

Biała Podlaska, 12 March 2026

prof. dr hab. Konrad Kamil Hozyasz

Zakład Pielęgniarstwa

Wydział Nauk o Zdrowiu

Akademia Bialska im. Jana Pawła II

ul. Sidorska 95/97, 21-500 Biała Podlaska

CRITICAL REVIEW

of the doctoral dissertation submitted by Maima Matin, M.Sc.

titled:

“Nutraceutical Intervention with Ginger (*Zingiber officinale*) Modulates Age-Related Liver Changes in Mice”

The doctoral dissertation of Ms Maima Matin, submitted for evaluation, was conducted under the supervision of Prof Artur Jóźwik and Prof Atanas G. Atanasov at the Institute of Genetics and Animal Biotechnology of the Polish Academy of Sciences, Jastrzębiec, 05-552 Magdalenka.

Matin’s research topic concerns the age-dependent effects of dietary ginger supplementation on liver antioxidant defence systems, activity of lysosomal enzymes, and inflammatory signalling in mice. The thesis includes two research articles and one review article published in international scientific journals indexed in the Journal Citation Reports (JCR) list. All three articles underwent rigorous external peer review by experts in the field. The articles are extensive and contain completed work.

The variety of research methods and results demonstrates a comprehensive approach to the subject. The articles are preceded by a list of abbreviations, summaries in English and Polish, and an independent introduction in English. This introduction is 46 pages long and extensively discusses the hallmarks of ageing, liver ageing, the therapeutic potential of ginger, the aim of the study and hypotheses, methodological overview, the results obtained in two experimental studies and a discussion. The introduction is followed by a list of 96 unnumbered references. Generally, the introduction demonstrates good space-to-information efficiency. The reviewed work has been prepared with great care and is impeccable in terms of editing form. The text is clear, written using appropriate scientific terminology, and is very readable.

Formal Assessment of the Doctoral Dissertation

The formal aspects of the dissertation are satisfactory. Experimental studies in a mouse model were performed after obtaining consent from the local Institutional Animal Care and Use Committee (permit No. 14186201). The PhD Candidate, with outstanding overall scientific achievements with an IF of 172.3 and a Hirsch index of 9 (Web of Science Core Collection), provided precise information on her own contribution to the publications included in the dissertation. According to this information, Ms Martin's participation in research and manuscript preparation ranges from 75 to 84%. Ms Maima Martin and co-authors declared that no Generative AI was used in the creation of the manuscripts.

This doctoral dissertation is based on the following:

- two original research articles:

1. Martin M, Wysocki K, Horbańczuk JO, Rossi L, Atanasov AG. Ginger (*Zingiber officinale*) dietary supplementation in mice regulates liver antioxidant defence systems in a dose- and age-dependent (manner). *Frontiers in Pharmacology* 2025;16:1597599

doi: 10.3389/fphar.2025.1597599

IF 4.8 (100 pkt. MNiSW)

2. Martin M, Łysek-Gładysińska M, Ksepka N, Frazzini S, Wieczorek A, Jóźwik A. Ginger supplementation supports liver health during aging through regulation of lysosomal function and molecular markers. *Animal Science Papers and Reports* 2025;43:385-404

doi: 10.2478/aspr-2025-0026

IF 1.1 (100 pkt. MNiSW)

The cumulative impact factor of these publications is 5.9, and the total score according to the (Polish) Ministry of Science and Higher Education (MNiSW) is 200. In both papers, Ms Martin is the first author. Moreover, in the article published in *Animal Science Papers and Reports*, the candidate is one of the two corresponding authors.

- one review article:

1. Martin M, Joshi T, Wang D, Tzvetkov NT, Martin FB, Wierzbicka A, Jóźwik A, Horbańczuk JO, Atanasov AG. Effects of ginger (*Zingiber officinale*) on the hallmarks of aging. *Biomolecules* 2024;14:940.

doi.org/10.3390/biom14080940

In this study, nine researchers contributed. Ms Matin was the first author, and her second supervisor, Prof A. Atanasov, was the corresponding author.

Substantive Evaluation

The interesting review article published in *Biomolecules* critically evaluated the available literature on ginger and ageing and was defined by the PhD candidate herself as an introduction to her own original research. In this article, the list of the hallmarks of ageing indicated in two influential reviews by Carlos Lopez-Otin and co-workers in *Cell* in 2023 was extended, with good justification, from 9 to 12. Matin's review paper is extensive; however, it only partially applies ageing processes at the liver level. For example, Table 1 lists 18 *in vitro* studies on the active ingredients of ginger that potentially modulate the hallmarks of ageing, but only one of them used a liver model (HepG2 cells). The paper shows that there are numerous *in vivo* studies assessing the effect of ginger supplementation in high-fat diet-fed rodents, and there is a lack of studies focusing on the effect of ginger on well-being when using a standard diet in experimental animals at different ages.

Ginger was domesticated 5,000 years ago by the Austronesian people. According to the FAO, in 2020, global ginger production reached over four million metric tons, with a value of over USD 3 billion, and there is a prospect for further rapid growth. All year round, every Polish discount store offers dried cranberries and fresh ginger. Consuming cranberries protects against the recurrence of urinary tract infections. The mass consumption of ginger in Poland is not due to its historically established indispensability in the kitchen, but to the widespread awareness of its health-promoting properties. However, it is in vain to look for guidelines on how healthy people from childhood to older age should consume ginger. As the PhD candidate rightly noted, "validating ginger as an intervention could pave the way for its use as a nutraceutical to support healthy ageing, particularly for the liver and metabolic health." As a reviewer with a strong clinical background, I appreciate and congratulate Ms Maima Matin and her supervisors for choosing this research topic.

Both research papers presented an intervention by supplementing a standard diet with ginger powder (without supplementation, 0.6% or 1.8%) in 144 male Swiss Webster mice in three equal age groups (3, 6, and 12 months old) for 3 months. The publication in *Frontiers in Pharmacology* reported the results of biochemical assays on liver homogenates, which measured total antioxidant capacity, DPPH radical scavenging capacity, vitamin C concentration, total phenolic content, superoxide dismutase activity, malondialdehyde levels, and reduced glutathione levels. When starting the study, it was initially assumed that the greatest increases in antioxidant defence under the influence of ginger supplementation would occur in the oldest mice. In general, this assumption was correct; however, evidence was found indicating that the antioxidant effects of ginger are likely mediated by both direct and indirect pathways with dose-dependent effects. While younger mice showed decreased DPPH radical scavenging with ginger supply, both middle-aged and older mice exhibited significantly increased activity. This is one of many observations made in this study that support the argument that age-specific responses highlight the need for a more personalised approach to ginger consumption. The publication in *Animal Science Papers and Reports* focused on the activities of lysosomal enzymes, the expression of pro-inflammatory and nutrient-sensing genes (TNF- α and

PI3K), and histological and ultrastructural changes in liver tissue after 3 months of ginger supplementation. It was shown that ginger may help preserve lysosomal function, exert both stimulatory and regulatory effects, and reduce inflammatory signalling in the ageing liver. Moderate ginger supplementation effectively preserved hepatocellular ultrastructure and improved lysosomal function, particularly in young and middle-aged mice. The observation of mild subcellular stress in aged mice highly supplemented with ginger (1.8%) stimulates reflection on the safety of ginger consumption *ad libitum* by older adults.

Detailed Comments

English and Polish summaries included an awkward statement about the inclusion of three works/publications investigating the therapeutic potential of ginger in the dissertation. The real investigation occurred in the two original publications, while the comprehensive review of the evidence linking ginger to the hallmarks of ageing is devoid of meta-analytical features; thus, it is well done but only a review.

In my opinion, the introduction section of the dissertation lacks a methodological chapter that describes the criteria for selecting the Swiss Webster mouse strain for research, explains the reasons for choosing only male animals, and details the procedure for determining the amounts of low and high ginger supplementation. Fortunately, for the dissertation evaluation, I found this information in a paper published in *Frontiers in Pharmacology*.

It is difficult to disagree with the Author that ginger is a promising candidate for translational research in geriatrics. However, as the results of Ms Matin's research showed that dietary ginger supplementation modulates age-associated liver alterations and this process is not uniform across the lifespan, the need for translational research for older persons' consumption also applies to the developmental age population.

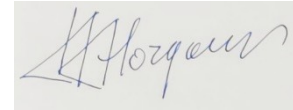
Overall Assessment and Final Conclusion

The doctoral dissertation submitted by Ms Maima Matin represents a significant and valuable contribution to the understanding of the health-promoting effects of ginger dietary supplementation at the liver level. I have no crucial critical remarks regarding the work and consider it to have high scientific merit. The results presented by the PhD candidate are original, constitute clear scientific novelty, and, to some extent, provide an innovative approach to the research problem. They hold substantial cognitive value and stimulate the conduct of confirmatory and detailed studies in a mouse model, even considering the variability associated with the oestrous cycle and clinical trials. The scope and quality of the results demonstrate that the problem of the impact of ginger on age-associated disturbances in hepatic homeostasis was addressed methodologically correctly and originally, thereby fulfilling the statutory requirements for doctoral dissertations. Importantly, this is a pioneering scientific work with a multi-parameter analysis, and its findings have been successfully published in two reputable, peer-reviewed, free-access journals, confirming their significance and quality. Ms Maima Matin has shown her ability for independent scientific investigation.

In conclusion, the doctoral dissertation meets the requirements set out in Art. 187 of the Act of July 20, 2018 – Law on Higher Education and Science (Journal of Laws 2023, item 742). It has been properly prepared, and the author has demonstrated the necessary skills to embark on the next

stage of her scientific career. Consequently, I recommend that the Scientific Council of the Institute of Genetics and Animal Biotechnology of the Polish Academy of Sciences in Jastrzębiec admit Ms Maima Matin to the next stages of the doctoral procedure.

The author declares that there are no conflicts of interest.

A handwritten signature in blue ink, appearing to read "H. Horgan", is enclosed in a light gray rectangular box.