Chaparral

Species (Family)

Larrea tridentata (DC.) Coville (Zygophyllaceae)

Synonym(s)

Creosote Bush. *L. tridentata* (south-western USA and northern Mexico) is now regarded as a separate species to *Larrea divaricata* Gav. (north-western Argentina).[1]

Part(s) Used

Herb

Pharmacopoeial and Other Monographs

Martindale 32nd edition[G43]

Legal Category (Licensed Products)

Chaparral is not included in the GSL.[G37]

Constituents[G22]

Amino acids Arginine, aspartine, cystine, glutamic acid, glycine, isoleucine, leucine, phenylalanine, tryptophan, tyrosine and valine.

Flavonoids More than 20 different compounds reported, including isorhamnetin, kaempferol and quercetin and their glycosidic and ether derivatives; gossypetin, herbacetin, and their acetate derivatives;[1–7] two C-glucosyl flavones.

Lignans Major constituent nordihydroguaiaretic acid (NDGA) (up to 1.84%), norisoguaiacin, dihydroguaiaretic acid, partially demethylated dihydroguaiaretic acid, 3'- demethoxyisoguaiacin.[8–10]

Resins 20%. Phenolic constituents on external leaf surfaces of *L. divaricata* and *L. tridentata* are reported to be identical, containing a number of flavone and flavonol glycosides, and two lignans (including NDGA).[5]

Volatile oils Many identified terpene components include calamene, eudesmol, limonene, α- and β-pinene, and 2-rossalene.[11]

Other constituents Two pentacyclic triterpenes,[12] saponins.

Other plant parts A cytotoxic naphthoquinone derivative, larreantin, has been isolated from the roots.[13]

Food Use

Chaparral is not used in foods, although a related species, *Larrea mexicana* Moric., also termed creosote bush, is listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates that creosote bush can be added to foodstuffs in small quantities, with a possible limitation of an active principle (as yet unspecified) in the final product.[G16] In the USA, NDGA is no longer permitted to be used as an antioxidant in foods following the results of toxicity studies in animals (*see* Side-effects, Toxicity).

Herbal Use

Chaparral has been used for the treatment of arthritis, cancer, venereal disease, tuberculosis, bowel cramps, rheumatism and colds.[G60]

Dosage

None documented.

Pharmacological Actions

In vitro and animal studies

Amoebicidal action against *Entamoeba histolytica* has been reported for a chaparral extract (0.01%).[14] This action may be attributable to the lignan constituents, which are documented as both amoebicidal and fungicidal.[9] NDGA has been reported to have antimicrobial activity against a number of organisms including *Penicillium* spp., *Salmonella* spp., *Streptococcus* spp., *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and various other pathogens and moulds.[8,15]

NDGA is an antioxidant, and has been documented to cause inhibition of hepatic microsomal enzyme function.[15–17]

Clinical studies

Medical interest in chaparral increased following claims that an aqueous infusion of the herb had caused the regression of a malignant melanoma in the cheek of an 85-year-old man.[18] However, results of a subsequent study that investigated the antitumour action of chaparral, as a tea, were inconclusive.[G60]

Side-effects, Toxicity

Acute hepatitis has been associated with chaparral ingestion.[19–21] Contact dermatitis to chaparral has been reported.[22,23] Chaparral-induced toxic hepatitis has been reported for two patients in different parts of the USA. The adverse effects were attributed to ingestion of a herbal nutritional supplement derived from the leaves of chaparral. Five cases of serious poisoning in the USA and another three in Canada have been linked to chaparral-containing products.[20,24] Some patients have developed irreversible reno-hepatic failure. Early investigations into the toxicity of NDGA concluded it to be low.[15] NDGA has been administered to humans, by intramuscular injection, in doses of up to 400 mg/kg body weight for 5–6 months, with little or no toxicity reported.[15] Documented oral LD_{50} values for NDGA include 4 g/kg (mouse), 5.5 g/kg (rat) and 830 mg/kg (guinea-pig).[15] Results of chronic feeding studies (two years, 0.25–1.0% of diet) in rats and mice reported no abnormalities in histological tests of the liver, spleen and kidney. Inflammatory caecal lesions and slight cystic enlargement of lymph nodes near the caecum were observed in rats at the 0.5% feeding level. At this point NDGA was considered to be safe for food use. However, two later studies in rats (using NDGA at up to 3% of the diet) reported the development of cortical and medullary cysts in the kidney.[15] On the basis of these findings, NDGA was removed from GRAS (Generally Recognised As Safe) status in the USA and is no longer permitted to be used as an antioxidant in foods.[15]

Contra-indications, Warnings

In view of the reports of acute hepatitis associated with chaparral ingestion, and the uncertainty regarding NDGA toxicity, consumption should be avoided. Excessive doses may interfere with monoamine oxidase inhibitor (MAOI) therapy, because of the documented amino acid constituents.

Pregnancy and lactation *In vitro* utero activity has been documented for chaparral.[G30] In view of the concerns regarding toxicity, chaparral should not be ingested during pregnancy or lactation.

Pharmaceutical Comment

The chemistry of chaparral is well studied and extensive literature has been published on the principal lignan component, NDGA. However, little documented evidence is available to justify the herbal uses of chaparral. In view of the concerns over the hepatic toxicity, the use of chaparral as a herbal remedy cannot be recommended.

References

See also General References G16, G18, G20, G22, G30, G31, G32, G36, G37, G43 and G60.

1 Bernhard HO, Thiele K. Additional flavonoids from the leaves of *Larrea tridentata*. *Planta Med* 1981; 41: 100–103.
2 Sakakibara M *et al.* 6,8-Di-C-glucosylflavones from *Larrea tridentata* (Zygophyllaceae). *Phytochemistry* 1977; 16: 1113–1114.
3 Sakakibara M *et al.* A new 8-hydroxyflavonol from *Larrea tridentata*. *Phytochemistry* 1975; 14: 2097–2098.
4 Sakakibara M *et al.* New 8-hydroxyflavonols from *Larrea tridenta*. *Phytochemistry* 1975; 14: 849–851.
5 Sakakibara M *et al.* Flavonoid methyl ethers on the external leaf surface of *Larrea tridentata* and *L. divaricata*. *Phytochemistry* 1976; 15: 727–731.
6 Chirikdjian JJ. Isolation of kumatakenin and 4',5-dihydroxy-3,3',7-trimethoxyflavone from *Larrea tridentata*. *Pharmazie* 1974; 29: 292–293.
7 Chirikdjian JJ. Flavonoids of *Larrea tridentata*. *Z Naturforsch* 1973; 28: 32–35.
8 Gisvold O, Thaker E. Lignans from *Larrea divaricata*. *J Pharm Sci* 1974; 63: 1905–1907.
9 Fronczek FR *et al.* The molecular structure of 3'-demethoxynorisoguaiacin triacetate from creosote bush (*Larrea tridentata*). *J Nat Prod* 1987; 50: 497–499.
10 Page JO. Determination of nordihydroguaiaretic acid in creosote bush. *Anal Chem* 1955; 27: 1266–1268.
11 Bohnstedt CF, Mabry TJ. The volatile constituents of the genus *Larrea* (Zygophyllaceae). *Rev Latinoam Quim* 1979; 10: 128–131.
12 Xue H-Z *et al.* 3-β-(3,4-Dihydroxycinnamoyl)-erythrodiol and 3β-(4-hydroxycinnamoyl)-erythrodiol from *Larrea tridentata*. *Phytochemistry* 1988; 27: 233–235.
13 Luo Z *et al.* Larreatin, a novel, cytotoxic naphthoquinone from *Larrea tridentata*. *J Org Chem* 1988; 53: 2183–2185.
14 Segura JJ *et al.* In-vitro amebicidal activity of *Larrea tridentata*. *Bol Estud Med Biol* 1979; 30: 267–268.

15 Oliveto EP. Nordihydroguaiaretic acid. A naturally occurring antioxidant. *Chem Ind* 1972: 677–679.
16 Burk D, Woods M. Hydrogen peroxide, catalase, glutathione peroxidasequinones, nordihydroguaiaretic acid, and phosphopyridine in relation to X-ray action on cancer cells. *Radiation Res Suppl* 1963; 3: 212–246.
17 Pardini RS *et al.* Inhibition of mitochondrial electron transport by nor-dihydroguaiaretic acid (NDGA). *Biochem Pharmacol* 1970; 19: 2695–2699.
18 Smart CR *et al.* An interesting observation on nordihydroguaiaretic acid (NSC-4291; NDGA) and a patient with malignant melanoma—a preliminary report. *Cancer Chemother Rep Part 1* 1969; 53: 147.
19 Katz M, Saibil F. Herbal hepatitis: subacute hepatic necrosis secondary to chaparral leaf. *J Clin Gastroenterol* 1990; 12: 203–206.
20 Clark F, Reed R. Chaparral-induced toxic hepatitis – California and Texas, 1992. *Morb Mortal Wkly Rep* 1992; 41: 812–814.
21 Gordon DW *et al.* Chaparral ingestion – the broadening spectrum of liver injury caused by herbal medicines. *JAMA* 1995; 273: 489–490.
22 Leonforte JF. Contact dermatitis from *Larrea* (creosote bush). *J Am Acad Dermatol* 1986; 14: 202–207.
23 Shasky DR. Contact dermatitis from *Larrea tridentata* (creosote bush). *J Am Acad Dermatol* 1986; 15: 302.
24 Anon. Toxic tea. *Pharm J* 1993; 250: 366.