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Thesis title: ***"Exploration on the mechanism of action of fisetin/Mimosine on MTH-1 mediated therapy against skin cancer"***

Findings:

Under the present work we tried to explore the therapeutic efficacy of Fisetin and Mimosine against skin cancer cells. In this study we explored the effectiveness of these drugs on DNA damage, apoptosis and MTH 1 expression.

The present work encloses the following findings: Mimosine and Fisetin were both found to effective against skin cancer cells, but fisetin was found to be more effective compared to Mimosine. The A431 cell line, which is a type of human squamous cell carcinoma, was found to be more sensitive to the compounds compared to the A375 cell line, which is a human malignant melanoma cell line. This indicates that the A431 cells were more responsive to the treatment. Both Mimosine and Fisetin were effective in inhibiting the formation of colonies and the ability of skin cancer cells to metastasize. This means that the compounds were able to suppress the growth and spread of cancer cells. The compounds induced cell cycle arrest at the G0/G1 phase by inhibiting CDK2, a cyclin-dependent kinase. This means that the compounds prevented cancer cells from progressing through the cell cycle, leading to a halt in cell division. Both compounds affected the mitochondrial membrane potential and the levels of reactive oxygen species (ROS) in skin cancer cells. Changes in mitochondrial function and increased ROS levels can contribute to cell death and have implications for cancer cell survival. The study found that both compounds influenced apoptotic pathways and DNA repair pathways. They modulated the expressions of genes such as p21, MTH1, p53, and caspase 3, which are involved in regulating cell death and DNA repair processes. The compounds caused extensive DNA damage by inhibiting MTH1. This was supported by various staining techniques (DAPI, Annexin V, FITC, Acridine orange, Ethidium bromide) and molecular dynamics (MD) simulations, which confirmed the occurrence of DNA damage. The study concludes that both Mimosine and Fisetin have the potential to be potent chemotherapeutic agents for treating human skin cancer. The findings suggest that these compounds could be considered for future drug development in the field of cancer treatment.

In summary, the study provides new insights into the mechanism of action of Mimosine and Fisetin. These compounds affect various cellular processes, including proliferation, apoptosis, cell cycle, ROS levels, mitochondrial function, nuclear condensation, and the functional properties of MTH1.