

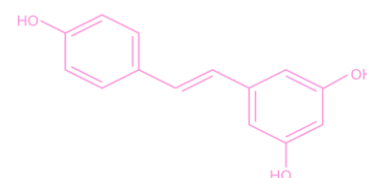
ABSTRACT

In recent years, there has been a dynamic development of research on organismal ageing, as well as a growing interest in bioactive compounds and nanomaterials in the context of mechanisms regulating longevity. Importance is attributed to sirtuins, enzymes involved in the regulation of metabolic processes, stress response, and the maintenance of cellular homeostasis. Despite numerous studies conducted on mammalian models and other selected model organisms, knowledge regarding the functioning of sirtuins in insects remains limited. Moreover, interactions between compounds such as resveratrol (RV), which is recognized as a modulator of sirtuin activity, and nanomaterials, including nanodiamonds (NDs), are still poorly understood, particularly in the context of their impact on ageing processes.

The first stage of this work included a literature review aimed at systematizing knowledge on the role of sirtuins in the regulation of ageing processes and summarizing information on the potential mechanisms of their modulation by bioactive compounds. Significant research gaps were identified, also regarding organisms other than classical laboratory models, including insects. The results of the review justified undertaking experimental studies focused on evaluating the effects of RV, NDs, and their combination on sirtuin activity and parameters related to longevity in a model organism - *Acheta domesticus*.

Stage II included preliminary studies, the aim of which was to assess the relationship between sirtuin activity, selection for longevity, and the organism's response to their potential modulators in the form of RV and NDs in *A. domesticus*. The obtained results showed that the longevity-selected strain (D) exhibited significantly higher sirtuin activity compared to the wild-type strain (H), which indicated a possible association of these enzymes with processes regulating survival in the studied insects. It was also indicated that insects selected for longevity (D strain) show a different response to modulators compared to the wild-type strain (H). At the same time, it was confirmed that both resveratrol and nanodiamonds may affect processes related to survival and enzymatic regulation, including sirtuins (SIRT1, SIRT6) and oxidative enzymes (SOD, catalase); however, their action is complex.

Stage III included the analysis of the effects of RV and NDs administered separately on survival, sirtuin activity, oxidative stress, and DNA damage. RV and NDs showed mainly short-term, context-dependent effects, without a sustained impact on the ageing process. In the H strain, NDs increased the median lifespan, while RV mainly affected the maximum lifespan of individuals, whereas in the D strain no significant changes were observed in these parameters,



which indicates greater stability of this strain. In the case of oxidative stress and sirtuin activity, no consistent trends were found, and the observed changes were transient and dependent on the developmental stage. The activity of SIRT1 and SIRT6 was not subject to sustained modulation, while SIRT6 increased its activity with age, independently of the applied factors. The effect on DNA damage was inconsistent, and in some cases, RV increased the level of damage markers, which suggests its dual action. Overall, the organism's response was strongly dependent on the strain and developmental stage.

Stage IV included the assessment of the effects of simultaneous administration of RV and NDs (RV+NDs). The results indicated a lack of a clear life-extending effect, as no changes were observed in the H strain, and in the D strain only a tendency towards an increase in maximum lifespan was observed. Oxidative stress parameters remained stable and showed only transient changes after the application of the combination (RV+NDs). The most pronounced effect concerned an increase in total sirtuin activity in the D strain, without sustained changes in SIRT1 and SIRT6. DNA damage markers showed transient increases (especially in the H strain), which indicated activation of repair mechanisms rather than accumulation of damage.

The obtained results allow the conclusion that both RV and NDs, as well as their combination, may modulate processes related to ageing; however, the mechanisms of these interactions are complex and dependent on many biological and environmental factors. The work highlights the important role of further research on the safety of nanomaterials and their interactions with bioactive compounds and also indicates the need to extend research to diverse biological models. *Acheta domesticus*, as an organism with a short life cycle and available selected strains, constitutes a valuable model for further studies on ageing mechanisms and the evaluation of the effects of new biologically active factors.

