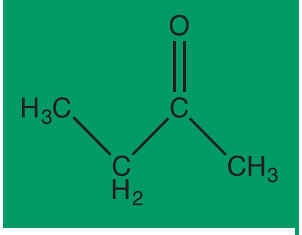

Toxic Tips

Methyl ethyl ketone

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INTRODUCTION

Chemical and Physical Description

Methyl ethyl ketone, C_4H_8O, also known as 2-butanone, methyl acetone, ethyl methyl ketone, and MEK, is a ketone that has both a methyl group and an adjacent ethyl group.[1] It is a colorless liquid with a minty or acetone-like odor.[2] MEK is soluble in water and miscible in alcohol, ether, and benzene.[3] It is highly volatile and flammable.[4] MEK vapor is heavier than air, having a density of 0.805 g/cm^3 at 20 °C.[1,4] The CAS registry number for methyl ethyl ketone is 78-93-3. Its molecular weight is 72.11.[5]

Uses and Typical Exposure Situations

Methyl ethyl ketone is used as a solvent in the manufacture and application of paints and paint removers, acrylic coatings, varnishes, and adhesives. It is used in food and pharmaceutical production and processing. MEK is also used as a sterilizing agent for bacterial spores on surgical instruments, dental instruments, and hypodermic needles. According to the National Occupational Exposure Survey (NOES) conducted by the National Institute for Occupational Safety and Health (NIOSH) from 1981 to 1983, an estimated 1,400,000 workers are potentially exposed to MEK in the U.S. MEK can enter the water supply via cement at the joint connections of PVC pipe. MEK can also be found in tobacco smoke.[6,7]

MEK is a natural component of various foods including milk, cheese, raw chicken breast, and nectarines. It is released into the atmosphere by plants and animals as a metabolic byproduct. It is also emitted by volcanoes and forest fires.[6,7]

Metabolism and Pharmacokinetics

Methyl ethyl ketone is absorbed rapidly by respiratory and dermal routes.[8] Due to its solubility in water, MEK is more rapidly absorbed by moist skin than dry skin.[6,7] When applied to dry skin, a plateau for the concentration of MEK in exhaled air is reached in 4–5 hours. But when MEK is applied to moist skin, it can be detected in expired air within 30 seconds and reaches maximum concentration around 10-15 minutes after application.[6] Because MEK is water soluble, it is easily distributed in the blood throughout the body. Because it is lipid soluble, MEK is evenly distributed among the tissues.[9] MEK is metabolized to 3-hydroxy-2-butanone, which is then reduced to 2,3-butanediol and a small portion is reversibly converted to 2-butanol.[6] 2,3-butanediol is eventually metabolized to carbon dioxide and water.[9] The majority of MEK is eliminated as carbon dioxide and water, primarily through the lungs.[7] MEK is quickly removed from the blood, having a plasma half-life ranging from 46 to 96 minutes in humans.[7] 2-3% of MEK absorbed into the body is eliminated unchanged via exhalation.[9] Another 3% on average is eliminated in the urine as metabolites 2,3-butanediol and 3-hydroxy-2-butanone.[8,9] There is insufficient evidence to support that MEK accumulates in body tissues.[4]

PATHOPHYSIOLOGY

Determinants of Toxicity

The airborne concentration of methyl ethyl ketone, the respiratory rate of the individual, and the time of exposure to the contaminated air determine the amount of toxicant absorbed through the respiratory system. The area of skin exposed, the concentration of the MEK, the moisture of the skin, and the length of time of skin contact determine the amount of MEK absorbed through the skin.[6]

Mechanisms of Action

MEK is known to potentiate the neurotoxicity of unbranched aliphatic hexacarbons, such as n-hexane. MEK also potentiates hepatic and renal toxicity of haloalkanes.[7] In one study, the effects of n-hexane, MEK, and a combination of both solvents were studied in rats. The solvents caused axon swelling by dramatically multiplying the number of neurofilaments. Other nonspecific alterations also occurred, including accumulation of clusters of phospholipids in the cytoplasm of Schwann cells and the accumulation of both phospholipids and glycogen in the axoplasm of nerve fibers. Schwann cells also underwent degenerative changes.[7] Additionally, MEK induces microsomal P450 activity. So repeated exposures may enhance the metabolism of future exposures to MEK.[6]

CLINICAL PRESENTATION

Effects Following Inhalation

MEK is known to cause irritation to the respiratory tract. Breathing MEK vapors can cause

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sufficient irritation of the mucous membranes of the nose and throat leading to coughing and wheezing. When sufficient concentrations are inhaled, dizziness, lightheadedness, headache, nausea, vomiting, and unconsciousness can occur.[1,10] Exposures to high levels of MEK can potentially cause damage to both the peripheral nervous system (PNS) and central nervous system (CNS).[11]

Effects Following Skin Exposure

MEK is a known skin irritant. Exposure can cause a rash or burning feeling.[10] Repeated exposure can cause inflammation and defatting of the skin.[4]

Effects Following Eye Exposure

Direct contact of the eyes with MEK can cause irritation, burning, and cornea damage.[4]

Carcinogenicity

Since there are no human carcinogenicity data and inadequate animal data, the carcinogenicity of MEK cannot be determined at this time.[7] However, mechanism-based structure-activity relationship (SAR) analysis determined that MEK is not likely to be carcinogenic. This type of analysis involves comparing a compound with unknown carcinogenic activity to compounds with a similar structure and known carcinogenic activity. Specifically, the structural features, functional properties, and probable mechanism(s) of action are evaluated.[12]

Reproductive Effects

Although it has been reported that MEK can cross the placenta and enter the human fetus, there is insufficient data to determine if MEK is a teratogen in humans.[7] One study in mice showed a statistically significant increase in the incidence of misaligned sternebrae in fetuses whose mothers were exposed to MEK for ten days at a concentration of 3,000 ppm during gestation (sternebrae are segments of bone in fetuses that fuse later in development to form the sternum).[13] The authors of this study concluded that MEK vapors at such levels cause mild developmental toxicity. MEK should be treated as a possible teratogen until more data is available.[10]

FIRST AID AND CLINICAL MANAGEMENT

In the case of high exposure by inhalation, move the individual to fresh air. Monitor the individual for breathing difficulties and administer oxygen if necessary. Mouth to mouth resuscitation should only be used if absolutely necessary. If MEK is ingested, the mouth of the individual should be rinsed with water and the contents spit out. Vomiting should not be induced. If eye exposure occurs, the eyes of the individual should be rinsed thoroughly with water for ten minutes. If skin exposure occurs, any contaminated clothing should be removed and the exposed skin should be thoroughly cleaned with soap and water. In severe exposure cases, further medical treatment should be provided as quickly as possible.[4]

HANDLING AND EXPOSURE

Accidental Release Measures

If a spill occurs, all sources of ignition should be immediately shut off and the area evacuated.[4] The spilled liquid should be absorbed with an inert absorbent such as diatomite, vermiculite, or sand. Dispose of the absorbent using methods approved by your Environmental Protection office.[1,4] Respiratory, eye and hand protection should be worn during clean up. The area where the spill occurred should be well ventilated and decontaminated .[4] MEK fires should be extinguished with alcohol foam, carbon dioxide, or dry chemicals.[11]

Storage Guidelines

MEK should be stored in tightly closed containers in cool, well-ventilated areas. It should be stored away from sources of ignition and heat.[4,10] MEK should be kept away from strong oxidizers.[1] Containers of MEK should be clearly and permanently labeled. Use original containers as much as possible.[4]

Reactivities and Incompatibilities

MEK is incompatible with strong oxidizers, such as trichloromethane/alkali chromium trioxide. It will ignite on contact with potassium tert-butoxide. MEK can form an explosive mixture with air.[4,11]

MEK produces explosive peroxides when reacted with hydrogen peroxide and hydrogen ion. Hydrogen ions (H^+) can originate from acid solutions, such as nitric acid or sulfuric acid.[4] Seven of these peroxides have been identified: 1,4,7-Trimethyl-1,4,7-triethyl-1,4,7-cyclononatriperoxane (I); 1,4,7,10,13,16-Hexamethy1-1,4,7,10,13,16-hexaethyl-1,4,7,10,13-pentaperoxy-l,16-dihydroperoxide (II); 1,4,7,10,13-Pentamethyl-l,4,7,10,13-pentaethyl-l,4,7,10-tetraperoxy-1,13-dihydroperoxide (III); 1,4,7,10-Tetramethy1-1,4,7,l0-tetraethyl-l,4,7-triperoxy-1,l0-dihydroperoxide; 2,2′-dihydroperoxy-2,2′-dibutyl peroxide (VI); 2,2-dihydroperoxybutane;1,4,7-Trimethyl-l,4,7-triethyl-l,4-diperoxy-l,7-dihydroperoxide (V); and 2,2-Dihydroperoxybutane (VII). The most abundant product is 2,2′-dihydroperoxy-2,2′-dibutyl peroxide (VI). The reaction mechanism of this product is shown in Figure 1, which is entitled Synthesis of a Peroxide From Methyl Ethyl Ketone and Hydrogen Peroxide. In reaction 1 of the mechanism, MEK, hydrogen peroxide, and H^+ react reversibly and form 2-hydroperoxy-2-butanol. This intermediate reacts with hydrogen peroxide and H^+ in reaction 2, forming 2,2-dihydroperoxybutane and water. The 2,2-dihydroperoxybutane then reacts with 2-hydroperoxy-2-butanol and H^+ in reaction 3, producing 2,2′-dihydroperoxy-2,2′-dibutyl peroxide and water. The other, less abundant products are formed by 2,2′-dihydroperoxy-2,2′-dibutyl peroxide continuing to react with the intermediate 2-hydroperoxy-2-butanol.[14,15]

Mixing MEK with 2-propanol will also produce explosive peroxides. MEK reacts vigorously with chloroform and alkali. Other incompatibilities of MEK include oleum, chlorosulfonic acid, isocyanates, pyridines, amines, ammonia, and inorganic acids.[4,11]

EXPOSURE CONTROLS

Sampling and Analysis

The Occupational Safety and Health Administration (OSHA) calls for the