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The Impact of Aerobic Exercise Combined with Lactobacillus Supplementation on the Expression of Adiponectin and Appl1 Genes in the Liver Tissue of Wistar Rats with Fatty Liver Disease

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1. Round 1

1.1 Reviewer 1

Reviewer:

The statement "NAFLD is closely associated with metabolic disorders such as obesity, type 2 diabetes, and dyslipidemia" could benefit from referencing more recent data or meta-analyses to strengthen the association between NAFLD and metabolic disorders.

The section on "temperature (22±3°C), relative humidity (30-60%), and 12:12 hour light-dark cycle" should explain how these controlled conditions align with best practices for animal studies related to metabolic research.

In the description of the Lactobacillus culture conditions, clarify the relevance of using "L-cysteine HCL" and how this enhances the culturing process, if applicable.

The statement "Motivation was provided through gentle tail touching; no electric shock was used" might benefit from a discussion on ethical considerations and the impact on the rats' stress levels.

The RNA extraction steps are detailed, but adding information on how RNA integrity was ensured post-extraction could improve the rigor of this section.

Consider elaborating on the statistical significance or biological relevance of the standard deviations presented for gene expression in the different groups.

The claim "The combination of aerobic exercise and Lactobacillus supplementation showed a positive effect on APPL1 gene expression" could be expanded to discuss potential mechanisms behind this synergistic effect.

Author revised the manuscript and uploaded the updated document.

1.2 Reviewer 2

Reviewer:

The phrase "Understanding these gene expression changes is vital for developing targeted therapeutic strategies for NAFLD" could be expanded to discuss specific therapeutic strategies currently under investigation.

The explanation of APPL1's role could include a discussion on how APPL1 specifically influences insulin signaling pathways in the liver to make the explanation more comprehensive.

The allocation of rats into groups is described clearly, but consider justifying why eight rats per group were deemed statistically sufficient for detecting significant differences.

The method of "oral tetracycline (140 mg/kg body weight)" could be strengthened by referencing past studies that used a similar approach to induce fatty liver and discussing its validity as a model.

The pairwise comparison results for adiponectin need a more in-depth explanation of how these differences translate to potential therapeutic benefits for NAFLD.

The sentence "Adiponectin regulates glucose and lipid metabolism through activation of various signaling pathways" could benefit from a more detailed discussion of specific pathways involved.

The statement "These effects are mediated through the activation of AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptors (PPAR)" might benefit from referencing additional studies to solidify this claim.

Author revised the manuscript and uploaded the updated document.

2. Revised

Editor’s decision after revisions: Accepted.

Editor in Chief’s decision: Accepted.