

# The Effect of Oral *Polypodium leucotomos* Extract (PLE) on Ultraviolet-induced Changes in the Skin

Indermeet Kohli, PhD, James L. Griffith, MD, Prescilia Isedeh, MD, Narumul Silpa-archa, MD, Mohammed Al-Jamal, MD, Henry W. Lim, MD, Iltefat H. Hamzavi, MD.

Multicultural Dermatology Center, Department of Dermatology, Henry Ford Hospital, Detroit, MI

**Introduction:** *Polypodium leucotomos* (PLE, Heliocare™) is a tropical fern from Central and South America that contains multiple polyphenols with anti-inflammatory, anti-oxidative, chemoprotective, and immunomodulatory properties demonstrated in numerous investigations. Recently, one of these investigations noted a reduction in subjectively graded erythema and increase in patient's minimal erythema dose following twice daily ingestion of 240 mg of PLE for 28 days.

**Objective:** To determine the effect of short-term PLE, specifically 2 doses, on clinical and histologic parameters following UV and visible light irradiation to subjects with skin phototypes I-III.

## Methods:

22 healthy subjects, skin phototypes I-III, were enrolled into an Institutional Review Board approved study.

- Day 1: subjects were irradiated with ultraviolet A1 (UVA1, 340-400 nm), ultraviolet B (UVB, 308 nm), and visible light (VL, 400-700 nm).
- Day 2: Subjective (Investigator Global Assessments, IGA, and Minimal Erythema Dose, MED) and objective clinical assessments (colorimetry assessments) of erythema and pigmentation plus histologic evaluations (unirradiated skin, irradiated skin pre-PL) were performed.
- Day 3: 240 mg of PLE was ingested 2 hours and 1 hour prior to irradiation with UVA1, UVB, and VL.
- Day 4: Subjective, objective, and histologic (irradiated skin post-PL) assessments were performed.

## Subjective results: IGA and MED

All 22 subjects displayed UVB-induced erythema, but limited to no response was observed for UVA1 and visible light.

17 of 22 subjects displayed decrease in clinical findings of UVB-induced erythema following 2 doses of PLE.



7 of 22 subjects exhibited an increase in MED following PLE ingestion. Yellow circle denotes site of MED. **SPF = 1.5**

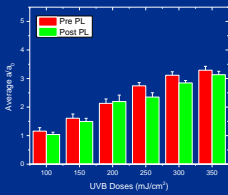
10 of 22 subjects exhibited an increase in objective erythema, which was not enough to raise the MED. Yellow circle denotes site of MED.

## Objective results: Colorimetry

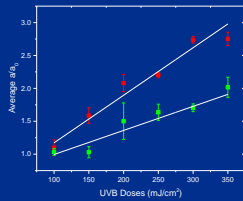
Average  $a^*/a_0$  for all sites of irradiation decreased by 7% ( $p < 0.05$ ) post-PLE, and 13% lower post-PLE in those showing a decrease in clinical erythema ( $p < 0.05$ ).  $a^*/a_0$  denotes intensity of erythema standardized to subject's innate basal cutaneous erythema.

Individually, most subjects (responders) showed a shift in their dose-response slope following PLE ingestion. The average decrease in slope for all subjects was 18% ( $p < 0.05$ ), and 35% in those showing a clinical response ( $p < 0.05$ ). Dose-response slopes of  $a^*/a_0$  were linear from 0.5-2.8 MED.

### Average $a^*/a_0$ for All subjects

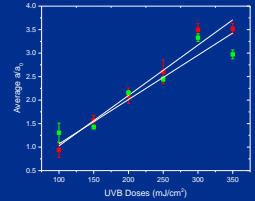


### Responder



### Dose-Response Slope:

### Non-Responder

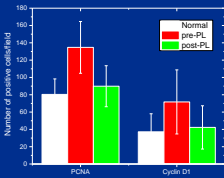


In the graphs above, **RED** is pre-PLE and **GREEN** is post-PLE.

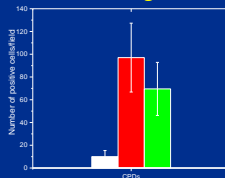
## Histologic Results:

### Proliferation:

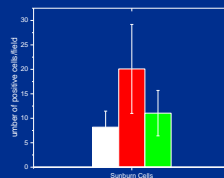
#### PCNA & Cyclin D1



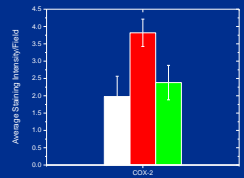
#### DNA Damage: CPDs



#### Apoptosis: Sunburn Cells



#### Inflammation: COX-2



- *Polypodium leucotomos* offers limited utility as SPF, but significant implications for reducing UVB-induced molecular damage. Most notably, both total DNA damage and proliferation amidst a background of unrepaired DNA damage were reduced.
- A near-immediate improvement in the photobiologic dose-response to UV radiation was observed in most subjects following ingestion of two 240 mg doses of PLE. This is manifested as greater reduction of erythema with every UVB dosing increment.

**Conflicts of Interest:** Only Drs. Lim<sup>1</sup> and Hamzavi<sup>2</sup> have relevant disclosures: Consultant – Ferndale<sup>1</sup>, Johnson & Johnson<sup>1</sup>, Sanofi<sup>1</sup>, Uriage<sup>1</sup>. Research support – Clinuvel<sup>1,2</sup>, Estee Lauder<sup>1,2</sup>, Ferndale<sup>1,2</sup>.