Prediction Xylen Detox with food intake containing CYP2E1 enzyme and glycine on workers in Surabaya car painting area Indonesia

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ABSTRACT

Introduction: Xylene is an aromatic hydrocarbon with colourless, flammable, and volatile characteristics. The main exposure occurs through inhalation, as paint solvent vapor is released during the spray-painting process and can be inhaled by workers in the car painting area in Surabaya.

One way to deal with xylene exposure in the workplace is to detoxify xylene through foods containing the enzymes CYP2E1 and Glycine.

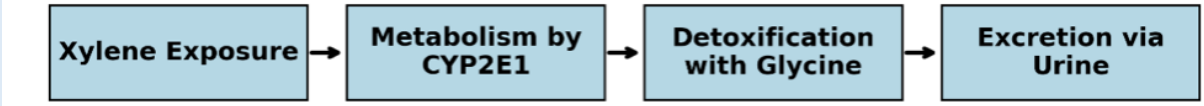
Objective: This study aims to predict the detoxification of xylene through food intake containing the CYP2E1 enzyme and glycine among workers in the car painting area of Surabaya, Indonesia. The primary goal is to evaluate how dietary factors influence xylene metabolism and elimination, potentially reducing occupational health risks associated with xylene exposure.

Methods: This is a cross-sectional observational study. The group being studied includes 2 strata of car painting workers and car retainer groups. Sampling was carried out through random sampling with proportional groups of 51 respondents including 36 painters and 15 workers in caulking areas. The research variables included weight, job time, weekly hours, work time per day, and xylene concentration. Once all variables had been gathered, each respondent's breathing rate and noncarcinogen intake were calculated. Lastly, we figure out the right amounts of foods with CYP2E1 enzymes and glycine.

Results: The level of xylene near the Surabaya car painting zone was above the threshold set for Xylen exposure at work. Foods that contain CYP2E1 enzyme are beef, brains. Glycine can be obtained from spinach.

Conclusion: The effective dose of food ingredients for xylen detox needed by each worker differs depending on the individual characteristics of each worker, ranging from body weight to length of work. Control with regular air checks to determine the condition of the xylene concentration level at work, providing air ventilation (local exhaust), specifically for partially enclosed workshops, using paint with safer organic solvents, and wearing personal protective equipment like a half-mask respirator with organic vapor cartridges, are steps taken to lower xylene levels.

Keywords: Xylen, CYP2E1 Enzyme, Glycine, Car Painting, Workers



Graphical Abstract: Prediction Xylen Detox with Food Intake Containing CYP2E1 Enzyme and Glycine on Workers in Surabaya Car Painting Area Indonesia

INTRODUCTION

Xylen is an aromatic hydrocarbon with colorless, flammable, and volatile characteristics. The vapor pressure of three isomers lies between 0.66 and 0.86 kPa [1–3]. The chemical industry produces xylene from petroleum [4,5]. The majority of xylene released into the environment directly enters the atmosphere [6–8]. In the atmosphere, photooxidation can immediately degrade xylene isomers[9–11].

Xylene can enter the body through inhalation, ingestion, and skin contact [12–14].

The main exposure pathway occurs through inhalation because the paint solvent vapors are produced from a spray-painting process that workers can inhale [15–17]. Individuals who are regularly exposed to high levels of solvent fumes may experience immediate effects like feeling drunk, tiredness, low stamina, headaches, feeling sick, shaking, difficulty balancing, or feeling down [18–20]. High xylene exposure can also have a major impact, namely acute inhalation disorders, eye and throat irritation, and disruption of reaction time [21,22].

Long-term exposure shows a significant decrease in radial and tibial nerve velocities and increased symptoms of numbness and cramps [4,23].

In addition, workers are exposed to steam and a mixture of tiny liquid particles (mist) that can easily penetrate the skin, particularly if proper personal protective equipment is not worn [24-25].

CYP2E1 is a key enzyme in the cytochrome P450 family that plays a significant role in the metabolism of various xenobiotics, including xylene. It is primarily found in the liver and catalyses the oxidation of xylene into methylbenzyl alcohol, which is subsequently converted into methylhippuric acid for excretion. The enzyme activates molecular oxygen to insert an oxygen atom into the xylene molecule, making it more water-soluble and easier to eliminate from the body. This biotransformation process is crucial in reducing the toxic effects of xylene and facilitating its detoxification through renal excretion 26.

Xylene is the most dominant material in spray painting in the automotive industry [27–29]. The research proposed by [30] shows that xylene content is the largest content in paint by 50%. Workers are exposed to xylene with a work duration of almost 8 hours a day for years in the painting area. Lundberg argues that at least 10 years of exposure are considered as criteria for diagnosing chronic toxic encephalopathy [31–33]. In [34] the average xylene concentration measurement results at five painting locations showed 146.47 ppm. This exceeds the limit set by the Minister of Manpower and Transmigration Regulation Number 13 of 2011 and Regulation No. 5 of 2018 [35-36].

Since the discovery of evidence of health problems due to exposure to xylene in workers, xylene was determined to be one of the harmful chemicals to human health [37–39]. In 2012, the American Conference of Governmental Industrial Hygienists (ACGIH) set the xylene Threshold Limit Value (TLV) at 435 mg/m3 (100 ppm) [40]. In 2005, the National Institute for Occupational Safety and Health (NIOSH) established a suggested exposure level of 100 ppm for an eight-hour workday [41]. In Indonesia, as per the Minister of Manpower and Transmigration Regulation No. 13 of 2011 and Regulation No. 5 of 2018, the threshold value is set at 434 mg/m3 (100 ppm).

Previous research in animals and humans has proven that benzene harms health. Xylene is distributed quickly to all body tissues, especially to adipose tissue. [42-43]

A study was conducted on spray workers in shipyards exposed to organic solvents found in solvent-based paints containing more than 50% xylene.

The results indicate complaints related to changes in mood, equilibration, and fatigue. This is following research conducted by [44] in PT X paint manufacturing

workers where 32.6% of respondents with exposure levels less than the threshold value experienced positive neurotoxic symptoms. Research [44] concluded the need for countermeasures to reduce the negative impact of xylene exposure on workers in the workplace. One way is to detoxify xylene through food [45–47]. During food-based detoxification, there's a biotransformation process where nonpolar toxins are converted into polar ones, making them water-soluble and easier to eliminate from the body.

METHODS

This research is a cross-sectional study where observations were made. The participants were divided into two groups, car painting workers and car pickers. We chose participants fairly, making sure each group was represented accurately. We ended up with 51 people in total, with 36 being painters and 15 working in caulking areas.

Study Design and Participant Selection: This cross-sectional study was conducted among Surabaya car painting and caulking workers. A total of 51 participants were included, consisting of 36 car painting workers and 15 caulking area workers. Participants were selected to ensure fair representation of both groups. Information on the study location, workforce size, and work schedules was obtained from the head of the Surabaya, Dodok and Cat Entrepreneurs Association (PPLDC).

Data Collection: Xylene Exposure Assessment: The concentration of xylene in the air was measured in five different car painting workshops in Surabaya. Air sampling was conducted using a GC/FID & HC analyser with the flame ionization detection method, following the NIOSH Method 1501 guidelines [48]. The sampling was conducted in collaboration with Prodia Laboratories and the Occupational Safety and Health Unit of East Java Province.

Determination of CYP2E1 Enzyme and Glycine Content in Food: CYP2E1 enzyme and glycine concentration in selected foods was determined based on literature sources and validated laboratory methods. Enzyme and amino acid content were analyzed using high-performance liquid chromatography (HPLC) and enzyme-linked immunosorbent assay (ELISA). The concentration values used in this study were as follows:

CYP2E1 Enzyme Content per 100 g of Food:

- Beef liver: 5.6 mg
- Beef brain: 1.8 mg
- Salmon: 6.6 mg
- Glycine Content per 100 g of Food:
- Seaweed: 3099 mg
- Tuna: 1436 mg
- Spinach: 648 mg

Calculation of Xylene Intake and Detoxification Dose: To determine the required intake of foods containing the CYP2E1 enzyme and glycine for xylene detoxification, we used the following formula:

Formula for effective doses per day for men:

Effective dose per day =

$$\{(Intake\ nk \times \frac{Mr\ Enzyme}{Mr\ Toxin}) - (\text{C enzyme} \times 70)\} \times \frac{100}{A}$$

Formula for effective doses per day for women:

Effective dose per day =

$$\{(Intake\ nk \times \frac{Mr\ Enzyme}{Mr\ Toxin}) - (\text{C enzyme} \times 70)\} \times \frac{100}{A}$$

Explanation: The calculation of non-carcinogenic xylene intake (nc) is as follows:

$$\frac{C\ x\ R\ x\ tE\ x\ fE\ x\ Dt}{Wb\ x\ 30\ x\ 365}$$

C: Xylene level (mg/m3)

R: Breathing rate (m3/hour)

Dt: Duration of working (years)

fE: Working time per week (days)

tE: Average of working time per day (hours)

Wb: Weight (kg)

Food Rich in (Tualeka, 2018)

C enzyme

CYP2E1 enzyme = 0.0000088 mmol/ml

Glycine = 0.00004 mmol/ml

Mr enzyme

CYP2E1 enzyme = 56849

Glycine = 75.07

A = Enzyme concentration in 100 grams of food, CYP2E1 enzyme

- Cow liver: 5.6 mg
- Cow brain: 1.8 mg
- Salmon: 6.6 mg Glycine
- Seaweed: 3.099 g = 3099 mg
- Tuna: 1.436 g = 1436 mg
- Spinach: 0.648 g = 648 mg

Determination of Effective Food Dose: The required daily intake of each food was estimated based on the calculated xylene intake and detoxification potential of the CYP2E1 enzyme and glycine. The calculation considered body weight, exposure levels, and dietary feasibility. Daily intake recommendations were determined in grams, ensuring practical and biologically feasible values.

RESULT

Xylen's concentration at work: Xylene concentration was measured in five workshops near the car painting zone along Jalan Pengenal in Surabaya, Indonesia. In this location, both open-air and semi-closed workshops are available. The final stage of painting a car is in an open field; a semi-closed workshop is usually used to paint a small part of the car.

Table 1. Xylen's Concentrations in Five Workshop Painting Cars in Surabaya, Indonesia.

Sample	Xylene concentration		Threshold		Note
	(mg/m3)	(ppm)	(mg/m3)	(ppm)	
Workshop A (Open)	137.64	31.7	434	100	<NAB
Workshop B (Open)	263.46	60.68	434	100	<NAB
Workshop C (Open)	286.26	65.93	434	100	<NAB
Workshop D (Semi-Closed)	1176.66	271	434	100	>NAB
Workshop E (Semi-Closed)	1480.59	341	434	100	>NAB
Average	635.98	146.47	434	100	>NAB

Based on the results of measurements made at five workshops around the Surabaya Identifier Road car painting area, the xylen concentration value was 635.98 mg /m3 (146.47 ppm), the high concentration reached 1480.59 mg/m3 (341 ppm), while the lowest recorded concentration was 137.64 mg/m3 (31.7 ppm). The mean xylene level exceeds the limit of Minister of Manpower and Transmigration Regulation Number 13 of 2011 and Permenaker No. 5 in 2018 of 434 mg / m3 (100 ppm) with two workshops exceeding the threshold limit.

Table 2. Characterization of Risk of Workers Exposed to Xylen.

Workers	Weight (kg)	C xylene (mg/m^3)	Dt (years)	fE (days)	tE (hours)	Breathing Rate (mg/m^3)	Intake (mg/kg day)	RfC (mg/kg)	RQ
1	50.1	137.638	11.5	365	6	0.576846306	3.644924856	38.86408	0.09378648
2	50.1	137.638	11.5	365	6	0.576846306	3.644924856	38.86408	0.09378648
3	50.1	137.638	11.5	365	6	0.576846306	3.644924856	38.86408	0.09378648

Workers	Weight (kg)	C xylene (mg/m³)	Dt (years)	fE (days)	tE (hours)	Breathing Rate (mg/m³)	Intake (mg/kg day)	RfC (mg/kg)	RQ
4	50.1	137.638	11.5	365	6	0.576846306	3.644924856	38.86408	0.09378648
5	50.1	137.638	11.5	365	6.5	0.576846306	3.948668594	38.86408	0.10160201
6	50.1	137.638	11.5	365	6.5	0.576846306	3.948668594	38.86408	0.10160201
7	50.1	137.638	11.5	365	6.5	0.576846306	3.948668594	38.86408	0.10160201
8	50.1	137.638	11.5	365	6.5	0.576846306	3.948668594	38.86408	0.10160201
9	50.1	137.638	11.5	365	6.5	0.576846306	3.948668594	38.86408	0.10160201
10	50.1	137.638	11.5	365	6.5	0.576846306	3.948668594	38.86408	0.10160201
11	50.1	137.638	11.5	365	6.5	0.576846306	3.948668594	38.86408	0.10160201
12	50.1	263.467	18	365	6.5	0.576846306	11.83077577	38.86408	0.30441417
13	58.7	263.467	18	365	6.5	0.61183044	10.70986046	38.86408	0.27557223
14	58.7	263.467	18	365	6.5	0.61183044	10.70986046	38.86408	0.27557223
15	58.7	263.467	18	365	6.5	0.61183044	10.70986046	38.86408	0.27557223
16	58.7	263.467	18	365	6.5	0.61183044	10.70986046	38.86408	0.27557223
17	58.7	263.467	18	365	6.5	0.61183044	10.70986046	38.86408	0.27557223
18	58.7	263.467	18	365	6.5	0.61183044	10.70986046	38.86408	0.27557223
19	58.7	263.467	18	365	6.5	0.61183044	10.70986046	38.86408	0.27557223
20	58.7	286.262	18	365	6.5	0.61183044	11.63647088	38.86408	0.29941456
21	58.7	286.262	18	365	6.5	0.61183044	11.63647088	38.86408	0.29941456
22	58.7	286.262	18	365	6.5	0.61183044	11.63647088	38.86408	0.29941456
23	58.7	286.262	18	365	6.5	0.61183044	11.63647088	38.86408	0.29941456
24	58.7	286.262	25.5	365	6.5	0.61183044	16.48500042	38.86408	0.42417063
25	58.7	286.262	25.5	365	6.5	0.61183044	16.48500042	38.86408	0.42417063
26	58.7	286.262	25.5	365	6.5	0.61183044	16.48500042	38.86408	0.42417063
27	58.7	286.262	25.5	365	6.5	0.61183044	16.48500042	38.86408	0.42417063
28	58.7	286.262	25.5	365	6.5	0.61183044	16.48500042	38.86408	0.42417063
29	58.7	286.262	25.5	365	6.5	0.61183044	16.48500042	38.86408	0.42417063
30	68.66	286.262	25.5	365	7	0.646440999	16.03635865	38.86408	0.41262677
31	68.66	286.262	25.5	365	7	0.646440999	16.03635865	38.86408	0.41262677
32	68.66	286.262	25.5	365	7	0.646440999	16.03635865	38.86408	0.41262677
33	68.66	1176.66	25.5	365	7	0.646440999	65.91633458	38.86408	1.69607356
34	68.66	1176.66	25.5	365	7	0.646440999	65.91633458	38.86408	1.69607356
35	68.66	1176.66	29	365	7	0.646440999	74.96367462	38.86408	1.92886797
36	68.66	1176.66	29	365	7	0.646440999	74.96367462	38.86408	1.92886797
37	68.66	1176.66	29	365	7	0.646440999	74.96367462	38.86408	1.92886797
38	68.66	1176.66	29	365	7	0.646440999	74.96367462	38.86408	1.92886797
39	68.66	1176.66	29	365	7	0.646440999	74.96367462	38.86408	1.92886797

Workers	Weight (kg)	C xylene (mg/m³)	Dt (years)	fE (days)	tE (hours)	Breathing Rate (mg/m³)	Intake (mg/kg day)	RfC (mg/kg)	RQ
40	73.64	1176.66	29	365	7	0.661904095	71.56605232	38.86408	1.84144477
41	73.64	1176.66	29	365	7	0.661904095	71.56605232	38.86408	1.84144477
42	73.64	1176.66	29	365	7	0.661904095	71.56605232	38.86408	1.84144477
43	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577
44	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577
45	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577
46	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577
47	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577
48	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577
49	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577
50	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577
51	73.64	1480.595	29	365	7	0.661904095	90.05179001	38.86408	2.31709577

Based on the results of Table 2, 19 respondents had an RQ value of more than one (RQ> 1), namely respondents 33 to 51. Therefore, the oxen detox calculation using foods containing the CYP2E1 and glycine enzymes was carried out on these 19 respondents because respondents with RQ> 1 had high health risks.

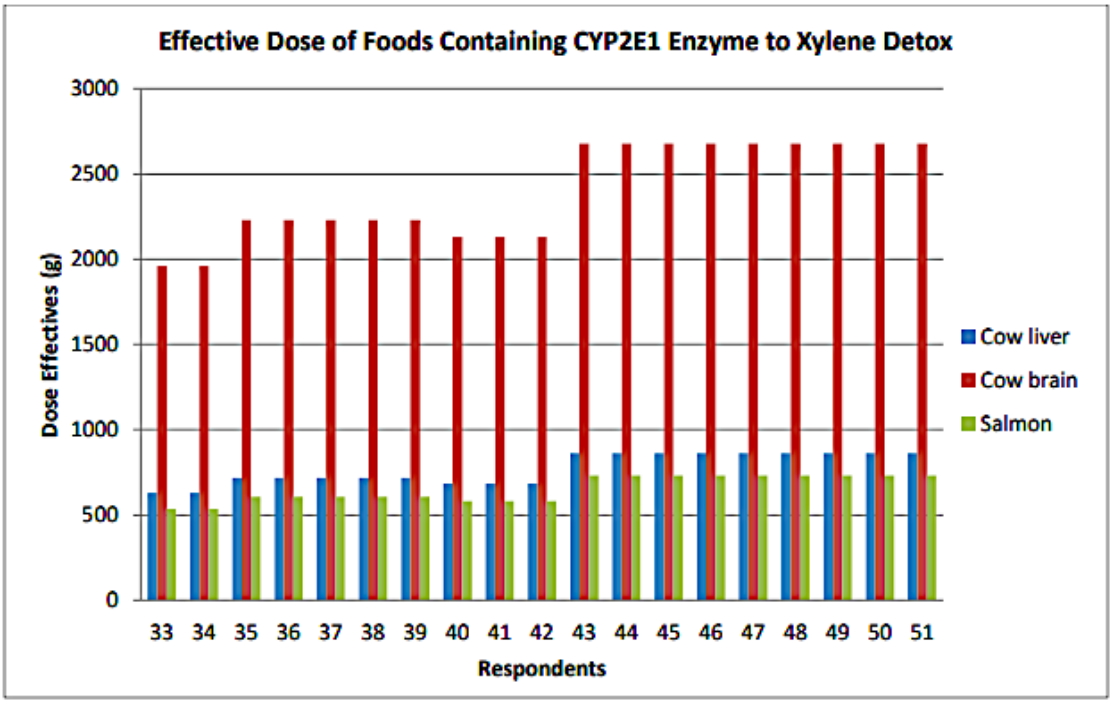


Figure 1. Effective intake dose of foods containing the CYP2E1 enzyme for xylene detoxification.

Figure 1 shows that cow brains have the highest effective dose, whereas salmon containing the CYP2E1 enzyme has the lowest dose among the food items. The highest effective doses for beef liver, beef brain, and salmon are 861,125 g, 2679,055 g, and 730,651 g

respectively (respondents 43-51). Meanwhile, the lowest effective dose of beef liver, beef brain, and salmon was 630,328 g, 1961,021 g, and 534,824 g (respondents 33-34).

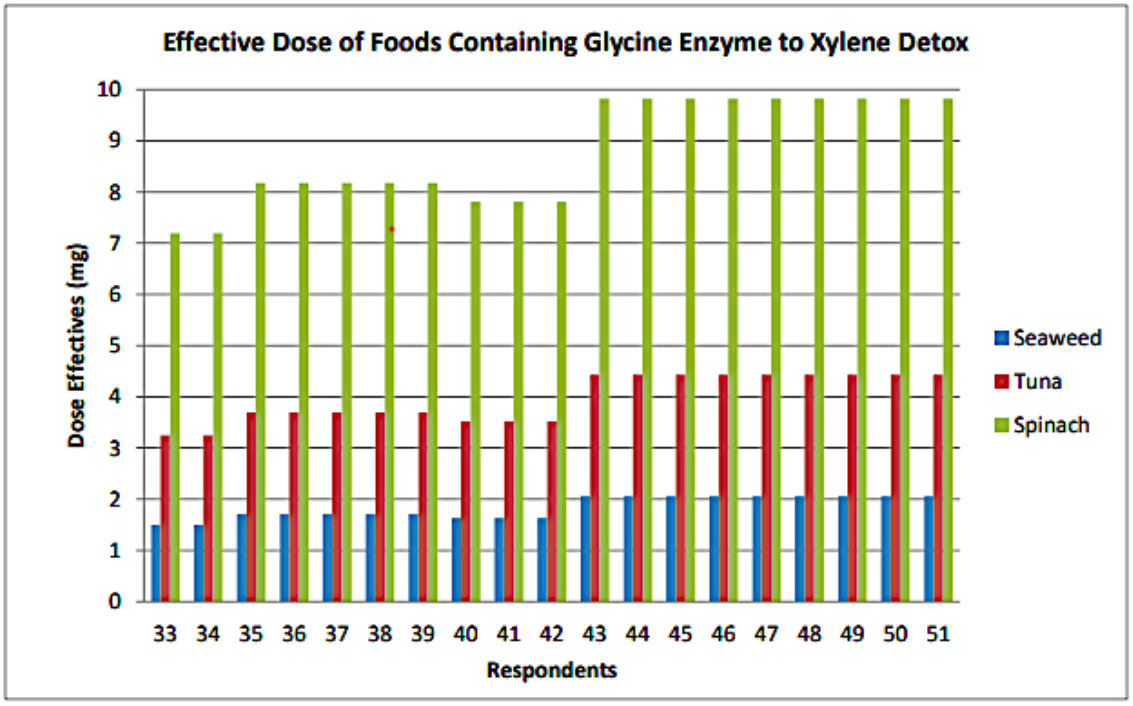


Figure 2. Effective intake dose of foods containing the glycine enzyme for xylene detoxification.

Figure 2 shows that spinach has the highest dose, while seaweed has the highest and lowest doses among the foods containing the Glycine enzyme. The highest effective doses for seaweed, tuna, and spinach were 2.054 mg, 4.434 mg, and 9.826 mg respectively (respondents 43-51). Conversely, the least effective doses for seaweed, tuna, and spinach were 1.504 mg, 3.245 mg, and 7.192 mg respectively (respondents 33-34).

DISCUSSION

According to the calculated results, the concentration of xylene in the vicinity of Surabaya's car painting area, Indonesia is an average of 199.3 ppm. This surpasses the workplace xylene exposure limit set by the 2004 Conference of Governmental Industrial Hygienists (ACGIH), NIOSH (National Institute for Occupational Health and Safety) in 2005, Minister of Manpower and Transmigration Regulation No. 13 of 2011, and Permenaker No. 5 in 2018, which is 434 mg/m3 or 100 ppm (8-day TWA).

According to the research analysis findings, each individual requires a specific effective dosage of food that differs depending on individual characteristics ranging from body weight to the length of service of the respondent.

In addition, the effective dose required by the body to detoxify xylene is influenced by the concentration of xylene in the body and the air. As the concentration increases, the required effective doses of beef liver, beef brain, salmon, seaweed, tuna, and spinach also increase due to the role of the CYP2E1 enzyme in xylene metabolism, which varies depending on exposure levels and individual physiological conditions [51–53].

Based on the calculation results, it is known that 43-51 respondents had the maximum effective dose of xylen detox from a total of 51 respondents. Food containing CYP2E1 requires 861,125 g beef liver, 2679,055 g beef

brain, and 730,651 g salmon, while glycine requires 3032,054 mg seaweed, 4,434 mg tuna, and 9,826 mg spinach. This is because respondents 43-51 have the longest working period of 29 years, so they have been continuously exposed to xylene for a long time. making the required food intake for xylene detoxification significantly higher.

CYP2E1 plays a crucial role in xylene metabolism, as it catalyzes the oxidation of xylene into methylhippuric acid, which is then excreted via urine. Prolonged exposure to xylene can lead to an upregulation of CYP2E1, potentially increasing metabolic clearance but also elevating oxidative stress due to reactive oxygen species (ROS) production. This suggests that individuals with prolonged exposure may require higher dietary intake of CYP2E1-inducing foods to maintain effective detoxification. Additionally, dietary sources of glycine contribute to the conjugation process, enhancing xylene elimination through the formation of hippuric acid. These metabolic interactions highlight the importance of selecting appropriate food sources to support enzymatic detoxification pathways.

The study's results clearly show how large the effective dose of each food is in the diagram, enabling workers to choose food according to their preferences and needs. If workers do not like vegetables such as seaweed and spinach, they can choose other types of food, such as salted fish or dry egg whites. Workers can also distribute their food intake over several days [49–51].

CONCLUSION

Most respondents exhibited xylene concentrations surpassing the threshold value (TLV). This study provides a novel approach by integrating dietary strategies to enhance xylene detoxification, focusing on the role of CYP2E1 and glycine intake. Consuming foods containing CYP2E1 enzymes (such as beef liver, beef brain, and salmon) and glycine (such as seaweed, tuna, and spinach) has been demonstrated to support xylene metabolism by facilitating oxidation and conjugation processes, which lead to its elimination. The necessary effective dose varies based on the worker's weight, duration of work, and xylene concentration in the workplace. Higher concentrations of xylene necessitate an increased consumption of foods rich in the enzymes CYP2E1 and glycine, which are essential for the body. Weight is another contributing factor to the varying intake among individuals. Weight, length of employment, and xylene concentration impact the non-carcinogenic intake of each person, thus influencing the required effective dose of food.

RECOMMENDATION

Five workshops in the car painting area of Jalan Pengenal Surabaya, Indonesia are advised to conduct periodic air checks to determine the condition of the xylene concentration level at work, provide air ventilation (local exhaust), especially in semi-enclosed workshops, opt for paints with higher safety standards, including those with fewer organic solvents. Additionally, ensure the proper use of personal protective equipment, such as half-mask respirators with organic vapor cartridges, to reduce exposure to xylene vapors. Workers are advised to maintain personal hygiene, such as washing hands with soap before and after work or before and after eating.

Abbreviations: CYP2E1, Enzim dalam keluarga cytochrome P450; ACGIH, American Conference of Governmental Industrial Hygienists; TLV, Threshold Limit Value; ROS, Reactive Oxygen Species; NIOSH, National Institute for Occupational Health and Safety; GC/FID, Gas Chromatography/Flame Ionization Detector; HC analyser, Hydrocarbon analyser; HPLC, High-Performance Liquid Chromatography; ELISA, Enzyme-Linked Immunosorbent Assay; TWA, Time-Weighted Average; RQ, Risk Quotient

Conflict of interest: The authors declare that they have no competing interests.

Authors' Contribution: All authors discussed the results and contributed to the final manuscript.

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