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Requirement Prediction for Toluene Detox with Foods Intake Rich in CYP2E1 Enzyme and Glycine to Prevent Nerve and Kidney Damage at Shoe Home Industry Workers in Romokalisari Surabaya

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Abstract

BACKGROUND: Toluene was an organic compound used in chemical and drug industries, the main source of toluene emissions from fires. To reduce and even eliminate toluene toxins in chemical component could be using detoxification by foods.

AIM: This research aimed to calculate the intake of foods rich in CYP2E1 enzyme and glycine to improve toluene detoxification.

METHODS: The type of research was a descriptive study. The subject of the study was 51 workers in Romokalisari Surabaya who had worked for more than or equal to 10 years. Variables were body weight, duration of working (years), working time per week (days), and working time per day (hours). The breathing rate, intake of non-carcinogen per respondent, can be calculated by variables before. Then, the effective dose of food rich in CYP2E1 enzyme and glycine will be obtained.

RESULTS: Majority respondents had toluene concentrations below the threshold limit value (TLV). The highest effective dose of foods rich in CYP2E1 enzymes such as beef liver, beef brain, and salmon was 239.61 g, 745.45 g, and 203.3 g. Also, foods rich in glycines such as seaweed, tuna, and spinach were 432.98 mg, 934.41 mg, and 2070.71 mg.

CONCLUSION: The level of adequacy of the CYP2E1 enzyme and glycine of each person was different and varied. The effective dose required by each respondent depending on weight, length of work, and concentration of benzene in the workplace. The greater the toluene concentration, the greater the needs for foods rich in CYP2E1 enzymes and glycine. Body weight can also be another factor in differences in individual intake. Weight, length of working, and toluene concentration can affect the intake of non-carcinogen in each which can affect the effective dose of foods.

Introduction

The use of chemicals, especially hazardous chemicals, can certainly provide a threat at work. This can be a potential source that can trigger danger to the health and safety of workers [1]. One of the chemicals that are dangerous or carcinogenic is toluene. Toluene has the formula $C_6H_5CH_3$, is a colourless liquid, but smells fishy and spicy like benzene. This material dissolves in diethyl ether, ethanol, benzene, chloroform, glacial acetic acid, carbon disulfide, and acetone, but is not soluble in cold water [2].

Some industries or companies are directly related to toluene, such as the informal industry sector, one of them which is the shoe industry. The informal sector industry plays a very big role in developing countries, including Indonesia. The informal industry sector is an unorganised, irregular, and mostly legal but not registered sector [3]. As Indonesia's population of 230 million increases and the world population reaches 7 billion, indirect demand for shoes will also increase [4]. One of the toluene-containing materials used in the shoe industry is glue.

The shoe industry is a home industry where location and place of the industry are in the house so that it is inseparable between shoemaking activities and household activities. One of the shoe home industries in Surabaya is in Romokalisari. In the production process, shoe artisans in Romokalisari use a variety of equipment, such as electric heating machines, nails, and hammerheads. The use of production materials depends on the high and low order; if ordered a lot, more raw materials are needed.

Workers usually glued using their fingers directly, without any personal protective equipment, either gloves or masks. The workplace air condition is also very hot, with a very strong smell of glue steam. Most workers even work bare-chested while smoking or even eating when they work. Even when resting, they rest and sleep in that room. The use of chemicals that can interfere with the health of shoe artisans includes the use of glue because in this process there is exposure to organic solvent vapour contained in the glue and is very likely to have an impact on health if continuously inhaled for a long time [5]. One of the chemicals contained in the glue used in shoe production is toluene.

Toluene exposure can cause eye and nose irritation, fatigue, confusion, dizziness, enlarged pupils, anxiety, muscle fatigue, insomnia, nerve damage, skin inflammation, even liver and kidney damage. The level of exposure also depends on the dose, duration, and work done [6].

To reduce and even eliminate toxins in chemical compounds in the body, a biotransformation process is needed. Biotransformation is a change in the toxin-catalysed by certain enzymes in living things. The purpose of biotransformation is to convert non-polar to polar, then to become hydrophilic so that it can be excreted out of the body. Biotransformation occurs in two phases. The first phase is the functional phase where the functional group matches the oxidation, reduction and hydrolysis reactions. Then the second phase is the conjugate reaction phase involving several types of endogenous metabolites in the body in the endoplasmic reticulum [7].

Research using food approaches as toluene detoxification is still very limited. Foods are rich in CYP2E1 enzymes such as beef liver, beef brains, and salmon [8], [9]. Food is rich in glycine such as tuna, seaweed, turkey skin, spinach, canned corned beef, etc. But there has never been researching that explains how much intake of these foods is needed to improve toluene detoxification, especially in populations that exposed to toluene in a long time.

Based on the background above, this research aims to calculate the intake of foods rich in CYP2E1 enzyme (beef liver, beef brain, and salmon) and glycine (seaweed, tuna, and spinach) are needed (effective dose) to detoxify toluene on shoe home industry workers in Romokalisari Surabaya.

Material and Methods

The research was a descriptive study. Subjects were workers in shoe home industry in Romokalisari Surabaya. The inclusion criteria were male workers who had worked in this industry for more than or equal to 10 years and willing to be used as research respondents. The sample of this research was 51 respondents.

Variables calculated were body weight, duration of working (years), working time per week (days), an average of working every day (hours) of respondents, toluene concentration at 9 points in this industry — a measurement of respondents weight using manual measurement method with body scales. Measurement of the duration of work, working time per week, an average of working every day were obtained with an in-depth interview with respondents. Then, measurement of toluene concentration in the work environment using the measurement method of NIOSH 1501 (2003) with aromatic hydrocarbon sampling method [10]. Air samples were taken using a calibrated personal sampler pump. The filter used to absorb toluene vapour was a charcoal tube SKC 226-01. Air samples were analysed using Gas Chromatography-Flame Ionization Detector (GC-FID). Willingness to participate in research was made in writing through informed consent, and this study had received prior ethical approval by the Ethics Committee of the Faculty of Public Health, Airlangga University with ethical number 516 KEP-K.

After getting all variables above, can be found breathing rate and intake non-carcinogen of toluene per respondents. Then, an effective dose of foods rich in CYP2E1 enzyme and glycine will be obtained by manual calculating, use the formula below :

$$\text{dose effective of food intake} = \left\{\left(\text{intake NC x}\frac{\text{Mr enzyme}}{\text{Mr toxin}}\right) - \text{C enzyme x 65 x 100A}\right.$$

Explanation:

Intake nc (non-carcinogen) = $\frac{C\ x\ R\ x\ tE\ x\ fE\ x\ Dt}{Wb\ x\ 30\ x\ 365}$

C: Toluene concentration (mg/m^3)

R: Breathing rate (m^3/hour)

Dt: Duration of working (years)

I: Working time per week (days)

tE: Average of working time per day (hours)

Wb: Weight (kg)

C enzyme = $C\ enzyme\ (normal) x\ Mr\ enzyme$ (Tualeka, 2018) [16].

CYP2E1 enzyme $= \frac{0.0000088\ mmol/ml}{56849}$

Glycine $= \frac{0.00004\ mmol/ml}{75.07}$

A = Content of enzyme in 100 grams of the food

CYP2E1 enzyme
- Beef liver : 5.6 mg
- Beef brain : 1.8 mg
- Salmon : 6.6 mg

Glycine
- Seaweed : 3.099 g
- Tuna : 1.436 g
- Spinach : 0.648 g

Results

Distribution of Toluene Concentration at Workplace

Figure 1 shows that the majority of respondents are at the workplace with toluene concentration below TLV. The TLV of toluene concentration in the air is 50 ppm, while, respondents who are at the workplace with toluene concentration above TLV are 8% (4 respondents).

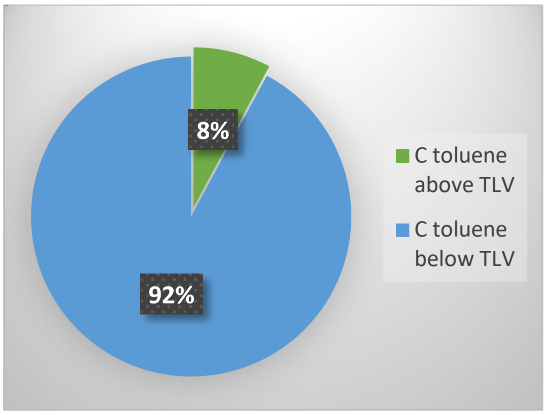

Figure 1: Distribution of Toluene Concentration in the Workplace

This respondent is in the same location (location 1). This location has the highest toluene concentration 138.6 ppm, while the lowest toluene concentration is 0.21, and the average of toluene concentration is 15 ppm.

Comparison between Toluene Concentration and Weight

The highest toluene concentration is 138.6 ppm (respondent 1-4), while the lowest is 0.21 ppm (respondent 46-51). The biggest weight on respondents is 82 kg (respondent 31), while the smallest is 0.41 kg (respondent 5).

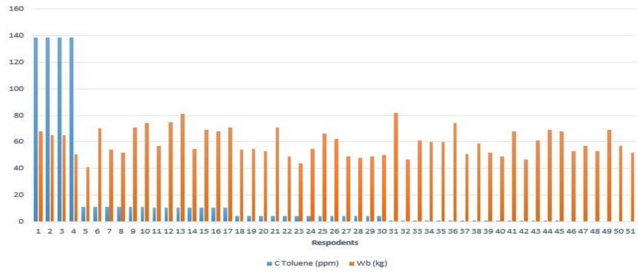

Figure 2: Comparison between Toluene Concentration and Weight

Based on Figure 2, the respondent who has the biggest weight isn't a workplace that has the highest toluene concentration while it had a similar result to lowest toluene concentration.

Effective Dose of Food Rich in CYP2E1 Enzyme to Toluene Detox

1. Effective Dose of Beef Liver to Toluene Detox

Figure 3 shows that the highest effective dose of beef liver to toluene detox is on respondent 2 (239,610 mg/239.61 g), while the lowest is on respondent 51 (317.33 mg).

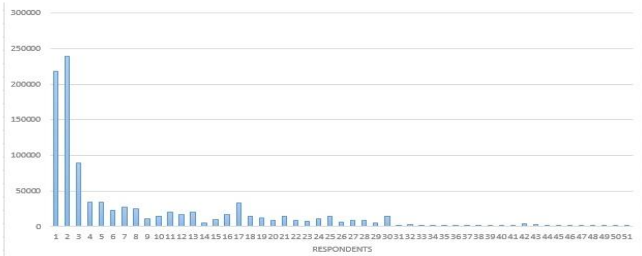

Figure 3: Effective Dose of Beef Liver to Toluene Detox

The average effective dose of beef liver to toluene detox on the respondent is 19.752 mg/19.75 g.

2. Effective Dose of Beef Brain to Toluene Detox

Figure 4 shows that the highest effective dose of the beef brain to toluene detox is on respondent 2 (745,456 mg/745.45 g).

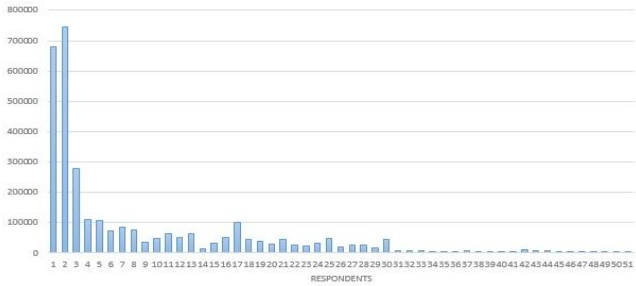

Figure 4: Effective Dose of Beef Brain to Toluene Detox

The lowest is on respondent 51 (987.25 mg). The average effective dose of the beef brain to toluene detox on the respondent is 61,451 mg/61.45 g.

3. Effective Dose of Salmon to Toluene Detox

Figure 5 shows that the highest effective dose of salmon to toluene detox is on respondent 2 (203,306 mg/20.33 g).

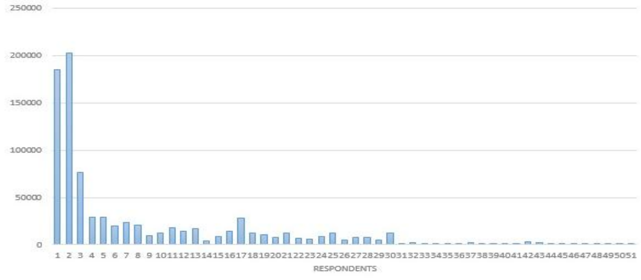

Figure 5: Effective Dose of Salmon to Toluene Detox

The lowest is on respondent 51 (269.25 mg). The average effective dose of salmon to toluene detox on the respondent is 16,759 mg/16.75 g.

Effective Dose of Food Rich in Glycine to Toluene Detox

1. Effective Dose of Seaweed to Toluene Detox

Figure 6 shows that the highest effective dose of seaweed to toluene detox is on respondent 2 (432.98 mg).

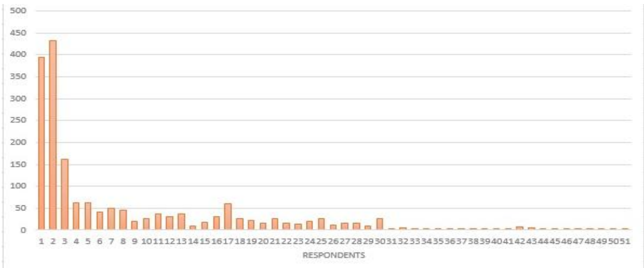

Figure 6: Effective Dose of Seaweed to Toluene Detox

The lowest is on respondent 51 (1.48 mg). The average effective dose of seaweed to toluene detox on the respondent is 35.7 mg

2. Effective Dose of Tuna to Toluene Detox

Figure 7 shows that the highest effective dose of tuna for toluene detox is on respondent 2 (934.41 mg) while the lowest is on respondent 51 (1.23 mg).

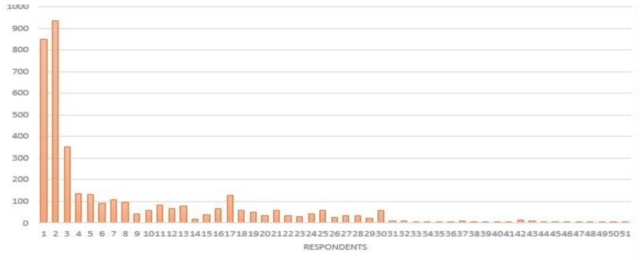

Figure 7: Effective Dose of Tuna to Toluene Detox

The average effective dose of seaweed to toluene detox on the respondent is 77 mg.

3. Effective Dose of Spinach to Toluene Detox

Figure 8 shows that the highest effective dose of seaweed to toluene detox is on respondent 2 (2070.71 mg/0.2 g).

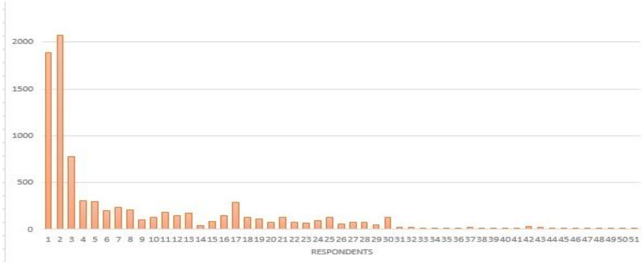

Figure 8: Effective Dose of Spinach to Toluene Detox

The lowest is on respondent 51 (2.74 mg). The average effective dose of seaweed to toluene detox on the respondent is 170.7 mg

Discussion

Threshold Limit Value (TLV), Weight, and Toluene Concentration

Distribution diagram analysis between toluene concentration and TLV shows that majority of respondents are at the workplace have toluene concentration below TLV. The TLV for toluene concentration according to The Regulation of Minister of Manpower and Transmigration Number PER13/MEN/X/2011 about The Threshold Limit Value of Physical and Chemical Factors at Workplace is 50 ppm (188.43 mg/m^3) [11]. Comparative diagram analysis between toluene concentration and weight of respondents shows that respondents with the biggest weight didn't have the highest toluene concentration, and it was similar to respondents with the smallest weight didn’t have the lowest toluene concentration. This research not by the research of Mukono that toluene had a small molecular mass that would be easily dissolved in fat. It was assumed that toxic with high solubility in fat (adipose) shows low concentration in the body [12]. This can be considered as a protection mechanism. So, it was concluded that there is low toluene toxicity in obese people than in thin people.

Detoxification of Toluene by Foods Rich in CYP2E1 Enzyme

Detoxification is very important to remove harmful chemicals in the body, especially toluene. Detoxification can be done foods approach, but this publicity still limited. Meanwhile, food-based nutrition continues to be a low-risk approach in the detoxification process. Several publications that had used cells, animals and clinical studies show that food-based components and nutrients could modulate the process of conversion and excretion of toxins from the body [13]. Toluene inhaled by a human while about 25-40% toluene will be excreted by expiration. The remaining 60-75% toluene will be metabolised in the liver became benzyl alcohol. Toluene will be converting to benzyl alcohol through a hydroxylation reaction. The reaction was carried out by members of the cytochrome P450 (CYP) in the liver, namely CYP1A1, CYP1A2, CYP2B6, CYP2C8, and CYP2E1 [14]. Then, benzyl alcohol will be metabolised to benzaldehyde by CYP and the alcohol dehydrogenase enzyme through an oxidation reaction. CYP was more active than the alcohol dehydrogenase enzyme. A small amount of benzaldehyde will be converted to benzylmercapturic acid while the majority of the others will be converted to benzoic acid. Benzoic acid will be metabolized to hippuric acid, which will be excreted through urine [15].

Consumption of suitable substances can detox toluene from the body, such as foods that contain CYP2E1 enzyme. High concentrations of CYP2E1 enzyme were found in some foods such as beef liver, beef brain, and salmon [9] (Minich & Hodges, 2015). The content of the CYP2E1 enzyme in 100 grams of the beef liver was 5.6 mg, in 100 grams of the beef brain was 1.8 mg, and 100 grams of salmon was 6.6 mg [16].

Based on the results, the effective dose of beef liver, beef brain, and salmon that the body requires for toluene detox from the body, as shown in Figure 3, 4, and 5. The effective dose of each food is different depending on the individual physical. The higher toluene concentration, the higher the mass of toluene detox for beef liver, beef beef, and salmon. This effective dose, also influenced by the weight and length of working of workers. This research by previous research, which states that it had a synergistic relationship with substance concentration [17]. The maximal consumption of beef liver is 239.6 g, the beef brain is 745.4 g, and salmon is 203.3 per day. Foods in the diagram can be chosen by each respondent based on the toluene concentration and individual taste. If respondents didn't interest to consume beef liver, they could consume beef brain and salmon, and vice versa. The consumption of each food can be regulated by each respondent, can be divided into several days according to the requirements of the foods intake of respondents.

Detoxification of Toluene by Foods Rich in Glycine

High burden of toxin in this modern life, diet supplementations with healthy foods should emphasise to support the metabolic detoxification phases. Evidence for toxin metabolism and elimination. Specific foods and nutrients can induce metabolic enzymes; one of them is glycine. When toluene enters the body, about 20% toluene will be excreted through the respiratory tract, while the remaining 80% will be metabolised into benzoic acid than will conjugate with glycine in the liver to form hippuric acid which will then be excreted through urine (ATSDR, 2000 [18]). To get glycine, one source is foods. Foods containing glycine include seaweed, spinach, tuna, long beans, leeks, corned beef, dried egg white, and so on [16].

Based on our results, the effective dose of seaweed, tuna, and spinach that the body needs from toluene detox, as shown in Figure 6, 7, and 8. The effective dose of each food is different depending on the individual physical. The higher toluene concentration, it will increase the mass of toluene detox for seaweed, tuna, and spinach. This effective dose, also influenced by the weight and length of working of workers. The maximal consumption of seaweed is 432.98 mg, tuna is 934.41 mg, while spinach is 2070.71 mg per day. Foods in the diagram can be chosen by each respondent based on the toluene concentration and individual taste. If respondents don’t like seaweed, they can consume tuna and spinach, and vice versa. The consumption of each food can be regulated by each respondent, can be divided into several days according to the needs of the foods intake of respondents.

In conclusion, the majority of respondents shows toluene concentrations below the threshold limit value (TLV). Intake of foods that contain CYP2E1 enzyme (Beef liver, beef brain, and salmon) and glycine (seaweed, tuna, and spinach) were expected to increase detoxification of toluene. The effective dose was required by the respondents depending on weight, length of working, and toluene concentration at the workplace. The greater the toluene concentration, it will increase the needs for foods rich in CYP2E1 enzymes and glycine that the body needs. Body weight can also be another factor in differences in individual intake. Weight, length of working, and toluene concentration could affect the intake of non-carcinogen of each which could affect the effective dose of foods.

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Data Availability

The manuscript data used to support the findings of this study have been deposited in the Analysis Of Relationship Between Benzene Vapor And Trans Content, Trans Muconic Acid Urin With Immunoglobulin A Decrease In Shoes In Kelurahan Tambak Oso Wilangun Surabaya" with accessed on http://repository.unair.ac.id/61400/ on Airlangga University/

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