

VII Symposium **PROGRESS IN CLINICAL AND FORENSIC TOXICOLOGY**

2-4 June 2005, Kraków, Poland

Poison Information Centre Erfurt

c/o HELIOS Klinikum Erfurt, Nordhäuser Str. 74, D-99089 Erfurt, Germany



Absinthe

Absinthe – Revival of an old poison

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24 h - Poison Emergency Call +49-361-730 730

History

Absinthe

- Origin of the name:
the origin is not known
- Dioskurides:
αψινθος = apsinthos = annoying
απινθος = apinthos = undrinkable
- Old Egypt:
Somi = Saam in Papyrus Ebers was used as an anthelmintic drug
- Romans:
- the winner of a race with harnessed bulls got a vermouth drink in the state house (capitol)
- Importance during thousands of years:
pharmaceutical and stimulating drug:

„vermouth is useful for everything“

Artemisia absinthium L.

- *Botanic name*
Absinthium absinthium L.
engl. wormwood
- *Botany*
Fam. Asteraceae (Compositae)
The **shrub or subshrub** gets **1 metre high**, the flowering stem is **whitish**, being closely covered with fine **silky hairs**. The leaves are also whitish on both sides. The globular **flowerhead** consists of **little greenish-yellow flowers**.



Foto: Arne Anderberg

Artemisia absinthium L.

- *Occurrence*

Northafrica, Southern Europe, Kashmir and Siberia, north and south of America; canton Vallais of the Switzerland

- *Cultivation*

The plant is cultivated for pharmaceutical purposes in Eastern Europe and in the USA



Artemisia absinthium L.

- *Indication as a pharmaceutical drug*
 - appetising bitter agent (Amarum aromaticum)
ingredient in tea for diseases of the stomach, liver or gallbladder
 - in pharmaceutical preparations with choleric, digestive or invigorating properties
 - Dosing in tea:
1-1.5 g (= 1 teaspoon) of the precision cut drug;
the mean daily dose should not exceed 2-3 g of the drug;
the period of application should not be longer than one week.

Artemisia absinthium L.

- *Pharmaceutical drug*

Absinthii herba = wormwood

during the bloom time collected and dried leaves and the tips of the blooming branches are used

- *Ingredients*

- Oleum Absinthii: 0.2 – 0.8 (-1.5) % ethereal oil with a dark green, sometimes blue or brown colour

- α -Thujone, cis-Epoxyocimen, trans-Sabinylacetat, Chysanthenylacetat, Sesquiterpene, α -Bisabolol, β -Curcumen, Spathulenol

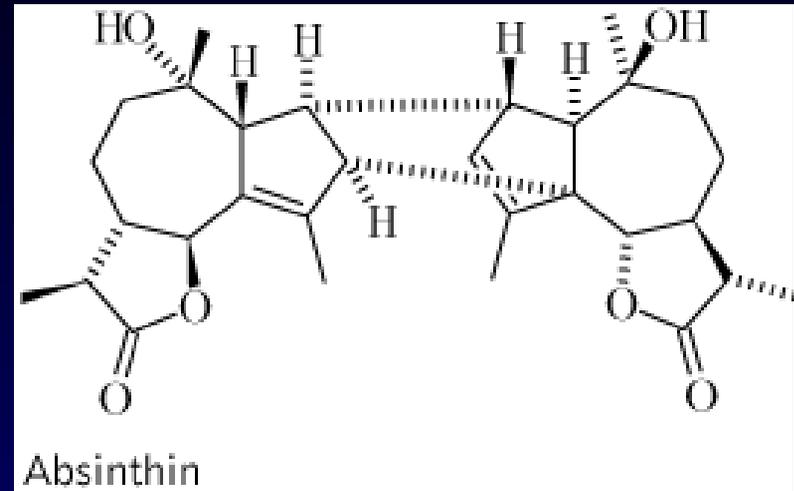
- Further ingredients: 0.2 – 0.5 % bitter agents

- **Absinthin (0.20 – 0.28 %)**

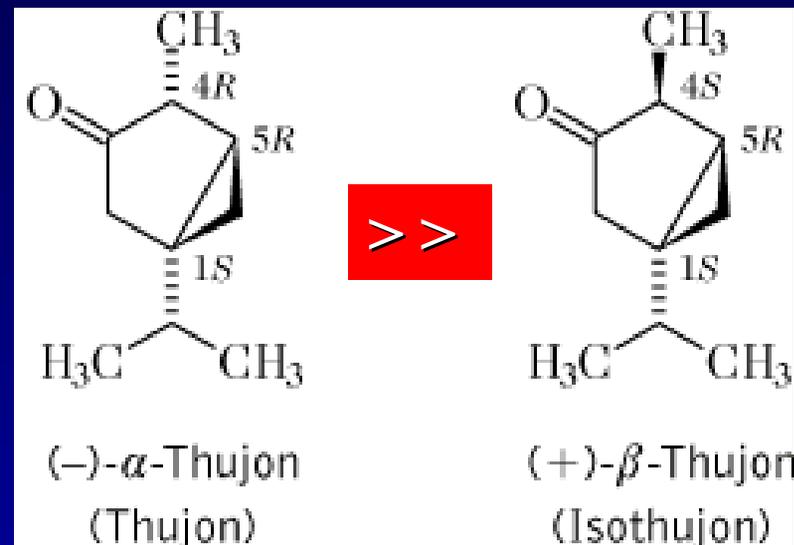
- Anabsinthin, Artabsin, Artabin, Matricin, Flavonolglykoside

Artemisia absinthium L.

- **Absinthin**
 - = dimer guaianolide
 - = sesquiterpene lactone
 - IBU¹ of the pure substance:
12.7 millions
 - in the tip of the sprout to 0.9%



- **Thujone**
 - = monoterpene
 - = derivate of isoprene
 - 10 .. 80 % of the ethereal oil



¹ reziprocal value of the drug concentration, at which a bitter taste is still noted

α -Thujone

- *pharmacological effects*
 - antinociceptive - analgetic
 - anthelmintic
 - insecticidal
- convulsive
 - porphyrinogenic
 - psychodelic ?

α -Thujone

- *Antinociceptive - analgetic effect*
 - in animal studies comparable with the effect of codeine and tetrahydrocannabinol
- *Anthelmintic effect*
 - against the roundworm *Ascaris lumbricoides* (Nematodes)
- *Insecticidal effect*
 - against the larva of the western corn rootworm beetle (*Diabrotica virgifera*)

α -Thujone

- *Convulsive effect*

Mechanism:

non-competitive inhibition of the GABA_A-receptors
(chloride channel)

Clinical features:

[acute] tonic-clonic convulsion

[chronic] manifestation of an epilepsy

Nicotine enhances the epileptogenic effects !

Treatment:

Diazepam; Phenobarbital sodium;

α -Thujone

- *Porphyrinogenic effect*

Mechanism:

enhanced production of porphyrin in hepatic chicken cells can cause acute intermittent porphyria

Clinical features :

acute abdominal pain, tachycardia, hypertonia, pain in extremities, pareses, polyneuritis, rhabdomyolysis with renal failure, red urine, convulsions, respiratory insufficiency

Diagnosis:

Porphobilinogen (PBG), delta-aminolaevulinic acid and total-porphyrin in 24-h-urine

Treatment:

continuous infusion of dextrose (4 to 6 g/kg/d).

infusion of haem-arginate (3 mg/kg/d) for 4 days.

(Normosang[®]: infoPoland@orphan-europe.com)

Prohibition

Absinthe

- Liqueur or distillate of vermouth (*Artemisia absinthium*) with characteristic green colour:
„Die grüne Fee“ (La fee verte) with an ethanol concentration of 70 % v/v and a concentration of thujone of 80 mg/L.
- Production was prohibited in **1923** in Germany as well as in the most of the other european countries.
(Exception: Great Britain and Czechia where production of absinthe with a concentration of thujone up to 10 mg/l stayed allowed.)



Revival

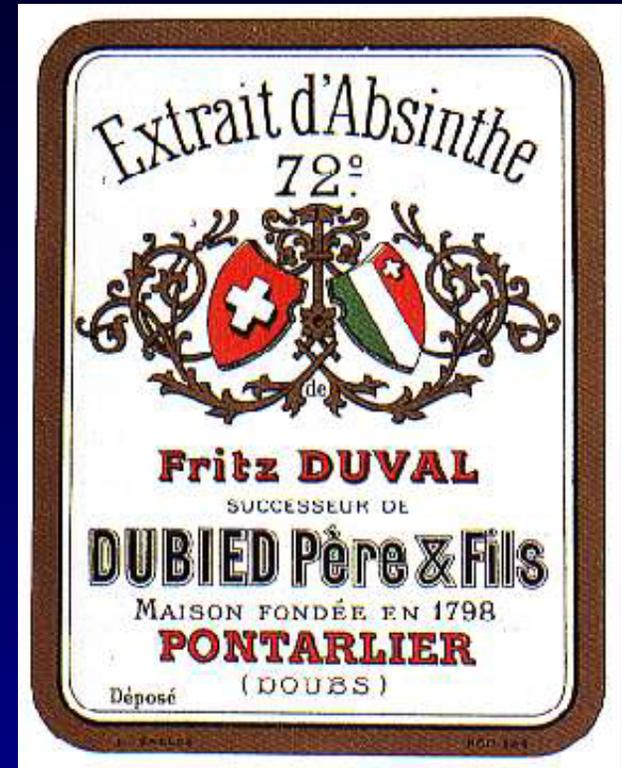
Absinthe

- The prohibition of absinthe was suspended in Germany in 1981; The oil out of vermouth, however, stayed forbidden.
- In the EU absinthe became allowed (Directive 88/388/EWG from 22.6.1988) in 1991 again.

Ethanol

α -Thujone

> 35 % v/v	max. 35 mg/L
> 25 % v/v	max. 10 mg/L
≤ 25 % v/v	max. 5 mg/L



Quelle: <http://www.lafeeverte.ch>

Thujone und THC

“We propose therefore that both thujone and THC exert psychomimetic effects by interacting with a common receptor in the central nervous system“ (Del Castillo J. et al.: Nature 1975; 253: 365-6)

TLZ

ZB WI 331

6.12.03

Doppelter Dreh beim Absinth

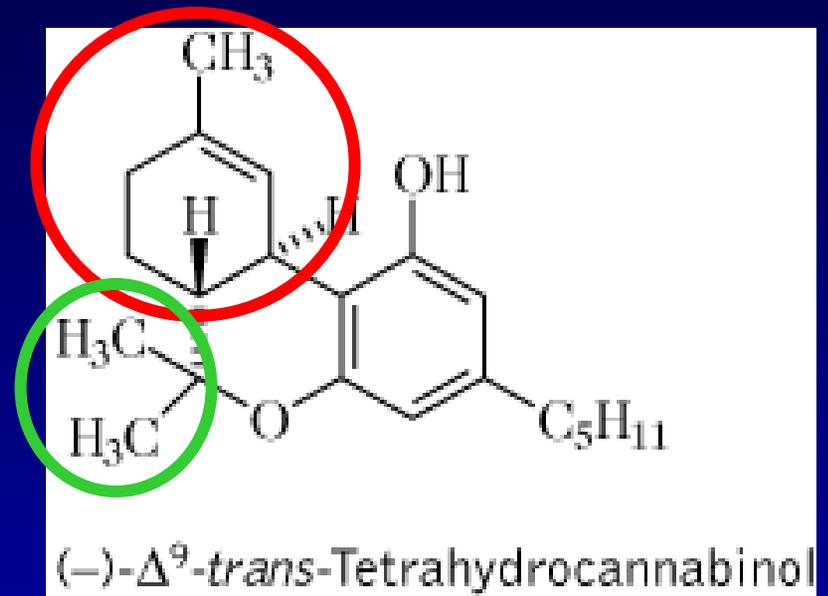
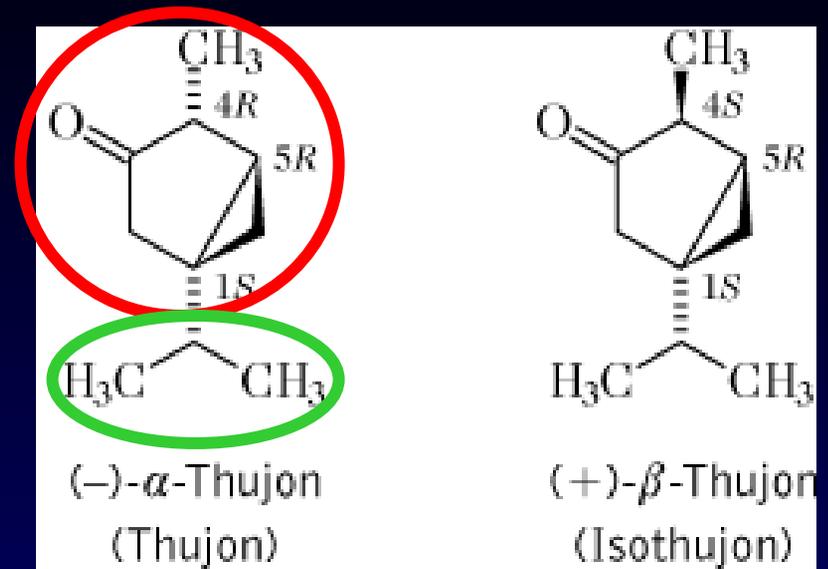
Neuer Kräuterbitter aus Magdeburg

Wermutöl gibt beiden Getränken eine berauschende Wirkung. Der Extrakt beinhaltet den erwähnten Wirkstoff Thujon, der eine ähnliche

Molekularstruktur besitzt wie der Wirkstoff der Cannabis-pflanze. Gerhard Mette nennt es „den doppelten Dreh“.

Thujone und THC

- similar biosynthesis
- similar molecular structure (terpenoids)
- Interactions with the *CB1-cannabinoid-receptor* ?
- replacement of [³H]CP55940, a cannabinoid-agonist at concentrations higher than > 10 μmol/L ~ 1.5 mg/L
- no intrinsic activity up to concentrations of 1000 μmol/L ~ 150 mg/L



Thujone und THC

Interactions with the CB1-cannabinoid-receptor

Conclusion:

„... the hypothesis that activation of cannabinoid receptors is responsible for the intoxicating effects of thujone is not supported by the present data.“

Meschler JP, Howlett AC: Pharmacol Biochem Behav. 1999 Mar;62(3):473-480

Symptoms

Absinthe

➤ **Louis Lewin in 1928:**

“A thirty years old man drunk 3 quarters of a litre absinthe (ethanol concentration was 60 % v/v) during a journey by train. Afterwards he got unconscious and sank to the ground. Three hours later he was taken to the hospital pulse- and breathless with a body temperature of 34.5°C. After gastric lavage, artificial respiration, electrical phrenical stimulation, exciting agents it was possible to improve breathing and cardial activity but the patient died 18 hours after ingestion“

Case series of the PIC Erfurt

Absinthe

- **Time period:** 1995 – 2004
- **Patients:** 6 male, 1 female; 17 to 35 years old
- **Cause of poisoning:** abuse (6), unknown (1)
- **Dose:** mostly unknown; in two cases max. 350 ml

- **Ethanol blood concentration:** mostly unknown; in two cases 1.9 and in one case 5.1 g/L, respectively.

- **Clinical features:** unconsciousness (1), convulsion (1), increase of pancreatic enzymes (1), gastrointestinal symptoms (1), hypothermia (1), bradykardia (1)

Conclusion

Absinthe

- There is *no evidence* that drinking of absinthe has similar psychogenic effects like cannabis as it is sayed in some advertisements.
- The reduction of thujone in legal absinthe beverages will reduce their *neurotoxic* and *porphyrinogenic effects* but will not eliminate them.
- The acute clinical predominant problems seen after ingestion of high amounts of absinthe beverages are mainly caused by the high overdose of *ethanol*.