## Hesperidin through Acting on Proliferating Cell Nuclear Antigen and Follicle Stimulating Hormone Receptor Expression Decreased Ovarian Toxicity Induced by Malathion

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Abstract: Background: Malathion is one of the most toxic agents widely used in agriculture throughout the world. This agent has adverse effects on the functions of multiple organs such as the reproductive system in both male and female genders. On the one hand, daily use of antioxidant supplementations such as hesperidin is capable to neutralize the deleterious impacts of malathion. Therefore, in this experimental study, the protective effects of hesperidin against ovarian toxicity induced by malathion were investigated. Material & Methods: Balb/c adult mice (n=32) were randomly divided into 4 groups including 1) the control group, treated with normal saline, 2) the Mal group, treated with 30mg/kg malathion, daily for 1 month, 3) Mal + Hes group, treated with 20 mg/kg malathion and 20 mg/kg hesperidin, daily for 1 month, and 5) Hes group, treated with 20 mg/kg hesperidin. At the end of the experimental period, mice were anesthetized and their drops of blood were collected to the assessment of some hormones such as LH, FSH, E2, and P4. Also, the right ovaries were used to H&E staining, and the left ovaries were used for IHC staining (PCNA and FSHR). Results: Histopathological assessments showed that the number of follicles, i.e. primordial, primary, and secondary, significantly decreased, while the atretic follicle counts remarkably increased compared to the control group (p<0.05). Hormonal levels revealed that the production of all mentioned hormones decreased in the Mal group in comparison with the control group (p<0.05). The expression of PCNA, as a proliferative marker, and FHSR, as a marker showing maturation, decreased when mice received malathion compared to the control group (p<0.05). Interestingly, treatment with hesperidin significantly neutralized the adverse effects of malathion on all mentioned parameters. Conclusion: Daily use of antioxidant supplementations such as hesperidin could alleviate the ovarian toxicity induced by malathion.

**Keywords:** malathion, ovary, antioxidant hesperidin, FSHR PCNA, ovary