

# **Beyond UVA+UVB Photoprotection: Approaches to Mitigate Oxidative Stress Associated with Boundary Region Wavelengths (Longest Ultraviolet A + High Energy Visible Light)**

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# Introduction, Objectives, and Methods

## Introduction

- Solar UV radiation damages skin primarily through the generation of reactive oxygen species (ROS).
- Although ultraviolet (UV) filters effectively block UVB and most UVA rays, they are less effective against the boundary region wavelengths:
  - Longest UVA (LUVA) wavelengths (380–400 nm), and
  - High energy visible light (HEVL; 400–760 nm).
- LUVA wavelengths penetrate deeper and are present year-round. HEVL, within the visible spectrum, has been shown to induce significant oxidative stress and skin pigmentation.
- Therefore, incorporating antioxidants (AOX) into sunscreens is essential for enhanced photoprotection.

## Objectives

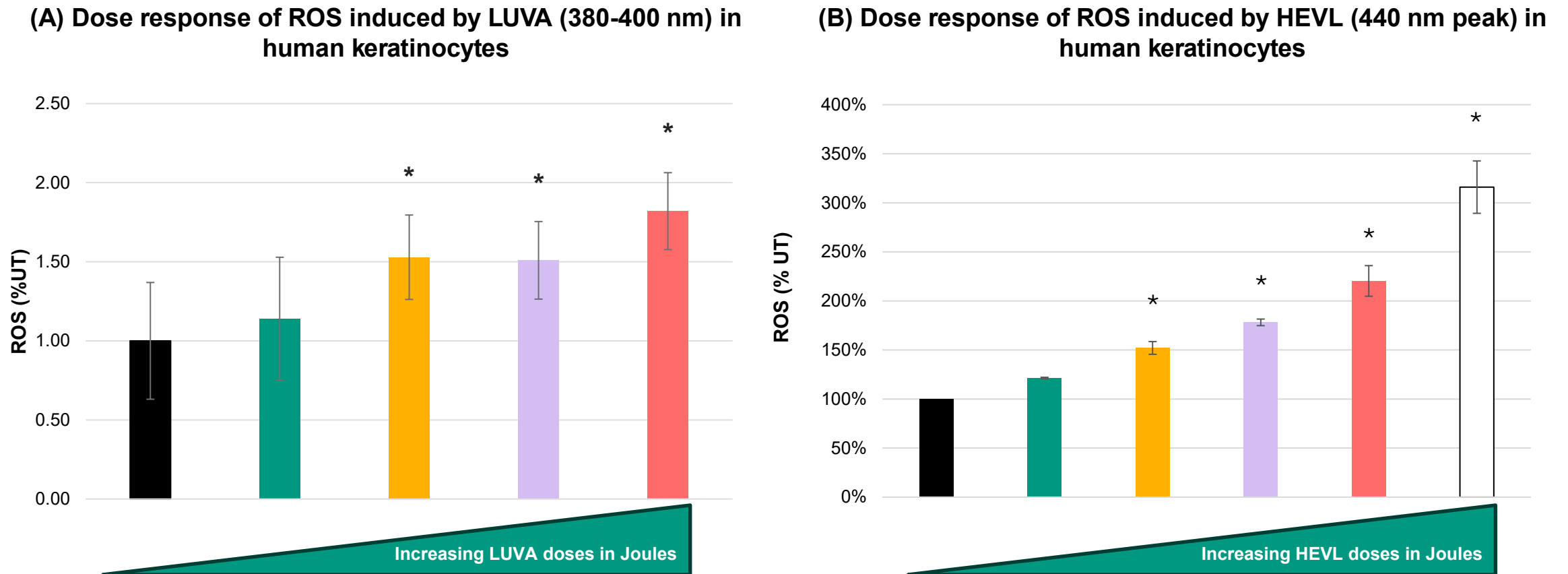
- To create a pre-clinical model to assess the oxidative damage caused by LUVA and HEVL wavelengths.
- To evaluate various AOX for their abilities to inhibit oxidative damage caused by the LUVA and HEVL wavelengths.

## Methods

- Human primary keratinocytes and/or fibroblast cells were exposed to LUVA and HEVL (Boundary Region Wavelengths). ROS levels were measured using a fluorescent dye and compared to untreated controls.
- Seven AOX were screened for their abilities to inhibit LUVA-induced ROS in human primary keratinocytes.
- A parthenolide-free Feverfew extract combined with Vitamin E was evaluated in primary human keratinocytes and fibroblasts, and compared with a marketed AOX against blue light and LUVA exposure.

# Dose Responses of Boundary Region Wavelengths Showed Significant Induction of ROS in Human Keratinocytes

Figure 1. ROS Induction of Boundary Region Wavelengths

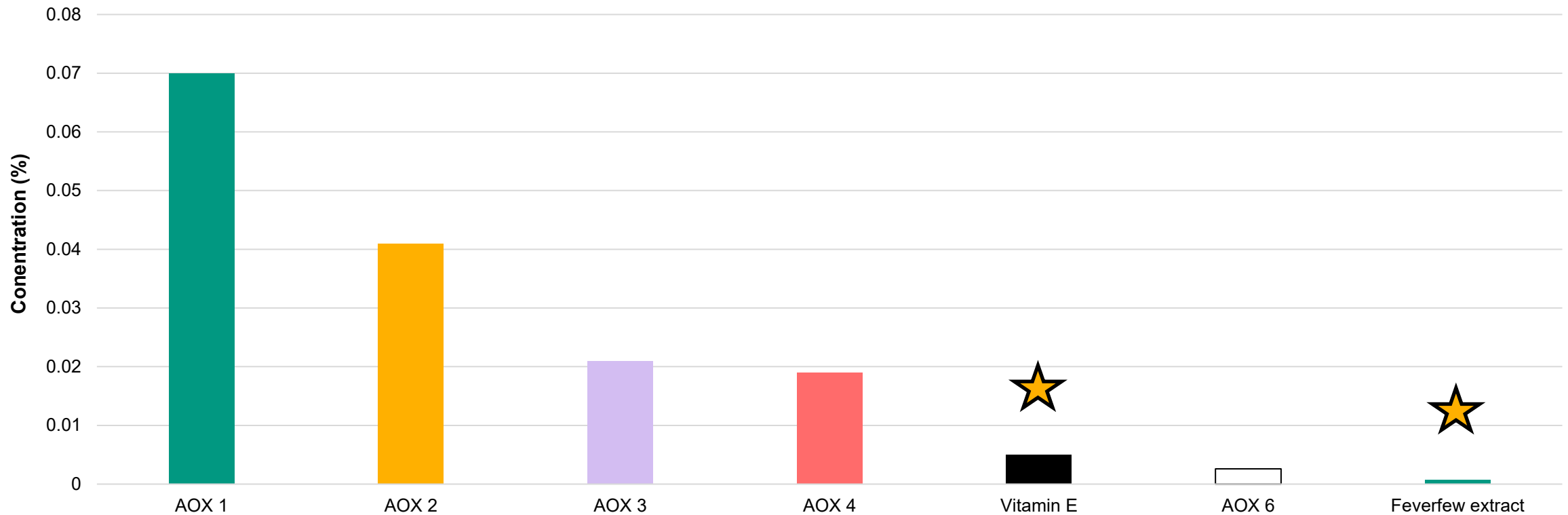


\*P<0.05 vs UT.

HEVL, high-energy visible light; LUVA, longest ultraviolet A; ROS, reactive oxygen species; UT, untreated

# AOX Revealed Different Potencies Against LUVA-induced ROS in Human Keratinocytes: Vitamin E and Parthenolide-free Feverfew Extract Were Potent ROS Inhibitors

Figure 2. IC<sub>50</sub><sup>a</sup> of AOX for LUVA-induced ROS Inhibition in Human Keratinocytes



<sup>a</sup> Higher IC<sub>50</sub> Indicates lower AOX potency. AOX pre-treatment revealed variable efficacy, with Vitamin E and parthenolide-free Feverfew extract emerging as potent AOX (denoted with a star). AOX, antioxidant; IC<sub>50</sub>, half-maximal inhibitory concentration; ROS, reactive oxygen species

# A Currently Marketed AOX in a Sunscreen was Used to Evaluate How the Proposed AOX Combination Performs Across Cell Lines

**Table 1. Assessment of AOX-mediated ROS Inhibition (%) Under Different Light Exposures in Two Different Skin Cell Types**

AOX	LUVA		HEVL	
	Keratinocytes	Fibroblasts	Keratinocytes	Fibroblasts
<b>A marketed AOX</b>	-	-	-	+
<b>Feverfew Extract + Vitamin E</b>	+	+	+	+

AOX activity was assessed in human keratinocytes and fibroblasts under LUVA or HEVL exposure; + denotes the presence of ROS inhibition; – denotes absence of ROS inhibition compared with irradiated controls; AOX, antioxidant; HEVL, high energy visible light; LUVA, longest ultraviolet A; ROS, reactive oxygen species.

## Conclusions

- A screening model was developed to differentiate AOX efficacy against boundary light exposure-induced ROS.
- This approach revealed that not all AOX are effective against boundary light exposure in different skin cell types.
- Although IC<sub>50</sub> values provide a useful comparative insight into AOX potency, the selection of AOX for sunscreen products must also consider factors such as stability, formulation compatibility, and patient safety or irritation potential to ensure suitability for real-world application.
- These results showed that Feverfew + Vitamin E is a powerful, broad-spectrum AOX combination, offering robust protection and suitability for real-world application.
- Feverfew + Vitamin E are anticipated to deliver benefits complementary to a broad-spectrum sunscreen's standard UV filters to reduce the potential for hyperpigmentation and oxidative stress in multiple skin cell types.