Genetic Damage Mitigation by Metformin in X-Ray-Irradiated Human Skin Perfusion Model

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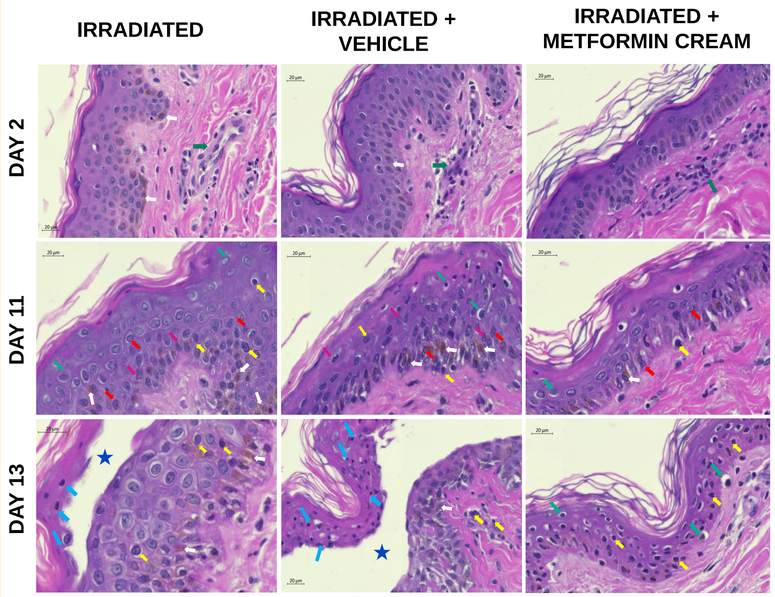
INTRODUCTION

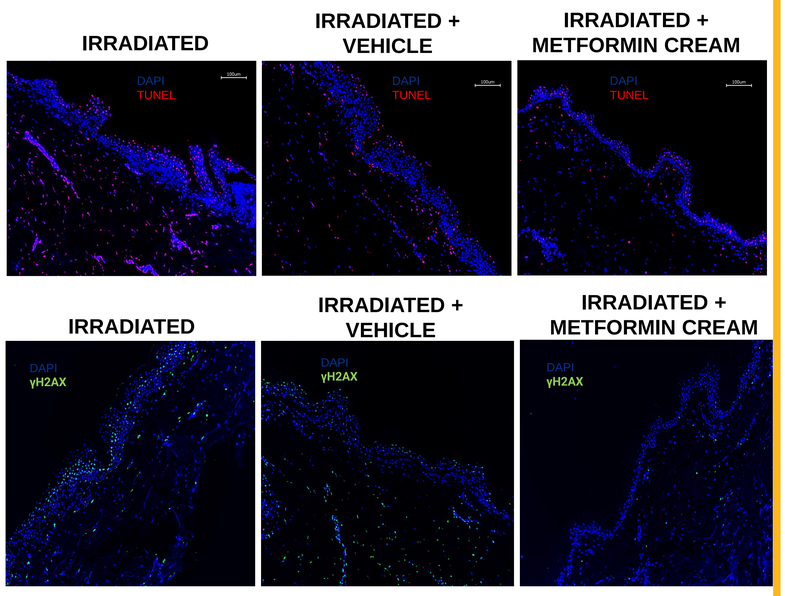
Radiation-induced DNA damage represents a critical challenge in both therapeutic and accidental exposure to ionizing radiation, particularly in the skin, where it leads to compromised integrity, genomic instability, and increased susceptibility to secondary injuries. Exposure to high-dose X-ray radiation, such as 10 Gy, induces double-strand DNA breaks, oxidative stress, and apoptosis, all of which can hinder tissue recovery and compromise skin function. Therefore, identifying agents capable of mitigating these effects is essential for enhancing skin recovery and reducing long-term complications. Metformin, a widely used anti-diabetic medication, has shown promise as a radioprotective agent due to its ability to activate AMP-activated protein kinase (AMPK), reduce reactive oxygen species (ROS), and enhance DNA repair pathways. This study evaluated the efficacy of topical metformin in reducing DNA damage in human skin following X-ray irradiation.

MATERIALS & METHODS

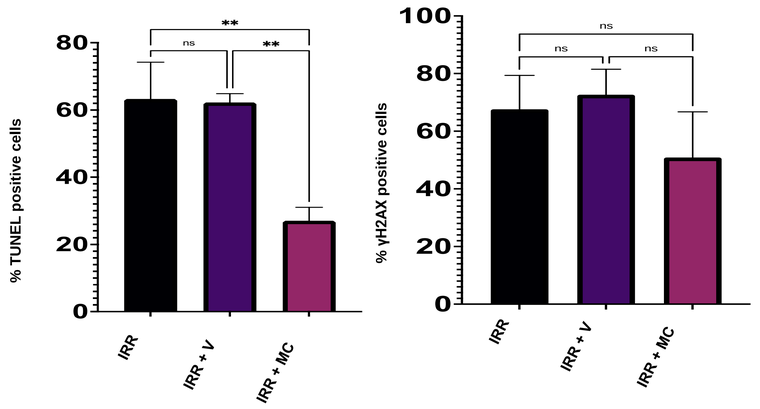
Skin flaps were exposed to 10 Gy X-ray radiation and treated with metformin cream, control cream, or left untreated. DNA damage markers (TUNEL staining and γH2AX foci) were assessed at days 2, 7, 11, and 13 post-irradiation. Metformin significantly reduced DNA damage and supported long-term repair, especially at later stages, compared to untreated skin.

RESULTS





Metformin significantly reduces radiation-induced cell death (TUNEL) and DNA damage (γH2AX) in skin cells



•H&E stained sections revealed reactive keratinocyte changes in epidermis and dermis of non-treated skin.

•Immunohistochemistry showed increased DNA damage, assessed by TUNEL activity and DS-DNA break (Gamma H2X).

•Quantification of TUNEL and Gamma H2X was calculated using the fluorescent intensity with ImageJ. It demonstrated significantly lower DNA damage and TUNEL activity in metformin-treated irradiated group, in comparison to irradiation only and control cream-treated groups This shows protective effects of metformin application in radiation-induced DNA damage.

CONCLUSIONS

•Metformin significantly mitigates radiation-induced genetic damage in human skin.

•It enhances DNA repair mechanisms and reduces apoptotic cell death.

•Metformin shows potential as a topical therapeutic agent for protection against ionizing radiations.

•It could be especially beneficial for patients undergoing radiotherapy.

•Metformin may also be useful in cases of accidental radiation exposure.

Metformin effectively reduces radiation-induced DNA damage and apoptosis while enhancing repair processes, highlighting its potential as a topical therapeutic agent for protecting human skin against ionizing radiation.