Sassafras

Species (Family)

Sassafras albidum (Nutt.) Nees (Lauraceae)

Synonym(s)

Ague Tree, Cinnamon Wood, Saloop, *Sassafras varifolium* (Salisb.) Kuntze, *Sassafras officinale* Nees & Eberm., Saxifrax

Part(s) Used

Inner root bark

Pharmacopoeial and Other Monographs

BHP 1983[G7]
Martindale 32nd edition[G43]
PDR for Herbal Medicines 2nd edition[G36]

Legal Category (Licensed Products)

Sassafras is not permitted for use in medicinal products.

Constituents[G2,G22,G41,G48,G64]

Alkaloids Isoquinoline-type about 0.02%. Boldine, isoboldine, norboldine, cinnamolaurine, norcinnamolaurine and reticuline.

Volatile oils 5–9%. Safrole as major component (80–90%), others include anethole, apiole, asarone, camphor, caryophyllene, coniferaldehyde, copaene, elemicin, eugenol, 5-methoxyeugenol, menthone, myristicin, α-pinene, α- and β-phellandrene, piperonylacrolein and thujone.

Other constituents Gum, mucilage, lignans (sesamin, desmethoxyaschantin), resin, sitosterol, starch, tannins and wax.

Food Use

Sassafras oil was formerly used as flavouring agent in beverages including root beer.[G58] However, in the 1960s safrole, the major component of the volatile oil, was reported to be carcinogenic.[G58] The use of safrole in foods is now banned, and its use in toilet preparations controlled.[G45] In the USA, safrole-free sassafras extract, leaf and leaf extract are approved for food use. In 1976, the US Food and Drugs Administration (FDA) banned interstate marketing of sassafras for sassafras tea.[G22]

Herbal Use

Sassafras is stated to possess carminative, diaphoretic, diuretic, dermatologic and antirheumatic properties. Traditionally, it has been used for cutaneous eruptions, gout and rheumatic pains.[G2,G7,G64]

Dosage

Bark 2–4 g or by infusion three times daily.[G7]

Liquid extract 2–4 mL (1:1 in 25% alcohol) three times daily.[G7]

Pharmacological Actions

Studies have concentrated on investigating the toxicity associated with the bark. However, aqueous and alcoholic extracts have been reported to elicit ataxia, hypersensitivity to touch, CNS depression and hypothermia in mice.[1] Both inhibition and induction of hepatic microsomal enzymes have been documented for safrole.[2,3] Enzyme-inducing activity was found to be a transient phenomenon, with activity falling after the onset of hepatic toxicity (*see* Side-effects, Toxicity).[2] Safrole is reported to induce both cytochrome P488 and P450 activities. Sassafras oil has been used as a topical antiseptic, pediculicide and carminative.[4]

Side-effects, Toxicity[G58]

The toxicity of sassafras is attributable to the volatile oil, and in particular to the safrole content. It is estimated that a few drops of sassafras oil are sufficient to kill a toddler and as little as one teaspoonful has proved fatal in an adult.[5] Symptoms of poisoning are described as vomiting, stupor and collapse. High doses may cause spasm followed by paralysis.[G58] Large amounts of the oil are reported to be psychoactive with the hallucinogenic effects lasting for several days.[G22] One of the components of the oil is myristicin, the hallucinogenic principle in nutmeg.

Sassafras has traditionally been used as an ingredient of beverages. To put the potential toxicity of sassafras into perspective, the following estimation has been made.[1] Extrapolation of results from animal toxicity studies indicate that 0.66 mg/kg may prove hazardous in humans.[1] By comparison, a cup of sassafras tea, prepared from a 2.5 g teabag, may provide up to 200 mg safrole, representing approximately 3 mg/kg.[1]

Safrole, the principal component of the volatile oil, was first recognised to be a hepatocarcinogen in the 1960s[6] and many animal studies have been documented concerning this toxicity.[7] Both benign and malignant tumours have developed in laboratory animals, depending on the dose of safrole administered.[2]

Both human and animal studies have shown that safrole gives rise to a large number of metabolites.[8] A sulfate ester (formed via a hydroxylated metabolite) has been established as the ultimate carcinogen for safrole with tumour incidence parallelling the rate of conversion to the ester.[9] Induction of cytochrome P450 activity has been associated with mutagenic and carcinogenic activity of the inducing agent.[10] The inducing effect of safrole on certain metabolising enzymes is thought to play a role in the carcinogenic activity of safrole. The liver has a high level of cytochrome P450 activity and is therefore susceptible to induction.[10]

Acute oral LD_{50} values for safrole have been reported as 1.95 g/kg (rats) and 2.35 g/kg (mice).[2] Major symptoms of toxicity are stated as ataxia, depression, diarrhoea, followed by death within 4 hours to seven days.[11] Rats fed safrole in their diet at concentrations of 0.25, 0.5 and 1.0% exhibited reduction in growth, stomach and testicular atrophy, liver necrosis, biliary proliferation and primary hepatomas.[G22] Animals have also developed tumours when fed safrole-free extracts.[G22]

Conflicting results have been reported from studies investigating the mutagenicity of safrole, using the Ames test and DNA repair test.[12,13] Purity of the safrole, test system employed, type of metabolic activation mix, and toxicity of the test system have been suggested as reasons for the observed variations.[12]

Contra-indications, Warnings

Sassafras should not be used internally or externally. Safrole, the major component in the volatile oil of sassafras, is hepatotoxic and even safrole-free extracts have been reported to produce tumours in animals. Sassafras essential oil is contra-indicated in internal and external use.[G58] Sassafras has been reported to inhibit and induce microsomal enzymes.

Pregnancy and lactation Sassafras is contra-indicated during pregnancy and lactation. The oil is reported to be abortifacient.[5]

Pharmaceutical Comment

In addition to its traditional herbal use for treating dermatological and rheumatic ailments, sassafras also used to be a common flavouring ingredient in beverages, in particular root beer. However, animal studies have revealed the carcinogenic and hepatotoxic potential of safrole, the major component of sassafras volatile oil. Consequently, the use of safrole is no longer permitted in foods and sassafras is not permitted as a constituent of licensed medicinal products.

Antiseptic and diuretic properties claimed for sassafras are probably attributable to the volatile oil, although no documented studies were found supporting the antirheumatic claims. Sassafras should not be used as a herbal remedy, either internally or externally.

References

See also General References G2, G7, G11, G18, G21, G22, G31, G32, G36, G41, G43, G48, G58 and G64.

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4 International Agency for Research on Cancer. *IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Some Naturally Occurring Substances, vol 10.* Geneva: WHO, 1976.

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6 Homburger F, Boger E. The carcinogenicity of essential oils, flavors, and spices: A review. *Cancer Res* 1968; 28: 2372–2374.

7 Opdyke DLJ. Sassafras oil. *Food Cosmet Toxicol* 1982; 20: 825–826.

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9 Bock KW, Schirmer G. Species differences of glucuronidation and sulfation in relation to hepato-

carcinogenesis. *Arch Toxicol* 1987; 10(Suppl.): 125–135.

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12 Sekizawa J, Shibamoto T. Genotoxicity of safrole-related chemicals in microbial test systems. *Mutat Res* 1982; 101: 127–140.

13 Swanson AB *et al.* The mutagenicities of safrole, estragole, eugenol, *trans*-anethole, and some of their known or possible metabolites for *Salmonella typhimurium* mutants. *Mutat Res* 1979; 60: 143–153.