New York State Integrated Pest Management Program | Cornell Cooperative Extension

Eugenol Profile

Active Ingredient Eligible for Minimum Risk Pesticide Use

Brian P. Baker and Jennifer A. Grant
New York State Integrated Pest Management, Cornell University, Geneva NY

Label Display Name: Eugenol

Active Components: Eugenol

CAS Registry #: 97-53-0

U.S. EPA PC Code: 102701

CA DPR Chem Code: 2095

Other Names: 4-Allyl-2-methoxyphenol, Allylguaiacol, 1,4-Eugenol; 1-Hydroxy-2-methoxy-4-propenylbenzene, 2-Methoxy-4-allylphenol, Eugenolum, 5-Allylguaiacol, Phenol; Eugenic acid

Other Codes: BRN: 1366759; Caswell 456BC; CCRIS 306; CRC: HDW90-Y; FEMA 2467; RTECS: SJ4375000; Flavis: 04.003; JECFA: 1529

Summary: Eugenol is a naturally occurring aromatic compound derived primarily from cloves, and used as a flavoring agent. As a pesticide, it has many uses. The EPA allowed eugenol to be used as an active ingredient in minimum risk pesticides because of its long history of human exposure and safe use as a food ingredient. However, it is not permitted for use on food crops because there is no established tolerance or exemption from tolerance.

Pesticidal Uses: While Eugenol is most often used as a mosquito repellent, or as an attractant to Japanese beetles and other beetles, it's also employed as an insecticide targeting wasps, yellow jackets, hornets and other stinging or biting insects, and against tent caterpillars. Eugenol may be applied as a fungicide or bactericide, and as a plant growth regulator to promote lettuce seed germination, or thin tree fruits.

Formulations and Combinations: Eugenol is often combined with other essential oils, particularly mint oil, cinnamon oil, and geraniol. In Japanese beetle traps, it is combined with 2-phenethyl propionate (PeP). Other ingredients reported in minimum risk products include water, citric acid, lauric acid, gum Arabic, xanthan gum, sodium acetate, vinegar, sodium lauryl sulfate, lecithin, mineral oil, sodium bicarbonate, and potassium oleate.

Basic Manufacturers: Firmenich, Florida Treatt, Fluka/Sigma-Aldrich, Givaudan, Merck, Penta Manufacturing, Schweizerhall, Wako, Kanto.

This document profiles an active ingredient currently eligible for exemption from pesticide registration when used in a Minimum Risk Pesticide in accordance with the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) section 25b. The profile was developed by the New York State Integrated Pest Management Program at Cornell University, for the New York State Department of Environmental Conservation. The authors are solely responsible for its content. The Overview Document contains more information on the scope of the profiles, the purpose of each section, and the methods used to prepare them. Mention of specific uses are for informational purposes only, and are not to be construed as recommendations. Brand name products are referred to for identification purposes only, and are not endorsements.

Safety Overview: Eugenol is classified as a flower oil by US EPA (McDavit and Matthews 2012). EPA waived toxicological data requirements for eugenol because of its long history of exposure to humans, and a determination that its use as a pesticide is unlikely to have adverse effects on human health (Shaukat 2010). Eugenol has been identified as a potential carcinogen by the Ames test, but it is not currently classified as a carcinogen by the National Toxicology Program or the International Agency for Research on Cancer.

Background

The primary uses of eugenol are as a fragrance and flavor. It is also used as a pesticide and has several applications in dentistry. Eugenol is a naturally occurring component of numerous plant essential oils, including those of cloves (*Szygium aromaticum, Eugenia aromatica, or Eugenia caryophyllus*), cinnamon (*Cinnamomum* spp.), basil (*Ocimum* spp.), allspice (*Pimenta dioica*), bay laurel (*Laurus nobilis*), turmeric (*Curcuma longa*), and other plants (Debboun et al. 2007; Khan and Abourashed 2010). It is an allyl chain-substituted guaiacol that is slightly soluble in water. First isolated from cloves in 1826 (ChemNetBase 2015), clove oil remains the primary commercial source of eugenol. Clove bud oil has between 60-90% eugenol, clove stem oil contains about 90-95% eugenol, and clove leaf oil has 82-88% eugenol (Khan and Abourashed 2010).

Eugenol can be synthesized by various methods (Brauer et al. 1963; Bhagat et al. 1982), but steam distillation of clove oil is the main process by which eugenol is isolated. Hydrodistillation is the traditional method used, and some eugenol is extracted using a synthetic solvent, such as dichlormethane. Supercritical extraction with carbon dioxide increases the oil yield from clove buds, but lowers the eugenol content (Guan et al. 2007). Indonesia is the world's largest producer of cloves, accounting for over half of the global production. The next three leading countries, Madagascar, Tanzania, and Sri Lanka, account for another 15% (FAO 2015). No other country accounts for more than 1% of global production.

Clove oil appears on the EPA 25(b) eligible active ingredient list as a separate entry and has a different pesticide classification code (220700). Closely related compounds include the isomer, isoeugenol (CAS #97-54-1) and the methylated form, methyl eugenol (CAS #93-15-2). These substances may occur as impurities in technical grade eugenol. Isoeugenol is rarely found in nature (Nurdjannah and Bermawie 2001); methyl eugenol is more common. For example, samples of the Mexican marigold (*Tagates lucida* or 'pericón' in Spanish) had higher levels of methyl eugenol than of eugenol (Franz and Novak 2009).

Chemical and Physical Properties

The molecular structure of eugenol is presented in Figure 1.

Figure 1

Molecular Structure of Eugenol

Source: EMBL 2015

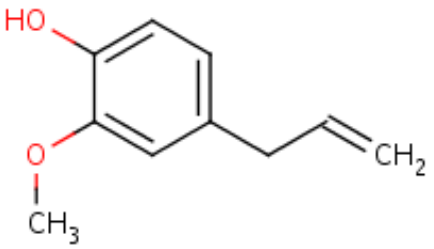

Table 1

Physical and Chemical Properties of Eugenol

Property	Characteristic/Value	Source
Molecular Formula:	$C_{10}H_{12}O_2$	(Merck 2015)
Molecular Weight:	164.20	(Merck 2015)
Percent Composition:	C-73.15%, H-7.37%, O-19.49%	(Merck 2015)
Physical state at 25°C/1 Atm.	Liquid	(Merck 2015)
Color	Colorless to pale yellow	(Merck 2015)
Odor	Odor of cloves	(Merck 2015)
Density Specific Gravity	1.0664 at 20°C	(Merck 2015)
Melting point	9.1-9.2° C	(Merck 2015)
Boiling point	255° C	(Merck 2015)
Solubility	Practically insoluble in water; Soluble in ether, most fixed oils	(Merck 2015)
Vapor pressure	< 0.1 hPa (< 0.1 mmHg) at 25 °C	(Sigma-Aldrich 2014)
pH	Not found	
Octonol/Water (K_{ow}) coefficient	log Kow = 2.49	(Dias et al. 2003; HSDB 2015)
Viscosity	Not found	
Miscibility	Miscible in alcohol, chloroform, ether, oils	(Merck 2015)
Flammability	Flash point: 112°C (closed cup)	(Sigma-Aldrich 2014)
Storage stability	Stable, incompatible with strong oxidizing agents	(Sigma-Aldrich 2014)
Corrosion characteristics	Not found	
Air half life	3.37 hrs.	(EPI 2012)
Soil half life	720 hrs.	(EPI 2012)
Water half life	360 hrs.	(EPI 2012)
Persistence	Not found	

Human Health Information

The EPA affirmed earlier studies concluding that registered pesticide products—specifically floral attractants, repellents, or insecticides—containing eugenol as an active ingredient create no adverse effects to humans when used according to label directions (US EPA 2000).

Acute Toxicity

The acute toxicity of eugenol is summarized in Table 2.

Table 2

Acute Toxicity of Eugenol

Study	Results	Source
Acute oral toxicity	Rat: 1,600-2,970 mg/kg Mouse: 2,400-3,750 mg/kg Guinea pig: 1,860-2,480 mg/kg	(Jenner et al. 1964; Gwynn 2014; Shaukat 2010)
Acute dermal toxicity	1,000 mg/kg	(Shaukat 2010)
Acute inhalation	Rat: 11 mg/kg	(LaVoie et al. 1986)
Acute eye irritation	Not found	
Acute dermal irritation	Severe irritation at 24 hours—Category II	(Shaukat 2010)
Skin sensitization	Not a sensitizing agent	(Shaukat 2010)

Eugenol is recognized as a skin and eye irritant (Gwynn 2014), and has sedative properties (Heuberger 2009). The oral LD_{50} values are somewhat variable (Jenner et al. 1964; Shaukat 2010; Gwynn 2014). While fatal overdoses are rare, they have occurred and there is no known antidote (HSDB 2015). Results for the murine local lymph node assay (LLNA) and guinea-pig maximization test (GPMT) were both positive, indicating that eugenol is a contact sensitizer and has the potential to cause allergic reactions (Hilton et al. 1996). These results show that eugenol stimulates the immune system and has the potential to increase the potential for eye and skin irritation. The test for respiratory sensitization was negative.

Sub-chronic Toxicity

The sub-chronic toxicity of eugenol is summarized in Table 3. Although some human health incidents involving eugenol pesticides have been reported to the EPA, they have waived most of eugenol's sub-chronic toxicity data requirements (McDavit and Matthews 2012). Those incidents were of minor injuries involving products formulated with multiple active ingredients including capsaicin, phenethyl propionate, pyrethrins, and (r,z)-5-(1-decynyl) dihydro-2(3H)-furanone. The EPA concluded that these reports did not indicate any risk from the use of eugenol, or geraniol and oil of the mustard—the other two flower oils involved in similar incidents. (McDavit and Matthews 2012).

Methods in a number of tests conducted on eugenol or isoeugenol were not comparable to the OPPTS Guidelines, mainly in terms of time periods. The exceptions, as described in Table 3, involved failure to meet guidelines due to duration of the experiments, or because doses included ingredients other than pure eugenol, which may have confounded the results. Oral doses increasing from 1,400-4,000 mg/kg body weight administered to rats over 34 days resulted in slight liver enlargement with yellow discoloration. Eugenol fed to rats produced slight enlargement of the liver and adrenal gland, with marked yellowish discoloration (Hagan et al. 1965). The forestomachs of the study's rats showed a moderately severe hyperplasia and hyperkeratosis of the stratified squamous epithelium associated with focal ulceration.

Eugenol is classified as an allergen (EMBL 2015). A Japanese study found the frequency of positive allergic reactions to patch tests on patients with cosmetic dermatitis was 2.6% for eugenol and 5.2% for isoeugenol (Itoh 1982). One study estimated that four out of every 1,000 Europeans are allergic to eugenol (Demyttenaere 2010). Estimates for sensitive populations vary. Patch tests for eugenol in patients suffering from 'cosmetic dermatitis' were positive in 2.6% (4/155) of cases in one study (IARC 1985).

Table 3

Sub-chronic Toxicity of Eugenol

Study	Results	Source
Repeated Dose 28-day Oral Toxicity Study in Rodents	No adverse effects at doses up to 2,000 mg/kg/day	(Sipes and Mattia 2006)
90-day oral toxicity in rodents	Rat: No adverse effect was observed at 79.3 mg/kg of body weight per day for 12 weeks Mice: No mortality or compound gross related effects or microscopic pathology	(Sipes and Mattia 2006; HSDB 2015)
90-day oral toxicity in non-rodents	Not found	
90-day dermal toxicity	Not found	
90-day inhalation toxicity	Rat: 0.77 – 2.58 mg/L for 4 hours per day for 14 days. Lost body weight reduced intake of food and water; no abnormalities observed in lung tissues	(Clark 1988)
Reproduction/development toxicity screening test	Not found	
Combined repeated dose toxicity with reproduction/development toxicity screening test	Not found	
Prenatal developmental toxicity study	Not found	
Reproduction and fertility effects	Not found	

Eugenol has been associated with a reddening irritation (erythema), and in some cases, ulcers and diffuse inflammation in some dental applications (Lilly et al. 1972). Inhaled eugenol via commercially available clove cigarettes is associated with pulmonary edema.

Chronic Toxicity

The chronic toxicity of eugenol is summarized in Table 4.

Table 4

Chronic Toxicity of Eugenol

Study	Results	Source
Chronic toxicity	Negative	(IARC 1985)
Carcinogenicity	Rats: Negative; Mice: Equivocal	(HSDB 2015)
Combined chronic toxicity & carcinogenicity	Not mutagenic to *Escherichia coli* or *Salmonella typhimurium* (see below); Genotoxic to Chinese hamster cells.	(IARC 1985; Maralhas et al. 2006)

Eugenol was not mutagenic to the *Salmonella typhimurium* strains TA1530, TA1535, TA1537, TA 1538, T A98 or TA 100 in the presence of S9 from the livers of polychlorinated biphenyl induced rats, Aroclor-induced Syrian hamsters, or mice. However, it was mutagenic to *S. typhimurium* TA 1535 and TA 100 in the absence of an exogenous metabolic system but not to strains TA 1537, TA 1538 or TA 98 in either the presence or absence of a metabolic system (IARC 1985). The International Agency for Research on Cancer

(IARC) concluded that given the widespread exposure and absence of human epidemiological data, no evaluation could be made of the carcinogenicity of eugenol to humans—even though eugenol is a potential carcinogen. Therefore, IARC considers eugenol as "not classifiable" as to its carcinogenicity to humans (Group 3) (IARC 1985). Eugenol has been identified as one of a number of naturally occurring pesticides that may be potential carcinogens (Ames, Profet, and Gold 1990). Assays done on cultures of Chinese hamster cells showed significantly greater mutation and reduplication than the control, which led to the conclusion that eugenol is genotoxic and a possible carcinogen (Maralhas et al. 2006). The results of a bacterial reverse mutation test for eugenol were negative (Shaukat 2010).

The National Toxicology Program concluded that eugenol was not carcinogenic to male or female rats. In mice, however, there was equivocal evidence of carcinogenicity because eugenol increased both carcinomas and adenomas of the liver in male mice at the 3,000 ppm dietary level, and an increase in the combined incidences of hepatocellular carcinomas or adenomas in female mice (HSDB 2015). Eugenol is not considered by California to be a chemical known to cause cancer. However, methyl eugenol was listed as a substance of "low carcinogenicity concern" by California in 2001 (Cal-EPA OEHHA 2016).

Human Health Incidents

Between April 1, 1996 and March 30, 2016, the National Pesticide Information Center (NPIC) received 20 reported human health incidents involving eugenol as an active ingredient (NPIC 2016). Most of these involved multiple active ingredients, and a number were EPA registered pesticides.

Environmental Effects Information

Effects on Non-target Organisms

The EPA conducted a risk assessment that supported a complete endangered species determination for eugenol and other flower oils in registered pesticide products. Due to the low use volume of these products and because they are not applied directly to water, the ecological risk assessment showed a "no effect" determination for endangered or threatened terrestrial or aquatic species (Moore 2011; McDavit and Matthews 2012). As with other flower oils, the EPA waived non-target organism data requirements for eugenol when used in registered pesticides (McDavit and Matthews 2012). These waivers were granted in May 1976 and re-granted in June 1990, prior to the establishment of criteria for exemption from registration (Moore 2011). Between April 1, 1996 and March 30, 2016, NPIC received 11 reports of animal related incidents involving eugenol as an active ingredient (NPIC 2016). Most of these involved multiple active ingredients and a number were EPA registered pesticides.

Available data for the effects of eugenol on non-target organisms are summarized in Table 5.

Table 5

Effects of Eugenol on Non-target Organisms

Study	Results	Source
Avian Oral, Tier I	Bobwhite quail (*Colinus virginianus*): >10,000 mg/kg bw	(Gwynn 2014)
Non-target plant studies	Not found	
Non-target insect studies	Not found (see below)	
Aquatic vertebrates	Rainbow trout: LC_{50} >10 mg/l (96 hr); 61.5 mg/L/24 hr	(Stroh et al. 1998; Gwynn 2014)
Aquatic invertebrates	*Daphnia magna* 1.11 mg/l (48 hr)	(Gwynn 2014)

Juvenile Coho salmon ((*Oncorhynchus kisutch*), a non-target aquatic vertebrate, responded to eugenol exposure with LC_{50} values of 67.6 mg/L at 24hr (Stroh et al. 1998). Efficacy as an herbicide also gives eugenol the potential to damage non-target plants (Tworkoski 2002). However, no data was found to support that concern. African clawed frogs (*Xenopus laevis*) exposed to 350 µg/L of eugenol for ten minutes suffered renal tubular apoptosis, hepatic necrosis, hyaline membranes in the lungs, and adipose tissue hemorrhages (Goulet et al. 2011).

Environmental Fate, Ecological Exposure, and Environmental Expression

The environmental fate and degradation of eugenol is summarized in Table 6.

Table 6

Environmental Fate, Ecological Exposure, and Environmental Expression of Eugenol

Study	Results	Source
Leaching series	Not found	
Photodegradation in water	Not found	
Photodegradation in air	Isoeugenol was 79% photodegraded after 10 days	(HSDB 2015)
Photodegradation in soil	Not found	
Ready biodegradability	Fully biodegradable	(HSDB 2015)

Eugenol is considered to be extremely volatile and degradable in air, soil, and water, including through microbial activity (Gwynn 2014). While there was no empirical data for photodegradation in soil and water, eugenol may degrade in water and on surfaces exposed to sunlight (HSDB 2015).

Environmental Incidents

Between April 1, 1996 and March 30, 2016, NPIC received 29 reported incidents involving eugenol as an active ingredient, but none were characterized as human health or animal related (NPIC 2016).

Efficacy

Eugenol has contact activity through the disruption of cell walls, membranes, or, in the case of microorganisms, organelles (Gwynn 2014). As noted above, the mode of action is dose-dependent; in some cases, it will serve as an attractant at low doses and a repellent at high doses.

Insecticidal activity

Eugenol is recognized as a relatively strong and moderately durable mosquito repellent (Moore et al. 2007). One study found that Terminix ALLCLEAR® Sidekick® mosquito repeller, a 25(b)-exempt repellent formulated with 13% eugenol along with cinnamon oil, geranium oil, peppermint, and lemongrass oil repelled the mosquito species *Aedes albopictus* and *Culex pipiens* at a rate not significantly different from a repellent having metafluthrin as its active ingredient (Revay et al. 2013). The authors concluded that the formulation "provided a consistent and satisfactory level of protection from biting mosquitoes." Eugenol also can act as an anti-feedant (Regnault-Roger 1997). A number of mosquito repellents use eugenol as a component, either in concentrated form or with cinnamon and clove oils.

Eugenol killed *Ochlerotatus caspius* mosquito larvae with the LC_{50} values of 7.53 mg/L for 24 hours and 5.57 mg/L for 48 hours; for *Aedes aegypti*, the LC_{50} was 33 mg/L in an experiment conducted in Lebanon (Knio et al. 2008). In a laboratory study, eugenol extracted from *Ocimum basilicum* and *O. sanctum* induced 100 percent mortality in *Anopheles stephensi*, *Aedes aegypti*, and *Culex quinquefasciatus* mosquitos at a dose of 7 L/ha in 30-35 minutes (Bhatnagar et al. 1993).

Eugenol at 0.25 mg/cm^2 was as potent in killing human head lice (*Pediculus capitis*) as the botanical insecticide pyrethrum and the synthetic pyrethroid δ-phenothrin, but was slightly less effective than the pyrethroids at 0.125 mg/cm^2 (Yang et al. 2003). The same study found eugenol vapor was a potent louse ovicide. At a dose of 1.0 mg/cm^2, only 3% of the louse eggs hatched.

By itself, Eugenol attracts Japanese beetle (*Popillia japonica*); when combined with PeP (2-Phenethyl Propionate) the result is a more effective trap attractant (McGovern et al. 1970; McGovern et al. 1973; Ladd et al. 1974, 1975). In Chinese experiments, the closely related Chinese scarab, *Popillia quadriguttata*, a pest of turf, soybean (*Glycine max*), corn (*Zea mays*), and horticultural crops, was trapped at a rate comparable to the results found with Japanese beetles (Chen et al. 2013). The white-spotted flower chafer (*Protaetia brevitarsis*)—a scarab beetle and a significant corn pest in China—was also trapped using this Japanese beetle bait, though not as effectively as *P. quadriguttata* (Chen and Li 2011). Another pest attracted by eugenol is the scarab beetle of peanuts, *Maladera matrida* (Ben-Yakir et al. 1995). These formulations are also effective attractants in experiments with other beetles, particularly those in the scarab family. Eugenol was attractive to *Euphoria sepulchralis,* though not as attractive as geraniol and eugenol + geraniol + phenyethyl propionate (7:3:3 ratio) (Cherry and Klein 1992). In experiments conducted in Israel's Negev Desert, eugenol by itself was found to be a superior attractant compared to PeP, geraniol, or lavender oil. However, when the lure was combined with methamidophos—an EPA-registered organophosphate insecticide and sold under the brand name 'Monitor'—the repellency of the insecticide overwhelmed the attraction of the eugenol (Ben-Yakir et al. 1995).

Eugenol is not acutely toxic to the post-harvest storage pests maize weevil (*Sitophilus zeamais*) and red flour beetle (*Tribolium castaneum*). Toxicity tests with *S. zeamais* found eugenol LD_{50} values were approximately 30 µg/mg insect. For *T. castaneum*, eugenol's LD_{50} was 30.7 µg/mg (Huang et al. 2002). Eugenol, at concentrations of 1 µL/kg grain, was effective at killing grain beetles *Sitophilus granarius*, *Sitophilus zeamais*, *Tribolium castaneum* and *Prostephanus truncates* under laboratory conditions in Germany (Obeng-Ofori and Reichmuth 1997). Eugenol's efficacy was confirmed under storage conditions (Obeng-Ofori and Reichmuth 1999). Bean weevil (*Acanthoscelides obtectus*) eggs, larvae, and adults are all susceptible to eugenol toxicity (Regnault-Roger et al. 2012). The LD_{50} of eugenol for wireworms (*Agriotes obscurus*)—a click beetle that is a pest in cereal and forage crops—was 516.5 µg/larva (Waliwitiya et al. 2005).

Eugenol and mixtures of eugenol with alpha-terpineol and cinnamic alcohol can be effective insecticides against American cockroaches (*Periplaneta americana*) (LC_{50} = 0.047 mg/cm^2) and German cockroaches (*Blattella germanica*) (LC_{50} = 0.021 mg/cm^2) (Enan 2001). Exposed American cockroaches demonstrated hyperactivity followed by hyperextension of the legs and abdomen, then fast immobilization followed by death. The above application rates are fairly low compared to other eugenol studies on cockroaches. Eugenol disrupts cockroach cell binding of octopamine (Price and Berry 2006). One study found that 0.206 mg/cm^2 of eugenol rendered 50% of tested American cockroaches immobile within 24 hours (knockdown), and 0.148 mg/cm^2 killed 50% of test organisms within 96 hours. The values were not significantly different, and the authors noted that at lower doses, eugenol was slightly more effective in inducing mor-

tality than as a knockdown (Ngoh et al. 1998). Tests of eugenol formulated with benzyl acetate and phenyl ethyl alcohol as additional active ingredients not eligible for use in minimum risk pesticides showed effective toxicity against the German cockroach (*Blatella germanica*), cat fleas (*Cunocephalides felis*), and Argentine ants (*Iridomyrmex humilis*) (Bessette and Knight 2000).

Carpenter ants (*Camponotus pennsylvanicus*) were susceptible to eugenol (LC_{50} = 0.012 mg/cm^2) (Enan 2001), but it did not deter the feeding of Formosan termites (*Coptotermes formosanus*) when applied directly to blocks of wood (Cornelius, Grace, and Yates 1997).

Eugenol demonstrated acaricidal activity against the dust mites *Dermatophagoides* spp (Choo et al. 2004) and *Tyrophagus* spp (Kim et al. 2003) in South Korean experiments. The LD_{50} of eugenol for *Dermatophagoides farinae* adults was 4.8 µg/cm^2 (0.48 kg/ha). For *Dermatophagoides pteronyssinus* adults, the LD_{50} was 3.7 µg/cm^2 (0.37 kg/ha) (Choo et al. 2004). Adult mites of the species *Tyrophagus putrescentiae*, the LD_{50} value for eugenol derived from clove bud oil is 12 µg/cm^2 (1.2 kg/ha)(Kim et al. 2003). Eugenol derived from pimento (*Pimenta dioica*) prevented oviposition of the cattle tick, *Boophilus microplus*, at doses of 1.0 mg/g of seed (Brown et al. 1998).

Molluscicidal activity

Snails and other mollusks are susceptible to eugenol toxicity and are also attracted to the odor. For example, a snail, *Lymnaea acuminate*, that serves as an intermediate host and vector of various helminthic parasites of the *Fasciola* genus was exposed to eugenol under various aquatic and terrestrial conditions in India (Agrahari et al. 2012). The LC_{50} varied widely depending on temperature and other abiotic conditions. Both starch and proline—the amino acid found in gelatins—were used as a base, along with a snail attractant. The 24 hour LC_{50} ranged between 2.55 and 10.73, with the greatest activity at elevated temperatures.

Herbicidal activity

Eugenol's phytotoxic properties were first recognized in the 1980s, but understanding the mode of action and testing its efficacy as an herbicide lagged by about 20 years. In an experiment that looked at the germination of weed species, eugenol was applied once to filter paper on top of seeds in a Petri dish. Eugenol prevented germination of hairy beggartick (*Bidens pilosa*) at a concentration of 10 µL per treated Petri dish and of coffee weed (*Cassia occidentalis*) in India at a concentration of 20 µL per treated Petri dish (Vaid et al. 2010). Another study in India compared the effects of eugenol on grassy and broadleaf weeds. The grassy weeds included barnyard grass (*Echinochloa crus-galli*), small canary grass (*Phalaris minor*), Asian sprangletop (*Leptochloa chinensis*), and johnsongrass, as well as four broadleaf weeds: goatweed (*Ageratum conyzoides*), Bengal dayflower (*Commelina benghalensis*), coffee weed, and hairy beggartick (Ahuja et al. 2015). The results showed eugenol inhibited grass root growth more than broadleaf. This effect was replicated on wild oats (*Avena fatua*) (Ahuja et al. 2015). The mode of action was thought to be the generation of reactive oxygen species (ROS) leading to oxidative stress and membrane damage in the root tissue. The phytotoxic properties of eugenol also make it effective as a fruit thinner. Eugenol was applied by an air-blast sprayer during bloom to Royal Gala, Ace Spur Delicious, Cameo, Sun Fuji, and Red Delicious apple trees, as well as to Harrow Beauty, John Boy, and Lovell peach trees. Rates ranged from 0-10% and the total amount was calibrated by variety. There was considerable variability among the varieties and growing seasons, but in general, the best results were obtained by 2-4% concentrations (Miller

and Tworkoski 2010). Higher concentrations tended to over-thin and reduce yields without significant increases to fruit size.

Fungicidal activity

Ten plant pathogens, including *Botrytis cinerea,* were cultured from diseased plants and exposed to eugenol under controlled conditions in China. The EC_{50} value of eugenol on *B. cinerea* growth was 38.6 µg/mL (Wang et al. 2010). The same study showed that eugenol had an EC_{50} value on *Sclerotinia sclerotiorum* of 39.94 µg/mL. The other species were moderately sensitive to eugenol with EC_{50} values ranging from 46.7 to 96.9 µg/mL.

Standards and Regulations

EPA Requirements

According to 40 CFR 180, eugenol does not have a tolerance and is not exempt from the requirement of a tolerance. Therefore, it is only permitted for non-food uses. As of 2017, there were 14 products registered with EPA that contained eugenol as an active ingredient (US EPA 2017).

FDA Requirements

Eugenol that meets the Food Chemicals Codex specification as food grade is Generally Recognized As Safe (GRAS), along with other clove derivatives [21 CFR 184.1257]. Eugenol is also permitted to be used in over-the-counter (OTC) drugs for the following uses: analgesic and anesthetic; fever blister and cold sores; poison oak, poison ivy and poison sumac treatments; and as an astringent [21 CFR 310.545]. Zinc oxide mixed with eugenol is permitted to be used as a dental cement [21 CFR 872.3275]. However, eugenol and other clove oil constituents are not approved as animal drugs, and the FDA has voiced concerns about its use as a fish anesthetic (FDA CVM 2007).

Other Regulatory Requirements

Synthetic eugenol is prohibited for use in organic farming under the USDA's National Organic Program (NOP) [7 CFR 205.105(a)]. Natural extracts of eugenol are allowed by the NOP and may be used as a botanical pesticide [7 CFR 205.206(e) and 7 CFR 205.602].

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) recommends an allowable daily intake of 2.5 mg/kg body weight (JECFA 2001).

Literature Cited

Agrahari, Pooja, V. K. Singh, and D. K. Singh. 2012. "Toxicity of Snail Attractant Pellets Containing Eugenol with Respect to Abiotic Factors against the Vector Snail Lymnaea acuminata." Biological Agriculture & Horticulture 28 (3):156–66. https://doi.org/10.1080/01448765.2012.712903.

Ahuja, Nitina, Harminder Pal Singh, Daizy Rani Batish, and Ravinder Kumar Kohli. 2015. "Eugenol-Inhibited Root Growth in Avena fatua Involves ROS-Mediated Oxidative Damage." Pesticide Biochemistry and Physiology 118 (February):64–70. https://doi.org/10.1016/j.pestbp.2014.11.012.

Ames, Bruce N, Margie Profet, and Lois Swirsky Gold. 1990. "Dietary Pesticides (99.99% All Natural)." Proceedings of the National Academy of Sciences 87 (19):7777–7781.

Ben-Yakir, D, A Bazar, and M Chen. 1995. "Attraction of Maladera matrida (Coleoptera, Scarabaeidae) to Eugenol and Other Lures." Journal of Economic Entomology 88 (2):415–20.

Bessette, S.M., and A.M. Knight. 2000. Controlling adult ants, adult cockroaches and adult fleas with a contact pesticide such as benzyl acetate, eugenol, and/or phenylethyl alcohol dispersed in a carrier; nontoxic to humans. US Patent Office 6,114,384, issued September 5, 2000. https://www.google.com/patents/US6114384.

Bhagat, Shib D, Raj K Mathur, and Narendra N Siddhanta. 1982. "Synthesis of New Derivatives of Eugenol and Isoeugenol." Journal of Chemical and Engineering Data 27 (2):209–210.

Bhatnagar, Mala, KK Kapur, Saba Jalees, and SK Sharma. 1993. "Laboratory Evaluation of Insecticidal Properties of Ocimum basilicum Linnaeus and O. sanctum Linnaeus Plant's Essential Oils and Their Major Constituents against Vector Mosquito Species." Journal of Entomological Research 17 (1):21–26.

Brauer, Gerhard M, Richard Warren Morris, and Willard B Howe. 1963. "Synthesis of Isomers of Eugenol." Journal of Research of the National Bureau of Standards 67 (3).

Brown, Heather A, Donna A Minott, Conrad W Ingram, and Lawrence AD Williams. 1998. "Biological Activities of the Extracts and Constituents of Pimento, Pimenta dioica L. against the Southern Cattle Tick, Boophilus microplus." International Journal of Tropical Insect Science 18 (01):9–16.

Cal-EPA. 2016. "Chemicals Known to the State to Cause Cancer or Reproductive Toxicity." Sacramento, CA: Cal-EPA. http://oehha.ca.gov/media/downloads/proposition-65//p65single05202016.pdf.

ChemNetBase. 2015. "Dictionary of Natural Products." Dictionary of Natural Products. 2015. http://dnp.chemnetbase.com.

Chen, Ri-zhao, Michael G. Klein, Cheng-fa Sheng, Yu Li, and Qi-yun Li. 2013. "Male and Female Popillia quadriguttata (Fabricius) and Protaetia brevitarsis (Lewis) (Coleoptera: Scarabaeidae) Response to Japanese Beetle Floral and Pheromone Lures." Journal of Asia-Pacific Entomology 16 (4):479–84. https://doi.org/10.1016/j.aspen.2013.08.001.

Chen, Ri-zhao, and Yu Li. 2011. "A Novel Plant Volatile Attractant Scheme to Protect Corn in China from the White-Spotted Flower Chafer (Coleoptera: Scarabaeidae: Cetoniinae)." Journal of Pest Science 84 (3):327–35. https://doi.org/10.1007/s10340-011-0353-6.

Cherry, RH, and MG Klein. 1992. "Attraction of Adult Euphoria sepulchralis (Coleoptera: Scarabaeidae) to Aromatic Compounds." Florida Entomologist, 383–385.

Choo, Jang Hee, Mi Youn Lim, and Sang Guei Lee. 2004. "Acaricidal Components of Medicinal Plant Oils Against Dermatophagoides farinae and Dermatophagoides pteronyssinus." Journal of Microbiology and Biotechnology 14 (3):631–634.

Clark, Gerald C. 1988. "Acute Inhalation Toxicity of Eugenol in Rats." Archives of Toxicology 62 (5):381–386.

Cornelius, Mary L, Kenneth J Grace, and Julian R Yates. 1997. "Toxicity of Monoterpenoids and Other Natural Products to the Formosan Subterranean Termite (Isoptera: Rhinotermitidae)." Journal of Economic Entomology 90 (2):320–325.

Debboun, Mustapha, Stephen P. Frances, and Daniel A. Strickman. 2007. Insect Repellents : Principles, Methods, and Uses. Boca Raton, FL: CRC Press.

Demyttenaere, JC. 2010. "Recent EU Legislation on Flavors and Fragrances and Its Impact on Essential Oils." In Handbook of Essential Oils. Science, Technology, and Applications, by K Hüsnü Can Baser and Gerhard Buchbauer, 917–948. Boca Raton, FL.

Dias, Neil C, Mohamed I Nawas, and Colin F Poole. 2003. "Evaluation of a Reversed-Phase Column (Supelcosil LC-ABZ) under Isocratic and Gradient Elution Conditions for Estimating Octanol–water Partition Coefficients." Analyst 128 (5):427–433.

EMBL. 2015. "Chemical Entities of Biological Interest." 2015. http://www.ebi.ac.uk/.

Enan, Essam. 2001. "Insecticidal Activity of Essential Oils: Octopaminergic Sites of Action." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology 130 (3):325–37. https://doi.org/http://dx.doi.org/10.1016/S1532-0456(01)00255-1.

EPI. 2012. "Estimation Programs Interface (EPI) Suite (V4.11)." Washington, DC: US EPA Office of Pesticides and Toxic Substances.

FAO. 2015. "FAO Stat." 2015. http://faostat3.fao.org/home/E.

FDA CVM. 2007. "Concerns Related to the Use of Clove Oil as an Anesthetic for Fish." Guidance for Industry 150. Rockville, MD: FDA CVM.

Franz, Chlodwig, and Johannes Novak. 2009. "Sources of Essential Oils." In Handbook of Essential Oils: Science, Technology, and Applications, by K Hüsnü Can Baser and Gerhard Buchbauer, 39–81. Boca Raton, FL: CRC Press.

Goulet, F, P Vachon, and P Helie. 2011. "Evaluation of the Toxicity of Eugenol at Anesthetic Doses in African Clawed Frogs (Xenopus laevis)." Toxicologic Pathology 39 (3):471–477.

Guan, Wenqiang, Shufen Li, Ruixiang Yan, Shaokun Tang, and Can Quan. 2007. "Comparison of Essential Oils of Clove Buds Extracted with Supercritical Carbon Dioxide and Other Three Traditional Extraction Methods." Food Chemistry 101 (4):1558–1564.

Gwynn, Roma L, ed. 2014. Manual of Biocontrol Agents. 5th ed. Alton, Hants, UK: British Crop Protection Council.

Hagan, Ernest C., Paul M. Jenner, Wm I. Jones, O. Garth Fitzhugh, Eleanor L. Long, J. G. Brouwer, and Willis K. Webb. 1965. "Toxic Properties of Compounds Related to Safrole." Toxicology and Applied Pharmacology 7 (1):18–24. https://doi.org/http://dx.doi.org/10.1016/0041-008X(65)90069-4.

Heuberger, Eva. 2009. "Effects of Essential Oils in the Central Nervous System." In Handbook of Essential Oils: Science, Technology, and Applications, by K Hüsnü Can Baser and Gerhard Buchbauer, 281. Boca Raton, FL: CRC Press.

Hilton, J., R. J. Dearman, I. Fielding, D. A. Basketter, and I. Kimber. 1996. "Evaluation of the Sensitizing Potential of Eugenol and Isoeugenol in Mice and Guinea Pigs." Journal of Applied Toxicology 16 (5): 459–64. doi:10.1002/(SICI)1099-1263(199609)16:5<459::AID-JAT366>3.0.CO;2-H.

HSDB. 2015. "National Library of Medicine Hazardous Substances Data Bank (HSDB)." 2015. http://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm.

Huang, Yan, Shuit-Hung Ho, Hsien-Chieh Lee, and Yen-Ling Yap. 2002. "Insecticidal Properties of Eugenol, Isoeugenol and Methyleugenol and Their Effects on Nutrition of Sitophilus zeamais Motsch.(Coleoptera: Curculionidae) and Tribolium castaneum (Herbst)(Coleoptera: Tenebrionidae)." Journal of Stored Products Research 38 (5):403–412.

IARC. 1985. "Allyl Compounds, Aldehydes, Epoxides and Peroxides." Iarc Monographs on the Evaluation of Carcinogenic Risks to Humans 36. Lyon, FR: International Agency for Research on Cancer. http://monographs.iarc.fr/ENG/Monographs/vol1-42/mono36.pdf.

Itoh, M. 1982. "Sensitization Potency of Some Phenolic Compounds--with Special Emphasis on the Relationship between Chemical Structure and Allergenicity." Journal of Dermatology 9 (3):223–33.

JECFA. 2001. Evaluation of Certain Food Additives and Contaminants. WHO Food Additives Series 55. Geneva, CH: World Health Organization. http://whqlibdoc.who.int/trs/WHO_TRS_901.pdf.

Jenner, PM, EC Hagan, Jean M Taylor, EL Cook, and OG Fitzhugh. 1964. "Food Flavourings and Compounds of Related Structure I. Acute Oral Toxicity." Food and Cosmetics Toxicology 2:327–343.

Khan, I. A., and Ehab A. Abourashed. 2010. Leung's Encyclopedia of Common Natural Ingredients Used in Food, Drugs, and Cosmetics /. 3rd ed. Hoboken, N.J. : John Wiley & Sons,. http://encompass.library.cornell.edu/cgi-bin/checkIP.cgi?access=gateway_standard%26url=http://app.knovel.com/web/toc.v/cid:kpLECNIUF1.

Kim, Eun-Hee, Hyun-Kyung Kim, Don-Ha Choi, and Young-Joon Ahn. 2003. "Acaricidal Activity of Clove Bud Oil Compounds against Tyrophagus putrescentiae (Acari: Acaridae)." Applied Entomology and Zoology 38 (2):261–266.

Knio, KM, J Usta, S Dagher, H Zournajian, and S Kreydiyyeh. 2008. "Larvicidal Activity of Essential Oils Extracted from Commonly Used Herbs in Lebanon against the Seaside Mosquito, Ochlerotatus caspius." Bioresource Technology 99 (4):763–768.

Ladd, TL, CR Buriff, M Beroza, and TP McGovern. 1975. "Japanese Beetles Coleoptera Scarabaeidae Attractancy of Mixtures of Lures Containing Phenethyl Propionate and Eugenol." Journal of Economic Entomology 68 (6):819–20.

Ladd, TL, MG Klein, KO Lawrence, and M Beroza. 1974. "Japanese Beetles - Duration of Attractancy in Field of Phenethyl Propionate plus Eugenol." Journal of Economic Entomology 67 (1):139–40.

LaVoie, EJ, JD Adams, J Reinhardt, A Rivenson, and D Hoffman. 1986. "Toxicity Studies on Clove Cigarette Smoke and Constituents of Cloves: Determination of the LD50 of Eugenol by Intratracheal Instillation in Rats and Hamsters." Archives of Toxicology 59:78–81.

Lilly, G. E., J. L. Cutcher, and M. D. Jendresen. 1972. "Reaction of Oral Mucous Membranes to Selected Dental Materials." Journal of Biomedical Materials Research 6 (6):545–51. https://doi.org/10.1002/jbm.820060606.

Maralhas, Alexandra, Ana Monteiro, Célia Martins, Michel Kranendonk, António Laires, José Rueff, and António S Rodrigues. 2006. "Genotoxicity and Endoreduplication Inducing Activity of the Food Flavouring Eugenol." Mutagenesis 21 (3):199–204.

McDavit, W. Michael, and Keith A Matthews. 2012. "Vegetable and Flower Oils Final Work Plan." Registration Review Case 8202. Washington, DC: US EPA Office of Pesticides and Toxic Substances. http://www.regulations.gov/contentStreamer?objectId=0900006480b5b0ce&disposition=attachment&contentType=pdf.

McGovern, TP, M Beroza, and TL Ladd. 1973. Phenethyl propionate and eugenol, a potent attractant for the Japanese beetle (Popillia japonica Newman). US Patent Office 3,761,584, issued September 1973.

McGovern, TP, M Beroza, TL Ladd, JC Inganci, and JP Jurimas. 1970. "Phenethyl Propionate, a Potent New Attractant for Japanese Beetles." Journal of Economic Entomology 63 (6):1727–1729.

Merck. 2015. The Merck Index Online. Cambridge, UK : Royal Society of Chemistry,. http://resolver.library.cornell.edu/misc/8496923.

Miller, Stephen S., and Thomas Tworkoski. 2010. "Blossom Thinning in Apple and Peach with an Essential Oil." Hortscience 45 (8):1218–25.

Moore, Jacob. 2011. "Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils." Registration Review OPP-2011-0628-0002. Washington, DC: US EPA Office of Pesticides and Toxic Substances. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2011-0628-0002.

Moore, Sarah J, Annick Lenglet, and Nigel Hill. 2007. "Plant-Based Insect Repellents." In Insect Repellents : Principles, Methods, and Uses, by Mustapha. Debboun, Stephen P. Frances, and Daniel A. Strickman, 275–303. Boca Raton, FL: CRC Press.

Ngoh, Shay P, Lionel EW Choo, Fung Y Pang, Yan Huang, Manjunatha R Kini, and Shuit H Ho. 1998. "Insecticidal and Repellent Properties of Nine Volatile Constituents of Essential Oils against the American Cockroach, Periplaneta americana (L.)." Pest Management Science 54 (3):261–268.

NPIC. 2016. "NPIC Special Report: 25(b) Incidents." Corvallis, OR: National Pesticide Informatiom Center.

Nurdjannah, N, and N Bermawie. 2001. "Clove." In Handbook of Herbs and Spices, by KV Peters, 154–63. Boca Raton, FL: CRC Press Boca Raton, Woodhead Publ. Ltd.

Obeng-Ofori, D, and CH Reichmuth. 1997. "Bioactivity of Eugenol, a Major Component of Essential Oil of Ocimum suave (Wild.) against Four Species of Stored-Product Coleoptera." International Journal of Pest Management 43 (1):89–94.

———. 1999. "Plant Oils as Potentiation Agents of Monoterpenes for Protection of Stored Grains against Damage by Stored Product Beetle Pests." International Journal of Pest Management 45 (2):155–159.

Price, DN, and MS Berry. 2006. "Comparison of Effects of Octopamine and Insecticidal Essential Oils on Activity in the Nerve Cord, Foregut, and Dorsal Unpaired Median Neurons of Cockroaches." Journal of Insect Physiology 52 (3):309–319.

Regnault-Roger, Catherine. 1997. "The Potential of Botanical Essential Oils for Insect Pest Control." Integrated Pest Management Reviews 2 (1):25–34.

Regnault-Roger, Catherine, Charles Vincent, and John Thor Arnason. 2012. "Essential Oils in Insect Control: Low-Risk Products in a High-Stakes World." Annual Review of Entomology 57:405–424.

Revay, Edita E., Amy Junnila, Rui-De Xue, Daniel L. Kline, Ulrich R. Bernier, Vasiliy D. Kravchenko, Whitney A. Qualls, Nina Ghattas, and Günter C. Müller. 2013. "Evaluation of Commercial Products for Personal Protection against Mosquitoes." Acta Tropica 125 (2):226–30. https://doi.org/10.1016/j.actatropica.2012.10.009.

Shaukat, Sadaf. 2010. "Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils." EPA-HQ-OPP-2011-0628-0004. US EPA, Office of Pesticides and Toxic Substances.

Sigma-Aldrich. 2014. "Eugenol Safety Data Sheet." MSDS 246700. St Louis, MO: Sigma-Aldrich. http://www.sigmaaldrich.com/msds.

Sipes, IG, and A Mattia. 2006. "Eugenol and Related Hydroxyallylbenzene Derivatives." JECFA Monograph 530. WHO Food Additive Series No. 1138. Rome, IT & Geneva, CH: Joint FAO/WHO Expert Committee on Food Additives. http://www.inchem.org/documents/jecfa/jecmono/v56je09.pdf.

Stroh, J, MT Wan, MB Isman, and DJ Moul. 1998. "Evaluation of the Acute Toxicity to Juvenile Pacific Coho Salmon and Rainbow Trout of Some Plant Essential Oils, a Formulated Product, and the Carrier." Bulletin of Environmental Contamination and Toxicology 60 (6):923–930.

Tworkoski, Thomas. 2002. "Herbicide Effects of Essential Oils." Weed Science 50:425–431.

US EPA. 2000. "Floral Attractants, Repellents, and Insecticides." Fact Sheet. Washington, DC: US EPA. http://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_G-105_25-Sep-00.pdf.

———. 2015. "Active Ingredients Eligible for Minimum Risk Pesticide Products." Washington, DC: US EPA Office of Chemical Safety and Pollution Prevention. https://www.epa.gov/sites/production/files/2015-12/documents/minrisk-active-ingredients-tolerances-2015-12-15.pdf.

———. 2017. "Pesticide Product Labeling System (PPLS)." 2017. http://iaspub.epa.gov/apex/pesticides/f?p=PPLS:1.

Vaid, S, DAIZY R Batish, HP Singh, and RK Kohli. 2010. "Phytotoxic Effect of Eugenol towards Two Weedy Species." Bioscan 5 (3):339–341.

Waliwitiya, Ranil, Murray B. Isman, Robert S. Vernon, and Andrew Riseman. 2005. "Insecticidal Activity of Selected Monoterpenoids and Rosemary Oil to Agriotes obscurus (Coleoptera: Elateridae)." Journal of Economic Entomology 98 (5):1560–65.

Wang, Chunmei, Jie Zhang, Hao Chen, Yongjian Fan, and Zhiqi Shi. 2010. "Antifungal Activity of Eugenol against Botrytis cinerea." Tropical Plant Pathology 35 (3):137–143.

Yang, Young-Cheol, Si-Hyeock Lee, Won-Ja Lee, Don-Ha Choi, and Young-Joon Ahn. 2003. "Ovicidal and Adulticidal Effects of Eugenia caryophyllata Bud and Leaf Oil Compounds on Pediculus capitis." Journal of Agricultural and Food Chemistry 51 (17):4884–4888.