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Essential Oil Poisoning

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INTRODUCTION

canelle noix de muscade armoise

A review of essential oils used in the natural product pharmacopoeia with detailed evaluations of nutmeg (myristicin, eugenol); eucalyptus (1, 8 cineole); mint (menthol); cinnamon (cinnamaldehyde); pennyroyal (pulegone, menthofuran); and absinthe or wormwood (thujones) is presented.

In a 1990 telephone survey of over 1500 US adults, 34% reported using at least one unconventional therapy within the previous year. Extrapolations of the data suggested that Americans make 425 million visits annually to providers of unconventional therapies (but only 388 million visits to primary care physicians), spending approximately $13.7 billion, of which $10.3 billion was out of pocket, on alternative remedies.[1] Herbal medicines are touted to the public as less toxic and more effective than conventional drugs for various ailments because they are 'natural' and are based on knowledge gained over thousands of years. While one can dispute the theory, toxicologists cannot afford to ignore the reality: herbal medicines, along with their toxicities, are a newly emerging growth industry in the US — elsewhere, their use has long been accepted.

Herbs used for medicinal purposes come in a variety of forms. Active parts of a plant may include leaves, flowers, stems, roots, seeds, and/or berries. They may be taken internally as pills or powders, dissolved into tinctures or syrups, or brewed in teas and decoctions. Salves, ointments, shampoos, or poultices may be applied to the skin, scalp, or mucous membranes. Many plants contain so-called essential oils that are distilled, packaged, and sold unregulated to the public for medicinal purposes. In this discussion, we will review the therapeutic use of essential oils, as well as the diagnosis and management of patients suffering ill effects from their medicinal or misuse, or from inadvertent exposures.

DEFINITIONS

Some definitions can help in the understanding of the toxicology of essential oils.

Essential Oil: Any of a class of volatile oils composed of a mixture of complex hydrocarbons (usually terpenes) and other chemicals extracted from a plant, usually by a method of distillation. Essential oils give the plant its characteristic aroma and will evaporate quickly off skin or another surface.

Essence: An essence is a concentrated fragrance, a perfume.

Fixed Oil: A fixed oil is a nonvolatile oil made of long-chain fatty acids (such as castor oil or safrole).

Carrier Oils: Essential oils used therapeutically in herbal remedies are too concentrated to be applied directly and must be diluted. Often only a few

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drops are put in carrier oil, such as safflower oil, in a therapeutic application.

THERAPEUTIC USES

Essential oils may be used by herbalists in a variety of ways. Topical applications, baths, inhalation, ingestion, or parenteral use have all been documented. Again some definitions are helpful in understanding what herbalists are intending through the prescription of essential oils to a patient.

Aromatherapy: The use of volatile oils in the treatment of certain health problems.
Carminative: An agent that aids in expelling gas from the gastrointestinal tract.
Rubefacient: An agent that reddens the skin and causes a localized feeling of warmth via cutaneous vasodilation.
Emmenagogue: An agent that influences menstruation and addresses problems related to menstrual flow.
Abortifacient: An agent that induces abortion.

Essential oils, like other herbal remedies, are used in a variety of ways therapeutically, as antimicrobials, antispasmodics, analgesics, sedatives, antidepressants, etc. Table 1 gives some examples of health conditions for which herbalists might include an essential oil as one aspect of management. This review is not intended to be prescriptive, and many of the purported therapeutic advantages of essential oils have not been proven scientifically. Their proponents cite an ancient, historical validity, which is unproven under the scrutiny of evidence-based medicine and yet to herbalists remains irrefutable. The 'doctrine of signatures' is cited by some. This ancient concept states simply that one can get a clue as to what an herb might be good for by what it looks like. For example, a cut whole nutmeg looks somewhat like the gyri of the brain. Thus the essential oil of nutmeg might be indicated for neurologic maladies. Or St. Johnswort has a red appearing sap; thus it must be good for blood abnormalities. Many essential oils do not have a single indication, but are used by herbalists to treat a bewildering array of seemingly disparate and unrelated diseases.

And yet some essential oils have scientifically demonstrable beneficial activity. In a randomized clinical trial, peppermint oil was found to have some benefit for adults suffering from irritable bowel syndrome.[2] Tea tree oil (TTO) is a popular medicament used for skin and wound care, for vaginal candidiasis, and for acne as a natural antiseptic. Derived from *Melaleuca alternifolia*, TTO has been shown by *in vitro* susceptibility testing to have significant bactericidal activity against *S. aureus* and many gram-negative bacteria. Several authors have found *in vitro* activity of TTO against *Streptococcus* species, which might make it useful in the treatment of impetigo.[3–5] Cytotoxicity of one of the components of TTO, terpinen-4-ol, which may solubilize bacterial cell membranes, can account for the observed germicidal actions of the essential oil.[6] The Chinese medical use of a wormwood (*Artemisia* spp) preparation, 'qinghaosu,' has been shown to approach the efficacy of chloroquine in the treatment of susceptible malaria.[7,8] The essential oils, *Artemisia nelagrica, Caesulia axillaris, Chenopodium ambrosioides, Cymbopogon citratus*, and *Mentha arvensis*

Table 1

Therapeutic Uses of Some Essential Oils

Essential Oil	Botanical Name	Purported Indications
Chamomile	*Chamaemelum nobile*	Eczema, asthma
Hyssop	*Hyssopus officinalis*	Nervous exhaustion, grief
Juniper	*Juniperus communis*	Arthritis, antibacteria, diuretic
Lavender	*Lavandula* spp	Many dysfunctions
Lemon Balm	*Melissa officinalis*	Sedative, antidepressant
Pennyroyal	*Hedeoma pulegioides*	Abortifacient
Peppermint	*Mentha* spp	Antispasmotic, carminative
Nutmeg	*Myristica fragrans*	Toothache, GI upset, halitosis
Rose	*Rosa* spp	Aphrodisiac, anxiety
Tea Tree	*Melaleuca alternifolia*	Antibacterial
Yarrow	*Achillea millefolium*	Antiinflammatory, antispasmodic

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have all been shown to have antifungal activity against *Trichophyton rubrum, Microsporum gypseum*, and 5 other fungal dermatophytes.[9] Such evidence may validate the topical use of these essential oil preparations for superficial fungal rashes.

GENERAL TOXICITY OF ESSENTIAL OILS

Table 2 presents some of the general toxic principles applying to herbs used commonly as essential oils or in other forms. Since these products are not under regulatory control of the FDA, they may be contaminated or adulterated with other chemicals and may not contain the specific herb that the buyer is seeking or may contain the herb at an unknown concentration. The nomenclature is confusing, so that 'black cohosh' for sale in different countries, or even different parts of the US, may contain one of several herbs, all of which share that description. In New England, cohosh comes from the baneberry plant (*Actaea* species), whereas in northern Appalachia, cohosh comes from *Cimicifuga racemosa* and in southern Appalachia, it refers to *Caulophyllum thalictroides*.

Table 2

General Toxicities of Essential Oils and Other Herbal Preparations

1. Product Management
   - Nomenclature: no international conventions, confusing synonyms
   - Quality control: no FDA regulation = buyer beware
2. Ingredients
   - Natural toxicants: no adverse effect safety testing
   - Complex mixtures of chemicals
   - Variable potencies: part of plant, maturity, time of year, year to year, geography, soil
   - Interactions with other herbs or medications
3. Circumstances
   - Excessive use
   - Inappropriate use
4. Host Characteristics
   - Sensitization/anaphylaxis
   - Placental transport/excretion into breast milk
5. Unknown Toxicities
   - Carcinogenesis
   - Mutagenesis
   - Embryotoxicity

The safety of essential oils for human consumption has not undergone the rigorous scientific testing typical of regulated drugs, especially in vulnerable populations such as children or pregnant women. These are complex mixtures of potent hydrocarbons; an essential oil may contain 40 or more different identifiable component chemicals, or may undergo phase 1 metabolism to even more potent toxicants. It is a challenge to determine which component chemicals in an essential oil may be beneficial and why, and which may be natural toxicants. Furthermore, the potency of an essential oil may vary with the conditions of harvesting of the herb. The concentration of the terpenes it contains may vary with the soil acidity and nutrients, season of the harvest, yearly climactic variations, geography of where it is grown, and other variables typically affecting the growing plant.

Many herbs are used together with other herbs. The adverse effects of cumulative or synergistic activities of different combinations of herbs and other herbs, or drugs and herbs, are poorly studied. Thus, the added potential for adverse effects of essential oil-herb or essential oil-drug interactions are often unknown.

There is always the potential for misuse of herbs in ways that were unintended. As with drugs, the potential for overdosing and/or abuse of herbs is present. For example, many patients will self-medicate with 15–20 different herbal preparations. Should they develop a hepatitis, it may be difficult to determine which is the offending agent. The 'spice cabinet syndrome' of abuse of nutmeg, cloves, cinnamon, or other essential oils by young adolescents has been documented.[10] Even a relatively nontoxic essential oil can produce severe toxicity when used in an unintended manner, such as the reported case of a 2-year-old who swallowed 10 mL tea tree oil and developed ataxia and confusion.[11]

Host characteristics may affect adverse reactions to the essential oils. An atopic individual, or one with a history of allergies and asthma, may be more sensitive to the chemicals found in the essential oil, and thus be more likely to develop a dermatitis or bronchospasm on contact with even a small therapeutic dose. Infants and young children, with immature liver enzymes, may be more sensitive to the effects of an hepatically metabolized essential oil because of their relative inability to detoxify it. Essential oils may well have some latent toxicities, such as teratogenesis or carcinogenesis not yet documented. For example, *plecanthus fruticosus*, an essential oil used in Romanian medicine to treat burns, was shown to be teratogenic in mice, causing predominantly anophthalmia.[12]

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TOXICITIES OF SPECIFIC ESSENTIAL OILS

Table 3 gives examples of specific toxic essential oils and the chemical constituents believed to be responsible for their toxic effects.

Nutmeg Poisoning

noix de cajou

The nutmeg is the seed kernel of the evergreen tree, *Myristica fragrans,* the outer shell of which is also the source of the spice, mace. Nutmeg was originally grown in the Malucca Islands of the South Pacific, but was successfully transplanted to Grenada, Trinidad, and other 'spice islands' of the Caribbean where it is grown commercially today.

Besides its common culinary use as a spice, fresh nutmeg oil is prescribed as a gastrointestinal (GI) stimulant, a carminative, for the treatment of rheumatism, for neurologic disorders, and as an emmenagogue. Introduced into Europe as early as the middle of the 12th century, abuse of the spice was recorded as early as the 1500s. It was well known among sailors, jail inmates, and most recently, adolescents as a cheap, readily available euphoriant. Unfortunately, the euphoria is short-lived and is accompanied by such an array of unpleasant side effects, that after the first experiment, repetitive abuse is unlikely.

The oil of the nutmeg spice contains a mix of aromatic allylbenzenes including the active principal, myristacin, as well as other complex hydrocarbons including alamecin, borneol, safrole, isoeugenol, geraniol, and eugenol. Myristicin has been characterized as causing both hallucinogenic as well as amphetamine-like symptoms. It can be metabolized endogenously to 5-methoxy-3,4-methylenedioxyamphetamine (MMDA), which may be the proximal mediator of some of its toxic effects. Alamecin may also be metabolized to a hallucinogenic agent. These compounds have been described as having LSD-like and monoamine oxidase inhibitor properties as well.

The fresh nutmeg contains much higher concentrations of the essential oil than the dried, powdered spice. An estimated 1–3 whole nutmegs can cause moderate toxicity when ingested, which translates to 5–15 g of the freshly ground spice.[13] A dose of 18 grams of freshly ground nutmeg has been associated with obtundation in a patient; such very large doses are said to be associated with liver failure and death.[14]

Usually, ingestion of 10–50 g of the fresh nutmeg produces clinical intoxication. Prominent nausea, vomiting, headache, and chest and abdominal pain are invariably an early part of the clinical picture and limit the abuse potential of the essential oil. Patients may experience a sense of impending doom, which precedes uncontrollable retching. Flushed skin, decreased salivation, tachycardia, and slightly elevated blood pressures, along with delirium, may remind the clinician of the anticholinergic syndrome. But these patients differ from those with an anticholinergic syndrome in that they present early on with pinpoint rather than dilated pupils and a depressed body temperature, rather than fever. Patients may develop other neurological symptoms besides hallucinations, including agitation, tremors, lethargy, confusion, delirium, or psychosis. The hallucinations are said to be visual and auditory, with distortions in color, time, and space. Symptoms may persist for up to 2–3 days.

Management of nutmeg poisoning includes oral decontamination with activated charcoal, supportive care including antiemetics, and, where necessary, sedation with a benzodiazepine medication. Reduction of visual and auditory environmental stimuli is also helpful in calming the agitated patient.

Table 3

Examples of Toxic Essential Oils and the Chemical Constituents Thought to Be Principally Responsible for Their Toxicity

Essential Oil	Toxic Chemical	Toxic Effect
Nutmeg	Myristacin, eugenol	Hallucinations
Eucalyptus	1,8 Cineole	Seizures
Mentha sp	Menthol, menthone	Ataxia, myalgia
Cinnamon	Cinnamaldehyde	Dermatitis
Pennyroyal	Pulegone	Hepatic necrosis
Wormwood	α or β Thujone	Seizures, dementia

Eucalyptus Poisoning

Eucalyptus oil has been recommended for the treatment of upper respiratory and other viral infections, and is also used in a liniment for muscle aches and strains. The active ingredient in the essential oil is eucalyptol, made of 1,8 cineole plus tannins in up to a 70% concentration. Eucalyptol is capable of hepatic microsomal induction, and thus may affect the metabolism of other drugs and chemicals. It is rapidly absorbed and has primary neurotoxicity.

While 80% of 42 children with eucalyptus poisoning remained asymptomatic in one study,[15] two other case series have documented symptoms in 65%[16] and 59%[17]

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of victims. Diagnosis is evident after accidental ingestion of eucalyptus oil because of its pungent odor on the breath. Small amounts may cause a rapid onset of nasal and epigastric burning, vomiting and GI distress, miosis, weakness, headache, ataxia, or even coma.[16,18] Hyperpnea, dyspnea, and pneumonia are also associated with aspiration of the volatile oil. Cyanosis and seizures are sometimes seen, especially in infantile poisoning, and have been associated with death.[16] As little as 0.6–5.0 mL of 100% eucalyptus oil causes severe illness in children;[17] and seizures and death were reported in an 8-month-old after ingestion of 30 mL of the oil.[16] In adults, symptoms may occur with an ingestion of as little as 1–2 teaspoons of eucalyptus.

While some victims of eucalyptus poisoning may require only close observation, in known large ingestions or when a poisoned patient presents with clinical symptoms, the clinician is still advised to contemplate decontamination with activated charcoal by most authors.[15–17] Respiratory support, antiemetics, and vasopressors are indicated in the management of some patients. Symptoms may be delayed by several hours, so that the suspected victim deserves a longer period of monitoring than usual.

Mentha Poisoning (*Mentha pulegium*; Peppermint)

Peppermint is not only an herbal remedy for abdominal pain and other discomforts, but is a ubiquitous flavoring in everything from gum to toothpaste. There are a wide variety of Mentha species, all of which contain various amounts of the chemicals menthol and menthone. In 2 separate analyses, more than 30 other chemicals were identified from different mint species, including pinene, limonene, diosphenol, eugenol, menthofuran, menthyl acetate, and many others.[19,20]

The actions of peppermint oil on the gut are complex. Some have found that it relaxes smooth muscle and invoke its effects on calcium channel receptors or the cholinergic nervous system, whereas others have found that it stimulates intestinal smooth muscle and can cause cramps and the urge to defecate and micturate.[21]

The clinical toxicity of peppermint includes a dermatitis associated with a sensitivity to menthol. Chronic urticaria, 'hot flashes,' and GI irritation are common in susceptible individuals. Diagnosis is possible by challenging the allergic individual with mint; besides eliciting symptoms, a characteristic basopenia is observed in the blood count after provocative testing. Since a wide variety of everyday foods and household products contains mint flavoring, strict surveillance to avoid offending foodstuffs is difficult.[22]

Essential oils from 2 different *mentha* species produced central nervous system depression and hypothermia when fed to rats.[20] Acute mentha reactions in humans can also include neurologic changes such as tremor, ataxia, drowsiness, or even coma. Myalgias and bradycardia are seen in some cases. In one instance, menthol drops were mistakenly instilled into the nose of a 2-month-old infant who subsequently developed dyspnea, unconsciousness, hyperextension of the extremities, and a metabolic acidosis.[18] Peppermint oil is also an irritant to the eyes and skin. It can cause GI symptoms, cramps, and diarrhea.

Management of mentha poisoning usually consists of supportive care and activated charcoal for recent ingestions.

Cinnamon Poisoning

canelle

Cinnamon is harvested from the bark of the *Cinnamon cassia nees ex blume* plant, a member of the *Lauraceae* family. Besides its use as a spice, cinnamon essential oil is promoted for a variety of medical conditions related to its properties as a stimulant, astringent, and carminative agent. However, fresh cinnamon oil contains appreciable amounts of cinnamic aldehyde (up to 80% of the oil), which can have sensitizing properties. Patients who develop cinnamon sensitivity usually develop an allergic dermatitis or urticarial lesions upon reexposure.

Cinnamon-dipped toothpicks are sucked on as a recreational activity.[23] However this practice may produce white mucosal lesions in the mouth that are quite similar to leukoplakia seen associated with squamous cell carcinoma. Additionally, oral cheilitis, welts, erythema, ulcers, and vesicles may be observed. The patient will complain of burning pain from such lesions. The condition, known as stomatitis venenata and mucositis, can develop into orofacial granulomatosis and must be differentiated from lupus, lichen planus, oral candidiasis, lichenoid mucositis, cheek biting, and malignant conditions.[24,25] A history of chronic cinnamon exposure reveals the correct etiology of the lesions, and abstinence from cinnamon results in their resolution. IgE testing and RAST tests are unhelpful to the diagnosis. A skin biopsy reveals characteristic perivascular infiltrates.

Other signs of acute cinnamon toxicity include facial flushing, shortness of breath, tachycardia, dizziness, and abdominal pain. Symptoms usually subside with abstinence from the use of the essential oil and only supportive care is necessary.

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Pennyroyal (Squaw Mint) Oil Poisoning

Pennyroyal oil is distilled from *Hedeoma pulegiodes* or *Mentha pulegium* and may be prescribed for a variety of medical conditions, including toothache, as a flea repellent, for chronic bronchitis, as an antiinflammatory agent, or for genitourinary complaints. Use of pennyroyal oil as an emmenagogue or as an abortifacient is becoming more common among young women. Four recently reported cases of pennyroyal oil poisoning included one woman who died from seizures, anoxic encephalopathy, cardiovascular collapse, and diffuse liver necrosis after ingesting for 2 weeks large amounts of pennyroyal extract, pennyroyal oil, and black cohosh in an attempt to induce an abortion.[26] *Yerba buena*, an herbal tea made from mint leaves, is popular in Hispanic and other cultures as an indigenous cure for infantile abdominal pain and colic. However, when pennyroyal oil–containing mint is used, life-threatening poisoning among treated infants has been reported.[27]

The active chemical in pennyroyal is pulegone, an aromatic ketone that undergoes bioactivation to menthofuran, a cyclohexanone. Both of these compounds, as well as other reactive intermediates derived from the metabolism of pulegone, can bind to subcellular proteins and cause cellular damage.[28,29] Pulegone and menthofuran also deplete cellular glutathione levels and make hepatocytes vulnerable to attack by oxidizing radicals.[30]

Gastrointestinal symptoms are noted at doses of pennyroyal oil as low as 10 mL, with cases of centilobular hepatitis following ingestion of 30 mL or more. Clinical symptoms and signs of poisoning are apparent soon after ingestion and may include nausea, vomiting, dizziness, abdominal pain, GI bleeding, hematuria, and a burning throat. Chemical hepatitis is usually detectable within 24 hours of ingestion. Later the patient will manifest liver dysfunction with secondary complications including coagulopathy, renal failure, seizures, and death.[31]

The active metabolite, menthofuran, can be detected by gas chromatography in urine, blood, and other tissues. Management of the affected patient includes oral decontamination by lavage if performed soon after ingestion and administration of activated charcoal, although charcoal's efficacy as an adsorbent in this circumstance is unproved. The similarity of the pathogenesis of pennyroyal-induced centrilobular hepatic necrosis to that produced by acetaminophen suggests a prominent role for *N*-acetylcysteine (NAC) as an antidote. Indeed, NAC was given to a child who had ingested life-threatening amounts of pennyroyal oil and the patient did not subsequently develop hepatitis.[26]

Absinthe (Wormwood, Mugwort) Poisoning

Wormwood grows as an ornamental bush with pale green leaves and bright yellow flowers. The essential oil of some species of *Artemisia* has been used for its antimalarial properties and also is an ingredient in the banned liqueur, absinthe. It has been speculated that Vincent Van Gogh, as well as other painters and literati towards the *fin de siecle* in France and other countries, suffered seizures, distorted perceptions, behavioral abnormalities, and other nervous system effects due to chronic absinthe-drinking.

Wormwood oil's toxicity relates to the active principal, thujone, a terpene with a biochemical and pharmacologic relationship to tetrahydrocannabinol. The acute toxicity of wormwood poisoning includes vomiting, restlessness, delirium, paranoia, and seizures. Chronic wormwood exposure can cause gastritis, deteriorating mentation, seizures, pica, visual effects, tremors, and coma. While wormwood-containing absinthe has been banned for more than 80 years, the herb and essential oil are still touted by herbalists as a cure for parasites and abdominal discomforts and are available as proprietary products.

CONCLUSIONS

Essential oils are potent aromatic hydrocarbons, usually containing complex mixtures of terpenes and other chemicals that are used alone or in combination with other herbal preparations in the treatment of many diseases and health conditions. Although their efficacy is largely unknown, some have been shown to have antimicrobial or other beneficial actions. Essential oils are no different than other herbal preparations in their inherent toxicities, related to product variation, adulteration, or contaminants, adverse reactions, overdose or misuse, and the possibility of as yet undetected toxicities, such as mutagenesis or carcinogenesis. Some essential oils, such as pennyroyal oil or wormwood, contain specific toxicants such that their risk far outweighs their potential for benefit. All need better scientific testing, in a variety of *in vitro*, animal, and human models, in order to ascertain, using evidence-based decision-making, their usefulness in medicine.

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