Caveat Emptor: Safety Considerations for Natural Products Used in Arthropod Control

John T. Trumble

Interest in natural products is growing rapidly, and shows no sign of abating. Sales of dietary supplements alone (not even including all herbal remedies) increased from 3.3 billion dollars in 1990 to over 6.5 billion dollars in 1996 (Kurtzweil 1998). According to Kurtzweil (1998), approximately one-half of the population in the United States uses these products. Given the size of the market, and an increasing interest in all things natural, it is not surprising that commercial products are being developed for a wide range of human and animal uses, including pest control.

The scientific community also has shown an interest in natural product development and use. Several journals are largely devoted to the study of the activity, chemistry, and use of natural products. Many other journals contain papers that describe the active ingredients or mode-of-action of herbs and other natural products (Table 1). In addition, Internet sites such as the Phytochemical and Ethnobotanical Database (www.ars-grin.gov/duke/) and HerbMed (http://www.herbmed.org/) offer detailed information on the active ingredients and recent scientific literature on plant species often used in herbal remedies.

Unfortunately, most natural products, including those used for insect control, are not always subject to rigorous testing. Many commercially available products are sold in the category of 'dietary supplements.' Materials sold in this classification are not routinely tested for content, quantity of ingredients, or safety (USDA 2001). These materials typically include products that are self-labeled as herbal remedies, aroma therapies, holistic cures, homeopathic treatments, or 'New Age' remedies. There are no regulations that provide limitations on the content or amount of ingredients; such decisions are solely at the discretion of the producer. For all of these products, the manufacturer is responsible for making sure that all the dietary ingredients are safe and the contents list is complete. Manufacturers and distributors are not required to register with the Food and Drug Administration (FDA) or get FDA approval before producing or selling dietary supplements (USDA 2001). This is in contrast to the category of 'food additives,' where FDA review and approval is mandatory.

Most consumers in the United States and Europe are accustomed to the rigorous labeling requirements required for drugs, food, and pesticides. Statements made on the labels for such products are approved only after extensive review by the FDA (or similar organizations in Europe). However, for dietary supplements or herbal remedies in the United States, the Federal Trade Commission (FTC) is responsible for handling advertising claims. Unfortunately, manufacturer claims for effectiveness are not evaluated for accuracy (USGAO 2000). However, following a manufacturers' statement of benefit, the FTC requires that labels include the disclaimer that "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent disease." This generic disclaimer often is footnoted in small letters beneath such benefit statements as "controls lice," "prevents infection," "improves health," "provides appropriate boundaries," "kills pests," "stimulates the immune system," and so on. In the case of herbal or new age remedies, particularly those found on the Internet, even the generic FTC warning statement is often omitted.

Many of the commercial products incorporate materials or compounds that are listed by the USDA as 'generally recognized as safe' (GRAS). These include materials that have a long history of food use (prior to 1958; Code of Federal Regulations 1999) with minimal problems, such as garlic. Unlike many of the more recent herbal control products, the active ingredients in these older materials have often been tested for efficacy, and results reported in the scientific literature. However, this does not ensure that the preparation or product will function effectively as formulated or advertised by a specific producer.

One area of concern is the use of mix-

Table 1. Numbers of manuscripts in selected journals investigating natural products as potential pest-control components

	Year	
Journal	**1999**	**2000**
Journal of Economic Entomology	**33**	**44**
Environmental Entomology	**9**	**17**
Journal of Medical Entomology	**11**	**14**
Journal of Phytochemistry	**14**	**10**
Journal of Chemical Ecology	**21**	**23**
Journal of Agricultural Food Chemistry	**11**	**25**
Journal of Ethnopharmacology	**3**	**3**
Journal of Natural Products	**5**	**5**
Entomologia Experimentalis et Applicata	**16**	**14**

tures of ingredients. While many individual materials may have a history of safe use, little scientific information is available on the efficacy or safety of mixtures promoted for insect control. Because some of these products or recipes are used on animals or humans, possible negative interactions with other drugs must be considered (Devine 2000). This is particularly problematic in the unregulated areas of the Internet where individuals promote recipes and "concoctions" containing multiple plant extracts or components that they believe have demonstrated value.

The Message Promoted to Consumers

The overwhelming message promoted by the manufacturers, distributors, and advocates of herbal or natural approaches to insect control is that 'natural is safe.' The literature often states that natural materials have been used for many years with no ill effects. Presumably, if any chronic problems occurred, they were ascribed to other causes. In addition, many recipes on the Internet describe a history of folk wisdom (from someone's neighbors, cousins, or friends) that provides 'proof' of efficacy. However, perhaps the most remarkable claim to safety is on the basis that these products or recipes "contain no chemicals." The disdain for 'chemicals' was typified by a statement at the invisiblegardener.com web site where Lyme disease is discussed (http://www.invisiblegardener.com/magazine/online_magazine/lyme_framed.html). Along with some useful information on clothing and tick removal, the following is stated: "Lyme disease is a reflection of weakening human immunity systems. All living beings are being attacked by chemicals and are breaking down in their ability to fight off diseases. . . .Chemicals weaken our society as a whole, weaken our biological systems." The apparent lack of understanding of simple chemistry in our modern society provides a distressing assessment of science education.

In an effort to assess the status of homeopathic or herbal control strategies for insect control, I examined the scientific literature and conducted Internet searches for terms such as homeopathy, natural pest control, ethnopharmacology, aroma therapy, new age control, and holistic pest control. I do not claim to have found all of the possible key words or even read more than 50% of the available information. However, after hundreds of hours spent researching this topic, several conclusions could be reached.

The first is that there is a surprisingly large number of entomologists, chemists, medical scientists, botanists, and biologists conducting scientifically sound research on the use of natural products. However, only a few small companies are emerging that are registering promising new arthropod control materials based on scientifically supported data. Most of these have chosen to obtain registration through the U.S. Environmental Protection Agency, rather than use the dietary supplement approach via the FDA and FTC. Nonetheless, the amount of peer-reviewed publication on natural products (Table 1) suggests that more registrations may be forthcoming.

A second conclusion is that many of the herbal products or recipes for insect control suffer from several non-trivial problems. The least important of these range from relatively minor misinterpretations to providing misinformation to the consumers. In some cases this could lead to potential discomfort for the consumer. For example, a natural repellant such as oil of eucalyptus advertised for use against one insect (e.g., mosquitos, Mosi-Guard Natural, http://www.masta.org/products/repellents/index.html) can serve as an attractant for another blood-feeding pest (e.g., certain biting midges, Braverman et al. 1999). However, more serious problems include recommendations likely to lead to contact dermatitis, exposure to carcinogens, mutagens, neurotoxins, use of materials known to cause organ failure.

Some examples of misinformation include statements such as "Mosquitoes suck juices from plants like grass, tree leaves, etc., in order to survive" from Garlic Barrier FAQs (http://www.garlicbarrier.com/facts.html). I was also surprised to read that the garlic product was systemic in plants because "the wheat is green where the Garlic Barrier was sprayed—showing that it was absorbed by the plant." Although this is an interesting observation, it does not provide proof the material is systemic. Another example is that "There is a plant-derived spray you can resort to in desperation. . . . It is called bT (*bacillus Thuringiensis*)" from the Organic Gardener at http://www.perc.flora.org/PEN/1995-07-08/supplement/cleary.html. Although incorrect (*Bacillus thuringiensis* Berliner is a bacterial pathogen of insects), misinformation of this nature is not likely to cause significant problems. Of more serious concern are comments such as the following from the Master Gardening Internet site (http://www.mastergardening.com/ticmasyarspr.html) that falsely state that a product is from a natural source when in fact it is a synthetic compound. The web site states that Tick Master Yard Spray is "Made with Permethrin, a chemical produced naturally by flowers to repel insects. This spray will bring comfort and safety to your backyard." My first thought was that this was a simple typographic error, and the statement should read 'pyrethrum' (an insecticidal chemical from certain species of plants in the genus *Chrysanthemum*). However, the label on the container pictured clearly lists 'permethrin,' a synthetic chemical thousands of times more active against insects than pyrethrum.

The popular literature on the Internet also includes many apparent contradictions. One example (http://www.earthhome.tripod.com/pest/html) is that "The last thing you want to do is fill your garden full of toxic chemicals. . .you run a risk of poisoning pets or even your kids, with this stuff around. Plus, who wants to eat food laced with pesticide." This is followed a few lines later with a description of a natural pesticide for aphids, June bugs, black spot, and rust: "Steep rhubarb leaves in boiling water. Strain and spray. This is VERY poisonous to humans too, keep out of reach of children." Another example of contradiction is at the Garlic Barrier web site (http://www.garlicbarrier.com/facts.html), where they note that many customers feed the product to their dogs to repel fleas. A few lines later they state that the product should not be eaten because "it is not food grade and is not made in conditions considered safe for foodstuffs."

Natural Insect Control Strategies

There are numerous examples of insect control strategies using natural products or concoctions that can be found in the homeopathy, herbal, and new age literature. Some of these probably work as described. Anyone who has worked in the field of plant-insect interactions is keenly aware of how many insect toxins there are and how remarkably efficacious they can be in certain circumstances. However, most researchers in this field also recognize that many of these toxins are active against mammalian systems, and therefore do not automatically equate 'natural' with 'safe.' In the following sections I describe a few of the more interesting insect control strategies. To provide some structure, I have catalogued these examples as the curious, the cautionary, the potentially hazardous, and the inexplicable.

The Curious. I was interested to read that ground-up remains of pest insects sprinkled over leaves, or water extracts of dead insects sprayed on plants, were repellent to living insects. The recommended approach (http://www.seedman.com/pest.html) is to collect as many different types of insects as possible in a garden, smash these into a paste, and then soak this paste overnight in water. "To make the best bug juice, use an old blender and add a little dishwashing detergent to the mix to make it adhere better." I was unable to find any scientific literature that supported the claim that extracts of dead insects can function as insect repellents. However, many soaps are known to be active against insects. This 'dead insect' theme is repeated frequently in the natural product literature.

A similar approach is also reported to be successful even for parasitic species. For example, a homeopathic remedy for fleas and ticks (Frontier Pet Remedy for Fleas and Ticks; http://www.alteredstatesherbs.com/alteredstatesherbs/fronpetremfo4.html) contains both *Pulex irritans* (the human flea) and "*Apis mellifica*" [sic] as ingredients. The other ingredients listed were *Cistus canadensis, Citricum acidum, Hypericum perforatum, Kali nitricum, Ledum palustre, Lycopodium clavatum, Mezereum, Pulsatilla, Stahpysagria,* sulphur, *Urtica urens* and alcohol. Of these, both sulphur and alcohol have a long history in insect control. I was, however, interested to read that the genus and species for citric acid is *Citricum acidum* (although perhaps this is a holdover from reporting terms in ancient Latin, which is sometimes seen in the homeopathic literature). The other plant materials have not been reported in the scientific literature as insect control agents, but St. John's wort, *H. perforatum* (Fig. 1), and stinging nettle, *Urtica urens*, have been studied for a variety of benefits and problems associated with ingestion (Ziyyat et al. 1997, Beckman et al. 2000, Lane-Brown et al. 2000, Williams et al. 2000). Regardless, the repeating theme that 'dead insects repel live insects' may justify additional investigation.

Fig. 1. Saint John's Wort, *Hypericum perforatum* L. Photo by Brother Alfred Brousseau, 1995, Saint Mary's College.

There are many examples of both commercial products and folklore remedies that use various herbs and spices for flea and tick control. A natural flea repellent powder is available (Rachel's Pest Powder; http://www.seedman.com/pest.html) that is made from "naturally ground" spearmint, peppermint, eucalyptus, rosemary, myrrh, goldenseal, and talc. I was unable to determine what constituted naturally ground. However, at least the first four ingredients can be found in many of the holistic remedies available on the Internet. Most of these recipes use dried ground herbs, but some include essential oils. The essential oils of peppermint and rosemary have been tested and found to be efficacious against lice (Veal 1996). The author suggested that phenols, phenolic ethers, ketones, and oxides (1,8-cineole) appear to be the major toxic components, but aldehydes and sesquiterpenes may also play a role. However, there are reports that rosemary oil can cause contact dermatitis (Fernandez et al. 1997) and contribute to occupational asthma (Lemiere 1996). In response to allergic concerns, some web sites suggest that when using herbs for insect repellency or control, the crushed leaves (or preparation) should be rubbed on a small portion of your skin (or your pet's skin) to determine if there will be an allergic reaction before treating your whole body. Of course, this assumes that any allergic reaction will not be profound.

On the lighter side, there are multiple reports on the Internet in sites promoting holistic remedies, natural pest management solutions, chat rooms, and even a magazine that describe the use of Bounce Fabric Softener sheets (Proctor and Gamble, Hunt Valley, MD) to repel mosquitoes and gnats. Only the magazine suggested a potential mode of action: "The best explanation I've heard about why this works: Have you ever seen bugs in a dryer?" (Hansen 2000). No scientific literature was available on this potential repellent.

Most of the material I read was for products designed to remove insects from humans, animals, and gardens. One claim was notably different. Apparently, partially digested caterpillars regurgitated from the crop contents of hornet larvae offer substantial potential benefits if ingested. According to the Meiji Milk Company of Japan, a juice made of 1.8% gut contents of the giant hornet greatly improves performance of athletes (and at least one swimming mouse, http://www.vaam-power.com/). The product, now with the commercial name VAAM, was used by the winner of the women's marathon at the 2000 Summer Olympics. Because this is a natural material, there are no concerns with athletic regulations for performance enhancing drugs. The product was created when scientists at the Institute of Physical and Chemical Research were curious how the giant killer hornet (*Vesper mandarin japonica*) could fly the equivalent of two marathons a day. They analyzed the contents of larval food passed by trophalaxis to the adults, and found a blend of 17 amino acids, which the chemists then aquire from other sources and re-create for the drink. Extracting commercial quantities from the larvae is not feasible, and apparently somewhat dangerous. This was the only commercial product I found manufactured based on an animal extract; plant-based compounds are far more popular.

The Cautionary. Plants produce a wide variety of insect-active toxins, many of which are dangerous to mammals as well as insects (D'Mello 1997). Some of these broadly toxic

Fig. 2. English lavender, *Lavandula angustifolia* P. Mill. Photo by Danel Vickerman.

chemicals are incorporated into commercial products or recipes because they can be readily collected from plants as natural sources. Many of these have a long history of use, while some are relatively new. However, just like FDA-approved synthetic materials that can be toxic to mammals, the administered dose of a natural product can be critically important. Unfortunately, documenting content of bioactive chemicals in plant preparations is not possible for the average user, and frequently not specified (or determined) by many manufacturers. Plants vary in chemical content with soil nutrition, exposure to stress factors, water availability, and a host of other environmental conditions. Thus, simply assuming that all plants are equal or that 'natural is safe' can be dangerous. The following includes a description of just a few of these plant products, beginning with one that is essentially benign.

Linalool. Linalool (3,7-dimethyl-1,6-octadien-3-ol) is a compound extracted from many plants including lavender (*Lavandula angustifolia*, Fig. 2) and basil (*Ocimum* spp., Fig. 3) (Ntezurubanza et al. 1985, Lis-Balchin and Hart 1999). This ingredient can be found in flea dips for dogs and cats. Acute oral (rat) and dermal (rabbit) exposure levels that cause 50% mortality are quite high (>2.7 g/kg), suggesting substantial safety margins for mammals (Opdyke 1979). Recent research suggests that the primary mode of action of linalool is on the nervous sys-

Fig. 3. Sweet basil, *Ocimum basilicum* L. Photo by Danel Vickerman.

tem, affecting ion transport and the release of acetylcholine esterase (Ryan and Byrne 1988, Re et al. 2000). There have been a few studies reported in the scientific literature that describe insecticidal activity against stored-product pests (Weaver et al. 1991, Sanchez-Ramos and Castanera 2000) and the potential for use against cat fleas (Hink et al. 1988). Thus, there is no question regarding insecticidal activity. This does not mean that all advertised claims for products containing linalool will be entirely accurate.

Flea Stop Plus Dip is a product that contains linalool. Advertising notes "our highly concentrated dip contains linalool which kills all four stages of fleas" (see http://gardenersalive.com/item_display.asp?ProductNumber=3317&PROG_NBR=12). I was curious how often the egg stage, which drops off the host, and the larval stage, which lives off the host, are actually contacted. This claim may have originated from the study by Hink et al. (1988) where insecticidal activity on carpets was assessed. Regardless, I could find no reports of any adverse effects on humans or animals from commercial products containing linalool, and there is ample scientific evidence that at least some are efficacious.

Melaleuca Oil. The oil of *Melaleuca alterniflora* Cheel (paperbark or tea tree, also several other hybrids and species, Fig. 4) has been used for centuries by aboriginal Australians as a traditional remedy for discomfort casued by insect bites, bruises, and other ailments (Budhiraja et al. 1999). The oil is now used medicinally in topical cream formulations (5-10% concentration) as antifungal, acne, and antimicrobial preparations (Bassett et al. 1990, Budhiraja et al. 1999, Syed et al. 1999). A formulation of 100% oil for topical use is also available on the Internet (see http://www.naturalice.com/). The oil is extracted from leaves and twigs of the plants, and in herbal recipes, frequently combined with other essential oils to control ectoparasitic insects on companion animals and humans. There are a wide range of other uses described in the literature and many commercial products containing the oil are currently available (Rubel et al. 1998).

Fig. 4. Tea tree, *Melaleuca alternilflora* Cheel. Photo by William Carson.

A great deal of research has been conducted on the active chemicals in *Melaleuca* oil. The most active components of the oil are terpenes (mostly terpinen-4-ol; a- and y-terpinene; 1,8 cineole; and terpinolene) and sesquiterpenes. The International Standard, ISO 4730 (ISO 1996), mandates a minimum concentration of 30% for terpinen-4-ol and a maximum concentration of 1,8 cineole of 15% in the oil. This latter material is also one of the arthropod-active ingredients in peppermint and rosemary essential oils (Veal 1996). The intraspecific variation in oil contents in *Melaleuca* species is substantial between geographic regions and within seasons (Butcher et al. 1994, Murtagh and Smith 1996), making chemical analysis of the oil important for standardization of products.

There have been several problems reported with the use of *Melaleuca* oil. The most common problematic response is contact dermatitis, with more than 30 human cases reported in the scientific literature in the 1990s (Knight and Hausen 1994, Bhushan and Beck 1997, Rubel et al. 1998, Hausen et al. 1999). This can be caused by the fresh oil, but is enhanced by the formation of degradation products that develop with photodegredation in either open or closed containers (Hausen et al. 1999). These degradation products include peroxides, epoxides, and such endoperoxides as ascaridol and 1,2,4-trihydroxy menthane. *Melaleuca* oil toxicosis in dogs and cats has been associated with depression, weakness, muscle tremors, and lack of coordination (Villar et al. 1994). In one case where the oil was diluted and used as a dip for fleas for three cats, all of the cats required veterinary care and one subsequently died (Bischoff and Guale 1998).

Products available for human use are generally available, including at least one for control of head lice (Naturallice, http://www.naturalice.com/). The concentration of *Melaleuca* oil is not specified, but the site recommends that "The head is wrapped in plastic wrap to avoid staining of the furniture." The exposure time is approximately one hour, which could be of concern if a contact dermatitis response occurs. The mode of action is under study scientifically, but this web site suggests that the compound is a neurotoxin "Because it is very difficult to kill the early nits before they have developed a nerve system, some nits may survive the treatment." Thus, additional one-hour applications may be necessary.

d-Limonene. The compound d-limonene (1-methyl-4-isopropenyl-1-cyclohexene) is often extracted with either pressure or steam from the peels of several citrus species, including orange, lemon, mandarin, lime, and grapefruit, and is present in a number of other essential oils (EPA1993). This compound is on the U.S. EPA's GRAS list. This versatile citrus extract has a remarkable variety of uses, including, among others, utility as an industrial degreaser, household cleaning agent, food flavoring, sewage scum remover, and pesticide. As a pesticide, this compound can be found in flea dips for dogs and cats, and pesticides used for indoor pest control. Data on d-limonene are insufficient for the EPA to provide values for an oral assessment, an inhalation assessment, or a carcinogenicity assessment (EPA 1993).

As with many pesticides, inadequate dilution can be problematic. Frank et al. (1992) described necrotizing dermatitis with sloughing of the skin following exposure to d-limonene. Cats appear to be particularly sensitive, with exposures causing hypersalivation, muscle tremors, ataxia, depression, and hypothermia (Hooser 1986, Powers et al. 1988). Fortunately, most treatments at the dose recommended by the commercial products tested were not a problem. However, repeated exposures to d-limonene cause a heightened sensitivity resulting in substantial allergic reactions (Karlberg et al. 1991). Contact dermatitis from d-limonene has also been reported in humans (Chang et al. 1997, Wakelin et al. 1998, Nilsson et al. 1999), so some caution may be advisable during application to animals. The Internet availability of inexpensive technical grade material, along with the many nebulous recipes offered on the Internet, enhance the potential for misuse by consumers.

An advertisment for the 607 d'limonene Bug Killer, a "safe, non-toxic insect control", suggests that the mode of action is the dissolving of the protective layer of wax from the exoskeletons of insects "causing them to suffocate and die" (Direct Chem 2001). I wondered if the writers meant 'desiccate,' but were unable to find any scientific literature on the subject. This product purportedly offers weeks of residual action on indoor structural surfaces (for ants, cockroaches, silverfish, and others) and bedding (for fleas). The mode of action for the residual activity was not explained.

The Potentially Hazardous. *Wormwood.* Wormwood (*Artimesia absinthium* L. and related species, Fig. 5) is readily available on the Internet in plant or extract form. It is sold under the names absinthe, absinthium, green ginger, and madderwort. *Artimesia absinthium* contains a-thujone, the active ingredient in absinthe. Absinthe was a popular stimulant/hallucinogen during the 19th century, but was banned in most countries by the early 1900s after being implicated as a causal factor in hallucinations, psychoses, and suicides (Reese 2000). The active ingre-

Fig. 5. Wormwood, *Artimesia* spp. Photo by Brother Alfred Brousseau, 1995, Saint Mary's College.

dient, a-thujone, has been identified as a potent neurotoxin impacting the gamma-amino butyric acid system (Hölld et al. 2000). According to Reese (2000), a-thujone is still available in stores in parts of Europe, but the European Commission limits the a-thujone content to 10 µg/g, compared with 260 µg/g in plants and extracts. Thus, the many procedures for extracting *A. absinthium* described on the Internet could produce much higher concentrations than 10 µg/g. Not surprisingly, there are reports in the medical literature of significant health problems associated with wormwood extracts (Weisbord et al. 1997).

Wormwood oil and *A. absinthium* plant parts and extracts have been used medicinally for centuries, with recipes recorded in ancient Egyptian and Syrian texts. Most current recipes focus on promoting liver function, increasing appetite, strengthening the stomach, relief of gout, and dealing with a variety of gastrointestinal complaints, especially the control of internal parasites. It has also been recommended in aromatherapy to 'increase psychic awareness.' Insects such as fleas and moths are reportedly repelled by judicious placement of dried and powdered forms (http://www.wormwood-absente.com/thujone.htm). Wormwood apparently was taken orally by thieves to avoid contracting the plague (repel fleas?) while stealing from sick individuals or corpses (Day 2001). There has also been the suggestion that a-thujone was perceived as an aphrodisiac in the aptly titled article "Absinthe Makes the Tart Grow Fonder: A Note on Wormwood in Christina Rossetti's Goblin Market" (O'Reilly 1996). However, this perception may have been due, in part, to the common alcohol delivery system. Regardless, the Internet and folk medicine texts contain innumerable recipes for human and animal use.

Most of the concoctions that include wormwood are confounded by the addition of several other plant components. One example is the commercial product Purge. This product has the interesting advertisement copy: "Are you hosting uninvited guests? - Kick them out with Purge!" (Healthwise International 2001). Purge contains wormwood, cloves, black walnut extract, and 24 other natural substances. Treatment lasts 50 days, not including a five-day break from medication at day 25. Similarly, deworming concoctions for pets often include dried, powdered rosemary, wormwood, and fresh ground garlic. In nearly all cases, potential interactions between components have not been scientifically studied, and safety is assumed because of the long history of use.

Pennyroyal. The mints known as pennyroyal, *Mentha pulegium* in Europe (Fig. 6) and *Hedeoma pulegioides* in the new world, have been used for centuries as insect repellants, insect control agents, and for a variety of medicinal purposes. The name pulegium is credited to Pliny the Elder, who named the plant for the common practice of spreading it over the floors of houses to control 'pulex' or 'pulices' (fleas) (Stuart 1979, Genders 1980). The term 'royale' was later added because the herb was used to rid the French royal apartments of fleas. Ultimately, the name for the herb corrupted to pennyroyal.

Fig. 6. Pennyroyal, *Mentha pulegium* L. Photo by Brother Alfred Brousseau, 1995, Saint Mary's College.

This herb can be found in many human and animal recipes for gout, colds, flu, flatulence, insect bite treatments and repellants, as well as flea and tick control, among others. The most dangerous use is as an abortifacient, where the effective dose results in the death of the mother as well. This serves as an excellent example of how the collective knowledge of a long history of use can be dangerously incorrect. Among the most entomologically interesting medical uses was a recipe to control *formication*, the feeling that thousands of ants are crawling on the affected body part. In most uses the plant or extract is meant to be ingested, but some recipes require dermal application.

Some scientific literature is available on the insect control potential of pennyroyal. The primary active ingredient has been tested in soil and on plant material against some major agricultural pests of economic importance, and appeared potentially useful (Rice and Coats 1994, Sanchez-Ramos and Castanera 2000). Similarly, the essential oil of a related species containing pulegone (*Hedomea mandonianum*) offered some control of *Triatoma* spp. vectors of Chagas disease (Fournet et al. 1996). Unlike the herbal supplement use, agricultural or urban structural registrations would require detailed toxicity and carcinogenicity studies prior to employment.

Both species of pennyroyal contain pulegone (a monoterpene). Upon ingestion, pulegone is oxidized by the cytochrome P-450 system into toxic metabolites including menthofuran (Nelson et al. 1992). These metabolites bind to proteins (Thomassen et al. 1992) causing loss of organ function, seizures, acute poisonings, and death (Anderson et al. 1996, Bakerink et al. 1996, Burkhard et al. 1999). Topical application for fleas on dogs have produced acute illness, vomiting, liver damage, and death (Sudekum et al. 1992). I could find no scientific studies that evaluated toxicity of pulegone following ingestion by companion animals (although laboratory rats were well represented). However, given the ingestion toxicity observed for humans, such use may not be advisable.

Nicotine. As an entomologist, I found it remarkable that herbal recipes containing nicotine for use on humans are still widely available on the Internet. In one example on the Medicinal herbFAQ web site (1999), a recipe for lice and gnats is offered: "It is easy to prepare. Buy a cigar or some rolling tobacco and boil the hell out of it in a liter or so of water. When cool, shlop it on your hair and cover your hair with a plastic shower cap or something like that for 20 minutes, then shampoo. One application should be enough, but I would often do a follow up about three or four days after the first application." Studies in the scientific literature stress the value of immediate washing following nicotine exposure (Zorin et al. 1999) and the importance of protective clothing (Gelbach et al. 1979). Thus, intentional application with prolonged exposure would appear contraindicated.

The Inexplicable. For a scientist, reading the New Age literature and some of the holistic writing is roughly the equivalent of suddenly entering a parallel universe where the rules of physics and chemistry do not apply. Biology is replaced by mysticism. Psychic awareness is paramount. Health relates to your vibrational status and medical doctors are replaced by holistic health practitioners. This is not to say that the recipients do not receive value for the prescribed treatment, but simply that the rules are so different that they can be difficult to comprehend by someone trained to look for repeatability

Fig. 7. Castor bean, *Ricinus communis* L. Photo by Brother Alfred Brousseau, 1995, Saint Mary's College.

at the $P < 0.05$ level. The number of potential examples on the Internet is legion, but I will present just two to provide some insight into the conundrum.

Flower Essences and Electrical Systems. Flea Free from Green Hope Farm offers "healing vibrational energy to animals and their electrical systems" (see http://www.naturalpet.com/essences.html). This flower essence mixture "strengthens animal's energy systems and helps them in the creation of appropriate boundaries." The advertising states that it is a combination of 30 flower essences that "provide powerful system strengtheners" that keep fleas, ticks, and black flies off of pets. It is also recommended for rashes, allergic reactions, and poison ivy. This essence is "very useful for people also in dealing with blackflies and other flying insects." I was pleased that this product could be used by humans; as a parent of teenagers, the concept of appropriate boundaries is particularly appealing.

Essential Oils as Vibrational Remedies. The invisiblegardener.com web site offered some insight into how essential oils can serve as vibrational remedies for defense against pests as well as diseases (http://www.invisablegardener.com/magazine/online_magazine/essential_oils_framed.htm). It was suggested that a healthy person vibrates at about 61-73 millihertz (mhz). Pure essential oils vibrate at 60-320 mhz. Because most diseases occur when vibrations in humans are too low (e.g., lupus occurs at ≈49 mhz, cancer at ≈42 mhz), using pure organic essential oils can provide a pure energy source for raising vibration levels to the desirable state. No information was presented that explained how these frequency values were determined or how incorporation into the human body would maintain original frequencies.

At 70 mhz, this would suggest an on-off cycle every 14.29 seconds for a healthy person. I was unable to relate this to a biological cycle, although it is not too different from a slow breathing period that occurs during deep sleep periods, or perhaps with sleep apnea. A colleague of mine (who requested anonymity) suggested that she has observed this cycle in attention spans of some undergraduate students, but could offer no evidential proof. I concur with a statement on the web site that additional research would be desirable.

Conclusions

Natural products are not always safer than synthetic products. Just because a plant has been used for centuries does not mean it is safe or even desirable (Hinkle 1995). Plants contain many toxins, some of which we can use for pest control purposes. However, some of these toxins can cause significant human or animal health effects, and many deaths have been reported. A great many, if not most, of the compounds in plants used in pest control have not been scientifically evaluated for effectiveness and safety.

Nearly any product or substance can be misused. Even relatively benign plant compounds can be dangerous if mixed or prepared incorrectly. Because toxins in plants vary with geography, season, environment, and soil nutrients, one cannot assume that homemade remedies will be consistent in terms of concentrations or effects.

A statement is not always true if you read it in a magazine or on the Internet. Testimonials from satisfied customers are not proof the product will function as advertised. The numbers of entomological mistakes and misconceptions in the natural products literature on insect control are enormous. Given that these products make up only a very small part of the merchandise available in the multibillion dollar natural products industry, the misinformation content must be truly staggering.

Nonetheless, there were some places where the homeopathic and new age products have an advantage over more conventional pest control materials. Product naming is one such category. The names tended to be descriptive and colorful. Some of the best included a repellant for armadillos called "Armadillo Armageddon" (with castor oil as the active ingredient, Fig. 7), a citronella-based mosquito repellant named "Don't Bite Tonight," a rabbit repellant called "Hare Today - Gone Tomorrow" (active ingredient capsicum extract), a mole repellant made with castor oil called "Mole-otov Cocktail," and "Bug N-Out," a citronella oil treatment to repel flies for use on dogs. However, my personal favorite was a product designed to reduce the devastating late night forays of whitetail deer into vegetable and flower gardens. This product is sold as "Not Tonight Deer."

Acknowledgements

Thanks to B. A. Mullens, M. K. Rust, W. C. Carson, G. Kund, J. Oross, and D. Vickerman for providing comments on the manuscript. W. Carson and G. Kund helped provide the data in Table 1.

References Cited

Anderson I. B., W. H. Mullen, J. E. Meeker, S. C. Khojasteh-Bakht, S. Oishi, S. D. Nelson, and P. D. Blanc. 1996. Pennyroyal toxicity: measurement of toxic metabolite levels in two cases and review of the literature. Ann. Intern. Med. 124: 726-734.

Bakerink, J. A., S. M. Gospe, Jr., R. J. Dimand and M. W. Eldridge. 1996. Multiple organ failure after ingestion of pennyroyal oil from herbal tea in two infants. Pediatrics 8: 944-947.

Bassett, I. B., D. L.Pannowitz, and R. S. Barnetson. 1990. A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne. Med. J. Aust. 153: 455-458.

Beckman, S. E., R. W. Sommi, and J. Switzer. 2000. Consumer use of St. John's wort: a survey on effectiveness, safety, and tolerability. Pharmacotherapy 20: 568-574.

Bischoff, K., and F. Guale. 1998. Australian tea tree (*Melaleuca alternifolia*) oil poisoning in three purebred cats. J. Vet. Diag. Invest. 10: 208-210.

Bhushan, M., and M. H. Beck. 1997. Allergic contact dermatitis from tea tree oil in a wart paint. Contact Dermatitis 36: 117-118.

Braverman, Y., A. Chizov-Ginsberg, and B. A. Mullens. 1999. Mosquito repellant attracts *Culicoides imicola* (Diptera: Ceratopogonidae). J. Med. Entomol. 36: 113-115.

Budhiraja, S. S., M. E. Cullum, S. S. Sioutis, L. Evangelista, and S. T. Habanova. 1999. Biological activity of *Melaleuca alternifola* (tea tree) oil component, terpinen-4-ol, in human myelocytic cell line HL-60. J. Manip. Physiol. Ther. 22: 447-453.

Burkhard, P. R., K. Burkhardt, C. A. Haenggeli, and T. Landis. 1999. Plant-induced seizures: reappearance of an old problem. J. Neurol. 46: 667-670.

Butcher, P. A., J. C. Duran, and M. U. Slee. 1994. Intraspecific variation in leaf oils of *Melaleuca alternifolia* (Myrtaceae). Biochem. Syst. Ecol. 42: 419-430.

Chang, Y. C., A. T. Karlberg, and H. I. Maibach. 1997. Allergic contact dermatitis from oxidized d-limonene. Contact Dermatitis 37: 308-309.

Code of Federal Regulations. 1999. Title 21, vol. 3, parts 170 to 199, revised as of April 1,

1999. U.S. Government Printing Office via GPO Access. CITE: 21CFR170.30 (http://www.cfsan.fda.gov/~lrd/cfr17030.html.)

Devine, N. 2000. Dangerous combinations; understanding the risks of mixing herbal products and drugs. NurseWeek 13: 26.

Direct Chem. 2001. 607 d'Limonene bug killer (http://www.directchem.com/607dlimbugki.html.

D'Mello, J. P. (ed.). 1997. Handbook of plant and fungal toxicants. CRC, Boca Raton, FL.

(EPA) Environmental Protection Agency. 1993. Integrated Risk Information System, d-Limonene; CASRN 5989-27-5 (http://www.epa.gov/iris/subst/index.html).

Fournet, A., A. Rojas de Arias, B. Charles and J. Bruneton. 1996. Chemical constituents of essential oils of muna, Bolivian plants traditionally used as pesticides, and their insecticidal properties against Chagas' disease vectors. J. Ethnopharmacol. 52:145-149.

Gehlbach, S. H., W. A. Williams, and J. I., Freeman. 1979. Protective clothing as a means of reducing nicotine absorption in tobacco harvesters. Arch. Environ. Health 34: 111-114.

Genders, R. 1980. The complete book of herbs and herb growing. Sterling, New York.

Hansen, T. 2000. Only in Corning. CNN Sports Illustrated. Posted: Monday May 29, 2000 (http://207.25.71.142/inside_game/tom_hanson/news/2000/05/29/inside_lpga/).

Hausen, B.M., J. Reichling, and M. Harkenthal. 1999. Degradation products of monoterpenes are the sensitizing agents in tea tree oil. Am. J. Contact Dermatitis 10: 68-77

Healthwise International. 2001. Purge (http://www.artnet.net/~healthwise/nutritn.htm#Purge).

Hink, W. F., T. A. Liberati, and M. G. Collart. 1988. Toxicity of linalool to life stages of the cat flea, *Ctenocephalides felis* (Siphonoptera: Pulaicidae), and its efficacy in carpet and on animals. J. Med. Entomol. 25: 1-4.

Hinkle, N. C. 1995. Natural born killers. Pest Control Tech. July 54, 56, and 116.

Höld, K. M., N. S. Sirisoma, T. Ikeda, T. Narahashi, and J. E. Casida. 2000. Alpha-thujone (the active component of absinthe):gamma-aminobutyric acid type A receptor modulation and metabolic detoxification. Proc. Natl. Acad. Sci. U.S.A. 97: 3826-3831.

Hooser, S. B. 1986. Effects of an insecticidal dip containing d-Limonene in the cat. J. Am. Vet. Med. Assoc. 189: 905-908.

(ISO) International Standards Organization. 1996. Essential oils—oil of Melaleuca, terpen-4-ol type (tea tree oil). ISO 4730. Oxford University Press, Oxford.

Knight, T. E., and B. M. Hausen. 1994. Melaleuca oil (tea tree oil) dermatitis. J. Am. Acad. Dermatol. 30: 423-427.

Kurtzweil, P. 1998. An FDA guide to dietary supplements. FDA Consum. Publ. 99-2323.

Lane-Brown, M. M. 2000. Photosensitivity associated with herbal preparations of St. John's wort (*Hypericum perforatum*). Med. J. Aust. 172: 302.

Lemiere, C., A. Cartier, S. B. Lehrer, and J.L. Malo. 1996. Occupational asthma caused by aromatic herbs. Allergy 51: 647-649.

Lis-Balchin, M., and S. Hart. 1999. Studies on the mode of action of the essential oil of lavender (*Lavandula angustifolia* P. Miller). Phytother Res. 13: 540-542.

Medicinal herbFAQ. 1999. (http://www.ibiblio.org/herbmed/mediher4.html#c2_2_1).

Murtagh, G. J., and G. R. Smith. 1996. Month of harvest and yield components of tea tree. II—oil concentration, composition and yield. Aust. J. Agric. Res. 47: 817-827.

Nelson, S. D., R. H. McClanahan, D. Thomassen, W. P. Gordon, and N. Knebel. 1992. Investigations of mechanisms of reactive metabolite formation from (R)-(+)-pulegone. Xenobiotica 22: 1157-1164.

Nilsson, U., K. Magnusson, O. Karlberg, and A. T. Karlberg. 1999. Are contact allergens stable in patch test preparations? Investigation of the degradation of d-limonene hydroperoxides in petrolatum. Contact Dermatitis 40: 127-132.

Ntezurubanza, L., J. J. Scheffer, and A. Looman. 1985. Composition of the essential oil of *Ocimum canum* grown in Rwanda. Pharm. Week. Sci. 7: 273-276.

Opdyke, D. L. 1979. Monographs on fragrance raw materials. Pergamon, New York.

O'Reilly, S. 1996. Absinthe makes the tart grow fonder: a note on ''wormwood" in Christina Rossetti's 'Goblin Market.' Victorian Poetry 34: 108-114.

Powers, K. A., S. B. Hooser, J. P. Sundberg, and V. R. Beasley. 1988. An evaluation of the acute toxicity of an insecticidal spray containing linalool, d-Limonene, and piperonyl butoxide applied topically to domestic cats. Vet. Hum. Toxicol. 30: 206-210.

Re, L., S. Barocci, S. Sonnino, A. Mencarelli, C. Vivani, G. Paolucci, A. Scarpantonio, L. Rinaldi, and E. Mosca. 2000. Linalool modifies the nicotinic receptor-ion channel kinetics at the mouse neuromuscular junction. Pharmacol. Res. 42: 177-181.

Reese, K. M. 2000. Mechanism worked out for neurotoxicity of absinthe. Chem. Eng. News 8 (May): 104.

Rice, P. J. and J. R. Coats. 1994. Insecticidal properties of several monoterpenoids to the house fly (Diptera, muscidae), red flour beetle (Coleoptera, tenebrionidae), and southern corn rootworm (Coleoptera: Chrysomelidae). J. Econ. Entomol. 87:1172-1179.

Rubel, D. M., S. Freeman, and I. A. Southwell. 1998. Tea tree oil allergy: what is the offending agent? Report of three cases of tea tree oil allergy and review of the literature. Aust. J. Dermatol. 39: 244-247.

Ryan, M. R., and O. Byrne. 1988. Plant insect coevolution and inhibition of acetylcholinesterase. J. Chem. Ecol. 14: 1965-1975.

Sanchez-Ramos, I. I., and P. Castanera. 2000. Acaricidal activity of natural monoterpenes on *Tyrophagus putrescentiae* (Schrank), a mite of stored food. J. Stored Prod. Res. 37: 93-101.

Stuart, M. (ed.). 1979. The encyclopedia of herbs and herbalism. Grosset & Dunlap, New York.

Syed, T. A., Z. A. Qureshi, S. M. Ali, S. Ahmad, and S. A. Ahmad. 1999. Treatment of toenail onychomycosis with 2% butenafine and 5% *Melaleuca alternifolia* (tea tree) oil in cream. Trop. Med. Int. Health 4: 284-287.

Sudekum, M. R. H., N. Poppenga, N. Raju, and W. E. Braselton. 1992. Pennyroyal oil toxicosis in a dog. J. Am. Vet. Med. Assoc. 200: 817-818.

Thomassen, D., N. Knebel. J. T. Slattery, R. H. McClanahan, and S. D. Nelson. 1992. Reactive intermediates in the oxidation of menthofuran by cytochromes P-450. Chem. Res. Toxicol. 5: 123-30.

(USDA) U.S. Department of Agriculture. 2001. Center for Food Safety and Applied Nutrition "Dietary Supplements" (http://www.cfsan.fda.gov/~dms/ds-faq.html).

(USGAO) United States General Accounting Office. 2000. Food Saftey: improvements needed in overseeing the safety of dietary supplements and functional foods. Congr. Comm. Rep. GAO/RCED-00-156.

Veal, L. 1996. The potential effectiveness of essential oils as a treatment for headlice, *Pediculus humanus capitis*. Complement Ther. Nurse Midwif. 2: 97-10.

Villar, D., M. J. Knight, S. R. Hansen, and W. B. Buck. 1994. Toxicity of Melaleuca oil and related essential oils applied topically on dogs and cats. Vet. Hum. Toxicol. 36: 139-142.

Wakelin, S. H., J. P. McFadden, J. N. Leonard, and R. J. G. Rycroft. 1998. Allergic contact dermatitis from d-Limonene in a laboratory technician. Contact Dermatitis 38: 164-165.

Weaver, D. K., F. V. Dunkel, L. Ntezurubanza, L. L. Jackson, and D. T. Stock. 1991. The efficacy of linalool, a major component of freshly-milled *Ocimum canum* Sims (Lamiaceae), for protection against postharvest damage by certain stored product Coleoptera. J. Stored Prod. Res. 4: 213-220

Weisbord, S. D., J. B. Soule, and P. L. Kimmel. 1997. Brief report: poison on line—acute renal failure caused by oil of wormwood purchased through the Internet. N. Engl. J. Med. 337: 825-827.

Williams, J. W., C. D. Mulrow, E. Chiquette, P. H. Noel, C. Aguilar, and J. Cornell. 2000. A systematic review of newer pharmacotherapies for depression in adults: evidence report summary. Ann. Intern. Med. 132: 743-756.

Ziyyat, A., A. Legssyer, H. Mekhfi, A. Dassouli, M. Serhrouchni, and W. Benjelloun. 1997. Phytotherapy of hypertension and diabetes in oriental Morocco. J. Ethnopharmacol. 58: 45-54.

Zorin, S., F. Kuylenstierna, and H. Thulin. 1999. In vitro test of nicotine's permeability through human skin. Risk evaluation and safety aspects. Ann. Occup. Hyg. 43: 405-413.

John T. Trumble is a professor of entomlogy with the Department of Entomology at the University of California, Riverside.