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NATURAL SOURCES OF FLAVOURINGS

REPORT N° 2

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Introduction

The present publication is 'Report N° 2 on natural sources of flavourings'. It provides safety-in-use evaluations of 58 natural sources of flavourings.

Report N° 1 contains 101 evaluated natural sources of flavourings.

Further 250 source materials are at present under evaluation by the Committee of experts.

The CoE numbers attributed in this report should be considered as provisional. Final numbering depends on the total number of natural sources of flavourings to be evaluated.

Classification system for natural flavouring sources and preparations

In the 3rd edition of the "Blue Book", natural flavouring sources were listed and classified into four categories (N1-N4). This approach has been refined by considering individual parts and preparations and allocating them a single classification or, in the case of preparations derived from the same part, a group classification. Flavouring source materials and preparations have been classified into six numbered categories as follows:

Category 1

Plants, animals and other organisms, and parts of these or products thereof, normally consumed as food items, herbs or spices in Europe for which it is considered that there should be no restrictions on use.

Flavouring preparations, which are not themselves consumed as food but which are derived from plants, animals and other organisms and parts of these or products thereof, normally consumed as food items, herbs or spices in Europe. These preparations, on the basis of the information available, are not considered a risk to health in the quantities used.

Category 2

Plants, animals and other organisms, and parts of these or products thereof, and preparations derived therefrom, not normally consumed as food items, herbs or spices in Europe.

These source materials and preparations, on the basis of the information available, are not considered to const a risk to health in the quantities used.

Category 3

Plants, animals and other organisms, and parts of these or products thereof, normally consumed as food items, herbs or spices in Europe which contain defined "active principles" or "other chemical components" requiring limits on use levels.

Flavouring preparations, which are not themselves consumed as food but which are derived from plants, animals and other organisms and parts of these or products thereof, normally consumed as food items, herbs or spices in Europe which contain defined active principles" or "other chemical components" requiring limits on use levels.

These source materials and preparations are net considered to constitute a risk to health n the quantities used provided that the limits set for the active principles" or the "other chemical components" are not exceeded.

Category 4

Plants, animals and other organisms, and parts of these or products thereof, and preparations derived therefrom, not normally consumed as food items, herbs or spices n Europe, which contain defined "active principles" or "other chemical components" requiring limits on use levels.

These source materials and preparations are not considered to constitute a risk to health in the quantities used provided that the limits set for the "active principles" or the "other chemical components" are not exceeded.

Category 5

Plants, animals and other organisms, and parts of these or products thereof, and preparations derived therefrom, for which additional toxicological and/or chemical information is required.

These could temporarily be acceptable provided that any limits set for the “active principles” or the “other chemical components” are not exceeded.

Category 6

Plants, animals and other organisms, and parts of these or products thereof, and preparations derived therefrom, which are considered to be unfit for human consumption n any amount.

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Datasheets of evaluated natural sources of flavourings

SYS NAME	**Allium ascalonicum** Strand
CE No	23
STEINMETZ No	-
FEMA No	-
ORDER	Liliiflorae
FAMILY	Liliaceae
NAME	**E** Scallion, Shallot **F** (Ail) échalotte, ciboule **D** Schalotte **I** Scalogno
SYNONYMS	Allium cepa var. aggregatum G. Don, Allium cepa var. ascalonicum Backer, Allium cepa var. multiplicans Bailey, Allium cepa var. solanina Alef., Porrum ascalonicum Rchb. (1,2) (may also be regarded as a variety of Allium cepa). Three distinguished provarieties: A. asc. provar. ascalonicum, A. asc. provar. chinense G. Don, A. asc. provar. majus G. Don (engl. scallion or fr. ciboule)
PARTS USED	Bulbs (1)
IMPORTANT CONSTITUENTS	Volatile compounds qualitatively similar to Allium cepa (CE No. 24) (1)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Meat products, soups (3)
LEVEL OF USE	Extract: meat products 500 ppm. Infusion*:* meat products 500 ppm. Concentrated juice: soups 500 ppm; Powder: soups 3000 ppm. Essential oil: soups 3 ppm (3)
PREPARATION	Extract, infusion, concentrated juice, powder, essential oil prepared from bulb
MAIN TOXICOLOGICAL DATA	See Allium cepa (CE No. 24)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Fresh bulbs are used in sauces, salads, pickles (1). Bulbs are used as food
CLASSIFICATION AND LIMITS	**Bulbs and preparations: Category 1**
NATIONAL/INT. EVALUATION	-
MAIN REFERENCES	(1) Hagers Handbuch der Pharmazeutischen Praxis (1993-1995), 5th Ed., Vol. 4-6 Drogen, Haenseler R. et al. (Eds.), Springer, Berlin (2) Mansfeld (1986) (3) IOFI 2000
DATA BASES USED	Keywords: Allium ascalonicum, Scallion, Shallot MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Allium cepa** L.
CE No	24
STEINMETZ No	-
FEMA No	Onion oil: 2817
ORDER	Liliiflorae
FAMILY	Liliaceae (Amaryllidaceae)
NAME	**E** Onion **F** Oignon **D** Zwiebel, Küchenzwiebel **I** Cipolla
SYNONYMS	Allium esculentum Salisb., Cepa esculenta S.F. Gray, Cepa vulgaris Renault, Kepa esculenta Rafin., Porrum cepa Rchb. (1). Main varieties (1)*:* var. aggregatum G. Don (D: Kartoffelzwiebel; also regarded as variety of A. ascalonicum) var. ascalonicum Backer (D: Schalotte; also regarded as own species A. ascalonicum see CE No. 23) var. cepa (D: gewöhnliche Küchenzwiebel, name E: common onion) var. cepiforme Regel (also regarded as identical with A. fistulosum) var. proliferum (Moench) Alef. (D: Catavissazwiebel; also regarded as own species A. proliferum or as A. cepa L. var. viviparum) var. viviparum (Metzg.) Alef. (D: Luftzwiebel)
PARTS USED	Bulbs
IMPORTANT CONSTITUENTS	Fresh bulbs contain organic sulfur compounds, including 0.2% trans-S-(1-propenyl) cysteine sulfoxide, alliin (S-allyl-L-cysteine sulfoxide), S-methyl-cysteine sulfoxide (‚methylalliin'), S-propylcysteine sulfoxide (‚propylalliin') which are converted to simpler, unstable sulfur compounds by the enzyme alliinase present when the onion is cut or crushed, and further to sulfides (di-, tri-, etc.) and other compounds that are responsible for the characteristic flavour and are recovered in the onion oil (yield 0.005-0.03%) (2,3). The flavour components of onion oil can be classified in the following categories: disulfides (mainly alkyl propenyl or propyl disulfides) and trisulfides as major constituents with dipropyl disulfide as main component (35% in the oil) and considerable quantities of methylpropyl disulfide, methylpropyl trisulfide, and dipropyl trisulfide; smaller amounts of tetrasulfides, monosulfides, oxygen compounds (carbonyls, aldehydes, furanes), thiols and thiophenes,. (2,4,5,6). By the action of heat methyl and propyl propenyl disulfides are converted into dimethylthiophenes (mainly 3,4-dimethylthiophene) and saturated disulfides (as dimethyl disulfide and dipropyl disulfide), which are present in steam distilled onion oil and are responsible for the characteristic flavour of fried onions (4). In onion extracts thiosulfonates (i.e. sulfonothioates; from freshly cut onions only), and cepaenes (α-sulfinyldisulfides) and zwiebelanes (bicyclic sulfur-containing derivatives) have also been characterized (4,7). Onions also contain about 0.25% cycloalliin (3-methyl-1,4-thiazan-5-carbonic acid-1-oxide), and γ-glutamyl amino acids (1). Other constituents are phenolic acids, flavonoids, sterols, saponins (8,9). The lachrymatory (tear-producing) principle in crushed or cut onion is thiopropanal S-oxide (propanethial S-oxide) produced from trans-S-(1-propenyl)-

	cysteine sulfoxide (double-bonded isomer of alliin) by alliinase (2)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked goods, fats and oils, frozen dairy, meat products, condiment/relish, soft candy, gelatin/pudding, soups, snack foods, nonalcoholic beverages, alcoholic beverages, gravies (8)
LEVEL OF USE	Onion oil: baked goods 12 ppm, fats and oils 826 ppm, frozen dairy 1.9 ppm, meat products 7.0 ppm, condiment/relish 52.7 ppm, soft candy 1.9 ppm, gelatin/pudding 2.0 ppm, soups 10.0 ppm, snack foods 20.0 ppm, nonalcoholic beverages 1.9 ppm, alcoholic beverages 1.0 ppm, gravies 3.4 ppm (8)
PREPARATION	Onion oil: by steam distillation of the crushed fresh bulbs that have been allowed to stand for some hours (yield 0.005%) (2). Oleoresin, fluid concentrated water extract: by special manufacturing processes from thermally pretreated bulbs; fluid extract in order to enhance some flavour top notes as well as the flavouring strength (8)
MAIN TOXICOLOGICAL DATA	Onions have similar pharmacological and toxicological properties as garlic (Allium sativum L. CE No. 26) (antihypercholesterolemic, hypoglycemic, antifungal, antibiotic, inhibiting platelet aggregation, increasing fibrinolytic activity, reducing gastric cancer risk) (9). No adverse effects on reproductive parameters and development observed after long-term administration of onions in rats and pigs (10,11,12)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Bulbs are used as food
CLASSIFICATION AND LIMITS	**Bulbs and preparations: Category 1**
NATIONAL/INT. EVALUATION	Onion oil: CFR 182.20, 582.20
MAIN REFERENCES	(1) Hagers Handbuch der Pharmazeutischen Praxis (1993-1995), 5th Ed., Vol. 4-6 Drogen, Haenseler R. et al. (Eds.), Springer, Berlin (2) Food. Technol. 24, 78-80 (1970) (3) Reineccius (1994) (4) J. Agric. Food Chem. 19: 984-999 (1971) (5) Maarse&Visscher, Volatile Compounds in Food: Qualitative and quantitative data. TNO-CIVO Analytical Food Institute: Zeist (1989) (6) J. Food Sci. 40: 1165-1167 (1975) (7) Bruneton J., Pharmacognosy, Phytochemistry, Medicinal Plants. Lavoisier, Paris (1995) (8) Fenaroli (1995) (9) Leung (1996) (10) Food Cosmet. Toxicol. 4: 569-576 (1966) (11) Food Cosmet. Toxicol. 4: 585-592 (1966) (12) Food Cosmet. Toxicol. 4: 593-599 (1966)

DATA BASES USED

Keywords: Allium cepa, onion
MEDLINE (1966-1999), EMBASE (1980-1999),
BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Allium porrum** L.
CE No	25
STEINMETZ No:	-
FEMA No	-
ORDER	Liliiflorae
FAMILY	Liliaceae
NAME	**E** Leek, porret **F** Ail à tunique, poireau **D** Lauch, Porree, Winterlauch **I** Porrina
SYNONYMS	Allium ampeloprasum β. porrum Gay, Allium laetum Salisb., Allium porrum var. maximum Schweinf., Porrum commune Rchb., Porrum sativum Mill., Porrum sectile Schult. Two varieties*:* var. porrum (D: Winterlauch), var. sectivum (D: Perlzwiebel) (1)
PARTS USED	Whole plant, bulb
IMPORTANT CONSTITUENTS	The whole plant contains between 0.005 and 0.02% essential oil which is very similar in composition to that of onion (Allium cepa L. CE No. 24) (2). Main components are dipropyl disulfide (49% in the oil) and methyl propyl sulfide (together 90% of the total disulfide fraction in the oil), furthermore propanethiol, dimethyl disulfide, dimethyl trisulfide, methyl propenyl disulfide, methyl propyl trisulfide, 2,5-dihydro-3,4-dimethylthiophen-2-one, allyl methyl sulfide, and various thiosulfinates (2,3,4). Levels of flavour and odour compounds, as measured by pyruvate determination in seedling roots (produced enzymatically from S-alk(en)yl-L-cysteine sulphoxides during germination; 7 μmol/g fresh weight of root) are lower than in onions (11 μmol/g) and garlic (27 μmol/g) (5). Four new sapogenins, porrigenins A and B, identified as (25R)-5 alpha-spirostan-2 beta,3 beta,6 beta-triol and (25R)-2-oxo-5 alpha-spirostan-3 beta,6 beta-diol, respectively, and neoporrigenins A and B were also isolated from Allium porrum. In addition, the known agigenin and its 25S epimer, neoagigenin, were also identified in the plant (6)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked products, meat products, soups, snacks
LEVEL OF USE	Essential oil from bulb: baked products 1 ppm, meat products 1 ppm, soups 3 ppm, snacks 1 ppm. Concentrated juice: soups 1000 ppm; Powder: soups 1000 ppm. Concrete: soups 500 ppm (7)
PREPARATION	Leek essential oil by steam distillation of freshly crushed whole leek or bulb. Concentrated juice, powder, concrete from the bulb
MAIN TOXICOLOGICAL DATA	See Allium sativum (CE No. 26). The sapogenins agigenin, porrigenin A and B exhibited cytotoxicity and high antiproliferative activity on four different tumor cell lines in vitro. All three compounds had a higher antiproliferative (IC_{50} 111-655 μg/ml at 48 h and 45-354 μg/ml at 72 h) than cytotoxic activity (IC_{50} 552-942 μg/ml at 24 h). Porrigenin B

	showed a higher antiproliferative activity (IC_{50} 45-74 μg/ml at 72 h) than porrigenin A (IC_{50} 110-270 μg/ml) and agigenin (IC_{50} 210-354 μg/ml) on all cell lines studied (6)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Whole plant is used as a food
CLASSIFICATION AND LIMITS	**Whole plant and preparations: Category 1**
NATIONAL/INT. EVALUATION	-
MAIN REFERERENCES	(1) Hagers Handbuch der Pharmazeutischen Praxis (1993-1995), 5th Ed., Vol. 4-6 Drogen, Haenseler R. et al. (Eds.), Springer, Berlin (2) Food. Technol. 24, 78-80 (1970) (3) Reineccius (1994) (4) J. Agric. Food Chem. 24 (6): 1147-1152 (1976) (5) Plant Pathol. 35(3): 370-376 (1986) (6) J. Nat. Prod. 60: 1003-1007 (1997) (7) IOFI 2000
DATA BASES USED	Keywords:Allium porrum, leek MEDLINE(1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Allium sativum** L.
CE No	26
STEINMETZ No	-
FEMA No	Garlic oil: 2503
ORDER	Liliiflorae
FAMILY	Liliaceae (Amaryllidaceae)
NAME	**E** Garlic, common garlic **F** Ail, ail blan **D** Knoblauch **I** Aglio, aglioti
SYNONYMS	Porrum sativum Rchb.; Three varieties*:* var. ophioscorodon (Link) Döll (syn. Allium scorodoprasum Lam. (D: Schlangenknoblauch or echte Rockenbolle), var. pekinense (Prokh.) Maek. (E: Peking garlic), var. sativum (syn. Porrum satuvum (L.) Rchb.(D: gewöhnlicher Knoblauch, E: common garlic) (1)
PARTS USED	Bulbs (2)
IMPORTANT CONSTITUENTS	Fresh bulbs contain organic sulfur compounds, including up to 1% alliin (S-allyl-L-cysteine sulfoxide) and S-methyl-L-cysteine sulfoxide (‚methylalliin'), enzymes (alliinase, peroxiddase, myrosinase), adenosin (0.05-0.6%), proteins (16.8% of dry wt, including alliinase), peptide glycosides (scordinines), carbohydrates (10-20%, with inulin-like polyfructosanes and mucilaginous compounds), minerals, vitamins (thiamine, riboflavin, niacin, etc), lipids, amino acids, phenolic compounds (caffeic acid, flavones) and others (3,4). As artefacts in the fresh bulb after enzymatically induced transformation of alliin also about 0.1% ajoenes (trans and cis), 4% 2-vinyl-1,3-dithiin, 0.1% 3-vinyl-1,2-dithiin, 0.3% diallylsulfide, 0.1% allylmethyl trisulfide and about 0.03% diallyl trisulfide (4). As the bulbs are crushed or cut, alliin is converted to allicin (diallyl thiosulfinate or S-allyl-2-propenethiosulfinate) by the enzymatic action of alliinase. Allicin (0.3% of fresh weight) is the source of the volatile constituents (0.1-0.36%, usually ca. 0.2%) recovered in ‚garlic oil': diallyl disulfide (20-50%), diallyl trisulfide (5-40%) and methyl allyl trisulfide (2-61%) as major components in the oil (26-30% each in oil of European origin (5)), furthermore considerable amounts of allyl alcohol, diallyl sulfide (0.5-10%) and dimethyl trisulfide (0.2-10%) (5,6,7,8,9), probably also some allyl tetrasulfide, divinyl sulfide, allyl vinyl sulfoxide (1,3). Garlic oil contains higher amounts of allyl disulfides than other Allium ssp. (10). A not further characterized antimicrobial principle has been described as garlicin (11)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked goods, fats and oils, frozen dairy, meat products, condiment/relish, soft candy, gelatin/pudding, snack foods, nonalcoholic beverages, gravies (2)
LEVEL OF USE	Essential oil: baked goods 9.7 ppm, fats and oils 23.0 ppm, frozen dairy 2.0 ppm, meat products 34.0 ppm, condiment/relish 34.5 ppm, soft candy 4.9 ppm, gelatin/

pudding 2.0 ppm, snack foods 10.0 ppm, nonalcoholic beverages 4.9 ppm, gravies 15.2 ppm (2)

PREPARATION

Essential oil by steam distillation of the crushed bulbs or cloves, sometimes from the whole plant (yield 0.2-0.4%) (2). Also extract, oleoresin (containing about 5% garlic oil) (3,12), dehydrated garlic powder (12), oil macerates (11)

MAIN TOXICOLOGICAL DATA

Garlic has numerous pharmacological properties mainly due to the volatile sulfur compounds including hyperglycemic activities in rabbits, lowering serum cholesterol (or lipids) in rabbits and humans, while raising levels of high-density lipoprotein cholesterol, hypotensive properties in humans and animals, antibacterial and antifungal properties, larvicidal and insecticidal activities, antitumor activities, amebicidal activities, antihepatotoxic activity in rats, antimycotic and antiviral (*in vitro* and *in vivo*), lowers blood viscosity, improves microcirculation; expectorant, diaphoretic and diuretic properties; antithrombotic activity (due to ajoene and thiosulfinates) (3). Allergic contact dermatitis with severe skin lesions has been reported in an infant and in an elderly man after intensive dermal contact with plasters of fresh garlic (13,14). Local inflammations with possible necrosis of the skin may also be induced with high doses or long exposure of garlic oil. Sensitization has been related mainly to diallylsulfide and also to allicin, allylpropyldisulfide and allylthiol (15). Fresh garlic may cause local irritation of the gastric mucosa, particularly in sensitive persons. Ingestion of 10-25 ml freshly pressed garlic juice resulted in transient burning in the stomach followed by nausea, sweating, dizziness for 30 minutes in healthy volunteers (16). Observed diarrhoeas after oral intake of garlic have been related to local irritation of the intestines by adenosin (17). Damage of gastric mucosa, reduced body weight and death (5 of 10 animals) were observed in rats after 3 weeks on 5 ml fresh raw garlic juice/kg bw&d. Swelling of the liver, hypertrophy of the spleen and adrenal glands, and decrease of erythrocytes with various morphological changes were observed after 3 and 8 days on fresh raw garlic juice, but these changes did not occur at any time on extracted-aged garlic juice (garlic extract) (18). Gastrointestinal irritation have also been reported in humans after oral exposure to garlic oil. Three daily doses of 1.250 mg garlic oil induced gastrointestinal effects with anorexia, nausea, vomiting, diarrhoea, loss of body weight and menorrhagia in a considerable number of patients (up to 50%) with ischemic heart disease in a study on long term-use of garlic (19). High doses of garlic oil have been shown to damage erythrocytes and reduce hemoglobin levels resulting in anemia, mainly due to the sulfur compounds dipropyldisulfide and S-methyl-cysteine sulfoxide (17,20, 21). Doses of 15-20 mg/kg bw/d of S-methyl-L-cystein sulfoxide (an alliin homologue) resulted in severe hemolytic anemia in animals (22). Garlic preparations inhibit the aggregation of thrombocytes, which is, in addition to the increase of the fibrinolytic activity in the plasma, used as therapeutic effect (17). Various dialkylsulfides (mainly di-n-propyl disulfide) have been shown to exert a goitrogenic effect by an antithyroidal activity (23), however, contradictory results have been found in other studies (17). Hepatotoxic effects with a

reduction of various liver enzymes and with focal areas of hepatic cell necrosis and infiltration by inflammatory cells have been observed after administration of garlic extract (aqueous extract at 20 ml/kg bw for 10 days) (24). Significant effects on liver enzyme activities have also been observed in rats treated with 100 mg allicin/kg bw&d for 15 days (25). Ingestion of fresh or dried garlic at moderate (i.e. therapeutic) doses is considered unlikely to result in serious adverse or toxic effects in humans (17). No adverse effects on body weight, urinary and hematological parameters, organs and tissues could be observed after oral doses of 2000 mg garlic extract/kg bw five times a week over 6 months in rats (26). Reduced body weight, reduced serum protein concentrations and a dedrease in total caecal microflora have been observed in rats after 4 weeks on 200 mg raw garlic extract/kg bw&d, however, none of these changes were observed after feeding boiled garlic extract (27). Dose-dependent cytotoxic effects have been seen in the bone marrow of mice (micronucleus test) and in chinese hamster embryo cells after exposure to freshly pressed garlic juice and to an alcoholic garlic extract, with the juice being considerably more cytotoxic than the extract (28). Cytotoxic effects have also been demonstrated for ajoen (an artefact formed from allicin during extraction) with an ED_{50} of 2-50 μg/ml *in vitro* (29). Garlic (boiled as fresh whole bulbs or cut into pieces, thus containing mainly alliin and allicin, respectively) and the pyrolysis products of alliin, methyiin and s-methyl-1-cysteine exerted mutagenic effects in Salmonella typhimurium TA98 and TA100 with S-9 mix (30). Garlic (no details on preparation given) also showed a weak mutagenic activity in a preliminary test on sex-linked recessive lethal mutations in Drosophila (31). However, mutagenicity tests (Ames-Tests) with pressed garlic juice and alcoholic garlic extract were negativ (28), and no genotoxic effects could be seen in the micronucleus test in mice after oral administration of powdered garlic (32). Weak mutagenic effects of an oleoresin prepared from Allium ascalonicum (CoE No. 23) have been observed in the Ames-Test (plate incorporation test and spot test) with streptomycin-dependent strains of S. typhimurium isolated from TA100 and TA98, however, comparative analysis of strains TA100 and TA98 and E. coli WP2 try^- hcr^- in the spot test gave a negative result (33). Data on embryotoxicity and teratogenicity are rare, but adverse effects are not to be expected (34). In a single study on reproduction toxicity, adverse effects have been observed in rats after oral exposure to dried garlic powder (50 mg/d for 45 and 70 days) with degenerative changes in testes (shrunken seminiferous tubule and Leydig cells nuclei) after 45 days and severe testicular lesions (spermatogenesis arrested at the primary spermatocyte stage) after 70 days, possibly as the result of the hypoglycemic and hypolipidaemic effects of garlic (35). A spermicid effect of garlic has been demonstrated *in vitro*, and was possibly related to its cytotoxic activity (36). An androgenic effect with a significant increase in the weight of seminal vesicles and epididymides and significantly elevated sperm count has been observed in mice after 100 mg/kg bw&d of an aqueous garlic extract for 3 months (37). Similar effects have been found in rats (17). No estrogenic or antiestrogenic effect has been seen in the

uterotrophic assay in prepubertal female mice after daily doses of 500 mg aqueous garlic extract per kg bw (i.p.) for three consecutive days (37). No adverse effect on the implantation has been seen in rats after aqueous, alcoholic or petrol-ether extracts of garlic (38)

DATA NEEDED No data required

SPECIFIC OBSERVATIONS Bulbs are used as a food

CLASSIFICATION AND LIMITS **Bulbs and preparations: Category 1**

NATIONAL/INT. EVALUATION Garlic oil, extract, oleoresin: GRAS (CFR 184.1317)

MAIN REFERENCES

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DATA BASES USED

Keywords: Allium sativum, garlic
MEDLINE (1966-1999), EMBASE (1980-1999),
BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Allium schoenoprasum** L.
CE No	27
STEINMETZ No	-
FEMA No	-
ORDER	Liliiflorae
FAMILY	Liliaceae
NAME	**E** Chives, cive garlic, civet **F** (Ail) civette, ciboulette **D** Schnittlauch, Binsenlauch **I** Cipollina, cipoletta
SYNONYMS	Allium tenuifolium Salisb., Cepa schoenoprasum Moench., Porrum schoenoprasum Schur., Schoenoprasum vulgare Fourr. (1). Four varieties*:* var. alpinum Gaudin, var. schoenoprasum, var. foliosum Regel, var. orientale Regel
PARTS USED	Leaves
IMPORTANT CONSTITUENTS	Freshly cut leaves contain γ-glutamylpeptides (non-volatile, sulfur-containing). Volatile sulfur-containing compounds are formed enzymatically after harvesting (mainly dipropyl disulfide, also *cis*- and *trans*-3,5-diethyl-1,2,4-trithiolane, pentyl hydrodisulfide, methyl pentyl disulfide, methyl-(2-propenyl)disulfide, and other di- and trisulfides) representing the most important constituents (total of 16.8% of the oil) of chive oil (yield of 0.038% by steam distillation) as in other Allium ssp. (2)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Meat products, soups, snacks
LEVEL OF USE	Herb extract: soups 500 ppm. Chive oil: meat products 10 ppm, soups 10 ppm, snacks 10 ppm (3)
PREPARATION	Chive oil by steam distillation of the fresh leaves, extract from the herb
MAIN TOXICOLOGICAL DATA	See Allium sativum (CE No. 26)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Leaves are used as a food
CLASSIFICATION AND LIMITS	**Leaves and preparations: Category 1**
NATIONAL/INT. EVALUATION	Chives: CFR 182.10, 582.10
MAIN REFERERENCES	(1) Hagers Handbuch der Pharmazeutischen Praxis (1993-1995), 5th Ed., Vol. 4-6 Drogen, Haenseler R. et al. (Eds.), Springer, Berlin (2) J. Food Sci. 48: 1858 (1983) (3) IOFI 2000
DATA BASES USED	Keywords: Allium schoenoprasum, chives MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Aloe barbadensis** Mill.
CE No	28
STEINMETZ No	-
FEMA No	2047 (Aloe, concentrated juice from leaves)
ORDER	Liliiflorae
FAMILY	Liliaceae (Asphodelaceae)
NAME	**E** Mediterranean aloe, aloe vera, Barbados aloe **F** Aloès, lloi **D** Echte Aloe, Aloe vera **I** Aloe
SYNONYMS	Aloe vera L. Webb et Berth. non Mill., Aloe vera (L.) N.L. Burm. f., Aloe chinensis Bak., Aloe elongata Murray, Aloe indica Royle, Aloe officinalis Forsk., Aloe perfoliata L., Aloe rubescens DC., Aloe vera „L." var. littoralis König ex Bak., Aloe vera „L." var. chinensis Berger, Aloe vulgaris Lam. (Aloe barbadensis is the source of Curaçao aloe; sources of Cape aloe (African aloe) are A. ferox Mill. and hybrids of this species with A. africana Mill. and A. spicata Baker), and also Aloe perryi Baker) (1)
PARTS USED	Leaves
IMPORTANT CONSTITUENTS	Curaçao aloe (dried leaf exsudate of Aloe barbadensis) contains 25-40% of the hydroxyanthracene-derivatives Aloin A (barbaloin) and B (diastereomeric 10-C-β-D-glucosylderivatives of aloeemodinanthrone), also 3-4% 7-hydroxyaloin A and B, 8-*O*-methyl-7-hydroxyaloine A and B, various esters (6´-p-cumaric acid- and ferulic acid ester), small amounts of the free 1,8-dihydroxyanthraquinone aloeemodin (0.05-0.5%) and chrysophanol; chromonderivatives with up to 30% of the aloeresin B (aloesin, an 8-C-glucosylchromone), aloeresin C (7-*O*-β-D-glucosid of aloeresin A) and aloeresin D (reduced and 7-methylated derivative of aloeresin A), 2'-*O*-cinnamoyl-aloeresin B, small amounts of the aloeson (aglykone of aloeresin B) (2,3). Also contains about 2% essential oil (1). The standardized extract prepared from Aloe ferox or Aloe barbadensis (Aloes extractum siccum normatum PhEur) contains 19.0-21.0% hydroxylanthracene derivatives calculated as aloin A (barbaloin). The gel contains 98.5-99.5% water. Other main constituents are polysaccharides (0.2-0.3% of fresh gel and 0.8-1.2% of dry matter), mainly an acetylated glucomannan (acetomannan; i.e. a mucopolysaccharide with glucose and mannose in a 1:3 ratio), and other carbohydrates (arabinose, galactose, xylose), minerals, vitamines, enzymes, amino acids and essential oil (4,5,6,7)
ACTIVE PRINCIPLES	Aloin/aloe-emodine
PRODUCTS IN WHICH USED	Aloe extracts are used in condiment/relish, soft candy, nonalcoholic beverages, alcoholic beverages (bitters, liqueurs, vermouths) (1), frozen dairy desserts, candy, baked goods, gelatins/puddings (7). Aloe vera gel is used in nonalcoholic beverages (Aloe vera juice) (6)

LEVEL OF USE

Concentrated juice (not further specified): condiment/ relish 48 ppm, soft candy 500 ppm, nonalcoholic beverages 190 ppm, alcoholic beverages 186 ppm (1). Aloes, leaf extract (not further specified)*:* non-alcoholic beverages 100 ppm, alcoholic beverages 1000 ppm, candy 2000 ppm (8)

PREPARATION

Crude, concentrated juice (latex) from the leaves (=Curaçao aloe), fluid, dry and soft extracts, tincture (10% in 80% ethanol (1). The extracts used in foods must be tinctures or greatly diluted extracts, as standard extracts (solid extract or fluid extract) would contain too much anthraglycosides to be safely used (6). Mucilaginous gel (Aloe vera gel) from parenchymatous tissue in the center of the leaf (6)

MAIN TOXICOLOGICAL DATA

Unwanted side-effects of the laxative effect may be mild to severe colic pains in the lower abdomen, resulting from spastic contractions of the smooth muscles of the intestines. Irritation of the large intestines may lead to reflectoric contractions of the uterus with abortive effects. Anthrones may induce a strong blood congestion in the abdominal vessels which might increase mentrual bleeding. Possible results of chronic use of Aloe as laxative are increased mucous production and reduced reabsorption of water and electrolytes from the large intestine which may lead to electrolyte dysbalance and loss of potassium with following paralysis of intestinal musculature, finally resulting in hyperaldosteronismus with possible damage of the kidney tubules (9). Chronic irritation of mucous membranes in the gastrointestinal tract by anthrones may lead to local damage. Toxic doses induce abdominal pain, hemorrhagic gastritis, bloody diarrhoe and nephrotoxic effects (letal dose 1 g for several days) (2). Aloin has a low acute toxicity (LD_{50} > 850 mg/kg KG in rats, LDLo cat oral 500 mg/kg). There are no data on the acute toxicity of aloeemodin. Cytotoxic effects of aloin and aloeemodin on chicken fibroblasts have been shown *in vitro* (10). Longterm exposure of Aloin in the diet (100 mg/kg bw&d for 20 weeks) was not carcinogenic in mice and did not lead to hepato- and nephrotoxic effects (11). Some recent *in vitro* data indicate that some anthranoids, including aloeemodin, have mutagenic and potentially tumour-promoting properties (9). Aloeemodin induced *tk*-mutations in mouse lymphoma L5178-cells and induced micronuclei in a dose-dependent manner in the same cell line. It also inhibited the topoisomerase II-mediated decatenation in mitochondrial DNA of C. fasciculata. Aloeemodin induced DNA damage in the SCGE/Comet-Assay. In a modified Comet-Assay resulted pretreatment with aloeemodin in a reduced effect of the potent non-intercalating topoisomerase II-inhibitor etoposide, which indicated an inhibition of the interaction of DNA and topoisomerase II by intercalation of aloeemodin. Overall these findings support the hypothesis that the genotoxicity of anthraquinones are at least partly the result of a non-covalent DNA-binding (12,13). Aloeemodin was mutagenic in various *in vitro* genotoxicity studies, whereas *in vivo* studies gave negative results. Ames-Test with Salmonella typhimurium strainTA 1537, TA 1538 and TA 98 without S9 positive; strain TA 1538 with S9 positive; SAL (+/- S9) positive; gene mutations in

mammalian cells at HGPRT locus (+/- S9) positive in one experiment, negative in two experiments; chromosomen-aberrations in CHO-cells in vitro (+/-S9) positive (Heidemann 1993). Ames-Test with Salmonella typhimurium: strain TA 1537 (+/-S9) positive, strain TA 102 (+/-S9) S9 negative, strains TA 1538, TA 1978 and TA 98 positive (without S9 strongly mutagenic potential, which was reduced by addition of S9); V79-HGPRT mutation test: weakly positive in one experiment, very weakly positive in the second experiment; UDS in primary rat hepatocytes: positive; transformation of C3H/M2 mousse fibroblasts *in vitro*: positive (Westendorf 1990). The authors concluded that the hydroxymethyl side chain in aloeemodin was essential for the genotoxic effect, which was however dependent on the activation of other functional groups such as phenolic hydroxyl groups in the vicinity of the hydroxymethyl group. Various *in vivo* genotoxicity studies, however, gave negative results: chromosome aberration assay in Wistar rats negative up to 2000 mg/kg KG; gene mutations (mouse spot) in mice (NMRI x DBA) negative up to 2000 mg/kg KG; micronucleus test in NMRI mice negative with 1500 mg/kg KG; UDS ex vivo in Wistar rats negative up to 1000 mg/kg KG (14)

DATA NEEDED Specification of preparations used for flavouring purposes

SPECIFIC OBSERVATIONS Aloe juice contains about 2% essential oil with an extremely bitter flavour. Apparently, the essentail oil is of little or no commercial use as a flavour ingredient (1)

CLASSIFICATION AND LIMITS **Leaf and preparations: Category 5; limits on aloin/aloe-emodin**

NATIONAL/INT. EVALUATION Concentrated juice from the leaves: CFR 172.510

MAIN REFERENCES

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DATA BASES USED

Keywords: Aloe vera, Aloe barbadensis
MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Angelica sylvestris** L.
CE N°	43
STEINMETZ N°	99
FEMA N°	-
ORDER	Umbelliflorae
FAMILY	Apiaceae
NAME	**E** Wild angelica **F** Angélique des bois, angélique sauvage **D** Wald-Engelwurz, echte Brustwurz **I** Angelica silvestre
SYNONYMS	Angelica silvestris L.
PARTS USED	Fruit, root
IMPORTANT COMPONENTS	Root: furocoumarins (qualitative composition): imperatorin, ostruthol, oxypeucedanin, archangelin, iso-imperatorin (1); + umbelliprenin, marmesin, oxypeuce-danin hydrate, xanthotoxin, phellopterin, byakangelicol, byakangelicin, 5-b-cyclolavandulyl-oxy-psoralen (2); + 4-(2'-hydroxy-3'-methoxymethylbutoxy)-7H-furo[3,2-g][1]-benzopyran-7-one (3); + heraclenol, heraclenin and bergapten (4); + tannins + volatile compounds. Essential oil of root: (Angelica sylvestris var. eliator Wahlenb.): mainly aliphatic hydro-carbons: nonane 18.7 %; heptane 0.5 %; terpenic hydro-carbons: α-pinene 16.2 %; β-pinene 0.7 %; β-phellandrene 12 %; α-phellandrene 0.9 %; γ-terpinene 0.6 %; terpinolene 1.6 %; + germacrene D; bicyclogermacrene; 5-pentyl-cyclohexa-1,5-diene; + alcohols: 2-undecanol; myrtenol; + esters; isoamyl isovalerate; isoamyl angelate; myrtenyl acetate (5). Fruits : furocoumarins : bergapten, heraclenol, heraclenin (4) + sesquiterpenic compound: bisabol-angelone (1,6)
ACTIVE PRINCIPLES	Furocoumarins
PRODUCTS IN WHICH USED	Beverages, foods
LEVEL OF USE	Fruit: beverages 3-25 g/l; food 2 g/kg. Essential oil of fruit: beverages 1-10 ppm; food 0.1-70 ppm. Roots: 3-25 g/l; food 6 g/kg. Essential oil of root: beverages 5-10 ppm; food: 5-10 ppm (IOFI, 1995)
PREPARATION	Essential oils of fruit and root
MAIN TOXICOLOGICAL DATA	Phototoxic and photomutagenic potency of tincture and extract preparations using Chlamydomonas as test system (7)
DATA NEEDED	Quantitative data on chemical composition of essential oil from fruit and, if necessary, 28-day oral study and mutagenicity studies
SPECIFIC OBSERVATIONS	Sometimes used as substitute of Angelica archangelica L.

CLASSIFICATION AND LIMITS **Root, and essential oil of root: Category 4; limits on furo-coumarins**
Fruit and essential oil of fruit: Category 5; limits on furocoumarins

NATIONAL/INT. EVALUATION -

MAIN REFERENCES

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DATA BASES USED Keyword : Angelica sylvestris
CHEMICAL ABSTRACTS (- JUNE 1997)

SYS NAME	**Asparagus officinalis** L.
CE No	2014 (530)
STEINMETZ No	-
FEMA No	-
ORDER	Liliiflorae
FAMILY	Liliaceae (Asparagaceae)
NAME	**E** Garden asparagus, white asparagus **F** Asperge **D** Gartenspargel **I** Asparago, sparagio
SYNONYMS	A. sativus Bank., A. altilis Aschers., A. hortensis Mill. Two varieties (1): Asparagus officinalis L. var. officinalis (Europe, North-Africa, Asia to Iran, West Sibiria, part of North America) Asparagus officinalis var. pseudoscaber (Grec.) Aschers. et Graebn. (Syn. A. pseudoscaber Grec.) (North-East Yugoslavia to West Ukraina) or two subspecies (2): ssp. officinalis (Syn. A. polyphyllus Steven, A. caspicus Hohen. ssp. prostratus (Dumort.) Corb.
PARTS USED	Shoots (stalks) (3)
IMPORTANT CONSTITUENTS	Shoots (spears and tips) contain cyclic and aliphatic sulfur-containing acids and esters (mainly methyl 1,2-dithiolane-4-carboxylate (up to 7 mg/kg raw asparagus) and asparagusic acid [1,2-dithiolane-4-carboxylic acid] (3-5 mg/kg raw asparagus, main component among at least 16 sulfur-containing growth inhibitors), and, among others, in traces dihydroasparagusic acid [β,β'-dimercapto-isobutyric acid], and S-acetyldihydro-asparagusic acid [β-S-acetyl-β'-mercaptoisobutyric acid]) (4,5); furthermore α-amino-dimethyl-γ-butyrothetin (an S-methylmethionine derivative) (6); furostanol saponins of which asparasaponin I was identified as a glycosidic bitter principle (25S-furost-5-ene-3β,22,26-triol-3-O-(2,4-di-α-L-rhamnopyranosyl-β-D-glucopyranoside-26-O-β-D-gluco-pyranoside with yield of diosgenin and yamogenin after hydrolysis), whereas asparasaponin II (25S-furost-5-ene-3β,22,26-triol-3-O-(α-L-rhamnopyranosyl-(1→4)-β-D-gluco-pyranoside-26-O-β-D-glucopyranoside) was not bitter (7,8); various flavonoids (rutin, hyperoside, isoquercitrin, cosmosiin [apigenin-7-O-D-glucoside],kaempferol-3-O-L-rhamno-D-glucoside) 9,10); amino acids (asparagine, arginine, tyrosine) (6) and aspartyl/γ-glutamyl dipeptides and S-substituted cysteine derivatives (S-(2-carboxy-n-propyl)-L-cysteine and S-(1,2-dicarboxyethyl)-cysteine as precursors of asparagusic acid) (11). More than 100 constituents (thiophenes, thiazoles, pyrroles, pyrazines, aldehydes, ketones, alcohols, and phenols) are formed during cooking, amounting to at least 20-30% of the flavour components in cooked asparagus. Dimethylsulfide is formed as the principal aroma constituent from S-methylmethionine. Decomposition of asparagusic acid leads to a cyclic compound (1,2-dithiacyclopentene), which is not very stable and delivers a pleasant smell like cooked asparagus. During this reaction 1,2,3-trithiane-5-carboxylic acid, which is only a minor constituent in uncooked asparagus shoots, is also formed as a higher homologue of asparagusic acid. The amount of asparagusic acid

	decreased from 3500 ppb to 150 ppb during heating for 30 minutes. The methyl ester of asparagusic acid is more stable and is not decomposed during heating (12,13). Methylmercaptan (a hydrolysis product of the S-containing compounds) or asparagine-aspartic acid monoamide is believed to be present in urine after eating asparagus, causing its peculiar odour (6)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Powder from shoots (stalks) used in soups (3)
LEVEL OF USE	Powder of shoots: soups 1200 ppm (3)
PREPARATION	Powder of shoots
MAIN TOXICOLOGICAL DATA	Asparagusic acid and its derivatives are very effective plant growth inhibitors and have also nematicidal properties (4).The sulfur-containing growth inhibitor 1,2,3-trithiane-5-carboxylic acid has been identified as responsible contact allergen of raw and cooked asparagus shoots with weak to moderate sensitizing capacity (13). Fibers isolated from the vegetable are claimed to have mutagen-adsorbing (cancer-preventing) properties (14)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Shoots are eaten as vegetables
CLASSIFICATION AND LIMITS	**Shoots: Category 1**
NATIONAL/INT. EVALUATION	-
MAIN REFERERENCES	(1) Zander (1984), Hagers Handbuch der Pharmazeutischen Praxis (1993-1995), 5th Ed., Vol. 4-6 Drogen, Haenseler R. et al. (Eds.), Springer, Berlin (2) IOFI 2000 (3) Tetrahedron Lett. 25: 2549 (1972) (4) J. Agric. Food Chem. 25: 455-459 (1977) (5) Leung (1996) (6) Nippon Shokuhin Kogyo Gakkaishi 14: 491 (1967); through Chem. Abstr. 69: 74477g (1968) (7) Agric. Biol. Chem 41: 1-8 (1977). (8) Z. Lebensm. Unters. Forsch. 155: 151 (1974) (9) Planta Med. 51: 288 (1985) (10) Agric. Biol. Chem. 45: 433 (1981), Phytochemistry 20: 2209 (1981) (11) J. Agric. Food Chem. 25: 459-463 (1977) (12) Am. J. Contact Dermatitis 7: 41-46 (1996) (13) Jpn Kokai Tokkyo Koho JP 6140764 (1986); through Chem. Abstr. 104: 220607J (1986)
DATA BASES USED	Keywords: Asparagus officinalis MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Capsicum annuum** L.
CE No	107
STEINMETZ No	240
FEMA No	Capsicum annum L. extract**:** FEMA No. 223 Capsicum annum L. oleoresin*:* FEMA No. 2234
ORDER	Tubiflorae
FAMILY	Solanaceae
NAME	**E**: Red pepper, Spanish pepper **F**: Piovre d'Espagne **D**: Paprika, Spanischer Pfeffer **I**: Peperone, pepe cornuto
SYNONYMS	C.annuum L.var.Longum Sendt; C.cerasiforme Lamk.; C. Longum DC.
PARTS USED	Fruit
IMPORTANT CONSTITUENTS	Capsaicin (1.67mg/gdry wt), dihydrocapsaicin, nordihydro-capsaicin, homocapsaicin, apigenin, solanine, solanidine, luteolin-7-O-α -apioglucoside, hexadecane, heptadecane, limonene, trans-ocymene, naphthelene, hexanol, cis-3-hexanol, linalool, hexanal, trans-2-hexanal, cis-3-hexanal, benzaldehyde, 2-heptanone, trans-2-hepten-2-one, nonen-4-one, isophorone, α-ionone, hexyl-butyrate, 2-ethylfuran, 2-penthylfuran, 3-isobutyl-3-methoxypyrazine, α-sitosterol, stigmasterol, cycloartenol, α-amirin, capsanthin (1-6)
ACTIVE PRINCIPLES	Capsaicin , glycoalkaloids
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, meat products, condiment, relish, soft candy, hard candy, gelatin, pudding, soups, nonalcoholic beverages, alcoholic beverages, breakfast cereal, other grains, fats and oils, milk products, cheese, processed vegetables, snack foods, nut products, gravies, fish products
LEVEL OF USE	Extract: baked goods 295 ppm, frozen dairy 330 ppm, meat products 198 ppm, condiment, relish 870 ppm, soft candy 450 ppm, gelatin, pudding 115 ppm, soups 1300 ppm, nonalcoholic beverages 167 ppm, alcoholic beverages 1200 ppm, hard candy 6 ppm. Paprika: baked goods 640 ppm, breakfast cereals 640 ppm, other grains 3100 ppm, fats, oils 6100. ppm, milk products 380 ppm, cheese 260 ppm, meat products 4600 ppm, processed vegetables 9200 ppm, condiment, relish 3800 ppm, soups 170 ppm, snack foods 5200 ppm, nonalcoholic beverages 1200 ppm, nut products 4600 ppm, gravies 470 ppm. Paprika oleoresin: baked goods 64 ppm, other grains 200 ppm, fats, oils 1900. ppm, cheese 630 ppm, frozen dairy 5 ppm, meat products 230 ppm, fish products 1000 ppm, processed vegetables 230 ppm, condiment, relish 840 ppm, soft candy 5ppm, gelatin, pudding 5 ppm, soups 13900 ppm, nonalcoholic beverages 30 ppm, alcoholic beverages 20 ppm, nut products 720 ppm, gravies 920 ppm (22)
PREPARATION	Extract, tincture, oleoresin. Paprika is the powder of the fruits from which the most pungent parts are removed

MAIN TOXICOLOGICAL DATA	Oral administration of 50 mg/kg b.w./capsaicin, or 0.5 mg/ kg b.w./day capsicum fruit crude extract to rats for 60 days, reduced significantly the gain in body weight. The reduction in body weight gain was more marked in rats fed with capsicum extract (8). In a 13-week toxicity study, nephrotoxicity was seen in male mice in the 1% dose group (21). There are conflicting data on the mutagenic activity of capsaicin and chili extract in bacterial systems. Both substances have been reported to be non mutagenic in bacteria (9,10). But capsaicin was subsequently reported to show a low level of mutagenic activity in TA98 strains of Salmonella in the presence of an Aroclor-induced activating system (11), and more recently to have higher mutagenic activity in this system (12). Certain fractions from extracts of Capsicum fruit have been found to possess profound clastogenicity as determined by induction of micronuclei in the mouse bone marrow cells (20). In the latter study has been reported a significant increase in bonemarrow micronuclei in the mouse at a dose of 7.5 but not at 1.8 mg/kg b.w. of capsaicin (12). In the other study, capsaicin administered intraperitonally to adult mice at dose of 0.4, 0.8 or 1,6 mg/kg b.w/day on five consecutive days, did not induce any mutagenic effect in male germ cells in vivo, studied using the sperm morphology assay and the dominant-lethal test (13). Chili is reported to act as a promoter of hepatocarcinogenesis (14) and to produce hepatomas when fed at the 10% level in the diet (15). Further chili and capsaicin have been shown to produce cirrhosis of the liver (15), damage to duodenal mucosa (16), and gastric ulcers which probably develop into intramucosal cancer of the skin (17). Moreover, has been reported an increased incidence of adenocarcinoma of the duodenum as a result of feeding 0.0625-1% capsaicin in the diet of mice for 35 days (11). Capsaicin has powerful actions on peripheral sensory C fibres; in some cases, central neurones or small myelinated fibres may also be affected (18). In a population-based case-control study conducted in Mexico City, chili peppers consumers were at high risk for gastric cancer compared with non-consumers (19). In a study with B6C3F1 mice fed a mixture of capsaicinoids at levels of 0. 0.025, 0.083 and 0.25% for 79 wks, a few jejunal and colonic tumors developed in both treated and control group, but capsaicinoids treatment did not increase their incidence (21). Limonene JECFA ADI not specified (1993). Linalool JECFA group-ADI 0-0.5 mg/kg bodyweight (1998)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Sweet peppers are used as foodstuff
CLASSIFICATION AND LIMITS	**Fruit and preparations: Category 3; limits on capsaicin and glycoalkaloids**
NATIONAL/INT. EVALUTATION	The SCF expressed an opinion on capsaicin 28 February 2002. (SCF/FS/FLAV/FLAVOUR/8 ADD 1 Final). The Committee concluded that the available data did not allow it to establish a safe exposure level for capsaicinoids in food. Capsicum annum *L.:* CFR 73.340, 182.10, 582.10.

Capsicum annum L. extract**:** CRF 182.20, 582.20; FEMA No. 223. Capsicum annum L. oleoresin*:* CFR 73.345, 182.20, 582.20; FEMA No. 2234

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DATA BASES USED

Keywords: Capsicum annum, red pepper, chemical composition, toxicity
NAPRLERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001)

SYS NAME:	**Capsicum frutescens** L.
CE No: **STEINMETZ No**: **FEMA No**:	108 241 -
ORDER **FAMILY**	Tubiflorae Solanaceae
NAME	**E** Cayenne pepper, **F** Piment, pment de cayenne **D** Cayennepfeffer, Chillie **I** Pepe di Guinea
SYNONYMS	Capsicum baccatum L., Capsicum fastigiatum L., Capsicum minimum Roxb.
PARTS USED	Fruit
IMPORTANT CONSTITUENTS	Capsaicin (0.45mg/g dry wt), caffeic acid, p-coumaric acid, hexanoic acid, lauric acid, mevalonic acid,2-isobutyl methoxypirazyne, valeric acid, isovaleric acid, ethyl acetate, n-exhanol, 3-methyl-1-pentanol, cis-3-hexenol, hexanol, benzaldehyde, 4-methyl-1-penthyl-iso-butyrate, isoamyl-isovalerate, 4-methyl-1-2-methylbutyrate, 3-methyl-1-penthyl-3-methyl butyrate, cis-3-hexenyl-iso-valerate, cis-3-hexenylvalerate, 4-methyl-1-penthyl-valerate, n-hexylvalerate, ethylsalicylate, iso-hexyliso-caproate, cis-3-hexenhylcaproate, iso-hexyl-caproate, hexylcaproate, isopenthyl-isocaproate, hepthyl-iso-caproate, dihydrocapsaicin, nordihydrocapsaicin, homo-dihydrocapsaicin (1-5)
ACTIVE PRINCIPLES	Capsaicin
PRODUCTS IN WHICH USED	Baked goods, fats, oils, milk products, frozen dairy, meat products, processed vegetables, condiment, relish, soft candy, hard candy, chewing gum, gelatin, pudding, soups, snack foods, gravies, non-alcoholic beverages, alcoholic beverages
LEVEL OF USE:	Red pepper: baked goods 580 ppm, fats, oils 350 ppm, milk products 1600 ppm, meat products 2300 ppm, processed vegetables 1100. ppm, condiment, relish 1300 ppm, soups 1200. ppm, snack foods 100 ppm, gravies 900 ppm. Oleoresin: baked goods 80 ppm, fats, oils 60 ppm, frozen dairy 30 ppm, meat products 150 ppm, condiments relish 300 ppm, soft candy 24 ppm, gelatin, pudding 20 ppm, nonalcoholic beverages 100 ppm, alcoholic beverages 900 ppm, gravies 50 ppm, hard candy 19 ppm, chewing gum 160 ppm.
PREPARATION	Fluid extract, tincture, oleoresins
MAIN TOXICOGICAL DATA	See Capsicum annuum (CE No 107)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	The dried and finely ground fruits are used as foodstuff, spices

CLASSIFICATION AND LIMITS	**Fruit and preparations: Category 3; limit on capsaicin**
NATIONAL/INT. EVALUTATION	Capsaicin:The SCF expressed an opinion on capsaicin 28 February 2002. (SCF/FS/FLAV/FLAVOUR/8 ADD 1 Final) The Committee concluded that the available data did not allow it to establish a safe exposure level for capsaicinoids in food
MAIN REFERENCES	(1) J.Chromatogr.,329,99,1985 (2) J. Agr. Food Chem.,19,1131,1971 (3) J. Agr. Food Chem.,28,156,1980 (4) J. of Chromatogr., 166,221,1978 (5) Z. Lebensm-Unters Forsch, 171,193,1980
DATA BASES USED	Keywords: Capsicum frutescens, cayenne pepper, chillies, chemical composition, toxicity data NAPRLERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001)

SYS NAME	**Coffea arabica** L.
CE No	148
STEINMETZ No	-
FEMA No	-
ORDER	Gentianales
FAMILY	Rubiaceae
NAME	**E** Coffee, Arabian coffee **F** Café, caféier d'Arabie **D** Kaffee, Arabischer Kaffee
I	**I** Caffé
SYNONYMS	Coffea vulgaris Moench. (80 varieties; the two 'original' varieties are C. arabica var. arabica (syn. var. typica) and C. arabica var. bourbon)
PARTS USED	Seeds (beans) (1)
IMPORTANT CONSTITUENTS	Green coffee beans contain 1.2% caffeine (commercial range 0.9-1.4%, all data on dry basis), 1.0% trigonelline (0.6-1.3%), 6.5% chlorogenic acids (5-10%; i.e. phenolic acids with 60-80% chlorogenic acid or 3-caffeoylquinic acid) (2), 1% caffeic acid and 0.4% quinic acid (3), 1% aliphatic acids, 16% coffee oil (7.4-17%; triglycerides with unsaponifiable fat), 45-50% polysaccharides (mostly a galactomannan), 8.1% sugars (mainly sucrose and traces of reducing sugars), 11% proteins, 0.5% free amino acids (mainly glutamic acid, aspartic acid and asparagine), 2% lignin, 3% pectins, 4.2-4.4% minerals (2), polyamines (putrescine, spermine, and spermidine), tannins (ca. 9%), B vitamins and traces of niacin. Also 0.005-0.025% theophylline and traces of theobromine (4,5). Roasted coffee beans (medium roast) contain slightly more caffeine (1.3%) than green coffee beans. Content in coffee oil (17%) and minerals (4.7%) also slightly increased, proteins (10%), lignin (2%) and pectins (3%) unchanged. Much lower concentrations of trigonelline (1.0% including roasted by-products), residual chlorogenic acid (2.5%), polysaccharides (33%) and sugars (0.0% sucrose and 0.3% reducing sugars) (2), tannins and polyamines, which are degraded and involved in flavour formation during roasting. Aliphatic acids (1.6%) and quinic acid (0.8%) increased. Caramelized or condensation products amount to 23%, volatile substances to 0.1% (over 700 compounds including carbonyl compounds, alcohols, acids, esters, terpenoid compounds, nitrogen- and sulfur-containing compounds, hydrocarbons, heterocyclic and aromatic compounds). Important flavour contributors out of the over 100 identified aroma compounds are furan derivatives (α -furfurylmercaptane), pyrazines, pyrroles, oxazoles, and acids (6). Furfural (content of 55-80 mg/kg, but also up to 255 ppm reported) and 5-methylfurfural (content of 50-70 mg/kg, but also up to 216 ppm reported) are the carbonyls present in highest concentrations. Methylglyoxal and glyoxal are further important carbonyl compounds, however they are present only in brewed coffee (methylglyoxal: 500-1000 μg/cup assuming 10-12 g roasted coffee per 150 ml of water) and instant coffee (methylglyoxal: 23-990 ppm or 100-150 μg/cup assuming 1.5 g instant coffee for 100 ml water) (2,7). Other

	important carbonyl compounds are 5-hydroxymethylfurfural, acetol, and diacetyl (7). Coffee oil extracted from roasted coffee beans contains mainly glycerides of fatty acids (mainly palmitic and linoleic acid) and 5-8% of unsaponifiable matter, which is rich in diterpenes specific for coffee (total content of 6.54%; 3.58% cafestol, 2.64% kahweol, 0% 16-O-methyl-cafestol, and both traces of cafestolene (0.2%) and kahweolene (0.12%) in the oil), and contains also squalene, n-nonacosane, lanosterol, sitosterol, stigmasterol, methyl-sterols, tocopherols and others (8)
ACTIVE PRINCIPLES	Caffeine
PRODUCTS IN WHICH USED	Coffee extract is widely used as a flavour ingredient in many food products, including alcoholic (e.g. liqueurs) and nonalcoholic beverages, frozen dairy desserts, candy, baked goods, gelatins and puddings, sweet sauces, and milk products (6)
LEVEL OF USE	Seeds, extract: nonalcoholic beverages 4300 ppm, alcoholic beverages 5'000 ppm, frozen dairy 4200 ppm, candy 3000 ppm, baked products 4000 ppm, desserts 2400 ppm, meat products 350 ppm, soups 200 ppm, snacks 1600 ppm. Seeds, dry extract: nonalcoholic beverages 2500 ppm, alcoholic beverages 70 ppm, frozen dairy 500 ppm, candy 100 ppm, desserts 500 ppm. Seeds, alcohol distillate 35 vol%: nonalcoholic beverages 1130 ppm, alcoholic beverages 15000 ppm, frozen dairy 2000 ppm, candy 400 ppm, baked products 8500 ppm, desserts 400 ppm. Seeds, alcohol distillate 85 vol%: nonalcoholic beverages 240 ppm, alcoholic beverages 1600 ppm, frozen dairy 200 ppm, desserts 300 ppm (28)
PREPARATION	Infusion, soft extract, dried extract, tincture (20% in 40 to 70% ethanol), distillate (65% proof alcohol) (1)
MAIN TOXICOLOGICAL DATA	Caffeine at a dose of 1 g or more would produce toxic effects in humans, including headache, nausea, insomnia, restlessness, excitement, mild delirium, muscle tremor, tachycardia, and extrasystoles. The fatal dose in humans is reported to be 10 g for adults and 5.3 g for children (9). It has been suggested that excessive use of caffeine-containing beverages, particularly coffee, influences the risk for coronary heart disease. The question is still open, despite a vast body of research (2). Caffeine has been reported to have mutagenic, teratogenic, and carcinogenic activities (10,11). Although possessing mutagenic properties in bacteria and lower eukaryotes, as well as clastogenic properties at high concentrations in cultured mammalian cells, there is general agreement that caffeine is not mutagenic in higher animals. The mutagenic effects occur only at concentration levels far in excess of those associated with human exposure to the drug (2). Human carcinogenicity data showed no association between caffeine consumption and mortality from cancers at all sites, except for bladder cancer (weak association) (2). To date, it has been concluded that caffeine is not classifiable with regard to its carcinogenicity to humans, due to inadequate evidence for the carcinogenicity in humans and experimental animals (2). The phenolic compounds chlorogenic acid and caffeic acid induce double-strand

DNA breaks, DNA aducts, mutations and chromosome aberrations in a great variety of test systems. On the other hand, they can also suppress the genotoxic activity of numerous carcinogenic compounds in both in vitro and in vivo assays (12). In contrast to earlier reports, chlorogenic acid is considered to have no allergenic properties (13). Some methods of coffee preparation are associated with an elevation in plasma levels of cholesterol and low-density lipoproteins (2). It has been shown that the diterpenes kahweol and cafestol are responsible for the raise in the serum cholesterol in humans. In healthy volunteers, serum cholesterol was increased by 32% after 30 days on a daily intake of 148 mg coffee diterpenes (cafestol and kahweol) (14). Others reported that each 10 mg cafestol consumed per day (corresponding to 2-3 cups of coffee brewed without the use of a paper filter) raises serum cholesterol by 0.15 mmol/l (about 3%) (15). It has been suggested that palmitic acid might also be involved in the hypercholesterolemic effect (8,16). Mutagenic compounds (not specified) are formed during the roasting procedure (17). These compounds have been shown to be mutagenic to bacteria but less to mammalian cells. There are no mutagenic effects in the presence of detoxifying enzymes in *in vivo* situations (18). In vitro experiments demonstrated that more than 50% of the total mutagenic activity of brewed coffee observed can be attributed to the activity of methylglyoxal (7). With respect to human toxicity, coffee and caffeine consumption in moderate to normal amounts is most unlikely to induce mutagenic effects in humans (18). In earlier, mainly epidemiologic studies, coffee drinking has been linked to cancer of the lower urinary tract (bladder) (19), breast (20), ovaries, prostate, (21) and others (22). However, most of these findings have been disputed by later reports (23,24,25,26,27). Final IARC evaluation reported that there is limited evidence for carcinogenicity to the urinary bladder, and that there is evidence suggesting lack of carcinogenicity of coffee to the female breast and the large bowel and inadequate evidence for carcinogenicity to pancreas, ovary and other sites (2)

DATA NEEDED No data required

SPECIFIC OBSERVATIONS The roasted seeds are used as a food ingredient

CLASSIFICATION AND LIMITS **Seeds and preparations: Category 3; limit on caffeine**

NATIONAL/INT. EVALUATION Coffee concentrate, coffee extract (Coffea spp.) and solid coffee extract: GRAS 182.20 (1). Caffeine*:* Labelling of caffeine (limits) regulated by Commission Directive 2002/67/EC. Several countries have national legislation with limits for caffeine in special food categories

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DATA BASES USED

Keywords: Coffea, Coffea arabica, Coffea vulgaris
MEDLINE (1966-1998), EMBASE (1980-1998),
BIOLOGICAL ABSTRACTS (1989-1998),
CC LIFE (2/97-2/98)

SYS NAME **Coffea canephora** Pierre ex Froehner

CE No 148A
STEINMETZ No -
FEMA No -

ORDER Gentianales
FAMILY Rubiaceae

NAME
E Coffee
F Café
D Kaffee
I Caffé

SYNONYMS Coffea robusta Lind. ex De Wild.

PARTS USED Seeds (beans) (1)

IMPORTANT CONSTITUENTS Green coffee beans contain 2.2% caffeine (commercial range 1.5-2.6%; all data on dry basis), 0.7% trigonelline (0.3-0.9%), 10% chlorogenic acids (i.e. phenolic compounds with 60-80% chlorogenic acid or 3-caffeoylquinic acid) (2), 1% caffeic acid and 0.4% quinic acid (3), 1% aliphatic acids, 10% coffee oil (7.4-17%; triglyceride with unsaponifiable fat), 50% polysaccharides (mostly a galactomannan), 4.4% sugars (mainly sucrose and minor amounts of reducing sugars), 11% proteins, 0.8% free amino acids (mainly glutamic acid, aspartic acid and asparagine), 2% lignin, 3% pectins, 4.4% minerals (2), polyamines (putrescine, spermine, and spermidine), tannins (ca. 9%), B vitamins and traces of niacin. Also 0.08-0.35% theophylline and traces of theobromine (4,5).
Roasted coffee beans (medium roast) contain slightly more caffeine (2.4%) than green coffee beans. Content in coffee oil (11%) and minerals (4.7%) also slightly increased, proteins (10%), lignin (2%) and pectins (3%) unchanged. Much lower concentrations of trigonelline (0.7% including roasted by-products), residual chlorogenic acid (3.8%), polysaccharides (37%) and sugars (0% sucrose, 0.3% reducing sugars) (2), tannins and polyamines, which are degraded and involved in flavour formation during roasting. Aliphatic acids (1.6%) and quinic acid (1.0%) increased. Caramelized or condensation products amount to 22.5%, volatile substances to 0.1%. Important flavour contributors out of the over 100 identified aroma compounds are furan derivatives (α-furfurylmercaptane), pyrazines, pyrroles, oxazoles, and acids (6). Furfural (content of 55-80 mg/kg and up to 255 ppm reported) and 5-methylfurfural (content of 50-70 mg/kg and up to 216 ppm reported) are the carbonyls present in highest concentrations. Methylglyoxal and glyoxal are further important carbonyl compounds, however they are present only in brewed coffee (methylglyoxal: 500-1000 μg/cup assuming 10-12 g roasted coffee per 150 ml of water) and instant coffee (methylglyoxal: 23-990 ppm or 100-150 μg/cup assuming 1.5 g instant coffee for 100 ml water) (2,7). Other important carbonyl compounds are 5-hydroxymethylfurfural, acetol, and diacetyl (7). Coffee oil extracted from roasted coffee beans contains mainly glycerides of fatty acids (mainly palmitic and linoleic acid) and 5-8% of unsaponifiable matter, which is rich in

	diterpenes specific for coffee (total content of 3.30%; 1.98% cafestol, 0.12% kahweol, 0.97% 16-O-methyl-cafestol and both traces of cafestolene (0.22%) and kahweolene (0.01%) in the oil) (8), and contains also squalene, n-nonacosane, lanosterol, sitosterol, stigmasterol, methylsterols, tocopherols and others. Levels of 239-250 mg cafestol and 5-8 mg kahweol have been measured per 100 g of green beans of C. canephora (9
ACTIVE PRINCIPLES	Caffeine
PRODUCTS IN WHICH USED	Coffee extract is widely used as a flavour ingredient in many food products, including alcoholic (e.g. liqueurs) and nonalcoholic beverages, frozen dairy desserts, candy, baked goods, gelatins and puddings, sweet sauces, and milk products (6)
LEVEL OF USE	Seeds, extract: nonalcoholic beverages 8600 ppm, alcoholic beverages 9'000 ppm, frozen dairy 9300 ppm, candy 9000 ppm, baked products 12700 ppm, desserts 6700 ppm (10)
PREPARATION	Infusion, soft extract, dried extract, tincture (20% in 40 to 70% ethanol), distillate (65% proof alcohol) (1)
MAIN TOXICOLOGICAL DATA	See Coffea arabica (CE No. 148)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Roasted seeds are used as a food ingredient
CLASSIFICATION AND LIMITS	**Seeds and preparations: Category 3; limit on caffeine**
NATIONAL/INT. EVALUATION	Coffee concentrate, coffee extract (Coffea spp.) and solid coffee extract: GRAS 182.20 (1). Labelling of caffeine (limits) regulated by Commission Directive 2002/67/EC. Several countries have national legislation with limits for caffeine in special food categories

MAIN REFERENCES

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(7) Kasai H. et al., Gann 73: 381 (1982)
(8) Mensink R.P. et al., J. Intern. Med. 237: 543-550 (1995)
(9) DeRoos B. et al., J. Agric. Food Chem. 45: 3065-3069 (1997)
(10) IOFI, results of an iquiry on natural source materials (IOFI circular letter 98/9), CEFS RD 5/8-44 (1999)

DATA BASES USED

Keywords: Coffea, Coffea robusta, Coffea canephora
MEDLINE (1966-1998), EMBASE (1980-1998),
BIOLOGICAL ABSTRACTS (1989-1998),
CC LIFE (2/97-2/98)

SYS NAME	**Crocus sativus** L.
CE No	157
STEINMETZ No	-
FEMA No	Saffron 2998, saffron extract 2999
ORDER	Liliiflorae
FAMILY	Iridaceae
NAME	**E** Saffron **F** Saffran **D** Echter Safran **I** Zafferano
SYNONYMS	Crocus autumnalis Sm., Crocus officinalis Martyn. (1), Crocus orientalis, Crocus hispanicus (2). Varieties (1,3): var. cartwrightianus, var. elwessii, var. hausknechtii, var. orsinii Parl., var. pallasii, var thomasii Ten.
PARTS USED	Stigmas
IMPORTANT CONSTITUENTS	Dried stigmas contain water-soluble dyes such as about 2% crocin 1 (crocetin-di-β-D-gentiobiosylester) and other ester derivatives of the carotinoid crocetin (4) and small amounts of crocin-2 and crocin-3. Bitter monoterpenes such as the glucoside picrocrocin (usually about 2%, up to 4% in freshly dried stigmas) and its aglycone β-hydroxycyclocitral (5). The latter yields safranal (2,2,6-trimethyl-4,6-cyclohexodienal) which gives the characteristic spicy, warm odour of the dried stigmas (6). Safranal is the main constituent (47%) in the 0.4-1.3% essential oil. Other terpene aldehydes comprise for another 35% of the essential oil: Seven constituents were identified as isophorone or isophorone-related compounds (3,5,5-trimethyl-4-hydroxy-1-cyclohexanone-2-ene, 3,5,5-trimethyl -1,4-cyclohexadione, 3,5,5-trimethyl-1,4-cyclohexadion-2-ene, 2,6,6-trimethyl-1-carboxaldehyde-4-hydroxy-1-cyclohexene (13.8% of essential oil, easily converted to safranal in the presence of catalytic amounts of acid) and other trimethyl-cyclohexan derivatives) (7). Saffron contains 10% fatty oil, amino acids, a saponin with oleanolic acid as aglycon and a steroid saponin (8), starch (ca. 13%), heteropolysaccharides (ca. 5.2% pentosan, ca. 6% pectine) and vitamin B_2 (0.01%) (9). Also small amounts of α- and β-pinene, and 1,8-cineole (eucalyptol); furthermore hydroxysafranal, 2-phenyl ethanol, 2-butenoic acid lactone and naphthalene (1,10)
ACTIVE PRINCIPLES	Eucalyptol
PRODUCTS IN WHICH USED	Baked goods, other grains, frozen dairy, condiment relish, meat products, soft candy, hard candy, nonalcoholic beverages, alcoholic beverages (3)
LEVEL OF USE	Saffron: baked goods 970 ppm, other grains 112 ppm, meat products 200 ppm, soft candy 4 ppm, nonalcoholic beverages 0.4 ppm, alcoholic beverages 150 ppm. Saffron extract: baked goods 25 ppm, frozen dairy 19 ppm, condiment/relish 85 ppm, soft candy 20 ppm, hard candy 8 ppm, nonalcoholic beverages 11 ppm, alcoholic beverages 8 ppm (3)

PREPARATION

Dried stigmas, tincture (10% in 80% and also lower strength ethanol) (3)

MAIN TOXICOLOGICAL DATA

Toxic principle is thought to be picrocrocin and its decomposition products (11). No clinical toxic effects reported at doses of up to 1.5 g per day. Heavily toxic at high doses: letal dose for humans 5 to 10 g of dried stigmas (11), abortive dose 10 g (1). Lower doses (from 1.2-2g up to 5 g) induce intoxications with vomiting, bleeding of the uterus, bloody diarrhoe, necrosis and bleeding of nose, lips and eye lids, vertigo, dizziness, yellow colouring of skin and mucous membranes, thrombocytopenia and uremia collapse. Target organ of acute intoxication is the kidney (inflammation, congestion, bleeding) (2,12,13). Mice treated with dimethyl-crocetin did not exhibit hematological or biochemical toxic effects up to 50 mg/kg at repeated doses (14). Saffron extract (10 g dried stigmas in 5 ml solvent) was not mutagenic in the Ames-Test with Salmonella typhimurium TA98 and TA100 with S9-mix (15). Ames-test on S. typhimurium TA1535 with crocin and dimethyl-crocetin up to 4 mg/plate was negative (16). Crocetin has a lipid reducing effect in plasma of laboratory animals; it reduced hyper-cholesterolemia and increases oxygen diffusion in plasma by up to 80% and lowers serum cholesterol levels by ca. 30% in rabbits. Crocetin binds to serum albumin (17,18,19). Ethanolic saffron extract inhibited cellular nucleic acid synthesis in HeLa cells *in vitro* in a dose-dependent manner (IC_{50} 100-150 μg/ml), however, did not affect protein synthesis up to 400 μg/ml (20). Anticancer activity of crocin and dimethyl-crocetin, measured as cytotoxicity (IC_{50} 7-39 μg/ml), has been demonstrated in a wide spectrum of murine tumors *in vivo* and human leukemia cell lines *in vitro* (14,16)

DATA NEEDED

No data required

SPECIFIC OBSERVATIONS

-

CLASSIFICATION AND LIMITS

Saffron: Category 3; limits on eucalyptol
Saffron extract: Category 4; limits on eucalyptol

NATIONAL/INT. EVALUATION

Saffron: CFR 182.10, 582.10, 73.500 (food colour additive); Safron extract: CFR 182.20, 582.20

MAIN REFERENCES

(1) Hager's Handbuch der Pharmazeutischen Praxis, 5th Ed., Haenseler R. et al. (Ed.), Springer Verlag, Berlin (1990)
(2) Wichtl M., Teedrogen. 2nd Ed., WVG, Stuttgart (1989)
(3) Fenaroli (1995)
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(15) Rockwell P., Nutr. Cancer 1: 10-15 (1993)
(16) Nair SC et al. Cancer Biotherapy 10: 257-264 (1995)
(17) Gainer J. and Jones J., Experientia 31: 548 (1978)
(18) Olin B.R, ed., Lawrence Rev. Nat. Prod. (April 1993)
(19) Miller T.L. et al. J. Pharm. Sci. 71: 173 (1982)
(20) Abdullaev F.I. et al., Biofactors 3: 201 (1992)

DATA BASES USED

Keywords: Crocus sativus, saffron
MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Cuminum cyminum** L.
CE No	161
STEINMETZ No	366
FEMA No	-
ORDER	Umbelliflorae
FAMILY	Apiaceae
NAME	**E** Cumin **F** Cumin **D** Kümmel, gewöhnlicher Kümmel, Wiesenkümmel **I** Cumino comune
SYNONYMS	-
PARTS USED	Fruit = seed
IMPORTANT CONSTITUENTS	Essential oil from fruit: terpenic hydrocarbons [α-pinene 0.5-1.3 %; β-pinene 13-20.1 %; γ-terpinene 14-29.5 %; limonene 0.37-0.7 % , myrcene 0.3- 1.1 % , p-cymene 8.5-17.6 %]; aldehydes [cuminaldehyde 32-32.4 %; p-mentha 1,3-diene,7-al 5.6-13 %; perillaldehyde 2.4 %]; alcohols (cuminyl alcohol 2.5-2.8 %; eucalyptol 0.2-0.4 %) (1,2,3)
ACTIVE PRINCIPLES	Eucalyptol
PRODUCTS IN WHICH USED	Baked goods, other grains, meat products, processed vegetables, fats, oils, condiment, relish, soups, snack foods, gravies, frozen dairy, fruit ices, alcoholic and nonalcoholic beverages, candy, seasonings, flavors
LEVEL OF USE	Cumin: baked goods 1900 ppm; other grains 40000 ppm; fats, oils 100 ppm; meat products 2800 ppm; processed vegetables 1200 ppm; condiment, relish 250 ppm; soups 4300 ppm; snack foods 610 ppm; gravies 2800 ppm. Cumin oil: baked goods 1 ppm; other grains 0.2 ppm; fats, oils 0.8 ppm; frozen dairy 0.66 ppm; fruit ices 0.36 ppm; meat products 50 ppm; processed vegetables 50 ppm; condiment, relish 100 ppm; candy 1 ppm; soups 50 ppm; snack foods 200 ppm; nonalcoholic beverages 0.018 ppm; alcoholic beverages 0.48 ppm; gravies 50 ppm; seasonings, flavors 100 ppm (4)
PREPARATION	Infusion, tincture, fluid extract, oleoresin, essential oil
MAIN TOXICOLOGICAL DATA	Cumin oil*:* oral LD50 (rat): 2.5 ml/kg. Distinct phototoxic effects reported for undiluted cumin oil, but none for its principal ingredient, cuminaldehyde (5). Cuminaldehyde: Metabolic studies (6). Cuminyl alcohol: oral LD 50 (rat) : 1.02 g/kg (7). Metabolic studies (6). c-cymene: Metabolism in rats and guinea-pigs (8)
DATA NEEDED	28-day oral study on cuminaldehyde and cuminyl alcohol
SPECIFIC OBSERVATIONS	Cumin seed is a foodstuff
CLASSIFICATION AND LIMITS	**Cumin seed and preparations: Category 5; limits on eucalyptol**

NATONAL/INT. EVALUATION UK FACC 1976, Appendix 2

MAIN REFERENCES

(1) Perfumer & Flavorist, June/July 1976, 1, p.8
(2) J. Agr. Food Chem., 1970, 18, p.234 & p.239
(3) Perfumer & Flavorist, Dec. 1980/Jan. 1981, 5, p.54; Apr/May 1987, 12, p.70; Jan/Feb 1990, 15, p.50; Jan/Feb 1995, 20, p.53
(4) Fenaroli, 1995, 1, p.107
(5) Food Cosmet. Toxicol., 1974, 12, p.869
(6) Scheline, 1991, p.90
(7) Food Cosmet. Toxicol., 1974, 12, p.871
(8) Xenobiotica, 1983, 13, p.503

DATA BASES USED Keywords: Cuminum cyminum, cumin
CHEMICAL ABSTRACTS (- JUNE 1996)

SYS NAME	**Cymbopogon martinii** (Roxb.) W. Wats. var. sofia
CE No	2046
STEINMETZ No	-
FEMA No	-
ORDER	Graminales
FAMILY	Gramineae
NAME	**E** Gingergrass **F** Gingergrass **D** Gingergras **I** -
SYNONYMS	Andropogon schoenanthus var. sofia
PARTS USED	Herb (1)
IMPORTANT CONSTITUENTS	Essential oil (0.1%) contains terpenes (d-α-phellandren, dipentene, d-limonene, d-l-carvon, geraniol, dihydrocumin alcohol, perillalcohol (Hoppe). Cympopogon martinii (Roxb.) W. Wats. var. sofia is grown in East India and Java on wet ground in contrast to Cympopogon martinii Stapf. var. motia (CE No. 40) which is grown in North Africa to East India, Java, Seychelles on dry ground and has more essential oil (0.3-1%) (2)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Essential oil is used in non-alcoholic and alcoholic beverages, frozen dairy, candies, baked goods, desserts, meat products, soups, snacks (1)
LEVEL OF USE	Essential oil of herb: non-alcoholic beverages 15 ppm, alcoholic beverages 68 ppm, frozen dairy 37 ppm, candies 22 ppm, baked goods 15 ppm, desserts 12 ppm, meat product 10 ppm, soups 10 ppm, snacks 10 ppm (1)
PREPARATION	Essential oil of herb (1)
MAIN TOXICOLOGICAL DATA	Geraniol: Not mutagenic in Salmonella typhimurium TA 100 (3). JECFA evaluation: 'No safety concern at current level of intake as flavouring agent' (2003). (+)-Limonene, JECFA ADI 0-1.5 (applies to total intake of limonene. Food additive intake should not exceed 0.075 mg/kg bw per day, which represents 5% of the maximum ADI) (1992)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	For use of essential oil of herb for flavouring purposes no distinction made between the botanical sources Cympopogon martinii (Roxb.) W. Wats. var. sofia and Cympopogon martinii Stapf. var. motia (CE No. 40) (1)
CLASSIFICATION AND LIMITS	**Herb, essential oil: Category 2**
NATIONAL/INT. EVALUATION	-

MAIN REFERENCES

(1) IOFI, Results of an inquiry on natural source materials (circular letter 98/4), RD5/8-43 (Oct. 1998)
(2) Hoppe, H.A. Drogenkunde, 8th Ed., de Gruyter, Berlin, New York (1975)
(3) NTP Technical Report 252 (1987)

DATA BASES USED

Keywords: Cympopogon martinii, gingergrass
MEDLINE (1966-1998), EMBASE (1980-1998),
BIOLOGICAL ABSTRACTS (1989-1998),
CC LIFE (2/97-2/98)

SYS NAME	**Dipteryx odorata** (Aubl.) Willd
CE No	178
STEINMETZ No	406
FEMA No	-
ORDER :	Rosales
FAMILY :	Leguminosae
NAME :	**E** Tonka bean **F** Feve de Tonka **D** Tonkabohne **I** Fava Tonka
SYNONYMS	Coumarouna odorata Aubl
PARTS USED	Fruit (1)
IMPORTANT CONSTITUENTS	Seeds, pentan/dichlormethane extract: >1 mg/kg: coumarin (3.6 g/kg), anethol. 0.1–1 mg/kg: 1-Pentanol, 4-terpineol,1-phenylpropanol, 2-phenylethanol, 2-butanone, hexanal, 2-nonanone, fenchon, nonanal, camphor, salicylaldehyde, carvone, 2-phenethylformate, p-cymen, hexacosan, 2-methylbutanoic acid, hexanoic acid, hexadecanoic acid, octadecanoic acid, linolenic acid, eicosanoic acid, o-hydroxycumaric acid, 2-hydroxyacetophenon(2). Seeds, methanol extract: Coumarin 23-25 g/kg, melilotic acid (o-dihydrocoumaric acid) 4 g/kg, methyl melilotate 0.33 g/kg, ethyl melilotate 0.36 g/kg (3). Tonka bean absolute: coumarin 390-510 g/kg melilotic acid (o-dihydrocoumaric acid) 6-7 g/kg, methyl melilotate 2 g/kg, ethyl melilotate 4 g/kg (3)
ACTIVE PRINCIPLES	Coumarin, camphor
PRODUCTS IN WHICH USED	Alcoholic beverages, ices, candy, baked products and desserts (1)
LEVEL OF USE	Extract: alcoholic beverages 10 mg/kg, candy 60 mg/kg. Absolute (20% coumarin): ices 10 mg/kg, candy 10 mg/kg, baked products 10 mg/kg, desserts 10 mg/kg. Infusion (0,75% coumarin): ices 200 mg/kg, candy 200 mg/kg, baked produkts 200 mg/kg, desserts 200 mg/kg (1)
PREPARATION	Extract, absolute and infusion (1)
MAIN TOXICOLOGICAL DATA	Anethol, JECFA ADI 0-2 mg/kg (51 meeting, 1998) (+)-Carvone, JECFA ADI 0-1 mg/kg (1990, maintained 1998), (-)-Carvone, JECFA ADI 'No safety concern at current levels of intake' (1998)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Fruit and preparations: Category 4; limits on coumarin and camphor**
NATIONAL/INT. EVALUATION	Tonka beans*:* Use of tonka beans and tonka extracts in food is prohibited in the U.S.

MAIN REFERERENCES

(1) IOFI (2000)
(2) Z Lebensm Unters Forsch, 193, 21-25, (1991)
(3) Z Lebensm Unters Forsch, 201, 278-282, (1995)

DATA BASES USED

Keywords: Dipteryx odorata, tonka bean
MEDLINE (1966-1999), TOXLINE (1965-1999), FSTA (1969-1999), ANALYTICAL ABSTRACTS (1980-1998)

SYS NAME	**Eriodictyon californicum** (Hook.et Arn) Tor.
CE No	182
STEINMETZ No	432
FEMA No	Yerba Santa, fluid extract: 31183118
ORDER	Tubiflorae
FAMILY	Hydraphyllaceae
NAME	**E** Santa herb, Yerba Santa, mountain balm, wild balsam, gum bush **F** Herbe de Santa **D** Santakraut, Bärenkraut **I** -
SYNONYMS	E. californica, E. glutinosum, E. glutinosa, E. crassifolium Benth., Eriodictyon crassifolium var. denudatum, Eriodictyon traskiae
PARTS USED	Herb
IMPORTANT CONSTITUENTS	Flavones: 3-4-5-trihydroxy-7-methoxy flavone (41%), eryodictyol, chrysderiol (11.4%), diosmetin, homo-eryodictyol (4.2%),eriodin, eriodionol, 3-5-7-trihydroxy-7-methoxy flavone, 3-5-7-trihydroxy-4-methoxy flavone-luteolin, persicogenin, velutin, tannic acid (1-3),4-5-7-trihydroxy-3-methoxy flavone, pinocembrin, sakuranetin (1-4)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, non-alcoholic beverages, alcoholic beverages
LEVEL OF USE	Yerba Santa, fluid extract: baked goods 500 ppm, frozen dairy 200 ppm, nonalcoholic beverages 60 ppm, alcoholic beverages 90 ppm (7)
PREPARATION	Extract
MAIN TOXICOLOGICAL DATA	Eriodictyol, diosmetin and luteolin are not mutagenic in the Salmonella/mammalian microsome test (5,6)
DATA NEEDED	Chemical composition and, if necessary, 28-day oral study on herb and extract
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Herb and extract, Category 5**
NATIONAL/INT. EVALUATION	Yerba Santa, fluid extract: CFR 172.510; FEMA No. 3118
MAIN REFERENCES	(1) Arch.Biochem.Biophys.32,121,1951; (2) Biochem. Syst. Ecol.13,5,1985; (3) Biochem. Syst. Ecol.11, 211, 1983; (4) J. Nat. Prod., 55, 357, 1992; (5) Biochem. Soc.Trans. 1489,1977; (6) Mut. Res.66,223,1979. (7) Fenaroli, 1995.

DATA BASES USED

Keywords: Eriodictyon californicum, Santa herb, chemical composition, toxicity data
NAPRALERT (1988-2001), CHEMABS(1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001)

SYS NAME	**Gentiana acaulis** L.
CE No	213
STEINMETZ No:	-
FEMA No	-
ORDER	Gentianales
FAMILY	Gentianaceae
NAME	**E** Stemless gentian, dwart gentian **F** Gentiane acaule **D** Stengelloser Enzian, Kochs Enzian **I** Genzianella
SYNONYMS	G. excisa W. D. J. Koch non K. B. Presl, G. kochiana Perr. et Song., Ericoila kochiana (Perr. et Song.) A. et D. Löve; today subdivided in two varieties: G. kochiana Perr. et Song. und G. clusii Perr et Song.
PARTS USED	Herb (1), whole plant (2)
IMPORTANT CONSTITUENTS	No data available on Gentiana acaulis L. Constituents assumed to be similar to other Gentiana ssp., i.e. the bitter secoiridoid glycosides (mainly gentiopicrin, also known as gentiopicroside, gentiamarin; in the whole plant), the acylglycosides of the secoiridoid sweroside: amarogentin, amaropanin and amaroswerin (mainly responsible for bitter taste; in the whole plant), the flavonoids (isoorientin and isovitexin, and their glucosides and/or derivatives; in the leaves), xanthones (mainly gentisin [1,7-dihydroxy-3-methoxyxanthone; also known as gentianin], isogentisin [1,3-dihydroxy-7-methoxyxanthone] and gentisein [1,3,7-trihydroxyxanthone]; in the roots) and high amounts of carbohydrates (mainly monosaccharides; in the roots) (see also Gentiana lutea L. CE No. 214) (3)
ACTIVE PRINCIPLES	Xanthones
PRODUCTS IN WHICH USED	Nonalcoholic beverages, alcoholic beverages, ices, candies, baked goods, gelatin desserts, other products (1, 2)
LEVEL OF USE	Herb, tincture: nonalcoholic beverages 575 ppm, alcoholic beverages 4000 ppm. Herb, essential oil*:* nonalcoholic beverages 10 ppm, alcoholic beverages 60 ppm, ices 60 ppm, candies 690 ppm, baked goods 60 ppm, gelatin desserts 30 ppm and other products 1030 ppm (1). Whole plant, extract: nonalcoholic beverages 250 ppm (2)
PREPARATION	Herb, tincture and essential oil (1); whole plant, extract (2)
MAIN TOXICOLOGICAL DATA	Genotoxicity: positive Rec assay with B. subtilis (water extract of radix from G. lutea L.); positiv Ames test with S. typhimurium TA100 (negative with TA98) with water extract (with and without metabolic activation) and with methanol or ethanol extract (with metabolic activation) (4,5). Mutagenic potential due to the xanthones gentisin and isogentisin, which are responsible for 76% of total mutagenic activity of methanol extract (6). Ames test with isolated xanthones positive with TA100 (+S9) for gentisein, gentisin and isogentisin. Isogentisin showed the

	highest mutagenic activity and was also positive with TA100 (7)
DATA NEEDED	Chemical composition and, if necessary, 28-day oral study on tincture, essential oil and extract
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Whole plant, herb and preparations: Category 5; limits on xanthones**
NATIONAL/INT. EVALUATION	-
MAIN REFERENCES	(1) IOFI, Results of an inquiry on natural source materials, letter to CEFS, September 1997 (2) IOFI, Results of an inquiry on natural source materials, letter to CEFS October 2001 (3) Hagers Handbuch der Pharmazeutischen Praxis, 5th Ed., R. Hänseler, et al. (eds.), Springer, Berlin (1990) (4) Morimoto I. et al., Mutat. Res. 97: 81-102 (1982) (5) Göggelmann W., Schimmer O., Genet. Toxicol. Diet 206: 63-72 (1986) (6) Morimoto I. et al., Mutat. Res. 116: 103-117 (1983). (7) Matsushima T. et al., Mutat. Res. 150: 141-146 (1985)
DATA BASES USED	Keywords: Gentiana acaulis, stemless gentian MEDLINE (1966-1997), EMBASE (1980-1997), TOXLINE (1965-1997), BIOLOGICAL ABSTRACTS (1989-1997)

SYS NAME	**Hamamelis virginiana** L.
CE No	222
STEINMETZ No	537
FEMA No	-
ORDER	Rosalas
FAMILY	Hamamelidaceae
NAME	**E** Witch Hazel **F** Hamamélis **D** Zaubernuss **I** -
SYNONYMS	-
PARTS USED	Leaf (8)
IMPORTANT CONSTITUENTS	Leaf: 3-10% tannins mainly gallotannins, calcium oxalate, 0.01-0.5% volatile oils (2,3,6). The volatile oil contain 9.7% of 2-hexen-1-al, 3.2% acetaldehyde, 3.5% α-ionone, 1% β-ionone and 0.2% safrole (2,3). Hamamelis water or distilled witch hazel: A trace of volatile oil consisting of eugenol, carvacrol. No tannins (6)
ACTIVE PRINCIPLES	Safrole, carvacrol
PRODUCTS IN WHICH USED	Beverages, alcoholic beverages and candy (8)
LEVEL OF USE	Leaf: beverages 5 mg/kg, alcoholic beverages 5 mg/kg, candy 5 mg/kg (8)
PREPARATION	Essential oil (8)
MAIN TOXICOLOGICALDATA	The leaf and the bark may cause irritation of the stomach and may in rare cases give rise to liver damage (2). 10/30 NIH black rat developed malignant fibrous histocytomas after sc. injections of total aqueous extract of witch once a week for up to 72 weeks, but the route of application seems irrelevant for flavouring purposes (4)
DATA NEEDED	Quantitative data on chemical composition and, if necessary, 28-day study and mutagenicity studies on essential oil
SPECIFIC OBSERVATIONS	The leaf and bark have been used for a long time in folk medicine and for external application without any report of poisoning. However, internal application, may, due to effect of the tannins give rise to irritation of the stomach and in rare cases liver damage
CLASSIFICATION AND LIMITS	**Leaf and preparations: Category 5; limits on safrole and carvacrol**
NATIONAL/INT. EVALUATION	-
MAIN REFERENCES	(1) List and Hörhammer 1967-1980 (2) Wichtl 1989 (3) Tyler 1988 (4) Kapadia et al.: Lloydia, 1977, 40, 619-20 (5) Wagner 1980 (6) Leung 1980

(7) Trease and Evans 1989
(8) IOFI (2000)

DATA BASES USED

Keywords: Hamamelis virginiana, witch hazel
MEDLINE (1966-1999), TOXLINE (1965-1999), FSTA (1969-1999), ANALYTICAL ABSTRACTS (1980-1998)

SYS NAME	**Hedeoma pulegioides** (L.) Pers.
CE No	223
STEINMETZ No	540
FEMA No	-
ORDER	Tubiflorae
FAMILY	Labiatae
NAME	**E** American pennyroyal , squawmint, tickweed **F** Menthe pouliot americain **D** Frauenminze, Amerikanische Pennyroyal, Amerikanische Poleiminze **I** -
SYNONYMS	Mentha pulegium
PARTS USED	Herb
IMPORTANT CONSTITUENTS	Essential oil: pulegone (30-80%), menthone, menthofuran, carvone, eucalyptol, 1-methyl-cyclohexan-3-one, geraniol, jasmone, limonene, limonene acetate, menthol, iso-menthone, octan-3-ol, α-pinene, β-pinene, piperitenone, piperitone (1-3)
ACTIVE PRINCIPLES	Pulegone, menthofuran, eucalyptol
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, soft candy, gelatin, pudding, non-alcoholic beverages, alcoholic beverages, hard candy, chewing gum
LEVEL OF USE	Essential oil: baked goods 22 ppm, frozen dairy 5.6 ppm, soft candy 19 ppm, gelatin, pudding 6 ppm, nonalcoholic beverages 6.4 ppm, alcoholic beverages 4.8 ppm, hard candy 2.3 ppm, chewing gum 0.6 ppm. (11)
PREPARATION	Essential oil
MAIN TOXICOLOGICAL DATA	Pennyroyal oil caused acute hepatic and lung damage, at doses of 400 mg/kg ip, in male Swiss-Webster mice. Cellular necrosis was localized to the centrilobular regions of the liver and bronchiolar epithelial cells of the lung (4). A case of massive pennyroyal ingestion, 24 g, by an 18-years-old girl for the purpose of abortion resulted in shock massive hepatic necrosis and death (5). Two additional young woman reported to the same poison center after ingesting approximately 7.5 ml of the oil. Both recovered without apparent overt liver damage (6). Eucalyptol**:** The subacute toxicity studies reported up to now in rats and mice suggested that mice were less susceptible than rats to the toxicity of eucalyptol. In fact, after gavage, the compound was found toxic in male rats at doses higher than 600 mg/kg while no effect was seen in mice up to 1200 mg/kg. However, the limitations and the quality of the study do not allow the extrapolation of a “no effect level” (7). Several reports in rat and brushtail possum show the formation of hydroxylated bicycled products of eucalyptol as main metabolites (8). Furthermore other metabolites which require ring opening have also been detected (9).Following the accidental exposure of human beings, death was reported in two cases after ingestion of 3.5-5 ml of essential eucalyptus oil, but a number of recoveries

	have also been described for much higher amounts of oil (10). (+)-Carvone JECFA ADI 0-1 mg/kg bodyweight (1990, maintained 1998). (-)-Carvone JECFA ADI 'no safety concern at current level of use' (1998). (+)-Limonene JECFA ADI not specified (1993)
DATA NEEDED:	28-day oral study and mutagenicity studies on essential oil
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Herb and essential oil: Category 5; limits on pulegone, menthofuran, eucalyptol**
NATIONAL/INT. EVALUTATION:	Pulegone and menthofuran: SCF (July 2, 2002)*:* The Commission noted that only a limited studies were available on pulegone and menthofuran, and considered that these data were inadequate for the derivation of an ADI. The Committee requires for pulegone and menthofuran a 90-day studies together with further studies on genotixicity. Moreover the Committee recommends that industry should provide better usage levels and analytical data on concentrations in relevant products in order to refine the intake estimates to be used in risk assessment. Eucalyptol: SCF: The available toxicological studies are limited and inadequate to derive an ADI. However, the available animal data do not indicate a cause of concern associated with the daily intake from food including hard candies estimated from the small amount of information available. For more precise risk characterisation further data on exposure and toxicity would be needed. American pennyroyal (Hedeoma pulegioides L.) oil**:** CFR 172.510
MAIN REFERENCES:	**(**1) J.Liq.Chromatogr. 6, 1175, 1983 (2) J.Pharm. Sci. 53, 1008, 1964 (3) J.Pharm.Sci.53,1407,1964 (4) Toxicol. Appl. Pharmacol. 65, 413, 1982 (5)Lancet 2, 580, 1961 (6) J. Amer. Med. Assoc. 242, 2873, 1979 (7) National Toxicological Program, April 1987 (8) Bull. Environ. Contam. Toxicol. 37, 759, 1986 (9) Xenobiotica, 10, 17, 1980; (10) Aust. Amm. Med. 4, 23, 1965 (11) Fenaroli, 1995
DATA BASES USED:	Keywords: Hedeoma pulegioides, pennyroyal, chemical composition, toxicity data NAPRALERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001)

SYS NAME	**Hyssopus officinalis** L.
CE No	235
STEINMETZ No	577
FEMA No	Hyssop: FEMA No.2589 Hyssop, extract : FEMA No. 2590 Hyssop, oil*:* FEMA No. 2591
ORDER	Tubiflorae
FAMILY	Labiatae
NAME	**E** Hyssop **F** Hysope **D** Ysop **I** Issopo
SYNONYMS	-
PARTS USED	Flowers, flower tips, herb, leaves
IMPORTANT CONSTITUENTS	Herb and leaves essential oil: pinocamphone (44.7%), methyleugenol (0.09-3.8%), estragole (4.8%), iso-pinocamphone (32%), α-pinene (7.3%), β-pinene (22%), α--terpinene (9.4%), camphene, myrcene, limonene (2.4%), cis-β-ocymene, α-3-carene, pinocamphene, α-caryophyllene, allo-aromadendrene, α-humulene, β-cadinene, cis-calama-nene, β-elemene, germacrene D, α-cadinene, bicyclogermacrene, α-cadinene, pinocampheol (1.1%), α-terpineol, myrtenol, linalool, methyl-myrtenol, nerolidol, spathulenol, trans-cadinol, pinocarvone, hydroxy-2-isopinocamphone, thujone (tr),nonanoic acid, myrtenic acid, pinic acid, pinonic acid,methyl myrtenate, myrtenyl acetate, terpinyl acetate, bornyl acetate, carvacrol, eucalyptol, hesperedin, hyssopin, tannin (1-4)
ACTIVE PRINCIPLES	Estragole, methyleugenol, eucalyptol, thujone, carvacrol
PRODUCTS IN WHICH USED	Alcoholic beverages, soft candy, baked goods, non-alcoholic beverages, chewing gum
LEVEL OF USE	Hyssop: alcoholic beverages 600 ppm. Hyssop extract: soft candy 300 ppm, alcoholic beverages 300 ppm. Hyssop oil: baked goods 16.5 ppm, soft candy 12.7 ppm, gelatin, pudding 30 ppm, nonalcolic beverages 8 ppm, alcoholic beverages 37ppm, chewing gum 0.4 ppm. (13)
PREPARATION	Extract, oil
MAIN TOXICOLOGICAL DATA	Commercial preparations of essences of hyssop have caused poisoning of human beings and were found to possess a convulsant action of central origin in rats. The neurotoxicity of hyssop appears to be related to the presence of two terpene ketones, pinocamphone and isopinocamphone, the former of which has powerful convulsant properties, and is lethal at doses above 0.05 ml/kg (5-8). Eucalyptol: The subacute toxicity studies reported up to now in rats and mice suggested that mice were less susceptible than rats to the toxicity of eucalyptol. In fact, after gavage, it was found toxic in male rats at doses higher than 600 mg/kg while no effect was seen in mice up to 1200 mg/kg. However, the limitations and the quality of the study do not allow the extrapolation of a “no effect level” (9). Several reports in rat and brushtail

	possum show the formation of hydroxylated bicycled products of eucalyptol as main metabolites (10). Furthermore, other metabolites which require ring opening have also been detected (11). Following the accidental exposure of human beings, death was reported in two cases after ingestion of 3.5-5 ml of essential eucalyptus oil, but a number of recoveries have also been described for much higher amounts of oil (12). (+)-Limonene JECFA ADI not specified (1993). Linalool JECFA group ADI 0-0.5 mg/kg bodyweight (1998)
DATA NEEDED	Chemical composition of flower and flower tips and, if necessary, 28-day oral study and mutagenicity studies. 28-day oral study on essential oil from herb and leaves
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Herb, leaves, flower, flower tips and preparations: Category 5; limits on estragole, methyleugenol, eucalyptol, thujone, carvacrol**
NATIONAL/INT. EVALUATION	Thujone: SCF: The Committee considered the available data inadequate to establish a TDI/ADI, but noted that some of the deficiensis in the database were being addressed in ongoing NTP studies and recommended that the results of these should be reviewed where available. Moreover the Committee does not consider it appropriate to use thujone as a chemically identified flavouring substance. Finally the Committee noted that the consumption of as much a 1 litre of an alcoholic beverage containing 5 mg/l, would result in an intake of about 0.08 mg thujone/Kg b.w. for a 60 Kg adult. This intake is about 100 times lower than the NOEL derived from a 14 week study in rats. Estragole and methyleugenol: SCF: have been demonstrated to be genotoxic and carcinogenic. Therefore the existence of a threshold cannot be assumed and the Committee could not establish a safe exposure limit. Consequently, reductions in exposure and restrictions in use levels are indicated. Eucalyptol: SCF: Available toxicological studies are limited and inadequate to derive an ADI. However, the available animal data do not indicate a cause of concern associated with the daily intake from food including hard candies estimated from the small amount of information available. For more precise risk characterisation further data on exposure and toxicity would be needed. Hyssop**:** CFR 182.10, 582.10; Hyssop, extract **:** CFR 182.20, 582.10; Hyssop, oil: CFR 182.20, 582.20
MAIN REFERENCES	(1) Riv. Ital. EPPOS 58, 129, 1976 (2) Egypt. J. Pharm.Sci.19, 177, 1978 (3) Parfuem. Kosmet. 67, 118, 1986 (4) Dev. Food Sci.18, 171, 1988 (5) Clin. Toxicol. 18, 1485, 1981 (6) Plant. Med. Phytoter., 14, 34, 1980 (7) Rev. E.E.G. Neurophysiol., 9, 12, 1979 (8) J. Neurol., 246, 667,1999 (9) National Toxicological Program, April 1987;

MAIN REFERENCES (contin.)

(10) Bull. Environ. Contam. Toxicol. 37,759, 1986
(11) Xenobiotica, 10, 17, 1980
(12) Aust. Amm. Med. 4, 23, 1965
(13) Fenaroli, 1995

DATA BASES USED

Keywords: Hyssopus officinalis, hyssop, chemical composition, toxicity data
NAPRALERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001)

SYS NAME	**Iris florentina** L.
CE No	241
STEINMETZ No	-
FEMA No	Orris concrete, liquid, oil: 2829, Orris root, extract: 2830
ORDER	Liliiflorae
FAMILY	Iridaceae
NAME	**E** Florentine orris, orris **F** Iris de Florence **D** (Florentiner) Schwertlilie **I** Giglio bianco, lirio de Florencia
SYNONYMS	Iris germanica var. florentina Dykes, I. florentina auct. vix L.
PARTS USED	Rhizomes, roots (peeled, after two years of aging) (1)
IMPORTANT CONSTITUENTS	Rhizomes contain 0.5% (of fresh weight) monocyclic and bicyclic triterpenes (= iridales, C_{31}) of which are >10% iriflorental, 1-10% iso-iridogermanal, traces (<1%) of 21-desoxyiridogermanal and iripallidal (2). Essential oil of buttery consistency (yield 0.1-2%) contains 75% myristic acid and to less extent oleic acid, methylmyristate and other esters (3). Furthermore, the ketones α-, β- and γ-irone ($C_{14}H_{22}O$) which are formed during storage by oxidative degradation of triterpenes; furthermore ionone, methylmyristate, oleic acid and esters. Isoflavones (irifloside, iridine, irisflorentine, irigenine, iristectorigenin, irisolone, iriflophenone) (4), C-glucosylxanthones (demethylirisxanthone, irisxanthone, magniferin, isomagniferin, 3,6-irisxanthone-dimethylether) (5) and phenolic compounds (acetovanillon [=apocynine], piceol, protocatechuic acid, sinapic acid) isolated from fresh rhizomes (5)
ACTIVE PRINCIPLES	Xanthones
PRODUCTS IN WHICH USED	Nonalcoholic beverages, alcoholic beverages, frozen dairy, candy, baked goods, desserts (6), chewing gum (1)
LEVEL OF USE	Roots concrete: nonalcoholic beverages 10 ppm, alcoholic beverages 1 ppm, frozen dairy 20 ppm, candy 30 ppm, baked goods 30 ppm, desserts 10 ppm. Roots essential oil: nonalcoholic beverages 2 ppm, alcoholic beverages 5 ppm, frozen dairy 5 ppm, candy 10 ppm, baked goods 10 ppm, desserts 10 ppm. Roots absolute: nonalcoholic beverages 1 ppm, frozen dairy 1 ppm, candy 1 ppm, baked goods 1 ppm, desserts 1 ppm. Roots infusion: nonalcoholic beverages 40 ppm, alcoholic beverages 200 ppm, frozen dairy 90 ppm, candy 50 ppm, baked goods 50 ppm, desserts 50 ppm (6). Concrete, liquid, oil: chewing gum 9 ppm. Root extract: chewing gum 4 ppm (1)
PREPARATION	Orris root, concrete, absolute, infusion (6). Derivatives: fluid extract, concrete and absolute essence, resinoid, and tincture (20% in 50 to 60% ethanol or 30% in 55% ethanol) (1)
MAIN TOXICOLOGICAL DATA	See Iris germanica L. (CE No. 243)

DATA NEEDED Chemical composition and, if necessary, 28-day oral study and mutagenicity studies on preparations

SPECIFIC OBSERVATIONS Of the various species Iris pallida Lam. is the best for extractive purposes, followed by I. germanica and I. florentina of which all are used as botanical sources of orris preparations (concrete, liquid, oil, root extract) (1)

CLASSIFICATION AND LIMITS **Rhizomes, roots and preparations: Category 5; limits on xanthones**

NATIONAL/INT. EVALUATION Orris, root, extract*:* CFR 172.510

MAIN REFERENCES

(1) Fenaroli (1995)
(2) Krick W. et al., Z. Naturforsch. C. 38: 179-184 (1983).
(3) BHP 83
(4) Arisawa M. et al., Chem. Pharm. Bull. 20: 2323-2328 (1973)
(5) Fujita M., Inoue T., J. Pharm. Soc. Jpn. 101: 1118-1121 (1981)
(6) IOFI, Results of an inquiriy on natural source materials (circular letter 99/7), CE CEFS RD 5/1-46 (2000)

DATA BASES USED Keywords: Iris florentina, Orris
MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Iris germanica** L.
CE No	243
STEINMETZ No:	-
FEMA No	Orris concrete, liquid, oil: 2829, Orris root, extract: 2830
ORDER	Liliiflorae
FAMILY	Iridaceae
NAME	**E** Garden iris, German flag, blue flower de Luce, German iris **F** Fleur-de-lis, iris d'Allemagne, iris flambé **D** Deutsche Schwertlilie, blaue Lilie **I** Fior di S. Marco, giaggiolo, giglio pavonazzo
SYNONYMS	Iris deflexa Knowles. et Westc., I. violacea Salvi, I. vulgaris Pohl
PARTS USED	Rhizomes, roots (peeled, after two years of aging) (1)
IMPORTANT CONSTITUENTS	Dried orris roots contain 0.2-0.4% Iris essential oil of buttery consistency ('orris butter', 'orris concrete'), flavonoids and isoflavones (irilone, irisolidone [5,7-dihydroxy-4,6'-dimethoxyisoflavone], irisolone, irigenin, tectoridin, homotectoridin, tectorigenin, dihydroquercetin-7,3'-dimethylether etc.) (2,3); 18 bicyclic and monocyclic triterpenes (iridals and cycloiridales) and their esters with iridogermanal (iridal) and α- and γ-irigermanal (cycloiridales) as major extractable lipids of rhizomes (1% of fresh weight) identified as irone precursors in fresh rhizomes (4,5,6); 20-50% starch (irisin) (7). No information on content in xanthones. Orris concrete ('orris butter'; yield 0.2-0.4%) contains 5-20% irones ($C_{14}H_{22}O$) formed during storage by oxidation from C_{31}-triterpenoids and responsible for the characteristic flavour (61.5% *cis*-α-irone, 0.8% *trans*-α-irone, 36.7% *cis*-γ-irone, 0% *trans*-γ-irone, 1.0% β-irone of total irones). The low content of trans-α-irone is typical for Iris germanica *L.* (6,8,9). In addition, twenty irone-related compounds containing 10 to 16 C-atoms identified in commercial 'orric concrete' of Moroccan origin (I. germanica) (9). Other, earlier reported ketones such as acetophenone, acetovanillon [4-hydroxy-3-methoxyacetophenone], acetoveratrone (3,7). Furthermore, 83-95% free or partially esterified fatty acids (e.g. mainly myristic acid, also palmitic acid, caprylic acid, lauric acid, pelargonic acid), terpene and sesquiterpene alcohols, aldehydes, esters (8). Orris absolute (alcoholic extraction or distillation of concrete, yield of 0.03-0.04% of dried rhizomes) contains 55-85% ketones (irones); esters (methylmyristate, methylcaprylate, methyllaurate, methyl-oleate, methyllinoleate), aldehydes (oleic, benzoic), alcohols (benzylic) and other ketones (acetophenone, acetovanillon) (8). Orris resinoid (yield 1-3.3%) contains 62-78% ketones (irones) (1,8)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Nonalcoholic beverages, alcoholic beverages, frozen dairy, candy, baked goods, desserts (10), chewing gum (1)

LEVEL OF USE

Roots concrete: nonalcoholic beverages 10 ppm, alcoholic beverages 1 ppm, frozen dairy 20 ppm, candy 30 ppm, baked goods 30 ppm, desserts 10 ppm. Roots essential oil: nonalcoholic beverages 2 ppm, alcoholic beverages 5 ppm, frozen dairy 5 ppm, candy 10 ppm, baked goods 10 ppm, desserts 10 ppm. Roots absolute: nonalcoholic beverages 1 ppm, frozen dairy 1 ppm, candy 1 ppm, baked goods 1 ppm, desserts 1 ppm. Roots infusion (extract): nonalcoholic beverages 40 ppm, alcoholic beverages 200 ppm, frozen dairy 90 ppm, candy 50 ppm, baked goods 50 ppm, desserts 50 ppm (10). Orris concrete, liquid, oil: chewing gum 9 ppm. Orris root, extract: chewing gum 4 ppm (1)

PREPARATION

Orris root, concrete, absolute, infusion (10). Derivatives: fluid extract, concrete and absolute essence, resinoid, and tincture (20% in 50 to 60% ethanol or 30% in 55% ethanol) (1)

MAIN TOXICOLOGICAL DATA

The isoflavone irigenin (5,7,3'-triydroxy-6,4',5'-trimethoxy-isoflavone) inhibited beef heart cyclic AMP phospho-diesterase *in vitro* (IC_{50} $1.1x10^{-5}$ M), showed an inihibitory effect on barium sulfate transport in the small intestine in mice *in vivo* and exerted cholinergic activity with effects on blood pressure and heart rate in rats (11). An aqueous extract (not further specified) was reported to reduced the activity of the smooth muscles *in vivo* and to have a musculotroph spasmolytic effect at the jejunum *in vitro* and *in vivo* (12). Fresh rhizomes are locally irritating and gastrointestinal irritation and nausea occurs after ingestion (7). Orris absolute was not skin irritating, sensitizating or phototoxic in humans and animals (13). Allergic reactions upon skin contact to dermal products containing dried rhizome are possible in sensitive persons (7). Benzyl alcohol, JECFA ADI 0-5 mg/kg bw (1979)

DATA NEEDED

Further data on chemical composition, ie presence of xanthones, and, if necessary, 28-day oral study and mutagenicity studies on preparations

SPECIFIC OBSERVATIONS

Of the various species Iris pallida Lam. is the best for extractive purposes, followed by I. germanica and I. florentina of which all are used as botanical sources of orris preparations (concrete, liquid, oil, root extract) (1)

CLASSIFICATION AND LIMITS

Rhizomes, roots and preparations: Category 5

NATIONAL/INT. EVALUATION

Orris, root, extract*:* CFR 172.510

MAIN REFERENCES

(1) Fenaroli (1995)
(2) Dhar K.L., Kalla A.K., Phytochemistry 11: 3097-3098 (1972); 12: 734-735 (1973)
(3) Pailer M., Franke F., Monatsh. Chem. 104: 1394-1408 (1973)
(4) Marner F.J. et al. J. Org. Chem. 47: 2531-2536 (1982)
(5) Marner F.J., Kerp B. Z. Naturforsch. 47c: 21-25 (1992)
(6) Krick W., Helv. Chim. Acta 67, 318-324 (1984)

(7) Hagers Handbuch der Pharmazeutischen Praxis, 5th ed., Suppl. Vol. 3, W. Blaschek et al. (eds.), Springer, Berlin (1998)
(8) Fusi P. Fitoterapia 48: 51-59 (1977)
(9) Maurer et al. Helv. Chim. Acta 72: 1400-1415 (1989).
(10) IOFI, Results of an inquiriy on natural source materials (circular letter 99/7), CE CEFS RD 5/1-46 (2000)
(11) Nikaido R., Planta Med. 46, 162-166 (1982).
(12) Cahen R., Trav. Soc. Pharm Monpellier 31: 325-334 (1971)
(13) Opdyke D.L.J, Food Cosmet. Toxicol. 13: 895-896 (1975)

DATA BASES USED

Keywords: Iris germanica, orris
MEDLINE (1966-1999), EMBASE (1980-1999),
BIOLOGICAL ABSTRACTS (1989-1999),
CC LIFE (6/97-6/99)

SYS NAME	**Iris pallida** Lam.
CE No	244
STEINMETZ No:	-
FEMA No	Orris concrete, liquid, oil: 2829, Orris root, extract: 2830
ORDER	Liliiflorae
FAMILY	Iridaceae
NAME	**E** White flag, orris **F** Iris **D** Blasse Schwertlilie **I** Giaggiolo odoroso
SYNONYMS	Iris glauca Salisb., I. odoratissima Jacq., I. pallidocaerulea Pers.
PARTS USED	Rhizomes, roots (peeled, after two years of aging) (1)
IMPORTANT CONSTITUENTS	Rhizomes contain up to 1% (of fresh weight) (2) monocyclic and bicyclic triterpenes (= iridales, C_{31}). Eighteen iridals and cycloiridales isolated (3) of which are >10% iripallidal, 1-10% iso-iridogermanal and α-irigermanal, traces (<1%) of desoxy-iripallidal (2,4). Iridals in the rhizomes and roots also esterified with long-chained fatty acids such as myristic acid, palmitic acid and stearic acid (4). Furthermore, isoflavones (iridine, iriflophenone, irigenin, irisflorentine, iristectorigenin B) (4). Essential oil of buttery consistency (*Iris* oil, 'orris butter', 'orris concrete') with constituents similar to Iris germanica (CE No. 243). The characteristically smelling irones (total of 0.035-0.079% in dried rhizome; 34% *cis*-α-irone, 5% *trans*-α-irone, 61% *cis*-γ-irone of total irones) are formed during storage from the iridales (5). No information on the content in xanthones
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Nonalcoholic beverages, alcoholic beverages, frozen dairy, candy, baked goods, desserts (6), chewing gum (1)
LEVEL OF USE	Roots concrete: nonalcoholic beverages 10 ppm, alcoholic beverages 1 ppm, frozen dairy 20 ppm, candy 30 ppm, baked goods 30 ppm, desserts 10 ppm. Roots essential oil: nonalcoholic beverages 2 ppm, alcoholic beverages 5 ppm, frozen dairy 5 ppm, candy 10 ppm, baked goods 10 ppm, desserts 10 ppm. Roots absolute: nonalcoholic beverages 1 ppm, frozen dairy 1 ppm, candy 1 ppm, baked goods 1 ppm, desserts 1 ppm. Roots infusion (extract): nonalcoholic beverages 40 ppm, alcoholic beverages 200 ppm, frozen dairy 90 ppm, candy 50 ppm, baked goods 50 ppm, desserts 50 ppm (6). Orris concrete, liquid, oil: chewing gum 9 ppm. Orris root, extract: chewing gum 4 ppm (1)
PREPARATION	Orris root, concrete, absolute, infusion (6). Derivatives: fluid extract, concrete and absolute essence, resinoid, and tincture (20% in 50 to 60% ethanol or 30% in 55% ethanol) (1)
MAIN TOXICOLOGICAL DATA	See Iris germanica L. (CE No. 243)

DATA NEEDED

Further data on chemical composition, ie presence of xanthones, and, if necessary, 28-day oral study and mutagenicity studies on preparations

SPECIFIC OBSERVATIONS

Of the various species Iris pallida Lam. is the best for extractive purposes, followed by I. germanica and I. florentina of which all are used as botanical sources of orris preparations (concrete, liquid, oil, root extract) (1)

CLASSIFICATION AND LIMITS

Rhizomes, roots and preparations: Category 5

NATIONAL/INT. EVALUATION

Orris, root, extract*:* CFR 172.510

MAIN REFERENCES

(1) Fenaroli (1995)
(2) Krick W. et al., Z. Naturforsch. C. 38: 179-184 (1983).
(3) Marner F.J., Kerp B. Z. Naturforsch. 47c: 21-25 (1992)
(4) Bicchi C., Rubiolo P., Phytochem. Anal. 4: 171-177 (1993)
(5) Bicchi C., Rubiolo P., Flavour Fragr. J. 8: 261-267 (1993)
(6) IOFI, Results of an inquiriy on natural source materials (circular letter 99/7), CE CEFS RD 5/1-46 (2000)

DATA BASES USED

Keywords*:* Iris pallida, orris
MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Leptospermum citratum** Chall.
CE No	260
STEINMETZ No	-
FEMA No	-
ORDER	Myrtiflorae
FAMILY	Myrtaceae
NAME	**E** Lemon tea-tree **F** - **D** Zitronenmyrte, Zitronenteebaum **I** -
SYNONYMS	L. petersonii FM Bailey, L. flavescens var. citratum
PARTS USED	Leaves
IMPORTANT CONSTITUENTS	Essential oil*:* 50-80 % citral, 35 % citronellal, grandifloron (ß-triketon), geraniol. (1, 2, 4). The oil was found to occur n several chemical varieties. One variety contained aldehydes ranging from high citronellal and low neral/geranial to low citronellal and high neral/geranial. Two oil chemotypes comprising mainly hydrocarbons were identified. One chemotype contained mainly mono-terpenes, while another contained mainly sesquiterpenes with either β-caryophyllene or globulol/viridiflorol/ spathulenol as major components. Another chemotype contained 21-38% geranyl acetate and 21-29% geraniol. (5)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Beverages, alcoholic beverages, candy, ice cream, baked products, soups, snacks. (6)
LEVEL OF USE	Beverages: 177 ppm. Alc. Beverages: 200 ppm. Candy dessert and ice cream: 500 ppm. Baked products: 265 ppm. Soups and snacks: 30 ppm (6)
PREPARATION	Essential oil
MAIN TOXICOLOGICAL DATA	Citral JECFA group ADI 0-0,5 mg/kg bodyweight (2003)
DATA NEEDED	Chemical composition and, if necessary, 28-day oral study and mutagenicity studies on leaves and essential oil
SPECIFIC OBSERVATIONS	Steam distillation yields 0,8-1,5 % essential oil. Note that the species Lemon tea-tree should not be confused with Tea-tree, Melaleuca alternifolis Cheel, which yields tea-tree oil
CLASSIFICATION UND LIMITS	**Leaves and preparations: Category 5**
NATIONAL/INT. EVALUATION	Citral: CE No. 109, Cat. A, part I Blue Book, 4 th Edition 1962
MAIN REFERENCES	**(**1) CRC Crit. Rev. Toxicol. 5, 189 (1977) (2) Hoppe: Drogenkunde Verlag de Gruyter (1975) (3) Rehm, S.: Kulturpflanzen der Tropen,Verlag Ulmer (1976)

(4) Gildemeister, E.: Ätherische Öle, Akademie Verlag (1959)
(5) Flav Fragr J, 15(5), 342-351 (2000)
(6) IOFI (1998)

DATA BASES USED

Keywords : Leptospermum citratum
RTECS, MEDLINE, TOXBIO, BIOSIS, SCISEARCH, TOXCAS, TOXLINE, EMBASE, TSCA (1970 – 1999), PUB MED, DIALOG FOOD (–2004)

SYS NAME	**Lippia citriodora** (Ort.) H.B.K.
CE No	264
STEINMETZ No	662
FEMA No	-
ORDER	Tubiflorae
FAMILY	Verbenaceae
NAME	**E** Lemon verbena, lemonscented verbena **F** Verveine odorante, verveine citronnée **D** Zitronenstrauch, echte Verbene **I** Cedrina, verbena
SYNONYMS	Lippia citriodora (Cav.) Kunth, Lippia triphylla sic, Aloysia citriodora Ort., A. triphylla Britton, Verbena triphylla L'Her. (O. Kuntze)
PARTS USED	Herb, leaves
IMPORTANT CONSTITUENTS	Herb and leaves essential oil*:* citral (35%), eucalyptol (12-15%), l-limonene (3.7-18.5%), linalool (1.3%), neral (6.9%), geraniol (9.9%), α-curcumene (4.6%), caryophyllene oxide (5.5%), citronal, 5-hydroxy-6,7,4' trimethoxyflavone (salvigenin), 5,3'-dihydroxy-6,7,4'-trimethoxyflavone (eupatorin), 5,7,3',4'-tetrahydroxy-6-methoxyflavone (eupafolin), 6-hydroxyluteolin, luteolin, luteolin-7-O-beta-D-glucoside, nepetin, 4',5,7-trihydroxy-6-methoxyflavone (hispidulin), 4',5-dihydroxy-6,7-dimethoxyflavone (cirsimaritrin), diosmetin, diosmetin-7-O-glucoside, chrysoeriol, apigenin, apigenin-7-O-glucoside, 5,7-dihydroxy-6,4'-dimethoxyflavone (pectolin-arigenin), 5,3',4'-trihydroxy-6,7-dimethoxyflavone (cirsiliol), caryphyllene-2,6-β-oxide, caryophyllene, caryophyllene epoxide, iso-caryophyllene, iso-caryophyllene epoxide, 2,5-dimethyl-2-vinyl-4-hexenal, , kubosone, trans-limonene epoxide, nerol epoxide, perillen, photocitral A, photocitral B, epi-photocitral A, trans,trans-photocitral, photonerol A, epi-photonerol A, photonerol B, cis-rose oxide, rosefuran (1-10)
ACTIVE PRINCIPLES	Eucalyptol
PRODUCTS IN WHICH USED	The leaves are used for flavouring beverages, dessert, fruit salads and jellies, for seasoning food and in herbal teas
LEVEL OF USE	-
PREPARATION	Fluid extract, tincture, concrete and absolute (15)
MAIN TOXICOLOGICAL DATA	Apigenin and diosmetin are not mutagenic in the Salmonella/mammalian microsome test. (11). Eucalyptol: The subacute toxicity studies reported up to now in rats and mice suggested that mice were less susceptible than rats to the toxicity of eucalyptol. In fact, after gavage, it was found toxic in male rats at doses higher than 600 mg/kg while no effect was seen in mice up to 1200 mg/kg. However, the limitations and the quality of the study do not allow the extrapolation of a “no effect level” (12). Several reports in rat and brushtail possum show the formation of hydroxylated bicycled products of eucalyptol as main

	metabolites (13). Furthermore other metabolites that require ring opening have also been detected (14). Following the accidental exposure of human beings, death was reported in two cases after ingestion of 3.5-5 ml of essential eucalyptus oil, but a number of recoveries have also been described for much higher amounts of oil (16). Citral, linalool JECFA group ADI 0-0.5 mg/kg b.w. (1998). (+)-Limonene JECFA ADI not specified (1993)
DATA NEEDED	Preparations used and level of use. 28-day oral study on relevant preparations
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Herb, leaves and preparations: Category 5; limit on eucalyptol**
NATIONAL/INT. EVALUATION	Eucalyptol: SCF: The available toxicological studies are limited and inadequate to derive an ADI. However, the available animal data do not indicate a cause of concern associated with the daily intake from food including hard candies estimated from the small amount of information available. For more precise risk characterisation further data on exposure and toxicity would be needed. CFR 172.510 (in alcoholic beverages only)
MAIN REFERENCES	**(**1) Helv. Chim. Acta 59, 1797, 1976 (2) Helv. Chim. Acta 59, 1803, 1976 (3) Helv. Chim. Acta 59, 1802, 1976 (4) Phytochemistry 367, 1971 (5) Planta Med. 54, 465, 1988 (6) “The Wealth of India” 6, 142, 1962 (7) J. Agr. Food. Chem., 47, 4579, 1999 (8) J. Essent. Oil Res., 8, 581, 1996 (9) J. Essent. Oil Res., 6, 523, 1994 (10) J. Essent. Oil Res., 8, 471, 1996, 11 Mut. Res. 75, 243, 1980 (12) National Toxicological Program, April 1987 (13) Bull. Environ. Contam. Toxicol. 37,759, 1986 (14) Xenobiotica, 10, 17, 1980; 16. Aust. Amm. Med. 4, 23, 1965 (15) Fenaroli, 1995
DATA BASES USED	Keywords: Lippia citriodora, vervain, chemical composition, toxicity data NAPRALERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PAASCAL (1973-2001)

SYS NAME	**Liquidambar styraciflua** L.
CE No	265
STEINMETZ No	664
FEMA No	Storax: 3036. Storax extract: 3037
ORDER	Rosales
FAMILY	Hamamelidaceae
NAME	**E** Sweetgum, redgum, American storax, storax **F** Copalme d'Amérique, styrax **D** Amerikanischer Amberbaum, Kaugummibaum, Satinnussbaum, Styrax **I** Storace
SYNONYMS	Styrax
PARTS USED	Exudate (2)
IMPORTANT CONSTITUENTS	Balsam (Storax)*:* 5-10% Styracin (cinnamoyl cinnamate), 5-10% free cinnamic acid, 33-50% resin (mainly cinnamic esters), vanillin, styrene and styrocamphene (1)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Exudate extract: ices,candy, baked products and desserts. Exudate resinoid: beverages, alcoholic bev-erages, ices, candy, baked products and desserts (2)
LEVEL OF USE	Exudate extract: ices 0.5 mg/kg, candy 0,. mg/kg, baked products 0.5 mg/kg, desserts 0.5 mg/kg. Exudate resinoid: beverages 2 mg/kg, alcoholic beverages 5 mg/kg, ices 5 mg/kg, candy 10 mg/kg, baked products 20 mg/kg, desserts 5 mg/kg (2
PREPARATION	Extract and resinoid (2)
MAIN TOXICOLOGICAL DATA	Vanilin JECFA ADI 0-10 mg/kg bw (1967)
DATA NEEDED	Level of use of exudate extract and resinoid. Quantitative chemical composition of preparations and, if necessary, 28-day oral study and mutagenicity studies
SPECIFIC OBSERVATIONS :	Another botanical source of Storax preparations is Liqudambar orientalis Mill. (Asian or levant storax)
CLASSIFICATION AND LIMITS	**Exudate and preparations: Category 5**
NATIONAL/INT. EVALUATION	-
MAIN REFERENCES	(1) Fenaroli (1995) (2) IOFI (2000)
DATA BASES USED	Keywords: Liquidambar styraciflua, Storax MEDLINE (1966-1999), TOXLINE (1965-1999), FSTA (1969-1999), ANALYTICAL ABSTRACTS (1980-1998)

SYS NAME	**Litsea cubeba** (Lour.) Pers.
CE No	491
STEINMETZ No	-
FEMA No	-
ORDER	Magnoliales
FAMILY	Lauraceae
NAME	**E** Mountain spice tree, mountain pepper **F** - **D** - **I** -
SYNONYMS	-
PARTS USED	Fruits
IMPORTANT CONSTITUENTS	Essential oil*:* lauric acid (34,8-75,4 %); citral (70 %); citronellol (11,9-20,4 %); citronellal (7,7-10 %); methylheptanone (20 %); decanonic acid (=capric acid); carvone; cymene; 1,4-cineole; hexanal; limonene; linalool; sabinene; ß-phellaandrene; α- and ß-pinene (1, 2, 3, 4, 5, 6, 7)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Beverages, icecream, candy, baked products, desserts, meat products, soups, snacks
LEVEL OF USE	Essential oil*:* beverages 7 ppm, icecream 14 ppm, candy 25 ppm, baked products 93 ppm, desserts 3 ppm, meat products 2 ppm, soups 1 ppm, snacks 10 ppm (IOFI 2000)
PREPARATION	Essential oil
MAIN TOXICOLOGICAL DATA	Citral, citronellol, linalool JECFA group ADI 0-0.5 mg/kg bodyweight (1998). (+)-Carvone JECFA ADI 0-0.1 mg/kg bodyweight (1998). Limonene JECFA ADI not specified (1993). Effective insecticide found in seed oil (9)
DATA NEEDED	28-day oral study and mutagenicity studies on essential oil from fruit
SPECIFIC OBSERVATIONS	Steam distillation yields essential oil, tangkallag-fat, from fruits (36%) and seeds (50 %) (2)
CLASSIFICATION UND LIMITS	**Fruit and preparations: Category 5**
NATIONAL/INT. EVALUATION	-
MAIN REFERENCES	**(**1) CRC Crit. Rev. Toxicol. 5, 189 (1977) **(**2) Hoppe: Drogenkunde, de Gruyter (1975) (3) Gildemeister: Ätherische Öle, Akademie (1959) (4) Y. Nat. Prod. 56, 1971-1976 (1993) et 59, 80-82 (5) Acta Botanica Sinica 25, 245-249 (1983) (6) J. Ess. Oil Res. 10, 381-386 (1998) (7) J. Ess. Oil Res. 8, 575-576 (1998) (8) Fd. Chem. Toxicol. 20, (Suppl.), 731 (1982) 9 (9) Mabberley, The Plant Book 2nd ed., Cambridge Universitey Press (1997)

DATA BASES USED	Keywords: Litsea cubeba RTECS, MEDLINE, TOXBIO, BIOSIS, SCISEARCH, TOXCAS, TOXLINE, EMBRASE, TSCA (1970 – 1999)

SYS NAME	**Malva sylvestris** L.
CE No	268
STEINMETZ No	690
FEMA No	-
ORDER	Malvales
FAMILY	Malvaceae
NAME	**E** High mallow **F** Grande mauve **D** Wilde Malve, Käsepappel **I** Malva
SYNONYMS	M. Mauretania L., M. erecta C.Presl., M. ambigua Guss., Althaea silvestris Alef.
PARTS USED	Flower tips, leaves (5)
IMPORTANT CONSTITUENTS	Anthocyanglucoside malvin and malvidin, sterculic acid, mucilages and tannic substances (1, 2, 3, 7, 8). Gossypetin-3-glucoside-8-glucoronide, hypolaetin 4-methylether-8-glucoronide (6). Leaves contain 8-O-glucosides of hypolaetins and isoscutullareins as well as gossypetin-3-O-glucoside. The presence of flavonoide sulphate is notable (9). Flowers contain anthocyanins, mainly malvin, 6''-malonylmalvin and delphinidin. Traces of coumarin (9)
ACTIVE PRINCIPLES	Coumarin
PRODUCTS IN WHICH USED	Beverages, candy
LEVEL OF USE	Flower extract: beverages 5 ppm, candy 250 ppm. Leaf extract: beverages 250 ppm, candy 1300 ppm. (IOFI 2000)
PREPARATION	Extract
MAIN TOXICOLOGICAL DATA	No data available
DATA NEEDED	28-day oral study and mutagenicity studies on extracts from leaves and flowers
SPECIFIC OBSERVATIONS	Herb is used for tea (folk medicine) 1,5-2 g/cup (4). Other uses are as food colour (1). Hydroalcoholic and glycolic extracts are used for flavouring purposes
CLASSIFICATION UND LIMITS	**Flowers, leaves and extract: Category 5; limits on coumarin**
NATIONAL/INT. EVALUATION	-
MAIN REFERENCES	(1) Hoppe: Drogenkunde, de Gruyter (1975) (2) Gessner: Gift- und Arzneipflanzen, Winter (1974) (3) Lindner: Toxikologie der Nahrungsmittel, Thieme (1986) (4) Wichtl: Teedrogen, WVG (1989) (5) Mc Guffin: Botanical safety handbook, CRC-Press (1997) (6) Phytochemistry 30, 987-990 (1991) (7) Phytochemistry 28, 499-500 (1989)

(8) J. Pharmaceut. Biomed. Analys. 14, 203-211 (1995)
(9) Teedrogen und Phytopharmaka, Wichtl, 4th ed, Wissenschaftliche Verlagsgesellschaft mbH Stuttgart (2002)

DATA BASES USED

Keywords : Malva sylvestris, mallow
RTECS, MEDLINE, TOXBIO, BIOSIS, SCISEARCH, TOXCAS, TOXLINE, EMBASE, TSCA (1970 – 1999), PUB MED (–2004)

SYS NAME	**Marrubium vulgare** L.
CE No	71
STEINMETZ No	695
FEMA No	Horehound, extract*:* 2581
ORDER	Tubiflorae
FAMILY	Labiatae
NAME	**E** Horehound, hoarhound, white hoarhound **F** Marrube blanc **D** Weisser Andorn **I** Marrobio bianco
SYNONYMS	Marrubium album sic, Marrubium hamatum Kunth.
PARTS USED	Herb, leaves
IMPORTANT CONSTITUENTS	Herb and leaves extract: bitter sesquiterpenes marrubiin (0.9%) and pre-marrubiin (0.15%), diterpene alcohols (marrubenol, marrubiol, peregrinol, vulgarol, phytol), flavonoids (apigenin, apigenin-7-O-glucoside, luteolin, luteolin-7-O-d-glucoside, quercetin-3-O-α-L-rhamnosyl-glucoside, iso-quercitrin), small amounts of pyrrolidine alkaloids (betonicine, stachydrine), traces of volatile oil (α-pinene, sabinene, camphene, tricyclene, p-cymole, limonene, fenchene, α-terpinolene (2.9%), isomenthon-8-thiol), alkaloids, ursolic and caffeic acid, gallic acid, tannins, choline (0.2%), β-sitosterol, β-bisabolol, β-elemene (1-7).
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, soft candy, gelatin, pudding, non-alcoholic beverages, alcoholic beverages, hard candy
LEVEL OF USE	Horehound (hoarhound) extract: baked goods 162 ppm, frozen dairy 9 ppm, soft candy 730 ppm, gelatin, pudding 29 ppm, nonalcoholic beverages 13 ppm, alcoholic beverages 255 ppm, hard candy 6200 ppm. (9)
PREPARATION	Extract and tincture
MAIN TOXICOLOGICAL DATA	Marrubiin exhibits antispasmodic and antinociceptive effects in mice (8). Limonene JECFA ADI not specified (1993)
DATA NEEDED	28-day oral study and mutagenicity studies on extracts
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Herb, leaves and preparations: Category 5**
NATIONAL/INT. EVALUATION	Horehound: CFR 182.10, 582.10. Horehound, extract: CFR 182.20, 582.20. Horehound, solid, extract: CFR 182.20, 582.20
MAIN REFERENCES	(1) Planta Med.55,105,1989 (2) Boll. Chim. Farm.105,787,1966 (3) Khim. Prir. Soedin. 4,345,1968

(4) Herba Pol.24,184,1978
(5) J. Pharm. Sci. 53, 895,1964
(6) Boll. Chim. Farm. 86,56,1947
(7) J.Chem.Soc.C.15,2014,1969
(8) Phytomedicine, 7, 111, 2000
(9) Fenaroli, 1995

DATA BASES USED:

Keywords: Marrubium vulgare, white hoarhound, chemical composition, toxicity data
NAPRALERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001)

SYS NAME	**Melaleuca leucadendron** (L.) L.Mant.
CE No	276
STEINMETZ No	701
FEMA No	Cajeput oil: 2225
ORDER	Myrtiflorae
FAMILY	Myrtaceae
NAME	**E** Cajeput **F** Cajeput **D** Cajeput **I** Cajeput
SYNONYMS	M. leucadendra (L.) L.
PARTS USED	Leaves
IMPORTANT CONSTITUENTS	Essential oil: 1 % in leaves: 50-70 % eucalyptol, pinene, limonene, dipentene, terpineole, sesquiterpene (1,2). Essential oil: 1.3% in leaves: 14-27% eucalyptol, terpineol, nerolidol and pinene (6). Essential oil is found in a range of 1.20-1.58% in leaves with a seasonal variation, content increasing from February to May and decreasing slightly in November. The oil was composed of 19 main components, representing 97.1 % of the oil. Eucalyptol was the main constituent, 64.3%, followed by α-terpineol, 11%, limonene, 6.7%, α-pinene, 4.2%, valencene 3.9%, β-pinene, 1.7%, ledol 1.2%, terpinene-4-ol, 0.8%, β-myrcene 0.6%, γ-terpinene 0.6%. The following components were found in an amount of 0.3% or less, p-cymene, benzaldehyde, γ-terpineol, 1-tetradecene, β-eudesmol, trans-pinene hydrate, terpinolene, α-eudesmol and linalool (7). Indonesian cajeput oil: α-thujen 0.6 %; α-pinene 4.3 %; β-pinene 2.7 %; myrcene 0.9 %; p-cymene 2.3 %; eucalyptol 65.2 %; γ-terpinene 1.9 %; terpineole 6.9 %; β-caryophyllene (4). Methyleugenol (5). Fruit: Chloroform extract contained 6 known triterpenoids; betulinic acid, acetyl betulinic acid, betulinaldehyde, pyracrenic acid, ursolic acid, ursolaldehyde, and one known sesquiterpene, globulol. From methanol extract the following compounds were isolated; quercetin, gallic acid, a phenolic stilbene piceatannol, a stilbene oxyresveratrol, and a dimeric stilbene scirpusin B (10)
ACTIVE PRINCIPLES	Methyleugenol, eucalyptol
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, meat products, condiment, soft candy, non-alcoholic beverages
LEVEL OF USE	Cajeput oil: baked goods 9,9 ppm; frozen dairy 1 ppm; meat products 3 ppm; condiment 2 ppm; soft candy 9,5 ppm; nonalcoholic beverages 2 ppm (3)
PREPARATION	Essential oil
MAIN TOXICOLOGICAL DATA	The essential oil possessed antimicrobial and antiviral activity when tested against B. subtiles, E. coli, Aspergillus niger and Candida albicans as well as Herpes simplex virus type 1 (7). Limonene JECFA ADI not specified (1993)
DATA NEEDED	28-day study and mutagenicity studies on essential oil

SPECIFIC OBSERVATIONS

The herb is also used in cosmetics. Other Melaleuca species are also used as botanical sources of cajeput oil. There are several Melaleuca species and varieties that may be confused with one another. According to some authors M. cajuputi Powell is another species than M. leucadendron, but according to others a synonym. Sometimes 'cajeput oil' is used synonymous to 'tea tree oil' . The main commercial source for tea tree oil is M. alternifolia (Maiden & Betche) Cheel, but other Melaleuca species may be used, i.e. also M. linariifolia Smith (8). Tea tree oil is said to contain less eucalyptol than cajeput oil, but a high amount of terpinen-4-ol. According to an Australian standard tea tree oil should contain at least 30% terpinen-4-ol and not exceed 15% eucalyptol (9)

CLASSIFICATION UND LIMITS

Leaves and essential oil: Category 5

NATIONAL/INT. EVALUATION

Cajeput : CFR 172.510

MAIN REFERENCES

(1) Hoppe: Drogenkunde, de Gruyter (1975)
(2) Gildemeister: Ätherische Öle, Akademie Verlag (1961)
(3) Fenaroli, CRC-Press (1995)
(4) Dt. Apoth. Ztg. 50, 53-62 (1999)
(5) Flavour Fragrance J. 3, 43-46 (1988)
(6) Hagers Handbuch der Pharmazeutischen Praxis, 4th ed., Springer, Berlin (1975)
(7) Phytother. Res. 18, 30-35 (2004)
(8) Teedrogen und Phytopharmaka, Wichtl, 4th ed, Wissenschaftliche Verlagsgesellschaft mbH Stuttgart (2002)
(9) Clin Tox 33(2), 193-4 (1995)
(10) Chem Pharm Bull 39(12), 3276-3278 (1991)

DATA BASES USED

Keywords : Melaleuca leucadendron, Cajeput
RTECS, MEDLINE, TOXBIO, BIOSIS, SCISEARCH, TOXCAS, TOXLINE, EMBASE, TSCA (1970 – 1999), PUB MED (–2004)

SYS NAME	**Melaleuca linariifolia** Smith
CE No	277
STEINMETZ No	-
FEMA No	-
ORDER	Myrtiflorae
FAMILY	Myrtaceae
NAME	**E** Paperbark tea-tree, flax-leaf paperbark, „Snow in Summer“ **F** - **D** - **I** -
SYNONYMS	M. linariifolia var. alternifolia (possibly hybrid population) (3, 4), Metrosideros hyssopifolia
PARTS USED	Leaves, twigs
IMPORTANT CONSTITUENTS	Essential oil: 1.2-2 % in leaves: α- and β-terpinene, p-cymol, terpinen-1-ol (1), phenols, eucalyptol (0.06-1.23% in leaves), sesquiterpenes (0.09-0.12% in leaves), terpenes (0.67-0.90% in leaves), sesquiterpenalcohols, sabinene, trans- and cis-sabinene hydrates, p-menthane, gamma-terpinene, terpinen-4-ol (0.55-0.74% in leaves), terpinolene (0.06-0.075% in leaves), α-pinene (0.015-0.02% in leaves), β-pinene (0.015-0.02% in leaves), α-thujene (0.015-0.02% in leaves), myrcene (0.015-0.02% in leaves), p-cymene (0.015-0.02% in leaves), melalilol (1,2,7)
ACTIVE PRINCIPLES	Eucalyptol
PRODUCTS IN WHICH USED	Soups
LEVEL OF USE	Essential oil: soups 5 ppm (8)
PREPARATION	Essential oil
MAIN TOXICOLOGICAL DATA	No data available
DATA NEEDED	Quantitative chemical composition, 28-day oral study, mutagenicity studies on essential oil
SPECIFIC OBSERVATIONS	The herb is also used in cosmetics and dental medicine. Note that there are several Melaleuca species and varieties that may be confused with one another. The main commercial source for tea tree oil is M. alternifolia (Maiden & Betche) Cheel but other Melaleuca species may be used, i.e. also M. linariifolia Smith (5). According to an Australian standard tea tree oil should contain at least 30% terpinen-4-ol and not exceed 15% eucalyptol (6). See also CE No. 276, Melaleuca leucadendron
CLASSIFICATION UND LIMITS	**Herb and essential oil: Category 5**
NATIONAL/INT. EVALUATION	-
MAIN REFERENCES	(1) Gildemeister: Ätherische Öle, Akademie Verlag (1961) (2) Phytochemistry 29, 3529-3534 (1990) (3) Plant System. Evolut. 194, 69-81 (1995) (4) J. Agric. Food. Chem. 37, 1330-1335 (1989)

(5) Teedrogen und Phytopharmaka, Wichtl, 4th ed, Wissenschaftliche Verlagsgesellschaft mbH Stuttgart (2002)
(6) Clin Tox 33(2), 193-4 (1995)
(7) Duke, James A. 1992. Handbook of phytochemical constituents of GRAS herbs and other economic plants. Boca Raton, FL. CRC Press
(8) IOFI, 2000

DATA BASES USED

Keywords : Melaleuca linariifolia
RTECS, MEDLINE, TOXBIO, BIOSIS, SCISEARCH, TOXCAS, TOXLINE, EMBASE, TSCA (1970 -1999)

SYS NAME	**Melissa officinalis** L.
CE No	280
STEINMETZ No	703
FEMA No	Balm: 2111 Balm leaves extract: 2112 Balm oil: 2113
ORDER	Tubiflorae
FAMILY	Labiatae
NAME	**E** Melissa, balm, lemon balm **F** Melisse **D** Zitronenmelisse **I** Melissa, cedronella
SYNONYMS	-
PARTS USED	Flower, flower tips, herb
IMPORTANT CONSTITUENTS	Herb essential oil: β-myrcene (0.12%), limonene (tr), cis-ocimene (0.13%), β-ocimene:trans (4.6%), octan-3-one (tr), p-cymene (tr); hept-5-en-2-one,6-methyl (0.6%), rose oxide,cis (0.12%); rose oxide, trans (tr); hex-3-en-1-ol,cis (0.16%), octan-3-ol (0.65%), oct-1-en-3-ol (0.65%), citronellal (23%), α-copaene (0.55%), iso-geranial (0.27%), β-bourbonene (0.12%), α-cubebene (0.86%), linalool (tr), citronellic acid methyl ester (2.2%), iso-pulegol (0.5%), β-elemene (0.3%), β-caryophyllene (10%), β-farnesene-trans (0.41%), humulene (0.72%), β-guaiaene (tr), neral (10%), geranic acid methyl ester (0.12%), D-germacrene (10.5%), α-muurolene (tr), bicyclogermacrene (tr), geranial (16.3%); trans-3-trans-6-α-farnesene (in shoots), geraniol acetate (0.9%), δ-cadinene (1.3%), β-citronellol (2.1%), χ-cadinene (2.1%), nerol (1.21%), α-cadinene (tr), geraniol (3.4%); farnese,allo:cis-2-trans-4-trans-6 (tr); β-caryophyllene-oxide (0.17%), humulene oxide (tr), germacra-trans-1(10)-trans-5-dien-4-ol (2.3%), T-cadinol (0.11%), T-muurolol (tr), δ-cadinol (tr), α-cadinol (0.36%), citronellic acid (tr). Dried leaves and flowering tips essential oil: β-elemene, geraniol, nerolidol, cis-ocymene, trans-ocymene, hept-1-en-3-ol; 6-methy-hept-5-en-2-onel; nonanal, pinocamphone, α-copanene, α-cubebene, α-bisabolene, β-cubebene, χ-elemene, β-cedrene, calarene, β-cadinene, α-cadinol, apigenin-7-O-β-d-glucoside, dehydroabietane, benzyl alcohol, α-cadinene, caffeic acid (2100 ppm), β-caryophyllene (29%), chlorogenicacid (1.9%), citronellal (2.2%), α-copaene (1.9%), p-coumaric acid (8.3 ppm), α-cubebene (0.1%), β-phenylethanol, geranial (17.3%), iso-geranial (0.4%), geranic acid, geraniol acetate, α-humulene (2.1%), linalool, luteolin-7-β-glucoside, myrcene, neral (11%), neric acid, nerol, octylbenzoate (2.6%), iso-quercitrin, rhamnocitrin, rosmarinicacid (1.15%), thymol, limonene, pulegol, iso-pulegol, trans-β-ocymene, α-terpineol, β-elemene, methyleugenol, damascenone, eugenol, neryl acetate, β-curcumene, germacrene D, β-selinene, α-murolene, δ-cadinene, δ-cadinol, α-copaene (1-8)
ACTIVE PRINCIPLES	Methyleugenol

PRODUCTS IN WHICH USED	Baked goods, frozen dairy, soft candy, gelatin, pudding, non-alcoholic beverages, alcoholic beverages
LEVEL OF USE	Balm leaves extract: baked goods 5000 ppm, frozen dairy 800 ppm, soft candy 3000 ppm, gelatin, pudding 3000ppm, nonalcoholic beverages 3000 ppm, alcoholic beverages 3000 ppm. Balm oil: baked goods 17 ppm, frozen dairy 5 ppm, soft candy 112 ppm, gelatin, pudding 112 ppm, nonalcoholic beverages 13 ppm, alcoholic beverages 15 ppm (10)
PREPARATION:	Essential oil, extract
MAIN TOXICOLOGICAL DATA:	β-Myrcene was not cytotoxic and mutagenic in V79 cells and in mammalian cells in vitro. However, is has antimutagenic properties (9). Methyleugenol evaluated as active principle by CoE. Citral (neral + geranial), citronellal, linalool, geranyl acetate:JECFA group ADI 0.5 mg/Kg bodyweight (1998). Eugenol JECFA ADI 0-2.5 mg/kg b.w./day (1982)
DATA NEEDED	Chemical composition of flower and, if necessary, 28-day oral study and mutagenicity studies on relevant preparations from flower
SPECIFIC OBSERVATIONS	The essential oil (very little known and of limited production) can yield good results in the formulation of compounded oils for liqueurs
CLASSIFICATION AND LIMITS	**Flower and preparations: Category 5** **Herb and preparations: Category 2** **Flower tips and preparations: Category 4; limit on methyleugenol**
NATIONAL/INT. EVALUATIONS:	Methyleugenol: SCF: Methyleugenol has been demonstrated to be genotoxic and carcinogenic. Therefore the existence of a threshold cannot be assumed and the committee could not establish a safe exposure limit. Consequently, reductions in exposure and restrictions in use levels are indicated. Balm: CFR 182.10, 582.10. Balm Leaves: CFR 182.10, 582.10. Balm leaves extract: CFR 182.20, 582.20. Balm oil: CFR 182.20, 582.20
MAIN REFERENCES	**(**1) Planta Med. 46, 91, 1982 (2) Pharm. Acta Helv. 63, 266, 1988 (3) Pharm. Acta Helv. 62, 19, 1987 (4) Pharm. Acta Helv. 60, 276, 1985 (5) Planta Med. Phytoter. 15, 149, 1981 (6) J. Pharm. Pharmacol. 38, 791, 1986 (7) Z. Lebensm Unters Forsch. 171, 193, 1980 (8) Z. Lebensm-Unters Forsch. 176, 116, 1983 (9) Environ. Mol. Mut., 18, 28, 1991 (10) Fenaroli, 1995
DATA BASES USED:	Keywords: Melissa officinalis L., Melissa, Balm, chemical composition, toxicity data NAPRALERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001).

SYS NAME	**Menyanthes trifoliata** L.
CE No	287
STEINMETZ No	-
FEMA No	-
ORDER	Gentianales
FAMILY	Menyanthaceae
NAME	**E** Buckbean, marsh trefoil, bogbean **F** Ményanthe, trèfle d'eau, trèfle des marais **D** Bitterklee, Fieberklee **I** Trifoglio fibrino, scarfano, trifoglio di palude
SYNONYMS	Menyanthes palustris Tourn, Trifolium palustre Bauh., T. castoris Thal, T. fibrinum Tab., T. palustre Dod.
PARTS USED	Leaves (harvested during the flowering season) (1)
IMPORTANT CONSTITUENTS	Leaves contain bitter secoiridoid glycosides (1%) with dihydrofoliamenthin as main component, the secoiridoid glycosides menthiafolin and swerosid as well as the iridoid loganin have been reported as minor constituents. The earlier reported presence of foliamenthin (2) has been disputed (3). Further constituents of the leaves are small amounts of tannins (1-7%), the flavonoids hyperosid (0.4-1.2%), rutosid (0.3-0.9%), and trifolin, the triterpenes and sterols lupeol, β-amyrenol, betulin, betulinic acid (0.1-0.8%) and α-spinasterol (0.07%), the coumarins scopoletin (6-methoxy-7-hydroxycoumarin), coumarin (α-benzopyrone) and the derivatives braylin (6-methoxyseselin) and scoparone (6,7-dimethoxycoumarin), and the terpenoid lactone loliolide (4), several phenolic acids (mainly bound caffeic acid) (2,5). Furthermore 1% menyanthine (melianthine), menyanthol and 0.067% essential oil (6). The monoterpene alkaloids gentianin and gentianidin are probably artefacts (7)
ACTIVE PRINCIPLES	Coumarin
PRODUCTS IN WHICH USED	Alcoholic beverages (bitters) (1,8)
LEVEL OF USE	No data available (8)
PREPARATION	Fluid extract, tincture (20% in 20% ethanol) (1)
MAIN TOXICOLOGICAL DATA	Preparations may irritate the stomach. High doses are purgative and may cause vomiting (2). Oral intake (medical treatment of anorexia or dyspepsia) of infusions prepared with 0.5-2.0 g of dried leaves per cup with daily doses of 1.5-3.0 g dried drug are tolerated without adverse effects (2)
DATA NEEDED	Use levels
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Leaves and preparations: Category 5; limits on coumarin**
NATIONAL/INT. EVALUATION	Buck bean, leaves and extract: CFR 172.510 (in alcoholic beverages only) (1)

MAIN REFERENCES

(1) Fenaroli (1995)
(2) Hagers Handbuch der Pharmazeutischen Praxis, 5th Ed., Suppl. 3, Blaschek W. et al. (Eds.), Springer, Berlin (1998)
(3) Junior P., Planta Med., 55, 83-8 (1989)
(4) Adamczyk U. et al., Plant. Méd. Phytothér. 24 : 73-78 (1990)
(5) Swiatek L. et al., Planta Med. 52: 530 (1986)
(6) Hoppe H.A., Drogenkunde, 8th Ed., de Gruyter, Berlin (1975)
(7) Wichtl M., Teedrogen, 2nd Ed., WVG, Stuttgart (1989)
(8) IOFI, Results of an inquiry on natural source materials, personal communication with CEFS (1998)

DATA BASES USED

Keywords: Menyanthes trifoliata, buck bean, marsh trefoil, bogbean
MEDLINE (1966-1998), EMBASE (1980-1998), BIOLOGICAL ABSTRACTS (1989-1998), CC LIFE (2/97-2/98)

SYS NAME	**Myroxylon balsamum** (L.) Harms
CE No	297
STEINMETZ No	741
FEMA No	3069(extract), 3070 (gum)
ORDER	Rosales
FAMILY	Leguminosae
NAME	**E** Tolu balsam **F** Baume de tolu **D** Tolubalsam **I** Balsamo del tolu
SYNONYMS	
PARTS USED	Exudate (4)
IMPORTANT CONSTITUENTS	Hexane soluble portion of balsam, ~ 32%: cinnamic acid ~20%, benzoic acid ~10%, eugenol, vanilin, benzyl ferulate, benzaldehyde, benzyl alcohol, ethyl benzoate, cinnamaldehyde, cinnamyl alcohol, methyl cinnamate, ethyl cinnamate, benzyl benzoate, benzyl cinnamate, cinnamyl benzoate, α-pinene, styrene, cis-ocimene, p cumene, α-bourneone, α-copaene, β-bourneone,, β-elemene, caryophyllene, α-curcumene, γ-muurolene, α-muurolene, β-selinene, δ-cadiene, α-cadiene, calamenene, α-calacorene, cadalene, 1,2-diphenylethane (1,2)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Beverages, alcoholic beverages, ices, candy, baked products and desserts (4)
LEVEL OF USE	Exudate resinoid: beverages 2 mg/kg, alcoholic beverages 8 mg/kg, ices 10 mg/kg, candy 15 mg/kg, baked products 20 mg/kg, desserts 10 mg/kg. Exudate essential oil: beverages 1 mg/kg, alcoholic beverages 2 mg/kg, ices 4 mg/kg, candy 4 mg/kg, baked products 10 mg/kg, desserts 4 mg/kg. Exudate absolute: beverages 1 mg/kg, alcoholic beverages 2 mg/kg, ices 4 mg/kg, candy 4 mg/kg, baked products 6 mg/kg, desserts 4 mg/kg (4)
PREPARATION	Resinoid, essential oil and absolute (4)
MAIN TOXICOLOGICAL DATA	Benzoic acid, JECFA ADI 0-5 mg/kg bw (1983). Benzaldehyde, JECFA ADI 0-5 mg/kg bw (1967). Benzyl alcohol, JECFA ADI 0-5 mg/kg bw (1979). Benzyl benzoate, JECFA ADI 0-5 mg/kg bw (1979). Vanilin, JECFA ADI 0-10 mg/kg bw (1967). Eugenol, JECFA ADI 0-2.5 mg/kg bw (1982)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Exudate and preparations: Category 2**
NATIONAL/INT. EVALUATION	-

MAIN REFERENCES

(1) J. Assoc. Off. Anal. Chem. 63, 1195 (1980)
(2) Perfumer and Flavorist 2, 56 (1977)
(3) Fenaroli (1995)
(4) IOFI (2000)

DATA BASES USED

Keywords: Myroxylon balsamum, tolu balsam
MEDLINE (1966-1999), TOXLINE (1965-1999), FSTA (1969-1999), ANALYTICAL ABSTRACTS (1980-1998)

SYS NAME	**Myroxylon balsamum** (L.) Harms var pereirae
CE No	298
STEINMETZ No	742
FEMA No	2116, 2117(oil)
ORDER :	Rosales
FAMILY	Leguminosae
NAME :	**E** Peru balsam **F** Beaume de Perou **D** Perubalsam **I** Balsamo del Peru
SYNONYMS	-
PARTS USED	Exudate (3)
IMPORTANT CONSTITUENTS	Peru balsam oi): Benzyl benzoate 65%, benzyl cinnamate 25%, benzoic + cinnamic acid 10-12%, nerolidol + farnesol 9%, vanilin 1%, cinnamyl cinnamate, methyl benzoate, methyl cinnamate, peruviol, cinnamyl alcohol.(1,2,34)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Beverages, alcoholic beverages, ices, candy, baked products and desserts (3)
LEVEL OF USE	Exudate essential oil: beverages 1 mg/kg, alcoholic beverages 2 mg/kg, ices 4 mg/kg, candy 4 mg/kg, baked products 6 mg/kg, desserts 4 mg/kg. Exudate resinoid: beverages 5 mg/kg, alcoholic beverages 8 mg/kg, ices 7 mg/kg, candy 10 mg/kg, baked products 30 mg/kg, desserts 30 mg/kg. Exudate absolute: beverages 3 mg/kg, alcoholic beverages 3 mg/kg, ices 3 mg/kg, candy 3 mg/kg, baked products 3 mg/kg, desserts 3 mg/kg. Exudate extract: beverages 5 mg/kg, alcoholic beverages 5 mg/kg, ices 4 mg/kg, candy 10 mg/kg, baked products 10 mg/kg, desserts 10 mg/kg (IOFI 2000)
PREPARATION	Essential oil, resinoid, absolute and extract (5)
MAIN TOXICOLOGICAL DATA	Benzyl benzoate, JECFA ADI 0-5 mg/kg bw (1979). Vanilin, JECFA ADI 0-10 mg/kg bw (1967). Benzoic acid, JECFA ADI 0-5 mg/kg bw (1983)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Exudate and preparations: Category 2**
NATIONAL/INT EVALUATION	-
MAIN REFERENCES	**(**1) Fenaroli (1995**)** (2) J. Chromatogr. 623, 395 (1992) (3) Guenther E., The essential oils, Vol. 5, p. 217, Huntigton, New York, R.E.Krieger Publ Comp 1975 (4) Freidel H.D., Ueber Peru- und Tolubalsam – neue Sesquiterpen Kohlenwasserstoffe aus Tolubalsam. Diss, Univ. Marburg 1986 (5) IOFI (2000)

DATA BASES USED	Keywords used: myroxylon balsamum, peru balsam. MEDLINE (1966-1999), TOXLINE (1965-1999), FSTA (1969-1999), ANALYTICAL ABSTRACTS (1980-1998)

SYS NAME	**Myrrhis odorata** (L.) Scop
CE No	299
STEINMETZ No	743
FEMA No	-
ORDER	Umbelliflorae
FAMILY	Apiaceae
NAME	**E** Sweet chervil, sweet cicely **F** Cerfeuil musqué **D** Wohlriechende Süssdolde, Spanische Kerbel **I** Finocchiella
SYNONYMS	-
PARTS USED	Aerial parts, root, fruit
IMPORTANT CONSTITUENTS	Fruit essential oil: alkenylbenzenes [mainly *trans*-anethole 76-85 %; methyleugenol, estragole 1.2-1.7%]; terpenic hydro-carbons [limonene 0.3-3.5 %; β-caryophyllene] (1,2). Leaf essential oil: *trans*-anethole 82-85 %; terpenic alcohols [α- and/or γ-terpinol 3.5-3.9%; terpinene-4-ol 0.3-0.6%; elemol 1.4-2.2%]; terpenic hydrocarbons [myrcene 0.3-1.9 %; γ-terpinene 0.2-0.8 %; longifolene 0.9-2.1 %; β-caryo-phyllene 1.0-1.7 %; β-bisabolene 1.1-1.7%; alloaroma-dendrene and/or germacrene D 2.0-2.9%; γ-muurolene and/ or β-selinene 0.8-1.9 %) (3)
ACTIVE PRINCIPLES	Estragole
PRODUCTS IN WHICH USED	Beverages, liqueurs
LEVEL OF USE	Not found
PREPARATION	Infusion, essential oil
MAIN TOXICOLOGICAL DATA	Trans-anethole: 2 years chronic/carcinogenic study in rats: NOEL 105-125 mg/kg/day (4). JECFA ADI 0-2 mg/kg bw (1998). Metabolic study in man (5). Review on genotoxicity studies (6)
DATA NEEDED	Use levels
SPECIFIC OBSERVATIONS	Essential oils used as source of *trans*-anethole
CLASSIFICATION AND LIMITS	**Fruit, herb, root, essential oils: Category 5; limits on estragole**
NATIONAL/INT. EVALUATION	UK FACC 1976, Appendix 2 (herb)
MAIN REFERENCES	**(**1) World Crops Prod. Util. Descr. 1982, 7, 165 (2) Economic Botany, 1990, 44, 174 (3) J. Essent. Oil Res., 1993, 5, 329 (4) Food Chem. Toxicol. 1989, 27, 11 (5) Xenobiotica, 1987, 17, 223 (6)Food Chem. Toxicol., 1988, 26, 87 (7) Mutat Res, 1995, 326, 199

DATA BASES USED

Keywords: Myrrhis odorata, chervil, cicely
CHEMICAL ABSTRACTS (1972-JUNE 1996)

SYS NAME	**Narcissus poeticus** L.
CE No	2080
STEINMETZ No	-
FEMA No	-
ORDER	Liliiflorae
FAMILY	Amaryllidaceae
NAME	**E** Narcissus, daffodil, pleasant's eye **F** Herbe à la vierge, jeanette **D** Dichternarzisse, weisse Narzisse, echte Narzisse **I** Fior-maggi
SYNONYMS	N. poeticus ssp. Poeticus, N. poeticus ssp. radiiflorus (Salisb.) Bak. (Syn. N. radiiflorus Salisb., N. exsertus Haw., N. stellaris Haw.), N. maialis Curt.
PARTS USED	Flowers (1)
IMPORTANT CONSTITUENTS	Six kaempferolglycosides isolated from flowers (2). The phenanthridine (isoquinoline) alkaloids lycorine (($C_{16}H_{17}O_4N$ or galanthidine, formerly named narcissine) and galanthamine, the glucoside scillaine (or scillitoxin) and narciclasine have been identified in flowers of other Narcissus ssp. (Narcissus jonquilla CE No. 2079) (3)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Nonalcoholic beverages, alcoholic beverages, candies (1)
LEVEL OF USE	Flowers, concrete: nonalcoholic beverages 10 ppm, alcoholic beverages 10 ppm, candy 10 ppm. Flowers, absolute: nonalcoholic beverages 1 ppm, alcoholic beverages 1 ppm, candy 1 ppm (6)
PREPARATION	Flowers, concrete and absolute (1)
MAIN TOXICOLOGICAL DATA	Ingestion of narcissus bulbs (Narcissus ssp.), containing as main toxics the alkaloids lycorine and galantamine also present in flowers, produces severe gastroenteritis and nervous symptoms (4). Low doses of lycorine, the most common toxic principle, cause salivation, vomiting, diarrhea, and at higher doses, paralysis and collaps. Galanthamine acts as cholinesterase inhibitor and has analgetic properties. Lycorine, narciclasine, and others are cytotoxic. Chewing of the stem of N. poeticus has been reported to cause a chill, shivering and a tendency to faint (5)
DATA NEEDED	Chemical composition and, if necessary, 28-day oral study and mutagenicity studies on relevant extracts
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Flowers and preparations: Category 5**
NATIONAL/INT. EVALUATION	-

MAIN REFERENCES

(1) IOFI, Results of an inquiry on natural source materials (circular letter 99/7), CE CEFS RD 5/1-46 (2000)
(2) Hagers Handbuch der Pharmazeutischen Praxis, 4th Ed., Vol. VI, P.H. List, L. Hörhammer (Eds.), Verlag, Berlin (1977-1979)
(3) Vigneau Ch. et al., Vet. Hum. Toxicol. 24: 133-135 +192 (1982)
(4) Tyler V.E. et al., Pharmacognosy, 9th Ed., Lea & Febiger, Philadelphia (1988)
(5) Bruneton J., Pharmacognosy, Phytochemistry, Medicinal Plants. Lavoisier, Paris (1995)
(6) IOFI (April 2000)

DATA BASES USED

Keywords: Narcissus poeticus, daffodil
MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Nepeta cataria** L.
CE No:	302
STEINMETZ No	755
FEMA No	-
ORDER	Tubiflorae
FAMILY	Labiatae
NAME	**E** Catmint, catnip. **F** Herbe aux chats, chataire (commune), menthe de chats **D** (Gewöhnliche) Katzenminze **I** Erba dei gatti
SYNONYMS	-
PARTS USED	Herb
IMPORTANT CONSTITUENTS	Herb, fresh: Lactones such as: mainly nepetalactone (70-90% of total lactones, up to 0.99% in plant)), 4-A-nepetalactone (nepetalactone-N1 up to 0.74%), epi-nepeta-lactone (up to 0.4%), 5,9-dehydro-nepetalactone, dihydronepetalactone. Others: limonene, geraniol, linolenic acid, 1R,5R,8S,9S-deoxyloganic acid, nepetalic acid, nepetol, nepetoglucosylester, β -sitosterol, tannin, ursolic acid, camphor, humulene, nepetalic anhydride. Content of essential oil: 0.2-1.3% (1,2,3,4,5,6,7)
ACTIVE PRINCIPLES	Camphor
PRODUCTS IN WHICH USED	Leaves and shoots are used for flavouring sauces, soups and stews (8)
LEVEL OF USE	No data found
PREPARATION	No data found
MAIN TOXICOLOGICAL DATA	The LD50 of catnip oil, the nepeta-lactone enriched fraction, and nepetalic acid were found in mice to be 1300 mg/kg, 1550 mg/Kg, and 1050 mg/kg respectively. Catnip oil (500 mg/kg) and nepetalic acid (62.5 mg/kg) were found to significanly increase hexobarbital sleeping time in mice (9). Rats trained on a Sidman avoidance schedule showed a significant decease in performance following ip injections of catnip oil (500-750 mg/kg), nepetalic acid (125-250 mg/Kg), and the nepetalactone-enriched fraction (500-700 mg/kg) (9). Moreover, it has been reported that catnip oil was being used as substitute for marjhuana (10,11). Camphor: TMDI 100 µg/kg b.w. based on the minimum lethal dose of 50 mg/kg, with a safety factor of 500 (12)
DATA NEEDED:	Use levels, 28-day oral study, mutagenicity studies on relevant preparations
SPECIFIC OBSERVATIONS	Dried leaves and flowering tops are used as a spice to prepare a sedative tea and as tidbit for domestic cats. Some young Americans are reported to smoke the dried leaves, reported to have effects in man similar to those observed with cannabis
CLASSIFICATION AND LIMITS	**Herb and preparations: Category 5; limits on camphor**

NATIONAL/INT. EVALUATION -

MAIN REFERENCES

(1) Phytochemistry 6, 1271, 1967
(2) Phytochemistry 14, 369, 1975
(3) Drug. Ther. 7, 178, 1977
(4) J.Org. Chem. 45, 3811, 1980
(5) PlantaMed. 39, 144, 1980
(6) PlantaMed. 47, 109, 1983
(7) Phytochemistry 11, 453, 1972
(8) Duke, Handbook of Medicinal Herb 1985
(9) Lloydia 41, 367, 1978
(10) J.A.M.A. 207, 1969
(11) Quart.J.Crude Drug Res. 12,1846,1972
(12) Toxicol.Lett. 19, 207, 1983

ATA BASES USED

Keywords: Nepeta cataria, catmint, catnip
NAPRALERT (1988-2001), BIOSIS (1973-2001), CHEMABS (1967-1999), TOXLINE (1969-1999), FSTA (1969-1999), MEDLINE (1966-1999)

SYS NAME	**Paullinia cupana** H.K.B.
CE No	323
STEINMETZ No	803
FEMA No	-
ORDER	Sapindales
FAMILY	Sapindaceae
NAME	**E** Guarana shrub, guarana **F** Guarana **D** Guarana **I** Cupana guarana
SYNONYMS	Paullinia sorbilis (Mart.) Ducke
PARTS USED	Seeds, guarana (pulp of the dried seeds)
IMPORTANT CONSTITUENTS	Guarana paste: tannins 12-15% ; starch 5-6 %; fats 3 %; resins 7 %; caffeine 2.6-7 % (with traces of theophylline, theobromine, adenine, guanine, hypoxanthine); saponins (1,2). Seeds: (% dry weight): caffeine 4.28; theobromine 0.015; theophylline 0.007; polysaccharides, disaccharides, tannins, saponins, fats, resins, mucuous substances, minerals and essential oil (3,4). Essential oil from guarana (qualitative composition): main components: di- and trimethylbenzenes, terpenic hydrocarbons [limonene, caryophyllene, α-copaene]; phenolic compounds [carvacrol (dominant component), 4-dimethylpropyl-phenol]; anethole and estragole (4). Guarana powder: up to 4.4 % caffeine (5)
ACTIVE PRINCIPLES	Caffeine, carvacrol, estragole
PRODUCTS IN WHICH USED	Non alcoholic beverages, liqueurs, candy
LEVEL OF USE	Guarana paste: nonalcoholic beverages 12 ppm; candy 10 ppm (1). Guarana seeds: beverages 7 g/l; foods 1g/kg (IOFI). Guarana gum: soft candy 20 ppm; nonalcoholic beverages 16 ppm; alcoholic beverages 10 ppm (6)
PREPARATION	Paste, gum , alcoholic extracts and distillates
MAIN TOXICOLOGICAL DATA	Guarana extracts: genotoxic effects assessed only in Salmonella typhimurium strain TA97 at a concentration of 30 mg/plate, and by lysogenic induction in Escherichia coli. Addition of S 9, catalase, superoxide dismutase or thiourea counteracted with the genotoxicity of guarana, suggesting that oxygen reactive species play an essential role in the genotoxicity of aqueous guarana extracts. This activity was related to the presence of a molecular complex formed by by caffeine and a flavonoid (catechin and epicatechin) in the presence of potassium (7). Caffeine: see Coffea arabica (CE No 148). Review on general toxicology; metabolism; effects on reproduction and prenatal toxicity, genetic and related effects in animals and humans; carcinogenicity studies in animals; evaluation of carcinogenic risks to humans; estimation of caffeine consumption (8,9). *Trans*-anethole: 2 years chronic/carcinogenic study in rats: NOEL 105-125 mg/kg/day (5). JECFA ADI 0-2 mg/kg bw (1998)

DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Seeds and preparations: Category 3; limits on caffeine, carvacrol and estragole**
NATIONAL/INT. EVALUATION	UK FACC 1976 ; Appendix 2. Caffeine: EU legislation on labelling of caffeine.
MAIN REFERERENCES	(1) Leung, 1980, 194 (2) Int. J. Pharmacogn., 1993, 31, 175 (3) Phytochemistry, 1995, 39, 1063 (4) Ztschr. Lebensm. Unters. Forsch., 1996, 203, .95 (5) MAFF data ref FSF 2550 , 14 January 1994 (6) Fenaroli, 1995, Vol 1, 143 (7) Mutat Res., 1994, 321, 165 (8) IARC Monograph 1991, Vol 51, 291 (9) Food Chem. Toxicol., 1988, 26, 645; 1992, 30, 533
DATA BASES USED	Keyword: guarana CHEMICAL ABSTRACTS (–1996)

SYS NAME	**Petroselinum crispum** (Mill.) Nym. ex A.W. Hill
CE No	326
STEINMETZ No	816
FEMA No	-
ORDER	Umbelliflorae
FAMILY	Apiaceae
NAME	**E** Parsley **F** Persil **D** (Krausblättrige) Petersilie **I** Prezzelmolo
SYNONYMS	Petroselinum sativum Hoffm., Petroselinum hortense auct non Hoffm., Apium petroselinum L., Carum petroselinum Benth. and Hook.
PARTS USED	Fruit (seed), herb (leaves, flowering tops), roots
IMPORTANT CONSTUENTS	Parsley leaves (one sample of fresh and four samples of dried leaves): furocoumarin content: psoralen 32.3-104.7 mg/g; bergapten 63.9-146.7 mg/g; xanthotoxin 5.3-53.0 mg/g; isopimpinellin 15.7-79.8 mg/g; with smaller amounts of isopimperatorin, oxypeucedanin, oxypeucedanin hydrate, saxalin and graveolone (1). Parsley leaf oil: terpenic hydrocarbons [α-pinene 0.7-7 %, camphene (trace), β-pinene 0.5-4.6 %, sabinene 0.1-0.3 %, myrcene 4.9-5.7 %, a-terpinene 0.8-1.3 %, limonene 1.6-3 %, β-phellandrene 0.9-26.1 %, (Z) and (E)-β-ocimene (trace), γ-terpinene 0.4 %, p-cymene 0.4-0.5 %, terpinolene 1.8-3.8 %, p-mentha-1,3,8-triene 30.1-30.3 %, p-mentha-1,4,8-triene trace-1%]; alkenylbenzenes [myristicin 1.5-14 %, apiol 0.9-8.1 %, α-p-dimethylstyrene 1.5-7.7 %] (2). Common parsley seed oil: terpenic hydrocarbons [α-pinene 10.1-16.9 %, β-pinene 6.9-10.7 %, limonene + β-phellandrene 1.3-3 %, terpinolene 0.2-0.5 %]; alkenylbenzenes [myristicin 2.4-36.9 %, allyl tetramethoxybenzene 1.3-29 %, elemicin 0-8.8 %, apiol 11.3-67 %] (3). Italian parsley seed oil: terpenic hydrocarbons [α-pinene 8.3-15 %, b-pinene 5.4-9.6 %, limonene +β-phellandrene 1.2-2.3 %, terpinolene 0.1-0.4 %]; alkenylbenzenes [myristicin 0.7-37.9 %, allyl, tetramethoxybenzene 0.6-20.8 %, elemicin 0-2 %, apiol 30.4-67.5 %] (3) Curly parsley seed oil: terpenic hydrocarbons [α-pinene 15.7-24.1 %, β-pinene 9.6-15.1 %, limonene + β-phellandrene 1.4-3.5 %, terpinolene 0-0.2 %]; alkenylbenzenes [myristicin 44.6-62.3 %, allyl tetramethoxybenzene 1.3-29 %, elemicin 0-12.2 %, apiol 0-7.2 %] (3)
ACTIVE PRINCIPLES	Furocoumarins, myristicin, apiol, elimicin
PRODUCTS IN WHICH USED	Baked goods, fats, oils, meat products, processed vegetables, condiment, relish, soups, snack foods, gravies, frozen dairy, gelatin, pudding, nonalcoholic and alcoholic beverages, candy (4)
LEVEL OF USE	Parsley: baked goods 7500 ppm; other grains 490 ppm; fats, oils 1600 ppm, meat products 4100 ppm; processed vegetables 15000 ppm; condiment, relish 5000 ppm; soups 5100 ppm; snack foods 720 ppm; gravies 420 ppm (4).

	Parsley oil: baked goods 24 ppm; frozen dairy 1 ppm; meat products 63 ppm; processed vegetables 1 ppm; condiment, relish 64 ppm; soft candy 6 ppm; gelatin, pudding 10 ppm; soups 66 ppm; nonalcoholic beverages 2 ppm; alcoholic beverages 2.2 ppm; gravies 6.2 ppm (4). Parsley oleoresin: baked goods 180 ppm; frozen dairy 10 ppm; meat products 180 ppm; condiment, relish 390 ppm; soft candy 50 ppm; gelatin, pudding 100 ppm; soups 37 ppm; nonalcoholic beverages 20 ppm; alcoholic beverages 18 ppm (4)
PREPARATION	Infusions and decoctions (from roots), essential oils, oleoresin (from seeds)
MAIN TOXICOLOGICAL DATA	d-Limonene, JECFA ADI not specified (1993)
DATA NEEDED	28-day oral toxicity study and mutagenicity studies on relevant preparations
SPECIFIC OBSERVATIONS	Parsley herb (leaves and flowering tops) is a foodstuff
CLASSIFICATION AND LIMITS	**Parsley herb and essential oil: Category 3; limits on furocoumarins, myristicin, apiol, elemicin** **Parsley seed, root and preparations essential oils: Category 5; limits on furocoumarins, myristicin, apiol, elemicin**
NATIONAL/INT. EVALUATION	UK FACC 1976 ; Appendix 2
MAIN REFERENCES	**(**1) Phytochemistry, 1994, 36, 869 (2) Perfumer & Flavorist, July/Aug 1996, 21, 65 (3) Bull. Soc. Pharm. Bordeaux, 1993, 132, 90 (4) Fenaroli, 1995
DATA BASES USED	Keywords : Petroselinum, Parsley CHEMICAL ABSTRACTS (-1967-1996)

SYS NAME	**Pimpinella anisum** L.
CE No	336
STEINMETZ No	838
FEMA No	-
ORDER	Umbelliflorae
FAMILY	Apiaceae
NAME	**E** Anise **F** Anis, anis vert **D** Anis **I** Anice
SYNONYMS	-
PARTS USED	Fruit (seed)
IMPORTANT CONSTITUENTS	Fruit: lipids 16 %, proteins 15 %, carbohydrates 50 %; coumarins and furocoumarins: 0.01 ppm (bergapten 0.005 ppm, xanthotoxin 0.005 ppm, scopoletin, umbelliferone, umbelliprenin (1). Anise oil: alkenylbenzenes [*trans*-anethole 75-90 %; estragole 1-5 %]; carbonyl compounds [anis-aldehyde 0.2- 2.5 %; anisketone 0.2-1 %]; terpenic hydro-carbons [β-caryophyllene, γ-himachalene, d-limonene] (2)
ACTIVE PRINCIPLES	Furocoumarins, estragole
PRODUCTS IN WHICH USED	Condiments, nonalcoholic and alcoholic beverages, meats, ice-creams, ices, candy, baked goods
LEVEL OF USE	Anise: baked goods 7600 ppm; fats, oils 4000 ppm; frozen dairy 5 ppm; meat products 2300 ppm; condiment, relish 1100 ppm; soft candy 7 ppm; nonalcoholic beverages 40 ppm; alcoholic beverages 380 ppm; gravies 150 ppm. Anise oil: baked goods 180 ppm; frozen dairy 61 ppm; meat products 28 ppm; condiment, relish 180 ppm; soft candy 680 ppm; nonalcoholic beverages 31 ppm; alcoholic beverages 570 ppm; gelatin, pudding 46 ppm; hard candy 1300 ppm; chewing-gum 5200 ppm (3)
PREPARATION	Fluid extract; tincture; infusion or decoction; essential oil
MAIN TOXICOLOGICAL DATA	Anise oil: LD 50 oral (rat) 2,25 g/kg, LD 50 dermal (rabbit) >5 g/kg Sensitization + (4). Trans-anethole: 2 years chronic/ carcinogenic study in rats: NOEL 105-125 mg/kg/day (5). JECFA ADI 0-2 mg/kg bw (1998) D-limonene JECFA ADI not specified (1993)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	The seed is a foodstuff
CLASSIFICATION AND LIMITS	**Fruit and preparations: Category 3; limits on furocoumarins, estragole**
NATIONAL/INT. EVALUATION	UK FACC 1976, Appendix 2 (fruit)

MAIN REFERERENCES

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(2) Perfumer & Flavorist, Aug/Sept 1976, 1, 31 - Aug/Sept 1980, 5, p.14, June/July 1983, 8, 65, Aug/Sept 1983, 8, 63, Aug/Sept 1986, 11, 73, April/May 1987, 12, 67.
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DATA BASES USED

Keywords: Pimpinella anisum, anise
CHEMICAL ABSTRACTS (1962 – 1995)

SYS NAME	**Pogostemon cablin** (Blanco) Benth.
CE No	353
STEINMETZ No	872
FEMA No	Patchouly oil: 2838
ORDER	Tubiflorae
FAMILY	Labiatae
NAME	**E** Patchouli **F** patchouli **D** Patschuli **I** -
SYNONYMS	Pogostemon heyneanus Benth., Pogostemon patchouly Pellet., Pogostemon patchouli Hook., Betonica officinalis Lor., Agastachye rugosa Kuntze, Elscholzia monastachia Lev. Et Van., Mentha auricularia Blanco.
PARTS USED	Leaves
IMPORTANT CONSTITUENTS	Leaves essential oil: pogostol (10%); benzaldehyde; 2-methylbutyric acid; o-cresol; cinnamaldehyde; cis-2-pentyl-cyclopropylcarboxilic acid; trans-2-pentyl-cyclopropylcarb-oxylic acid; eugenol, guaiacol; heptanoic acid; 2-methyl-hexanoic acid; nonanoic acid; octanoic acid; patchoulan-1-2-diol; alpha-patchoulene; beta-patchoulene; delta-patchoulene; patchouli alcohol; patchoulol; pentanoic acid; 4-methylpentanoic acid; phenol; dimethylphenol; p-vinyl-phenol; seychellene; 3-(4-Methylpentanoyl-)3; 1-dihydro-6-methyl-1; 2-pyran-2; 4-dione 3(2-methylbutyryl-)3; 4-dihydro-6-methyl-1; 2-pyran-2, 4-dione; eriodictyol,3-4^{1}-7-tri-0-methyl; 3-4^{1}-7-tri-0-methyl kaempferol; ombuine; patchypodol; kumatakenin; retusin; licochalcone A; ombulin; 5-7-dihydroxy-3^{1}-4^{1}-dimethoxy flavanone; ternatin (1-11). Leaves essential oil: patchouli alcohol (31-43%), pogostone (0.85%), other compounds over 1% were beta-patchoulene, beta-elemene, transcaryo-phyllene, delta-guaiene, seychellene, alpha-patchoulene, aciphyllene, alpha-guaiene. Content of 0.6-0.8% essential oil in leaves (Luo J. et al., Zhong Yao Cai, 25 (1) (2002): 21-23 (article in chinese, abstract in English). Content of essential oil in plant: 1.5-5.8% (Duke, James A. 1992. Handbook of phytochemical constituents of GRAS herbs and other economic plants. Boca Raton, FL. CRC Press)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, meat products, soft candy, gelatin, pudding, non-alcoholic beverages, alcoholic beverages, hard candy, chewing gum
LEVEL OF USE	Patchouli oil: baked goods 2.2 ppm, frozen dairy 2.1 ppm., meat products 0.1 ppm., soft candy 2.2 ppm., gelatin, pudding 1.1 ppm., nonalcoholic beverages 1.0 ppm., alcoholic beverages 1.0 ppm., hard candy 760 ppm., chewing gum 1100. ppm
PREPARATION:	Essential oil
MAIN TOXICOLOGICAL DATA	No adverse effects on growth, food consumption, hematology, blood chemistry, liver and kidney weights or

	the gross and microscopic post-mortem appearance of major organs were observed in rats given patchouly oil (commercial grade) at level of 2% in the diet. (12). Benzaldehyde JECFA ADI (expressed as benzoic acid equivalents) 0-5 mg/kg bodyweight (1996, 2001). Eugenol JECFA ADI 0-2.5 mg/kg bodyweight (1982)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Leaves and preparations: Category 2**
NATIONAL/INT. EVALUATION	Patchouly oil: CFR 172.510
MAIN REFERENCES	(1) Phytochemistry 17, 1664, 1976 (2) Chem. Pharm. Bull. 16, 1608, 1968 (3) J. Pharmacobiol. Dyn. 10, 49, 1987 (4) Process Biochem. 12, 5, 1977 (5) Fitoterapia 55, 370, 1985 (6) Phytochemistry 14, 2712, 1975 (7) J. Agr. Fd. Chem., 48, 642, 2000 (8) Phytomedicine, 6, 89, 1999 (9) Planta Med., 64, 646, 1998 (10) Korean J. Pharmacol., 29, 18, 1998 (11) Chim. Pharm. J. (Taipei), 47, 431, 1995 (12) Fd. Cosmet. Toxicol. 3, 563, 1965
DATA BASES USED:	Keywords: Pogostemon cablin, patchouli, chemical composition, toxicity data NAPRALERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001)

SYS NAME	**Polianthes tuberosa** L.
CE No	354
STEINMETZ No	-
FEMA No	3084
ORDER	Liliiflorae
FAMILY	Agavaceae
NAME	**E** Tuberose **F** Tubereuse **D** Tuberose **I** Tuberosa
SYNONYMS	Amica nocturna Rumph.
PARTS USED	Flowers
IMPORTANT CONSTITUENTS	Methyl benzoate, methyl anthranilate, benzyl alcohol, butyric acid, probably phenyleacetic acid, methyl salicylate, eugenol, geraniol, nerol, farnesol. Flowers contain 0.036-0.09% essential oil (1)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, soft candy, gelatin/pudding, nonalcoh olic beverages, alcoholic beverages (1)
LEVEL OF USE	Tuberose oil: baked goods 3.3 ppm, frozen dairy 1.6 ppm, soft candy 3.2 ppm, gelatin/pudding 1.7 ppm, nonalcoholic beverages 1.2 ppm, alcoholic beverages 0.7 ppm (1)
PREPARATION	Concrete (yield 1.2-1.5%), absolute, essential oil (distilled from concrete with yield 3-6%) (1,2)
MAIN TOXICOLOGICAL DATA	Benzyl alcohol, JECFA ADI 0-5 mg/kg bw (1979). Butyric acid, JECFA no safety concern at current levels of intake when used as a flavouring agent (1997). Eugenol, JECFA ADI 0-2.5 mg/kg bw (1982). Methyl anthranilate, JECFA ADI 0-1.5 mg/kg bw (1979). Methyl benzoate, JECFA no safety concern at current levels of intake when used as a flavouring agent (2001). Methyl salicylate, JECFA no safety concern at current levels of intake when used as a flavouring agent, the 1967 ADI of 0-0.5 mg/kg bw was maintained (2001)
DATA NEEDED	Quantitative data on chemical composition and, if necessary, 28-day oral study and mutagenicity studies on relevant preparations
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Tuberose flowers and essential oil: Category 5**
NATIONAL/INT. EVALUATION	Tuberose oil: CFR 182.20, 582.20
MAIN REFERENCES	(1) Fenaroli (1995) (2) Reineccius G., Source Book of Flavours. 2nd Edition, Chapman & Hall. London (1994)

DATA BASES USED

Keywords: Polianthes tuberosa, Tuberose
MEDLINE (1966-1999), EMBASE (1980-1999),
BIOLOGICAL ABSTRACTS (1989-1999),
CC LIFE (6/98-6/99)

SYS NAME	**Potentilla erecta** (L.) Raeusch.
CE No	493
STEINMETZ No	899
FEMA No	-
ORDER	Rosales
FAMILY	Rosaceae
NAME :	**E** Common tormentil, tormentil **F** - **D** Blutwurz **I** -
SYNONYMS	Potentilla tormentilla Stokes, P. sylvestris Neck.
PARTS USED	Root (6)
IMPORTANT CONSTITUENTS	Rhizome: tannins 15-22% (of a nonhydrolysable type including different catechins). One of the major constituents is agrimoniin (1%) (3)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Alcoholic beverages (2,3,6)
LEVEL OF USE	Root extract: alcoholic beverages 200 mg/kg (6)
PREPARATION	Extract
MAIN TOXICOLOGICAL DATA	Mice, which received a dose corresponding to 1200 mg rhizome/kg bw orally or a dose corresponding to 800 mg/kg bw did not show any symtoms of acute intoxication(3). A dose corresponding to 400 mg rhizome/kg bw administrered p.o. in rats lowered the blood pressure by 5% in hypertensive rats. Antibacterial, antiviral and antiinflammatory effects of the rhizome of Potentilla erecta (L.) are described (5)
DATA NEEDED	Concentration of extract. Quantitative data on chemical composition and, if necessary, 28-day oral study and mutagenicity studies
SPECIFIC OBSERVATIONS	The rhizome has been used for its adstringent properties in folk medicine for a long time. No side effects have been described
CLASSIFICATION AND LIMITS	**Root and preparations: Category 5**
NATIONAL/INT EVALUATION	-
MAIN REFERENCES	**(**1) Martindale (1982) (2) List and Hörhammer (1967-80) (3) Lund and Rimpler: Dtsch. Apoth. Ztg. (1985), 125, 374 (4) Wichtl (1984) (5) Chem. Pharm. Bull. (1985), 33, 3977 (6) IOFI (2000)
DATA BASES USED	Keywords: Potentilla erecta, tormentil. MEDLINE (1966-1999), TOXLINE (1965-1999), FSTA (1969-1999), ANALYTICAL ABSTRACTS (1980-1998)

SYS NAME	**Pterocarpus santalinus** L.
CE No	379
STEINMETZ No	923
FEMA No	-
ORDER	Rosales
FAMILY	Leguminosae
NAME :	**E** Red sandalwood tree, red saunders **F** Santal rouge **D** Roter Sandelbaum **I** Sandalo rosso
SYNONYMS :	-
PARTS USED	Wood (1,2)
IMPORTANT CONSTITUENTS	Derivatives of benzoxanthenons, santalin A and B, small amounts of volatile oil containing up to 50% of cedrol, pterocarpol, iso-pterocarpol, pterocarptriol and eudesmol (2,3)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Extract: alcoholic beverages and meat products. Essential oil: beverages, alcoholic beverages, ices, candy, baked products and desserts (5)
LEVEL OF USE	Wood extract: alcoholic beverages 10 mg/kg, meat products 300-900 mg/kg. Wood essential oil: beverages 2 mg/kg, alcoholic beverages 2 mg/kg, ices 5 mg/kg, candy 5 mg/kg, baked products 5 mg/kg, desserts 5 mg/kg (5)
PREPARATION	Extract and essential oil (5)
MAIN TOXICOLOGICAL DATA	No data available. No side effect found in therapeutic doses (the level of therapeutic doses is not indicated) (4)
DATA NEEDED	Quantitative data on chemical composition and, if necessary, 28-day oral study and mutagenicity studies
MAIN REFERENCES	**(**1) Fenaroli, 1995 (2) List and Hörhammer, 1967 (3) Wichtl, 1989 (4) Braun , 1987 (5) IOFI (2000)
SPECIFIC OBSERVATIONS	No toxicological data are available but the wood has been used as a spice and colouring agent in fish products for many years without any known side effects
CLASSIFICATION AND LIMITS	**Wood and preparations: Category 5**
NATIONAL/INT EVALUATION	-
DATA BASES USED	Keywords: Pterocarpus santalinus, red sandalwood MEDLINE (1966-1999), TOXLINE (1965-1999), FSTA (1969-1999), ANALYTICAL ABSTRACTS (1980-1998)

SYS NAME	**Salvia lavandulifolia** Vahl
CE No	413
STEINMETZ No	-
FEMA No	Sage, Spanish, oil: 3003
ORDER	Tubiflorae
FAMILY	Labiatae
NAME	**E** Spanish sage **F** Sauge a feuilles de lavande **D** Lavendelblättriger Salbei **I** Salvia
SYNONYMS	Salvia officinalis L. ssp. lavandulaefolia Gams
PARTS USED	Herb
IMPORTANT CONSTITUENTS	Essential oil: eucalyptol (11.8-41.2 %), camphor (10-39%), α-pinene (5%), α-thujene, tricyclene, camphene (5-30%), β-pinene (6-19%), sabinene, myrcene, α-phellandrene, α-terpinene, limonene (1-41%), cis-β-ocimene, trans-β-ocimene, p-cymene, terpinolene, cis-allo-ocimene, α-terpinene, α-p-dimethyl-stirene, trans-sabinene hydrate, α-cubebene, linalool (0.2-11.2%), α-gurjunene, cis-α-bergamotene, linalyl acetate (0.1-10.2%), isocaryophyllene, bornyl acetate, iso-bornyl acetate, terpinen-4-ol, β-caryophyllene, aromadendrene, δ-terpineol, allo-aromadendrene, cis-sabinyl acetate (12.8%), iso-borneol, cis-sabinol, α-humulene, borneol (1.5-6.4%), α-terpineol, α-terpinyl acetate, δ-cadinene, geranyl acetate, bisabolene, nerol, carvone, geraniol, β-spathulene, viridi-florene, humulene epoxide II, viridiflor, spathulenol (1-11)
ACTIVE PRINCIPLES	Eucalyptol, camphor
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, meat products, condiment, relish, soft candy, gelatin, pudding, non-alcoholic beverages, alcoholic beverages, gravies
LEVEL OF USE	Spanish sage, oil: baked goods 21 ppm, frozen dairy 11 ppm, meat products 40 ppm, condiment, relish 17 ppm, soft candy 21 ppm, gelatin, pudding 5 ppm, nonalcoholic beverages 7 ppm, alcoholic beverages 5 ppm, gravies 40 ppm
PREPARATION	Essential oil
MAIN TOXICOLOGICAL DATA	Terpinen-4-ol: kidney irritation by commercially available Juniper oil depend on the content of terpinen-4-ol (12). In another study two slightly different Juniper oil batches were tested in male Sprague-Dawley rats. Animals were dosed orally for 28 days with 100-333 and 1000 mg/kg bw/d (1st batch) and 100-300 and 900 mg/kg bw/d (2nd batch). Additionally, terpinene-4-ol, a known component of *Juniper* oil (10 mg%), was tested with the same experimental design at 400 mg/kg. Neither of the tested substances induced changes in function or morphology of the kidney at the tested doses (15). Camphor: TDI 100 μg/kg b.w., based on minimum lethal dose of 50 mg/kg, with a safety factor of 500 (18). The oil of Salvia

lavandulifolia showed neurotoxic effect in rats when injeeted (i.p.) with 4 ml/kg (13). A fraction of essential oil of S. lavendulifolia, containing 50% sabinyl acetate had a dose-dependent abortifacient effect in mice. This work underlines the potential risk induced by the uncontrolled use of such essential oil in aromatheraphy (14). Borneol: Ames test negative (16), but positive with Bacillus subtilis rec-assay at 10 mg per dish (5). α-Pinene: not mutagenic in Ames tests; weak tumour-promoting effect on mouse skin when applied after a single dose of known carcinogen; foetotoxic only at a maternally toxic dose level when administered orally to pregnant rats with several other terpenes; repeated administration at lower levels in rats caused enzyme induction. In man, has been given orally in combination with several other terpenes to treat gallstones (17). Eucalyptol: The subacute toxicity studies reported up to now in rats and mice suggested that mice were less susceptible than rats to the toxicity of eucalyptol. In fact, after gavage, it was found toxic in male rats at doses higher than 600 mg/kg while no effect was seen in mice up to 1200 mg/kg. However, the limitations and the quality of the study do not allow the extrapolation of a "no effect level" (19) Several reports in rat and brushtail possum show the formation of hydroxylated bicycled products of eucalyptol as main metabolites (21). Furthermore other metabolites which require ring opening have been also detected (20).Following the accidental exposure of human beings, death was reported in two cases after ingestion of 3.5-5 ml of essential eucalyptus oil, but a number of recoveries have also been described for much higher amounts of oil (22). Linalool, linalyl acetate, citral (neral + geranial) JECFA group ADI 0.5 mg/kg b.w. (1998). (+)-Carvone JECFA ADI 0-1 mg/kg body weight (1998). Limonene JECFA ADI not specified (1993)

DATA NEEDED: 28-day oral study and mutagenicity studies on essential oil

SPECIFIC OBSERVATIONS Fresh leaves are used in herb butters, cheeses liqueurs, pickles salads and vinegars

CLASSIFICATION AND LIMITS **Herb: Category 3; limits on eucalyptol, camphor**
Essential oil: Category 5; limits on eucalyptol, camphor

NATIONAL/INT. EVALUATION Eucalyptol: SCF: the available toxicological studies are limited and inadequate to derive an ADI. However, the available animal data do not indicate a cause of concern associated with the daily intake from food including hard candies estimated from the small amount of information available. For more precise risk characterisation further data on exposure and toxicity would be needed. Sage, Spanish, oil: CFR 182.20, 582.20

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(21) Xenobiotica, 10, 17, 1980
(18) Vet. Hum. Toxicol. 26, 8, 1984
(19) National Toxicological Program, April 1987
(20) Bull. Environ. Contam. Toxicol. 37, 759, 1986
(21) Xenobiotica, 10, 17, 1980
(22) Aust. Amm. Med. 4,23,1965

DATA BASES USED:

Keywords: Salvia, Spanish sage,
chemical composition, toxicity data
NAPRALERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001)

SYS NAME	**Salvia sclarea** L.
CE No	415
STEINMETZ No	1012
FEMA No	Clary (sage): 2320 Clary (sage) oil: 2321
ORDER	Tubiflorae
FAMILY	Labiatae
NAME	**E** Clary sage, clary wort **F** Sauge sclaree, toute-bonne **D** Muskatsalbei, Muskateller-Salbei **I** Sclarea, Erba moscatella
SYNONYMS	-
PARTS USED	Flower, herb.
IMPORTANT CONSTITUENTS	Herb essential oil: estragole (49.0%), linalool (9.3%), linalyl acetate (19.2%), terpinen-4-ol (0.27%), α-terpineol acetate (4.3%), α-terpineol (7.5%), α-pinene (0.2%), α-thujene (0.01%), β-pinene (0.22%), sabinene (0.19%), myrcene (1.01%), car-3-ene (0.11%), p-cymene (0.06%), limonene (0.2%), eucalyptol (3.23%), β-ocimene (0.8%), χ-terpinene (0.08%), linalool oxide (0.05%), β-caryophyllene (0.22%), germacrene D (0.18%), nerol acetate (0.42%), geranyl acetate (0.15%), nerol (0.02%), geraniol (0.07%), eugenol methyl ether (1.97%), α-endesmol (0.13%), β-endesmol (0.28%), camphor. Flower essential oil: α-pinene (0.1%), camphene (tr), β-pinene (0.1%), myrcene (0.25%), limonene (0.15%), eucalyptol (tr), hex-3-ol (0.15%), hex-2-en-1-ol (0.1%), α-copaene (0.5%), linalool (17%), linalool acetate (14.3%), α-terpineol (15.1%), geraniol (2.15-6.5%), geranyl acetate (7.5%), manool (2.5%), sclareol (5.2%), camphor (1-12)
ACTIVE PRINCIPLES	Estragole, eucalyptol, camphor
PRODUCTS IN WHICH USED	Nonalcoholic beverages, alcoholic beverages, baked goods, frozen dairy, condiment, relish, soft candy, non-alcoholic beverages, alcoholic beverages
LEVEL OF USE	Clary: nonalcoholic beverages 9 ppm, alcoholic beverages 145 ppm. Clary oil: baked goods 13 ppm, frozen dairy 3.9 ppm, condiment, relish 20 ppm, soft candy 5 ppm, nonalcoholic beverages 2 ppm, alcoholic beverages 100 ppm
PREPARATION	Essential oil
MAIN TOXICOLOGICAL DATA	Camphor: TDI 100 μg/kg b.w. based on the minimum lethal dose of 50 mg/kg, with a safety factor of 500 (17). Estragole: evaluated as active principle by CoE. Terpinen-4-ol: kidney irritation by commercially available Juniper oil depends on the content of terpinen-4-ol (13). In another study two slightly different Juniper oil batches were tested in male Sprague-Dawley rats. Animals were dosed orally for 28 days with 100-333 and 1000 mg/kg bw/d (1st batch) and 100-300 and 900 mg/kg bw/d (2nd batch). Additionally, terpinene-4-ol, a known component of Juniper oil (10 mg%), was tested with the same experimental design at

400 mg/kg. Neither of the tested substances induced changes in function or morphology of the kidney at the tested doses (14). Geranyl *acetate:* Food-grade geranyl acetate (containing approx. 29% citronellyl acetate) was not carcinogenic for F344/N rats (50 m/f, 1000 or 2000 mg/kg bw for 103 weeks) and B6C3F1 mice (50 m/f, 500 or 1000 mg/kg bw for 103 weeks) (15). Geraniol: not mutagenic in S. typhimurium TA 100 (15). α-Pinene: not mutagenic in Ames tests; weak tumour-promoting effect on mouse skin when applied after a single dose of known carcinogen; foetotoxic only at a maternally toxic dose level when administered orally to pregnant rats with several other terpenes; repeated administration at lower levels in rats caused enzyme induction. In man, has been given orally in combination with several other terpenes to treat gallstones (16). Eucalyptol: the subacute toxicity studies reported up to now in rats and mice suggested that mice were less susceptible than rats to the toxicity of eucalyptol. In fact, after gavage, it was found toxic in male rats at doses higher than 600 mg/kg while no effect was seen in mice up to 1200 mg/kg. However, the limitations and the quality of the study do not allow the extrapolation of a "no effect level" (17) Several reports in rat and brushtail possum show the formation of hydroxylated bicycled products of eucalyptol as main metabolites (18). However other metabolites which require ring opening have been also detected (19).Following the accidental exposure of human beings, death was reported in two cases after ingestion of 3.5-5 ml of essential eucalyptus oil, but a number of recoveries have also been described for much higher amounts of oil (20). Linalool, linalyl acetate, citral (nerol + geraniol) JECFA group ADI 0.5 mg/kg b.w. (1998). Limonene JECFA ADI not specified (1993)

DATA NEEDED 28-day oral study and mutagenicity studies on essential oil

SPECIFIC OBSERVATIONS Clary sage is used in the formulation of liqueurs and soft beverages

CLASSIFICATION AND LIMITS **Herb, flower and preparations: Category 5; limits on estragole, eucalyptol, camphor**

NATIONAL/INT. EVALUATION Eucalyptol: SCF: The available toxicological studies are limited and inadequate to derive an ADI. However, the available animal data do not indicate a cause of concern associated with the daily intake from food including hard candies estimated from the small amount of information available. For more precise risk characterisation further data on exposure and toxicity would be needed. Estragole: SCF: Estragole has been demonstrated to be genotoxic and carcinogenic. Therefore the existence of a threshold cannot be assumed and the Committee could not establish a safe exposure limit. Consequently, reductions in exposure and restrictions in use levels are indicated. Clary (sage): CFR 182.10, 582.10. Clary (sage) oil: CFR 182.20, 582.20.

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DATA BASES USED:

Keywords:: Salvia sclarea, Clary sage, chemical composition, toxicity data
NAPRALERT (1988-2001), CHEMABS (1967-2001), BIOSIS (1973-2001), FSTA (1969-2001), TOXLINE (1969-2001), MEDLINE (1966-2001), PASCAL (1973-2001).

SYS name	**Sambucus canadensis** L.
CE No	416
STEINMETZ No	1013
FEMA No	Flowers: 2406
ORDER	Dipsicales
FAMILY	Caprifoliaceae
NAME	**E** American elder, sweet elder **F** Sureau du Canada **D** Kanadischer Holunder **I** Sambuco **SP** Sauco
SYNONYMS	**-**
PARTS USED	Flowers, leaves, fruit (1, 2, 7)
IMPORTANT CONSTITUENTS	Leaves: *n*-Hexane extract: *n*-alkanes (C25-C31, mainly *n*-nonaconsane), α- and β-amyrin palmitates, sitosterol, small amounts of stigmasterol and campesterol. EtOH extract: urosolic and oleanolic acid. H2O extract: rutin (3). Seeds and leaves: sambunigrin, a mandelonitrile glycoside, which liberates HCN on hydrolysis (2). When leaves were tested for sambunigrin content in 9 populations of S. canadensis 4 of the populations did not produce sambunigrin at all. In one population all individuals tested produced sambunigrin, in three populations an occasional individual tested positive, and in one population some individuals constantly tested positive whereas others tested negative (4). Fruit: methanol extract: anthocyanes (derivatives of cyanidin) (5, 6)
ACTIVE PRINCIPLES	Hydrocyanic acid (sambunigrin)
PRODUCTS IN WHICH USED	Flowers: baked goods, frozen dairy, soft candy, gelatin, pudding, non-alcoholic beverages, alcoholic beverages (2). Fruit: jellies, pies, sauces, alcoholic drinks (7)
LEVEL OF USE	Flower extract: baked goods 30 ppm, frozen dairy 44 ppm, soft candy 30 ppm, gelatin and pudding 30 ppm, non-alcoholic beverages 500 ppm, alcoholic beverages 14 ppm (2)
PREPARATION	Fluid extract, tincture (2)
MAIN TOXICOLOGICAL DATA	No data found
DATA NEEDED	Use and use levels for fruits, leaves and preparations. Chemical composition of flowers and preparations. 28-day oral study and mutagenicity studies of preparations
SPECIFIC OBSERVATIONS	**-**
CLASSIFICATION AND LIMITS	**Flowers, leaves, fruits, preparations: classification 5; limits on hydrocyanic acid**
NATIONAL/INT.EVALUATION	Elder flowers: CFR 182.10, 582.10. Elder flowers extract: CFR 182.20, 582.20. Elder tree leaves extract: 172.510 in alcoholic beverages only, not to exceed 25 ppm prussic acid in the flavor (2). Hydrocyanic acid in flavours has limits in foodstuffs by EU Council Directive 88/388/EEC

MAIN REFERENCES

(1) Hagers Handbuch der Pharmazeutischen Praxis, 4th ed., Springer, Berlin (1975).
(2) Fenaroli, 3rd ed, CRC-Press (1995).
(3) Phytochemistry, 14: 187-1872 (1975).
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DATA BASES USED

Keywords: Sambucus canadensis
FSTA (1969-2000), BIOSIS (1973-1995), TOXLINE (1966-1995), PUBMED (-2004), TOXNET (-2004), PFAF (-2004)

SYS NAME	**Sesamum indicum** L.
CE No	429
STEINMETZ No	1056
FEMA No	
ORDER	Tubiflorae
FAMILY	Pedaliaceae
NAME	**E** Sesame, gingelly **F** Sesame **D** Sesam **I** Sesamo
SYNONYMS	S.luteum Retz; S. occidentale Heer et reg.; S. oleiferum Moench.; S. orientale L.
PARTS USED	Seed
IMPORTANT CONSTITUENTS	Sesamin (0.01-0.1%); sesamolin (0.01-038%); sesamol (0.001-0.1%); β-sitosterol; stigmasterol; cycloartenol; campesterol; 24-methylcycloartenol; α-amyrin; δ-avenasterol; palmitic, stearic, oleic, arachidic, and linoleic acids; protein sugars; guaiacol; furfuryl alcohol; 2-acethyl-3-methyl furan; pentanal; acethylpyrazine; 2-acethylpyrrole; α-formylpyrrole; hexanal; heptanal; 2-heptanal; octanal; 2-acethyl-furan; 2-hexenal (1-8)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	The seed is used for flavouring bread. The oil is used in baking and flavouring confections. (12)
LEVEL OF USE	Seed >1000 mg/kg (IOFI)
PREPARATION:	Oil
MAIN TOXICOLOGICAL DATA	Sesame oil prepared from sesame seed with different roasting temperature (unroasted, 180, 200 and 220°C) was not mutagenic in S. typhimurium TA98 and TA100 strains, with or without S9 mix.; a weak mutagenicity was found only in the oil prepared with 240 and 260°C of roasting temperatures on TA98 strain with S9 mix, but no on the TA100 strain (9). The brominated sesame oil was administered in the diet to miniature swine at level, 0.5, 25, 50 and 500mg/kg b.w. for 17 weeks. Ataxia, marked fatty degeneration of the hepatic plate cells, renal tubular epithelial cells, and neutral fat increased in the myocardium, were seen in the pigs fed 500mg/kg. Moreover a increased in LDH, SGOT, and SGPT values were observed at the 50mg/kg dose level: The kidney-to-body weight ratios were also increased at all dose level (10). In rats high level (0.5%) of brominated sesame oil in the diet for 105 days, produce toxicological effect such as cardiac myocytolysis, thyroid hyperplasia, fatty liver, testicular atrophy and renal damage. At the 0.1% of dietary level, only fatty changes in the liver were observed (11)
DATA NEEDED	No data required

SPECIFIC OBSERVATIONS Seeds are eaten after being parched. They are the source of a semi-drying oil used in salads shortenings, margarine, or culinary purposes. Popular in Japanese kichen

CLASSIFICATION AND LIMITS **Seed and oil: Category 1**

NATIONAL/INT. EVALUATION -

MAIN REFERENCES

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(2) J.OilTechnol.Assoc., 10, 128, 1978
(3) Haryana Agric. Univ. J. Res., 3, 667, 1973
(4) Nippon Nogei Kagaku Kaishi, 41, 526, 1969;
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(6) J.Am. oil Che. Soc., 49, 225, 1972
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(8) Shokuhin Eiseigaku Zasshi, 23, 742, 1982
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(10) Toxicology, 5, 319, 1976
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(12) Fenaroli, 1995

DATA BASES USED Keywords: Sesamum indicum, sesame
NAPRALERT (1988-2001), BIOSIS (1973-2001), CHEMABS (1967-1999), TOXLINE (1969-1999), FSTA (1969-1999), MEDLINE (1966-1999)

SYS NAME	**Silybum marianum** (L) Gaertn.
CE No	2103
STEINMETZ No	1064
FEMA No	-
ORDER	Campanulales
FAMILY	Compositae
NAME	**E** Lady's thistle **F** Chardon Notre Dame **D** Mariendistel **I** Cardo Mariano
SYNONYMS	Carduus Marianus L.
PARTS USED	Flowering tops, seed.
IMPORTANT CONSTITUENTS	Seed extract: silymarin (a mixture of silybin, silydianin and isosilybin); silychristin; betaine; linoleic, oleic, palmitic, arachidic, and behenic acids (1-11). Flowering tops extract: apigenin; kaempferol; apigenin-7-O-glucuronide; apigenin-7-O-glucoside; silandrin-3-desoxy-isosilybin; silymarin-3-desoxy-silydianin; 5,7-dihydroxy-chramone; luteolin; luteolin-7-glucoside; kaempferol-7-glucoside (12-15)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Liqueurs
LEVEL OF USE	0.5 kg/1000L finished flavoured product (liqueur) (IOFI)
PREPARATION	Extract
MAIN TOXICOLOGICAL DATA	Seed extract administered to mice by i.m. injection (1ml every day for 1 week) did not have any toxic effect (16). The liver protective effect of flavonolignans from Silybum Marianum, has been established in vivo and in many in vitro liver damage models (17-20)
DATA NEEDED	Quantitative data on chemical composition and, if necessary, 28-day oral study and mutagenicity studies on extracts
SPECIFIC OBSERVATIONS	-
CLASSIFICATION AND LIMITS	**Flowering tops, seeds and preparations: Category 5**
NATIONAL/INT. EVALUATION	-
MAIN REFERENCES	(1) Pak.J.Ind.Sci.Res., 26,244,1983 (2) Tluszcze Jadalne, 24,11,1986 (3) Nanjing Yaoxueyuan Xuebao, 16,12,1986 (4) Herb. Hung., 23,53,1984 (5) Res. Ind., 27, 37,1982 (6) Pharmazie, 37,1,1982 (7) Planta Med., 38,377, 1980 (8) J.C.S. Chem. Camm., 696, 1979 (9) Spectroscopy Letters, 23, 1007, 1990 (10) Grasas y Aceites, 38, 93, 1987 (11) J. Chromat., 281, 263, 1983 (12) Sci. Pharm., 49, 157, 1981 (13) Planta Med., 43, 121, 1981

(14) Planta Med. 54, 44. 1988
(15) Phytochemistry, 28, 1751, 1989
(16) Akak Nauk Azerbidzzhan SSR No 6 71-75, 1954
(17) Arzneim-Forsch, 23, 148, 1973
(18) Arzneim-Forsch., 23, 159, 1973
(19) Arzneim-Forsch., 23, 160, 1973
(20) Eur. J. Drug Metab. Pharmacokinet., 15, 333, 199

DATA BASES USED

Keywords: Silybum Marianum
NAPRALERT (1988-2001), BIOSIS (1973-2001), CHEMABS (1967-1999), TOXLINE (1969-1999), FSTA (1969-1999), MEDLINE (1966-1999)

SYS NAME	**Smilax aristolochiifolia** Mill.
CE No	2104A
STEINMETZ No	-
FEMA No	-
ORDER	Liliiflorae
FAMILY	Liliaceae (Smilacaceae)
NAME	**E** Mexican sarsaparilla, wild liquorice **F** Salsepareille **D** Osterluzeiblättrige Stechwinde **I** Salsapariglia
SYNONYMS	Smilax medica Schlechtend. et Cham., S. milleri Steud., S. ornata Lem. (by some authors regarded as different species)
PARTS USED	Roots (1)
IMPORTANT CONSTITUENTS	Qualitatively similar to Smilax regelii (CE No. 434) with a content of 0.5-3% steroidal saponins in the roots, mainly the bisdesmosidic furostanolglycoside sarsaparilloside (= bisdesmosidic glycoside of (25S)-5β-furostan-triol-(3β, 22α, 26); yielding parillin), desgluco-parillin and desgluco-desrhamno-parillin (2,3,4)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Nonalcoholic and alcoholic beverages, frozen dairy, candies (5)
LEVEL OF USE	Root, extract: nonalcoholic beverages 20 ppm, alcoholic beverages 30 ppm, frozen dairy 10 ppm, candies 10 ppm (5)
PREPARATION	Extract („plant“, not further specified) (5)
MAIN TOXICOLOGICAL DATA	see Smilax regelii (CE No. 434)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Sources of „Sarsaparilla radix“ are S. aristolochiifolia, S. regelii and S. officinalis (1)
CLASSIFICATION AND LIMITS	**Roots and preparations: Category 2**
NATIONAL/INT. EVALUATION	Mexican Sarsaparilla Root: CFR 175.510
MAIN REFERERENCES	(1) Hagers Handbuch der Pharmazeutischen Praxis 1993-1995), 5th Ed. Vol. 4-6 Drogen, Haenseler R. et al. (Eds.), Springer, Berlin (2) Tschesche R. et al., Chem. Ber. 102: 1253-1269 (1969) (3) Tschesche R. et al., Liebigs Ann. Chem. 699: 212 (1966) (4) Mahato S.B. et al., Phytochemistry 21 (5) : 959-978 (1982) (5) IOFI, Results of an IOFI inquiry on natural source materials (circular letter 99/7) CE CEFS RD 5/1-46 (2000)

DATA BASES USED

Keywords: Smilax aristolochiifolia, Sarsaparilla
MEDLINE (1966-1999), EMBASE (1980-1999),
BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Smilax officinalis** Kunth in H.B.K.
CE No	2104
STEINMETZ No	-
FEMA No	-
ORDER	Liliiflorae
FAMILY	Liliaceae (Smilacaceae)
NAME	**E** Guajaquil-, Ecuador- or Jamaika sarsaparilla **F** Salsepareille **D** Stechwinde **I** Salsapariglia
SYNONYMS	-
PARTS USED	Roots, roots with part of rhizomes (1)
IMPORTANT CONSTITUENTS	Qualitatively similar to Smilax regelii (CE No. 434). Three new (monodesmosidic) steroidal saponins have been isolated from the rhizomes and their structures established, i.e. sarsasapogenin 3-*O*-*beta*-D-glucopyranosyl-(1-->4)-[*alpha*-L-arabinopyranosyl-(1--> 6)-*beta*- D-glucopyranoside, neotigogenin 3-*O*-beta-D-glucopyranosyl-(1-->4)-[*alpha*-L-arabinopyranosyl-(1-->6)]-*beta*- D-glucopyranoside and 25*S*-spirostan-6 *beta*-ol 3-*O*-*beta*-D-glucopyranosyl-(1-->4)-[*alpha*-L-arabinopyranosyl-(1--> 6)]-*beta*- D-glucopyranoside, the latter compound being an uncommon steroidal aglycone (2)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Nonalcoholic and alcoholic beverages, frozen dairy, candies (3)
LEVEL OF USE	Root extract: nonalcoholic beverages 20 ppm, alcoholic beverages 30 ppm, frozen dairy 10 ppm, candies 10 ppm (3)
PREPARATION	Extract („plant“, no further information) (3)
MAIN TOXICOLOGICAL DATA	see Smilax regelii (CE No. 434)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Sources of „Sarsaparilla radix“ are S. aristolochiifolia, S. regelii and S. officinalis (1). The species S. officinalis is not listed in Zander (4), however, listed in Schultze (5). Botanically, the species is only incompletely known (1)
CLASSIFICATION AND LIMITS	**Roots, rhizomes and preparations: Category 2**
NATIONAL/INT. EVALUATION	-
MAIN REFERERENCES	(1) Hagers Handbuch der Pharmazeutischen Praxis (1993-1995), 5th Ed. Vol. 4-6 Drogen, Haenseler R. et al. (Eds.), Springer, Berlin (2) Bernardo RR et al. Phytochemistry 43: 465-469 (1996)

(3) IOFI, Results of an IOFI inquiry on natural source materials (circular letter 99/7), CE CEFS RD 5/1-46 (2000)
(4) Zander R., Handwörterbuch der Pflanzennamen, 13. Auflage, F. Encke, G. Buchheim, S. Seybold (Ed.), Verlag Eugen Ulmer, Stuttgart (1984)
(4) Schultze-Motel J. (Ed.) Rudolf Mansfeld Verzeichnis landwirtschaftlicher und gärtnerischer Kulturpflanzen, Vol. 3, p. 1353-1363, Springer, Berlin (1986)

DATA BASES USED

Keywords: Smilax officinalis, sarsaparilla
Medline (1966-1999), Embase (1980-1999), Biological Abstracts (1989-1999)

SYS NAME	**Smilax regelii** Killip et C.V. Morton
CE No	434
STEINMETZ No	-
FEMA No	3009
ORDER	Liliiflorae
FAMILY	Liliaceae (Smilacaceae)
NAME	**E**Honduras sarsaparilla, Jamaican sarsaparilla **F** Salsepareille de l'Honduras **D** Honduras-Sarsaparille **I** Salsapariglia di Honduras
SYNONYMS	Smilax grandifolia Regel, S. ornata J.D.Hook., S. saluberrima Gilg, S. utilis Hemsl. (1)
PARTS USED	Roots (2)
IMPORTANT CONSTITUENTS	Roots and rhizomes contain steroids (sarsapogenin, smilagenin, tigogenin, neotigogenin, diosgenin, yam-ogenin) and their glycosides (1-3% steroidal saponins (3), i.e. spirostanol- and furostanolglycosides) including sarsasaponin, smilasaponin (yielding smilacin), sar-saparilloside (yielding parillin), and sterols and other triterpenes (sitosterol, sitosterol glucoside [sitosteroline], stigmasterol, pollinastanol) (4,5,6), a trace of volatile oil (2,5)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, soft candy, nonalcoholic beverages (root beer) (2)
LEVEL OF USE	Sarsaparilla root, alcoholic extract (Smilax ssp.): baked goods 2000 ppm, frozen dairy 200 ppm, candies 1000 ppm, nonalcoholic beverages 13 ppm. Sarsaparilla bark, alcoholic extract: nonalcoholic beverages 220 ppm, candies 150 ppm (7)
PREPARATION	Fluid extract and dried water-alcohol extract (2)
MAIN TOXICOLOGICAL DATA	Irritating effect on mucous membranes due to saponins. High dosages have a strong diuretic effect and induce nausea, irritation of the stomach, nephritis, shock, paralysis of heart and CNS (8,9,10). The saponins may cause gastric irritation or temporary kidney impairment. Sarsaparilla saponins facilitate the absorption of other drugs by the body. Sarsaparilla is reported to have hepatoprotective (11), diuretic, and antiinflammatory activity (12,13). Acute administration of sarsaparilla extract in the dose range of 0.5 to 3.0 g/kg bw did not produce any adverse effects or mortality in mice over a period of 24 hours. Oral doses of 100 mg/kg bw extract to 20 male and female mice during 90 days did not influence behavior and growth of animals and had no significant effects on hemoglobin content, erythrocyte and leucocyte count compared to controls. (11). Biological properties of the bisdesmosidic furostanolglycosides differ significantly from monodesmosidic spirostanolglycosides: sarsaparillosid has a low hemolytic index (in isolated erythrocytes)

compared to parillin (<4000 vs. 250'000) (14) and no bacteriostatic and fungicidal activity (4)

DATA NEEDED No data required

SPECIFIC OBSERVATIONS Other sources of Sarsaparilla extract are Smilax officinalis Kunth (CoE Nr. 2104) (also called Honduras sarsaparilla), S. aristolochiifolia Mill. (Syn. S. medica (Mexican sarsaparilla)), S. febrifuga Kunth (Ecuadorean sarsaparilla), S. ornata Lem., and undetermined Smilax species (Ecuadorean or Central American sarsaparilla) (2,6). Sources of „Sarsaparilla radix" are S. aristolochiifolia, S. regelii and S. officinalis (1)

MAIN REFERENCES

(1) Hagers Handbuch der Pharmazeutischen Praxis (1993-1995), 5th Ed., Vol. 4-6 Drogen, Haenseler R. et al. (Eds.), Springer, Berlin
(2) Fenaroli (1995)
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(5) Karrer (1958)
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(7) IOFI, Results of IOFI inquiries concerning natural source materials, Letter to CoE, October 2001
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(9) Roth L. et al., Giftpflanzen – Pflanzengifte, 3rd Ed., p. 609-610, ecomed Landsberg (1988)
(10) Jaretzki R., Pharmazie 6: 115-117 (1957)
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(13) Ageel A.M. et al., Drugs Expl. Clin. Res. 15: 369 (1989)
(14) Steinegger E., Hänsel R., Pharmakognosie, 5th Ed., Springer Verlag, Berlin (1992)

CLASSIFICATION AND LIMITS **Roots and preparations: Category 2**

NATIONAL/INT. EVALUATION Sarsaparilla extract: CFR 172.510 (food use)

DATA BASES USED Keywords: Smilax regelii, Sarsaparilla
MEDLINE (1966-1999),EMBASE (1980-1999),
BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Styrax benzoin** Dryand.
CE No	439
STEINMETZ No	-
FEMA No	Benzoin: 2132. Benzoin resin: 2133
ORDER	Theales
FAMILY	Styracaceae
NAME	**E** Benzoin **F** Benjoin **D** Benzoë, Benzoin, Benzoe-Storax **I** Benzoino **ESP** Benjui
SYNONYMS	-
PARTS USED	Resinoid
IMPORTANT CONSTITUENTS	Resin consists mainly of two alcohols combined with cinnamaic acid, free cinnamoic and benzoic acids (5). Resin: Mainly esters of cinnamaic and bezoic acids together with free acids. Sumatra benzoin (Styrax benzoin) contains 70-80% coniferyl cinnamate, cinnamyl cinnamate and coniferyl benzoate; about 10% free cinnamic acid, small amounts of benzoic acid and traces of benzaldehyde, vanillin and styrene. Siam benzoin (S.tonkinensis) contains 60-80% coniferyl benzoate and cinnamyl benzoate, about 12% free benzoic acid, d-siaresinolic acid and traces of cinnamic acid and vanillin (1,4)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Baked goods, frozen dairy, soft candy, gelatin, pudding, non-alcoholic beverages, alcoholic beverages, chewing gum (1, 2)
LEVEL OF USE	Baked goods 15 ppm, frozen dairy 3 ppm, soft candy 6 ppm, gelatin and pudding 5.8 ppm, non-alcoholic beverages 5.8 ppm, alcoholic beverages 5.7 ppm, chewing gum 9.6 ppm.(2) 20% in chewing gum (IOFI)
PREPARATION	Crude benzoin, benzoin resinoid, tincture and fluid extract
MAIN TOXICOLOGICAL DATA	Vanillin JECFA ADI 0-10 mg/kg bw (1967). This ADI was maintained at the 57th meeting (2001)
DATA NEEDED	28-day study and mutagenicity studies on resinoid
SPECIFIC OBSERVATIONS	Botanical sources of benzoin are also Styrax paralleloneurus Perkins, S. tonkinensis (Pierre) Craib ex Hartwick, or other species of the section Anthostyrax of the genus *Styrax*. Benzoin resinoid is prepared by extraction of the crude resinoid. Benzoin, especially Siam benzoin, has antioxidant and preservative properties and is therefore used in cosmetics
CLASSIFICATION AND LIMITS	**Benzoin and preparations: Category 5**
NATIONAL/INT.EVALUATION	Benzoin: CFR 172.515. Benzoin resin: CFR 73.1, 172.510

MAIN REFERENCES

(1) Leung, Encyclopedia of Common Natural Ingredients, J. Wiley & Sons, New York (1980)
(2) Fenaroli, Handbook of flavour ingredients, 3rd ed, CRC Press (1995)
(3) Duke, Handbook of Medicinal Herbs, CRC Press (1986)
(4) Samuelsson, Drugs of Natural Origin, Apotekarsocieten (1999)
(5) Mabberley, The Plant Book, 2nd ed, Camebridge University Press (1998)

DATA BASES USED

Keywords: Styrax benzoin
PUBMED, TOXNET, PFAF (-2004)

SYS NAME	**Uncaria gambir** (Hunter) Roxb.
CE No	465
STEINMETZ No	**-**
FEMA No	-
ORDER	Gentianales
FAMILY	Rubiaceae (Chinchonaceae)
NAME	**E** Gambir, pale catechu, gambir catechu **F** Gambir **D** Gambir, Catechu **I** Gambir
SYNONYMS	Ourouparia gambir Roxb., Ourouparia gambir Baill., Ourouparia gambier Hunt., Nauclea gambir Hunt., Cinchona kattu-kambar Steud., Uruparia gambir O. Kuntze, Uncaria gambir var. latifolia S. Moore
PARTS USED	Leaves and young branches (1)
IMPORTANT CONSTITUENTS	Dried aqueous extract of fresh leaves and young branches (Gambir) contains condensed tannins (8-47%; mainly catechutannic acid [approx. 24%]; catechu red, gambir fluorescin) and hydrolysable tannins (with gallic acid, ellagic acid, catechol); high amounts of flavonoids: catechins (30-58%; mainly d-catechin and also dl-catechin), the chalkan-flavan dimers gambiriine A_{1-3} and gambiriine B_{1-3}, the epiafzelechin-catechin dimer gambiriine C and quercetin (2,3,4,5). Furthermore, several yohimbine (indol) alkaloids including gambirtannine (0.013%), dihydrogambirtannine (0.0067%), neooxy-gambirtannine (0.0017%), and oxogambirtannine (0.017%) (6). Other alkaloids such as roxburghine A to E, each constituted from a heteroyohimbin- and a monoterpenoid-C_{10} part (at 0.0005-0.005% each) have been reported in fresh leaves (7,8,9), however, their occurrence in the fresh parts has been questioned and there are no reports on their presence in the preparations used (4)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Used as flavour component in major categories of food products, including alcoholic and nonalcoholic beverages, frozen dairy desserts, candy, baked goods, and gelatins and puddings (3)
LEVEL OF USE	No data available (10,11)
PREPARATION	Extracts (dried aqueous extract of fresh parts [Gambir]) tincture and crude (3)
MAIN TOXICOLOGICAL DATA	Oral intake of dried leaves (traditional medical use for the treatment of nose-bleeding, boils, sores, ulcers, hemorrhoids) (3) at doses of 0.5-2 g/day or of tincture at doses of 2.5-5 ml/day is tolerated without adverse effects (4). Pharmacological and toxicological properties of the tannins are adstringent, antibacterial, liver protectant activity (3). D-Catechin showed a protective acitivity in antibody-dependent liver cell cytotoxicity (4). An anti-

mutagenic activity of catechin has been reported in various strains of Salmonella typhimurium (12)

DATA NEEDED Use and use levels. 28-day oral study and mutagenicity studies on relevant preparations

SPECIFIC OBSERVATIONS Might also be used as food additive for its colouring properties (11)

MAIN REFERENCES

(1) Fenaroli (1995)
(2) Hoppe H.A., Drogenkunde, 8th Ed., de Gruyter, Berlin, New York (1975)
(3) Leung A.Y., Foster S., Encyclopedia of common natural ingredients, 2nd Ed., John Wiley&Sons, New York (1996)
(4) Hagers Handbuch der Pharmazeutischen Praxis, 5th Ed., Suppl. 2+3, Blaschek W. et al. (Eds.), Springer, Berlin (1998)
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(6) Merlini L. et al., Tetrahedron 23: 3129-3145 (1967)
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(8) Merlini L. et al., Tetrahedron Lett. 1571-1574 (1967)
(9) Merlini L. et al., Phytochem. Rep. 11: 1525-1526 (1972)
(10) IOFI, Results of an inquiry on natural source materials, circular letter 98/4, CEFS RD 5/8-43 (1998)
(11) IOFI, Results of an inquiry on natural source materials, personal communication with CEFS (1998)
(12) Nagabhushan M. et al., J. Cancer Res. Clin. Oncol. 114: 177-182 (1988)

CLASSIFICATION AND LIMITS **Leaves, young branches and preparations: Category 5**

NATIONAL/INT. EVALUATION Gambir: CFR 172.510 (1)

DATA BASES USED Keywords: Uncaria gambir, gambir
MEDLINE (1966-1998), EMBASE (1980-1998),
BIOLOGICAL ABSTRACTS (1989-1998),
CC LIFE (2/97-2/98)

SYS name	**Viburnum prunifolium** L.
CE No	480
STEINMETZ No	**-**
FEMA No	Bark extract: 2538
ORDER	Dipsicales
FAMILY	Caprifoliaceae
NAME	**E** Black haw, American sloe, stagbush **F** Viorne américain **D** Kirschblättriger Schneeball **I** Viburno **SP** Viburno
SYNONYMS	Viburnum prunifolium L. var. bushii (Ashe) Palmer§ Steyermark; Viburnum prunifolium L. var. globosum Nash ex. Schneid
PARTS USED	Bark from branches
IMPORTANT CONSTITUENTS	Bark: amentoflavone, triterpenes (α-amyrine, β-amyrine), coumarin, scopoletin, scopolin, aesculetin, chlorogenic acid, isochlorogenic acid, salicylic acid, tannins (2%), viburnin. Four iridoid glycosides of valeriana-type. (1). Bark extract: salicin (saligenin glucoside), viburnin and a trace of essential oil (2). Bark water extract: 1-methyl-2,3-dibutyl hemimellitate (4)
ACTIVE PRINCIPLES	Coumarin
PRODUCTS IN WHICH USED	Nonalcoholic and alcoholic beverages (2)
LEVEL OF USE	Nonalcoholic beverages 6 ppm, alcoholic beverages 0.5 ppm (2)
PREPARATION	Fluid extract, tincture, dried water alcoholic extract
MAIN TOXICOLOGICAL DATA	No data found
DATA NEEDED	28-day study and mutagenicity studies on preparations
SPECIFIC OBSERVATIONS	Fruits edible after frost (3)
CLASSIFICATION AND LIMITS	**Bark and preparations: Category 5; limits on coumarin**
NATIONAL/INT.EVALUATION	Bark extract: CFR 172.510
MAIN REFERENCES	**(**1) Wichtl, Teedrogen und Phytopharmaka, 4th ed, Wissenschaftliche Verlagsgesellschaft mbH Stuttgart (2002) (2) Fenaroli, Handbook of flavour ingredients, 3rd ed, CRC Press (1995) (3) Mabberley, The Plant Book, 2nd ed, Camebridge University Press (1998) (4) J Org Chem, 34(12): 4202-4203 (1969)
DATA BASES USED	Keywords: Viburnum prunifolium PUBMED, FSTA, PFAF, TOXNET (-2004)

SYS name	**Vitis vinifera** L.
CE No	485
STEINMETZ No	1206
FEMA No	**-**
ORDER	Rhamnales
FAMILY	Vitaceae
NAME	**E** European grape, grapevine **F** Vigne, vigne vinifère **D** Weinrebe, Weinstock **I** Vite
SYNONYMS	-
PARTS USED	Fruit (grapes), leaf, seed, lees of wine
IMPORTANT CONSTITUENTS	Leaf: flavonoids (4-5%) including quecitrin, isoquercitrin, rutin, quercetin, kaempferol. Oleanolic acid, tannins, organic acids (tartaric-, malic-, mono-p-cumarylic acid) (1). Fruit: flavonoids including kaempferol-3-mono-glucoside, quecetin-3-monoglucoside, myricetin-3-monoglucoside. Tannins, including catechin and epicatechin, organic acids and other common plant constituents (1). Anthocyanin pigments (delphinidin, petunidin, malvidin, cyanidin and peonidin) (2). Seeds: fatty oil (10-20%; linolic acid, palmitic- and myristic acid), sitosterin, tocopherol, tannins (1). Lees of wine: main non-volatile constituent: tartaric acid. Essence: Ethyl octanoate 19%, ethyl decanoate 25.5%, ethyl dodecanoate 13%, ethyl myristate 8.5%, ethyl palmitate 14%, ethyl stearate 2.5%, ethyl oleate 3%, ethyl linolate 7.5%, ethyl linolenate 2%, isoamyl octanoate 0.1%, isoamyl decanoate 0.4%, isoamyl dodecanoate 0.1%, isoamyl myristate 0.15%. (IOFI 2001)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Beverages, foods, sauces (IOFI 1994, 2001)
LEVEL OF USE	Leaves: 1 g/L in beverages. Seeds: 1 g/L in beverages and 36g/kg in foods. Lees of wine*:* 0.6 g/L in beverages and 2.1 g/kg in foods (sauces) (IOFI 1994, 2001)
PREPARATION	Extract
MAIN TOXICOLOGICAL DATA	Many studies have been carried out concerning constituents from different parts of grapevine, especially from fruits and seeds. Studies have mainly focused on the protective effect of substances found in the different parts of the plant. No relevant toxicological findings have emanated from literature found since the 4th millennium BC in Egypt and Syria, and since 2500 BC in the Aegean (5). The fruits and leaves have been used as foodstuffs during thousands of years
DATA NEEDED	Quantitaive chemical data on preparations from leaves, seeds and lees of wine and, if necessary, 28-day oral study and mutagenicity studies on preparations
SPECIFIC OBSERVATIONS	**F**uit and leaf are foodstuffs. Grape skin extract (enocianina) is used as food colorant. Seed oil is used as cooking oil. (4)

CLASSIFICATION AND LIMITS	**Fruit, leaves, seeds, lees of wine: Category 1**
NATIONAL/INT.EVALUATION	Grape skin extract: US: Grape skin extract has been approved for food use in beverages only, with specific restrictions CFR 73.170
MAIN REFERENCES	**(**1) List and Hörhammer (1967-80) (2) Am J Enol Vitic 29(1), 42-49 (1978) (3) Eur J Drug Metabol Pharmaco 1, 15-30 (1978) (4) Leung, Encyclopedia of common natural ingredients, J Wiley & Sons, New York (1980) (6) Mabberley, The Plant Book, 2nd ed, Camebridge University Press (1998).
DATA BASES USED	Keywords: Vitis vinifera CHEMICAL ABSTRACTS (1969-92), FSTA (1969-92), BIOSIS 1973-92, TOXLINE (1969-92), PUBMED (-2004)

SYS NAME	**Yucca filamentosa** L.
CE No	487
STEINMETZ No	-
FEMA No	3120
ORDER	Liliiflorae
FAMILY	Agavaceae
NAME	**E** Joshua tree, yucca, Adams needle, bear grass, Spanish bayonet, thready **F** Yucca **D** Faden-Palmlilie, Yucca **I** Yucca
SYNONYMS	Yucca angustifolia hort. non Pursh., Yucca brevifolia Engelm., Yucca arborescens Trel., Yucca smalliana Fern., Yucca draconis var. arborescens, Clistoyucca arborescens
PARTS USED	Leaves (1)
IMPORTANT CONSTITUENTS	Leaves are rich in steroidal saponins (Yuccoside B, C, E; 0.6% cristalline steroidsapogenins) (2,3) with the major sapogenin being sarsapogenin and tigogenin (1,4)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Nonalcoholic beverages (root beer) (1,5)
LEVEL OF USE	Yucca leaves, extract (Yucca ssp.): nonalcoholic beverages 600 ppm (1,5)
PREPARATION	Solid extract prepared by hot-water extraction (1)
MAIN TOXICOLOGICAL DATA	See Yucca schidigera (CE No. 487A)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Yucca extracts (Yucca ssp.) are extensively used as foaming agent in root beer, other frothy drinks and dairy drinks (1,6)
CLASSIFICATION AND LIMITS	**Leaves and preparations: Category 2**
NATIONAL/INT. EVALUATION	Yucca (Joshua tree), leaf: CFR 172.510

MAIN REFERENCES

(1) Leung A.Y., Foster S., Encyclopedia of common natural ingredients, 2nd Ed., John Wiley&Sons, New York (1996)
(2) Mahato S.B. et al., Phytochemistry 21: 959-978 (1982)
(3) Waclaw-Rozkrutowa B., (1972) through CA (1972) 78 (9): 55300p
(4) Wall M.E., Fenske Ch.S., Econ. Bot. 15: 131-132 (1961)
(5) Fenaroli (1995)
(6) Rice J., Food processing USA 44: 58 (1983)

DATA BASES USED	Keywords: Yucca filamentosa, Yucca brevifolia, Joshua tree MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)

SYS NAME	**Yucca schidigera** Roezl ex Ortigies
CE No	487A
STEINMETZ No	-
FEMA No	3121
ORDER	Liliiflorae
FAMILY	Agavaceae
NAME	**E** Mohave Yucca **F** Yucca **D** Palmlilie**,** Yucca **I** Yucca
SYNONYMS	Yucca mohavensis Sarg.
PARTS USED	Leaves (1)
IMPORTANT CONSTITUENTS	Yucca extracts (*Yucca ssp.*) are rich in steroidal saponins (generally max. 1-2% sapogenin of dry wt) with the major sapogenin being sarsapogenin and tigogenin (1,2). Mohave yucca extract contains 60% solids (3)
ACTIVE PRINCIPLES	Not known
PRODUCTS IN WHICH USED	Nonalcoholic beverages (root beer) (4)
LEVEL OF USE	Yucca (Mohave) leaves, extract (Yucca ssp.): Nonalcoholic beverages 600 ppm (1,4)
PREPARATION	Solid extract (ca. 60% solids) prepared by hot-water extraction (1)
MAIN TOXICOLOGICAL DATA	In a 12-week diet study in rats, Mohave yucca extract (containing ca. 60% solids; doses of 540, 1080 and 2160 mg/kg bw of Yucca solids, 5 rats per sex and dose group) was non-toxic with respect to various blood parameters (erythrocyte count, hemoglobin, red cell fragility, total and differencial leucocyte count, blood glucose), organ weights and histopathology, urine analysis. The extract showed about half the hemolytic activity *in vitro* as commercial soap bark saponin (extract of Quillaja saponaria CE No. 391) and one third of the activity of soya-bean saponin extract. Saponins are rarely hemolytic *per os* (3). Water extracts of another Yucca ssp. (Yucca glauca Nutt.) have shown antitumor activity against B16 melanoma (5). Effects of long-term exposure of small amounts of yucca extracts (i.e. yucca saponins) in humans are not known. Yucca extract has been used for effective treatment of arthritis, however not scientifically proved. Also used for various skin diseases in traditional medicine (6). Saponins are generally good antifungal and antibacterial agents (7)
DATA NEEDED	No data required
SPECIFIC OBSERVATIONS	Yucca extracts (Yucca ssp.) are extensively used as foaming agent in root beer, other frothy drinks and dairy drinks (1,8)

MAIN REFERENCES

(1) Leung A.Y., Foster S., Encyclopedia of common natural ingredients, 2nd Ed., John Wiley&Sons, New York (1996)
(2) Wall M.E., Fenske Ch.S., Econ. Bot. 15: 131-132 (1961)
(3) Oser B.L., Food Cosmet. Toxicol. 4: 57-61 (1966)
(4) Fenaroli (1995)
(5) Foster S., Duke J.A., A Field Guide to Medicinal Plants: Eastern and Central North America. Houghton Mifflin Co., Boston (1990)
(6) Mahato S.B. et al., Phytochemistry 21: 959-978 (1982)
(7) Tyler V.E. et al., Pharmacognosy, 9th Ed., Lea & Febiger, Philadelphia (1988)
(8) Rice J., Food processing USA 44: 58 (1983)

CLASSIFICATION AND LIMITS **Leaves and preparations: Category 2**

NATIONAL/INT. EVALUATION Yucca (Mohave), leaf: CFR 172.510

DATA BASES USED Keywords: Yucca schidigera, Yucca mohavensis, Yucca, Mohave
MEDLINE (1966-1999), EMBASE (1980-1999), BIOLOGICAL ABSTRACTS (1989-1999)