Photoprotection Beyond the UV Spectrum

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Disclosure

- **Investigator:**
  - Estée Lauder
  - Ferndale
  - Allergan
Photoprotection

- Shade
- **Sunscreens**
- Clothing
- Hat
- Sunglasses
- **Non-topical agents**

Sunlight & Reactive Oxygen Species

ROS is generated following exposure to:

- UV, especially UVA
- Visible light (Liebel, F. JID 7/12; 132:1901)
Antioxidants & Sunscreens

Sunscreen + antioxidants >> sunscreen alone in:

• Suppressing UV-induced pigmentation, depletion of Langerhans cells, induction of MMP9

• Suppressing infrared A induction of MMP1
Ground Level
Spectrum of Sunlight
Role of Visible Light
UVA1 vs Visible Light
(Mahmoud, BH, et al. J Invest Dermatol 8/10; 130:2092)

70 minutes of sun exposure

UVA1
20 J/cm²

UVA1: 340-400 nm

Immediate

1 week
UVA1 vs Visible Light

(Mahmoud, BH, et al. J Invest Dermatol 8/10; 130:2092)

70 minutes of sun exposure

UVA1
20 J/cm²

Visible light
320 J/cm²

Immediate

1 week
Skin Type IV-VI vs Skin Type II
(Mahmoud, BH. J Invest Dermatol. 8/10; 130:2092. Detroit)
Visible light may have a role on conditions aggravated by sun exposure such as PIH and melasma, esp. in dark-skinned individuals.

Currently available organic (chemical) UV filters are not sufficient to protect the skin from the effect of visible light.

Antioxidants may be beneficial
Non-Topical Photoprotection
Polypodium leucotomos Extract
Polypodium leucotomos

(Caccialanza, M. PPP 2/07; 23:46; Tanew, A. JAAD 1/12; 66:58

• Fern plant extract – Central America

Courtesy of Teresa Hoyjo,
MD, Mexico
Polypodium leucotomos Extract


• Antioxidative and anti-inflammatory properties
• Suppresses:
  – Clinical changes induced by UVB, PUVA
  – Development of PMLE
• ? Role in visible light photoprotection
Acute Effects of *Polypodium leucotomos* Extract


- PLE, 240 mg 2 hr and 1 hr before UVB irradiation resulted in:
  - Decrease of UV erythema
  - Inhibition of markers of DNA damage and apoptosis (sunburn cells, cyclobutane pyrimidine dimers), inflammation (COX-2), and proliferation (cyclin D1, Ki67, PCNA)
Polypodium leucotomos Extract

- Study on the effect of PLE on visible light induced changes is on-going
Afamelanotide
**α-MSH & Analogues**


Afamelanotide (Scenesse®; CUV1647):

- Similar to α-MSH, linear 13 amino acid peptide.
- The 4\textsuperscript{th} and 7\textsuperscript{th} amino acids of α-MSH have been replaced in afamelanotide.
- Binds to MC1R
α-MSH & Analogues


Afamelanotide (Scenesse®; CUV1647):

• Resistant to enzymatic breakdown, prolonging its duration of action at MC1R → stimulation of melanocyte proliferation and upregulation of tyrosinase activity

• Melanin:
  – Neutral density filter
  – Scavenges reactive oxygen species
α-Melanocyte Stimulating Hormone Analogues

Haylett, AF… Rhodes, LE. BJD 2/11; 164:407. Manchester, UK)

**EPP:**
- Afamelanotide, 20 mg s.c., twice, 60 days apart

**Solar urticaria:**
- Afamelanotide, 16 mg s.c., once

**Both:**
- Increased tolerance to artificial light
- Increased melanin content
Afamelanotide for Erythropoietic Protoporphyria

Afamelanotide for EPP: EU & US


• Randomized, double-blind, placebo-controlled study
• EU (74 pts): 5 subcutaneous implants, every 60 days
• US (94 pts): 3 implants
• Duration of pain-free time following sun exposure was longer in the treatment gr.
• Improved quality of life
• Adverse effects: headache, nausea, nasopharyngitis, and back pain
Melanotan I and/or II, “synthetic analogue of α-MSH”

- Cyclic molecule.
- Through internet, tanning salons, gyms
- Not approved by FDA or any other regulatory agencies
- Come as powder. Self-inject substance
- Purity unknown
**α-MSH & Analogues**


- Melanotan I and/or II, “synthetic analogue of α-MSH”
  - Increased skin pigmentation.
  - Reports of development of eruptive nevi, dysplastic nevi, melanoma.
  - Interacts with a wide range of melanocortin receptors:
    - MC3R in GI tract: nausea
    - MC3/4R in brain: somnolence, penile erection, decreased appetite
Nicotinamide
Oral Nicotinamide


- UV inhibits ATP production → energy crisis → prevents optimal skin immune response and DNA repair
- Oral nicotinamide (500 mg bid):
  - Blocks the inhibitory effect of UV on ATP production
  - Minimizes UV-immunosuppression
  - Enhances DNA repair
  - Unlike niacin, does not produce flushing reaction (niacin: lower lipid levels)
A Phase 3 Randomized Trial of Nicotinamide for Skin-Cancer Chemoprevention

Oral Nicotinamide (N=386)


Actinic keratoses

Figure 3. Change from Baseline to Month 12 in Number of Actinic Keratoses.
### Oral Nicotinamide (N=386)


<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Placebo mean no. of lesions/person</th>
<th>Nicotinamide</th>
<th>Rate Ratio (95% CI)</th>
<th>Relative Difference, % (95% CI)</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td><strong>12-mo intervention period</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NMSCs</td>
<td>2.4</td>
<td>1.8</td>
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<td>23 (4 to 38)</td>
<td>0.02</td>
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<td>BCCs</td>
<td>1.7</td>
<td>1.3</td>
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<td>20 (-6 to 39)</td>
<td>0.12</td>
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<tr>
<td>SCCs</td>
<td>0.7</td>
<td>0.5</td>
<td></td>
<td>30 (0 to 51)</td>
<td>0.05</td>
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<tr>
<td><strong>6-mo postintervention period</strong></td>
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<td></td>
<td></td>
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<tr>
<td>NMSCs</td>
<td>0.8</td>
<td>0.8</td>
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<td>-17 (-59 to 14)</td>
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<tr>
<td>BCCs</td>
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<td>-6 (-53 to 26)</td>
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<tr>
<td>SCCs</td>
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<td>0.3</td>
<td></td>
<td>-59 (-163 to 4)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

![Graph showing relative differences and rate ratios for different subgroups.](image-url)
Nicotinamide and Renal Transplant Patients

(Chen, AC,… Halliday, GM, Damian, DI. Br J Dermatol Nov 2016; 175:1073. Sydney, Australia)

- Phase II trial (evaluates effectiveness and safety)
- Randomized, controlled: 11 renal transplant patients, 11 controls
- Nicotinamide 500 mg bid vs placebo
- 36% decrease of NMSCSs, 16% decrease of AKs
- Trend, but not statistically significant.
- No safety concerns were noted
Non-Topical Photoprotection

- Promising as an adjunctive photoprotective measure
- Not to replace current regimen of photoprotection