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# Effects of supplementation rich in CYP2E1 and decarboxylase enzymes on leukocytes of smoking workers exposed to benzene at Osowilangon shoe industry home in Surabaya

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**ABSTRACT**

**Background:** Exposure to benzene in the shoe industry is a risk factor for immune system disorders, especially in the leucocyte profile. Supplementation of enzymes such as CYP2E1 and decarboxylase could potentially protect against the toxic effects of benzene, especially in workers who smoke.

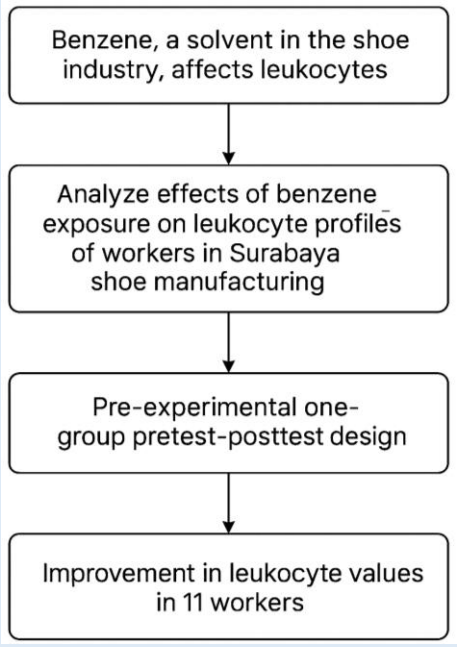
**Objectives:** This study aims to analyze the effect of CYP2E1 and decarboxylase-rich enzyme supplementation on the leukocyte profile of smokers exposed to benzene in a home-based shoe industry in Surabaya.

**Methods:** This study employs a quantitative approach with a pre-experimental one-group pretest-posttest design. The study was conducted in two locations of the home shoe industry in RW 1 and RW 2 Tambak Osowilangun Village, Surabaya. The sample consisted of 27 workers who fulfilled the inclusion criteria.

**Results:** The cross-tabulation results showed that most non-smoking workers experienced a decrease in leukocyte values after receiving enzyme supplementation, from 14 people (58.3%) to 5 people (20.8%), indicating an improvement in leukocyte values in 9 people. Overall, 11 workers (41%) had improved leucocyte values after the intervention.

**Conclusion:** Supplementation of CYP2E1 and decarboxylase enzymes contributed to the improvement of the leukocyte profile in smokers exposed to benzene, suggesting the potential of this intervention in reducing the toxic effects of benzene in the work environment.

**Keywords:** safety to work, benzene, leukocytes, home industry, shoemakers




**Graphical abstract:** Effects of Supplementation Rich in CYP2E1 and Decarboxylase Enzymes on Leukocytes of Smoking Workers Exposed to Benzene at Osowilangon Shoe Industry Home in Surabaya

## INTRODUCTION

Benzene is a solvent that is commonly used in glues, adhesives, and paints in the shoe production process. Long-term exposure to benzene vapor is known to have toxic effects, especially on the hematopoietic and immune systems (1,2). Although in some developed countries, such as Europe and North America, benzene exposure has decreased, in some Asian countries, including Indonesia, this exposure remains a serious occupational health problem, particularly in home industries that lack adequate supervision (3-4).

Several studies have shown that shoe repair workers have a risk of benzene exposure that exceeds the threshold value and experience major health risks (1,5,6). Workers are also reported to experience hematological disorders, such as changes in leukocyte counts and an increased incidence of cells with linked nuclei and micronuclei, indicating genetic damage due to oxidative stress (7,8).

In work environments such as the Tambak Osowilangun home shoe industry in Surabaya, workers generally use glue in open containers, without gloves or masks, and work in enclosed spaces with poor ventilation. These conditions increase the risk of continuous inhalation of high levels of benzene vapor.

Chronic exposure to benzene can increase the activity of CYP2E1 enzymes involved in the bioactivation of toxic compounds, as well as generate free radicals that trigger oxidative stress (9-10). One potential approach to mitigate such toxic effects is by enzyme supplementation, particularly those containing CYP2E1 and decarboxylase, to support metabolism and neutralize the oxidative impact of chemical exposure. A similar approach was demonstrated in a study on xylene exposure among car painting workers in Surabaya, which found that food intake containing CYP2E1 enzymes and glycine could support detoxification and reduce occupational health risks (11). This supports the potential of targeted enzyme-based interventions in reducing the toxic effects of aromatic hydrocarbons such as benzene.

The use of enzyme supplementation in this study also reflects the development of functional food science that emphasizes the role of bioactive compounds-both animal and plant-derived-in improving health and reducing disease risk. As stated in recent literature, the identification and validation of bioactive compounds through systematic research is an important step in legitimizing functional food interventions in the context of public health (12). This study is novel in its approach, which combines monitoring the hematological status of shoe home industry workers exposed to benzene with CYP2E1 and decarboxylase enzyme supplementation interventions. To date, no study has examined the direct effect of enzyme supplementation on leucocyte profile in a population of informal workers in the home-based shoe sector.

This study aimed to analyze the effect of enzyme supplementation rich in CYP2E1 and decarboxylase on the leukocyte profile in smokers exposed to benzene in a home-based shoe industry in Surabaya.

## METHODS

This research uses an experimental quantitative approach with a pre-experimental one-group pretest-posttest design, which is research that explains the cause-and-effect relationship (causality) between one variable and another by involving only one experimental group without a control group, which will be given a pretest and posttest.

This research was in the shoe home industry in community-level administrative units (Rukun Warga/ RW) 1 and 2 Tambak Osowilangun Surabaya Village, with a total of 2 research locations in several home industries. This research began in July 2023 until December 2023. The population in this study was all groups of shoe workers from several Tambak Osowilangun Surabaya shoe home industries.

Respondents were given the intervention in the form of supplements containing CYP2E1 and decarboxylase enzymes. The supplement was administered orally as 500 mg twice a day (morning and

evening) after meals, for 14 consecutive days. Supplement administration was done in person and supervised by the research team at the work site. Research respondents were recruited following the inclusion criteria:

1. Not in the period of menstruation or menstruation.
2. Not in a pregnant condition.
3. Not taking certain drugs or anesthesia, and alcohol.
4. Workers are in good health (not disabled).

The sample of this study was a group of shoe workers who fit the inclusion criteria which led to 27 workers who were shoe craftsmen workers in Tambak Osowilangun Surabaya participating. There are two variables, namely the independent variable (characteristics of workers, including age, gender, length of service, nutritional status, smoking habits, exercise habits, history of having diseases, and use of PPE) and the dependent variable (improvement in leukocyte values).

**Data collection method**: Blood was taken from a vein, using a 5cc syringe, taken as much to 5cc, put in a vacuum tube with EDTA, and without EDTA as much as 2.5 cc each. The collected blood was put into an ice box then the blood sample was taken to the TDC (tropical disease centre) Laboratory for testing. Blood sampling was done by authorized medical personnel (doctors or nurses) who are experts in their fields.

**Data Processing and Analysis:** The data used will be analyzed using the SPSS (Statistical Product and Services Solutions) computer program. Data presentation was done in the form of a frequency distribution table accompanied by a narrative. The data analysis used in this study was descriptive analysis.

## RESULTS

**Identifying Worker Characteristics:** Based on the descriptive results of worker characteristics presented in Table 1, the shoe home industry in Tambak Osowilangun Surabaya shows that the average age of workers is 52.4 years, with the youngest age being 37 years old and the oldest being 67 years old. Based on the interview results, workers' smoking habits showed that the average cigarette consumption among smokers was 20.3 cigarettes/day (range: 19–22 cigarettes/day). When calculated across the entire study population, including both smokers and non-smokers, the average was 2.3 cigarettes/day. However, most of the workers did not smoke, as many as 24 people (88.9%).

**Table 1.** Results of Frequency Distribution Analysis of Characteristics of Home Industry Workers of Shoe Tambak Osowilangun Surabaya

| Worker Characteristics Variables | Category | Frequency (f) | Percentage (%) |
|---|---|---|---|
| **Age** | Productive age group: 15-64 years old | 23 | 85.2 |
| | Non-productive age group >65 years | 4 | 14.8 |
| | Total | 27 | 100 |
| | Mean (SD) | 52.4 years (9.7) | |
| | Max Value | 67 year | |
| | Min Value | 37 year | |
| **Sex** | Male | 8 | 29.6 |
| | Female | 19 | 70.4 |
| | Total | 27 | 100 |
| **Smoking habit** | No smoking | 24 | 88.9 |
| | Heavy smokers: (>16 cigarettes/day) | 3 | 11.1 |
| | Total | 27 | 100 |
| | Mean (SD) | 2.3 cigarettes/day (6.6) | |

| Worker Characteristics Variables | Category | Frequency (f) | Percentage (%) |
|---|---|---|---|
| | Max Value | 22 cigarettes/day | |
| | Min Value | 19 cigarettes/day | |
| **History of disease** | Has a history of disease | 18 | 66.7 |
| | No history of disease | 9 | 33.3 |
| | Total | 27 | 100 |
| **Use of personal protective equipment** | Yes, every day | 3 | 11.1 |
| | Sometimes | 2 | 7.4 |
| | Never | 22 | 81.5 |
| | Total | 27 | 100 |

Source: Results of Researcher Data Collection Using Questionnaires, 2023

**Table 2.** Cross Tabulation Analysis of Leukocyte Values Before and After Administration of Cyp2e1 Enzyme and Decarboxylase Enzyme for Home Industry Workers of Tambak Osowilangun Shoe Industry Surabaya

| Pretest Leukocytes | Posttest Leukocyte Normal (N) | Posttest Leukocyte Abnormal (ABN) | Total |
|---|---|---|---|
| | n | % | n |
| **Normal (N)** | 11 | 100 | 0 |
| **Abnormal (ABN)** | 11 | 68.8 | 5 |
| **Total** | 22 | 81.5 | 5 |

Source: Results of Researcher Data Processing Using SPSS (2024)

### Identifying Leukocyte Values of Home Industry Workers of Tambak Osowilangun Surabaya Shoe Industry

Description

u/L: Leukocyte Value Unit

n: Frekuensi

N: Normal

ABN: Abnormal

Based on the cross-tabulation results in Table 2, it was found that before the administration of CYP2E1 and decarboxylase enzymes, there were 16 workers (59%) with abnormal leucocyte values. After the intervention, the number of workers with abnormal leucocyte values decreased to 5 people (18.5%). Thus, there were 11 workers (40.5%) who had improved leucocyte values after enzyme supplementation.

**Analyzing the Difference in Leukocyte Values Before and After Supplementation Rich in CYP2E1 Enzymes and Decarboxylase Enzymes for Home Industry Workers of Tambak Osowilangun Surabaya Shoe Industry:** The analysis used is descriptive analysis to analyze the impact of supplementation rich in CYP2E1 enzymes and decarboxylase enzymes between two or more variables; the complete analysis results as shown in Table 3. following:

**Table 3.** Descriptive Results of Differences in Leukocyte Values Before and After Supplementation Rich in CYP2E1 Enzymes and Decarboxylase Enzymes on the Improvement of Leukocyte Values

| Parameters | Group A: Normal Pretest (11 workers) | | | Group *B: Pretest Abnormal (16* workers*)* | | |
|---|---|---|---|---|---|---|
| | *Pretest (N)* | *Posttest (ABN)* | Difference | *Pretest (N)* | *Posttest (ABN)* | Difference |
| **Frequency (n)** | *8,2* | *8,5* | 0,3 | *6,5* | *11* | 4,5 |
| **Mean** | *8,2* | *11,3* | 3,1 | *7,6* | *11* | 3,4 |
| **Median** | *10,2* | *12,6* | 2,4 | *11* | *11,3* | 0,3 |
| **Maximum** | *4,2* | *2,5* | 1,7 | *3,8* | *10,9* | 7,1 |
| **Minimum** | *3,3* | *8,8* | 5,5 | *3,6* | *0,3* | 3,3 |

Source: Results of Researcher Data Processing Using SPSS (2024)

u/L: Leukocyte Value Unit

n: Frekuensi

N: Normal

ABN: Abnormal

Based on the results in Table 3, it is known that before supplementation, the average abnormal leucocyte value of workers was 8.5 u/L, with the lowest value of 2.5 u/L and the highest of 12.6 u/L. After supplementation, the average abnormal leucocyte value was 11.0 u/L, with the lowest value being 10.9 u/L and the highest being 11.3 u/L. From the data distribution, the number of workers with abnormal leucocyte values before supplementation was 16 people (59%), and afterwards it was 5 people (18.5%). This shows that the administration of CYP2E1 and decarboxylase enzymes had an impact on the improvement of leucocyte values in 11 workers (41%).

**Comparing Leukocyte Values Before and After Administration of Cyp2e1 Enzyme and Decarboxylase Enzyme Based on Characteristics of Home Industry Workers of Tambak Osowilangun Surabaya Shoe Industry:** Based on the results of the research data obtained, cross tabulation based on individual characteristics with the complete worker leukocyte value can be seen in Table 4 as shown:

**Table 4.** Results of Cross Tabulation Analysis of Smoking Habits and Leukocyte Values Before and After CYP2E1 and Decarboxylase Enzyme Supplementation

| Smoking Habit | Total Workers | Pre-test Normal (N) | Pre-test Abnormal (ABN) | Post-test Normal (N) | Pre-test Abnormal (ABN) | Improvement (ABN to N) |
|---|---|---|---|---|---|---|
| **Non- Smoker** | 24 | 10 (41,7%) | 14 (58,3%) | 19 (79.2%) | 5 (20.8%) | 9 |
| **Heavy Smoker (>16 cig/day)** | 3 | 1 (33,3%) | 2 (66,7%) | 3 (100%) | 0 (0%) | 2 |
| **Total** | 27 | 11 (40,7%) | 16 (59,3%) | 22 (81.5%) | 5 (18.5%) | 11 |

Source: Results of Researcher Data Processing Using SPSS (2024) Description

N: Normal leukocyte count

ABN: Abnormal leukocyte count

Improvement (ABN to N): Number of workers whose leukocyte count improved from abnormal to normal after supplementation

Based on the cross-tabulation of the distribution of workers' smoking habits, most workers with non-smoking habits had improved leukocyte values, from 14 people (58.3%) to 5 people (20.8%), indicating improvement in 9 workers. In the heavy smoker group (>16 cigarettes/day), of the 3 people observed, all showed improvement in leucocyte values after supplementation.

## DISCUSSION

**Smoking Habit:** The results of this study showed that among Tambak Osowilangun Surabaya home-based shoe industry workers, most were non-smokers, as many as 24 people (88.9%). According to (13) Smoking can increase the risk of benzene exposure even in minute quantity. This is because smoking can accelerate the absorption process of benzene in the body due to the disruption of the cilia in the respiratory tract (14-15). In addition, the concentration of toluene in cigarette smoke ranges from 5-90 µg/cigarette (16), and it is estimated that each cigarette contains 80-100 µg of benzene, with absorption rates reaching 50%, resulting in an accumulation of up to 1000 µg of benzene/day for active smokers (17). Smoking also affects liver cell health (18) The main site of benzene metabolism (19). Therefore, workers who smoke have a higher susceptibility to health problems due to benzene exposure.

**Changes in Leukocyte Values Before and After Enzyme Supplementation:** Before the intervention, 16 workers (59%) had abnormal leucocyte values, and 11 workers

(41%) were within the normal range. After CYP2E1 and decarboxylase enzyme supplementation, workers with regular leucocyte values increased to 22 (81%), while those with abnormal values decreased to 5 (19%). Overall, there were 11 workers (41%) who had improved leucocyte values. These results indicate that enzyme administration plays a role in improving leucocyte values. This is in line with the theory that benzene exposure can cause myeloid stem cell failure and reduce blood cell production (20-21), as well as increase the risk of anemia as found in Pulogadung industrial workers (22).

**Effects of Benzene Exposure and the Role of Enzyme Supplementation**: An increase in leucocyte count (leukocytosis) is generally a response to chronic infection or toxic exposure (7,23,24). In this study, leukocytosis was likely caused by the length of working life (>20 years), leading to chronic exposure to benzene vapor. Research (25) showed that hematological changes due to benzene exposure can occur even at exposure levels previously considered safe. Exposure to benzene is also associated with hematopoietic system disorders, including abnormal leucocytes, which have the potential to develop into blood cancers such as leukemia. The role of CYP2E1 and decarboxylase enzymes in the detoxification of toxic compounds may help reduce the impact of oxidative stress from this exposure.

**Relationship with Smoking Habit:** The cross-tabulation results showed that in non-smokers, enzyme supplementation showed an improvement in leucocyte values in 9 workers. However, these results suggest that smokers also experienced a positive response to the intervention, albeit to a lesser extent. Study (26) showed that smokers with a consumption of 33 cigarettes/day can absorb 1.8 mg of benzene per day. However, as stated in (27,28), cigarette content does not affect hemoglobin levels directly, but rather reduces the ability of hemoglobin to bind and distribute oxygen. Exposure to toxic substances in cigarette smoke can increase levels of reactive oxygen species (ROS), which trigger oxidative stress (29–31). This oxidative stress is characterized by increased levels of malondialdehyde (MDA), which follows the finding that smoking affects the oxidative status of the body.

This study makes a novel contribution to the field of occupational toxicology by demonstrating that enzymatic intervention can be an alternative approach in mitigating the hematological effects of chronic benzene exposure. This approach fills the gap of previous studies that mainly focus on the description of exposure or exposure effects without including biological intervention strategies.

## CONCLUSIONS

Based on the results and discussion of this study, it can be concluded that the provision of enzyme supplementation rich in CYP2E1 and decarboxylase to home-based shoe industry workers in Tambak Osowilangun Surabaya contribute to the improvement of leukocyte values. A total of 11 workers (41%) had improved leucocyte values after the intervention, of which 9 were non-smokers. This finding suggests that enzyme supplementation has the potential to have a positive effect on leucocyte profiles, especially in non-smoking individuals with long-term exposure to benzene. These results demonstrate the potential of the enzyme supplementation approach as an innovative strategy in the health protection of workers exposed to benzene, especially in the cottage industry which often lacks regular monitoring.

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