. Dengue hemorrhagic fever is an acute infectious viral disease usually affecting infants and young children and can be often fatal. *Aedes Aegypti*, the transmitter of the disease is a day-biting mosquito that lays eggs in clear water containers, such as flower vases, cans, rain barrels, old rubber tyres, etc. The adult mosquitoes rest in dark places of the house.

One should not allow water to stagnate, as this forms a breeding ground for malaria's deadly carriers, the anopheles mosquito. At community level, drain out water completely and prevent stagnation. For efficient control, spraying can be undertaken using pesticides by certified authority. At home, you should change water in flowerpots, buckets, coolers etc. at least twice a week. Cover the ventilation of socket outlet pipes with proper nets. Mosquito nets and door screens also help. However, if these methods are not convenient the use of mosquito repellents like mats, coils, aerosol, sprays, vaporisers, body creams, etc., regularly, to keep mosquitoes away, is necessary.

HOW HUMAN SWEAT ATTRACTS MOSQUITOES

Scientists from the Yale University's Department of Molecular, Cellular, and Developmental Biology have figured out how malarial mosquitoes are attracted to the smell of human sweat. The molecular mechanism lies in the nerve cells of the female anopheles mosquito that help the insect to detect a human victim from miles away. An odorant in sweat called 4-methylphenol activates olfactory cells through a lock, or receptor, on those cells that is termed AgOr1. Once triggered, those cells then alert the mosquito to a potential meal. The discovery has big potential, for it opens the way to a new generation of mosquito repellents that neutralise 4-methylphenol. Alternatively, 4-methylphenol could be used in bait traps to lure mosquitoes to their death. Only female mosquitoes carry AgOr1 — and female mosquitoes are the biggest carrier of the malaria parasite *Plasmodium falciparum. P. falciparum* is passed on to humans when the mosquito takes a blood meal. It then proliferates in the bloodstream and passes onto other mosquitoes that feed on the same host, thus perpetuating the cycle.

POTENT DRUGS AGAINST MALARIAL PARASITE

Quinine and other drugs like chloroquine, mefloquine, and primaquine are potent against malaria. However, malarial parasite is one that does not easily give up its fight for survival and are constantly evolving new immunity. With so many strains of parasites, remedies are only partially successful. More the anti-malarial drugs used, the greater the resistance the parasite develops to them, making it difficult to control the ailment.

Quite often, malaria is not easy to diagnose and by that, the severity of attack has intensified. In addition, most people tend to take medication only until the fever and more severe symptoms abate; after which they become negligent leading to relapse. Nevertheless, for the treatment to be effective, it is essential that the patient go through the entire course of medication prescribed.

One cannot depend on medication alone to prevent malaria. Avoidance of bites is the best protective plan. Consistent use of these measures, during day and night, will not only prevent malaria and filaria, but also dengue, the daytime biting mosquito disease. It is advisable to carry some form of mosquito repellent while travelling viz., sprays, creams, lotions, mats, or coils and use as felt necessary.

PESTICIDES TO CONTROL MOSQUITOES

Pesticides used in controlling harmful mosquitoes play a very important role in protecting the life and health of the populace. The use of DDT (1,1,1-trichloro-2,2-bis(p-chloropenyl)ethane) to control the mosquito vector of the malarial parasite is well known. DDT was largely responsible in reducing the incidence of the disease, saving millions of lives during Second World War and in the 1950 and 1960's. Ironically, the use of DDT to control agricultural crops, pests, and mosquitoes was stopped, as it found a way in the food chain causing the death of birds. DDT's value in controlling disease that were vectored by pests and the service it rendered in saving millions of soldiers, farmers across Europe after the war was forgotten. Had the WHO (World Health Organisation) spray program been continued, malaria would have been eradicated and this author would not have suffered the fever recently to feel the urge to pen this article.

MOSQUITO REPELLENTS

Humans have battled against mosquitoes by applying plant extracts on skin, burning twigs, shrubs, bark, etc., a practice that was common in India and China from the early days of civilisation. However, mosquito coils that are very handy and convenient to use, owe its origin to Japan. In addition to the convenience, it is also economical for regular use. Mosquito coils are so popular across boundaries that it is manufactured in all parts of the world.

Mosquito repellents were first commercialised for use in 1890. At one time, pyrethrum seed powder was mixed with kerosene to create a sprayable liquid insecticide. In 1910, powdered dried pyrethrum flowers replaced pyrethrum seed powder. Use of pyrethrum made these mosquito repellents an effective insecticide. Mosquito repellents in the initial days were in the shape of incense sticks. Manufacturing it in the form of incense sticks that lasted for a few minutes was time consuming and ineffective to keep mosquitoes away all night. Constant effort by the manufacturers to alleviate the inefficiency in manufacture and cater to demand led to the discovery of machines that mass-produced mosquito repellents of uniform quality. The shape gradually evolved into the present spiral shape making it effective to burn for longer duration, almost 8-12 hours, enough for a good night's sleep.

The main active used in mosquito coils are derivatives extracted from Pyrethrum flowers (*Chrysanthemum cinerariaefolium Vis*), that have insecticidal properties. A native plant of Dalmatia (Yugoslavia), Herzegovina and Montenegro, it is cultivated on a commercial scale all over the world. However, Kenya, Tanzania, and Rwanda produce more than 80% of the total production. About 70% of the pyrethrum produced goes in making fly sprays and insecticidal aerosols, 20% in mosquito coils and the rest 10% in formulations like powder, liquid sprays, ointments, and creams.

In India, pyrethrum cultivation started in Kashmir and the Nilgiri hills in 1931. Now it is cultivated commercially in parts of Kashmir, Kodaikanal and Lucknow. Pyrethrins is extracted from the flowers as concentrated oleoresins by solvent extraction using organic solvents, namely petroleum ether, ethylene dichloride, etc. The extract is used as is or after due refining in insecticide formulations. Total pyrethrin active obtained is between 1.0-1.5%. Today, however, synthetic derivatives of Pyrethrum are major actives used in mosquito control.

An effective mosquito repellent active should possess the following properties.

1. It should have a good 'Knock down' i.e., the compounds are fast acting causing flying insects to fall out of air and rendered incapable of co-ordinated movement.
2. It should posses a good "Kill" i.e., the compounds should be effective in killing the insects.
3. The active should be photo-stable, i.e. it should not break down in sunlight.
4. It should possess good insecticidal toxicity, but low mammalian toxicity.

An active having good "Kill" properties acts very slowly. However, it is very effective, in combination with compounds that have a good "Knock" down property.

Natural pyrethrum's insecticidal action is due to the combined action of the six-pyrethrum molecules that constitute it. Each molecule possesses different biological roles and complements each other so that, in totality, natural pyrethrum extract not only has a good knock down effect, but also have good mosquito repellence. Pyrethrum, however, has low photo stability. This enables the mosquito to recover when exposed to sub-lethal doses. To increase the kill property of pyrethrum, it is combined with a synergist like piperonyl butoxide in a mosquito formulation. Piperonyl butoxide is also prepared from the oil of sassafras, a natural product.

First generation synthetic pyrethroids had similar properties as natural pyrethrum, viz.; good "Knock down" and low photo stability. Use of synergists did not really help in increasing the kill property. Second generation pyrethroids had good "Kill" property, but poor "Knock down" properties. Subsequent generations, now available, are more photostable and have a good "Kill" and good "Knock down" properties. Nowadays, most commercial mosquito repellents with synthetic pyrethroids use a combination of one or more chemicals as actives to improve insecticidal activity. The most common chemical actives are Resmethrin, Bioresmethrin, d–Phenothrin, Tetramethrin, Bioallethrin, and p-Allethrin.

Despite the many advantages that chemical pesticides provide in controlling plant pests, most have serious limitations, as well. Not only do they have to be applied carefully because of possible hazards to humans and animals, but also insects often develop resistance to them very quickly. Natural pyrethrum has neither of these drawbacks. It is safe and effective, and it has been in use for years without any sign of insect resistance developing. In addition, new means are being devised for improving it and making it

more effective. People believe that an insect proceeding toward an environment or source of food senses pyrethrin vapours released from a mosquito repellent, makes an about turn, and flees from the pyrethrin vapours that are distasteful and malodorous in nature. This is far from the truth, as pyrethrins have low vapour pressure and are non-volatile and odourless under normal conditions. The mild flowery odour of pyrethrum extract is due to the natural pyrethrum essential oils and not from the active insecticide pyrethrins present in the extract.

SO HOW DOES PYRETHRIN REPEL?

Pyrethrins act as nerve toxicants on insects. They act on the insect's nerves initially by hyper stimulating or over exciting, the nerves to a point that ultimately, the nerve synapses are blocked. The repellence effect is the insect's physical manifestation due to pyrethrin stimulation and excitation on the nerves. The insects become hyperactive get confused making their movements unregulated. A small amount of pyrethrin is sufficient to cause this effect. This behaviour of mosquitoes to pyrethrin is called as repellent.

A female mosquito that feeds on mammals, needs a blood meal in order to lay eggs. She combines her sense of heat detection and chemical detection of stimulants (water vapour and carbon dioxide) and detects her hosts. The mosquito uses the tarsi footpads of the third pair of legs to detect heat. Her antennae detect presence of water vapour and carbon dioxide. Pyrethrin stimulates the mosquito's nervous system and the tarsi, antennae do not function normally, and she is not able to find the host correctly. The mosquito then flies in a different direction until her nerves and organs function normally and she is able to find her blood meal. Thus, the mosquito behaves in a manner not necessarily against hostile environment, but in favour of an area where her nervous system functions normally, helping her locate a host and get a satisfying bloody meal.

Pyrethrin activity on the nervous system of amphibians and mammals are limited, when compared to studies designed and generated with insects. It is assumed that pyrethrin does affect animal nervous system in a similar manner as tremors, hyper-excitability, etc., has been observed in animals. Significant data relating to acute and chronic toxicity, teratogenic, carcinogenic, mutagenic, and allergenic are available. Pyrethrum has a long history of use on humans and animals. When used at normal labelled dosages and specified patterns, it is safe and not a health hazard. Among all insecticides available for use, pyrethrin is supposed to be the safest one to humans. Synthesis and sale of pyrethrin, the active present in natural pyrethrum, have significantly helped in overcoming the industry's dependence on pyrethrum harvest and vagaries of nature. Similarly the invention of the automatic coil making machine has helped in eliminating the various blockade that earlier existed in manufacturing mosquito repelling coil, truly making it a mass-marketed product.

Allethrin is the chemical used in leading mosquito repellent products. A high power committee of WHO has reviewed and approved allethrin for use in household insecticides in 1989, based on exhaustive toxicology data submitted by Sumitomo (Japan) & Aventis (Germany). The Central Insecticide Board, Ministry of Agriculture, Government of India, based on data submitted on chemistry, bio-efficacy, and toxicology, also approves allethrin.

MOSQUITO COILS

Mosquito coils are the most common form of mosquito repellents. They are cheaper than other product forms and can be used in the absence of electricity. The main disadvantage is the smoke that is released on lighting it and its tendency to break into pieces easily. An 8-10 hour coil burns effectively up to 8-10 hours when there is no airflow on the coil. Coil will burn for less duration if there is a breeze. It is advisable to keep unused coils inside the pack and avoid burning coils on a damp floor or places that are wet as it can absorb moisture and stop burning.

The following are the important steps to manufacture mosquito coils.

Preparation of raw material

Extracted residue of pyrethrum flower, dried petals of pyrethrum flowers, or a synthetic active is pulverised with sawdust acquired from cedar, cypress wood, etc., to a proper size by an atomiser.

Blending and kneading of secondary material

A fixed amount of a suitable binder added to the pulverised sawdust and pyrethrin active are blended well in a mixer. The blend is kneaded thoroughly with water, along with coloured pigments, emulsifiers, anti-mould preservative, etc. The amount of water is adjusted at this point in the process.

Crushing, moulding and punching

The thoroughly blended and kneaded mixer of ingredients is then crushed as uniform as possible. It is then made out in the form of a board of uniform thickness. The product is then punched out into the spiral shape of fixed length and breath by a mould-punching machine and then kept for drying.

Drying

The product obtained is arranged in a drying net and passed through a low temperature drying process, during which time the water content is reduced by about 20%. The product then passes through a quick high temperature drying process reducing the water content by a further 40%. Fragrance is sprayed now and the coil allowed to cool.

Packing

On complete drying, the product is packed in boxes for sale.

MOSQUITO REPELLENT MATS

They are made generally of cardboard impregnated with an active ingredient combined with a synergist. Generally, allethrin is used as an active along with piperonyl butoxide. It is heated to a temperature of above 150°C when the added active vaporizes in a controlled manner to drive away the mosquitoes. Perfume added in repellent mats is used to indicate that the heater is switched on. Blue colour is added to differentiate between used and unused mates. If colour does not change, it indicates you heater is not giving the right temperature. Mats are effective ideally when room size is 30-cu.m.

LIQUID VAPORISERS

They are product forms where mosquito repellent actives are dissolved in solvent,

generally deodorised kerosene. On electrical heating, the solvent evaporates along with the active in a phased manner through a wick to repel mosquitoes. Fragrances and colour pigments are used in the mix to indicate that the vaporiser is on and for aesthetic values.

LOTIONS & CREAMS

Mosquito repellent creams and lotions are product forms very popular with travellers. Lotions can be a simple alcoholic solution with an insect repellent active or can also be formulation with different ingredients to give a better skin feel. Similarly, general cream formulations with a mosquito repellent active serve the purpose. However, creams and lotions are suitable only for travelling or outdoor use. It is not recommended for daily use as they are meant to be rubbed on the skin. This can clog the pores and prevent natural breathing of skin. For effective control, that should be used thoroughly on exposed skin as mosquitoes bite body parts not applied with lotion or cream. Contact of the material with eyes and lips should be avoided.

DEET (N,N-diethyl-m-toluamide) developed by the US Army and the Department of Agriculture in 1950 is claimed to be the most effective mosquito repellent, and is very popular around the world. DEET does not kill the mosquitoes, but its vapours discourage the mosquitoes to sit on the subject. Most repellents contain 10-30% DEET in the formulae.

AEROSOLS / SPRAYS

An aerosol consists of a metal can containing the insecticide and a propellant material. The contents are held in the can under pressure. When the spray button is pressed, the valve is opened and the pressure forces the mixture of insecticides and propellant up a dip tube to produce a spray.

Aerosols are convenient for use and are highly effective, compared to other repellent products, though the effect can be temporary or long-lasting depending on the type of aerosol used. When aerosol is used, the gas molecules evaporate into fine particles that remain air borne for a long time. Mosquitoes that encounter these particles are exterminated. The effect is immediate, unlike mats, coils, and vaporisers where the action compounded is present in a gaseous state. However, separate specialised spray cans for mosquitoes are to be used, as aerosols meant for other crawling insect's viz., cockroaches, etc., are not safe for spraying in the air. For effective control, few 'puffs' are sufficient to cover the whole area. Avoid keeping aerosols in damp areas like bathrooms and open places and near open flame.

MARKET SCENARIO

The Indian market for various mosquito repellents like coils, mats, lotions and vaporisers is Rs. 500-600-crore, growing annually at 7-10%. Almost all of them use synthetic pyrethroids, that is, the Allethrin group of compounds.

The journal of the Indian Academy of Sciences affiliated to Indian Council of Medical Research (ICMR), informs that a survey carried out by the Malaria Research Centre (MRC) revealed that mosquito repellents widely used in the country are harmful to health. It recommends that their use should be avoided or discouraged. The MRC survey, carried out in nine states, covered both users and medical practitioners in urban and rural areas.

The results have revealed that 11.8% of the users of synthetic pyrethroids, across all age groups and both sexes, "complained of a variety of acute toxicity effects, either soon after or within a few hours of use of repellents." The most common complaint was breathing problem, followed by eye irritation, often accompanied by bronchial irritation, headache or skin reaction. In two cases, persons who did not suffer from asthma became asthmatic.

Of those using DEET-based cream, 11.4% reported skin reaction and itching. Of the 286 doctors covered in the survey, 165 or 57.6% reported acute toxicity following use of repellents. A report of the Indian Toxicological Research Centre records serious health consequences by use of repellents. It states that even those who do not immediately feel any adverse effects may be in long-term danger. Although symptoms disappear shortly after withdrawal, those who do not suffer acute toxicity and continue to use these repellents for extended periods may suffer neurotoxic and immunotoxic hazards.

TRIED AND TESTED NATURAL METHOD

Mosquito nets or a 'Neem cream' made up of 5 parts neem oil and 95 parts coconut or mustard oils are safer alternatives. Burning neem oil in kerosene is also very effective.

A 'SALINE SOLUTION' FROM KOCHI

Meanwhile, the Kochi Corporation in Kerala, an area where mosquito is an endemic scourge, has under directions from the Kerala High Court tried out a novel and cost-effective method of reducing the mosquito population at the larvae stage itself. It has conducted experiments where the salinity of water in canals and stagnant pools, major breeding grounds for the mosquito, is increased by adding seawater.

The Corporation, in an affidavit submitted, has told the High Court that the experiment conducted was successful and mosquito larvae were found morbid in the canal portions where salinity was increased. This confirms the view proposed by National Institute of Oceanography (NIO), after series of experiments extending over years, that when the salinity level reaches 30-ppt (the normal percentage of salt in the sea), mosquito larvae cannot survive beyond 3-hours. Even at lower concentrations of 15-ppt, they are dead in 12-hours. In addition, when the concentration is around 60-ppt, the larvae perish within an hour.

There is no way to tell if a mosquito is carrying the virus. Therefore, one must protect oneself from all mosquito bites. All it takes is a few precautionary measures. Maintain a clean environment and healthy hygienic habits.

These not being the cases, then use personal protection agents — natural or otherwise — like mosquito repellents, aerosols, creams, coils, vaporising mats, and nets to lead a happy, healthy, and hygienic life.

Declare war on mosquitoes. They are easier to kill. Malaria and dengue are not. They kill!