

## **Abstract**

**Introduction:** Leukemia refers to the neoplastic proliferation of lymphoid and myeloid cells as a result of mutations in blood-forming stem cells. Leukemia is characterized by the abnormal accumulation of immature white blood cells (blasts) in the blood and organs. However, these cancer cells in large numbers are unable to perform the normal functions of blood cells, thus increasing susceptibility to infection. N-ethyl-n-nitrosourea (ENU) is an alkylating agent with the chemical formula, which is a very strong mutagen. Among the plant flavonoids, hesperidin is a bioactive compound that exists in the epicarp, endocarp, and mesocarp of different citrus species. Recent studies have shown the antioxidant, anti-inflammatory, anti-cancer, antiviral, and protective effects of this compound against cardiovascular disorders.

**Materials and Methods:** Female mice were divided into three groups of seven: the control group, the ENU group, and the hesperidin+ENU group. Hesperidin (20 mg/kg, intraperitoneally) was injected once a day for 30 days into the mice of the hesperidin+ENU group. Normal saline was injected intraperitoneally once a day into the control and ENU mice for 30 days. On the 31st day, ENU (80 mg/kg, single dose, intraperitoneally) was injected into the mice of the ENU group and the hesperidin+ENU group. Mice were monitored for weight changes and general condition for 90 days. At the end of 150 days after ENU injection, they were euthanized by ketamine/xylazine injection (65 mg/kg ketamine and 13 mg/kg xylazine, intraperitoneally). Fresh blood samples were collected from the hearts of mice and analyzed.

**Results:** Our results showed that hesperidin significantly increases the survival of mice up to 86% after exposure to ENU and prevents noticeable weight changes after exposure to ENU. Also, hesperidin improved parameters including mitochondrial membrane potential (MMP), reactive oxygen species (ROS), lipid peroxidation, and lysosome membrane damage. But there was no significant change in the level of reduced glutathione (GSH) and oxidized glutathione (GSSG).

**Discussion and Conclusion:** Finally, our results showed that hesperidin could significantly prevent the toxic effects of N-ethyl-n-nitrosourea.

**Keywords:** leukemia, N-ethyl-N nitrosourea, Hesperidin.