Evaluation of
Chamomile flower, roman, oil
for Use as a Cigarette Ingredient

January 2006

INTRODUCTION

Chamomile flower, roman oil (CAS # 8015-92-7) is currently used worldwide at levels below **5 ppm** in selected cigarette brands manufactured and/or distributed by Philip Morris International. This document is a review of current published toxicology information of chamomile flower, roman oil abstracted from online toxicity databases.

TOXICITY DATA ON UN-BURNED MATERIAL

The following information was generated from the MICROMEDEX database tool http://csi.micromedex.com on January 3rd 2006, unless otherwise indicated.

Overview

Chamomile flower, roman oil is obtained by steam distillation from the florets of *Anthemis nobilis.*[1]

As a food flavouring additive, the material has been assessed under the provisions of the *Federal Food, Drug and Cosmetic Act, section 201 (s)*, by the Expert Committee of the USA Flavour and Extract manufacturers' Association (FEMA), to be generally recognized as safe (GRAS) under current conditions of use.

Chamomile flower, roman oil is a common cosmetic ingredient.

This material appears on the "List of Permitted Additives to Tobacco Products in the United Kingdom" (Department of Health, 2003) at a maximum level permitted for inclusion in cigarettes of 0.15 % w/w tobacco.

Roman chamomile oil is relatively non-toxic following acute exposure. The acute oral LD50 in rats was greater than 5 g/kg[2]. Dermal application of 5 g/kg to rabbits did not result in any deaths. Oral administration of 300 to 500 mg/kg to rats was reported to cause slight behavioral depression; doses of 150 mg/kg and below had no effect[3].

Undiluted Roman chamomile oil applied to the backs of hairless mice produced no irritating effects[2]. When applied full strength to intact or abraded rabbit skin for 24 hours under occlusion, Roman chamomile oil was only mildly irritating[2].

[1] http://www.thegoodscentscompany.com, viewed on January 3rd, 2006.

[2] Opdyke, D.L.J. Monographs on fragrance raw materials: Chamomile. Food and Cosmetics Toxicology 12(Suppl.):1423-1425, 1974.

[3] Fundaro, A. and Cassone, M.C. Actions of the essential oil of chamomile, cannella, assenzio, mace and oregano on operative behavior in rats. *Boll. Soc. It. Sper* 56: 2375-2380, 1980.

Liver regeneration was followed over a 10-day period in partially hepatectomized rats (5-16 Charles River rats per group) given Roman chamomile oil subcutaneously at a dose level of 50 mg/kg/day for 7 days or in the diet at 0.35% (350 g/kg/day) for 10 days[4]. Liver regeneration was calculated from the dry liver weight by taking the product of the weight at surgery by factor of 0.46 and subtracting this from the weight at necropsy. The objective was to investigate the effects of several oils, including chamomile oil, on the extent of liver regeneration. No effects on liver regeneration were seen with either oral or sc Roman chamomile treatment.

Chamomile has been reported to cause allergic contact dermatitis. Patch testing with 5% chamomile in petrolatum was conducted in 290 patients with eczematous dermatitis; only one developed positive reaction to chamomile oil[5]. Kligman (1973)[6] conducted a maximization test on 25 normal human volunteers. Roman chamomile oil was tested at a concentration of 4% in petrolatum with no sensitization reactions. Hausen (1979)[7] performed patch testing with various extracts including chamomile in 25 individuals with prior allergy to different Compositae plants. Two subjects were allergic to chamomile and cross-reactions to chamomile were seen in 10 subjects. Barry (1995)[8] reported that majority of reports of contact dermatitis refer to A. cotula ("stinking dog-fennel") and related species. This species is known for its high contents of the allergenic sesquiterpene lactone, anthecotulide. If present at all, only traces of this lactone are contained in Roman chamomile.

A patch test in a 34-year old woman with a history of atopic dermatitis elicited a positive reaction to essential oil of chamomile (25%). The lactone nobilin was extracted from the Roman chamomile in the compress and was considered the probable sensitizer[9]. In yet another case report, an 82-year old man with itchy eczema was patch tested with the European Standard series and the fragrance mix series and found to be allergic to chamomile extract and sesquiterpene lactones[10].

Several incidences of anaphylactic reactions have been reported in the literature in association with drinking chamomile tea (type unspecified). Within 1 to 20 minutes of drinking the tea, symptoms including abdominal pain, vomiting and diarrhea, breathing difficulties, swelling of the

[4] Gershbein, L. L. Regeneration of rat liver in the presence of essential oils and their components. *Food Cosmet. Toxicol.* 15:173-181, 1977.

[5] Meneghini, C. L., Rantuccio, F. and Lomuto, M. Additives, vehicles and active drugs of tropical medicaments as causes of delayed type allergic dermatitis. *Dermatologica* 143:137-147, 1971.

[6] Kligman, A.M. Report to RIFM 11 October, 1973. [In Opdyke, D.L.J. Monographs on fragrance raw materials: Chamomile. *Food and Cosmetics Toxicology* 12(Suppl.):1423-1425, 1974.]

[7] Hausen B.M. The sensitizing capacity of Compositae plants. III. Test results and cross-reactions in Compositae-sensitive patients. *Dermatologica* 159(1):1-11, 1979.

[8] Berry, M. Herbal products – 6. *The chamomiles. Pharm. J.* 254(6827):191-193, 1995.

[9] Giordano-Labadie, F., Schwarze, H. P. and Bazex, J. Allergic contact dermatitis from chamomile used in phytotherapy. *Contact Dermatitis* 42(2):247, 2000.

[10] Bossuyt, L. and Dooms-Goossens, A. Contact sensitivity to nettles and camomile in "alternative" remedies. *Contact Dermatitis* 31(2):131-132, 1994.

eyes, lips and throat, hives and itching skin were reported[11,12,13,14]. The patients who exhibited these reactions were also allergic to other pollens such as ragweed and mugwort, suggesting that prior sensitization to these pollens resulted in cross sensitization to the chamomile pollen contained in the tea. The likely mechanism is an IgE mediated immunological reaction as indicated by ELISA antibody tests.

Jarolim et al. (1998)[15], in a case report, described an anaphylactic reaction from an enema containing chamomile extract (Kamillosan) given to a woman in labor. Within minutes, the patient developed nausea, urticaria, laryngeal edema, tachycardia and hypotension. Further testing through immunoblot techniques revealed a cross reactivity of proteins in chamomile to birch pollen allergens.

No phototoxic effects were reported for Roman chamomile oil when exposed to sunlight or UV light after undiluted application to the backs of mice and miniature pigs[16,17].

The following information was generated from the RTECS – Registry of Toxic Effects of Chemical Substances, a database of MICROMEDEX Systems (http://csi.micromedex.com) January 3rd 2006.

Health hazard data

Acute toxicity
LD50/LC50 - LETHAL DOSE/CONC 50% KILL

Rat

LD50 - ROUTE: Oral; DOSE: >5 gm/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (12,853,1974)]

[11] Benner, H.B. and Lee, H.J. Anaphylactic reaction to chamomile tea. *J. Allergy Clin. Immunol.* 52(5):307-308, 1973.

[12] Casterline, C.L. Allergy to chamomile tea. *Letter to JAMA* 244: 331, 1980.

[13] Palacios, A.S., Schamann, F., Marrerro, J.A.G., Parra, V.R. and Suarez, E.M. Anaphylactic reaction with chamomile. Cross-sensitivity with Artemisia pollen. *Clin Exp Allergy* 20: 123, 1990. (Abstract)

[14] Subiza, J., Subiza, J.L., Hinojosa, M., Garcia, R., Jerez, M., Valdiveso, R. and Subiza, E. Anaphylactic reaction after the ingestion of chamomile tea: a study of cross-reactivity with other composite pollens. *J. Allergy Clin. Immunol.* 84: 353-358, 1989.

[15] Jarolim, E.J., Reider, N., Fritsch, R. and Breiteneder, H. Fatal outcome of anaphylaxis to chamomile-containing enema during labor: a case study. *J Allergy Clin. Immunol.* 102: 1041-1042, 1998.

[16] Forbes, P.D., Urbach, F. and Davies, R.E. Phototoxicity testing of fragrance raw materials. *Food Cosmet. Toxicol.* 15; 55-60, 1977.

[17] Small, E. Culinary Herbs. NRC Press, Ottawa, Canada. pp. 197-200, 1997.

Rabbit

LD50 - **ROUTE:** Skin; **DOSE:** >5 gm/kg [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (12,853,1974)]

Irritation

SKIN - STANDARD DRAIZE TEST

Rabbit

ROUTE: Skin; DOSE: 500 mg/24H; REACTION: Moderate [Food and Cosmetics Toxicology. (London, UK) V.1-19, 1963-81. For publisher information, see FCTOD7. (12,853,1974)]

TOXICITY DATA ON BURNT MATERIAL

Data on the toxicity of chamomile flower, roman oil as a cigarette ingredient has been evaluated in a series of studies. The results of these studies may be found in the following references:

R.R. Baker et *al*., 2004, "An overview of the effects of tobacco ingredients on smoke chemistry and toxicity", Food and chemical toxicology, 42S:53-83. **PEER REVIEWED**

E.L. Carmines, 2002, "Evaluation of the Potential Effects of Ingredients Added to Cigarettes. Part I: Cigarette Design, Testing Approach and Review of Results," Food and Chemical Toxicology, 40:77-91. **PEER REVIEWED**

K. Rustemeier et al, 2002, "Evaluation of the Potential Effects of Ingredients Added to Cigarettes Part II. Chemical Smoke Composition," Food and Chemical Toxicology, 40:93 - 104. **PEER REVIEWED**

Roemer et al, 2002, "Evaluation of the Potential Effects of Flavor Ingredients Added to Cigarettes. Part 3. In Vitro Genotoxicity and Cytotoxicity," Food and Chemical Toxicology, 40:105-111. **PEER REVIEWED**

P.M. Vanscheeuwijck et al, 2002, "Toxicological Evaluation of Cigarettes without and with the Addition of Flavor Ingredients to the Tobacco. Part 4. Subchronic Inhalation Toxicity," Food and Chemical Toxicology, 40:113-131. **PEER REVIEWED**

These studies indicate that the ingredients used in the production of cigarettes do not increase the overall toxicity of cigarette smoke.

CONCLUSION

Cigarette smoking causes lung cancer, heart disease, emphysema and other serious diseases in smokers. Smokers are far more likely to develop serious diseases, like lung cancer, than non-smokers. There is no "safe" cigarette. Government health warnings about smoking apply to all cigarettes, regardless of the ingredients added, including those containing only tobacco and paper.

While Philip Morris International has not conducted human studies on the health effects of ingredients used in cigarette manufacture, studies have been conducted using scientifically accepted in vitro and in vivo toxicity assays with various ingredient mixtures (see Toxicity Data on Burnt Material above). These studies show there is no meaningful difference in the composition or toxicity of smoke when the smoke from cigarettes with added ingredients is compared to the smoke from cigarettes without added ingredients. These findings are supported by similar studies from the published literature. It is our scientific judgment, based on the best available data, that chamomile flower, roman oil used in our cigarettes does not increase the overall toxicity of cigarette smoke.