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RECENZJA

rozprawy doktorskiej Maima Matin, MSc „Interwencja nutraceutyczna z imbirem (*Zingiber officinale*) moduluje zmiany w wątrobie związane z wiekiem u myszy”.

REVIEW

Doctoral dissertation Maima Matin, MSc ”Nutraceutical Intervention with Ginger (*Zingiber officinale*) Modulates Age-Related Liver Changes in Mice”

1. Dissertation topic

The work presented to me for evaluation was carried out at the Institute of Genetics and Animal Biotechnology of the Polish Academy of Sciences. The presented doctoral dissertation is based on a documented scientific output dedicated to the ginger modulation age-related liver changes in mice. It together form an interesting and coherent work, with each paper addressing a complementary aspect of the research problem. Collectively, it provide a comprehensive and well-structured contribution to the field, integrating individual findings into a unified narrative that enhances the broader significance of the work. The present doctoral research therefore aimed to investigate whether chronic dietary ginger supplementation can mitigate age-associated hepatic deterioration by influencing redox balance, lysosomal function, inflammatory signaling, and tissue ultrastructure.

2. Candidate's knowledge and summary of work

The candidate carefully describes the current state of knowledge related to the research conducted by the doctoral candidate, and the subsections are well written. She comprehensively

presents the experimental design and methodology, providing detailed descriptions of the animal model, biochemical assays, enzymatic analyses, gene expression techniques, and histological evaluations. The applied methods are appropriate, well-justified, and ensure the reliability of the results.

The dissertation includes results from three thematical coherent publications including first publication „Effects of Ginger (*Zingiber officinale*) on the Hallmarks of Aging. Biomolecules” is a review of existing knowlede. It provides a comprehensive review of evidence linking ginger and its bioactive compounds to the hallmarks of aging, drawing on in vitro, in vivo, and clinical studies. It highlights ginger’s antioxidant, anti-inflammatory, and pro-autophagic properties relevant to aging biology. Based on these findings, animal studies were designed to further investigate and validate these effects.

Second publication „Ginger (*Zingiber officinale*) dietary supplementation in mice regulates liver antioxidant defense systems in a dose- and age-dependent” experimentally evaluated the effects of dietary ginger supplementation on hepatic antioxidant status in mice across three age groups (3, 6, and 12 months). Control animals showed age-related changes within liver. Ginger modulated these parameters in an age- and dose-dependent manner, improving antioxidant defenses in middle-aged and older mice, while young mice showed reduced DPPH activity. The higher dose consistently increased glutathione across all groups. Ginger reduced lipid peroxidation (MDA), particularly in young mice, with limited effects in older animals, while SOD activity remained unchanged, indicating a predominant action via non-enzymatic antioxidant pathways. Overall, ginger enhanced hepatic antioxidant defenses, especially in aged liver tissue. As a novel finding, a differential effect of the intervention on the liver was observed across different age groups of mice.

The third paper „Ginger Supplementation Supports Liver Health During Aging Through Regulation of Lysosomal Function and Molecular Markers” provides a deeper and more detailed look at the ultrastructure of liver cells. The cellular and molecular mechanisms underlying liver aging and the effects of ginger supplementation were investigated. Aging was associated with increased lysosomal enzyme activity, mitochondrial damage, hepatocyte hypertrophy, and lipofuscin accumulation, reflecting impaired cellular homeostasis and proteostasis and Ginger supplementation modulated these changes. However, high-dose supplementation in aged animals induced mild ultrastructural stress, highlighting a dose-dependent response. Overall, the study demonstrated that ginger influences key pathways involved in hepatic aging, including lysosomal function, inflammation, and nutrient signaling.

3. Independent work skills of the candidate

The Candidate presents experience in biochemical, molecular, and cellular methodologies. Importantly, these skills were not only acquired but also applied and further developed within the framework of the doctoral research. The ability to integrate diverse experimental techniques into a coherent research strategy reflects a high level of methodological awareness and scientific rigor.

Moreover, the Candidate shows understanding of the broader implications of the research, including its potential applications in evidence-based nutrition and therapeutic strategies targeting inflammation and age-related disorders what is an important indicator of scientific maturity.

The Candidate has also demonstrated a commitment to teaching and academic engagement. Delivered lectures and participation in doctoral forums indicate the ability to transfer knowledge effectively and engage with both academic and broader audiences. This pedagogical activity complements the research profile and reflects readiness for future academic responsibilities.

The scientific activity of the Candidate is noteworthy. The publication record, comprising 35 peer-reviewed articles (including 30 with Impact Factor), reflects exceptional productivity and strong engagement in international research collaboration. The thematic coherence of the publications, focusing on natural products, nutraceuticals, and molecular mechanisms of aging and disease, further strengthens the scientific value of the work.

4. Original contribution of the dissertation

The present study provides a perspective on the role of dietary ginger supplementation in modulating age-related hepatic dysfunction. Unlike previous studies focusing on single pathways, this work simultaneously examines redox balance, lysosomal activity, inflammatory signaling, and ultrastructural changes, revealing their coordinated regulation during aging.

A novelty lies in demonstrating that ginger preferentially enhances non-enzymatic antioxidant systems. Furthermore, the study identifies a context-dependent and age-specific response, with older organisms showing greater sensitivity to intervention, changes also showed dose-response relationship,

Collectively, these findings position ginger as a multi-target, context-dependent geroprotective agent, advancing current understanding of how phytochemicals modulate complex aging processes beyond simple antioxidant activity.

The research interests are clearly defined and relevant. The focus on health-promoting properties of natural products, particularly ginger (*Zingiber officinale*), and their role in modulating aging-related processes, oxidative stress, and immune responses, represents an important and timely research direction.

5. Questions

1. The proposed future research, aimed at elucidating interactions between bioactive compounds and immune signaling pathways with clear potential for translational impact in the prevention and management of chronic diseases. Ginger was marked as a candidate for future translational studies in geriatric health, particularly for interventions targeting age-related liver dysfunction and sets the stage for future investigations.
What further investigations could be conducted to deepen the insights acquired from this doctoral research?
2. It would be interesting to examine how ginger affects not only the liver of aging animals, but also animals with liver diseases. Are you aware of any models that could be used for this purpose?
3. Are the dosages administered to mice relevant and both used doses are safe for humans?
Can the same product used in mice also be used in humans?
4. What should be the duration of administration - continuous or intermittent? In the work presented, ginger was integrated into the diet, enabling the mice to consume it continuously. How can this be connected to human application?
5. Should the outcomes of ginger be taken into account for administration to young individuals considering the differing results when compared to older individuals? If not, at what age should supplementation commence?

6. Final opinion

In summary, I conclude that the doctoral candidate is capable of independently formulating and solving a scientific problem, appropriately selecting research techniques, and conducting a discussion of the obtained results. All of this demonstrates that she has the ability to carry out independent research, demonstrates independence and creativity. The doctoral dissertation of Maima Matin is valuable and may make a contribution to improving and refining the positive ginger influence on liver function. The doctoral candidate demonstrated theoretical knowledge in the field of the conducted research, as well as skills in carrying out research work.

Maima Matin's doctoral dissertation, entitled "Nutraceutical Intervention with Ginger (*Zingiber officinale*) Modulates Age-Related Liver Changes in Mice" meets the requirements specified in Article 187 of the Act of 20 July 2018, the Law on Higher Education and Science. Therefore, with full conviction, I recommend that the Scientific Council of the Institute of Genetics and Animal Biotechnology of the Polish Academy of Sciences in Jastrzębiec, Poland admit Maima Matin to the next stages of the doctoral process.

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