Chapter 5
Substance Properties of Methanol

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5.1 Physical Properties of Pure Methanol

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Methanol (also known as CH_3OH, methyl alcohol, hydroxymethane, wood alcohol, or carbinol) is a widely used basic raw material. It is a colourless neutral polar liquid that can be mixed with water and most other organic solvents in any ratio. It acts, owed to its polarity, as a solvent for many inorganic salts. The flammability of methanol (flash point 12.2 °C, ignition temperature 470 °C) can cause safety problems. For this reason, there exist many international guidelines for safe handling, explosion protection and electrical equipment to handle methanol. Methanol also is a substance of high toxicity that is rapidly and almost completely adsorbed orally (via the gastrointestinal tract), by inhalation, or through the skin.

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Table 5.1 Physical properties of pure methanol

Molecular weight	32.04 g mol^{-1}
Critical temperature	512.5 K (239 °C; 463 °F)
Critical pressure	8.084 MPa
Critical density	0.2715 g cm^{-3}
Critical compressibility factor	0.224
Specific gravity	
Liquid	
(25°/4 °C)	0.7866
(20°/4 °C)	0.7915
(15°/4 °C)	0.7960
Vapour	1.11
Vapour pressure	
20 °C (68 °F)	12.8 kPa (1.856 psia) (96 mm Hg)
25 °C (77 °F)	16.96 kPa (2.459 psia) (127.2 mm Hg)
Latent heat of vapourisation	
25 °C (77 °F)	37.43 kJ mol^{-1} (279.0 cal g^{-1})
64.6 °C (148.3 °F)	35.21 kJ mol^{-1} (262.5 cal g^{-1})
Heat capacity at constant pressure	
25 °C (77 °F) (101.3 kPa)	
Liquid	81.08 Jmol^{-1} K^{-1} (0.604 calg^{-1} K^{-1}) (0.604 Btu lb^{-1} °F^{-1})
Vapour	44.06 J mol^{-1} K^{-1} [1] (0.328 calg^{-1} K^{-1}) (0.328 Btu lb^{-1} °F^{-1})
Coefficient of cubic thermal expansion	
20 °C	0.00149 per °C
40 °C	0.00159 per °C
Boiling point	
760 mm Hg (101.3 kPa)	64.6 °C (148 °F)
Freezing point	−97.6 °C (−143.7 °F)
Reid vapour pressure	32 kPa
Flash point	
Closed vessel	12 °C (54 °F)
Open vessel	15.6 °C (60.1 °F)
Auto ignition temperature	470 °C (878 °F)
Viscosity	
Liquid	

(continued)

Table 5.1 (continued)

−25 °C (−13 °F)	1.258 mPa·s
0 °C (32 °F)	0.793 mPa·s
25 °C (77 °F)	0.544 mPa·s
Vapour	
25 °C (77 °F)	9.68 μPa·s
127 °C (261 °F)	13.2 μPa·s
Surface tension	
20 °C (68 °F)	22.6 mNm^{-1}
25 °C (77 °F)	22.07 mNm^{-1}
Refractive index	
15 °C (59 °F)	1.33066
20 °C (68 °F)	1.32840
25 °C (77 °F)	1.32652
Thermal conductivity	
Liquid	
0 °C (32 °F)	207 $\text{mWm}^{-1}\ \text{K}^{-1}$
25 °C (77 °F)	200 $\text{mWm}^{-1}\ \text{K}^{-1}$
Vapour	
100 °C (212 °F)	14.07 $\text{mWm}^{-1}\ \text{K}^{-1}$
127 °C (261 °F)	26.2 $\text{mWm}^{-1}\ \text{K}^{-1}$
Heat of Combustion	
Higher heating value	726.1 kJmol^{-1}
(25 °C, 101.325 kPa)	(22.7 kJg^{-1})
Lower heating value	638.1 $\text{kJmol}^{-1}{}_{\text{[calc]}}$
(25 °C, 101.325 kPa)	(19.9 kJg^{-1})
Flammable limits (in air)	Lower 6.0 (v/v) %
	Upper 36.5 (v/v) %

With its boiling point of 65 °C and melting point of −96 °C, methanol can be stored in tanks, distributed via pipelines, and transported by tank cars. The miscibility of methanol with water is a great advantage in case of a methanol accident (fire or spilled liquid).

The physical properties of pure methanol are summarised in Table 5.1 [1].

5.2 Toxicology

Katja Schulz

5.2.1 Occurrence of Methanol

In free form, methanol occurs in nature in just a few plants (cotton plants, some grasses and heracleum fruit). In conjugated form, as ester and ether, methanol occurs in the pectin of fruit as a supporting substance and in the lignin as the lignified part of the plant cell wall. The enzymatic degradation of pectin and lignin leads to the production of methanol.

Alcoholic beverages contain methanol in varying concentrations. It originates from the pectin of the fruit or fruit skins that were used for the production of alcoholic beverages. The highest concentrations of methanol can therefore be found in fruit spirits. Due to its toxicity, maximum amounts of methanol have been stipulated for spirits. Depending on the fruit used, these maximum amounts are between 1,000 and 1,500 g per hectolitre of pure alcohol [2].

Contrary to fusel alcohol, methanol is not a byproduct of alcoholic fermentation. Nonfermented soft drinks, such as fruit juices, also contain methanol if fruit or fruit skins have been used for production. Pectin-rich natural fruit juices contain 24–230 mg of methanol per litre [3]. The fruit as such contains harmless amounts of methanol [4].

Tobacco smoke has a low concentration of methanol, derived from the pyrolytic cleavage of the lignin-containing part of the tobacco. Contrary to many other substances contained in tobacco, methanol is not of toxicological concern.

A large part of the methanol that can be found in the atmosphere stems from plant emission [5, 6]. The atmospheric methanol has an estimated lifetime of about 12 days by reaction with OH radical [7]. It is oxidise to carbon dioxide and water.

Up until the beginning of the twentieth century, methanol was produced by using dry wood for distillation. The wood was heated to approximately 500 °C, and the contained lignin was thermally decomposed. Among other substances, the distillate contains methanol. The name “wood alcohol” for methanol is derived from the occurrence of alcohol in wood. Another historical name for methanol is carbinol. The production of methanol by isolation from natural occurrences is long forgotten. For about 80 years now, methanol has been produced on a large scale by catalysing carbon monoxide and hydrogen. For details, see Chaps. 3 and 4 of this book.

5.2.2 Use of Methanol

With an annual production of several million tonnes worldwide, methanol is one of the most common chemicals. Above all, methanol is used as a base material in the chemical industry, such as in the production of formaldehyde, acetic acid and methyl tert-butyl ether. Methanol is also used as a fuel additive. According to the European norm for petrol fuels, it is permitted to add 3 vol% of methanol to gasoline. Experiments with higher contents of methanol in gasoline (regular and diesel) have been carried out, and they are feasible without any problems if the automobile has been technically modified. Pure methanol can also be used as fuel in adapted motors. Due to its toxicity and above all its physicochemical properties (easily flammable, relatively low boiling point, burning with a hardly visible flame), additional safety measures are required.

Methanol is also used in the industry as a technical solvent or as an ingredient of solvent mixtures. Because methanol is known to be toxic, it is no longer allowed in household chemicals or do-it-yourself supplies in Germany, except in a few cases. The Federal Institute for Risk Assessment decided on these measures because numerous accidents caused by confusion (some of which also involved children) were registered. Exceptions are made for gasoline for model aircraft with high methanol levels (e.g. helicopters) and generators in small motorboats as well as for fuels used in (Belgian) fireplaces in the living area that were installed in Germany [8].

Methanol is no longer used in motor coolants or windshield defrosters. During World War II, methanol was employed because there was a lack of other conventional defrosters (glycerin and glycol). At that time, many accidents happened because people confused it with ethanol [3]. Today, the key defroster is isopropanol and not methanol. In the past, denaturated alcohol was produced by adulteration ethanol with methanol [9–12]. Today, methanol is no longer used as denaturant.

As described in detail in this book, another major field of application for methanol is its application as an energy source.

5.2.3 Biological Effects of Methanol

Toxicokinetics

The topic of toxicokinetics comprises all processes concerning the fate of a toxic substance in the body. They are subdivided into resorption, distribution, metabolism, storage and excretion. Metabolism, storage and excretion are also brought together under elimination, as the concentration of the substance and usually its effect are reduced.

Resorption

Methanol is rapidly and almost completely absorbed orally (via the gastrointestinal tract) or by inhalation (via the lungs). Maximum blood levels are reached after 30–90 min upon oral absorption. Methanol can also be absorbed dermally (via the skin).

Methanol is usually uptaken when ethanol is confused with methanol or with adulterated alcoholic beverages. In the past, when ethanol was denatured with methanol, there were cases of intoxication due to the consumption of these spirits. Today, denaturated alcohol is produced by adulteration with methyl ethylketone and denatonium benzoate. Denatonium benzoate is one of the bitterest substances known and therefore has a warning effect. Methanol, however, tastes nearly the same as ethanol, so its taste does not keep people from drinking it accidentally.

When homemade spirits made with poorly separated forerun are consumed, they can rarely lead to methanol intoxication because the antidote ethanol is always contained in it, too.

Methanol is a relatively volatile substance, so that it can also be inhaled, such as when working with solvents containing methanol in the industry or when extracting substances with methanol in laboratories.

Distribution

Methanol, like ethanol, is distributed uniformly to body water content because it is very well soluble in water. The approximate value of this body water content is 0.7 times the body weight of men and 0.6 times the body weight of women.

Metabolism

The liver oxidatively metabolises methanol. First, its metabolism goes through the same steps as ethanol metabolism. With the help of the enzyme alcohol dehydrogenase (ADH), an enzymatic oxidation of methanol to formaldehyde takes place. Compared with ethanol, the chemical reaction of methanol takes much longer if caused by ADH. In rats, the oxidation rate for methanol is 25 mg/kg/h, whereas for ethanol it is 175 mg/kg/h [4, 13–15]. Even if other metabolic pathways come to the fore with rats (catalase/peroxidase), the rate of elimination is comparable with humans [16].

In a second reaction, the aldehyde dehydrogenase (AIDH) enzyme immediately oxidises formaldehyde to formic acid. In monkeys, the biological half-life of formaldehyde in blood is 1.5 min [16]. Only a minor amount of the developed formate is eliminated via the kidneys (less than 5 % of the methanol uptake).

The metabolism of formic acid (or of the formate) produces CO_2 very slowly. This is done in two ways: There is a metabolism depending on catalase and a C_1-metabolism depending on tetrahydrofolic acid in the liver and the retina [17, 18]. The mechanism depending on tetrahydrofolic acid is of greater importance [19]. This oxidation step depends on the supply of active folic acid. Thus, folic acid can be used to increase formic acid elimination in cases of intoxication [20]. The metabolism of methanol in humans is shown in Fig. 5.1.

Due to the very slow metabolism and the poor elimination of the formate, there is an accumulation of formic acid leading to a reduction of the hydrogen carbonate concentration with a subsequent acidosis. With methanol intoxications, acidose is a typical and life-threatening pathology that can last several days. In extreme cases, it can reduce the blood pH from normal values between 7.35 and 7.45 to less than 7.0. In addition, there is an extensive acid-base imbalance.

Formic acid inhibits an enzyme of the respiratory chain, mitochondrial cytochrome oxidase, by bonding the sixth coordination area of Fe^{3+} in the heme molecule [21, 22]. The more severe the acidose, the more inhibited the cellular respiration. The inhibition of cellular respiration leads to the production of lactic acid, which makes the acidosis worse [16, 17, 22–24]. This cycle is called circulus hypoxicus. The cause of death with methanol intoxications is usually respiratory paralysis.

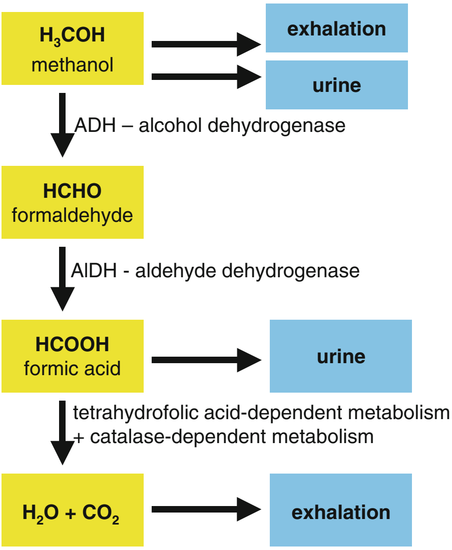

Fig. 5.1 Metabolism of methanol in humans

Storage

Methanol is not stored in the human body. Because it is eliminated only slowly, there is a risk of accumulation if taken repeatedly.

Excretion

Due to the slow ADH oxidation compared with ethanol, methanol is exhaled to a high degree (30–60 %) via the lungs non-metabolised [16]. To a low degree (<5 %), it is also eliminated non-metabolised via the kidneys.

Most of the methanol is oxidatively metabolised in the liver. A small amount of the metabolic intermediate formic acid (<5 %) is eliminated via urine. Formaldehyde is virtually undetectable due to its rapid metabolic pathway to formic acid. Formic acid is then metabolised to CO_2 and H_2O.

5.2.4 Toxicodynamics

Toxicodynamics characterise the kind and strength of the effect of poisons on the organism. Methanol toxicity in humans and higher mammals such as monkeys is characterised by a latent period of many hours followed by metabolic acidosis and ocular toxicity. Methanol competes with ethanol for the ADH enzyme; this is called competitive antagonism. Due to ethanol's higher affinity for ADH, methanol can be displaced. This property is used advantageously on treatment of methanol intoxication. To date, the mechanism causing damage to the optic nerve as a result of methanol intoxication has not yet been discovered.

Acute Toxicity

The difficulty in identifying methanol intoxication is mainly due to methanol being a classic latent poison, which implies that symptoms occur several hours or days after ingestion of the toxic agent. The temporary development of methanol intoxication is shown in Fig. 5.2. In addition, methanol is sensorily hardly ever distinguishable from ethanol and primarily shows a less pronounced inebriation than ethanol.

An excellent review article describes the toxicity of methanol [25]. Here, the author classified the methanol poisoning in humans into four stages:

1. A central nervous system depression of short duration, but milder than that seen following ethanol ingestion
2. An asymptomatic latent period of 12–24 h following ingestion of methanol, where no signs or symptoms are noted
3. After the latent period, severe metabolic acidosis occurs
4. Complaints that are characteristic of ocular toxicity are described, followed by blindness, coma, other central nervous system signs, and death

The acute toxicity of methanol after ingestion is shown primarily by narcotic effects, much like inebriation from ethanol but milder. At small but toxic dosages, drowsiness might not occur. After an asymptomatic latent period, symptoms such as respiratory failure, circulation failure and renal insufficiency are the consequence of metabolic acidosis. This acidosis may persist for several days. In this stage, laboratory investigations show a severe anion gap acidosis. At this time, methanol itself is completely metabolised and therefore not detectable in blood and urine.

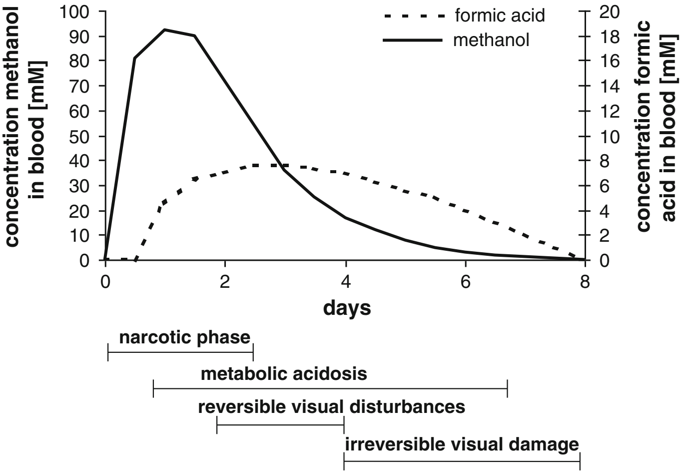

Fig. 5.2 Temporary development of acute methanol intoxication [16]

With methanol intoxications, pathological changes of the central nervous system (a toxic neuropathy) are observed. The optic nerve appears to be particularly sensitive. Also, the acoustic nerve may be concerned. After a latent period of approximately 2 days, methanol causes typical visual disturbances with retina edema. This stage may be reversible. If the edema persists for a substantial period of time and the damage is sufficiently severe, optic nerve atrophy including permanent blindness will ultimately result.

These observations at the optic nerve and the optic system can be detected on autopsy in fatal cases of methanol intoxications with longer survival times [22, 26–30]. The intoxication mechanism of ocular toxicity has not been definitely clarified. Probably, the combination of metabolic acidosis and formic acid inhibition of cytochrome c oxidase in the optic nerve results in histotoxic hypoxia, which is responsible for the ocular and central nervous system toxicity of methanol [17, 18, 31, 32].

The sensitivity to ocular toxicity of methanol is individually different. About half of the survivors of intoxications suffer from visual disturbances and approximately one in four suffers from permanent visual damage. There is a risk of blindness with a dosage of only 5–15 mL in adults [13, 33]. Blindness may occur even if the metabolic acidosis is treated. In cases of methanol-induced toxic optic neuropathy, high-dose corticosteroids are assumed to prevent the irreversible degeneration of the optic nerve in the early stages of intoxication [32].

Death occurs as a result of the metabolic acidosis, mostly in the form of respiratory paralysis. The lethal dosage of methanol in adults is approximately 30–100 mL [13, 33]. Children are more sensitive to the risk of blindness and more likely to die from an intoxication. The lethal dosage depends on the amount of simultaneously consumed ethanol with an antidotal effect, the filling of the stomach and the individual susceptibility.

Chronic Toxicity

Chronic intoxication can occur through repeated ingestion of small but not acutely toxic amounts, such as in the form of fumes between industry and commerce. This can lead to toxic neuropathies, alterations in vegetative area with headache, dizziness, or painful digestive disorders, and even a degeneration of the visual and auditory nerves leading to functional limitations and possibly to blindness and deafness [16, 34].

Toxicity tests for teratogenicity in experimental animals (rats) led to malformations due to high methanol concentrations. For humans, methanol is classified in the gestational group C, meaning there is no need to fear embryonal and fetal impairment with compliance of the maximal allowable concentration (MAC) and biological exposure limit (BEL) values [35].

5.2.5 Treatment of Methanol Intoxication

The treatment of methanol poisoning depends on the amount of ingested methanol, the concentration of methanol determined in the blood, and the occurring symptoms. Mostly, the amount of incorporated methanol is unknown. If it can be estimated, there is usually no need for treatment up to an ingestion of 0.1 g/kg body weight (BW) with adults [33]. Methanol dose levels of 1 g/kg BW or higher are required for severe intoxication leading to death [25]; consequently, the intensive-medical treatment is necessary.

The determination of methanol in the blood/serum is absolutely essential, particularly for the assessment of the severity of the poisoning. Serum-methanol concentrations are toxic from 200 mg/L and life threatening from 500 mg/L [33] or 900 mg/L [36–38]. Especially in the earliest stage of poisoning, when there is no recognisable pathology as is usual with latent poisons; the poisoning can only be identified and treated effectively if the analyte methanol is detected in the blood. If the typical symptoms of methanol poisoning (visual disturbances and metabolic acidosis) occur, the treatment and the progress of the poisoning become much more difficult than at the stage without severe symptoms.

If methanol was recently ingested, the primary decontamination is the gastric lavage, in which case the patient must be conscious. An antidote treatment should follow with ethanol or 4-methyl-pyrazol (Fomepizole), which is supposed to prevent methanol metabolism to the toxic metabolites formaldehyde and formic acid. The application of ethanol competitively inhibits the metabolism of methanol at the ADH enzyme due to its approximately 10 times higher substrate specificity compared with ethanol. An ethanol treatment with a blood alcohol concentration of about 1 per million [20, 33, 34] lasting several hours to days is desirable. The pharmaceutical agent 4-methyl-pyrazol is an inhibitor for the ADH enzyme. It binds to ADH and thereby also inhibits the metabolism of methanol. 4-Methyl-pyrazole has long been known as an inhibitor of ADH [39], but it has only been used as such for the last 10 years [40–44]. Both cases of antidote treatment reduce the action of ADH on methanol by competitive inhibition, and more methanol can be exhaled or excreted non-metabolised by the kidneys.

Metabolic acidosis is treated with a sodium bicarbonate solution or Tris buffer containing the agent trometamol, possibly for several days. In addition, a high dose of folic acid is recommended [16, 33, 34]. It increases the metabolism of the toxic formic acid in the blood through the folate cycle. With methanol poisoning, the human folic acid deposits are not sufficient for proper metabolisation of the toxic metabolite formic acid.

In severe or expectedly severe cases (from an intake of about 25 mL of methanol with a serum methanol concentration from about 500 mg/L or severe acidosis), hemodialysis should be carried out as well [33]. In this way, the concentrations of methanol, formaldehyde and formic acid in the blood are substantially reduced.

The measures described here serve to prevent or to treat life-threatening metabolic acidosis. Against methanol-induced toxic optic neuropathy, these measures are not certainly effective. Tephly [25] wrote: “Death may occur if patients are not treated for metabolic acidosis, and blindness may result even if treatment for metabolic acidosis is performed”. Therefore, high-dose corticosteroids are assumed to prevent the irreversible degeneration of the optic nerve in early states of intoxication [32].

5.2.6 Risks and Dangers by Exposition of Methanol

Until quite recently, the most frequent source of methanol intoxication has been the confusion with ethanol by people who are unaware of the danger. Today, methanol is not used in household chemicals in higher concentrations in Germany, with the exception of the few applications mentioned above. In other countries, these regulations may not be in place, so there household chemicals containing methanol may be an important source of intoxication. Also, methanol individual and mass poisonings from illegal spirits have occurred in countries with a poor ethanol supply or adulterated alcoholic beverages.

In the chemical industry, methanol is a commonly employed organic solvent and reactant in organic synthesis procedures. In the more recent literature, there are no reports of poisonings due to the use of methanol in laboratories or as an industrial chemical. Because methanol is very volatile (boiling point = 65 °C), vapours may form by exposure with methanol or methanol-containing mixtures. If these vapours are inhaled, they can cause toxic effects. People with occupational exposure are likely to be exposed to methanol by inhalation or resorption via the skin.

For protection of human health, threshold values concerning the handling of chemicals have been stipulated. These values are based on toxicological aspects. The MAC is the maximum permissible average concentration of an agent in the form of gas, vapour, or suspended matter in the air at the workplace that does not normally harm (based on present knowledge) most of the people exposed to it for a long time (8 h/day, 5 days/week, all of their working life). The MAC values are, however, not reliable limits for separating the dangerous from the harmless zone. MAC values exist for more than 600 substances, including methanol. The MAC for methanol is 200 mL/m^3 (ppm) and 270 mg/m^3, respectively [35]. The odour threshold for methanol, however, is 2,000 ppm [45]. It is many times higher than the MAC value. Consequently, there is no warning effect for humans.

The BEL is the highest quantity of an agent or of its metabolites allowed in humans (blood or urine) or the subsequent variation of a biological indicator that usually does not harm the workforce, even if exposed repeatedly and for a long time. The BEL values apply to healthy people under the same work time conditions as with MAC values. The values are not applicable to the general population. The BEL value for methanol is 30 mg/L in urine [35].

The MAC and BEL values are prepared, checked and updated every year by the Senate Commission for the control of health hazards of the German Research

Foundation. Even if the values cannot be applied to the general population, they help to estimate the potential risk and the toxicity.

Exposure to methanol during its production or processing is not the only risk leading to poisoning, except for poisoning through ingestion due to a confusion with ethanol. If pure methanol is used as a fuel for vehicles, additional sources of exposure need to be taken into account. However, this excludes the well-established addition of methanol to fuel.

A powerful argument that speaks for the use of methanol as a fuel for vehicles is its reduced environmental impact compared to the gasoline and diesel emissions. In contrast to currently used fuels, methanol completely combusts to carbon dioxide and water. Pollutants such as particulate matter, oxides of nitrogen and ozone are reduced through the usage of methanol as automotive fuel [46, 47]. On the other hand, the concentrations of two gaseous pollutants are expected to increase: formaldehyde and methanol [48, 49]. Formaldehyde is a byproduct resulting from the incomplete combustion of methanol.

Besides the continuous emission of methanol while driving, it may also be emitted when the motor is ignited, as uncombusted material in the exhaust, from its evaporation during refuelling, through the daily heating of the fuel tank, and in special cases such as engine malfunctions. In personal garages and service stations, the estimated methanol concentrations represent the highest exposure levels; in parking garages and roadway tunnels, concentrations are lower [50]. Even at the highest estimated exposure levels, the concentrations are below the MAC threshold limit value of 270 mg/m^3. Back in 1987, the Environmental Protection Agency identified the importance of technically evaluating the relevant health issues with the two pollutants methanol and formaldehyde [51]. The conclusion of this study was that methanol-powered motor vehicles are applicable to these situations as well.

However, it is necessary to consider all special cases, such as accidents or leaking fuel lines, for methanol-powered vehicles. The latter situation can cause dangerously high methanol concentrations, not only in the interior of the vehicle but also in personal garages and service stations. The MAC value is then assumed to be exceeded. In such cases, the immediate main risk lies in the ignition of the methanol fuel. Such cases can be found in literature [52].

In the beginning of the twentieth century, methanol was a widely spread substance on the consumer goods market, as a pure substance, an additive to several products, and an often-used chemical at the workplace. At that time, the documented number of methanol poisonings was extremely high [50, 53–59]. In most cases, methanol was taken in orally. Many poisonings resulted from methanol as an adulterant in alcoholic beverages [60–64]. Other cases occurred due to the extensive presence of methanol at the workplace in combination with a lack of work safety measures and ignorance towards the corresponding dangers. The results of a survey carried out in the United States in 1904 showed that about 2 million people worked in jobs where they had to use methanol. The most common professions were painters, glaziers, varnishers, launderers, boot and shoemakers, painters and lithographers [50, 55]. In this context, literary sources also give proof of accidents caused by inhalation or percutaneous uptake of lethal amounts of methanol [39, 56, 58, 65]. Today, these accidents are basically a thing of the past and hardly ever take place in industrialised countries.

However, if methanol is introduced as a fuel for motor vehicles, larger quantities of methanol would have to be stored and transported. Occasionally, the media report about accidents involving trucks or freight cars that transported pure methanol or methanol blends [66, 67]. These accidents conflict with the equally dangerous accidents with regular or diesel fuels.

5.2.7 Mass Poisoning and Accidents Caused by Methanol

In the past, besides single methanol poisonings, there were also some mass poisonings and incidents that concerned larger groups of people. For example, mass poisonings occurred in Estonia in September 2001 from the consumption of illegal spirits containing 50–100 % of methanol. Consequently, 154 people were poisoned and 68 of them died [68]. In March 2009, three students from Lübeck died in Turkey during a class trip, where they drank alcohol adulterated with methanol [69, 70]. In Bali in May 2009, 25 people died after drinking methylated rice wine [73]. In textbooks, there is evidence of historic mass poisonings from methanol [71].

As mentioned, one cannot rule out the possibility that accidents with tankers or freight cars carrying methanol will continue to happen at greater frequency. There is a serious risk of inhalation exposure to pure methanol vapour for emergency responders and the people involved in the accident, in addition to the risk of the methanol igniting. However, methanol fires can extinguished with plain water, in contrast to petroleum fires. In 1981, an accident occurred with a methanol-powered racing car at the Indianapolis Motor Speedway, where methanol ignited when the car was being filled [52]. Burning methanol has an invisible flame. The racecar driver and a member of the pit team were burning without any visible flames. Injecting water to the opening of the tank now prevents this kind of accident from happening while the car is filled. Since 2007, all vehicles in the Indianapolis race have run with ethanol.

In the literature, there are reports on numerous Swedish cases that have taken place between 1980 and 1983 involving accidental burns with domestic fire-lighting fluids containing methanol as an igniting fluid [72]. These accidents occurred while using this fluid for lighting barbecues or filling lamps and stoves, caused by negligence or inadequate knowledge of the dangers of methanol used for igniting.

5.2.8 Environmental Toxicology of Methanol

Methanol is completely miscible with water. It exhibits relatively high mobility if introduced into an aqueous environment. Methanol is readily biodegradable and shows no bioaccumulation. Methanol does also not persist in the environment [45]. Regular and diesel fuels, in contrast to methanol, are not readily biodegradable and show an appreciable potential for bioaccumulation. Furthermore, in contrast to methanol, regular and diesel fuel may cause cancer by long-term exposure [74, 75].

Despite the recognised human toxicity by direct (oral) ingestion of methanol, the properties related to environmental behaviour indicate only a marginal possibility of human exposure to methanol concentrations via consumption of contaminated water or food or contact with contaminated water or soil [76].

5.2.9 Conclusion

The toxicology of methanol has been discussed. The highest risk of intoxication exists for an accidental oral intake of methanol when it is confused with ethanol. Through governmental regulations to not allow methanol-containing chemicals in household or do-it-yourself products, the risk of methanol intoxication is reduced.

In contrast, the handling of methanol as base material for chemical industry, automotive fuel and industrial processes is easily technological realisable. Using qualified persons and safety measures, the risk of intoxication from methanol exposure likely is decreased.

5.3 Transport, Storage and Safety Handling

Elisabeth Brandes and Thomas Schendler

Because of its properties, methanol is subject to classification as dangerous good for transport and as a dangerous substance for handling, use and storage. Transport, handling and use classifications are based on European or international regulations [77–80], whereas storage instructions are based on national regulations, such as those in Germany (the *Betriebssicherheitsverordnung* [81] and the *Gefahrstoffverordnung* [82] and the respective downstream regulations *Technische Regeln für Betriebssicherheit* [TRBS] or *Technische Regeln für Gefahrstoffe* [TRGS]). Furthermore, the European Directives 94/9/EC [83], 1999/92/EC [84], and 98/24/EC [85] apply when methanol is produced or used in industrial processes.

5.3.1 Transport

Methanol is classified as a class 3 flammable liquid in packing group II, with a subsidiary risk of being toxic for transport on roads according to the ADR [86], on rail according to the RID [87], on inland waterways according to the ADN [88], for sea transport according to IMDG Code [89], and for air transport [90]. ADR, RID, ADN and IMDG are the European implementations of the Recommendations on the Transport of Dangerous Goods [91] elaborated and developed further by the United Nations.

Within these transport regulations, the classification as a class 3 flammable liquid is based on the substance's flashpoint. The class 3 designation includes substances meeting the following criteria:

- Liquid
- Vapours pressure of not more than 300 kPa (3 bar) at 50 °C
- Not completely gaseous at 20 °C and at standard pressure of 101.3 kPa
- Flashpoint of not more than 60 °C [86–90]

The class 3 flammable liquid designation is further divided into three packing groups that reflect the degree of danger associated with the substance/article and the requirements of the packaging and—in combination with toxicological and environmental dangers—of stowage (see Table 5.2).

Table 5.2 Classification of dangerous goods with class 3 flammable liquid designation

Packing group	Flash point (closed cup)	Initial boiling point (°C)
I	–	≤35 °C
II	<23 °C	>35 °C
III	≥23 °C and ≤60 °C	>35 °C

Furthermore, "the heading of Class 6.1 covers substances of which it is known by experience or regarding which it is presumed from experiments on animals that in relatively small quantities they are able by a single action or by action of short duration to cause damage to human health, or death, by inhalation, by cutaneous absorption or by ingestion [86–90]". This dangerous goods class 6.1 toxic substances designation is furthermore divided into three packaging groups, which reflect the degree of danger associated with the substance/article and the requirements of the packaging and—in combination with toxicological and environmental dangers—of stowage (see Table 5.3).

For many dangerous goods, a specific identification number is given. Together with its name and classification code, it listed in the respective regulations. For methanol, the following transport classification is valid: UN 1230 Methanol, 3 (6.1) II. It is based on its boiling point of 65 °C, its flash point of 9 °C and its classification as toxic (see Sect. 5.2) corresponding to the major hazard on the basis of the order of precedence [86–90].

Table 5.3 Classification of dangerous goods with class 6.1 toxic substances designation

	Packing group	Oral toxicity LD_{50} (mg/kg)	Dermal toxicity LD_{50} (mg/kg)	Inhalation toxicity by dusts and mists LC_{50} (mg/L)
Highly toxic	I	≤ 5	≤ 50	≤ 0.2
Toxic	II	>5 and ≤ 50	>50 and ≤ 200	>0.2 and ≤ 2
Slightly toxic	III	>50 and ≤ 300	>200 and $\leq 1{,}000$	>2 and ≤ 4

LD_{50} median lethal dose, LC_{50} median lethal concentration

For sea transport, special stowage requirements apply [89], namely "clear of living quarters." Depending on the number of passengers on board, stowage is allowed on deck only. Special regulations concerning the amount of shipped methanol apply for transport by air [88]. For passenger aircraft the maximum amount of the packaging is 1 L; for cargo aircraft, the maximum amount of the packaging is 60 L.

5.3.2 *Handling and Use*

With respect to handling, methanol is classified as a flammable liquid (category 2), with acute inhalation toxicity, acute dermal toxicity, acute oral toxicity (category 3) and specific target organ toxicity for single exposure (category 1), according to Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP regulation) [80]. The CLP regulation is the EU implementation of the Globally Harmonised System for the Classification and Labelling of Chemicals [92], elaborated and developed further by the United Nations. This CLP regulation replaced the former Council Directive 67/548/EEC in 2010 [93]. Within this CLP regulation, a flammable liquid is defined as a liquid with a flash point of not more than 60 °C. The criteria in Table 5.4 apply for the respective categories in Regulation (EC) No 1272/2008.

In the CLP regulation, acute toxicity is defined as "adverse effects occurring following oral or dermal administration of a single dose of a substance or a mixture, or multiple doses given within 24 h, or an inhalation exposure of 4 h." The hazard classes of acute toxicity are differentiated into acute oral toxicity, acute dermal toxicity and acute inhalation toxicity. The limiting values for these categories are given in Table 5.5.

Table 5.4 Criteria for the respective categories

Category	Criteria
1	Flash point <23 °C and initial boiling point ≤35 °C
2	Flash point <23 °C and initial boiling point >35 °C
3	Flash point ≥23 °C and ≤60 °C

Table 5.5 Limiting values for the categories of acute toxicity

Exposure route	Category 1	Category 2	Category 3	Category 4
Oral (mg/kg body weight)	$ATE \leq 5$	$5 < ATE \leq 50$	$50 < ATE \leq 300$	$300 < ATE \leq 2{,}000$
Dermal (mg/kg body weight)	$ATE \leq 50$	$50 < ATE \leq 200$	$200 < ATE \leq 1{,}000$	$1{,}000 < ATE \leq 2{,}000$
Inhalation vapours (mg/L)	$ATE \leq 0.5$	$0.5 < ATE \leq 2.0$	$2.0 < ATE \leq 10.0$	$10.0 < ATE \leq 20.0$

ATE: acute toxicity equivalence, which equals the mean lethal dose (LD_{50})/mean lethal concentration (LC_{50}) where available or as calculated from range test results or classification categories.

The criteria for the classification and the limiting values for the categories according to the CLP regulation are identical to those of the transport regulations, except that category 4 is of no relevance for transport classification. However, the principle precedence of hazard is only an aspect within the transport classification. This means that, for handling and use, each hazard assigned to a substance/mixture is of similar significance.

5.3.3 Storage

Currently, no European or international storage regulations exist. The German regulation on flammable liquids, which has regulated the storage conditions in nonportable vessels for flammable liquids, came out of force in 2002. The related downstream regulation (*Technische Regel brennbare Flüssigkeiten* 01) [94], however, is still valid until the new storage regulations that are being developed at the moment come into force. This is foreseen for the end of 2012. The requirements for the storage of methanol in nonportable vessels have been and will be based on its hazards of flammability and acute toxicity (see above). For the storage in portable vessels, TRGS 510 applies [95].

5.3.4 Safe Handling in Industrial Processes

According to Council Directives 89/391/EEC [96] and 98/24/EC [97] on the introduction of measures to encourage improvements in the safety and health of workers at work, the employer is supposed to take measures with respect to the safety and health of the workers. If hazards caused by potentially explosive atmospheres may arise during industrial processes, Directive 1999/92/EC on the minimum requirements for improving the safety and health protection of workers who are potentially at risk from explosive atmospheres [84] has to be applied. This

Table 5.6 Safety characteristic data of methanol [100, 101]

Safety characteristic	Ambient (20 °C[a], 1 bar)	Temperature dependence	Pressure dependence
Flash point	9 °C	Only existing at ambient conditions	
Lower explosion point	8 °C	–	Exponential increase
Lower explosion limit	6.0 vol%	Relative linear decrease −12.5 % per 100 K	More or less independent
Upper explosion limit at 50 °C	50.0 vol%	Relative linear increase ≈ + 10.0 % per 100 K up to ≈ 400 °C	Linear increase up to 30 bar
Limiting oxygen concentration, N_2	8.1 vol%	Linear decay up to ≈ 400 °C	Linear decay up to 30 bar
Automobile ignition temperature	440 °C	–	Exponential decay
Maximum experimental safe gap (MESG)	0.92 mm	Linear decay ≈ −15.5 % per 100 K	$\sim 1/p$
Minimum ignition energy	0.2 mJ	Linear decay	$\sim 1/p^2$
Maximum explosion pressure (p_{max})	850 kPa	$\sim T_0/T$; T in K	$\sim p/p_0$

[a] Unless other information is given in column 1

European Directive contains the minimum requirements that can be extended by the EU member states when transferred to national legislation. For Germany, this is done by the *Betriebsicherheitsverordnung* [85] and the *Gefahrstoffverordnung*. Accordingly, an explosion risk assessment has to be conducted. Depending on its result, an explosion protection document has to be prepared where specific measures have to be laid down to ensure a safe working environment and appropriate surveillance during the presence of workers. The Guide of Good Practice for implementing Directive 1999/92/EC [98] helps to fulfil this requirement. The specific measures are based on the individual safety characteristic data of the respective substance/mixture.

Because of its flashpoint, methanol is able to form an explosive atmosphere at ambient conditions, as well as during processes that are run at elevated pressure or temperatures. An explosion risk assessment for methanol would, therefore, result in “formation of explosive atmosphere possible”. The explosion protection document should then list possible measures to handle the associated hazards. Such a measure based on the safety characteristic data of methanol (see Table 5.6) might include the following:

- Prevention of the formation of hazardous explosive methanol/air
  This can be done by keeping the concentration of the methanol/air mixture below the lower explosion limit, either by dilution with air/inert gas or by using process temperatures that are below the flashpoint/lower explosion point, because then the concentration of the methanol is expected to be below the lower explosion limit. TRBS 2152 [99] part 2 recommends a safety distance of

−3 to −5 K from the flashpoint and 1–2 K from the lower explosion point. Another measure is to stay below the limiting oxygen concentration by dilution with an inert gas (e.g. nitrogen).

If it is not possible to reliably prevent the formation of a hazardous explosive atmosphere, hazardous areas have to be assigned (zoning), taking into account the likelihood of the formation of explosive atmospheres.

- Avoidance of the ignition of explosive atmospheres

  The most widespread ignition sources are hot surfaces (related safety characteristic: automobile ignition temperature [AIT]; see Table 5.6), electrical sparks (related safety characteristic: MIC; see Table 5.6), flames (related safety characteristic: maximum experimental safe gap [MESG]; see Table 5.6), and electrostatic discharges (related safety characteristic: minimum ignition energy [MIE]; see Table 5.6). Only explosion-protected equipment fulfilling the requirements of Directive 1994/9/EC [83] is allowed within the respective zones.
- Mitigation of the detrimental effects of an explosion

  If the ignition of hazardous explosive atmospheres cannot be excluded, the detrimental effects of an explosion have to be mitigated. This can be done by limiting the effects of an explosion to an acceptable extent, such as by explosion-resistant design, explosion relief based on the safety characteristic p_{max}, or the prevention of flame and explosion propagation through gaps designed on the basis of MESG.

If process conditions other than ambient apply, it has to be taken into account that safety characteristic data are temperature and pressure dependent. The lower explosion limit (LEL) decreases with increasing temperature; the influence of pressure is negligible. The upper explosion limit (UEL) increases with increasing temperature and pressure. The limiting oxygen concentration, MESG and MIE decrease with increasing pressure and temperature. The AIT decreases with increasing pressure, whereas the LEP increases with increasing pressure. The pressure and temperature dependence are not constant; they vary from substance to substance and from safety characteristic to safety characteristic. Therefore, the use of individual data is recommended.

Reference to Section 5.1

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