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Acute Poisoning with Pine Oil – Metabolism of Monoterpenes –

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Zusammenfassung. Nach suizidaler Einnahme von 400–500 ml Terpentinöl wurde ein 49jähriger Mann in der Klinik aufgenommen. Da ein mehrfaches der Letaldosis eingenommen worden war, wurden Hämoperfusionen mit Aktivkohle und Amberlite sowie eine Hämodialyse durchgeführt.

Die Zusammensetzung des eingenommenen Terpentinöls wurde durch Gaschromatographie/Massenspektrometrie bestimmt. Vier Monoterpene wurden identifiziert: 57% α-Pinen, 8% β-Pinen, 26% Caren, 6% Limonen sowie 3% höhere Kohlenwasserstoffe. Die Blut- und Urin-Monoterpenspiegel wurden fortlaufend bestimmt. Monoterpene werden offensichtlich schlecht im Gastrointestinaltrakt resorbiert. Der resorbierte Anteil reichert sich in den lipophilen Gewebekompartimenten an und wird langsam metabolisiert und über die Nieren ausgeschieden. Die Hauptabbauwege sind Hydratation, Hydroxylierung, Umlagerungen und Acetylierung. Fünf Metaboliten konnten nachgewiesen werden.

Abstract. A patient attempting suicide ingested 400–500 ml pine oil and was admitted to the clinic. Since more than the lethal dose had been ingested hemoperfusions with activated charcoal and amberlite and a hemodialysis were performed.

The composition of the ingested pine oil was determined by gaschromatography/mass spectrometry. Four monoterpenes were identified: 57% α-pinene, 8% β-pinene, 26% carene, 6% limonene and 3% other hydrocarbons. The blood and urine monoterpene concentrations were continuously monitored. The data suggest that monoterpenes are poorly resorbed in the gastrointestinal tract. The resorbed portion of the hydrocarbons cumulates in the lipophilic body compartments and is slowly metabolized and then excreted by the kidneys. The main metabolic pathways are hydratation, hydroxylation, rearrangement, and acetylation. Five metabolites were identified.

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Key words: Acute intoxication – Metabolism of monoterpenes – Gas-chromatography/mass spectrometry – Hemoperfusion

Introduction

Pine oil is a commonly used solvent for varnish and polish. In former times it was recommended as an expectorans or used in hyperemic liniments (Wirth 1967). Pine oil consists of a mixture of monoterpenes with the general formula $C_{10}H_{16}$. These monoterpenes are unsaturated cyclic hydrocarbons with a high lipophilia.

Suicidal intoxications with ingestion of high quantities of pine oil have been scarcely reported in literature whereas accidental intoxications of children seem to happen more often. The lethal dose is in the range of 60–120 g for adults (Moeschlin 1980).

The most common poisoning symptoms reported in literature are impaired consciousness, psychomotoric excitation, delirium, head ache, nausea, ataxia, pareses, gastroenteritis, tachycardia, toxic nephritis, and renal failure (Braun 1975; Hagen 1939; Ludewig 1974; Moeschlin 1980; Werner 1932; Wirth 1967). The monoterpenes are partly excreted via the lungs which leads to a violet-like odor of the exhaled air. As far as to our knowledge no data on resorption, blood level, metabolism, and extracorporal detoxication have been published.

Table 1 gives a survey on intoxications and suspected intoxications with pine oil reported to the "Beratungsstelle für Vergiftungserscheinungen Berlin" from 1979–1980. Nearly all cases exept two were accidental poisonings. No fatal poisonings were observed.

Table 1. Intoxications and suspected intoxications with pine oil reported to the "Beratungsstelle für Vergiftungserscheinungen Berlin" (1966–1979)

	Children (1–11 years)	Adults (37–45 years)
Cases	78	6
No symptoms	38	1
Gastroenteritis, vomiting	12	4
Leukocytosis	7	–
Somnolence	4	1
Fetor ex ore	11	–
Ataxia	3	–
Erythem	4	–

Case Report

A 49 year old male (height 185 cm, body weight 85 kg) drank 400–500 ml pine oil after an argument with his wife. One hour later he was admitted to the clinic

in an extreme state of psychomotoric excitation. The patient exhaled an intensive odor of pine oil and complained about head ache. Besides an erythem of mouth and larynx a flush of the face, ataxia, and a spontaneous hyperventilation were observed. The circulatory parameters and the laboratory data were in the normal range. After continuous stomach lavage 250 ml paraffine oil and saline laxatives were given. Since more than the lethal dose of pine oil had been ingested hemoperfusions with activated charcoal and amberlite and a hemodialysis were performed (Fig. 1). Extracorporal detoxication was stopped when the monoterpene concentration in blood fell beyond 1 µg/ml.

With a latence of 10 h after ingestion the consciousness of the patient was impaired and the circulatory parameters became instable although a hypovolemy could be excluded. After infusion of dopamine and dobutamine the circulatory functions stabilized. The EEG recorded the second day revealed a decelerated activity. No eleptogenic activities could be detected. The patient had a retrograde amnesia for the period of somnolence and sopor. At this time a leukocytosis (21,000/mm^3), a slight raise of the transaminases, and a reduction of the pseudocholinesterase (1,446 U/l) were observed. The renal functions were not affected except a transient oliguria which was due to the drop of the blood pressure (Fig. 1). Three weeks later the patient left the clinic without any bodily complaints.

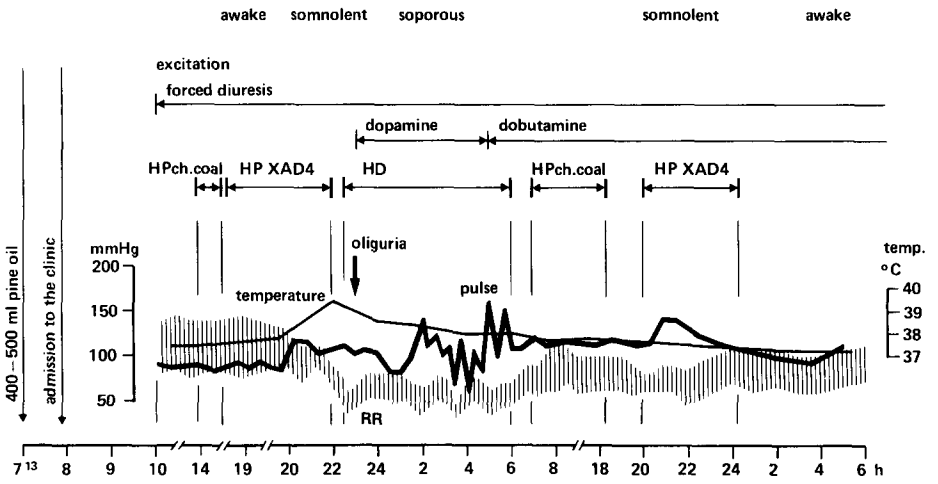

Fig. 1. Clinical course of the intoxication

Methods and Results

Since pine oil is a mixture of several isomeric monoterpenes gaschromatography/mass spectrometry is the best suited analytical method. Spectra were measured with a Finnigan gaschromatograph/mass spectrometer 4021 (GC

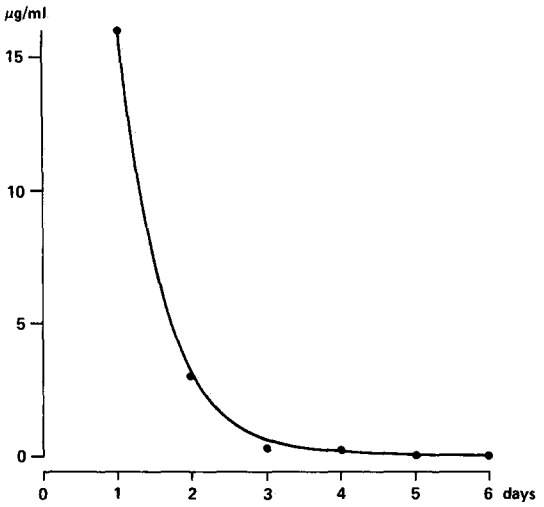

Fig. 2. α-Pinene blood concentrations

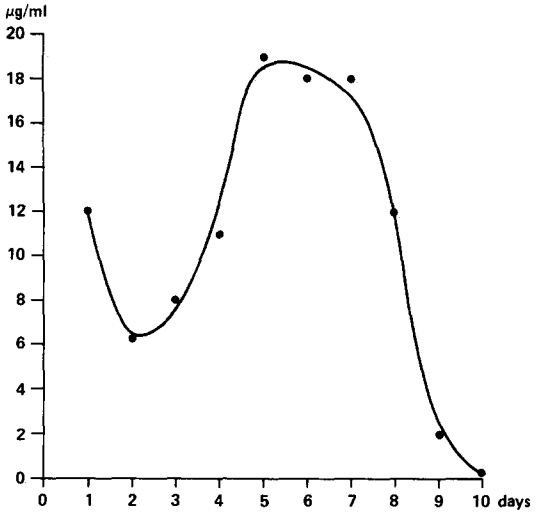

Fig. 3. Bornylacetate urine concentration

conditions: injection port 140° C, column temperature 100–130° C, 3° C/min, jet separator 250° C, 2% OV 1 on chromosorb G, length 3 m). For identification the electron impact mass spectra of the monoterpenes were run against the spectra library MSDS 3.1 of the 4021 data system. Since isomeric monoterpenes yield very similar mass spectra (Reed 1963) the retention times of the corresponding reference compounds were used as an additional conformation for structure elucidation. The pine oil which had been ingested consisted of four monoterpenes: 57% α-pinene, 8% β-pinene, 26% carene, 6% limonene, and 3% other hydrocarbons. Analysis of blood and urine were carried out at least 10 h after withdrawal of the samples. Monoterpenes have a comparatively low boiling

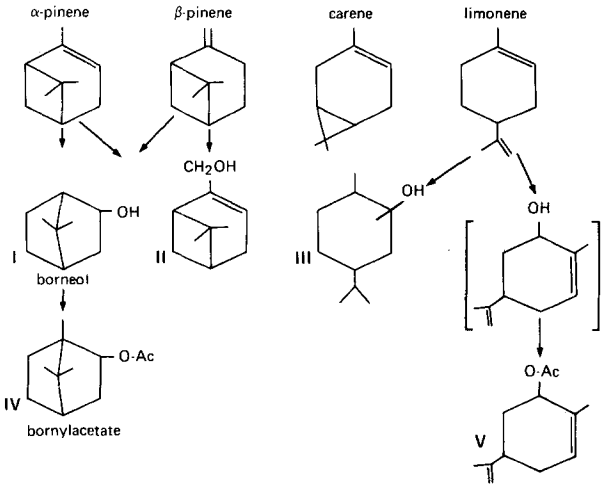

Fig. 4. Metabolism of monoterpenes

point. Therefore concentrating procedures after solvent extraction had to be avoided. 1–2 ml heparinized blood or urine were shaken 5 min with 0,2 ml pentane (nanograde Mallinckrodt) in a screw stoppered tube (internal standard 20 µg dodecane). After centrifugation 1–5 µl of the pentane layer were directly injected into the GC of the GC/MS 4021. The detection limit for α-pinene was 1 µg/ml, the recovery was 92% ± 6% SD.

α-Pinene was the monoterpene with the highest concentration in blood (Fig. 2). The metabolites of the monoterpenes could be detected solely in urine whereas in blood only the original monoterpenes were identified. The main metabolite is bornylacetate IV (Fig. 3). Metabolism occurs via hydratation, hydroxylation, rearrangement, acetylation, and reduction (Fig. 4). III is generated by hydratation and reduction of the double bond. The position of the hydroxylgroup of III could not be determined unequivocally. Ten days after ingestion a total of ~ 100 mg bornylacetate was excreted with the urine.

Hemoperfusions (Scribner shunt) were performed with a flow of ~ 150 ml/min. The clearance for α-pinene was calculated form the α-pinene blood concentrations before and after passage of the hemoperfusion cartridge: HP activated charcoal 46 ml/min, HP amberlite 133 ml/min.

Discussion

There is a striking difference between the ingested amount of pine oil (400–500 ml) and the renal excretion of bornylacetate (100 mg). This discrepancy may be explained by three effects:

1. Probably an unknown portion of the pine oil could be removed by stomach lavage.
2. The chemical and physical properties of monoterpenes are very similar to aliphatic hydrocarbons, e.g., paraffine oil which suggests that the resorption

behaviour in the gastrointestinal tract which is very poor may be similar, too. In humans the resorption of paraffine oil is 0.05% (Heckers 1978).
3. Part of the resorbed monoterpenes is exhaled via the lungs and possibly excreted with the bile.

The high affinity of the monoterpenes to lipophilic body compartments may be partly responsible for the comparatively low α-pinene blood level. The renal excretion of metabolized monoterpenes reaches its peak level 5 days after ingestion. This indicates that the resorbed portion of the monoterpenes is slowly metabolized and then excreted via kidneys. Treatment of the urine with glucuronidase gave no hint on formation of glucuronides. The less lipophilic monoterpene alcohols and acetates probably cause the nephrotoxicity observed by some authors (Moeschlin 1980). Unfortunately no feces samples were collected. Analyses of the feces might have answered the question whether monoterpenes are excreted with the bile.

Metabolism occurs via reduction hydratation, hydroxylation followed by rearrangement, and acetylation. I, II, IV are probably generated from α- and β-pinene. III and V are most likely metabolites of limonene. The precursor of V could not be detected (Fig. 4).

Hemoperfusion eliminates monoterpenes quite effectively from the blood compartment thereby protecting the renal functions. Amberlite is more effective than activated charcoal. However, monoterpenes accumulated in tissues cannot be removed effectively by hemoperfusion which is demonstrated by the delayed excretion of bornylacetate. Therefore hemoperfusion – with exception of the acute stage of the intoxication – has a limited therapeutic value. Prevention of the resorption of pine oil by stomach lavage and instillation of paraffine oil is the most effective therapy.

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