ChemicalWatch Factsheet OIL OF LEMON EUCALYPTUS (PMD)

What is Oil of Lemon Eucalyptus

Oil of lemon eucalyptus, specifically p-menthane-3,8-diol (PMD), its component that contains pesticidal properties, is an alternative to toxic mosquito repellents and most likely acts by masking the environmental cues that mosquitoes use to locate their target. Oil of lemon eucalyptus is the common name of one of the natural oils extracted from the leaves and twigs of the lemon-scented gum eucalyptus plant, *Eucalyptus citriodora Hook*, also called *Corymbia citriodora Hook*. Many other compounds have been identified and extracted from the eucalyptus, including citronellol, limonene and linalool. PMD is also chemically synthesized for commercial use, as is normally the case with insect repellents manufactured in the U.S. The term PMD is often used interchangeably with oil of lemon eucalyptus when it is used as an insecticidal repellent. However, PMD and the "pure" unrefined oil of lemon eucalyptus are chemically distinct.

The use of PMD has a long history, but only recently became important as a commercial repellent in the U.S. Oil of lemon

eucalyptus has been used for many years in China as a product known as Quwenling (translated as "effective repellent of mosquitoes"). Researchers in the U.S. began investigating this product in the early 1990s and identified PMD as the active ingredient. In 2000, EPA registered oil of lemon eucalyptus/ PMD as a 'biopesticide repellent' -meaning that it is derived from natural materials. Its products can be applied to human skin and clothing for

ChemicalWatch Stats

CAS Registry Number: 42822-86-6 Chemical Class: Botanical Use: Mosquitoes, ticks, biting flies, gnats, and no-see-ums Toxicity rating: Least-toxic Signal Words: Warning Health Effects: Eye irritation Environmental Effects: None known

unknown. Specific sensory receptors provide mosquitoes with the information they need to detect a source blood meal. Host location is determined by many factors, including lactic acid, ammonia, carbon dioxide, octenol, phenols, temperature, and humidity. It is believed that these products do not repel insects, but that they simply mask or confuse the attractive signals that humans emit so that mosquitoes are unable to locate their target.

Efficacy

When compared to the "pure" oil of lemon eucalyptus, PMD showed far superior repellent activity under laboratory conditions. PMD has also shown remarkable ability to repel mosquitoes when compared to DEET –the most popular synthetic commercial insect repellent which has been linked to serious adverse effects, especially in children.

When used in the field on humans in Tanzania, PMD gave complete protection from biting for between 6 and 7.75 hours. In comparison to DEET, there was no significant difference regarding efficacy and

> duration of protection when used against the Anopheles mosquito, Africa's chief malaria vector. In fact, PMD has been found to be equally efficacious compared to lower concentrations of DEET. In tests against a 10% DEET repellent, PMD products, such as the Repel Brand (with 26% oil of lemon eucalyptus or 65% PMD), were shown to prevent bites for 4 to 7 hours after application for aggressive species of mosquito and for

the purpose of repelling insects, such as mosquitoes, biting flies and gnats, and is formulated as a spray and a lotion.

Note: "Pure" oil of lemon eucalyptus (e.g. essential oil) has not received similar testing for safety and efficacy and is not registered with EPA as an insect repellent.

Mode of Action

The mechanism by which PMD and other repellents repel insects is

greater than 12 hours for less aggressive mosquitoes –a period of prevention greater than the studied DEET repellent. Studies have found that concentrations of PMD at 20-50%, at various formulations, can provide between 2-12hr protection against different mosquito species.

Other studies have shown that PMD also gives protection against the biting midge, *Culicoides variipennis Coquillett*, the deer tick, *Ixodes ricinis L.*, and the stable fly, *Stomoxys calcitrans L*. Recently, A Beyond Pesticides Factsheet – A Beyond Pesticides Factsheet – A Beyond Pesticides Factsheet – A Beyond Pesticides Factsheet

it has also been shown that burning the leaves of the lemon-scented gum eucalyptus (*E. citriodora Hook*) could provide a cost-effective means of household protection (in addition to mosquito nets) in sub-Sahara Africa.

Toxicity

In EPA studies using laboratory animals, PMD showed

no adverse effects except for eye irritation. The technical material is categorized as an eye irritant, while the diluted end use products are expected to be milder. In rare cases, skin irritation can occur, but PMD is not classified as a skin sensitizer. As a result of eye irritation,

PMD is classified in Toxicity Category I for the technical product and Toxicity Category II for the end-use product, and must carry "Warning" on the product label. Acute toxicity studies have shown low toxicity. The oral and dermal LC50 (dose required for 50% mortality) are both more than 2000mg/kg in rats. At high doses (5000mg/kg) significant dermal irritation was noted at the site of test material application, which included erythema, edema, dermal lesions, necrosis, and desquamation, which dissipated after day 7.

There is little epidemiologic data on the effects of PMD. Developmental toxicity and mutagenicity studies submitted for PMD registration showed no treatment-related signs of toxicity.

Avoid Repellents Containing DEET

DEET (N,N-diethyl-meta-toluamide) is commonly used as an insect repellent but its use has become highly controversial. Scientists have raised concerns about the use of DEET and seizures among children, even though EPA claims that there is not enough information to implicate DEET with these incidents. DEET is quickly absorbed through the skin and has caused adverse effects including large blisters and burning sensations. Laboratory studies have found that DEET can cause neurological damage, including brain damage in children.

DEET labels are required to include the following directions: Do not apply over cuts, wounds, or irritated skin; Do not apply to hands or near eyes and mouth of young children; Do not allow young children to apply this product; Use just enough repellent to cover exposed skin and/or clothing; Do not use under clothing; After returning indoors, wash treated skin with soap and water; Wash treated clothing before wearing it again; and, Use of this product may cause skin reactions in rare cases.

Duke Medical University pharmacologist Mohamed Abou-Donia, Ph.D. conducted numerous studies in rats, which clearly demonstrate that frequent and prolonged applications of DEET cause neurons to die in regions of the brain that control muscle movement, learning, memory and concentration. Rats treated with an average human dose of DEET (40 mg/kg body weight) performed far worse than control rats when challenged with physical tasks requiring muscle control, strength

and coordination. With heavy exposure to DEET and other insecticides, humans may experience memory loss, headache, weakness, fatigue, muscle and joint pain, tremors and shortness of breath.

Further research by Dr. Abou-Donia shows even greater impacts when DEET exposure occurs in combination with pharmaceuticals and other pesticides, including permethrin, an insecticide commonly used for public mosquito control. According to Dr. Abou-Donia, "Never use insect repellents on infants, and beware of using them on children in general. Never combine insecticides with each other or use them with other medications. Even an antihistamine could interact with DEET to cause toxic side effects... Until we have more data on potential interactions in humans, safe is better than sorry."

For more information on alternatives to using DEET, see Beyond Pesticides mosquito and insect-borne diseases webpage: www.beyondpesticides.org/mosquito.



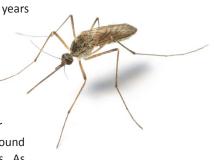
Environmental fate

Little to no data exists for the environmental fate of PMD. However, PMD is not expected to adversely impact the environment or wildlife.

Regulation

PMD was first registered with the EPA in 2000 with the issuance of its Biopesticide Registration Eligibility Document for the registrant-S.C. Johnson & Son, Inc. As part of its assessment, EPA stated in its document that since PMD is intended for direct application to the skin, including that of infants and children, FQPA considerations apply. It states, "The requirements for a biochemical pesticide registration include only one developmental study (in one species), and there are usually no data available which demonstrate whether young animals are differentially affected upon exposure to that pesticide. Therefore, the ten-fold FQPA safety factor could be retained for biochemical pesticides." As such, product labels specify that it is not to be used on children younger than three years of age.

According to EPA, PMD as an active ingredient is considered GRAS (generally recognized as safe), is used to flavor foods and medicines, and is found in many consumer products. As a result, EPA concluded that an



assessment of aggregate exposure was not necessary. The Centers for Disease Control and Prevention (CDC), after an evaluation of information contained in peer-reviewed scientific literature and data available, recommends the use of PMD products to help people avoid the bites of disease carrying mosquitoes.

Citations

1 USDA. Plant Profile: Corymbia citriodora (Hook.) K.D. Hill & L.A.S. Johnson. Natural Resource Conservation Service Plants Database. Available at http://plants.usda.gov/java/profile?symbol=COCI4.

- 2 Frost, A. C. (2005). Oil of Lemon Eucalyptus as an Insect Repellent. Alternative Medicine Alert, AHC Media LLC(August 2005).
- 3 Mustapha, D., Frances, S. P., Strickman, D., (2006). Chapter 20: PMG (p-Menthane-3,8-diol) and Quwenling. Insect Repellents: Principles, Methods and Uses. New York, NY: CRC Press.
- 4 U.S. EPA. 2000. p-Menthane-3,8-diol (011550) Biopesticide Registration Eligibility Document. Office of Prevention, Pesticides and Toxic Substances. Washington DC.
- 5 Ref #3

6 Ref #3

7 U.S. EPA (2000). p-Menthane-3,8-diol (011550) Fact Sheet. In: Office of Prevention Pesticides and Toxics, ed. Washington DC.

8 CDC. 2008. Updated Information regarding Mosquito Repellents. West Nile Virus: Division of Vector Borne Infectious Diseases. Altanta, GA. Available at http://www.cdc.gov/ncidod/dvbid/westnile/repellentupdates.htm.

9 Davis, E. E., & Bowen, M. F. (1994). Sensory physiological basis for attraction in mosquitoes. J Am Mosq Control Assoc, 10(2 Pt 2), 316-325; Schreck, C. E., Kline, D. L., & Carlson, D. A. (1990). Mosquito attraction to substances from the skin of different humans. J Am Mosq Control Assoc, 6(3), 406-410; Frost, A. C. (2005). Oil of Lemon Eucalyptus as an Insect Repellent. Alternative Medicine Alert, AHC Media LLC(August 2005).

10 Watson, R. R., & Preedy, V. (2009). Botanical Medicine in Clinical Practice. Cambridge, MA: CABI.

- 11 Trigg, J. K. (1996). Evaluation of a eucalyptus-based repellent against Anopheles spp. in Tanzania. J Am Mosq Control Assoc, 12(2 Pt 1), 243-246.
- 12 Katz, T. M., Miller, J. H., & Hebert, A. A. (2008). Insect repellents: historical perspectives and new developments. J Am Acad Dermatol, 58(5), 865-871.

13 Ref #9

14 Trigg, J. K., & Hill, N. (1996). Laboratory Evaluation of a Eucalyptus-based Repellent against Four Biting Arthropods. Phytotherapy Research, 10(4), 313-316; Elmhalli, F. H., Palsson, K., Orberg, J., & Jaenson, T. G. (2009). Acaricidal effects of Corymbia citriodora oil containing para-menthane-3,8-diol against nymphs of Ixodes ricinus (Acari: Ixodidae). Exp Appl Acarol, 48(3), 251-262.; Gardulf, A., Wohlfart, I., & Gustafson, R. (2004). A Prospective Cross-Over Field Trial Shows Protection of Lemon Eucalyptus Extract Against Tick Bites. Journal of Medical Entomology, 41(6), 1064-1067.

16 Ref #6

17 Ref #9

- 18 Ref#4
- 19 Ref #4
- 20 Ref #8

¹⁵ Ref #2