Journal of Chemistry Insights and Discoveries
Publisher: BioLuster Research Center Ltd.
Journal Home Page: Journal of Chemistry Insights and Discoveries
Journal DOI: https://doi.org/10.71193/jcid

Review Report

Final Title: Evaluation of anti-obesogenic and anti-diabetic effects of tauroursodeoxycholic acid in Swiss albino rats: possible blockage of CHOP-dependent mitochondrial shuttling of TBP-2 and antagonism of streptozotocin-induced type 2 diabetes
Submission Title: Evaluation of anti-obesogenic and anti-diabetic effects of tauroursodeoxycholic acid in Swiss albino rats: possible blockage of CHOP-dependent mitochondrial shuttling of TBP-2 and antagonism of streptozotocin-induced type 2 diabetes
Submission Date: October 15, 2025
Initial Editorial Assessment: October 17, 2025
Sent for Review: October 20, 2025
Review Completed: November 15, 2025
Accepted: November 25, 2025
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Round 1

Reviewer 1
Name: Unwilling to disclose
Conflict of Interest: None
Date of Reviewer's Comments: November 01, 2025
Date of Author Response: November 09, 2025

Reviewer 1 Comments	Author Response
Reviewer Recommendation: Revision Required 1. Write keywords in alphabetical order.	Thank you very much for your comment. All keywords were alphabetically arranged.
2. In line 129, the author writes "their combined effects on diabetes prevention, particularly in a diet-induced model of insulin resistance, remain inadequately explored". Give references of this statement.	Thank you very much for your comment. We could not find any published studies reporting the combined effects of TUDCA and UDCA on diabetes prevention, particularly in diet-induced models of insulin resistance. TUDCA and UDCA exert overlapping but distinct effects on endoplasmic reticulum (ER) stress, inflammation, and bile acid–mediated signaling pathways. Co-treatment may yield additive or synergistic benefits through complementary modulation of ER stress, mitochondrial function, and FXR/TGR5 signaling; however, interactions between the two compounds in the context of diet-induced insulin resistance have not been systematically investigated.
3. Why are only male mice used in this experiment?? Why not female mice?	Thank you very much for your comment. Male rats are used predominantly in HFD + STZ-induced T2D models because they develop insulin resistance and hyperglycemia more consistently due to the absence of estrogen's metabolic protection, gain weight faster, and exhibit less hormonal variability, leading to greater model reproducibility and efficiency.
4. Give the proper size of cages and How many rats were kept in each cage?	Thank you very much for your comment. Information regarding the cage size (430 × 270 × 150 mm) and the number of rats housed per cage (4–5) has been included in the Materials and Methods section of the manuscript.
5. In Figure 1, two pictures should be in same size.	Thank you very much for your comment. In Figure 1, the two pictures were made the same size.

Reviewer 2
Name: Unwilling to disclose
Conflict of Interest: None
Date of Reviewer's Comments: November 02, 2025
Date of Author Response: November 09, 2025

Reviewer 1 Comments	Author Response
Reviewer Recommendation: Accept Submission	-
1. In the whole manuscript, a lot of space problem is observed. For example, "5.2±0.19", there should be space. Carefully review the whole manuscript.	Thank you very much for your comment. The manuscript was reviewed very carefully, and all the space problems have been corrected.
2. In line 246, "5.90±o.46 mmol/L" corrected the number.	Thank you very much for your comment. The value 5.90 ± 0.46 mmol/L has been correctly included in the manuscript.
3. In line 254, the author said "whereas none (0%) of the rats in the treatment group showed signs of diabetes". What are signs of diabetes you mean here explain with references.	Thank you very much for your comment. The term "signs" was replaced with "symptoms." This determination was based on the blood glucose levels measured after 6.0 hours of fasting and 2.0 hours following oral glucose loading.
4. Line 271 needs strong reference.	Thank you very much for your comment. Line 271 in the manuscript accurately describes and reflects the overall findings of our study, which is discussed in detail later (or in the following paragraphs).

5. Lines 289 and 302 require references.	Thank you very much for your comment. The following sentence was newly added: “A comparison of postprandial blood glucose in the rats that became diabetic in both groups after the second STZ dose until Day 90 revealed a significant reduction in PBG in the supplemented diabetic rats compared to the unsupplemented diabetic rats ($p<0.0001$).” This finding serves as strong support for the subsequent statement.
6. Rewrite the line “While further mechanistic and translational studies are warranted” in conclusion.	Thank you very much for your comment. The line was written correctly.

Round 2

Reviewer 1 Name: Unwilling to disclose Conflict of Interest: None Date of Reviewer’s Comments: November 13, 2025 Date of Author Response: Not required	
Reviewer 1 Comments	**Author Response**
Reviewer Recommendation: Accept Submission	-
Reviewer 2 Name: Unwilling to disclose Conflict of Interest: None Date of Reviewer’s Comments: Not responded Date of Author Response: Not required	
Reviewer 2 Comments	**Author Response**
Reviewer Recommendation: Not responded	-

DOI: https://doi.org/10.71193/jcid.20250009 | Journal of Chemistry Insights and Discoveries | 02(01): 20250009