Review of: "Toxicity of Olea africana in Artemia Salina and Mice"

Hoang-Dung Tran

Potential competing interests: No potential competing interests to declare.

INTRODUCTION SECTION

"Olea africana is an ornamental tree with green, glossy leaves, a large trunk, and inconspicuous but fragrant flowers [9]. It is found in Asia (South East) and Africa (East and South). In folk medicine, various communities use the plant to treat urinary tract and eye infections, kidney problems, sore throat, headaches, and backaches. It is also used as a styptic, emollient, hypotensive, antimalarial and febrifuge [10][11][12]. The scientific literature is replete with pharmacological reports on Olea africana's anthelmintic, antibacterial, antihypertensive, and anti-diarrheal activities [10][11][13][14]. Moreover, triterpenoids, coumarins, secoiridoid glucosides, phenolic glucosides, and lignans are among the phytochemical compounds found in Olea africana [11][15][16][17][18]. Others include saponins, alkaloids, tannins, flavonoids, anthraquinones, and glycosides [13]. However, studies on the safety of Olea africana are scarce [19]. As a result, the current study investigated the toxicity of the ethanol extract of Olea africana in two animal models; mice and brine shrimp."

Comment: This section provides a wealth of information about Olea africana and its activities in folk medicine and scientific literature. However, there needs to be a clearer delineation between different pieces of information. Furthermore, it is essential to present the rationale behind the current study's decision to investigate the toxicity of ethanol extract from Olea africana using two animal models, mice and brine shrimp.

METHODS SECTION

2.3. Sample Preparation and Extraction: The description of "100 µg/mL" appears twice for the fourth group (groups 3, 4, and 5) in the "Brine Shrimp Cytotoxicity Assay." It seems to be an error, and you may need to correct this duplication.

2.4. Animals Used in Experiments: It would be useful to provide information about the gender of the mice and their age (if available) for a comprehensive understanding of the study's subjects and potential applicability of results across different age and gender groups.

2.7. Sub-acute Toxicity in Mice: Further elaboration on why specific doses of the extract were chosen for the sub-acute toxicity experiment would enhance the reader's understanding of the rationale behind the dosage selection.

RESULTS SECTION

This section includes the findings of the study on the toxicity of ethanol extract from the Olea africana tree concerning both Artemia salina (a small shrimp species) and mice. Specifically, this section comprises:

Toxicity in Artemia Salina and Mice: Table 1 and the accompanying text describe the LC50 and LD50 of the ethanol extract from Olea africana for Artemia salina and mice, respectively. The LC50 indicates the concentration at which 50% of Artemia salina would be fatally affected (2275.84 µg/mL), and the LD50 signifies the dose causing 50% mortality in mice (4297.30 mg/kg). However, there is no further analysis regarding the significance of these figures.

Effect on Body Weight and Organ-to-Body Weight Ratio: This part compares changes in body weight and organ-to-body weight ratios between the group treated with the extract and the control group. Nonetheless, there is limited statistical analysis of the meaningful differences among the groups.

Effect on Hematological and Biochemical Parameters: This section demonstrates alterations in hematological and biochemical markers after treating mice with the ethanol extract from Olea africana. There are significant changes observed in some indicators like ALT, AST, total protein, and bilirubin, but no detailed statistical analysis is provided regarding these differences.

Histopathology: This section presents results from examining tissue samples of the liver and kidneys of treated mice. It identifies pathological features such as fibrosis and cellular damage in the liver and kidneys. However, a deeper analysis is needed to understand the clinical significance of these changes.

Counterarguments and Considerations:

Small Sample Size: The number of samples in the experimental groups might be considered small (n = 35 in the acute toxicity experiment on mice and n = 28 in the sub-acute toxicity experiment on mice). A larger sample size could offer a more comprehensive insight into the extract's impact.

Unclear Acute Toxicant: In the section discussing acute toxicity in mice, the toxicant is not clearly defined. It is referred to as "pure water solution." This lack of clarity might hinder comparisons with other studies and understanding the actual toxicity of the extract.

Differences in Body Weight and Organ Ratios: The "Sub-acute toxicity in mice" section reports non-significant differences in body weight and organ-to-body weight ratios compared to the control group. However, it remains unclear whether these minor differences have clinical relevance.

Impact on Biological Indices: Some biological indices within the experimental group are reported as differing from the control group. Yet, there is no specific explanation provided for the clinical significance of these differences or whether they might negatively affect the health of the mice.

Organ Impact: The "Histopathology" section provides information about changes in liver and kidney organs due to exposure to the extract. However, the description of these changes lacks clarity and requires additional information about their nature and severity.

Explaining Results: The "Results" section needs to provide more detailed explanations regarding the clinical significance and limitations of the findings. While some results are labeled as "significantly different," there is no discussion on the clinical importance of these differences.

Lack of Discussion on Risk from Histopathological Findings: Although the "Histopathology" section presents pathological features in the liver and kidneys, there is no detailed analysis of the clinical relevance of these changes. Additional discussion is needed to address how these features might impact the health of humans or animals.

Need for Dosage and Duration Analysis: The article does not provide detailed information about how dosage and treatment duration affect the outcomes. This is important to understand the extent of extract toxicity and the potential accumulation of toxins in the body over prolonged use.

Overall, the "Results" section should be enriched with more comprehensive statistical analysis and a deeper discussion of the clinical significance of observed changes to strengthen the persuasiveness and scientific rigor of the findings.

DISCUSSION SECTION

The discussion presents important findings related to the acute and subacute toxicity of the ethanol leaf extract of Olea africana. However, there are certain aspects that require further consideration and critical examination:

Acute Toxicity Comparison: While the study compares the LC50 values of the current ethanol extract with a previous study using an aqueous extract of Olea africana in Artemia salina, the direct comparison might be limited due to differences in extraction methods and solvent properties. A comprehensive understanding of the reasons for these differences would enhance the validity of the conclusions.

Interpretation of Non-Toxicity: The discussion suggests that Meyer and Clarkson’s criteria suggest the extract may be considered non-toxic. However, these criteria and their applicability to plant extracts should be discussed further, considering that toxicity thresholds can vary based on species, exposure routes, and duration.

LD50 Interpretation: The comparison of the LD50 value for the ethanol extract with a previous study using a methanol extract warrants a deeper exploration. Different solvent properties could influence the extract's toxicity, and thus, a more comprehensive analysis is necessary to determine the overall toxic potential.

Subacute Toxicity Significance: While the study transitioned from acute to subacute toxicity evaluation due to the absence of observed toxicity, the choice of duration (28 days) should be discussed more thoroughly. A rationale for this duration's appropriateness and its alignment with potential clinical scenarios would add clarity.

Impact on White Blood Cells: The observation of significantly higher white blood cell levels in treatment animals could be attributed to multiple factors, including inflammation, infection, or immune responses. Further investigation is necessary to ascertain whether this elevation indicates an immune challenge directly linked to the extract's effects.

Sodium Levels: The discussion highlights significantly lower sodium levels in mice given the extract, but the reasons for

this effect remain unclear. Speculation about cellular malfunction and death due to insufficient sodium requires a more grounded scientific explanation.

Liver Function Indicators: While the discussion attributes liver damage indicators like ALT, AST, ALP, and GGT elevation to the extract, additional factors such as metabolic variation and the potential for secondary effects should be addressed. Further analysis and context are needed to solidify the conclusion.

Histopathology Confirmation: The discussion concludes that histopathology confirms liver and kidney damage due to extract administration. However, the extent of the damage, its clinical relevance, and the correlation between histopathological findings and physiological consequences require a deeper exploration.

Conclusion Interpretation: The conclusion states that prolonged administration of the extract is associated with significant toxic concern, and therefore, should be used with caution. While this is a reasonable recommendation based on the findings, a more nuanced interpretation could address the potential for dose-dependent effects, variations in individual susceptibility, and the extrapolation of these results to real-world scenarios.

In summary, while the discussion provides valuable insights into the toxicity profile of the ethanol leaf extract of Olea africana, a more comprehensive and nuanced consideration of the limitations, underlying mechanisms, and potential confounding factors would enhance the validity and applicability of the conclusions.