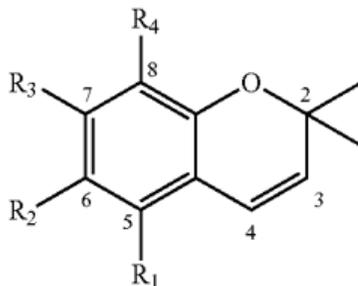


## INVENTION DISCLOSURE

We have developed insecticidal compositions containing chromene derivatives based on a chromene amide isolated from *Amyris texana*. At lower concentrations our chromene derivatives (synthetic or natural), are also useful for repelling blood-sucking and biting insects, ticks and mites.

Dengue fever and yellow fever are caused by arboviruses which are transmitted by female mosquitoes belonging to the genus *Aedes*, particularly *Ae. aegypti*. Symptoms of dengue infection in humans include headache, fever, exhaustion, severe muscle and joint pain, swollen glands (lymphadenopathy), and rash. Other symptoms include bleeding gums, severe pain behind the eyes, and red palms and soles. The more severe form of this viral illness is dengue viral hemorrhagic fever which includes headache, fever, rash, and evidence of hemorrhage in the body. This form of dengue fever is life threatening and can progress to dengue shock syndrome, the most severe stage of the illness. Our invention helps to fight this disease by acting as a pesticide and/or a repellent for those mosquitoes.

The compounds that work excellently in our invention have the formula:



where  $R_1 = \text{CH}_2\text{OH}$ , hydrogen, hydroxy, or aralkoxy, and  $R_2, R_3, R_4 = \text{H}$

We found that it is convenient to dispense the compounds of our invention into the environment in vapor form (e.g., an aerosol) preferably using devices that allow a slow sustained release of these compounds into the environment from a sealed canister.

The compositions and compounds can also be used for killing and/or repelling harmful or troublesome blood-sucking and biting insects, ticks and mites including mosquitoes (for example *Aedes*, *Culex* and *Anopheles* species including but not limited to Tiger mosquitoes, *Aedes aboriginis*, *Aedes aegypti*, *Aedes albopictus*, *Aedes cantator*, *Aedes sierrensis*, *Aedes sollicitans*, *Aedes squamiger*, *Aedes sticticus*, *Aedes vexans*, *Anopheles quadrimaculatus*, *Culex pipiens*, and *Culex quinquefasciatus*), sand flies (for example *Phlebotomus* and *Lutzomyia* species), bed bugs (for example *Cimex lectularius*), owl gnats (*Phlebotoma*), blackfly (*Culicoides* species), buffalo gnats (*Simulium* species), biting flies (for example *Stomoxys calcitrans*), tsetse flies (*Glossina* species), horseflies (*Tabanus*, *Haematopota* and *Chrysops* species), house flies (for example *Musca domestica* and *Fannia canicularis*), meat flies (for example *Sarcophaga carnaria*), flies which cause myiasis (for example *Lucilia cuprina*, *Chrysomya chloropyga*, *Hypoderma bovis*, *Hypoderma lineatum*, *Dermatobia hominis*, *Oestrus ovis*, *Gasterophilus intestinalis* and *Cochliomyia hominivorax*), bugs (for example *Cimex lectularius*, *Rhodnius prolixus* and *Triatoma infestans*), lice (for example *Pediculus humanus*, *Haematopinus suis* and *Damalina ovis*), louse flies (for example *Melaphagus orinus*), and fleas (for example *Pulex irritans*, *Ctenocephalides canis* and *Xenopsylla cheopis*), sand fleas (for example *Dermatophilus penetrans*), and blood-feeding ticks include (for example, *Ornithodoros moubata*, *Ixodes ricinus*, *Ixodes scapu-*

*laris*, *Boophilus microplus*, *Amblyomma americanum*, and *Amblyomma hebreum*., and mites include, for example, *Sarcoptes scabiei* and *Dermanyssus gallinae*).

The compounds, which can be used in undiluted or diluted form, can be converted into formulations customary for pesticides or repellents. They can be used in all the presentation forms customary in cosmetics and public health pesticides, for example in the form of solutions, emulsions, gels, ointments, pastes, creams, powders, sticks, sprays or aerosols from spray cans.

For use in the non-cosmetic sector, the compounds can be incorporated, for example, into granules, oily spraying agents or slow release formulations.

The formulations are prepared in a known manner by mixing or diluting the compounds with solvents (for example xylene, chlorobenzenes, paraffins, methanol, ethanol, isopropanol or water), carriers (for example kaolins, aluminas, talc, chalk, highly disperse silicic acid and silicates, nanoclays), emulsifying agents (for example polyoxyethylene fatty acid esters, polyoxyethylene fatty alcohol ethers, alkylsulphonates and arylsulphonates) and dispersing agents (for example lignin, sulphite waste liquors and methylcellulose).

The compounds can be mixed with one another in the formulations or can also be used as mixtures with other known active compounds (for example sunscreen agents). The formulations in general contain between about 0.1 and about 95% (e.g., 0.1-95%) by weight of active compound. For repellent use we believe that much lower concentrations (up to 2.5%) are desirable.

For protection from mosquitoes, the compounds are generally either applied to human or animal skin, or items of clothing and other objects are treated with the compounds. Preferably, the compounds are dispensed into the environment (e.g., outdoors or indoors) in vapor form (e.g., an aerosol).

The compositions contain a carrier and the compound. The repellent is generally applied with a carrier component. The carrier component can be a liquid or a solid material. As is known in the art, the vehicle or carrier to be used refers to a substrate such as a gel, polymers, or the like. All of these substrates have been used to release insect repellents and are well known in the art

We haven't tested all the concentrations, but believe that that pesticidal / insecticidal effective concentrations of the compound in the compositions may vary between about 0.1 and about 95% by weight. Of course, the precise amount needed will vary in accordance with the particular carrier used; the type of area or object to be treated; the number of hours or days of activity needed; and the environment in which the area or object is located.

The compounds may be used with other repellents or mosquito control agents (e.g., insecticides, chemosterilants or the like). When used, these agents should be used in an amount which will not interfere with the effectiveness of the compound.

#### PRIOR ART SEARCH

We have run a search and found one patent that could be of some relevance to our invention (for the patent attorney to determine). This is patent US 4,716,238 that makes reference to chromene derivatives. A copy of this patent is attached.

#### EXPERIMENTAL

The syntheses of analogs are known in the literature (De la Fuente, G., et al., *Phytochemistry*, 30: 2677-284 (1991)). The compounds are known in the literature, but we believe that their use as insecticides / pesticides is novel.

Bioassay for mosquito repellent activity: Repellency screening test for experimental chemicals were carried out to identify candidates that might be useful repellents. The repellent efficacy was compared to that of the standard repellent, DEET. Experimental compounds were assessed in one of two ways: (1) a range of concentration was evaluated to determine the minimum effective dosage (MED) which was the concentration threshold of where the repellent began to fail and allowed bites, or (2) a predetermined concentration of each repellent was applied to cloth and the activity was evaluated over several days (or in some cases months) (Katritzky, A. R., et al., Proc. Nat. Acad. Sci. (US), 105, 7359-7364 (2008); Katritzky, A. R., et al., Journal of Med. Entomol., 47: 924-938 (2010)).

On the basis of these findings we would like to protect our invention. We have a large amount of experimental data, so please let us know what you would need to file a complete patent application, and we will provide it. To assist us, please send us a draft of the patent application in which we can fill any missing information.