LITERATURE REVIEW

Judul Literature Review:

Ethylene oxide (EtO)

Oleh:

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FAKULTAS KEDOKTERAN
UNIVERSITAS TARUMANAGARA
JAKARTA

2023

Ethylene oxide (EtO)

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Background

One of the chemical agents which being used in industrialization. The major use of the ethylene oxide (its derivate product) is the production of solvents, antifreeze, textiles, detergents, adhesives, polyurethane foam, and pharmaceuticals. Smaller amounts are present in fumigants, sterilants for spices and cosmetics, as well as during hospital sterilization of medical equipment.[1] EtO was first prepared in 1859 by Wurtz using potassium hydroxide solution to eliminate hydrochloric acid from ethylene chlorohydrin. The chlorohydrin process developed from Wurtz's discovery and industrial production of EtO began in 1914. The direct catalytic oxidation of ethylene, discovered in 1931 by Lefort, has gradually superseded the chlorohydrin process. Currently, Ethylene oxide is produced by direct oxidation of ethylene with air or oxygen. Virtually all Ethylene oxide produced is further reacted to derivative products. Its most important derivative is ethylene glycol, which is used for the manufacture of polyester and in automotive antifreeze. Other Ethylene oxide derivatives include surfactants, solvents, amines and poly(ethylene) glycols. EtO also has several direct uses, including use as a sterilant and the treatment of spices and other foodstuffs. United States production of Ethylene oxide in 2004 was 8,315 million (8.3 billion) pounds, according to National Petrochemical & Refiners Association's (NPRA) Petrochemical Surveys 4 Quarter 2003, highlighting its role as an important industrial chemical.[2] Ethylene oxide is a colorless, odorless gas but can smelled like sweet etheric odor, which is both flammable and highly reactive. Most importantly, It can't smelled until reaches levels that can cause serious harm to human health (NIOSH, 1989).[3] EtO is irritating to the respiratory tract, skin, and eyes. Inhalation is the most common route of EtO exposure and high concentrations may cause coughing, dizziness, drowsiness, headache, nausea, sore throat, and vomiting. Repeated or prolonged contact may cause skin sensitization. Eye contact may cause redness, pain, or blurred vision. EtO is a human carcinogen.[4] So we must make sure whether the level of ethylene oxide in the workers' body beyond the limit level or not. the level of ethylene oxide in human body can be measured by biological monitoring.

Problem statement

Ethylene oxide will risk to human health but there is some ways to measure EtO in human body.

Objective

The objective of these paper are : To provide general information about ethylene oxide.

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Overview of Ethylene Oxide

Identity, physical and chemical properties

Ethylene Oxide (EO), sometimes referred to as oxirane, is the simplest cyclic ether. It is a colorless gas or liquid and has a sweet, etheric odor.

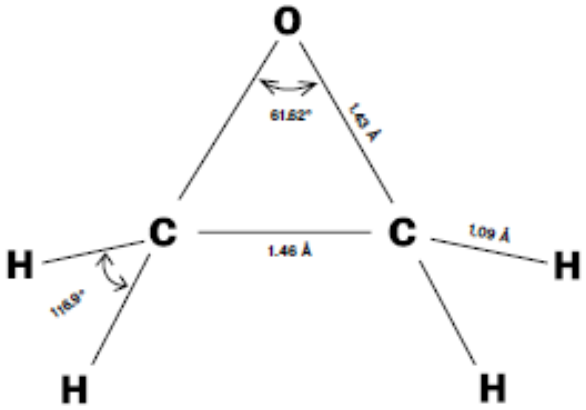

Figure 1. the molecule of ethylene oxide[2]

Some relevant physical and chemical properties of ethylene oxide are listed below:

Chemical name: Ethylene oxide

Synonyms: ethene oxide, oxirane, 1,2-epoxyethane, dimethylene oxide

Structural formula: CH2OCH2

CAS No.: 75-21-8

EC No.: 200-849-9

Molecular formula: C2H4O

Molecular weight: 44.05 g/mol

Melting point: -112 °C

Boiling point: 10.5 °C (1.013 hPa)

Conversion factor 20 °C, 101.3 kPa: 1 ppm = 1.83 mg/m3; 1 mg/m3 = 0.55 ppm

Ethylene oxide is highly flammable and has a flash point below -18°C. It is flammable in air at all concentrations above 2.6 % (by volume). There is no upper flammable limit as normally conceived in that exothermic decomposition replaces combustion at the higher ranges up to 100 % ethylene oxide vapour. Due to its low boiling point and flammability, ethylene oxide is, in some respects, similar to LPG. However, an essential difference is that ethylene oxide is fully miscible with water. Another important

difference is that ethylene oxide has an unusually low minimum ignition energy for mixtures in air. The lowest value at about 10.4 % ethylene oxide by volume is 0.06mJ and this figure is similar to the ignition energy of about 0.02mJ required by hydrogen/air mixtures. Ethylene oxide is a highly reactive chemical which reacts exothermically, especially in the presence of a catalyst, with impurities/compounds such as water, alcohols, ammonia, amines, acids/bases and rust. These reactions can be self-accelerating and strongly exothermic, even with only traces of the compound present. Pure ethylene oxide vapour decomposes explosively if ignited even in the absence of air. Ethylene oxide decomposition is initiated if the chemical is heated to about 560°C, the auto-decomposition temperature (ADT). Decomposition is catalysed by metal acetyl ides as well as the metals copper, silver, mercury, and their alloys. Increasing pressure lowers the ADT. The presence of rust may also initiate decomposition at a lower temperature due to the formation of a hot spot caused by polymerisation. Ethylene oxide is stable at room temperature in the absence of catalysts/contaminants. Purely thermal initiation of polymerisation begins at around 100°C. Polymerisation of ethylene oxide is highly exothermic and, if the temperature is not controlled by removal of heat at a sufficient rate, the polymerisation is self-accelerating. This can lead to vaporisation of unreacted ethylene oxide and also possibly to explosive decomposition of the vapour. This polymerisation can be promoted by impurities or contamination which act as catalysts, for example by acids, bases, metal oxides and anhydrous chlorides of iron, aluminium and tin.[2] The Occupational Safety and HealthAdministration (OSHA) has recomended *Permissible Exposure Limit (PEL)* – A limit on workplace exposure of one (1) part EtO per million parts of air (1 ppm) as an eight-hour time-weighted average (8-hour TWA). The threshold Limit Value (TLV), an ACGIH workday exposure level, is the same as the OSHA PEL: 1 ppm. The Action Level (AL) An airborne concentration of 0.5 ppm Ethylene oxide average as an 8-hour TWA. And OSHA Short Term Exposure Limit (STEL) – An excursion limit of 5 ppm EtO averaged over a sampling period of 15 minutes.[6] The Products derived from EO have many different uses. Some of these products (or uses) include monoethylene glycol use as antifreeze for engines, production of polyethylene terephthalate (polyester fibers, film, and bottles), and heat transfer liquids and deicing of aircraft and runway; diethylene glycol for polyurethanes, polyesters, softeners (cork, glue, casein and paper), plasticizers, gas drying and solvents; Triethylene Glycol for polyurethanes, lacquers, solvents, plasticizers, gas drying and humectants (moisture-retaining agents); Poly(ethylene) Glycols for cosmetics, ointments, pharmaceutical preparations, lubricants (finishing of textiles and ceramics), solvents (paints and drugs) and plasticizers (adhesives and printing inks); Ethylene Glycol Ethers for Brake fluids, detergents, solvents (paints and lacquers), and extractants for SO2, H2S, CO2 and mercaptans from natural gas and refinery gas; Ethanolamines for chemicals for textile finishing, cosmetics, soaps, detergents and natural gas purification; ethoxylation products of fatty alcohols, fatty amines, alkyl phenols, cellulose; poly(propylene glycol) for detergents and surfactants (nonionic), biodegradable detergents, emulsifiers and

dispersants. Ethylene oxide also has direct uses as a sterilizing agent for medical devices and equipment and as a fumigant for spices. Ethylene oxide is unlikely to be found in the general environment. No significant natural sources of ethylene oxide are known. From IARC 2004 states for some ethylene oxide can be found in cigarret. Ethylene oxide is released to air from some agricultural fumigation, Chemical manufacture, manufacturing industries, Car exhaust, Spices at extremely low levels.[7]

Toxicokinetics of Ethylene Oxide

Absorption, distribution,metabolism, and excretion

Ethylene oxide is very soluble in biological tissues such as blood. Absorption is very fast, especially across the lungs, with uptake into the body of a large proportion of the amount inhaled. Skin absorption is less common. Ethylene oxide is rapidly distributed throughout the body, and rapidly broken down in the body by hydrolysis or by conjugation with glutathione. Residual ethylene oxide and its breakdown products are mainly excreted through the urine, usually within a few hours after exposure.[8] The mammalian metabolic pathways of ethylene oxide are shown in Figure. 2 and can be summarized as follows: Ethylene oxide is converted (*a*) by enzymatic and non-enzymatic hydrolysis to ethylene glycol, which is partly excreted as such and partly metabolized further via glycolaldehyde, glycolic acid and glyoxalic acid to oxalic acid, formic acid and carbon dioxide; and (*b*) by conjugation with glutathione (GSH) followed by further metabolism to *S*-(2-hydroxyethyl)cysteine, *S*-(2-carboxymethyl)cysteine and *N*-acetylated derivatives (*N*-acetyl-*S*-(2-hydroxyethyl)cysteine (also known as *S*-(2-hydroxyethyl)mercapturic acid or HEMA) and *N*-acetyl-*S*-(2-carboxymethyl)cysteine) mainly excreted through the urine, which are partly converted to thio-diacetic acid. The glutathione-*S*-transferase (GST) activity towards ethylene oxide in cytosolic fractions from human livers was low Metabolism of ethylene oxide to the GSH conjugate and ethylene glycol is generally considered to be the major pathway for the elimination of DNA-reactive ethylene oxide. However, strongly suggestive evidence *in vitro* was presented by Hengstler *et al.* (1994) that glycolaldehyde is formed by further metabolism of ethylene glycol and that this derivative leads to DNA–protein crosslinks and DNA strand-breaks (as measured with the alkaline elution assay) after in-vitro incubation with human mononuclear peripheral blood cells. [7,8,9]

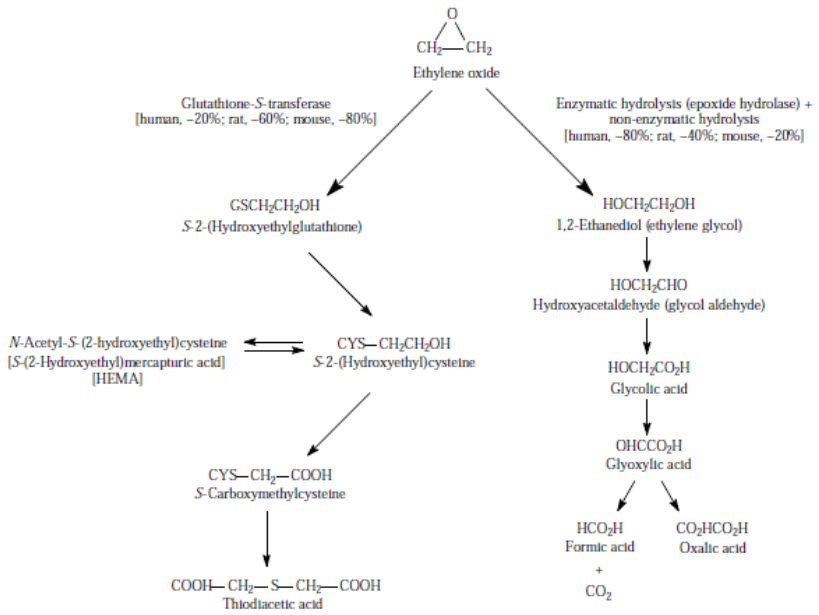

Figure.2 Metabolism of ethylene oxide[7]

Exposure information

Human Exposure

1.Non occupational exposure

Most ethylene oxide is released into the atmosphere (WHO, 2003). Ethylene oxide degrades in the atmosphere by reaction with photochemically produced hydroxyl radicals. The half-life of ethylene oxide in the atmosphere, assuming ambient concentrations of 5 × 105 hydroxyl radicals/ cm3, was reported to be 211 days. Neither rain nor absorption into aqueous aerosols is capable of removing ethylene oxide from the atmosphere (National Library of Medicine, 2005). Mainstream tobacco smoke contains 7 mg/cigarette ethylene oxide (IARC, 2004). With the possible exception of cigarette smoke, other non-occupational sources of exposure to ethylene oxide (e.g. residues in spices and other food products (Jensen, 1988; Fowles *et al.*, 2001) and in skin-care products (Kreuzer, 1992) are expected to be minor. Ethylene oxide is formed during the combustion of fossil fuel, but the amount is expected to be negligible (WHO, 2003). Hospital patients may be exposed during dialysis when the equipment has been sterilized with ethylene oxide (IPCS-CEC, 2001).[9]

2.occupational exposure

Workers may be exposed to ethylene oxide during its production or use in the manufacture of other chemicals. Because ethylene oxide is highly explosive and reactive, the processing equipment generally consists of tightly closed and highly automated systems, which limit occupational exposure. Exposures occur primarily during the loading or unloading of transport tanks, product sampling procedures, and equipment maintenance and repair (CHIP, 1982). The Toxic Chemical Release Inventory listed 197

industrial facilities that produced, processed, or otherwise used ethylene oxide in 1988 (US EPA, 1990). Industrial workers may also be exposed to ethylene oxide during sterilization of a variety of products, such as medical equipment and products (surgical products, single-use medical devices, etc.), disposable health care products, pharmaceutical and veterinary products, spices, and animal feed. Although much smaller amounts of ethylene oxide are used in sterilizing medical instruments and supplies in hospitals and for the fumigation of spices, it is during these uses that the highest occupational exposure levels have been measured (IARC, 1994). There was a wide range in reported concentrations (from 0 to about 1500 mg/m3), depending on operation, conditions, and duration of sampling for workers in US hospitals where ethylene oxide is used as a gaseous sterilant for heat -sensitive medical items, surgical instruments, and other objects and fluids coming in contact with biological tissues. Based on a limited field survey of hospitals, it was reported that concentrations of ethylene oxide near malfunctioning or improperly designed equipment may reach transitory levels of hundreds or even a few thousand milligrams per cubic metre, but time-weighted average (TWA) ambient and breathing zone concentrations were generally below about 90 mg/m3 (CHIP, 1982).[9]

Exposure effect

A. Acute exposure

Ethylene oxide has a high odor threshold (>250 ppm). Its odor threshold is too high to provide an adequate warning of hazardous concentrations. The effects of inhalation exposure to EO are concentration and time dependent. Concentrations of several hundred ppm may be tolerated for a few minutes without significant immediate health effects; however, similar concentrations may cause severe injury, especially if inhaled for longer periods. Short-term exposures to EtO vapors may cause irritation of exposed surfaces, including eyes, skin, nose, throat and lungs. Irritation of the lungs can lead to secondary infections, which may lead to pneumonia. Short-term exposures may also affect the central nervous system, leading to symptoms such as drowsiness, disorientation, nausea and vomiting. Convulsions and limb weakness may also occur. These symptoms may be expected to reverse within a few days after cessation of acute exposure.

B. Skin and eye contact

Liquid EtO can cause freezing of the skin by evaporative cooling. It is also highly irritating to the eyes and skin and even dilute solutions can cause blistering or severe damage to the skin or eyes. EtO liquid and solutions easily and rapidly penetrate cloth, leather and some types of rubber, and can produce blistering if clothing or footwear contaminated with EO is not removed.

C. Chronic exposure

Repeated dermal exposure to EO, or materials treated with EtO, may lead to skin sensitization (allergic) reactions. Repeated exposure to high inhalation concentrations may result in respiratory sensitization (asthmatic) symptoms. A possible association with long term exposure to EO and cataract formation has also been reported. Long-term exposure to EO may also result in neurological effects similar to those observed in cases of acute short-term exposure. Many of the effects may be non-specific, including headaches, nausea, lethargy, numbness and memory loss. There may also be a reduced sense of smell and/or taste, and muscle weakness particularly in the legs. The potential short-term and long-term effects of EtO on the nervous system are regarded as reversible.There have been a few epidemiological reports of increased spontaneous abortions in pregnant hospital or dental sterilizer workers exposed for short times to relatively high EtO concentrations . However, methodological questions have raised doubts about the conclusions drawn in these studies. Experimental animal studies have shown reproductive effects in rodents exposed to EtO. Effects include a decrease in the number and weight of offspring in rats exposed to high levels of EO. The potential effects of EtO on male and female reproduction and development have been the subject of research for many years and research into this area continues.. Because EO is reactive, it is capable of directly combining with proteins and DNA when absorbed into the body. EO can react with DNA in tissues to form various DNA adducts. Ongoing research is focused on the repair of these DNA adducts and the possible existence of an exposure threshold associated with the formation of DNA adducts and associated repair mechanisms. The potential for EO to cause cancer, reproductive, developmental or genetic effects has been examined in experiments using laboratory animals and also by studying exposed human worker populations in epidemiological studies. Based primarily on animal data and on cytogenetic changes in exposed workers, the International Agency for Research in Cancer (IARC) classified EtO as a known human carcinogen. In 2002, the U.S. National Toxicology Program classified EtO as “known to be a human carcinogen” based on “sufficient evidence of carcinogenicity from studies in humans. In April 2004, NIOSH issued a worker notification bulletin summarizing the results of several recent human studies. Ongoing research is being conducted by numerous investigators, including some sponsored by the American Chemistry Council’s Ethylene Oxide/Ethylene Glycols Panel, to explore the potential for EtO to cause cancer.[9]

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