SUMMARY OF DATA FOR CHEMICAL SELECTION

Cedarwood Oil
8000-27-9

BASIS OF NOMINATION TO THE CSWG

Cedarwood oil is brought to the attention of the Chemical Selection Working Group (CSWG) as the active component of widely used insect repellants.

Three distinct cedarwood oil products, Virginia cedarwood oil, Texas cedarwood oil, and Western red cedar (*Thuja plicata*) oil, can be identified. The common major ingredients in the Virginia and Texas oils are cedrol, ∀-cedrene, and thujopsene, but the relative percentages vary depending on the origin of the cedar trees used to produce the oil. Western cedarwood oil contains methyl thujate and thujic acid.

Virginia cedarwood oil is widely used as a fragrance in soaps, air fresheners, household detergents, and cosmetics. The National Institute for Occupational Safety and Health (NIOSH) estimated that nearly 118 thousand workers are potentially exposed to Virginia cedarwood oil based on data collected in the 1980s. It is also the active ingredient in cedar balls/wood blocks used as moth repellants and in bug blocks. Because of concerns about the toxicity of naphthalene ("moth balls") and high concentrations of Deet (active ingedient in many bug blocks), the market for cedarwood oil products is expected to grow.

Although cedarwood oil has been described as a powerful abortifacient, very little data on the toxicity of any of the three cedarwood oils was found in a review of the available literature. Cedar shavings used as bedding have been reported to stimulate drug-metabolizing enzymes in rodents and affect the mortality of rat pups.

SELECTION STATUS

ACTION BY CSWG: June 20, 2002

Studies requested:

- Subchronic study (90 day) of Virginia cedarwood oil

Priority: Moderate

Rationale/Remarks:

- Widespread exposure to Virginia cedarwood oil even though production volumes are greater for Texas cedarwood oil, which has greater usage as a chemical intermediate.

- Potential substitute for naphthalene moth balls

- Lack of basic toxicology data on this product

- Reregistration eligibility has already been determined by EPA; additional toxicological data will not become available through this avenue.

INPUT FROM GOVERNMENT AGENCIES/INDUSTRY

Dr. Esther Rinde from the US Environmental Protection Agency (EPA) provided information on the status of testing required by the Reregistration Eligibility Decision (RED) for cedarwood oil.

CHEMICAL IDENTIFICATION

Cedarwood oils are extracted from several members of the family Cupressaceae, which includes true cedars, junipers, and cypresses. In the US, cedarwood oil is harvested mainly from *Juniperus virginiana* (Eastern red cedar or Virginia cedar), *Juniperus ashei* or *mexicana* (Texas cedar), and *Thuja plicata* (Western red cedar). According to the Food and Agriculture Organization of the United Nations (FAO), Western red cedar is the least used of the three (FAO, 1995a & 1995b).

Cedarwood oil, Virginia

CAS Registry Number: 8000-27-9

Chemical Abstracts Service Name: Cedarwood oil, Virginiana (Allured FFM, 1999; ChemID, 2002). CAS registry number also applied to Chinese cedarwood oil (*Cupressus funebris*), Kenyan or East African cedarwood oil (*Juniperus procea*), and Moroccan or Atlas cedarwood oil (*Cedrus atlantica*) (ChemID, 2002; FAO, 1995a)

Synonyms and Trade Names: Cedar oil; cedarwood oil; red cedarwood oil; EPA Pesticide Chemical Code 040505 (ChemID, 2002)

Chemical and Physical Properties:

Description: Light yellow to pale brown viscous liquid; sometimes solidifies at room temperature; cedar odor (Gerhartz, 1988)

Density: d^{25} 0.939-0.958 (Gerhartz, 1988)

Solubility: Soluble in ethanol (Gerhartz, 1988)

Texas Cedarwood oil

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

CAS Registry Number: 68990-83-0

Chemical Abstracts Service Name: Texas cedarwood oil (Allured FFM, 1999; ChemID, 2002)

Synonyms and Trade Names: Texan cedarwood oil (ChemID, 2002)

Chemical and Physical Properties:

Description: Brown to reddish-brown, viscous liquid; may partially solidify at room temperature; cedar odor(Gerhartz, 1988)

Density: d^{20} 0.954-0.967 (Gerhartz, 1988)

Solubility: Soluble in ethanol (Gerhartz, 1988)

Western red cedar oil

CAS Registry Number: 68917-35-1

Chemical Abstracts Service Name: *Thuja plicata* oil (STNEasy, 2002)

Synonyms and Trade Names: Western red cedarwood oil (Laurel Laboratories, Inc., 2002)

Cedarwood oil components: The composition of cedarwood oils varies depending on the source. Cedrol and thujopsene are the major components of Texas and Virginia oils; Virginia oils also contain significant quantities of ∀-cedrene (Mookherjee & Wilson, 1996). The volatile oil from Western juniper has been reported to contain 15-40% cedrol (Kurth & Ross, 1954). Methyl thujate and thujic acid are the primary ingredients found in Western red cedarwood oil (Laurel Laboratories, Inc., 2002). The principal constituents of cedarwood oils are shown in Table 1.

Table 2 summarizes the chemical and physical properties of the major components of Virginia and Texas cedarwood oils.

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

Table 1. Chemical Composition of Cedarwood Oils

Component	CAS No.	Texas Oil (%)	Virginia Oil (%)	Western Red Cedarwood Oil (%)
Thujopsene	470-40-6	60.4	27.6	-
Cedrol	77-53-2	19.0	15.8	-
∀-Cedrene	469-61-4	1.8	27.2	-
∃-Cedrene	546-58-1	1.6	7.7	-
∀-Copaene	3856-25-5	2.8	6.3	-
Widdrol	6892-80-4	1.1	1.0	-
Methyl thujate		-	-	65
Thujic acid		-	-	25
∃-Thujaplicin	499-44-5	-	-	1
∀-Thujaplicin		-	-	1

Source: Lawrence, 1993; Laurel Laboratories, Inc., 2002; Mookherjee & Wilson, 1996

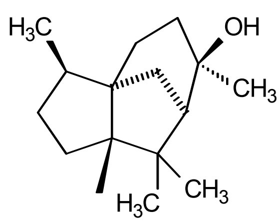
Technical Products and Impurities: The composition of cedarwood oils is complex and varies depending on the species of trees used in the extraction process. The International Organization for Standardization (ISO) and the Fragrance Manufacturers Association (FMA) provides standards for Texas and Virginia cedarwood oils. The ISO standard specifies an alcohol content (expressed as cedrol) of 35-48% with a minimum cedrol content of 20% for Texas cedarwood oil. For Virginia oil, a maximum cedrol content of 14% is specified. Compositional data for American oils, as specified by the FMA standards are somewhat different. The FMA standard specifies the alcohol content

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

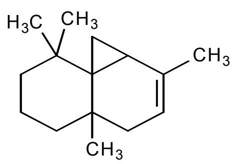
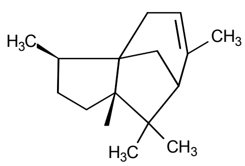
(cedrol and related isomers) for Texas oils as 25-42% and for Virginia oils as 18-38% (FAO, 1995a).

Chinese and *Cedrus atlanticus* cedarwood oil imports are also commercially available (AromaWeb, 2001; Schreiber, 1996). Chinese cedarwood oil from *Cupressus funebris*, which is widely used in the US, has a composition very similar to Texas cedarwood oil (Gerhartz, 1988; Schreiber, 1996). The FMA requires an 8% minimum alcohol content for Chinese cedarwood oil (FAO, 1995a).

Table 2. Chemical and Physical Properties of Major Components of Virginia and Texas Cedarwood Oils

Component	Synonyms	Chemical and Physical Properties/Percentage in oil
Cedrol [CAS No. 77-53-2]  Mol. Wt.: 222.37 $C_{15}H_{26}O$	(+)-Cedrol (ChemID, 2002)	Crystalline solid, needles from dil. methanol (Merck, 2001; Sigma-Aldrich, 2002a) Melting Point: 86-87 EC (Merck, 2001)

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

Thujopsene [CAS No. 470-40-6]  Mol. Wt.: 204.35 $C_{15}H_{24}$	(-)-Thujopsene, widdrene (ChemID, 2002)	Colorless, clear liquid (Merck, 2001; Sigma-Aldrich, 2002a) <u>Boiling Point</u>: 120EC (Merck, 2001); 258-260 EC (Sigma-Aldrich, 2002a) <u>Flash Point</u>: 104EC (Sigma-Aldrich, 2002a) <u>Solubility</u>: Insoluble in water, soluble in common organic solvents (Sigma-Aldrich, 2002a)
∀-Cedrene [CAS No. 469-61-4]  Mol. Wt.: 204.36 $C_{15}H_{24}$	Cedr-8-ene, (ChemID, 2002)	Colorless, clear liquid (Sigma-Aldrich, 2002a) <u>Boiling Point</u>: 261-262EC (Sigma-Aldrich, 2002a) <u>Flash Point</u>: 104EC (Sigma-Aldrich, 2002a) <u>Solubility</u>: Insoluble in water, soluble in benzene (Sigma-Aldrich, 2002a)

Virginia cedarwood oil [CAS No. 8000-27-9], Texas cedarwood oil [CAS No. 68990-83-0], (+)-cedrol (∃99.0 %) [CAS No. 77-53-2], (-)-thujopsene (∃97.0 %) [CAS No. 470-40-6], (-)-∀-cedrene (∃99.0 %) [CAS No. 469-61-4], (+)- ∃-cedrene (~97 %) [CAS No. 546-28-1], (-)-∀-copaene (~95 %) [CAS No. 3856-25-5], and ∃-thujaplicin (99%) [CAS No. 499-44-5] are available from Sigma-Aldrich (Sigma-Aldrich, 2002b).

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

EXPOSURE INFORMATION

Production and Producers:

Manufacturing Process: Virginia cedarwood oil is produced by steam distillation of sawdust, finely chipped waste wood from the manufacture of cedarwood products, or from stumps and logs of *Juniperus virginiana*. Texas cedarwood oil is obtained by steam distillation of chopped wood from *Juniperus ashei* or *Juniperus mexicana*. Although the most popular method for precessing cedarwood for oil production is steam distillation, some cedarwood oils are also produced through solvent extraction (Australian National University, 1999; Gerhartz, 1988; Schreiber, 1996).

Producers and Importers: Thirteen US producers or distributors of cedarwood oil are listed by Chemical Sources International (2002).

According to recent issues of chemical directories, cedarwood oil is manufactured and/or distributed by Berje Inc.; Brutanicals, Inc.; The Lebermuth Co., Inc.; Penta Manufacturing Co.; Polarome International, Inc.; Ruger Chemical Co., Inc.; and Spectrum Chemical MFG Corp. (Hunter, 2001; Tilton, 2001).

Production/Import/Export Level: Virginia and Texas cedarwood oils, *Thuja plicata* oil, cedrol, ∀-cedrene, and thujopsene are listed in the EPA Toxic Substances Control Act (TSCA) Inventory (ChemID, 2002).

The Port Import/Export Reporting Service (PIERS) reported cedarwood oil imports with a cargo weight of 23,302 pounds over the 11 month period from April 3, 2001 to February 20, 2002. For the 18-month period between September 12, 2000 and March 16, 2002, PIERS reported cedarwood oil exports with a cargo weight of 96,012 pounds (Dialog Information Services, 2002a, 2002b).

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

Use Pattern: The US production of cedarwood oil in 1984 was reported to be 1,400 tons for the Texas oil and 240 tons for the Virginia oil (FAO, 1995b). The production of cedarwood oil is expected to rise because of government incentive programs for the use of red cedar trees (Adams, 1987; Oklahoma State University, 2001).

Although Texas cedarwood oil is produced in larger quantities than cedarwood oil from the Eastern cedar *(Juniperus virginiana)*, it is used almost exclusively as feedstock for the manufacture of chemical derivatives, such as cedrol, cedryl methyl ether, acetyl cedrene, and cedryl acetate. Imports of Chinese cedarwood oil are also used to produce these derivatives. In contrast, Virginia cedarwood oil is widely used in the fragrance industry, among others (FAO, 1995b; Gerhartz, 1988; Schreiber, 1996).

Virginia cedarwood oils have many commercial uses. They are used to restore the smell of cedar to furniture and in cosmetic formulations, including shampoos for humans and animals, aftershave lotions, soap bars, and perfumes. They are also found in insect repellents, massage oils, incense oils, and shavings used as bedding for small animals. *Thuja plicata* or *Cedrus atlantica* cedarwood oils may also be used in some of these products (Absorbine Jr., 2002; Adams, 1987; Australian National University, 1999; Aroma-essence.com, 2002; Cedarcide, 2002; Country Cottage Works, 2002; Drugstore.com, 2002; FAO, 1995b; Frontier Natural Products Co-op, 2002; Lady Lorelei, 2002; POCO, LLC, 2002; Resource Management Group, 2002; Sawyer, 2002; Skeeter Defeater, 2002).

Cedarwood oil alcohols and terpenes are food additives considered by the US Food and Drug Administration (FDA) to be Generally Recognized as Safe (GRAS). These food additives are used as flavor enhancers, flavoring agents, or adjuvants. Food use of cedarwood oil terpenes was estimated to be 166,666 lb in 1987 (EPA, 1993; FDA, 2002; Clydesdale, 1997).

Cedarwood oil and thickened cedarwood oil have laboratory uses as immersion oils for light microscopy and for clearing microscope sections (Baker's Chemicals, 2002; PolySciences, Inc., 2001; Sigma-Aldrich, 2002b).

Cedarwood oil, in combination with other products, is used as a homeopathic remedy and is sold as a vaporizing ointment for topical use (Health Canada, 2002).

A total of 349 patents using cedarwood oil were on file with the US Patent and Trademark Office (USPTO) as of May 2002 (US Patents and Trademark Office, 2002).

Human Exposure:

Occupational Exposure: The National Occupational Exposure Survey (NOES), which was conducted by the National Institute for Occupational Safety and Health (NIOSH) between 1981 and 1983, estimated that 117,858 workers in 7,990 facilities representing 67 industries were potentially exposed to Virginia cedarwood oil in the workplace. The NOES database does not contain information on the frequency, level, or duration of exposure to workers of any chemical listed therein (Sigma-Aldrich, 2002a).

Cedarwood oil exposure may also occur in laboratories as a result of its use as immersion oil (PolySciences, 2001).

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

Environmental Exposure: ∀-Cedrene, a constituent of cedarwood oil, has been found in chemical wastes in the water of the Great Lakes. The sources of ∀-cedrene may derive from natural plant products or pulp mills (Passino-Reader *et al*., 1997).

Consumer Exposure: The largest number of human exposures to cedarwood oil occurs among consumers using insecticide products, deodorants, soaps, air fresheners, floor polishes, and sanitation supplies containing cedarwood oil. Consumers are potentially exposed to cedarwood oil through inhalation and dermal contact.

Although registration as a pesticide is no longer required by EPA for cedarwood oil, several formulations have been registered as pesticides in the past. These formulations include: ready-to-use liquids containing 0.48% cedarwood oil, wood blocks containing 2-8% cedarwood oil, and pet collars with 0.5% cedarwood oil (EPA, 1993). Two pesticides, Bug Block sunscreen and insect repellent, containing 0.46% Texas cedarwood oil, and Nexa cedarwood oil moth protection, containing 40% Virginia cedarwood oil, are registered with the state of California as pesticides (California EPA, 2001).

Two typical products for human topical use, Cedarcide (2002) and Skeeter Defeater (2002) contain 1 and 5% cedarwood oil, respectively.

<u>Environmental Occurrence</u>: Cedarwood oil contains natural products found in cedar, juniper, and cypress woods and steam distillation derivatives of such products.

<u>Regulatory Status</u>: No standards or guidelines have been set by NIOSH or the Occupational Safety and Health Administration (OSHA) for occupational exposure to or workplace allowable levels of cedarwood oil. Cedarwood oil is not listed on the American

Conference of Governmental Industrial Hygienists (ACGIH) list of compounds for which recommendations for a Threshold Limit Value (TLV) or Biological Exposure Index (BEI) are made.

Cedarwood oil was initially registered in 1960 as a pesticide to repel moths from clothing. As such, cedarwood oil was subject to the requirements for reregistration eligibility promulgated in 1988. EPA issued its Reregistration Eligibility Decision (RED) document for cedarwood oil in 1993. The RED profiles the use of cedarwood oil as a natural repellant/feeding depressant and fungicide used in houses and on pets or their bedding to repel fleas, moths, and mildew. Based on information collected as the result of the RED, EPA deregulated cedarwood oil in 1996 and no longer requires manufacturers of cedarwood oil products to register them as pesticides (EPA, 1993; Rinde, 2002).

Cedarwood oil is not listed as a hazardous substance, priority pollutant, or toxic pollutant under the Clean Water Act.

EVIDENCE FOR POSSIBLE CARCINOGENIC ACTIVITY

Human Data: No epidemiological studies or case reports investigating the association of exposure to cedarwood oil and cancer risks in humans were identified in the available literature.

Reports describing cedarwood oils as irritants or sensitizers appear to be rare (Botanical Dermatology Database, 2001). Cedarwood oil (no origin specified) produced no response in humans after 48 h when administered as a patch test at a concentration of 8% in petrolatum (HSDB, 2002). The Danish Environmental Protection Agency (2002) classified cedarwood oil used in household and cosmetic detergents as a rare sensitizer fragrance based on the results of patch tests on patients with cosmetic dermatitis and controls.

Historically, nineteenth century medical compendiums contain several reports of abortion and death in humans after oral consumption of relatively large amounts of cedarwood oil (Allen, 1877; HSDB, 2002).

Animal Data: No 2-year carcinogenicity studies of cedarwood oil or its components in animals were identified in the available literature.

The LD_{50} values for Virginia cedarwood oil and cedrol are given in Table 3.

Table 3. Acute Toxicity Values for Cedarwood Oil and Cedrol

Compound	Species	Route of administration	LD_{50} (g/kg)
Virginia cedarwood oil	rat	oral	>5
Virginia cedarwood oil	rabbit	dermal	>5
Cedrol	rabbit	dermal	>5

Source: Sigma-Aldrich (2002a)

Several limited studies reported a possible correlation between the use of cedarwood bedding and an increased incidence of spontaneous cancer in animals:

$ American-born C3H-A^{vy} and C3H-A^{vy}fB mice raised in the US have nearly a 100% incidence of liver and mammary tumors. These strains, bred and reared in Australia on sawdust bedding from Douglas fir, had almost no spontaneous incidence of mammary and liver tumors, particularly after the first generation. In contrast, virtually all C3H-A^{vy} mice reared in Australia but kept on US bedding (cedar) and fed US diets developed mammary tumors. The authors expressed their opinion that the cedar appeared to be the "carcinogenic" agent, noting that the results involved a limited number of animals (Sabine *et al.*, 1973).

$ Sabine (1975) conducted follow-up studies to further examine the role of cedar bedding vs other parameters on the spontaneous incidence of tumors in the susceptible strains of mice. Sabine concluded that:

> Based on data accumulated over 5 years, the incidences of mammary tumors and hepatomas in three strains of mice (C3H-A^{vy}, C3H-A^{vy}fB, and CBA/J) housed on Douglas fir sawdust bedding were significantly lower than the reported figures from US laboratories.
>
> Following submission of his paper, Sabine became aware of a publication by Dr. Heston, of the US National Cancer Institute (NCI). Heston had provided the Australian investigators with their initial colony of C3H-A^{vy} and C3H-A^{vy}fB mice. When Heston bedded two groups of mice on either ¾ pine sawdust and ¼ cedar shavings or pine sawdust, both groups developed very high incidences of spontaneous mammary tumors and hepatomas. Heston attributed the lower incidences of spontaneous tumors seen in the Australian study to higher ectoparasite infestations and slightly lower growth rates (Heston, 1975).

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

Burkhart and Robinson (1978) described a high rate of rat pup deaths, which the authors felt was probably caused by Eastern cedarwood bedding, either through ingestion of inhalation of toxic compounds in the bedding or through the milk of the dams.

Vlahakis (1977) reported that the first generation of C3H-A^{vy}fB crossbred mice had the same high incidences of mammary and liver tumors whether they were raised using pine bedding or a mixture of pine plus red cedar shavings.

Short-Term Tests: No *in vitro* or *in vivo* studies evaluating cedarwood oil or its components for mutagenic activity were found in the available literature.

Other Biological Effects:

Hexobarbital Sleeping Time: Housing the animals using cedarwood bedding resulted in a highly significant reduction of hexobarbital sleeping time in C3H-A^{vy}, CBA/J, and Swiss Albino mice, indicating induction of the enzymes responsible for hexobarbital oxidation. Using the same methodology, the authors demonstrated enzyme induction in CBA/J mice from Virginia cedarwood oil (Sabine, 1975).

The increase in the duration of hexobarbital hypnosis following exposure of Swiss-Webster mice to cedar shavings was previously reported by Wade and coworkers at the University of Georgia. These investigators then exposed mice to various fractions of cedarwood for up to 10 days and measured the duration of hexobarbital anesthesia, which suggested that cedrol and cedrene were the causative agents (Wade et al., 1968).

Insecticidal Properties: Cedarwood shavings from *Juniperus virginiana* arrested the life cycle at the 1st instar stage of the Peanut Trash Bug (*Elasmolomus sordidus*). It also

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

caused the death of colonies of Indian Moths (*Plodia interpunctella*) and Forage Mites (*Tyrophagus putrescentiae*). Virginia cedarwood oil (3%), cedrene (2%), and cedrol (2%) were all highly toxic to Peanut Trash Bug colonies. Cedarwood oil and cedrene also affected the reproductive behavior of adults or hatchability of eggs. Colonies of German cockroaches (*Blatella germanica*) were not affected by cedarwood from *Juniperus virginiana* (Sabine, 1975).

Components of cedarwood oils:

$ Cedrene prevented the butylated hydroxytoluene (BHT)-induced inhibition of lung tumors caused by intraperitoneal injection of urethan in strain A mice (Malkinson & Beer, 1984).

$ The effect of cedrene on *in vitro* hepatic metabolism was studied in Sprague-Dawley rats. Administration of cedrene using the oral, intraperitoneal and inhalation routes, increased the ethylmorphine *N*-demethylase activity and cytochrome P-450 content, while it had no effects on aniline hydroxylase activity (Hashimoto *et al*., 1972).

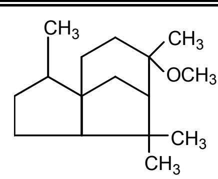
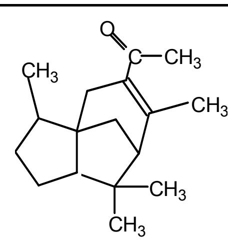
$ ∃-Thujaplicin, a compound found in the heartwood of the western red cedar (*Thuja plicata*), was teratogenic when administered to ICR mice at very high doses. *In vitro*, ∃-thujaplicin induced growth retardation and malformation of cultured embryos harvested at 9 days of gestation. *In vivo*, 420-1,000 mg/kg of ∃-thujaplicin, given orally to pregnant ICR mice on day 9 of gestation, induced cleft palates and lips, facial dysmorphism, and other malformations at doses of 560 mg/kg or above in 18-d old fetuses. The oral LD_{50} for ∃-thujaplicin was 750-800 mg/kg (Ogata *et al.*, 1999).

- Ecotoxicological studies on ∀-cedrene showed that the EC_{50} was 0.044 mg/L at 48 h for *Daphnia pulex* (Passino-Reader *et al*., 1997).

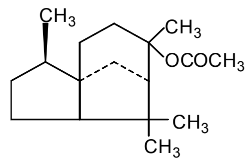
Structure Activity Relationships:

Three derivatives of the major chemical constituents of cedarwood oil were selected for review. These chemicals were cedrol methyl ether [CAS No.67874-81-1], acetyl cedrene [CAS No.80449-58-7], and cedryl acetate [CAS No. 77-54-3]. No information on the carcinogenicity or genotoxicity of these compounds in a search of the National Library of Medicine TOXNET databases, including TOXLINE. No information on any of these chemicals was located in the 1999 version of CancerChem, the CD-ROM version of NCI's *Survey of Compounds Which Have Been Tested for CarcinogenicomActivity* (PHS-149), available from GMA Industries, Inc.

Table 4. Information on Derivatives of the Major Components of Cedarwood Oil.

Compound	Structure	Uses
Cedrol methyl ether CAS No.: 67874-81-1		Fragrance in cosmetics (Allured FFM, 1999; Gerhartz, 1988)
Acetyl cedrene CAS No.: 80449-58-7		Fragrance (Allured FFM, 1999; Bledsoe, 1997)

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

Cedryl acetate CAS No.: 77-54-3		Fragrance in perfume, fixative, food additive (Allured FFM, 1999; FDA, 2002; Gerhartz, 1988)

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

References

Absorbine Jr. (2002) Bug Block®. *Absorbine Jr.® Products*. [http://www.absorbinejr.com/ products/ bug_block.htm]. Searched May 7, 2002

Adams, R.P. (1987) Investigation of *Juniperus* species of the United States for new sources of cedarwood oil. *Econ. Bot.*, **41**(1), 48-54

Allen, T. (1877) *The Encyclopedia of Pure Materia Medica*, vol. 5 Hyd-Lyc, Philadelphia, PA, Boericke & Tafel. [http://www.homeoint.org/allen/juni.htm]. Searched December 17, 2001

Allured FFM (1999) Cedarwood oil, cedrol, cedrene, cedryl acetate, acetylcedrene. Allured's Flavor and Fragance Materials, ed. (On CD-ROM), Carol Stream, IL, Allured Publishing Corp.

Aroma-essence.com (2002) *Kidscents*. [http://www.aroma-essence.com/catalog/kidscents.html]. Searched May 5, 2002

AromaWeb (2001) Atlas cedarwood essential oil. *E.O. Profiles*. [http://www.aromaweb.com/ essentialoilsaf/atlascedarwood.asp]. Searched December 17, 2001

Australian National University (1999) *Cedarwood oil: it's history, harvesting, processing, yield, and uses*. The Australian National University. [http://sres.anu.edu.au/associated/fpt/nwfp/ cedarwood/cedarwood.html]. Searched May 5, 2002

Baker's Chemicals (2002) Results of Search for: cedarwood oil. *Baker's Chemicals*. Virtual Scientific Industries. [http:www.virtual-scientific.com/Catalog/products/chemicals/ chemicals1.htm]. Searched May 17, 2002

Bledsoe, J.O. (1997) Terpenoids. In: Krokshwitz, J.I. & Howe-Grant, M., eds., *Kirk-Othmer Encyclopedia of Chemical Technology*, 4th ed., vol. 23, New York, John Wiley & Sons, Inc., p 839

Botanical Dermatology Database (2001) Cuppressaceae (Cypress family). *Botanical Dermatology Database*. [http://216.51.100/]. Searched May 2, 2002

Burkhart, C.A. & Robinson, J.L. (1978) Hugh rat pup mortality attributed to the use of cedar-wood shavings as bedding. *Lab. Animals*, **12**, 221-222

California EPA (2001) California Environmental Protection Agency Department of Pesticide Regulation, *USEPA/OPP Pesticide Related Database Queries: Cedarwood oil.*

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

[http://www.cdpr.ca.gov/]. Searched December 19, 2001

Cedarcide (2002) Chemical free, 100% natural pest control. *Cedarcide*. [http://www. pestproducts. com/cedarcide.htm]. Searched May 1, 2002

Chemical Sources International (2002) *All Chemical Suppliers for: Cedarwood oil* [http://db/chemsources.com]. Searched May 16, 2002

ChemID (2002) Cedarwood oil, cedarwood oil Texas, *Thuja plicata* oil, cedrol, alpha-cedrene, thujopsene, acetyl cedrene, cedrol methyl ether, 3-thujopsanone. *ChemIdplus*. National Library of Medicine, Bethesda, MD. Records No. 008000279, 068990830, 068917351, 000077532, 000469614, 000470406, 080449587, 125783655, 067874811, 025966794. [http://chem.sis.nlm. nih.gov/chemidplus/]. Searched May 9 and 13, 2002

Clydesdale, F. M., ed. (1997) Cedarwood oil alcohols. *Food Additives. Toxicology, Regulation, and Properties.* (On CD-ROM), Boca Raton, FL, CRC Press, Inc.

Country Cottage Works (2002) Country Cottage Works aromatherapy blends! *Blended Oils.* [http://www.countrycottageworks.com/boil.htm]. Searched May 22, 2002

Danish Environmental Protection Agency (2002) *Environmental and Health Assessment of Substances in Household Detergents and Cosmetic Detergent Products.* [http://www.mst.dk/ udgiv/publications/ 2001/87-7944-596-9/html/kap12_eng.htm]. Searched May 5, 2002

Dialog Information Services (2002a) *PIERS Imports (US Ports) (File 573)*, Palo Alto, CA. Searched April 25, 2002 [Accession Nos. 0024967128, 0023643954, 0023091615, 0021582468, 0020784810, 0019469008]

Dialog Information Services (2002b) *PIERS Exports (US Ports) (File 571)*, Palo Alto, CA. Searched Searched April 25, 2002 [Accession Nos.0024038447, 0023971590, 0023952622, 0023871459, 0018773530, 0018713411, 0018711860, 00186903233, 0018653985, 0018652219, 0018638069]

Drugstore.com (2002) *Dove. Beauty Bar, sensitive skin*. [http://www. drugstore.com]. Searched May 3, 2002

EPA (1993) *Reregistration Eligibility Decision (RED) Cedarwood Oil*. Washington, DC, US Environmental Protection Agency, EPA 738-S-93-012, 169 pp

FAO (1995a) *Flavours and Fragances of Plant Origin*. Food and Agriculture Organization of the United Nations. [http://www.fao/org/docrep/V5350e/V5350e00.htm]. Searched May 2, 2002

FAO (1995b) *Non-Wood Forest Products from Conifers.* Food and Agriculture Organization of the United Nations. [http://www.fao/org/docrep/x0453e/X0453e00.htm]. Searched May 2, 2002

FDA (2002) "Everything" Added to Food in the United States. *EAFUS: a Food Additive Database*. US Food and Drug Administration. [http://www.cfscan.fda.gov/~dms/eafus.html]. Searched May 8, 2002

Frontier Natural Products Co-op (2001) Red cedarwood essential oil. *Aromatherapy Pat's Picks*. [http://www.frontierherb.com/Aromatherapy/AromaNotes/Note12.html]. Searched December 17, 2001

Gerhartz, W., ed. (1988) Flavors and Fragrances. In: Elvers, B., Rousanville, J.F., & Schulz, G., eds., *Ullmann's Encyclopedia of Industrial Chemistry*, Vol. A11, VCH Publishers, p. 171, 176, 177, 219, 220

Hashimoto, M., Davis, D.C. & Gillette, JR. (1972) Effect of different routes of administration of cedrene on hepatic drug metabolism. *Biochem. Pharmacol.*, **21**, 1514-1517

Health Canada (2002) Cedarwood oil. *Drug Product Database*. [http://www.hc-sc.gc.ca/hpb/drugs-dpd/]. Searched May 5, 2002

Heston, W.E. (1975) Testing for possible effects of cedar wood shavings and diet on occurrence of mammary gland tumors and hepatomas in C3H-A^{vy} and C3H-A^{vy}fB mice. *J. Natl. Cancer Inst.*, **54**, 1011-1014

HSDB (2002) Cedarwood oil. *HSDB (Hazardous Substances Data Bank)*, National Library of Medicine, Bethesda, MD. [http://toxnet.nlm.nih.gov/]. Searched May 9, 2002

Hunter, D., ed. (2001) *Chemical Week 2001 Buyers' Guide*, New York, Chemical Week Associates, p. 190

Kurth, E.F. & Ross, J.D. (1954) Volatile oil from Western Juniper. Report No. C-3. Oregon Forest Products Laboratory. [http://juniper.orst.edu/kurth.htm]. Searched May 6, 2002

Lady Lorelei (2002) *Sense of Serenity. Woodland mists*. [http://www.lunarace.com/opinioa.html]. Searched May 1, 2002

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)

Laurel Laboratories, Inc. (2002) *An Introduction to the Oil of Western Red Cedarwood Pacific*.. [http://home.istar.ca/~daijones/index.html]. Searched May 8, 2002

Lawrence, B.M., ed. (1993) Cedarwood oil. *Essential Oils* (1988-1991). Carol Stream, IL, Allured Publishing Corp., pp 176-177

Malkinson, A.M. & Beer, D.S. (1984) Pharmacologic and genetic studies on the modulatory effects of butylated hydrxytoluene on mouse lung adenoma formation. *J. Natl. Cancer Inst*., **73**(4), 925-933

Merck (2001) Thujopsene, Cedrol.9470, 1923. *The Merck Index*, 13th ed. (On CD-Rom), Rahway, NJ, Chapman & Hall [Monograph Numbers 1923 & 9470]

Mookherjee, B.D. & Wilson, R.A. (1996) Oils, essential. In: Krokshwitz, J.I. & Howe-Grant, M., eds., *Kirk-Othmer Encyclopedia of Chemical Technology*, 4th ed., vol. 17, New York, John Wiley & Sons, Inc., p 644-645

Ogata, A., Ando, H., Kubo, Y., Nagasawa, H., Ogawa, H., Yasuda, K. & Aoki, N. (1999) Teratogenicity of thujaplicin in ICR mice. *Food & Chem. Toxicol.*, **37**, 1097-1104

Oklahoma State University (2001) *Turning a problem into profit*. [http://www.okstate.edu/ag/impact/impact1.htm]. Searched December 17, 2001

Passino-Reader, D.R., Hickey, J.P. & Ogilvie, L.M. (1997) Toxicity to *Daphnia pulex* and QSAR predictions for polycyclic hydrocarbons representative of Great Lakes contaminants. *Bull. Environ. Contam. Toxicol.*, **59**, 834-840

POCO, LLC (2002) *Welcome to POCO, LLC*. Port Orford Cedar Oil, LLC. [http://12.32.114.93/Aboutus.htm]. Searched May 1, 2002

PolySciences, Inc. (2001) Result of Search for: cedarwood oil. *Online Catalog*. [http://www.polysciences.com/]. Searched May 17, 2002

Rinde, E. (2002) Personal communication (telephone conversation) from Esther Rinde, PhD, US Environmental Protection Agency, to Marta De Santis, PhD, Technical Resources International, May 7, 2002

Resource Management Group (2002) *Cedar Info*. [http://rmg.8k.com]. Searched May 6, 2002

Sabine, J.R. (1975) Exposure to an environment containing the aromatic red cedar, *Juniperus virginiana*: procarcinogenic, enzyme-inducing and insecticidal effects. *Toxicology*, **5**, 221-235

Sabine, J.R., Horton, B.J., and Wicks, M.B. (1973) Spontaneous tumors in C3H-A^{vy} and C3H-A^{vy}fB mice: high incidence in the United States and low incidence in Australia. *J. Natl. Cancer Inst.*, **50**, 1237-1242

Sawyer (2002) Insect repellent ingredients. *Products and Knowledge to Increase Your Outdoor Enjoyment.* [http://www.sawyerproducts.com/Insect_Repellent/repellents_ingredients.htm]. Searched May 6, 2002

Schreiber, W.L. (1996) Perfumes. In: Krokshwitz, J.I. & Howe-Grant, M., eds., *Kirk-Othmer Encyclopedia of Chemical Technology*, 4th ed., vol. 18, New York, John Wiley & Sons, Inc., p 183, 190

Sigma-Aldrich (2002a) Cedarwood oil, Virginia cedarwood oil, cedrol, ∀-cedrene, and thujopsene. *Material Data Sheets.* [http://www.sigma-aldrich/com]. Searched May 20, 2002

Sigma Aldrich (2002b) Cedarwood oil, Virginia cedarwood oil, Texas cedarwood oil, cedrol, ∀-cedrene, ∃-cedrene, ∀-copaene, thujopsene, and ∃-thujaplicin. *Sigma Aldrich Search Results.* [http://www.sigma-aldrich/com]. Searched May 20, 2002

Skeeter Defeater (2002) Cedarwood soap. *Skeeter Defeater*. [http://www.worldpromo.com/wholesale/cedarwood_soap.htm]. Searched May 1, 2002

STNEasy (2002) Result of Search for: *Thuja plicata* oil. Scientific & Technical Information Network, Chemical Abstracts Services, Inc. [http://stneasy.cas.org]. Searched May 15, 2002

Tilton, H., ed. (2001) Cedarwood oil. *OPD 2002 Chemical Buyers Directory*, New York, Schnell Publishing Co., p 180

US Patents and Trademark Office (2002) Results of search (all years) of database for cedarwood oil: 349 patents, *Welcome to the USPTO Web Patent Databases.* [http://www. uspto.gov/]. Searched May 17, 2002

Vlahakis, G. (1977) Possible carcinogenic effects of cedar shavings in bedding of C3H-A^{vy}fB mice. *J. Natl. Cancer Inst.*, **58**, 149-150

Wade, A.J., Holl, J.E., Hilliard, C.C., Molton, E. & Greene, F.E. (1968) Alteration of drug metablolism in rats and mice by an environment of cedarwood. *Pharmacology*, **1**, 317-328

Prepared for NCI by Technical Resources International, Inc. to support nomination under contract no. N02-CB-07007 (CSWG:05/02; NTP: 9/02)