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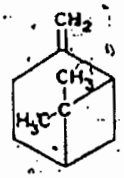
(3)

β-PINENE

Synonyms: Nopinene; 2(10)-pinene.
Structure:



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Description and physical properties: A colourless liquid.
Occurrence: β-Pinene often accompanies α-pinene in turpentine oils. It is also found in various other essential oils, including those of lemon, nutmeg, hyssop, coriander and cumin seed. *d*-β-Pinene has been identified in sulphate turpentine oil and in the oil of *Ferula galbaniflua*; *l*-β-Pinene is found in Oregon Balsam, Douglas fir needle oil, petitgrain oil and in various abies and pinus species (Guenther, 1949).
Preparation: By isolation from American turpentine oil.
Uses: In public use since the 1930s. Use in fragrances in the USA amounts to approximately 15,000 lb/yr.

Concentration in final product (%):

	Soap	*Detergent*	*Creams, lotions*	*Perfume*
Usual	0·03	0·003	0·01	0·2
Maximum	0·3	0·03	0·05	1·2

Analytical data: Gas chromatogram, RIFM no. 75-119; infra-red curve, RIFM no. 75-119.

Status

β-Pinene was given GRAS status by FEMA (1965), is approved by the FDA for food use (21 CFR 172.515) and was included by the Council of Europe (1974) in the list of artificial flavouring substances that may be added temporarily to foodstuffs without hazard to public health. CAS Registry No. 127-91-3.

Biological data

Acute toxicity. Both the acute oral LD_{50} in rats and the acute dermal LD_{50} in rabbits exceeded 5 g/kg (Moreno, 1975). The oral LD_{50} in rats for β-pinene from the sulphate pulping of wood was found to be 4·7 g/kg and the signs of intoxication included local irritation, central nervous system depression and death from respiratory failure (Hercules, Inc., 1962).

Inhalation. The LCt_{50} values (lethal concentrations for the shortest period causing death) for inhalation of saturated β-pinene vapour (19·6 mg/litre) for rats, guinea-pigs and mice were 627, 608 and 627 mg/litre/min, respectively; the vapour produced local irritation in eyes, nose and lungs with effects on the central nervous system (Hercules, Inc., 1962).

Irritation. β-Pinene applied full strength to intact or abraded rabbit skin for 24 hr under occlusion was moderately irritating (Moreno, 1975). Tested at 12% in petrolatum, it produced no irritation after a 48-hr closed-patch test on human subjects (Epstein, 1975).

Sensitization. A maximization test (Kligman, 1966; Kligman & Epstein, 1975) was carried out on 19 volunteers. The material (RIFM no. 75-119) was tested at a concentration of 12% in petrolatum and produced no sensitization reactions (Epstein, 1975).

In experiments with oil of turpentine it was shown that only the autoxidation products of the oil and not the terpenes themselves were eczematogenic. On autoxidation of oil of turpentine, only minimal amounts, if any, of eczematogen were formed from β-pinene while Δ^3-carene was the main or sole source of eczematogen (Pirilä & Siltanen, 1955, 1956 & 1958). The more thoroughly β-pinene was purified to remove Δ^3-carene, the lower, as a rule, were the eczematogenic effects of its oxidation products (Pirilä, Kilpiö, Olkkonen, Pirilä & Siltanen, 1969; Pirilä, Pirilä & Siltanen, 1966). Hellerstrom, Thyresson & Widmark (1957) showed that β-pinene, one of the four most frequently occurring constituents of turpentine oil, is not a reactor and could not be oxidized into an eczematogenic agent for human skin. Grimm & Gries (1967), however, have reported reactions to β-pinene in patients sensitized to oil of turpentine and one case of hypersensitivity to gum turpentine was reported to be due chiefly to β-pinene (Keil, 1947).

β-Pinene induced in human volunteers a pronounced contact allergic erythema accompanied by headaches, coughing and sleeplessness (Mikhailov & Berova, 1970; Michailov, Berowa & Zuzulowa, 1970).

Metabolism. When β-pinene in propylene glycol was injected iv in a dose of 0·6 μg/kg into a young pig and a human subject, 3% was exhaled within 3 hr (Römmelt, Zuber, Dirnagl & Drexel, 1974). Both α- and β-pinene are converted in the rabbit into conjugated glucuronides of undetermined

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nature, and on heating with dilute acids these glucuronides give the aromatic hydrocarbon, cymene (Williams, 1959).

Percutaneous absorption. β-Pinene was found to be readily absorbed onto the skin of rats (Valette & Cavier, 1954). Analysis of the breath of young pigs and a human subject during and after a 30-min soaking (without inhalation of bath volatiles) in baths containing a pine-needle-oil (*Pinus pumilio*) additive indicated percutaneous absorption of β-pinene and other terpenes in amounts capable of producing therapeutic effects (Römmelt *et al.* 1974).

Carcinogenesis. When mouse skin was painted alternately with either benzo[*a*]pyrene or dibenz-[*a,h*]anthracene and with a mixture of terpenes containing β-pinene, the incidence of malignant skin changes was lower and the latent period was longer than in mice treated with the carcinogens alone (Benko, Tiboldi & Bardox, 1963).

Cytotoxicity. β-Pinene inhibited the growth of ascites sarcoma BP 8 mouse-cell cultures by 10% at a concentration of 0·1 mM and by 100% at 1 mM (Pilotti, Ancker, Arrhenius & Enzell, 1975).

Pharmacology. Rabbits fed 1 g cholesterol/day for 3 months and given daily 2 ml of a mixture of terpenes, including β-pinene, remained largely free of atheromatosis of the aorta (Benkö, Macher, Szarvas & Tiboldi, 1961). β-Pinene administered to rats sc in a dose of 500 mg/kg, or inhaled in the form of an aerosol for four daily 15-min periods, did not significantly affect either pentobarbitone sleeping time or the levels of pentobarbitone in the brain (Jori, Bianchetti & Prestini, 1969). Exposure of male rats to turpentine vapours (essentially α- and β-pinene) in a concentration of 3–4 mg/litre for a 6-hr exposure period on three consecutive days, had no effect on hexobarbitone sleeping time or the lethal effect of parathion but increased both the number of deaths due to heptachlor and the benzpyrene-hydroxylase activity (Sperling, Ewenike & Farber, 1972).

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