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Education on the Dangers of Exposure to Chemicals that Affect Male Reproduction and the Potential of Xanthone as an Antioxidant through the Nrf2-Keap1 and Gpx4 Pathways for PKK Mothers in RW 01 Sidomoro, Gresik

Author

Ernawati[1*], Carissa Arshanty Naisya Salsabila[2], Mochammad Kharis[3], Achmad Maulana Rafi'Uzzaky Aziz[4]

Correspondence

[1]Lecturer Nursing Study Program, Universitas Muhammadiyah Gresik.
[2]Students of Gresik 1 State Junior High School Gresik
[3] Lecturer logistics engineering, Semen Indonesia International University
[4]Airport Authority Office Region IX, Ministry of Transportation, Indonesia.
***E-mail: ernawati@umg.ac.id**

Abstract

Exposure to hazardous chemicals such as 2-methoxyethanol has the potential to reduce reproductive health quality, particularly through damage to Leydig cells as producers of testosterone. The low level of public knowledge, especially among women in Family Welfare Movement (PKK) groups as key actors in family health, may lead to a lack of awareness of chemical risks and the importance of prevention efforts through healthy lifestyles and the use of natural antioxidant compounds such as xanthone.

This community service activity aimed to increase the knowledge and understanding of PKK members in RW 01 Sidomoro, Gresik regarding the dangers of chemical exposure to male reproductive health and the role of xanthone in cellular protection mechanisms through the Nrf2–Keap1 and Gpx4 pathways.

The methods used included educational counseling through interactive lectures, visual media, discussions, and question-and-answer sessions. Understanding was evaluated using pre-test and post-test questionnaires written in simple language. The activity was attended by 120 participants. The evaluation results showed that after the counseling, all 120 participants had received the information, with 110 people (91.7%) demonstrating good understanding of the dangers of 2-methoxyethanol, the function of Leydig cells, the role of xanthone as an antioxidant, and preventive measures that can be implemented at the family level. Meanwhile, 10 people (8.3%) had not fully understood the material, particularly the scientific terms and molecular mechanisms.

Overall, this educational counseling activity was effective in improving reproductive health literacy and awareness of the importance of protection against chemical exposure. In conclusion, follow-up assistance and repetition of the material using more practical and visual approaches are needed to help all participants achieve optimal understanding.

Keywords: Xanthone; Leydig cells; 2-methoxyethanol; reproductive health; community education

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Introduction

Male reproductive health is an essential component of human resource development, yet it often receives less attention than female reproductive health. Several reports indicate a downward trend in semen quality, testosterone levels, and an increase in male infertility rates over the last decades in many countries, including Indonesia (Kumar & Singh, 2021; Prasetya et al., 2021). One of the major contributing factors to impaired reproductive function is exposure to environmental and industrial chemicals that are toxic to the reproductive system. In the context of rapid industrialization and the extensive use of chemicals in various sectors, families living in industrial areas are at risk of chronic exposure to toxic compounds (Sutrisno & Hartati, 2022).

Among the chemicals known to exert toxic effects on the male reproductive system is 2-methoxyethanol (2-ME). This compound belongs to the ethylene glycol ether group and is widely used as a solvent in paints, inks, cleaners, and several manufacturing processes (Zhang et al., 2020). Experimental studies have shown that 2-ME exposure can decrease sperm count and motility, lower testosterone levels, and cause histological damage to the testes, particularly to Leydig cells and germ cells (Li et al., 2021; Rahman et al., 2023). The mechanism of 2-ME toxicity is strongly associated with increased oxidative stress, free radical formation, disruption of mitochondrial function, and activation of apoptotic pathways in testicular cells (Wang et al., 2020).

Leydig cells are the primary producers of testosterone, which is essential for spermatogenesis, the development of secondary sexual characteristics, and the maintenance of male sexual function. Damage to Leydig cells directly reduces testosterone production and ultimately impairs fertility (Chen et al., 2022). Under chemical exposure such as 2-ME, Leydig cells become one of the main targets of injury due to elevated reactive oxygen species (ROS) and decreased endogenous antioxidant capacity (Samarasinghe et al., 2021). Therefore, strategies to protect Leydig cells against oxidative stress are critical in preventing reproductive disorders caused by toxic chemicals.

One of the most important cellular defense mechanisms against oxidative stress is the nuclear factor erythroid 2–related factor 2 (Nrf2)–Kelch-like ECH-associated protein 1 (Keap1) signaling pathway. Nrf2 is a transcription factor that induces the expression of various antioxidant and detoxifying enzymes, such as heme oxygenase-1 (HO-1), superoxide dismutase (SOD), catalase (CAT), glutathione S-transferase (GST), and glutathione peroxidase (GPx) (Bellezza et al., 2020). Under basal conditions, Nrf2 is bound to Keap1 in the cytoplasm and undergoes proteasomal degradation. When oxidative stress increases, Nrf2 dissociates from Keap1, translocates into the nucleus, and activates the transcription of antioxidant genes (Tonelli et al., 2020). Activation of the Nrf2–Keap1 pathway has been shown to play a pivotal role in protecting different tissues, including testicular tissue, from oxidative injury (Zhang et al., 2021).

Glutathione peroxidase 4 (Gpx4) is another key enzyme involved in the detoxification of lipid peroxides and in the prevention of ferroptosis, a form of iron-dependent regulated cell death driven by lipid peroxidation (Feng & Stockwell, 2018; Imai et al., 2021). Gpx4 is crucial for maintaining the integrity of cellular and organelle membranes, including those of Leydig and germ cells in the testes. Adequate Gpx4 expression and activity are required to prevent excessive oxidative damage under chemical exposure or other stress conditions. Recent studies indicate that exposure to reproductive toxicants can reduce Gpx4 expression and trigger testicular injury via ferroptosis mechanisms (Liu et al., 2022). Thus, agents capable of sustaining or enhancing Nrf2 activation and Gpx4 activity hold great potential as protectants for testicular cells.

In recent years, natural bioactive compounds have attracted great interest as potential protective agents against male reproductive damage. One promising group of compounds is xanthones, polyphenolic molecules abundant in mangosteen (Garcinia mangostana) pericarp and several other plants (Obolskiy et al., 2009). Xanthones and their derivatives, such as α-mangostin and γ-mangostin, possess strong antioxidant, anti-inflammatory, antiapoptotic, and anticancer activities (Liang et al., 2021). Experimental studies demonstrate that xanthones can reduce ROS levels, improve antioxidant status, and protect various cell types from oxidative injury (Pothitirat et al., 2020; Syahputra et al., 2022). In the context of reproductive health, animal experiments report that mangosteen peel extract or isolated xanthones can improve semen quality and restore testicular histology disrupted by oxidative stress (Yuliani et al., 2021;

Nugroho et al., 2023).

The molecular mechanisms underlying the protective effects of xanthones on testicular cells are thought to include activation of the Nrf2–Keap1 pathway and increased expression of antioxidant enzymes, including Gpx4. In vitro studies show that xanthone derivatives can modulate Nrf2–Keap1 interaction, enhance Nrf2 nuclear translocation, and induce antioxidant gene expression (Nguyen et al., 2021). Moreover, xanthones may preserve mitochondrial function and inhibit intrinsic apoptotic signaling by regulating the Bcl-2/Bax ratio (Rinartha et al., 2022). However, data that specifically characterize the interaction between xanthone and key proteins such as Nrf2, Keap1, and Gpx4 in the context of Leydig cell protection against 2-methoxyethanol toxicity remain limited. In this situation, in-silico analysis and molecular dynamics simulations play an important role in clarifying the potential and mechanism of xanthone at the molecular level.

In-silico techniques, including molecular docking and molecular dynamics (MD) simulations, allow prediction of binding affinities and complex stability between ligand molecules and target proteins. These approaches are time- and cost-efficient and provide mechanistic insights before conducting in vitro or in vivo studies (Sousa et al., 2021). For xanthone and the Nrf2–Keap1–Gpx4 axis, molecular docking can be used to assess the ability of xanthone to interact with active sites or regulatory domains of Nrf2, Keap1, and Gpx4. Subsequently, MD simulations can evaluate the stability of xanthone–protein complexes under near-physiological conditions, including conformational changes, binding energy, and non-covalent interactions (Kumari et al., 2020). Such analyses provide a strong scientific foundation for the development of xanthone as a phytopharmaceutical candidate for male reproductive protection.

Parallel to these biomedical aspects, low reproductive health literacy and poor awareness of chemical hazards in the general population must be addressed. In Indonesia, survey studies reveal that public knowledge about male infertility risk factors, including industrial chemical exposures, is still limited (Setiawan et al., 2020; Lestari et al., 2022). Housewives and community health cadres, particularly those involved in the Family Welfare Movement (Pemberdayaan dan Kesejahteraan Keluarga, PKK), play strategic roles as agents of behavioral change at the household level. Nevertheless, they often lack access to specific information regarding reproductive toxicants and preventive strategies (Rosyada & Wulandari, 2021).

PKK RW 01 Sidomoro, Gresik, is an example of a community located in an area with substantial industrial activity. This situation highlights the importance of targeted educational programs on reproductive health, focusing on the hazards of chemicals such as 2-methoxyethanol and practical measures to reduce exposure, including the promotion of diets or supplements rich in natural antioxidant compounds like xanthones. Integrating basic and in-silico research findings on the protective mechanisms of xanthone with community service activities in PKK settings is expected to generate a dual impact: first, contributing to the scientific understanding of Leydig cell protection mechanisms; second, enhancing community literacy and awareness regarding male reproductive health.

The community service activity discussed in this paper was designed based on in-silico findings on xanthone interactions with Nrf2, Keap1, and Gpx4 and their implications for Leydig cell protection against 2-methoxyethanol exposure. Educational materials were prepared in simple, nontechnical language, accompanied by visual media and everyday examples, so that scientific concepts such as oxidative stress, antioxidants, and the Nrf2–Keap1–Gpx4 pathway could be more easily understood. Participants' understanding was evaluated using pre- and post-test questionnaires.

The activity was attended by 120 PKK members. Evaluation showed that 110 participants (91.7%) demonstrated good comprehension of the topics after the educational session, whereas 10 participants (8.3%) still encountered difficulties, especially in understanding scientific terminology and detailed molecular mechanisms. These findings suggest that educational interventions that translate scientific research into community-friendly messages are effective in improving reproductive health literacy, although follow-up sessions and repeated explanations remain necessary to achieve more uniform comprehension. Consequently, this community service program not only provides direct practical benefits to PKK RW 01 Sidomoro, Gresik, but also serves as a model for integrating basic research, in-silico approaches, and community-level health education.

Overall, the background above underscores the urgency of developing natural compound-based protective agents such as xanthones against Leydig cell damage induced by 2-methoxyethanol, while simultaneouslystrengthening community education on chemical hazards and preventive strategies. In-silico and molecular dynamics studies offer a robust scientific basis for elucidating xanthone's interactions with the Nrf2–Keap1 pathway and Gpx4. At the same time, community service activities through educational counseling within PKK structures play a strategic role in translating this scientific knowledge into improved awareness, attitudes, and health behaviors at the family level.

Method

Study Design

This community service activity employed a quasi-experimental one-group pre-test–post-test design. The program was developed to translate findings from in-silico research on the protective potential of xanthone via the Nrf2–Keap1 and Gpx4 pathways into practical reproductive-health education for community members. The main outcome was the change in participants' knowledge and understanding regarding: (1) hazards of chemical exposure, particularly 2-methoxyethanol, to male reproductive health; (2) the role of Leydig cells and testosterone; and (3) the protective role of antioxidants, including xanthone-rich foods or supplements.

Setting and Participants

The activity was conducted in RW 01 Sidomoro, Gresik, an area with considerable industrial activity and an active Family Welfare Movement (PKK) organization. The target population consisted of PKK members and adult residents involved in family health activities.

Inclusion criteria were: (1) registered PKK members or residents aged ≥18 years; (2) able to communicate in Bahasa Indonesia; and (3) willing to participate for the entire session and to complete both pre- and post-tests. Individuals with hearing or cognitive impairments that would substantially limit participation were excluded.

A total of 120 participants were recruited using consecutive sampling through PKK announcements and personal invitations distributed by local cadres. All participants who attended on the day of the program and met inclusion criteria were enrolled.

Development of Educational Materials

Educational materials were developed based on a narrative synthesis of in-silico and experimental literature on 2-methoxyethanol toxicity, oxidative stress, Leydig cell damage, and the protective mechanisms of xanthone through the Nrf2–Keap1 and Gpx4 pathways. Complex molecular concepts were simplified into community-friendly messages.

Content development consisted of three modules:

Module 1

Male reproductive health basics

Structure and function of the testes, the role of Leydig cells and testosterone, factors affecting male fertility, and the concept of oxidative stress.

Module 2

Chemical exposure and 2-methoxyethanol

Common household and industrial sources of chemicals, specific explanation of 2-methoxyethanol as a glycol-ether solvent, potential routes of exposure, and its documented impacts on testicular structure and function.

Module 3

Antioxidants and xanthone

General role of antioxidants in cellular defense; introduction to Nrf2–Keap1 and Gpx4 as "cellular shields"; explanation of xanthone as a natural antioxidant found in mangosteen and other plants; summary of in-silico findings on xanthone–protein interactions; and practical recommendations for healthy behaviors and dietary sources of antioxidants.

Each module was translated into a PowerPoint presentation, printed leaflets, and simple infographics. Scientific terms were consistently accompanied by analogies (e.g., "Leydig cells as testosterone factories," "Nrf2 as a master switch for antioxidant soldiers") to enhance comprehension.

Educational Intervention

The intervention was delivered in a face-to-face group session at the RW 01 community hall. The session lasted approximately 120 minutes and included the following components:

Opening and baseline assessment (15 minutes)

The facilitator explained the objectives, procedures, and voluntary nature of participation. After verbal consent, participants completed a pre-test questionnaire assessing baseline knowledge.

Interactive lecture (45 minutes)

The primary investigator delivered the three educational modules using slides and infographics. Visual aids included simplified diagrams of the testes, ROS generation, and xanthone–Nrf2–Gpx4 interactions, presented without mathematical or highly technical details.

Group discussion and question–answer session (30 minutes)

Participants were divided into small groups (8–10 people) to discuss key points, such as everyday sources of chemical exposure and feasible prevention strategies at the household level. Each group then presented one question or concern, which was addressed by the facilitator using lay language.

Summary and reinforcement (15 minutes)

Main messages were reiterated, emphasizing avoidable household hazards, the importance of protective equipment for family members working in industry, and the potential role of antioxidant-rich foods. Leaflets summarizing the session were distributed.

Post-test and feedback (15 minutes)

Participants completed an identical post-test questionnaire. A short feedback form captured perceived clarity, relevance, and satisfaction with the session.

Throughout the intervention, participatory methods (probing questions, examples from daily life, and local dialect where appropriate) were used to increase engagement.

Instrument for Knowledge Assessment

Knowledge was measured using a structured, self-administered questionnaire developed specifically for this program. Item generation was guided by the three content domains of the modules and reviewed by two experts in reproductive health and one expert in community health education to ensure content validity.

The final questionnaire consisted of 15 items:

5 items on basic male reproductive anatomy and the role of Leydig cells;

5 items on chemical exposure and 2-methoxyethanol risks;

5 items on antioxidants, Nrf2–Keap1/Gpx4 pathways, and xanthone.

Each item was presented as a statement with "true/false/don't know" options, or as multiple-choice questions with one correct answer. To keep the language accessible, scientific terms were followed by brief explanations in brackets. A pilot test with 10 PKK members from another RW was conducted to ensure clarity; minor wording changes were made based on feedback.

Each correct answer was scored as 1 and incorrect/"don't know" as 0. Total scores ranged from 0 to 15. For descriptive interpretation, participants with scores ≥11 were classified as "understand," while those with scores <11 were classified as "do not fully understand."

Data Collection and Management

Data were collected on paper forms during the session. Each participant received a unique code to pair pre- and post-test responses without recording names, thus maintaining confidentiality. After the activity, all questionnaires were checked for completeness and entered into a spreadsheet by two independent data clerks. Discrepancies were resolved by referring to the original forms.

Demographic data collected included age, education level, occupation, and involvement in PKK activities. These variables were used descriptively to characterize the participants.

Data Analysis

Descriptive statistics were used to summarize participant characteristics and knowledge scores. Continuous data (knowledge scores) were presented as mean ± standard deviation (SD), while categorical data (understand/not fully understand) were presented as frequencies and percentages.

Knowledge improvement was assessed by comparing pre- and post-test mean scores using a paired-samples t-test if data met normality assumptions, or a Wilcoxon signed-rank test otherwise. The proportion of participants categorized as "understand" before and after the intervention was compared descriptively. For the purpose of the abstract and main results, the numbers of participants classified as understanding (n = 110) and not fully understanding (n = 10) after the intervention were highlighted.
All analyses were performed using standard spreadsheet functions; significance for statistical tests, if applied, was set at $p < 0.05$.

Ethical Considerations

This community service activity was designed in accordance with ethical principles for health promotion programs. The protocol, including the content of educational materials and questionnaires, was reviewed and approved by the institutional ethics committee of the sponsoring university. Permission to conduct the activity was also obtained from the village head and the PKK leadership of RW 01 Sidomoro.

Participation was entirely voluntary. Before data collection, the facilitator explained the objectives, procedures, potential benefits, and the absence of risks beyond those of daily life. Participants were informed that their answers would be kept confidential, would be used only in aggregated form for academic reporting, and that they could withdraw at any time without consequences. Verbal informed consent was obtained because literacy levels varied, and the activity was considered minimal risk.

Quality Assurance

To enhance the reliability and consistency of the intervention, all facilitators participated in a short training session covering: (1) key messages to be delivered; (2) standardized explanations for technical terms; and (3) strategies for addressing questions without contradicting current scientific evidence. The delivery of the session was monitored using a simple checklist to ensure that all planned components (pre-test, three modules, discussion, summary, post-test) were completed within the allocated time.

Results and discussions

Figure 1. Socialization activities the potential of xanthones as antioxidan

In the photo documentation of the activity, the atmosphere at the RW 01 Hall, Sidomoro Village, on January 29, 2025, at 3:30 PM WIB, showed all participants and committee members enthusiastically participating in the activity, "Education on the Dangers of Chemical Exposure to Reproductive Health and the Potential of Xanthone as an Antioxidant through the Nrf2–Keap1 and Gpx4 Pathways for Family Welfare Movement (PKK) Women in RW 01, Sidomoro, Gresik."

In several key photos, the presenter is seen standing among the committee members. Her expression is serious yet communicative, conveying information systematically. PKK women from RT 1 to RT 11 sat attentively. They were neatly dressed, some in green PKK uniforms, others in casual yet modest attire. The angle of the photo clearly shows their focus and concentration on the material being presented.

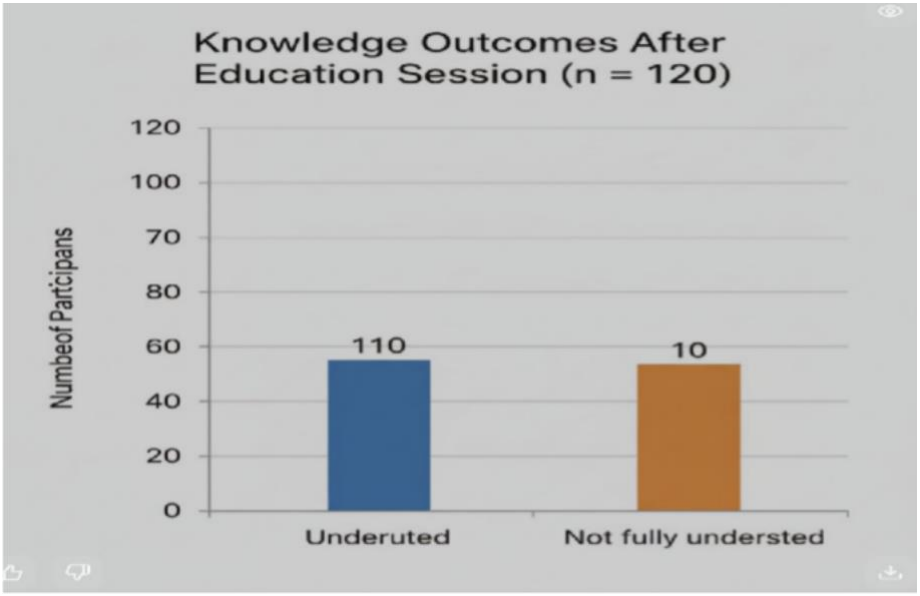

Figure 2. shows the shift in participants' knowledge levels

A total of 120 participants attended the community education session and completed both pre- and post-tests. All respondents were female PKK members or housewives residing in RW 01 Sidomoro, Gresik. The majority were in the age range of 30–49 years, reflecting the productive age group commonly responsible for family health decision-making. Most participants had completed at least junior high school, with a smaller proportion having completed senior high school or higher education. Only a few participants reported previous exposure to formal information about male reproductive health or specific chemical hazards, indicating that the topic was relatively new for the community.

Baseline Knowledge

Pre-test results showed that baseline knowledge of male reproductive health, chemical exposure, and antioxidant mechanisms was generally low to moderate. Several participants had heard of infertility or "difficulty in having children," but few could specifically identify male factors as an important contributor. The majority understood that the testes produce sperm, yet only a small subset could correctly identify Leydig cells as the structures responsible for testosterone production.

Knowledge about chemical hazards was particularly limited. Many participants associated chemical danger solely with food additives or visible pollution (e.g., smoke, bad smells) and were unfamiliar with glycol-ether solvents such as 2-methoxyethanol or their presence in industrial products. Likewise, the concept of oxidative stress and free radicals was largely unknown or only vaguely recognized from mass media without clear understanding.

Regarding antioxidants and natural protective agents, participants tended to associate antioxidant benefits with general notions of "vitamins" or "fruits and vegetables are healthy," but they were not aware of specific bioactive compounds such as xanthones or their potential role in protecting reproductive cells. This baseline picture justified the need for structured, context-appropriate education.

Post-Intervention Knowledge

After the 120-minute educational session, clear improvements in knowledge and understanding were observed. Quantitatively, all 120 participants completed the post-test, and classification based on total scores revealed that 110 participants (91.7%) met the criterion of "understand," whereas only 10 participants (8.3%) remained in the "not fully understand" category.

Male reproductive health and Leydig cells

Most participants were able to correctly identify the basic structure of the male reproductive system, the function of the testes, and the specific role of Leydig cells in testosterone production. They could also articulate, in simple terms, why damage to Leydig cells could lead to decreased fertility in men. Many participants remarked that they had never previously considered that exposure to chemicals at the workplace or in the environment could harm male reproductive organs rather than only affecting the lungs or skin.

Chemical exposure and 2-methoxyethanol

Understanding of chemicals and their potential dangers improved substantially. Participants were able to name at least one type of product or industry where solvents such as 2-methoxyethanol might be used, even though they did not memorize the exact chemical name. They grasped the main routes of exposure such as inhalation of vapors, skin contact, or contamination brought home on clothing and connected these with the risk of long-term health consequences, including male reproductive problems.

Antioxidants, Nrf2–Keap1/Gpx4 pathway, and xanthone

Although the molecular details remained challenging for some, most participants could explain antioxidants as the body's "defense army" against harmful "chemical attacks" or "rust" in cells. The simplified explanations of Nrf2 as a "master switch" that turns on antioxidant defenses, and Gpx4 as a "guardian of cell membranes," were well received. Participants recalled xanthone as a powerful natural antioxidant found in mangosteen peel and a potential supporter of these cellular defenses. Many were able to list antioxidant-rich foods commonly available in local markets and to identify them as part of a preventive strategy.

Remaining Knowledge Gaps

Despite the overall positive outcome, 10 participants did not reach the "understand" category based on the predetermined score threshold. Analysis of their answer patterns and informal post-session conversations suggested several contributing factors:

Lower formal education levels and limited literacy, which made comprehension of even simplified scientific explanations more challenging.
Difficulty in remembering unfamiliar terminologies (Nrf2, Gpx4, Leydig cells, 2-methoxyethanol) even when analogies were provided.
Limited concentration due to childcare or household responsibilities carried out simultaneously during the session.
These participants generally understood the broad message that "some industrial chemicals can harm male reproduction and healthy lifestyles with antioxidant-rich foods are important," but struggled to correctly answer more specific questions related to names or precise mechanisms.

Participant Feedback

Qualitative feedback from participants indicated high levels of satisfaction with the program. Many expressed appreciation that the session introduced a "new perspective" on family health, especially concerning the role of fathers' health and workplace exposures in determining fertility. Participants reported that the use of pictures, everyday analogies, and interactive discussion made complex topics more accessible.
Several participants suggested that future sessions could be extended to involve husbands and adolescent sons, arguing that direct engagement with male family members might further strengthen behavior change. Others requested additional materials such as posters or short videos that could be shared via messaging applications to reinforce key messages after the session.

DISCUSSION

Effectiveness of Community-Based Education

The findings demonstrate that a single, well-structured educational intervention can significantly improve community knowledge and understanding of male reproductive health, chemical hazards, and the protective potential of natural antioxidants. The increase from generally low baseline knowledge to 91.7% of participants reaching the "understand" category underscores the receptiveness of PKK members to scientifically grounded health information when it is communicated in a culturally and linguistically appropriate manner.
These results are consistent with previous studies showing that targeted health education in community settings can effectively improve knowledge and attitudes about sensitive or lesser-known health issues (Lestari et al., 2022; Wicaksono et al., 2024). In the context of male reproductive health, the involvement of women as primary caregivers and household managers is particularly strategic, as they often influence both nutritional choices and occupational health practices within the family.

Translating Complex Mechanisms into Lay Language

A unique strength of this program lies in its attempt to translate complex toxicological and molecular mechanisms—such as 2-methoxyethanol-induced oxidative stress and the Nrf2–Keap1/Gpx4 pathways—into messages understandable to the general public. The use of analogies (e.g., "factories," "guards," and "switches") and visual representations allowed participants to grasp the essence of molecular processes without memorizing technical details. This aligns with health communication literature emphasizing that abstract biomedical concepts should be framed using concrete metaphors and narratives to enhance public comprehension and retention.
By connecting the in-silico findings on xanthone–protein interactions with everyday examples of mangosteen and antioxidant-rich diets, the intervention bridged the gap between laboratory research and community practice. Rather than presenting xanthone merely as an experimental compound, it was introduced as part of a broader lifestyle message: reducing hazardous exposures while strengthening the body's natural defense systems through diet and behavior.

Implications for Reproductive Toxicology and Public Health

From a public health perspective, the program highlights the importance of raising awareness about reproductive toxicants in communities located near industrial areas. While occupational safety regulations typically focus on workers, the potential for take-home exposure to family members, including pregnant women and children, is often under-recognized. By educating PKK members about 2-methoxyethanol and similar solvents, the intervention encourages households to adopt precautionary measures such as proper storage of chemicals, advocating for personal protective equipment (PPE) for working family members, and seeking information when new chemicals are introduced in workplaces.
Moreover, the emphasis on Leydig cell health and testosterone production expands community understanding of male fertility beyond simplistic notions of "sperm count." Participants learned that hormonal regulation and cellular integrity are equally crucial, and that chemical insults can silently

disrupt these processes over time. This resonates with scientific findings that glycol-ether solvents can alter testicular morphology, hormone production, and spermatogenesis through oxidative stress and apoptosis (Li et al., 2021; Rahman et al., 2023; Wang et al., 2020).

Role of Xanthone and Antioxidants

The integration of xanthone as an example of a natural antioxidant with potential protective effects via Nrf2–Keap1 and Gpx4 pathways served both educational and translational research purposes. While the community activity did not directly evaluate biological outcomes, it introduced participants to the idea that certain plant-derived compounds may support cellular defense systems. This notion is supported by in-vitro and in-vivo studies indicating that xanthone derivatives can activate Nrf2, enhance expression of antioxidant enzymes, reduce ROS levels, and protect tissues from oxidative damage (Nguyen et al., 2021; Pothitirat et al., 2020; Syahputra et al., 2022; Yuliani et al., 2021; Nugroho et al., 2023).

By framing xanthone not as a stand-alone "magic pill," but as a representative of a wider class of phytochemicals found in fruits, vegetables, and herbal sources, the program avoided over-medicalization while still conveying the potential of evidence-based phytotherapy. Participants were encouraged to adopt a balanced diet rich in colorful fruits and vegetables, including locally available mangosteen when in season, as part of a holistic approach to health.

Remaining Challenges and Future Directions

Despite the positive outcomes, the fact that 8.3% of participants did not achieve the "understand" category highlights persistent barriers. Lower literacy, unfamiliarity with scientific language, and competing responsibilities during the session may reduce the effectiveness of one-time interventions. To address this, future programs could:

Implement repetitive and multi-modal reinforcement

Follow-up sessions, community posters, and short video messages circulated through social media or messaging apps can help repeat and reinforce key points beyond the initial training.

Simplify assessment tools

While the 15-item questionnaire captured a range of domains, some questions may have remained too technical for participants with very low education. Adapting the instrument to rely more on practical scenarios and pictorial questions may better reflect real-world understanding.

Involve male family members

Including husbands and adolescent boys in separate or joint sessions may increase the direct relevance of the information and encourage shared responsibility for reproductive health. Men working in industrial settings could be engaged in discussions about workplace safety and PPE usage to reduce both personal and household exposures.

Link with health services and policy

Collaboration with local health centers and occupational health authorities would allow educational efforts to feed into broader strategies for monitoring chemical exposures and reinforcing regulations in surrounding industries.

Limitations

Several limitations should be acknowledged. First, the study used a one-group pre-test–post-test design without a control group, making it difficult to completely rule out external influences on knowledge changes. However, the brief time frame between pre- and post-tests and the absence of similar concurrent programs suggest that the observed improvement is largely attributable to the intervention.

Second, knowledge was measured immediately after the session, so the durability of learning over longer periods remains unknown. Longitudinal follow-up would be needed to assess retention and behavior change, such as consistent use of PPE by workers or increased consumption of antioxidant-rich foods at home.

Third, the classification of "understand" versus "not fully understand" was based on an arbitrary cut-off score. While this threshold provided a useful snapshot, it may not fully capture the nuances of partial understanding. Future research might incorporate qualitative interviews or focus group discussions to explore how participants integrate new knowledge into their beliefs and practices.

Finally, although the educational content was grounded in contemporary toxicology and in-silico research, the community program itself did not directly test biological endpoints such as biomarkers of oxidative stress or hormonal levels. Consequently, conclusions are limited to knowledge and self-reported understanding, rather than physiological outcomes.

Strengths and Contribution

Despite these limitations, the program has several strengths. It is one of a relatively small number of initiatives that explicitly connects advanced molecular research—particularly in-silico studies on xanthone and Nrf2–Keap1/Gpx4 pathways—with community health education. The collaboration between academic researchers and PKK cadres demonstrates how scientific findings can be translated into accessible messages that support evidence-informed decision-making at the family level.

Additionally, the activity provides a practical model for community service in industrially exposed areas: identify a relevant toxicant (2-methoxyethanol), elucidate its mechanisms of harm, explore potential protective agents (xanthone), and design an educational intervention tailored to local sociocultural conditions. This model could be adapted for other chemicals, such as pesticides or heavy metals, and for other vulnerable populations beyond PKK groups.

In summary, the results show that community-based education rooted in current scientific evidence can substantially enhance understanding of chemical reproductive hazards and natural protective mechanisms among PKK members in RW 01 Sidomoro, Gresik. While further work is needed to ensure long-term retention and behavioral change, this program represents an important step toward integrating toxicological research, phytochemical insights, and community empowerment to safeguard male reproductive health in industrial environments.

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