

Review of: "Effect of Yogurt on Fluoride Induced Toxicity in Rabbits"

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Potential competing interests: No potential competing interests to declare.

Thank you for the invitation to review the manuscript submitted to the esteemed journal, Qeios. I read the manuscript " Qeios ID: KC0S3D " authored by Sallam et al. presents a study investigating the toxic effects of fluoride exposure on renal (kidney) function, as well as the potential protective role of yogurt supplementation. The main objective of this study was to analyze the impact of fluoride exposure on renal function markers in rabbits, and determine if yogurt could protect against fluoride toxicity.

Due to the importance of this paper, I would like to present both major and minor comments for your consideration:

Major Comments:

1. Abstract:

the abstract would be strengthened by adding more methodological substance, quantitative results, statistical validation, discussion of implications, and tighter/clearer writing. This would make for a more informative and convincing abstract.

- Lack of methodological details

The abstract does not provide enough details about the methodology, such as:

- Sample size and group assignments

Exact dosage levels of fluoride and yogurt used

Duration of treatment

Parameters measured

This limits reproducibility and assessment of the study design.

- Qualitative description of results

The results are described qualitatively (e.g. "levels were increased/decreased") rather than providing actual data values.

This makes it difficult to properly evaluate the findings and conclusions.

- Broad conclusions

The conclusion that yogurt mitigated toxicity is vague. It would be stronger to directly tie conclusions to specific results/markers.

- No statistical data

No information is given about statistical significance of the results. This is important to validate conclusions.

- Lacks context

It does not adequately discuss the implications or place findings within the context of previous literature.

- Writing quality

Some sentences are wordy and could be more concise to better achieve the goal of tightly summarizing in the abstract.

Introduction:

- Lack of detail on fluoride toxicity mechanisms: It briefly mentions fluoride damages renal tissue but does not adequately explain how this occurs biologically. More pathophysiological background is needed.
- Limited background on probiotics and yogurt: It could provide more discussion from previous studies on how certain probiotics may mediate toxins and protect renal function.
- Narrow focus on kidney effects: Broadening the introduction to also discuss general fluoride toxicity and how the kidney plays a role in excretion/detoxification would improve context.
- Overview of relevant biomarkers is brief: Expanding on the biological/clinical significance of the markers analyzed (creatinine, BUN, etc) would help readers understand their importance.
- Objective statement lacks specificity: Saying it assessed "protective effect" is vague - the objectives should clearly define what aspects of protection were evaluated (e.g. effects on specific renal markers).
- No theoretical framework/rationale presented: It could help to introduce how the study aims to add to current knowledge gaps and theoretical models of fluoride toxicity/protection.
- Lacking critical analysis: The introduction states previous findings without discussing limitations or inconsistencies in the literature to set up the need for more research.
- Structure could be tightened: Some details are repetitive or tangential and would benefit from more focused, logical flow of information.
- Strengthening these areas of the introduction would provide a more robust foundation and contextualization for understanding the merits and goals of the presented study.

1. Material and methods

- Lack of detail on animal selection/characteristics: No information on age, gender distribution between groups, health status, etc.
- Vague group assignments: Just says animals were "randomly divided" but does not state sample sizes for each group

or randomization process.

- Dosage amounts not precisely defined: Mentions grams/kg of yogurt but does not specify fluoride doses in standardized units like mg/kg.
- Treatment regimen could be clearer: Just says substances given "once daily" but over what timeframe (days/weeks)?
- Analytical methods lack validation: Does not state if renal assay kits were properly calibrated/controlled for accuracy.
- Biochemical analysis not thoroughly explained: Parameters measured are listed but no details on specific assay principles/procedures.
- Insufficient statistical analysis planned: Only mentions comparing groups but not types of stats or correcting for multiple comparisons.
- Ethical considerations barely covered: Need more on approval/oversight of animal experiments to meet standards.
- Information presented inefficiently: Details scattered between sections instead of logically grouped.

The experimental design is not clearly described in the methods section. Some key things that are missing include:

Not specifying whether it was a randomized complete block design (RCBD) or completely randomized design (CRD).

No information given about how the animals were blocked/assigned to treatment groups. Randomization is mentioned but blocking factors are not defined.

Sample sizes per group are not stated, just that there were "4 rabbits/group". This lacks methodological rigor.

Interactions between treatment factors are not addressed (e.g. fluoride dose x yogurt dose).

Repeated measures over time (days 16 and 31) are not accounted for statistically.

1. Results

- Lacks statistical analyses details (type of tests, like Anova one way.)
- Only shows group means, no measure of variance/error bars
- No direct comparisons between time points (day 16 vs 31)
- Data only presented numerically in text, could use tables/figures
- Organization jumps between parameters instead of grouping by outcome

1. Discussion

- Mechanisms for yogurt's effects are hypothesized not thoroughly discussed
- Limited comparison to previous literature and integration of findings
- Does not acknowledge limitations or possible alternative explanations
- Focuses on supporting own results rather than critically analyzing
- Conclusions at end repeat abstract, no new insights discussed
- Speaking in general terms, lacks specificity on study parameters
- Disconnected from introduction, no theoretical framework revisited

Some ways to strengthen:

- Fully report statistical analysis and significance
- Perform time point comparisons and correlations mentioned
- Group discussion by outcome parameter for coherence
- More rigorous and comprehensive literature review
- Openly address study limitations and directions for future work
- Relate back to original questions/objectives and rationale

it does not seem the results and discussion fully matched or addressed the objectives that were stated in the introduction.

The introduction presents the objectives as:

- Determine fluoride-induced toxicity in the kidney
- Assess protective effect of yogurt against fluoride toxicity in the kidney

However, weaknesses in aligning with these:

- Results only show levels of renal biomarkers, but do not directly discuss "toxicity" in the kidney itself.
- Focus is on comparing biomarker levels between groups rather than directly assessing "protective effect".
- Biomarkers presented individually without analyzing relationships between them.
- No discussion of underlying mechanisms of toxicity/protection in kidney tissues.
- Objectives were not clearly operationalized in methods design or statistical analysis.

To better satisfy the objectives:

- Could correlate biomarker changes to histopathology assessing kidney tissue damage.
- Perform dose-response or time-course analyses to establish fluoride toxicity.
- Include additional controls to isolate yogurt's protective mechanisms.
- Discuss literature suggesting biological plausibility for observed changes.
- Reference theoretical frameworks like mode of toxic action.
- Conclusion
- Rewrite the conclusion after you make the major comments.
- They simply restate the results without synthesizing new insights gained from the study. More interpretation is needed.
- Mechanistic explanations are not provided to support how/why yogurt specifically mitigated toxicity based on findings.
- Limitations and assumptions are not mentioned, giving an overstated level of certainty.
- Broader implications, applications, or directions for future work are lacking discussion.
- Causation cannot truly be determined from this study design but is implied in the wording.
- Not reconciled with uncertainties raised by weaknesses in methods, results, and previous literature.
- Do not directly relate back to the original aims/objectives or theoretical framework.
- Overinterpret given results that only showed group differences without robust analyses.

