On the potential of menthol propyleneglycol carbonate in wood protection against termites

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Introduction

Well-documented risks to human health, increased awareness on the toxicity of pesticides, pest resurgence and resistance, environmental pollution and infrastructure degradation have prompted the search for environmentally-friendly, safe and non-toxic applications in pest management. To understand the processes influencing insect ecology and behavior, Poseidon embarked on a project that began in 1990 to identify a wide variety of natural biochemicals with the objective of selecting compounds that may be useful in practical situations. Analogues of natural compounds that showed promising results were evaluated for improved efficacy under laboratory conditions. The selection of these compounds took into account their potential for further development, their impact on the environment, and their safety for human use.

As a "generally recognized as safe" (GRAS) compound, menthol would have been an ideal eco-friendly material for a repellent. But studies have documented its low repellent potency. Depending upon formulations and concentrations, the repellent effect of menthol and its isomers are generally less than one hour and therefore are unsuitable for effective use. However, a novel compound derived from menthol has now been identified. Menthol propyleneglycol carbonate (MR-08, MPC) demonstrated a high efficacy as repellent against a variety of insect species. It is referred in Poseidon's inventory and in succeeding references in this presentation as MR-08. The chemical structure is shown in Fig. 1.

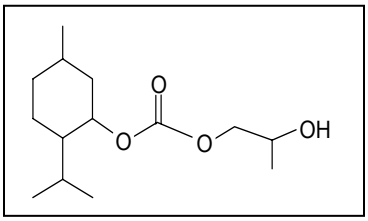

Fig. 1. Structure of menthol propyleneglycol carbonate (MR-08).

MR-08 is also a GRAS (generally recognized as safe by the US FDA) food ingredient and is referenced as number 3806 in the U.S. FEMA GRAS list and as number 444 on the JECFA (Joint FAO/WHO Expert Committee on Food Additives) list. The latest JECFA assessment conducted in 1999 of menthol and its derivatives, including MR-08, reaffirmed this compound's safety for use as an ingredient in food and cosmetics. The known physical properties of this compound are described in Table I.

Table 1. Physical, chemical and toxicological properties of menthol propyleneglycol carbonate

Molecular Weight	Carbonic acid, 5-methyl-2-(1-methylethyl) cyclohexyl ester [1R-(1a, 2ß, 5a)]	
Common Name	menthol propyleneglycol carbonate	
CAS Number	0030304-82-6	
Trade Name	MR-08	
Physical Properties	Form /Color Boiling Point Range Melting Point Flashpoint Ignition Temperature Vapor Pressure Density Solubility in Water Partition Coefficient	liquid / colorless 158.0-173.0°C (9.3 mbar) < -21.0°C 153°C c.c. 276.0 °C < 0.1 mbar (25.0°C) 0.014 g/cm^3 (20.0°C) < 0.100 g/l (20.0°C) n-octanol/water 0.70 (log POW)
Toxicity Profile	Acute Oral Toxicity Acute Dermal Toxicity Ames Test Sensitization Eye Irritation Skin Irritation	LD_{50} >2,000 mg/kg rat LD_{50} >2,000 mg/kg rat no mutagenicity non-sensitizing,guinea pig irritant, rabbit eye non-irritant, rabbit
Ecological Profile	Biodegradability Fish Toxicity Daphnia Toxicity Bacterial Toxicity Algal Toxicity	78% (Strum-Test, LC_{50} 24 mg/ l / 96h Daphnia magna EC_{50} 8.8 mg / l / 48h EC_{50} >62.5 mg / l / 3h EC_{50} 62 mg / l / 72h

MR-08's potential as an insect repellent

Potent vaccines against malaria, dengue fever, and the West Nile virus have yet to be discovered.

While ineffective against the Anopheles mosquito that transmits malaria, recent studies conducted by medical entomologists show that the chemical DEET *(N,N-diethyl-m-toluamide)* which is found in varying concentrations in most mosquito repellents on the market today is still the most effective in driving away mosquitoes, including *Aedes aegypti* , the species that carries yellow fever. Concerns over DEET's safety have diminished. However, repellents containing DEET tend to be sticky, have an unpleasant smell, burn when it gets into eyes and on lips, and tend to melt plastic objects and synthetic fabrics that it comes into contact with. Repellents based on plant extracts such as Citronella perform poorly in keeping away mosquitoes and bugs. Mosquito- and fly-borne diseases are still plaguing the world today.

Among the notorious diseases carried by mosquitoes is dengue fever, which infects 50 million every year and causes deaths among five percent of victims. Another is yellow fever, which infects 200,000 people, killing more than 30,000 worldwide. In recent years, the West Nile virus, carried by the mosquito species *Culex pipiens,* has emerged as a scourge, causing high fevers, neurological problems and even death. This virus killed 264 people in the United States in 2003.

MR-08's efficacy as an insect repellent

MR-08's protection time for human beings against mosquito bites was tested in the laboratory. Adult mosquitoes *(Culex quinquefasciatus)* were kept inside a screened chamber measuring 2 ft x 2ft x 2ft at a density of 200 mosquitoes per chamber. The mosquitoes were aged 3 to 10 days after emergence from larvae and starved for 24 hours prior to each test.

The tests involved volunteers each inserting an arm treated from the elbow to the tips of the fingers with a formulation containing MR-08 mixed with a Pond's-type base cream into the mosquito-filled chamber.

And there is malaria, a debilitating, often fatal disease transmitted by the female Anopheles mosquito, which continues to be one of the world's most infectious killers well into the 21st century. The World Health Organization (WHO) estimates that 40 percent of the world's population, especially in the world's poorest countries in sub-tropical and tropical regions, is threatened by malaria. Two million die from it, most of them children under the age of five.

Flies are a nuisance to people during work and at leisure time. But the health hazard they pose is constantly alarming. Flies spread diseases as they feed on food for human consumption and on filth. The fly carries disease-causing organisms on itself and within, and transmission of the disease occurs when the fly lands on people or their food.

Among fly-borne diseases, the more common and prevalent ones include dysentery, diarrhea, typhoid, cholera; eye infections, poliomyelitis and certain skin infections. About 10 million children in the developing world die each year due to diseases that can be prevented through proper sanitation and nutrition techniques. Diarrheal disease for instance, is among the top five causes of deaths among children under five years of age.

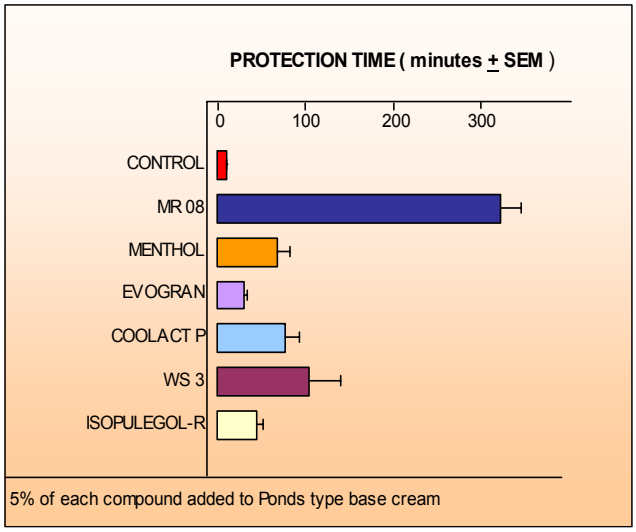

Fig. 2. Comparison of the effect of MR-08 and other menthol isomers on prevention of biting on arms of human volunteers (n=3 volunteers) by the mosquito, Culex quinquefasciatus.

The data in Fig. 2 showed that MR-08 was superior to menthol and other isomers with a protection time of approximately 280 minutes. All other compounds show protection time from bites of about 60 minutes or less.

Summary of the repellent effects of MR-08

Table 2 summarizes the effect of MR-08 in a wide variety of insect pests. In all species studied thus far, we have seen dramatic repellent effects that make this biochemical a unique product for many applications, especially those where food and human contact are involved.

Table 2. Efficacy of MR-08 against the following species:

Organisms	Delivery System	Protection Time
Mosquitoes *Culex quinquefasciatus*	Cream/lotion Laboratory test on human volunteers	5 hours, 5% to 40% depending on formulation
	Cream Field test on human volunteers	4 hours, 10% in cream
Houseflies *Musca domestica*	Spray on bait, up to 50% concentration in ethanol	4 hours
Stable flies	50% concentration in ethanol	8 hours
Ants *Monomonium pharaonis*	Impregnation of paper at 30 $\mu g/cm^2$	12 hours
Fire Ants *S. invicta*	50% in alcohol, spray	5 hours
Termites *Coptotermes vastator*	24 hour soaking of wood at 20% in ethanol	> 6 months
	Sand barrier test	Complete prevention of termite migration

MR-08's potential in wood protection against termite infestation

Wood Preservatives

The demand for wood protection coatings and preservatives is expected to increase just over two percent annually to total $3.0 billion in 2007, with the strongest growth seen in applications for interior products such as furniture and cabinets. The building industry has long used lumber treated with chromated copper arsenate (CCA). The wood is pressure treated or impregnated with this chemical to preserve and protect it against termites and rotting. Aware of the risks of arsenic, a highly toxic metal and known carcinogen present in CCA, manufacturers of wood-preserving chemicals voluntarily agreed to phase-out CCA products in December 2003 in the United States. Since January 2004, CCA-treated products are no longer allowed for residential use.

The alternatives to CCA however, alkaline copper quaternary and copper azole, are expensive. With the withdrawal of CCA-treated wood for residential use, there is a potential market of 68 percent in the U.S. and Canada waiting to be filled by other viable, cost-effective alternatives. The U.S. Forest Service for instance, is developing a commercially-available naptha-based compound that works well to prevent decay-causing fungi and kill subterranean termites.

Termites cause an estimated two billion dollars in damage annually in the U.S. and are a major problem in the warm and humid Southeast. Termites travel as far as 100 yards from their nests in search of food and can eat through plastic pipe and thin metal. They have also demonstrated an ability to survive standard termiticide treatment by avoiding traditional termite baits.

Sand Barrier Test. The effect of MR-08 on the milk termite, *Coptotermes vastator,* was compared to DEET using the sand barrier test method. Collection of termites is in accordance of ASTM D3345.

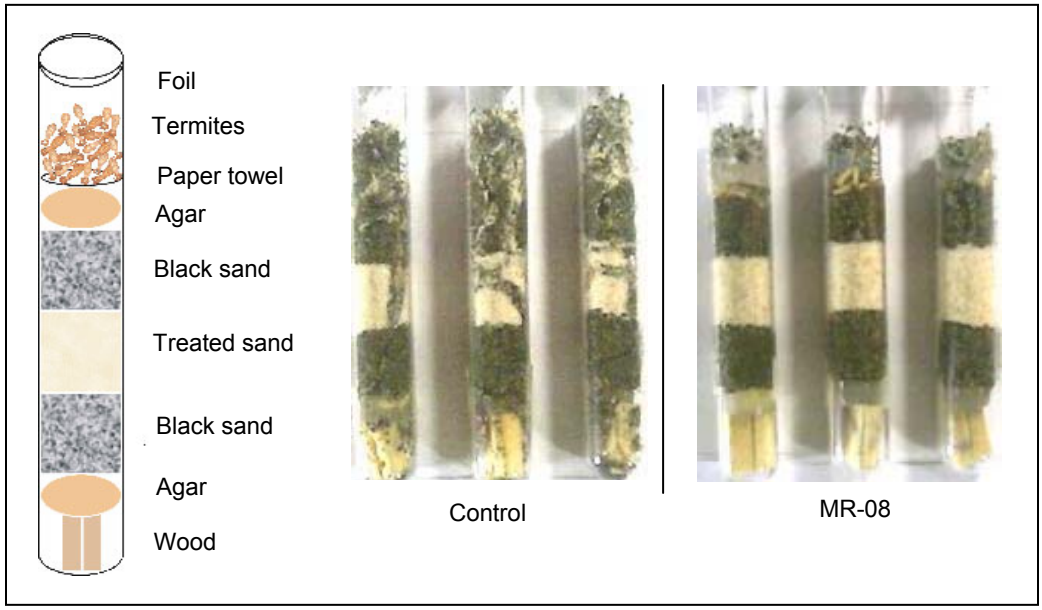

Fig 3. Distances traveled by the termites through the sand barrier. In the control group, the termites have reached the wood blocks by day 6 and burrowed to a distance of 7 cm. In MR-08 treated sand barriers, the termites remained stationary at 1 cm and no damage to the wood blocks until the termination of the test on day 12.

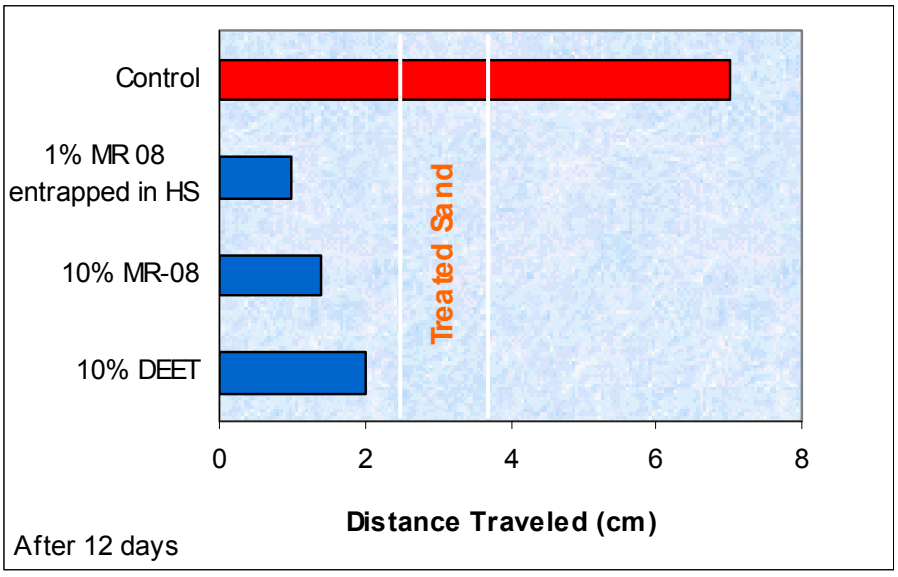

Fig.4. Effect of MR-08 against termites in the sand-barrier test. MR-08 is slightly better than DEET when tested. It is significant to note that when MR-08 was entrapped in a microtubule at one tenth the concentration, it produced a more effective inhibition of termite migration compared to the higher concentration of DEET or MR-08. This suggests that slow release technology may contribute to lower requirement of the active ingredient.

Wood Test

In this study, MR-08 was dissolved in ethanol at a concentration of 10% (w/w) and pieces of pre-weighed soft wood were immersed in the solution for 24 hours. Controls were represented by wood impregnated with ethanol alone. After impregnation, the wood was allowed to air-dry to remove the ethanol, which has a lower flash point. The dry wood was re-weighed to determine the total amount of MR-08 absorbed into the wood. The weight of MR-08 absorbed was 26 milligrams per gram of wood.

The wood test samples were placed on a termite mound under ambient natural outdoor conditions for a period of the study. At the end of the test period, the wood samples were cleaned of debris and termites, dried in the sun and weighed. Wood preservation was determined by the amount of weight loss during the test period.

The data show that termites were able to destroy the wood in the control group within the period of the study. When periodically checked visually, termites are seen within the wood samples in the control group.

However, when MR-08 was impregnated into the wood, the termites were completely prevented from consuming the wood as evidenced by the minimal weight loss of the experimental wood samples. Fig. 5 shows the photographs of the wood after exposure to termites.

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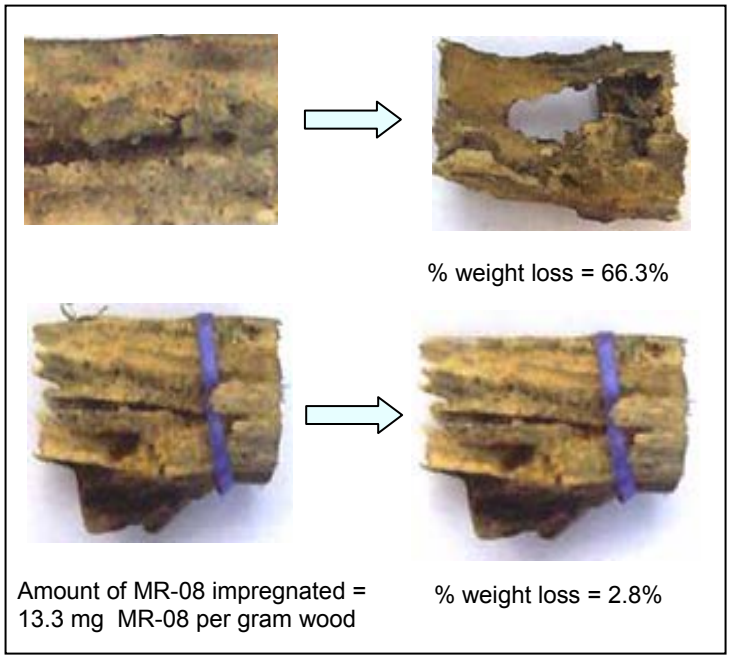

Fig. 5. Effect of MR-08 on prevention of wood damage by the wood termite (Coptotermes vastator). MR-08 was impregnated into the wood overnight using an ethanolic solution and the wood sample placed in a termite mound for 2 weeks.

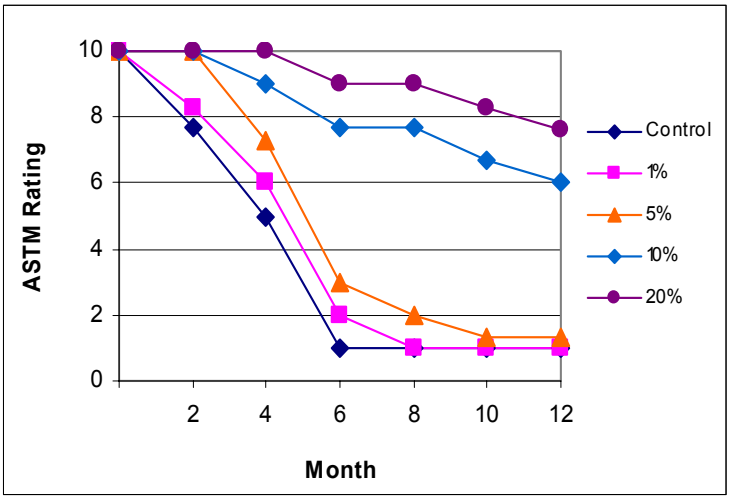

Fig. 6. The effect of MR-08 at various concentrations in protecting wood substrates against termite damage. Standardized wood samples were impregnated with MR-08 and placed in termite mounds. The samples were taken for evaluation at each month of exposure.

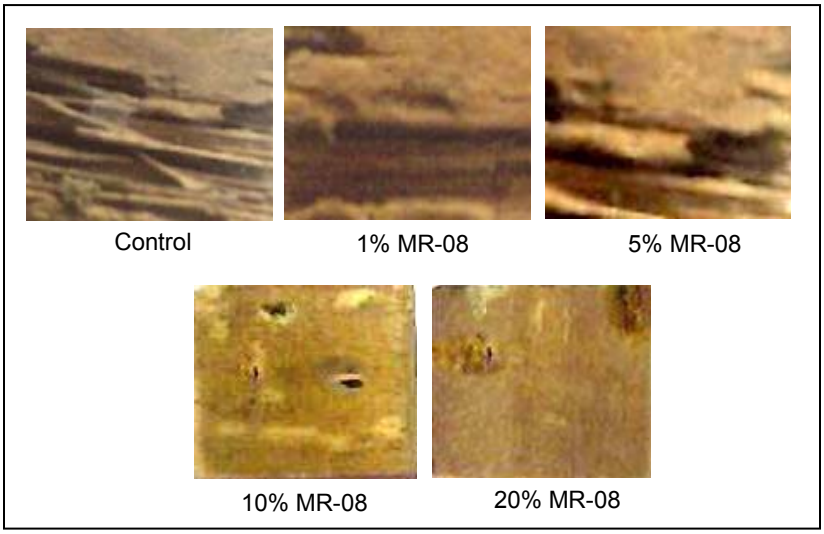

Fig. 7. Photographs of wood samples at four (4) months after single superficial impregnation of wood with various concentrations of MR-08.

The protective effect of MR-08 is dependent on the concentration used for impregnation. The study is in progress and shows effective protection at the higher concentrations

Prospects of MR-08 on wood protection

The data demonstrate that superficial impregnation with MR-08 produced a long lasting effect on preventing attack by termites. In normal wood treatment, the active ingredients are pushed through the core of the wood under high pressure and vacuum. This enabled protection time of many years compared to the old method of dipping the wood in preservatives.

Poseidon expects that MR-08 will also show years of performance time when perfused throughout the lumber under pressure. By novel encapsulation techniques, MR-08 can remain inside the interstices of the wood to permit the slow release of the compound and further extending the life span of the wood. These studies are currently in progress.

Intellectual Property Rights

The international patent for MR-08 was published in 24 March 2005 (International Publication Number WO 2005/025313 A1). This PCT patent went into its national phase filings in various countries in March 2006.

Summary

The data described in this report show that MR-08 is an effective agent in repelling a wide range of insects. As a termite repellent, MR-08 also demonstrated a prolonged inhibition of termite infestation than would have been predicted from the studies on mosquitoes, ants and houseflies alone. The data suggest that MR-08 may represent a new class of nontoxic repellent substances and a new market opportunity for consumer repellents and the pest control industry.

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