ORGANIC SOLVENTS I

Prof. Dr. Benay Can Eke

ORGANIC SOLVENTS

- Organic solvents are the liquid substances that are widely used in our homes, industry, households, and many other businesses

Where are they used…….

- 1) Solvent (melting / thinning of materials such as rubber, plastics, lacquer, varnish, paint),
- 2) Extraction Agent
- 3) As adhesive
- 4) Antifreeze (in cars),
- 5) Cleaner
- 6) Specific uses depending on chemical structures

Classification of Organic Solvents by Functional Groups

- ***Saturated hydrocarbons : Methane, ethane, propane, butane***
- ***Unsaturated hydrocarbons: Ethylene***
- ***Cyclic hydrocarbons: Cyclohexane***
- ***Aromatic hydrocarbons: Benzene, toluene***
- ***Chlorinated hydrocarbons: Chloroform, Carbontetrachloride,***
- ***trichlorethylene, perchlorethylene***
- ***Alcohols: Ethyl alcohol, methyl alcohol***
- ***Aldehydes and ketones: formaldehyde***
- ***acids***
- ***esters***
- ***amines***

- Low molecular weight
- Flammable, explosive
- Low boiling point
- vapour pressure is high at room temperature
- Volatile
- Oil / water solubility (dimethylsulfoxide-glycol ethers)

Exposure routes

Inhalation

Skin

GI

- Dose
- Exposure time
- Individual factors are important …

Effects on the Central Nervous System 1:

Headache

dizziness

Fatigue

unconsciousness

Death

Effects on Central Nervous System 2

For long-term exposure;

Behavioral changes

Sensory organs (sight, hearing)

Memory (coordination disorders, confusion)

Emotional (irritability, restlessness, depression**)**

Behavioral changes are observed

in the Sensory organs some changes are observed (sight, hearing)

in Memory (coordination disorders, confusion)

Emotionallly irritability, restlessness, depression were observed

Effects on skin;

Allergy

Dermatitis

Effects on Respiratory System;

irritation

- **Other effects;**
  Liver toxicity (carbon tetrachloride, chloroform)
  Kidney toxicity (glycol ethers)
  Heart (trichloroethane, CS2)
  Substance addiction (glue snuffing)
  Teratogenic

Cancer

Benzene-Group 1

Dichloromethane - Group 2B

Biological Monitoring

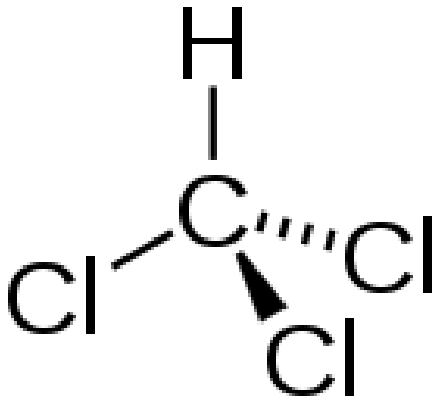
Urine

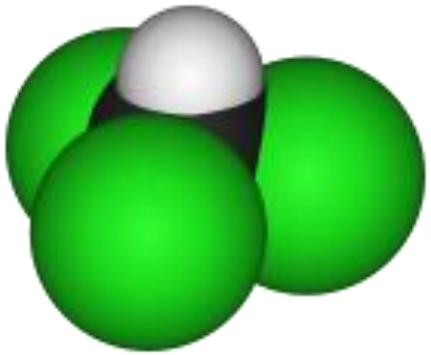
Blood

Workplace environment air

CHLOROFORM

Chemical name	Trichloromethan
Synonyme	chloroform
Chemical formula	$CHCl_3$
Molecular weight	119.38 g/mol
Physical state	Colorless liquid
Density	1.48 g/cm³, liquıd
Solubility	0.8 g/100 mL (20 °C)
Melting point	-63.5 °C
Boiling point	61 °C





The practical use of chloroform was initiated by James Young Simpson 1847 in a patient for labor.

- Due to liver toxicity was abandoned in 1900s for this purpose.
- Today; widely used for industrial purposes

Exposure, Distribution

Inhalation

Skin

Oral

After absorption, chloroform rapidly dissolves in fatty tissues, brain, liver, kidneys.

Adipose tissue> brain> liver> kidney> blood

TOXIC EFFECT OF CHLOROFORM

The main organs of chloroform are central nervous system, liver and kidneys.

In addition, toxic effects were observed in respiratory, cardiovascular and gastrointestinal systems.

METABOLISM

- Chloroform is primarily metabolized in the liver, but metabolism occurs in other tissues, such as kidneys.

METABOLISM

At low chloroform concentrations, is metabolised by **CYP2E1**.

This enzyme level is induced by different chemicals (eg alcohol).

In high chloroform concentrations, is metabolised also by CYP2B1 / 2..

METABOLISM

Oxidation reaction

The main product in the presence of oxygen is the fast and stable **phosgen**e gas formed by the dihydrochlorination of trichloromethanol.

$$2CHCl_3 + NADPH + H^+ + O_2 \longrightarrow 2\ CCl_3OH + NADP^+$$

$$CCl_3OH \longrightarrow CCl_2O + HCl$$

Reduction reaction

In the absence of oxygen, the main metabolite is **dichloromethane /**free radical.

ELIMINATION

Chloroform is primarily excreted by the lung.

90% of chloroform is excreted in the form of CO_2 with the lungs. 0.01% is excreted in the urine.

As a result of repeated contact with, chloroform was found to be in the postmortem tissue samples at the very low levels . Because the excretion and metabolism is fast.

CHLOROFORM/ CANCER

There is insufficient data on human studies to evaluate chloroform as a potential carcinogen in humans.

Group 2B (possible carcinogen)

In animals, there was an increase in the incidence of various types of liver and kidney tumors with various ways of exposure to chloroform.

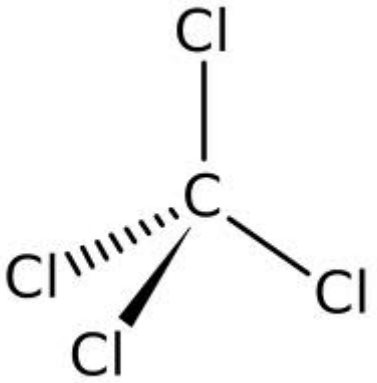
TREATMENT

- Symptomatic and supportive treatment
- O_2 support

- Respiration, excretion, kidney function
- electrolyte, acid-base balance
- Mental status
- Blood sampling
- Clinical diagnosis (chloroform determination in blood)

CARBON TETRACHLORIDE

Chemical name	Tetrachloromethan
Synonyme(s)	carbontetrachloride
Chemical formula	CCl_4
Molecular weight	153.82 g/mol
Physical state	Colorless liquid
Density	1.58 g/cm³, liquid
Solubility	0.8 g/100 mL (20 °C)
Melting point	-22.6 °C
Boiling point	77 °C



CARBON TETRACHLORIDE

- Cleaner and oil remover
- Fire extinguisher
- Pesticides
- antihelmintic
- Freon propellant was used in the coolers.
- Today, its use is restricted.

- **CARBON TETRACHLORIDE**

- Due to its high lipid solubility, it accumulates in fatty tissues (such as adipose tissue, liver).

- Most of the absorbed carbontetrachloride is excreted with the lungs unchanged.

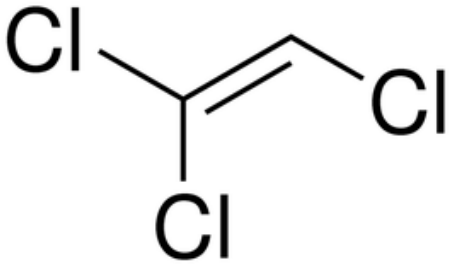
- The remainder is bioactive by metabolizing with CYP 2E1, resulting in the formation of the trichloromethyl radical.

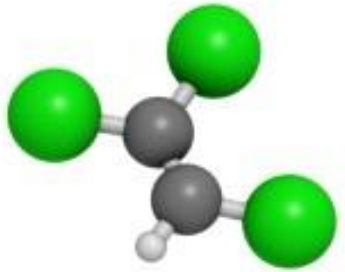
- This radical; The peroxyl radical resulting from the reaction with oxygen initiates lipid peroxidation.

- toxicity
- treatment
- Structurally similar to chloroform.

TRICHLORETHYLENE

Chemical name	Trichloroetylene
Synonyme(s)	Trilen, tri
Chemical formula	C_2HCl_3
Molecular weight	131.39 g/mol
Physical state	Colorless liquid
Density	1.47 g/cm³, liquid
Solubility	0.1 g/100 mL (20 °C
Melting point	-73°C
Boiling point	87 °C





TRICHLORETHYLENE

inhalation

Skin

Oral

It is rapidly dispersed in tissues after absorption.

TRICHLORETHYLENE

- TCE is transformed into trichloroethanol, trichloroacetic acid and trichloroethanol-glucuronide conjugates by the oxidative metabolism pathway.
- TCE is excreted in the urine as metabolites
- TCE is also excreted by the lung as unchanged metabolites

TRICHLORETHYLENE

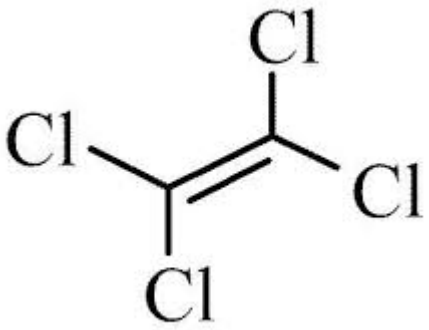
- Acute effects (inhalation, oral) excitement, headache,nausea and vomiting, coordination disorder and numbness. Coma, cardiac arrhythmias and death.
- In dermal exposure; erythema and irritation.
- For long exposures; serious irritations

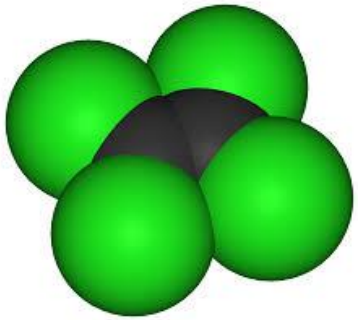
TRICHLORETHYLENE

- ***Chronic exposure;***
- ***Neurological, liver and kidney damage***
- ***Chronic dermal exposure; causes dermatitis.***
- ***Group 2A (most likely carcinogen)***

TETRACHLORETHYLENE

Chemical name	Tetrachloroetylene
Synonyme	Perchloroetylene
Chemical formula	C_2Cl_4
Molecular weight	165.83 g/mol
Physical state	Colorless liquid
Density	1.63 g/cm³, liquid
Solubility	150 mg/L (25 °C)
Melting point	-19°C
Boiling point	121 °C





- TETRACHLORETHYLENE

- It is a chlorinated hydrocarbon compound used in dry cleaning, textile industry, degreasing of metal parts, dyeing and stain removal and synthesis of chemicals.

- TCE and PER are also toxicokinetically similar to the chemical structure.

- TETRACHLORETHYLENE
- The toxic effects of tetrachlorethylene, which is widely used in the dry cleaning industry /environmentally friendly solvents.
- The Environmental Protection Agency (EPA) offers the wet cleaning method as an alternative to dry cleaning.
- biodegradable detergents.

CARBON DISULFIDE

Chemical name	Carbon disulfide
Synonyme	
Chemical formula	CS_2
Molecular weight	76.14 g/mol
Physical state	Colorless liquid
Density	1.63 g/cm³, liquid
Solubility	0.22g /100 ml (22 C)
Melting point	-111.6°C
Boiling point	46.3 °C

CARBON DISULFIDE

- Carbondisulfide is most used in the production of viscose silk and cellophane.
- It is also used in the manufacture of carbon tetrachloride, dithiocarbonates, thiocyanates and urea
- disinfecting the soil of the cereals stored in agriculture laying down the animals nested in the soil

- **CARBON DISULFIDE**
- Frequent exposure to 30-60 ppm CS_2 in the air results in headache, dizziness and hysterical behavior.

- In addition to these symptoms, mental disorder and confusion are caused by inhalation of 330 ppm CS_2 for several hours.
-
- In general, inhalation of carbon sulfide > 500 ppm causes a systemic toxic effect. Exposure to 2000-4000 ppm CS_2 vapors for a few hours results coma and death.

- **CARBON DISULFIDE**
- Exposure to high concentrations of CS2 for a long time, peripheral nervous system disorder, neurobehavioral disorder can be observed .

- It is also affect the cardiovascular system.

- Chronic exposure to CS2 causes encephalopathy. Depending on this, headache, sleep disturbance, general fatigue, emotional changes are observed.

- It also causes peripheral neuropathy.
- Another neurotoxic effect of carbon sulfide is the eye.

- Biological monitoring of carbon sulfide exposure:
- a) **CS2 determination in blood**:.

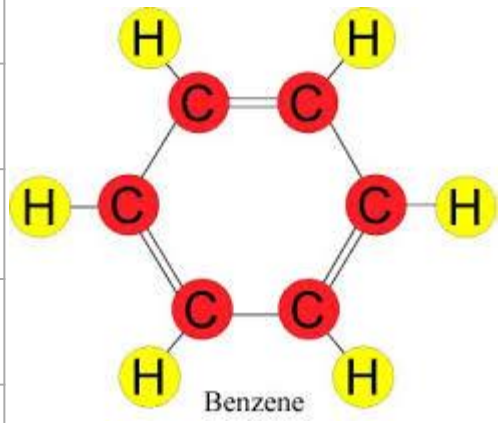
- b) **Iodine-azide test in urine:**
- c) **Determination of specific metabolites**: It has been shown that the determination of 2-thiothiazolidine-4-carboxylic acid from the metabolites of CS2 in urine can be used in biological monitoring. However, since the half-life of this metabolite is short, it is recommended that the urine sample should be taken immediately at the end of the work.

- d) **Antabus method**: For individuals who are very sensitive to CS2, the Antabus method is recommended. For this purpose, 0.5 g of disulfiram (Antabus) is administered orally to the person to be investigated for CS2 sensitivity. After 4-5 hours, diethyldithiocarbamate (DDC) is determined, there is an inverse ratio between the amount of DDK excreted in urine and sensitivity to CS2. Generally, 0.5 g of Antabus is administered orally, and those with DDK excretion over 150 mg / g creatinine in urine are taken to workplaces where CS2 production is performed.

- **n-HEXANE ve 2- HEXANONE**
- The major 6-carbon (hexacarbon) solvents used in industry include n-hexane, 2-hexanone (methyl n-butyl ketone) and cyclohexane. These organic solvents are generally among the "pests" in the industry.
- in recent years it was observed peripheral neuropathy with these chemical.

BENZENE

Chemical name	Benzene
Synonyme	Benzol
Chemical formula	C6H6
Molecular weight	78.11 g/mol
Physical state	Colorless liuqid
Density	0.87 g/cm³, liquid
Solubility	1.79 g/L (15 °C
Melting point	5.5 °C
Boiling point	80.1 °C



BENZENE

- Benzene is a by-product of petroleum and coal tar.
- As solvent and adhesive in benzene industry,
- extraction of fats and oils,
- Lubrication and cleaning of metal tools,
- In various chemical and pharmaceutical industries, in printing, In dry cleaning was used.

BENZENE

- Inhalation, Skin, GI.
- Benzene, which is absorbed, accumulates primarily in the tissues, erythrocytes, heart and skeletal muscle.
- Acute exposure
- Sleepiness, dizziness, delirium, loss of consciousness, respiratory arrest and death.
- Chronic exposure has a significant effect on the blood table: anemia and leukemia.

- **Muzaffer Aksoy, 1915-2001**

- As a result of Aksoy's work on the shoemakers, the fact that benzene caused leukemia was revealed.

- In chronic benzene poisoning,
- Hematologic disorders - Leukopenia, Anemia

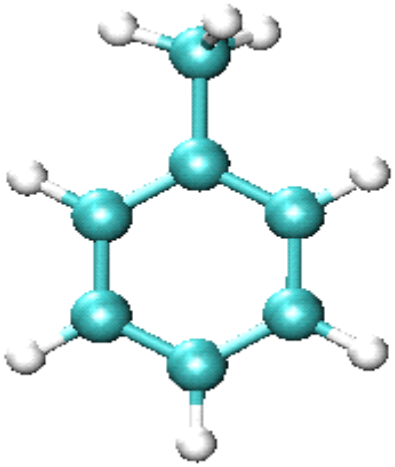
- Determination of benzene and its metabolites: Determination of phenol in urine is an important criterion. In general, phenol in the urine is more than 20 mg / L is considered as an indicator of benzene exposure.

- In addition, the relation between the ratio of inorganic sulphate / organic sulphate and the amount of inhaled benzene in urine was determined.
- Normally this rate is 85%.
- 60% when exposed to 40-75 ppm benzene;
- 40% when exposed to 75-100 ppm benzene;
- When exposed to 100-200 ppm benzene, it falls below 40%

- Determination of benzene in blood and urine in expiration air

TOLUENE

Chemical name	Toluen
Synonyme	Toluol
Chemical formula	C6H5CH3
Molecular weight	92.1 g/mol
Physical state	Colorles liquid
Density	0.9 g/cm³, liquid
Solubility	Insoluble in water.
Melting point	-94.5 °C
Boiling point	110.6 °C



- It is widely used in industry as a solvent in paints, varnishes, gums, lacquers and lacquers. There is also a place in the chemical industry.

- toluene does not cause hematological disorders.

- **(Glue sniffing habit)**
- euphoria, coma
- It has been observed hallucinations and antisocial behavior by inhalation of vapors in toluene
- Severe hepatic/ renal disorders can be observed with chronic exposure

Metabolism:

It was found that 68% was excreted as a

hippuric acid conjugate.

MOBİLYA İŞÇİLERİNDE TOLUEN VE KSİLEN MARUZİYETİNİN BİYOLOJİK İZLENMESİ

N.Vural, Y.Duydu, R.Kahraman

Ankara Üniv.Ecz.Fak.Toksikoloji A.B.D., 06100 Tandoğan - Ankara

ÖZET

Bu çalışmada vernik ve cila yapan mobilya işçilerinde, tiner maruziyetinin biyolojik indikatörü olarak toluen ve ksilen metabolitleri araştırılmıştır. Bu amaçla, mobilya işçilerinin idrar örneklerinde (n=57) toluen metabolitleri olan hippürik asit (HA) ve o-kresol (o-kr), ksilen metaboliti olan m-metilhippürik asit (m-MHA) düzeyleri gaz kromatografisi yöntemi ile ölçülmüştür. Ayrıca, mesleksel olarak maruz kalmayan kişiler (n=30) kontrol grubu olarak seçilmiştir. Mobilya işçilerinde HA düzeyi 2.90 ± 0.04 g/g kreatinin, o-kr düzeyi 1.53 ± 0.07 mg/g kreatinin ve m-MHA düzeyi ise 1.80 ± 0.04 g/g kreatinin olarak saptanmıştır. Bulgular kontrol grubuna göre anlamlı olarak yüksek ($p<0.01$) bulunmuş ve işçilerin 100 ppm civarında toluen ve ksilene maruz kaldığı yorumu getirilmiştir.

- Casarett & Doull’s Toxicology: The Basic Science of Poisons, 9th edition, 2018
- Toksikoloji , Prof. Dr. Nevin VURAL , Ankara Üniversitesi Eczacılık Fakültesi Yayınları No: 73, 2005