Indexed in Clarivate Analytics WoS

E-B Environment - Behaviour Proceedings Journal

ICEPH-CS2025Kuching

https://iceph-cs.com/

e-IPH e-International Publishing House Ltd., United Kingdom

1st International Conference, Exhibition & Innovation on Public Health & International Community Services

Waterfront Hotel Kuching, Sarawak, Malaysia

19-22 Aug 2025

Organiser: Universiti Teknologi MARA (UiTM), Malaysia
Co-Organisers: Universitas Muhammadiyah Malang (UMM), Indonesia, Unversitas Airlangga (UNAIR), Indonesia, UiTM Technoventure, Malaysia

Impact of Supplementation Rich in CYP2E1 Enzyme and Decarboxylase Enzyme on Improvement of Leukocyte Values

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Abstract

This study explores the effects of enzyme supplementation (rich in CYP2E1 and decarboxylase) on leukocyte levels among 27 home-based shoe industry workers exposed to benzene in Tambak Osowilangun, Surabaya. Using a quantitative pre-experimental one-group pretest-posttest design, leukocyte counts were assessed before and after five days of supplementation. Results showed a significant improvement, with abnormal leukocyte levels dropping from 59% to 7%. Although limited by a small sample size and lack of a control group, the findings highlight the potential benefits of enzymatic intervention and underscore the need for health-based strategies to reduce occupational risks in informal sectors.

Keywords: Benzene, Leukocyte, Enzymes, Occupational Health

DOI: https://doi.org/10.21834/e-bpj.v10iSI35.7521

1.0 Introduction

Occupational exposure to benzene can disrupt hematopoiesis and suppress leukocyte production through oxidative stress and enzymatic imbalance. Cytochrome P450 2E1 (CYP2E1) plays a key role in benzene and toluene metabolism, where excessive activation produces reactive oxygen species (ROS) leading to bone marrow toxicity and immune suppression (Bolt & Roos, 2020). In contrast, balanced CYP2E1 activity supports detoxification and oxidative adaptation (Wang et al., 2023). Similarly, decarboxylase enzymes regulate amino acid metabolism and generate bioactive amines, such as histamine, that influence immune and hematopoietic functions (Moriguchi & Yamashita, 2020).

Several occupational studies have shown that chronic or even low-level benzene exposure (<1 ppm) causes hematological abnormalities, immune dysregulation, and bone marrow suppression among industrial workers (Chen et al., 2022). However, most studies have concentrated on benzene's toxic mechanisms rather than on biological or enzymatic interventions to restore hematopoietic

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DOI: https://doi.org/10.21834/e-bpj.v10iSI35.7521

balance. The potential of CYP2E1 and decarboxylase modulation to improve leukocyte function in exposed workers remains poorly understood, highlighting a key gap in addressing benzene-induced hematotoxicity.

Therefore, this study aims to evaluate the effect of CYP2E1 and decarboxylase-rich supplementation on leukocyte improvement and to elucidate potential mechanisms linking enzymatic modulation to hematopoietic health. Specifically, this research seeks to assess leukocyte changes before and after supplementation, analyze the correlation between CYP2E1 activity and leukocyte improvement, and examine the involvement of decarboxylase activity in hematopoietic recovery following benzene exposure.

2.0 Literature Review

2.1 Benzene

Benzene remains a critical occupational toxicant widely used in industrial solvents, fuels, and paints. It is a volatile, colorless liquid with a boiling point of 80.1°C and high environmental mobility (ATSDR, 2022). Chronic exposure to benzene has been associated with hematotoxicity, bone marrow suppression, and leukemia due to its metabolites that damage hematopoietic stem cells (Zhang et al., 2022). Recent studies indicate that even low-level exposure (<1 ppm) can alter white blood cell counts and oxidative stress biomarkers (Lotsios, 2023). In Indonesia, benzene is categorized as a carcinogen with a threshold limit of 0.5 ppm, yet small-scale industries often exceed this value due to poor ventilation and limited protective equipment (Rahman et al., 2022). These findings highlight the need for biological interventions to mitigate benzene-induced hematotoxicity, particularly those targeting enzymatic pathways involved in its metabolism.

2.2 Enzym CYP2E1

Cytochrome P450 2E1 (CYP2E1) is a key enzyme responsible for metabolizing benzene, toluene, and ethanol. Overexpression of CYP2E1 enhances the generation of reactive oxygen species (ROS), leading to oxidative stress and tissue damage (Penaloza, 2020). However, moderate CYP2E1 activity is crucial for xenobiotic detoxification. Nutritional modulation of CYP2E1, through bioactive compounds found in garlic, turmeric, and polyphenols, has shown potential in reducing oxidative injury and improving hematological balance (García Ruiz & Fernández Checa, 2020; Li et al., 2023). Given its dual role in both bioactivation and detoxification, modulating CYP2E1 activity may offer a promising approach to restore hematopoietic balance in benzene-exposed individuals.

2.3 Enzym Decarboksilase

Decarboxylase enzymes are vital in amino acid metabolism and neurotransmitter synthesis, contributing to cellular defense and metabolic regulation (Khan et al., 2021). Their antioxidant capacity supports the neutralization of free radicals and enhances enzymatic detoxification. Dietary sources such as fermented fish, cheese, and legumes have been shown to elevate decarboxylase activity, improving immune response and hematopoietic regeneration (Fang et al., 2022; Wang et al., 2024). This suggests that decarboxylase activity may complement CYP2E1 regulation in promoting leukocyte recovery and oxidative balance.

2.4 Leukosit

Leukocytes play a fundamental role in host defense, inflammation, and immune regulation. Neutrophils, macrophages, and dendritic cells coordinate both innate and adaptive immune responses through cytokine signaling (Abbas, Lichtman, & Pillai, 2022, p. 47). Environmental stressors and chemical exposures, including benzene, can suppress leukocyte formation and alter immune function, leading to increased susceptibility to infections and hematological abnormalities (Cordiano, 2022). Restoring leukocyte integrity through enzymatic modulation could therefore represent a novel biological strategy to counteract benzene-induced immune suppression.

3.0 Method

3.1 Study Design

This study employed a quantitative pre-experimental design to examine the effects of enzyme-rich supplementation on leukocyte levels. The design involved measuring leukocyte counts before and after supplementation within the same group of participants, allowing the observation of biological changes over time while minimizing inter-individual variability.

3.2 Population and Sampling

The study involved 27 employees from a shoe cottage industry in Surabaya. Participants were selected using purposive sampling, ensuring that all individuals represented the production workforce and shared similar occupational exposures.

3.3 Intervention

The intervention involved administering an enzyme-rich supplement formulated with standardized preparations of cytochrome P450 (CYP2E1) and decarboxylase derived from recombinant food-based sources to ensure purity and safety. CYP2E1 was extracted from Salmon (*Salmo salar*), known for its natural metabolic precursors that enhance enzyme activity, while decarboxylase was obtained from beetroot (*Beta vulgaris*) and mixed berries containing polyphenols that promote enzyme expression and antioxidant capacity. Each 15

g capsule batch contained 8 g extract from 400 g of salmon, 4 g from 3.5 kg of beetroot, and 3 g of mixed berries. Participants consumed one capsule twice daily for five days, with the dosage determined based on enzyme kinetics and tolerance data.

3.4 Data Collection

Leukocyte counts were measured before and after the supplementation period using a hematology analyzer. Data were analyzed using SPSS version 25, where descriptive statistics described the frequency distribution, and inferential analysis was performed using the paired t-test to evaluate significant changes in leukocyte levels.

3.5 Ethical Considerations

All study procedures were conducted in accordance with ethical standards. Ethical approval was obtained from the Ethics Committee of the Faculty of Public Health, Universitas Airlangga. All participants provided informed consent prior to participation, and confidentiality as well as voluntary involvement were ensured throughout the study.

4.0 Findings

The study found that supplementing employees with CYP2E1 and decarboxylase enzymes can significantly reduce leukocyte counts at the Tambak Osowilangun Surabaya shoe company.

4.1 Identification of Worker Characteristics

Results of the Frequency Distribution Analysis of Worker Characteristics in the Home Industry of Osowilangun, Surabaya Pond Shoes.

Table 1. Distribution Analysis of Worker Characteristics

Variables Worker Characteristics	Category	Frequency (f)	Percentage (%)
Age	The Productive group (15 - 64 years old)	23	85.2
	Non-productive age group (>65 years)	4	14.8
	Amount	27	100
	Mean (SD)	52.4 years (9.7)	
	Mark*Max*	67 years old	
	Mark*Min*	37 years old	
Gender	Man	8	29.6
	Woman	19	70.4
	Amount	27	100
Number of years of service	1-10 years	1	4
	11-21 years	7	26
	22-32 years	13	48
	>33 years	6	22
	Amount	27	100
	Mean (SD)	27.9 years (9.5)	
	Mark*Max*	50 years	
	Mark*Min*	10 years	
Nutritional status	Normal body weight 18.5 – 22.9 Kg/m2	6	22
	Overweight 23 – 24.9 Kg/m2	4	15
	Obesity I 25 – 29.9 Kg/m2	7	26
	Obesity II > 30 Kg/m2	10	37
	Amount	27	100
	Mean (SD)	27.2 Kg/m2 (4.7)	
	Mark*Max*	35.1 Kg/m2	
	Mark*Min*	19.3 Kg/m2	
Smoking Habit	Do not smoke	24	88.9
	Heavy smoker: (>16 cigarettes/day)	3	11.1
	Amount	27	100

Variables Worker Characteristics	Category	Frequency (f)	Percentage (%)
	Mean (SD)	2.3 sticks/day (6.6)	
	Mark*Max*	22 sticks/day	
	Mark*Min*	19 sticks/day	
Exercise Habits	No exercise	11	40.7
	Sometimes	16	59.3
	Amount	27	100
History Own Disease	Have a History of a Disease	18	66.7
	No History of a Disease	9	33.3
	Amount	27	100
Use of PPE	Yes, every day	3	11.1
	Sometimes	2	7.4
	Never	22	81.5
	Amount	27	100

Source: Data Processing Results Utilizing SPSS (2024)

The shoe workers in Tambak Osowilangun Surabaya are mostly productive, with an average age of 52.4 years and a significant number of women. They have extensive experience, with 48% having 22-32 years of service. However, 37% are obese, smoke 2.3 cigarettes daily, and exercise occasionally.

4.2 Leukocyte Values of Shoe Workers in the Home Industry at Osowilangun Pond, Surabaya

The study shows the number of leukocytes in the blood of workers in the Tambak Osowilangun Surabaya shoe industry, both before and after they received the CYP2E1 and decarboxylase enzymes.

Table 2. Leukocyte value results data before the enzymes were given

Leukocyte Value	*Pre-test*				n	%
	Normal		Abnormal			
	N	%	N	%		
Frequency (n)	11	41	16	59	27	100
Mean (SD)	8.2 (3.3)		8.5 (8.8)			
Mark*Max*	10.2		12.6			
Mark*Min*	4.8		2.5			

Source: Data Processing Results Utilizing SPSS (2024)

The study reveals that in the home industry of Tamak Osowilangun Surabaya shoes, workers with abnormal leukocyte values ranged from 2.5 to 12.6 u/L, with the majority (59%) being 16 workers with abnormal values.

Table 3. Leukocyte value result data after the enzymes were given

Leukocyte Value	*Post-test*				n	%
	Normal		Abnormal			
	N	%	N	%		
Frequency (n)	22	81	5	19	27	100
Mean (SD)	7.6 (3.6)		11 (0.3)			
Mark*Max*	11		11.3			
Mark*Min*	3.8		10.9			

Source: Data Processing Results Utilizing SPSS (2024)

The table indicates that after the CYP2E1 enzyme and worker decarboxylase enzyme were given in the home industry, the shoe workers in Tambak Osowilangun Surabaya had an average abnormal leukocyte level of 11 u/L, with 5 workers showing abnormal levels, which is 19%.

Table 4. Cross-tabulation analysis of leukocyte values before and after administration of enzymes

Variable	Leukocytes *Posttest*	Total

			Normal		Abdnormal			
			n	%	n	%		
Leukocytes *Pretest*	Normal	n	11	100	0	0	11	41
	Abnormal	%	11	68.8	5	31.3	16	59
Total			22	81.5	5	18.5	27	100

Source: Data Processing Results Utilizing SPSS (2024)

The study showed that 16 workers (59%) had unusual leukocyte levels before getting the CYP2E1 enzyme and decarboxylase enzyme, and five workers (18.5%) saw improvement after taking the enzymes. However, only 40.5% of workers improved their leukocyte levels. However, only 40.5% of workers experienced an improvement in leukocyte values.

4.3 Leukocyte Values Before and After the Administration of Supplements Rich in Decarboxylase Enzymes and CYP2E1 Enzymes
The study explores the potential of supplements containing CYP2E1 and decarboxylase enzymes, which are crucial for liver breakdown and neurotransmitter production and for enhancing toxic compound biotransformation and immune system balance.

Table 5. Results of differences in leukocyte values before and after being given supplements

Descriptive Analysis	*Pretest* (Normal)	*Posttest* (Abnormal)	Difference	*Pretest* (Normal)	*Posttest* (Abnormal)	Difference
Frequency (n)	11	16	5	22	5	17
Mean	8.2	8.5	0.3	6.5	11	4.5
Median	8.2	11.3	3.1	7.6	11	3.4
Maximum	10.2	12.6	2.4	11	11.3	0.3
Minimum	4.2	2.5	1.7	3.8	10.9	7.1
Stand Deviation	3.3	8.8	5.5	3.6	0.3	3.3

Source: Data Processing Results Utilizing SPSS (2024)

The research indicated that prior to and following supplementation with CYP2E1 and decarboxylase enzymes, the mean abnormal leukocyte value among workers was 8.5 u/L, with 59% exhibiting abnormal values. Post-supplementation, the mean abnormal leukocyte value was 11 u/L, with 41% of workers showing improvement.

Although abnormal leukocyte cases decreased from 59% to 19%, the mean value within the abnormal subgroup increased because many workers moved into the normal range after supplementation, leaving only a small remaining group (n = 5) with higher individual values. Thus, the rise in the subgroup mean reflects a reduced sample size and value distribution, not a worsening condition.

4.4. *Comparison of Leukocyte Values Before and After the Administration of CYP2E1 Enzyme and Decarboxylase Enzyme Based on Worker Characteristics*
Based on the research data obtained, a cross-tabulation based on individual characteristics and the leukocyte value of workers was carried out.

Table 6. Results of cross-tabulation analysis of worker characteristics with worker leukocyte values

Variables	Leukocytes *Pretest* (Normal)		Leukocytes *Posttest* (Abnormal)		n	Leukocytes *Pretest* (Normal)		Leukocytes *Posttest* (Abnormal)		n
	n	%	n	%		n	%	n	%	
Age										
15-64 Years	10	43.5	13	56.5	23	20	87	3	13	23
>65 Years	1	25	3	75	4	2	50	2	50	4
Total	11	40.7	16	59.3	27	22	81.5	5	18.5	27
Gender										
Woman	9	47.4	10	52.6	19	16	84.2	3	15.8	19
Man	2	25	6	75	8	6	75	2	25	8
Total	11	40.7	16	59.3	27	22	81.5	5	18.5	27
Years of service										
1-10 years	0	0	1	100	1	1	100	0	0	1

Variables	Leukocytes *Pretest* (Normal)		Leukocytes *Posttest* (Abnormal)		n	Leukocytes *Pretest* (Normal)		Leukocytes *Posttest* (Abnormal)		n
	n	%	n	%		n	%	n	%	
11-22 years	3	42.9	4	57.1	7	5	71.4	2	28.6	7
22-32 years	5	38.5	8	61.5	13	11	84.6	2	15.4	13

Source: Data Processing Results Utilizing SPSS (2024)

Table 7. Results of Cross-Tabulation Analysis of Worker Characteristics with Worker Leukocyte Values

Variables	Leukocytes *Pretest* (N)		Leukocytes *Posttest* (TN)		n	Leukocytes *Pretest* (N)		Leukocytes *Posttest* (TN)		n
	n	%	n	%		n	%	n	%	
>33 years	3	50	3	50	6	5	83.3	1	16.7	6
Total	11	40.7	16	59.3	27	22	81.5	5	18.5	27
Nutritional status										
(Normal BB) 18.5-22.9 Kg/m2	0	0	4	100	4	3	75	1	25	4
(*Overweight*) 23-24.9 Kg/m2	3	50	3	50	6	5	83.3	1	16.7	6
(Obesity I) 25-29.9 Kg/m2	4	57.1	3	42.9	7	6	85.7	1	14.3	7
(Obesity II) >30 Kg/m2	4	40	6	60	10	8	80	2	20	10
Total	11	40.7	16	59.3	27	22	81.5	5	18.5	27
Smoking Habit										
Do not smoke	10	41.7	14	58.3	24	19	79.2	5	20.8	24
>16 sticks/day	1	33.3	2	66.7	3	3	100	0	0	3
Total	11	40.7	16	59.3	27	22	81.5	5	18.5	27
Exercise Habits										
No Exercising	6	37.5	6	54.5	12	14	87.5	3	12.5	17
Exercise Sometimes	5	45.5	10	62.5	15	8	72.7	2	27.3	10
Total	11	40.7	16	59.3	27	22	81.5	5	18.5	27
History of Having a Disease										
Having a Disease	7	38.9	11	61.5	18	14	77.8	4	22.2	18
Have No Disease	4	44.4	5	55.5	9	8	88.9	1	11.1	9
Total	11	40.7	16	59.3	27	22	81.5	5	18.5	27
Use of PPE										
Never	10	45.5	12	54.5	22	18	81.1	4	18.2	22
Sometimes	0	0	2	100	2	1	50	1	50	2
Yes, Every Day	1	33.3	2	66.7	3	3	100	0	0	3
Total	11	40.7	16	59.3	27	22	81.5	5	18.5	27

Source: Data Processing Results Utilizing SPSS (2024)

Supplementation with CYP2E1 and decarboxylase enzymes improved white blood cell counts, with the strongest response seen in workers aged 22–32, as well as among female and obese workers. Health behaviors also appeared to influence outcomes, as smokers showed greater changes and most workers reported slight increases in physical activity, suggesting that even low-frequency exercise may support immune function. While the supplementation showed potential benefits for workers with long-term exposure and limited PPE use, these findings remain preliminary.

5.0 Discussion

This study shows that chronic benzene exposure in informal shoe-making settings disrupts hematopoietic function by impairing leukocyte production. Benzene metabolism via the CYP2E1 pathway generates reactive oxygen species and toxic intermediates that damage bone marrow and immune cells (Bolt & Roos, 2020; Wang et al., 2022). The enzymatic supplementation used in this study, containing CYP2E1 and decarboxylase, showed a substantial reduction in abnormal leukocyte levels, from 59% to 19%, and a mean increase from 8.5 to 11.0 U/L, indicating significant biological improvement ($p < 0.05$, paired t-test). These findings confirm the capacity of enzyme-rich supplementation to restore hematopoietic balance by modulating oxidative metabolism and enhancing immune regeneration.

However, with a one-group pretest–posttest design and only a 5-day intervention, these findings should be viewed as preliminary and not conclusive. The observed improvements cannot be attributed solely to supplementation, as factors such as diet, hydration, rest, baseline inflammation, and variable benzene exposure may have influenced the results. Thus, the data provide only an early exploratory signal rather than evidence of efficacy. Larger randomized controlled trials with longer interventions and biomarker measurements are needed to confirm these observations and clarify underlying mechanisms.

From a mechanistic standpoint, CYP2E1 plays a dual role in both the activation and detoxification of xenobiotics. Moderate exogenous supplementation may promote a regulated increase in enzyme activity that accelerates benzene clearance while reducing the accumulation of toxic intermediates (Garcia Ruiz & Fernández Checa, 2020). Meanwhile, decarboxylase enzymes contribute to amino acid metabolism and the production of bioactive amines such as histamine and serotonin, which stimulate bone marrow and leukocyte proliferation (Moriguchi & Yamashita, 2020; Wu et al., 2023). Antioxidant compounds from beetroot and mixed berries may have boosted glutathione peroxidase and catalase activity, reducing oxidative damage to leukocytes and contributing to the observed hematological improvement.

The variation in leukocyte recovery among participants may be explained by physiological and behavioral factors. Younger workers (aged 15–64 years) demonstrated a stronger response, possibly due to better hematopoietic regeneration and cellular resilience (Lv et al., 2024). Female workers showed greater leukocyte improvement, aligning with evidence that estrogen modulates immune responses and enhances antioxidant enzyme expression (Penaloza et al., 2020). Interestingly, workers with obesity also showed positive responses despite baseline inflammation, suggesting that enzymatic activity can still function effectively within metabolically challenged environments (García Samuelsson et al., 2025). These findings indicate that enzyme supplementation remains beneficial across diverse nutritional and metabolic profiles.

Lifestyle-related factors also influenced outcomes. Workers who occasionally exercised exhibited higher improvements, consistent with studies showing that moderate physical activity boosts immune cell circulation and antioxidant enzyme function (Nieman, 2020). Although smoking generally elevates baseline leukocyte counts due to chronic inflammation (Dietrich & Fowler, 2014), the improved leukocyte normalization observed among smokers after supplementation may reflect reduced oxidative burden and improved detoxification capacity. Nevertheless, these interpretations warrant caution and should be verified with larger, controlled studies.

The low rate of personal protective equipment (PPE) use (11%) underscores the structural health vulnerability of informal workers. PPE alone cannot mitigate internal oxidative or hematopoietic damage once exposure has occurred (NIOSH, 2008). Therefore, enzymatic supplementation, as demonstrated here, may serve as an effective complementary strategy. However, biochemical interventions should not replace fundamental occupational health controls, such as ventilation improvement, hazard communication, and routine biomonitoring.

Statistically, the paired t-test showed a significant pre–post difference in leukocyte levels ($p < 0.05$), and the effect size (Cohen's $d = 0.72$) suggests a medium-to-large biological impact. However, causality cannot be inferred due to the one-group pre-experimental design, and uncontrolled factors such as diet, hydration, and residual benzene exposure may have influenced the results. The 5-day duration also limits interpretation to short-term responses rather than sustained hematological changes.

Future research should employ randomized controlled trials with larger samples and extended intervention periods (≥4 weeks) to determine dose–response relationships and long-term stability of leukocyte recovery. It would also be valuable to measure oxidative biomarkers and gene expression profiles of CYP2E1 and decarboxylase to elucidate mechanistic pathways at the molecular level.

6.0 Conclusion and Recommendation

Most workers were female, aged 15–64 years, with long work experience and predominantly classified as obesity class II. They were mostly nonsmokers, exercised occasionally, had a history of illness, and rarely used PPE. Before supplementation, the mean leukocyte count was 8.5 U/L with 59% abnormal. After five days of CYP2E1 and decarboxylase supplementation, the mean increased to 11 U/L and abnormal values dropped to 19%, with 41% showing improvement. These findings suggest a potential benefit of enzyme-rich supplementation in helping restore leukocyte balance disrupted by benzene exposure.

Although promising, this study's pre-experimental design without a control group and short duration limits causal inference and long-term conclusions. External factors such as diet, rest, and residual benzene exposure may have affected results. Future studies should

use randomized controlled or longitudinal designs with larger samples and further explore the enzymatic mechanisms in oxidative stress reduction. Continuous biomonitoring, health education, and strict safety practices are recommended to sustain these benefits.

Acknowledgment
The authors express sincere appreciation to the Indonesia Endowment Fund for Education (LPDP), Ministry of Finance of the Republic of Indonesia, for funding this study and supporting its publication. We also thank all participants for their cooperation and willingness to be involved.

Article Contribution To The Related Field of Study
This study advances occupational health and safety research by introducing CYP2E1 and decarboxylase enzyme supplementation as a novel and practical approach to reduce the hematological effects of benzene exposure.

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