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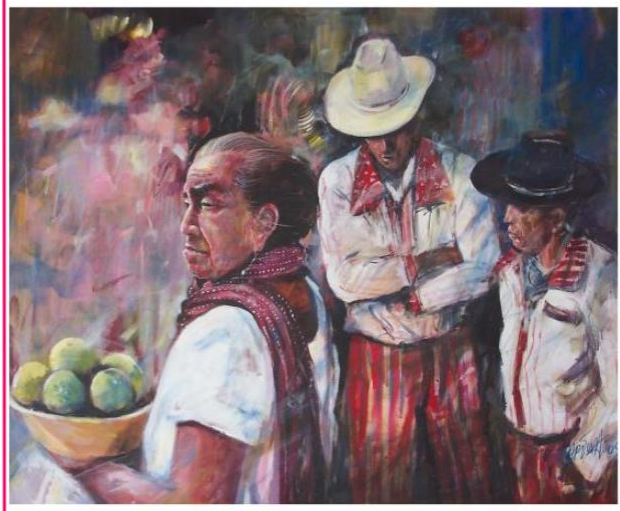

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Detoxification toxin carcinogenic and non-carcinogenic

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Abstract

The purpose of this analysis is to determine the detoxification of cancer-causing and non-cancerous toxins. A comprehensive literature search was conducted to identify, biotransformation and detoxify toxins as well as various supporting studies. Original research articles published in English academic journals were obtained through literature searches with electronic databases such as Scopus, ScienceDirect, PubMed and Google Scholar. Various sources and studies state that detoxification of toxins can be carried out using food. Foods that can detoxify toxins are enzyme-rich foods in stage two biotransformation such as foods containing the enzymes CYP2E1, glutathione and sulfation.

Keywords: Detoxification; Toxin; Cancer; Non-Cancer.

Desintoxicación toxina carcinogénica y no cancerígena

Resumen

El propósito de este análisis es determinar la desintoxicación de toxinas cancerígenas y no cancerosas. Se realizó una búsqueda exhaustiva en la literatura para identificar, biotransformar y desintoxicar toxinas, así como diversos estudios de apoyo. Los artículos originales de investigación publicados en revistas académicas en inglés se obtuvieron a través de búsquedas bibliográficas con bases de datos electrónicas como Scopus, ScienceDirect, PubMed y Google Scholar. Diversas fuentes y estudios afirman que la desintoxicación de toxinas se puede llevar a cabo utilizando alimentos. Los alimentos que pueden desintoxicar toxinas son alimentos ricos en enzimas en la

biotransformación de la etapa dos, como los alimentos que contienen las enzimas CYP2E1, glutatión y sulfatación.

Palabras clave: Desintoxicación; Toxina; Cáncer; No cáncer.

1. INTRODUCTION

The development of the industrial sector causes more and more potential hazards and risks faced by the workforce. One of the potential hazards and risks in the industrial sector is the use of various chemicals used as raw materials and by-products. The chemicals that are widely used especially in the industrial sector are Benzene, Toluene and Xylene, also known as BTX. The main sources of BTX exposure come from cigarette smoke, workshops, burning of motor vehicles and emissions from industry. Other sources of exposure can come from steam or gas from products containing benzene such as glue, paint, household coating wax and detergent soap (HANDOYO, 2014).

BENZENE, TOLUENE and XYLENE (BTX) are chemicals that are included in the category of chemicals that are toxic to health, both carcinogenic or triggering cancer (GAMMON et al., 2008; REID et al., 2012; WHITE et al., 2012; 2014), and increase oxidative stress (BAE et al., 2010) and non-carcinogenic such as affecting the hematopoietic system, central nervous system and reproductive system (HAN et al., 2011). BTX belongs to a type of air pollutant Polycyclic Aromatic Hydrocarbon (PAH) compound. PAHs are formed due to

incomplete combustion of organic matter, spread in the environment and take the form of a mixture. The main sources of PAH exposure to humans are the work environment, passive and active smokers (Suzuki and Yoshinaga, 2007), food and water and air pollution (NETHERY et al., 2012).

BTX is a Volatile Organic Compound (VOC). VOC is a carbon-containing compound which evaporates at a certain pressure and temperature or has high vapor pressure at room temperature. The most commonly known VOC is solvent, but there are also other types of monomers and fragrances (TUNSARINGKARN et al., 2012). VOCs are very dangerous and come to the attention of many circles so that many countries make special regulations to reduce the impact of the VOC. This is because VOCs react with Nitrogen Oxide (NOx) if exposed to sunlight will form a ground level ozone and smoke or fog. At certain concentrations in the air, ozone can affect health and the environment.

In high levels of exposure, BTX toxic properties can cause neurotoxic symptoms. Exposure to high levels of BTX can continuously cause damage to the human bone marrow, DNA damage to mammalian cells and damage to the immune system. Exposure to low BTX levels can result in irregular heartbeat, headaches, dizziness, nausea and even fainting if exposure is continued for a long time. Early manifestations of toxicity are anemia, leukocytopenia and thrombocytopenia (SINGH and TOMER, 2012). In air pollution, the general impact of continuous exposure to air pollution can cause lung cancer, heart disease and other diseases that are risk factors for death (LANGRISH and MILLS, 2014).

Several studies have been carried out to analyze BTX toxin exposure with effects that can be caused. TUNSARINGKARN et al. (2012) conducted research on people who worked in a gas station environment, people who worked around gas stations and people who were around gas stations every day in Bangkok, Thailand. The results showed that all workers had significant BTX exposure. In addition, workers also experience symptoms such as headaches (61%), fatigue (29%) and throat irritation (11%). Exposure to benzene and toluene is significantly associated with fatigue. Research XIONG et al. (2016) conducted on refueling workers stated that long-term exposure to low BTX concentrations can reduce the ability of antioxidants and increase the risk of DNA damage.

To prevent the occurrence of acute or chronic health effects due to exposure to toxins, detoxification of toxins in the body needs to be done. The purpose of this analysis is to determine the detoxification of cancer-causing and non-cancerous toxins. Detoxification is done by removing impurities from the blood in the liver, where toxins are processed to be eliminated. This article will discuss about toxins with types and properties of carcinogens and non carcinogens, toxin biotransformation and detoxification of toxins and various studies reported throughout the world.

2. METHODOLOGY

A comprehensive literature search was conducted to identify toxins, biotransformation of toxins and detoxification of toxins and

various supporting studies. Original research articles published in English academic journals were obtained through literature searches with electronic databases such as Scopus, ScienceDirect, PubMed and Google Scholar. The keywords used in the search are 'benzene', 'toluene', 'xylene', 'benzene biotransformation', 'toluene biotransformation', 'xylene biotransformation', 'benzene detoxification', 'toluene detoxification', 'xylene detoxification', ' health effects of benzene exposure ',' health effects of toluene exposure 'and' health effects of xylene exposure '. These terms are considered to have something in common with the topic being analyzed. Apart from using an electronic database, it also uses several books to strengthen information. The results were further refined to identify research conducted from 1980 to 2019.

3. RESULTS and DISCUSSION

Toxin

Benzene (C6H6) is a liquid aromatic hydrocarbon that is volatile in air and difficult to dissolve in water. Other properties of benzene are colorless, flammable and has a sweet characteristic odor (PILLAY, 2013). Benzene is a raw material used for the manufacture of plastics, resins, synthetic fibers, dyes, detergents, medicines and pesticides (SMITH, 2015). Benzene can also be found in gasoline used in the chemical and pharmaceutical industries (ATSDR, 2007). The International Agency for Research on Cancer stipulates that benzene is classified in group 1 which is carcinogenic in humans. Of these toxins, benzene is considered the most dangerous chemical and benzene exposure has a serious impact on human health (SUSYANTI et al.,

2019). The threshold value of benzene in the workplace air permitted according to the American Conference of Governmental Industrial Hygienists (ACGIH) (2015) does not exceed 0.5 ppm for 8 hours/day or 40 hours/week.

Exposure to benzene can enter the human body through the respiratory tract, digestive tract and skin contact. However, the biggest absorption of benzene is through the respiratory tract (about 70% - 80%) in the first five minutes and (20% -60%) until the next hour. Acute health effects from benzene exposure can experience several signs and symptoms such as drowsiness, dizziness, irregular heartbeat, headaches, tremors, confusion, unconsciousness until death. Chronic health effects of benzene exposure are carcinogenic, mutagenic, toxic for the reproductive system and central nervous system, toxic for the liver and urinary system, especially for disorders of the blood. Benzene can cause a decrease in blood cell production which is a result of disruption in the spinal cord (IRIS, 2003; MSDS, 2007). The Department of Health and Human Services (DHHS) stipulates that benzene causes cancer in human blood-forming organs, called leukemia (CDC, 2013). The International Agency for Cancer Research and the Environmental Protection Agency have also determined that benzene is carcinogenic to humans (ATSDR, 2007).

Several studies were conducted to analyze benzene exposure with effects that can be caused. A research conducted by TUNSARINGKARN et al. (2012) at gas station workers in Bangkok, Thailand showed that chronic exposure to benzene at work caused nervous system and haematological disorders with symptoms of

headache, drowsiness and fatigue. Meanwhile, the results of a study conducted by PELUSO et al. (2013), children who lived near the Sarroch industrial area, Island of Sardinia, Italy industrial area experienced a significant increase in DNA damage where the industrial area produced a complex mixture of air pollutants, one of which is benzene. The measured air concentrations of benzene and ethyl benzene around the industrial area exceed the regulatory limits for air quality standards. Research ABPLANALP et al. (2017) found that benzene exposure was associated with an increased risk of cardiovascular disease and deficits in angiogenic cell circulation in smokers and nonsmokers.

Several studies have shown that exposure to benzene can also increase free radicals and reduce the body's antioxidant status, especially the enzyme glutathione (GSH). Research conducted in Jakarta and Iraq shows that gas station workers who are exposed to benzene are more vulnerable to DNA damage due to free radicals (TUALEKA, et al., 2019). The results of research conducted by TUALEKA et al. (2019), also shows that there was a significant and reciprocal relationship between malondialdehyde and glutathione levels, which means that the higher the level of malondialdehyde, the lower the level of glutathione in the worker's body. Chen's research (1992) showed that serum malondialdehyde (MDA) content increased while the activity of erythrocyte superoxide dismutase (SOD) and erythrocyte glutathione peroxidase (GSH-Px) decreased in workers exposed to air benzene in the work environment by 50.21 mg / m3. This research was carried out by measuring lipid peroxide and the activity of relevant enzymes in workers exposed to benzene. Malondialdehyde (MDA) is a compound that can describe the activity

of free radicals in cells so that it is used as an indication of oxidative stress caused by free radicals.

Toluene ($C_6H_5CH_3$) is an aromatic hydrocarbon compound which is volatile, colorless, in the form of a clear liquid with a characteristic fishy and spicy aroma. This is a good solvent. This material is soluble in diethyl ether, ethanol, benzene, chloroform, glacial acetic acid, carbon disulfide, and acetone, but it does not dissolve in cold water. Toluene is generally used in the industrial sector in the process of making paints, solvent paints, nail polish, lacquers, adhesives, and rubber as well as in several processes of printing and tanning leather. The International Agency for Research on Cancer stipulates that toluene is classified in group 3, which is non-carcinogenic in humans (ATSDR, 2017). The toluene threshold value in the workplace air permitted according to the American Conference of Governmental Industrial Hygienists (ACGIH) (2015) must not exceed 20 ppm for 8 hours/day or 40 hours/week.

Exposure toluene can enter the human body through the respiratory, digestive and skin contact. However, as much as 40% - 60% of toluene exposure is absorbed by the body through the respiratory tract (IPCS, 2000). That is because toluene is a volatile compound that will be easily inhaled by workers exposed to toluene (ATSDR, 2017). Workers who are exposed to toluene continuously can result in eye and nose irritation, fatigue, confusion, dizziness, pupillary enlargement, anxiety, muscle fatigue, insomnia, damage to the central nervous system, skin inflammation, even liver and kidney

damage. The level of exposure also depends on the dose, duration, and occupation.

Several studies have shown that toluene exposure can cause health effects. Research by FARADISHA et al. (2019) in plastic bag printing industry workers showed that there was a significant relationship between toluene exposure, health risk characteristics (RQ) and toluene concentrations in the workplace above the threshold value based on ACGIH (2011). CHATURVEDI (2010) conducted a study of shoemaking workers in Agra in the Indies showing the results that acute exposure to toluene can cause kidney toxicity such as renal acidosis, hematuria, proteinuria and increased serum creatinine. Research by FREI, CHOBER-HALSTENBERG and THERAPY (1999) shows that there are 60 workers in Denmark and 81 workers in France doing dialysis and kidney transplants due to toluene exposure. Meanwhile, research conducted by BRAUTBAR and WILLIAMS (2002) states that exposure to toluene vapors can cause interference with liver function characterized by increased levels of Alanine Amino Transferase (ALT) and Aspartate Amino Transferase (AST).

Xylene is an aromatic hydrocarbon in three isomeric forms, namely meta-xylene, ortho-xylene and para-xylene. Total xylene refers to the three xylene isomers. The xylene mixture is a mixture of three isomers and usually also contains 6-15% ethylbenzene. Xylene is a colorless liquid at room temperature with a distinctive aroma, volatile and burning, not mixed with water but mixed with alcohol and other chemicals. Xylene is also widely used as a solvent in the printing, rubber and leather industries. Apart from that, it is also used as a cleaning agent, thinner for paints and in varnishes. About 92% of the xylene mixture is mixed into gasoline. The International Agency for

Research on Cancer stipulates that xylene is classified in group 3, which is non-carcinogenic in humans (ATSDR, 2007). The threshold value of xylene in the workplace air permitted according to the American Conference of Governmental Industrial Hygienists (ACGIH) (2015) does not exceed 100 ppm for 8 hours / day or 40 hours / week.

Exposure to xylene can enter the human body through the respiratory, digestive and skin contact. However, most of the xylene that enters the body is through the respiratory tract. 50-75% of xylene exposure that is inhaled can be absorbed by the lungs. Xylene does not accumulate significantly in the human body. Acute exposure to xylene with high concentrations can cause irritation to the skin, eyes, nose and throat, difficulty in breathing, impaired lung function, slow response to visual stimulation, memory disorders, stomach discomfort and possible liver and kidney disorders. Both acute and chronic exposure to high concentrations of xylene can have an effect on the nervous system and some people who are exposed to very high concentrations in a short time cause death (ATSDR, 2007).

Several studies were conducted to analyze xylene exposure with effects that can be caused. UCHIDA and NAKATSUKA (1993) conducted extensive research and reported signs and symptoms in workers who were chronically exposed to xylene mixtures. A significant increased in throat and nose irritation was found in workers who were chronically exposed to xylene smoke. In addition, decreased lung function and dyspnea were reported by HIPOLITO (1980) among histology technicians who were chronically exposed to xylene in the

laboratory. In the same study, cardiovascular effects such as flushing, palpitations and chest pain appeared among histology technicians. Meanwhile, a study of a group of workers in Turkey showed that there was an increase in hearing damage in a group of workers in the paint and painting industry. A total of 131 workers exposed to organic solvents in the form of xylene and 85 dB noise at work experience higher hearing damage than workers who are only exposed to the same level of noise (RAJAN and MALATHI, 2014).

Toxin Biotransformation

Biotransformation or metabolism is defined as xenobiotic / toxin changes catalyzed by a certain enzyme in living things. The purpose of biotransformation is to convert non-polar (easily soluble in fat) poisons into polar (easily soluble in solvent compounds). After that, it is converted into hydrophilic (easily soluble in water) so that it can be removed from the body (TUALEKA, 2013)

Phase I Reaction Phase II Reaction

Non polar → Polar → Hydrophilic

Oxidation-Reduction Conjugation

Hydrolysis

Non-polar chemicals include lipophiles and very stable lipophiles. Lipophil is a fat soluble toxin such as benzene toluene, xylene. Lipophils are very stable, lipophiles that are difficult to be decomposed / degraded so that there is accumulation in fatty tissue including benzopirin, DDT, PCB or poly chlorine bipenyl. Polar is a compound that dissolves easily in polar solvents such as methanol, etandiol, phenol. Hydrophilic toxins include hipuric acid, s-phenyl mercapturic acid, trans-trans muconic acid. Important organs in the

biotransformation process are the liver (high), lung, kidney, intestine (medium) and other tissues (low).

4. CONCLUSION

Detoxification is a constellation of physiological and psychological processes by which the body identifies, neutralizes and removes toxic substances, which are by-products of metabolism. Detoxification can be known by first analyzing the type and nature of carcinogens and non-carcinogens of the toxin and the process of biotransformation of the toxin. Various sources and studies state that detoxification of toxins can be carried out using a food approach. Foods that can detoxify toxins are enzyme-rich foods in stage 2 biotransformation such as foods containing the enzymes CYP2E1, glutathione and sulfation. Based on this analysis, a comprehensive strategy is needed to increase the consumption of foods containing CYP2E1, glutathione and sulfation enzymes in each individual that aims to increase the detoxification of toxins to avoid acute or chronic health effects due to toxin exposure.

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