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The Dose Makes the Poison: A Survey-Based Analytical Study Exploring the Relationship between Quantity and Effect in Toxicology (The Case of Derna City, Libya)

Sajeda A. El-mansory
Department of Zoology, Faculty of Science, University of Derna, Derna, Libya.
*E-mail: anamnoomy@gmail.com

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ABSTRACT

This study investigates the principle of "The dose makes the poison" using a survey-based analytical approach, focusing on public awareness and perception of toxic exposure in Derna City. An electronic questionnaire was distributed, and responses from 100 participants were recorded to assess their understanding of how the quantity of a toxic substance influences its effect. The analysis explores variations in residents' responses and relates them to classical toxicological theories. Results reveal varying levels of awareness regarding toxic dosage and its effects, alongside some misconceptions. These findings highlight the need for improved public education on toxicology to enhance community health outcomes. The study provides valuable insights into the community's interpretation of toxicological principles and suggests that targeted awareness campaigns could effectively address knowledge gaps. Overall, this research offers a foundation for future environmental health monitoring and public health strategy, emphasizing the importance of community engagement and promoting informed decision-making in toxic exposure management in Derna City.

INTRODUCTION

The phrase "The dose makes the poison" stands as one of the foundational principles of toxicology, originally articulated by the Swiss physician and alchemist Paracelsus in the 16th century. He stated, "All things are poison, and nothing is without poison; only the dose permits something not to be poisonous." This statement captures a profound scientific truth: the harmful or beneficial nature of any substance is not absolute but depends entirely on the amount to which an organism is exposed. Even water, essential for life, can become toxic if consumed in excessive amounts, while substances considered poisons may have therapeutic value in the right dosage (Carney, 2025).

In toxicological science, the relationship between dose and effect known as the dose-response relationship is a critical concept. It is used to determine how different levels of exposure to a substance influence its biological impact. This concept guides the establishment of safety thresholds, such as the LD_{50} (lethal dose for 50% of a population) and ED_{50} (effective dose for 50%), and plays a crucial role in public health, pharmaceutical development, environmental safety, and regulatory decision-making.

Toxicity is not determined by the substance alone, but by several interacting factors: the dose, the route of exposure (oral, dermal, inhalation), the duration of exposure (acute or chronic); the individual's physiological characteristics (age, weight, genetic profile), and external factors such as environmental conditions. Understanding these dynamics allows scientists and policymakers to predict toxic risks and mitigate harm while making safe and beneficial use of chemical substances.

In this research, we aim to explore the relationship between dose and toxicity in depth, not only through literature and scientific theory, but also by incorporating practical analysis. One of the key components of this study was the development, distribution, and analysis of a questionnaire designed to measure public awareness, perception, and understanding of the principle that "the dose makes the poison." The results of this questionnaire provided valuable insights into how well this concept is understood outside scientific communities and helped identify potential gaps in public knowledge that may affect health and safety decisions. Through a combination of theoretical study and empirical research, this paper seeks to highlight the importance of dosage in toxicology and demonstrate its relevance in real-life contexts

Revisiting Paracelsus: The Dose Concept in Modern Toxicology:

Philippe Grandjean's study delves into the historical context of Paracelsus's assertion that "the dose makes the poison," highlighting its enduring relevance in contemporary toxicology. The research discusses how this principle laid the groundwork for concepts like the No-Observed-Adverse-Effect Level (NOAEL) and the distinction between hazard and risk. Grandjean emphasizes the complexities introduced by modern environmental exposures, genetic predispositions, and the challenges in assessing the toxicity of industrial chemicals.

At the time that Paracelsus coined his famous dictum, 'What is there that is not poison? all things are poison, and nothing is without poison. Solely the dose determines that a thing is not a poison', embryonic toxicology was a focused discipline that mainly dealt with occupational poisonings and side effects of pharmaceuticals, such as mercury. While Paracelsus paved the way for the modern threshold concept and the no-adverse effect level, modern-day toxicology is now tussling with highly complex issues, such as developmental exposures, genetic predisposition and other sources of hyper susceptibility, multiple causes of underestimated toxicity, and the continuous presence of uncertainty, even in regard to otherwise well-studied mercury compounds. Further, the wealth of industrial chemicals now challenges the 'untested-chemical assumption' that the lack of documentation means that toxic potential can be ignored. Unfortunately, in its ambition to provide solid evidence, toxicology has been pushed into almost endless replications, as evidenced by the thousands of toxicology publications every year that focus on toxic metals, including mercury, while less well-known hazards are ignored. From a public health viewpoint, toxicology needs to provide better guidance on decision-making under ever-present uncertainty. In this role, we need to learn from the stalwart Paracelsus the insistence on relying on facts rather than authority alone to protect against chemical hazards. (Grandjean, 2016).

Many scientific studies have addressed the principle of "the dose makes the poison" as a cornerstone of toxicology. These studies have confirmed that the effect of any substance on a living organism depends on the dose, not just the nature of the substance. The following is a summary of the most prominent findings of these studies:

In examining the modern dimensions of Paracelsus's maxim, he noted that dose remains the primary factor in determining the toxicity of any substance, but the modern world faces additional complexities such as chronic exposure and genetic variation among individuals. He stated:" The dose concept remains valid but increasing complexity in chemical exposures and individual vulnerability challenges traditional toxicology" (Grandjean, 2016).

This indicates the need to update toxicity assessment methods to keep pace with the challenges of the times. A comprehensive overview of toxicology concepts was provided; emphasizing that understanding the dose-response relationship is the foundation of risk assessment. Klaassen & Watkins (2015) stated that" Understanding dose-response relationships is essential for predicting the potential risks and determining the safety thresholds of chemical substances".

This reflects the importance of adopting the dose as a criterion in setting regulatory standards. The importance of determining the "internal dose" that reaches the site of action in the body was discussed, explaining that simply knowing the amount of exposure is not enough. " Risk assessment must consider not just the exposure dose, but also the internal dose that reaches the target site" (Robinson, 2018). This reinforces the need for a deeper understanding of how the body reacts to chemicals.

Hamilton and Kozul-Horvath study is a practical example of low-dose toxicity, showing that chronic exposure to low levels of arsenic can have adverse effects on growth and development. They stated: "Even low doses of arsenic, previously considered safe, can disrupt fetal and postnatal development" (Hamilton & Kozul-Horvath, 2012)

Exposure to arsenic in drinking water, even at relatively low concentrations, has been linked to increased risks of cancer and other chronic health effects" (National Research Council, 1999).

This suggests that the concept of a "safe dose" may need to be reconsidered in some cases. This study addressed the basic concepts of toxicology, emphasizing that the dose determines whether a substance is toxic or not. The fundamental principle of toxicology is that the dose determines the effect. No substance is without risk" (Extoxnet, 1993).

Arsenic exerts its toxicity through multiple mechanisms, including interference with cellular respiration and oxidative stress, which complicates the establishment of a universally 'safe' dose" (Abernathy *et al.,* 1999).

This study aimed to assess individuals' awareness of the concept of "the dose makes the poison" and its relationship to the risk of overdose, through an online survey that included a diverse group of participants.

MATERIALS AND METHODS

This study adopted a descriptive-analytical approach to explore the toxicological principle of "the dose makes the poison," focusing on public understanding of dose-response relationships and awareness of the health impacts of varying exposure levels to chemicals and drugs. The study consisted of a literature review and a quantitative survey conducted through a self-administered questionnaire.

Participants and Sampling:

A total of 100 individuals from the general population participated in the study. There were no specific inclusion or exclusion criteria, as the aim was to gather a broad and diverse range of responses without targeting a particular demographic or occupational group.

Data Collection Tool:

The primary tool for data collection was a structured questionnaire.

- Demographic questions (such as age and education level.
- Knowledge-based items related to toxicological principles.
- Behavioral and attitudinal questions focusing on participants' handling of chemicals and medications.

The questionnaire was reviewed for clarity and content accuracy and then distributed online and/or in person. The data collection took place over a two-day period, from April 24 to April 25, 2025.

Data Analysis:

The responses were compiled and analyzed using Microsoft Excel. Descriptive statistics such as frequencies, percentages, and averages were calculated to interpret participant responses and to identify trends and general awareness levels.

Ethical Considerations:

Participants were informed of the purpose and voluntary nature of the study. Anonymity and confidentiality were strictly maintained throughout the data collection and analysis process. No personal or identifying information was collected.

RESULTS AND DISCUSSION

Demographic Distribution:

After collecting and analyzing the questionnaires, the results for gender and age group were as follows:

• Gender: The vast majority of participants were female (98.8%).

• Age Groups: The most participating age group was 18-25 years, representing 77.8%, followed by 26-35 years, representing 14.8%.

Participants' knowledge of the saying "The dose makes the poison":

The analyzing data as in Figure 1 show that Participants' knowledge of the previously mentioned proverb "The dose makes the poison" is as follows:

53 % of participants have heard the saying "The dose makes the poison" and understand its meaning.

33 % have never heard it before.

% 14 have heard it but do not know its meaning.

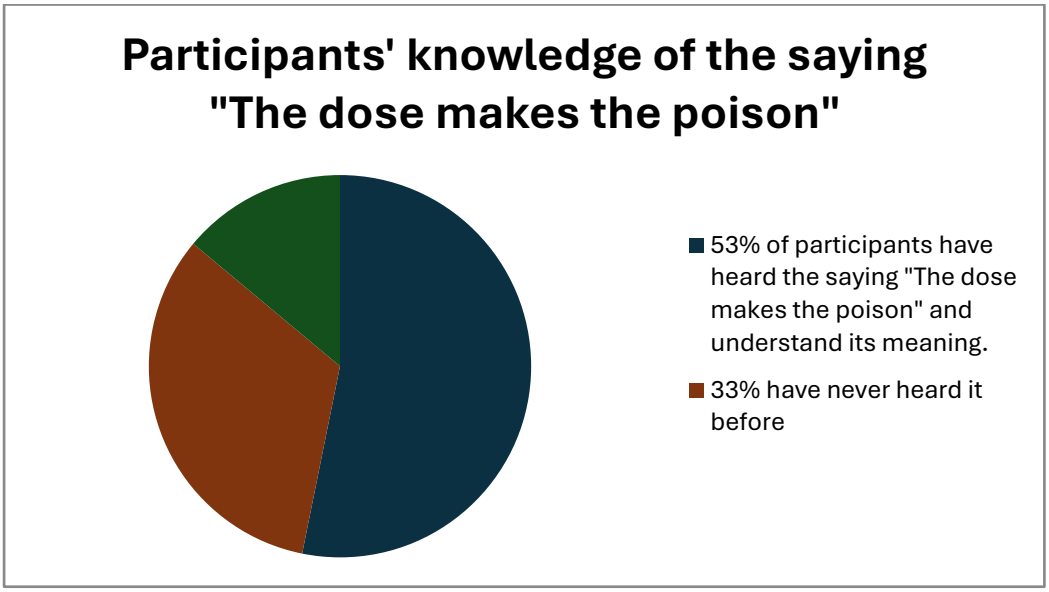

Fig. 1. Participants' knowledge of the saying "The dose makes the poison"

Participants' Awareness of the Risks of Overdose:

Figure 2 shows participants' awareness of the risks of overdose as follows: %90 of participants believe that an overdose of any substance, even natural ones, can be toxic. This reflects a high level of awareness of the risks associated with overdose.

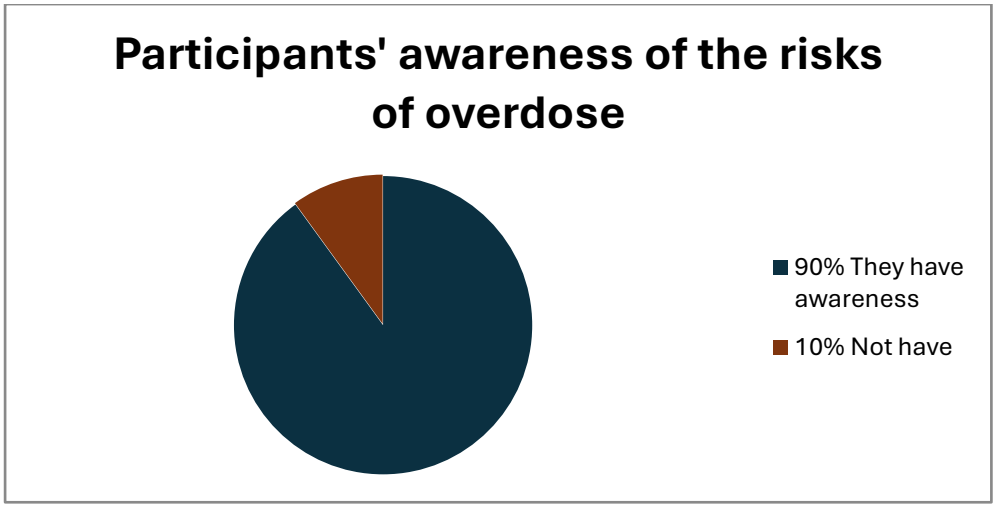

Fig. 2. Participants' awareness of the risks of overdose

Medication Behavior:

As for the medication behavior, the results were as follows:76.5 % of participants never took a higher medication than the recommended dose without consulting a doctor, while 23.5% did. But 5% of participants did not use pain relievers weekly, while 28.4% used them 1-2 times weekly.

Participants' Attitudes Toward Vitamin Use:

The study (Fig.3) revealed the participants' opinions about taking vitamins and nutritional supplements as follows:

% 63 of participants believe that taking vitamins and nutritional supplements requires medical supervision.

% 37 believe there is no need for such supervision.

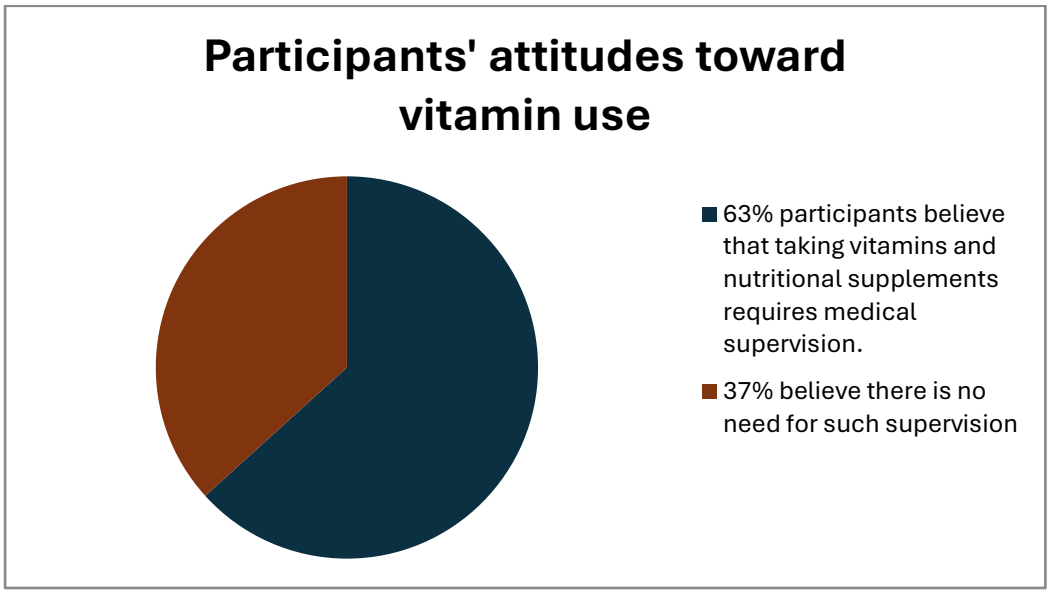

Fig. 3. Participants' attitudes toward vitamin use.

The Importance of Awareness:

97.5% of participants believe there is an urgent need to educate the community about the dangers of overdose.

Factors Influencing Toxicity (from the participants' perspective) :

While the study showed (Fig. 4) that the factors affecting toxicity from their point of view, according to their understanding are as follows:

•Dose was the most frequently selected factor, at 34%.
•Chronic illness came in second, at 26%.
•Type of substance came in third, at 21%.
•Age was the most significant factor, at 10%.
• Duration of exposure was the last, at 9%.

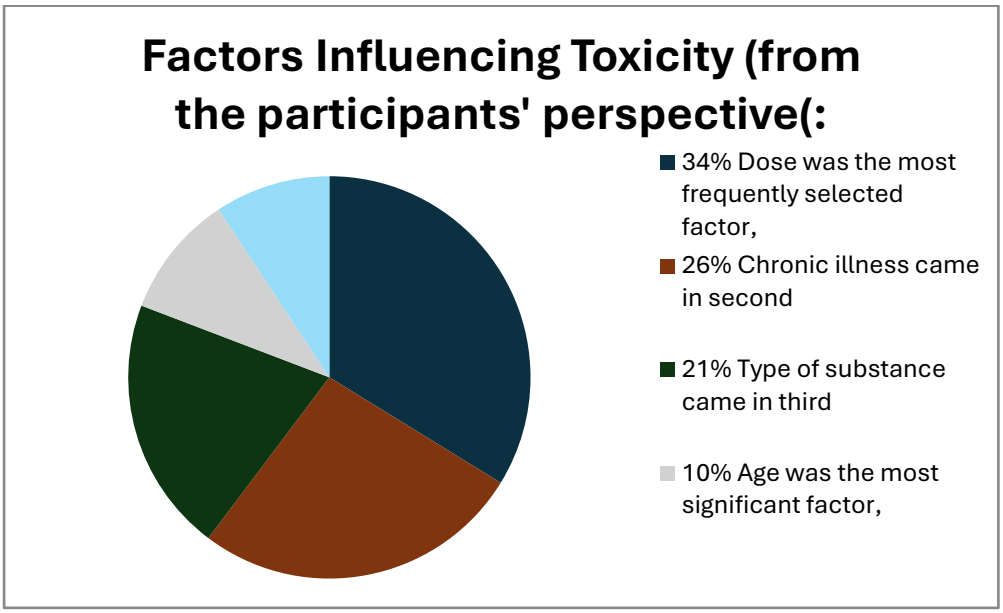

Fig. 4. Factors Influencing Toxicity (from the participants' perspective.

DISCUSSION

The findings of this study reinforce the central toxicological principle that "the dose makes the poison," as originally stated by Paracelsus in the 16th century and reaffirmed by contemporary researchers (Carney, 2025; Grandjean, 2016). More than 90% of participants recognized that an overdose of any substance, whether natural or synthetic, can lead to toxic outcomes. This reflects a baseline understanding of dose-dependent toxicity within the general population, aligning with the foundational concepts of toxicology that emphasize the importance of exposure level over substance type (Klaassen & Watkins, 2015; Extoxnet, 1993).

Nevertheless, the study also identified significant gaps in knowledge. Approximately one-third of participants (32%) had never heard of the phrase "the dose makes the poison." This echoes Grandjean's (2016) observation that, despite the historical endurance of Paracelsus' dictum, public health communication often fails to translate scientific knowledge into practical awareness, particularly when addressing complex exposures and genetic variability. Such findings highlight the need for targeted awareness programs that simplify toxicological principles for lay audiences.

A more concerning discrepancy emerged between knowledge and behavior: although most participants acknowledged the dangers of overdose, nearly one-quarter (23%) admitted to consuming medications at higher-than-recommended doses without medical consultation. This behavioral gap illustrates the limitations of knowledge alone in shaping safe practices. Hamilton and Kozul-Horvath's (2012) work on low-dose arsenic exposure provides a

parallel, showing that harmful outcomes can occur even when the risks are underestimated or disregarded. The current study's findings therefore underscore the need for educational interventions that go beyond knowledge transfer, addressing behavioral and cultural attitudes toward medication use and self-dose.

The results on dietary supplements further emphasize this point. While participants generally reported low-frequency use of vitamins and painkillers, over one-third (35.8%) believed that supplements could be taken without medical supervision. This perception is problematic given evidence that even substances perceived as "safe" may produce harmful effects at certain doses (Abernathy *et al.,* 1999; National Research Council, 1999). It also reflects the persistence of a lay/public health misconception that "natural" equates to "harmless," a view that directly conflicts with the toxicological principle that risk is dose-dependent rather than substance-dependent (Carney, 2025).

Finally, when asked about factors influencing toxicity, participants largely emphasized dose, consistent with toxicological theory. However, other critical determinants including age, duration of exposure, and genetic predisposition were under-recognized. This finding aligns with Robinson's (2018) call for a more nuanced understanding of internal dose and variability in susceptibility. In modern toxicology, the dose concept remains valid but is complicated by cumulative exposures, developmental stages, and individual biological differences (Grandjean, 2016). Raising awareness of these additional dimensions is essential to bridge the gap between scientific understanding and public perception.

Taken together, the results of this study support the universality of Paracelsus' maxim while simultaneously revealing persistent challenges in translating toxicological knowledge into safe behavior. The findings highlight both progress such as general awareness of overdose risks and ongoing deficits, such as behavioral inconsistencies and incomplete recognition of non-dose factors. Addressing these gaps requires multidisciplinary strategies that combine education, behavioral science, and public health initiatives to ensure that the principle "the dose makes the poison" is not only understood but effectively applied in everyday decision-making.

Recommendations:

Based on the findings, the following recommendations can be made:

1 .Enhance awareness programs: Through media and health campaigns that highlight the risks of overdose and explain the concept in a simplified manner to the public.

2 .Integrate toxicology concepts into school curricula: Especially at the middle and high school levels, to help build a scientific foundation in individuals from an early age.

3 . Encourage healthy behaviors: Via campaigns focusing on the importance of adhering to recommended doses and avoiding the use of any supplements or medications without professional consultation.

4 . Involve specialists in awareness efforts: Such as pharmacists and doctors, as they play a key role in guiding individuals and correcting misconceptions directly.

5. Further studies: To explore the relationship between awareness levels and healthy behaviors more deeply, especially across different age groups.

Declarations:

Ethical Approval: This study was conducted through survey-based data collection from the public. Participation was voluntary, and the confidentiality and privacy of respondents were ensured. No animals or medical interventions were involved.

Conflict of interest: The authors declare no conflict of interest.

Author's Contributions: Sajeda A. El-mansory designed the research, acquired the data, recorded the measurements, analyzed the data, wrote the manuscript, and discussed the results.

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