Enhanced UVA-induced cyclobutane pyrimidine dimer formation by silymarin without increased mutagenesis in cultured epithelial cells

E Fidrus[1]; P Fehér[2]; Cs Hegedűs[1]; EA Janka[1]; G Paragh[3]; I Bácskay[2]; É Remenyik[1]

1 Department of Dermatology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary

2 Department of Pharmaceutical Technology, University of Debrecen, Debrecen, Hungary

3 Departments of Dermatology and Cell Stress Biology, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

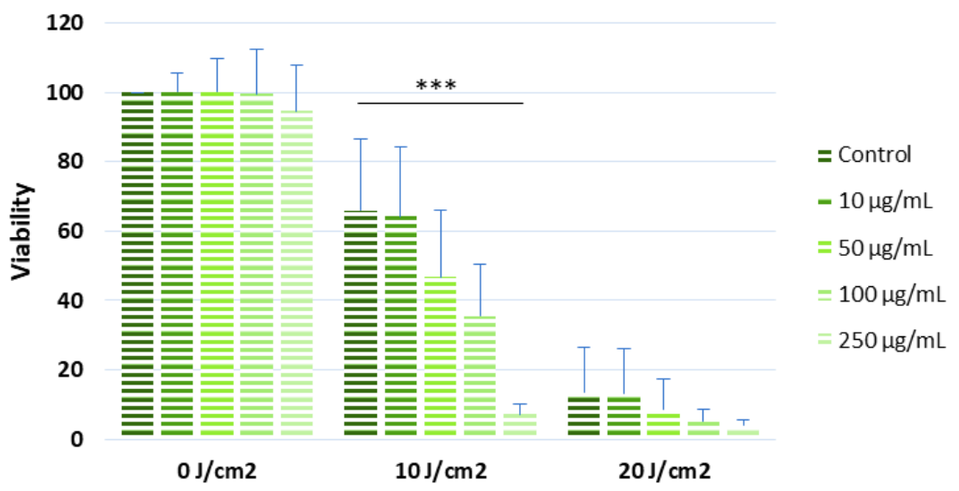
Introduction. Silymarin is a phytophenol extracted from the seeds of milk thistle (*Silibum marianum*). The application of the plant extract in the UV-protection of the skin is intensively studied due to its antioxidant and anti-inflammatory properties. However, the possible phototoxic effect of the polyphenol was also shown. Based on these findings the dermatological application of this polyphenol is fairly controversial.

ROS scavenger ⟷ **UV-A photosensitizer**

Aim of study: to investigate the effects of silymarin on the viability, ROS (reactive oxygene species) production, CPD (cyclobutane pyrimidine dimer)-formation and mutagenesis on UVA-exposed epithelial cells.

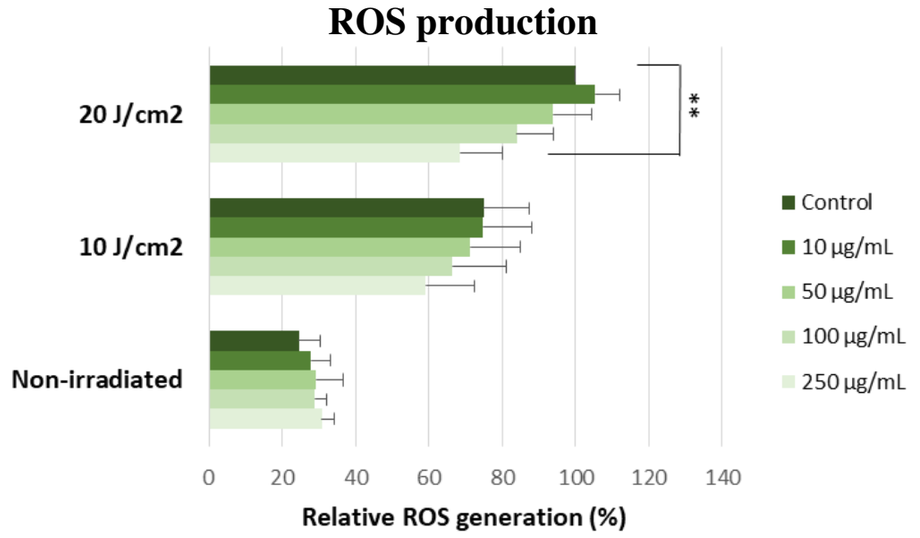
Materials and methods.
HaCaT immortalized keratinocyte and CHO (Chinese hamster ovary) cell lines were treated with silymarin for 30 min, then exposed to 10 or 20 J/cm^2 UVA. Viability, ROS production, cyclobutane pyrimidine dimer (CPD) formation and HPRT gene mutagenesis of the cells were measured by flow cytometry, CPD-specific ELISA and HPRT gene mutation assay, respectively.

Cell viability



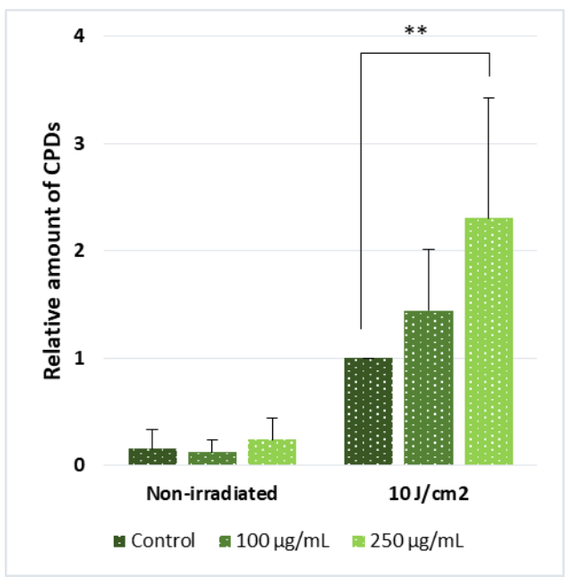
Silymarin treatment significantly enhanced UVA-induced apoptosis after 10 J/cm^2 UVA-treatment

ROS production



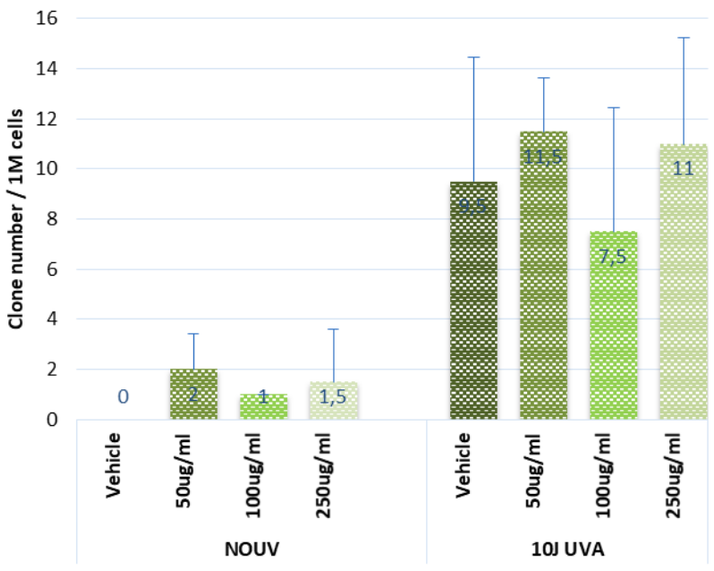
Contrarily to the photosensitizer effect, silymarin significantly reduced intracellular ROS after UVA treatment.

CPD generation



Silymarin enhanced UVA-induced CPD formation in DNA after UVA-irradiation.

HPRT mutagenesis



Silymarin treatment did not influence UVA-induced muation of the cells despite the increased CPD formation.

Conclusion.

- In our experiments, both **antioxidant** effect and **photosensitizer** properties of silymarin were demonstrated.
- Silymarin-treated cells showed **increased UVA-induced DNA damage without the change of UVA-mutagenesis**.
- We provide evidence for the **complex effects of silymarin in modifying UV response** and thus the need for careful consideration before using silymarin in dermatological preparations.

Acknowledgments: Our work was supported by the European Regional Development Fund co-financed by the European Union (GINOP- 2.3.2-15-2016-00005) and the Hungarian National Research Development and Innovation Fund (OTKA K120206).