IN SUPPORT OF HIGH SPF
A clinical discussion on why High SPF sunscreens contribute significantly to public health

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Disclosures:
J and J – A, H, I
Beiersdorf – C, H

Skin Cancer is an Epidemic
There are more skin cancers in the US than all other cancers combined

Analysis of Trends in US Melanoma Incidence and Mortality
US Annual Deaths From Melanoma
Estimated number of annual deaths from melanoma in the United States from 2009 to present

Analysis of Trends in US Melanoma Incidence and Mortality
Lifetime Risk of Developing Invasive Melanoma in the United States
Changes in the annual lifetime risk of developing invasive melanoma in the United States from 1930 to 2016

Sunburn, Skin Aging and Skin Cancer are Caused by Same Wavelengths of Sunlight
**SUN PROTECTION IS VITAL TO SKIN HEALTH**

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**Sunscreen Use Clinically Shown to Prevent Squamous-Cell Carcinomas**

- Sunscreen used daily vs discretionary use over 4 year time period
- Use of an SPF 16 product, weight of product brought in every 3 months measured

**RESULTS:**
- 45% fewer SCC lesions in subjects using daily SPF 16 sunscreen (p<0.05)

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**Study Shows Sunscreen Usage Associated with Reduction in Melanoma Incidence**

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**Skin cancers in Australia prevented by regular sunscreen use**

- Estimated the proportion of skin cancers that would have occurred but were likely prevented by regular sunscreen use
- Regular sunscreen use prevented around 14,190 persons from developing SCCs (PF 9.3%) and 1,730 from Melanoma (PF 14%)

**Conclusions:**
- Prevailing levels of sunscreen use probably reduced skin cancer incidence by 10-15%
- Sunscreen should be a component of a comprehensive sun protection strategy

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**MM risk using SPF<15 vs SPF >15**

- Percentage improvement with regular use of SPF>15

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**Norwegian Women Study N = 143,844**

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**Ghavam et al, J Clin Oncol, 2016**

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**“Well, don’t just stand there looking for sunscreen.”**
Development of SPF

- Correlation of indoor solar simulator with natural sunlight
- Natural sunlight effects could be duplicated with solar simulator

Sayre et al, Arch Dermatol, 1978

How high an SPF is high enough?
**SPF 50+ Status**

- Sunscreens with SPF of 50 or more are available in some other developed countries, including New Zealand, the US and many European countries
- Australia and other countries have an SPF 50+ cap

**SPF Cap 50+?**

- Higher SPFs have better protection at “real world” application concentrations
- 50+... Is it 51 or 100?

**SPF Cap 50+?**

- Higher SPFs have better protection at “real world” application concentrations
- 50+... Is it 51 or 100?

- What will be the incentive to develop a better sunscreen if there is no way to reflect that on the label?

### Sunscreen Use Not Only Protects, But Promotes Reversal of Photodamage

Daily use of a facial photostable broad spectrum sunscreen (SPF 30) over one year significantly improves clinical evaluation of photaging

- 12 Subjects, phototype 1-3
- Standard 2 mg/cm² sunscreen application rate
- MED observations at 24 hours
- 3mm punch biopsies taken at 24 hours
- SPF 55 sunscreen contained:
  - 5% octyl salicylate, 10% homosalate, 6% oxybenzone, 3% avobenzone, and 2.8 % octocrylene


### Despite Decades of Science, Education, Sunscreen Compliance is Low

- Only 39.1% of American households purchase sunscreen
- Only 30% of women and >15% of men use sunscreen on face and exposed skin

THE CASE FOR HIGH SPF – WHY IT MATTERS...

High SPF Offers Meaningful Margin of Safety

High SPF is Durable in Real World Use

High SPF is Valuable even In Shade

It’s Not About How Much Is Blocked

High SPF Offers Better Protection in Beach Setting
In-vivo comparison of SPF 100 vs 50 in Actual Use Conditions

High SPF formulation more effective during intense UV exposures
- SPF 85 formulation tested vs. SPF 50
- 56 subjects applied sunscreen to face while skiing at Vail, Colorado 1/13/08
- 1 application only at start of day
- Average hours exposed 5.0 hours
- Noon Sun 22 minutes = 1 MED
- 7/28 sunburned SPF 50 vs. 1/28 SPF 85 (p=0.02)
- **Conclusion:**
  - SPF 85 formulation more effective than SPF 50 in protecting from sunburn with a single application in a high UV test environment

Russak et al, JAAD 2010

High SPF Sunscreen Provides Significant Clinical Benefit in Actual Use Conditions:

SPF 100+ is More Effective than SPF 50+

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Federal Register / Vol. 76, No. 117 / Friday, June 17, 2011 / Proposed Rules

We are only aware of one study that examined the relative effectiveness of sunscreen products with SPF values of 50 compared to products with SPF values above 50. Russak et al. compared the sunburn protection provided by an SPF 85 sunscreen product compared to an SPF 50 sunscreen product (Ref. 3). In the double-blind study, each subject was randomly assigned to apply the SPF 85 product to one side of the face and the SPF 50 product to the other. Following a one-time morning application, subjects went skiing or snowboarding during a bright, sunny day at a well-known ski resort.

However, this single study summary is not an adequate basis upon which we may conclude that sunscreen products with SPF values above 50 provide additional sun protection compared to an SPF 50 sunscreen product. For example, we cannot determine from the summary the amounts of sunscreen products applied, length of sun exposure for individual subjects, or the time of day during which subjects were exposed to the sun. Furthermore, although current sunscreen directions instruct consumers to apply sunscreen products no less frequently than every two hours, the subjects in this study were explicitly told not to apply sunscreen products.

For each subject:
1. How much sunscreen was used?
2. How much time did each individual subject spend in the sun?
3. Were there reapplications [not allowed in study]?
**BACKGROUND**

- In the 2011 proposed monograph, the US Food and Drug Administration requested additional data stating "there is currently insufficient evidence that there is clinical benefit to the consumer at SPF above 50.”

- In real-world settings, consumers apply sunscreens at densities lower than are used to clinically determine SPF and the linear dependence of SPF to application density is well established.

**Sunscreen – Proposed Rule on SPFs**

- Proposing to limit SPF to “50+”
  - Acknowledged that SPFs higher than 50 have been substantiated and results are validated and repeatable
  - Additional data demonstrating additional clinical benefit above SPF 50 are being collected by the FDA
- Sunscreens labeled with SPFs above 50 may remain on the market until this proposed rule becomes final, provided they follow the appropriate SPF test.
- Depending on how this proposed rule is finalized, these products may/may not be able to continue on the market.

**SPF levels vs. UVB absorption**

Marginal increase in UVB protection from SPF 50 to SPF 100 is only 1%

**Underusage of Sunscreen**

Large variation in sunscreen application (many use less than recommended 2mg/cm²)

Users received a mean SPF of 20-50% of expected due to inadequate application

Underprotection due to inadequate application might explain why sunscreen use has been reported in some studies as a risk factor for melanoma

Stokes et al., Photodermatol Photoinmunol Photomed, 1997

**Promotional sunscreen with real world application**

But this assumes sunscreen applied at tested concentration (2mg/cm²)

Typically, 25-50% of rated amount applied
Impact of under application of sunscreen

- SPF of sunscreens are tested using a thickness of 2 mg/cm²
- Investigations show that sunscreen under natural conditions is applied insufficiently with amounts about 0.39 to 1.0 mg/cm²
- Missing areas and UV radiation exposure before sunscreen application are other pitfalls that reduce the protective effect of sunscreens considerably

Patients Under Apply Sunscreen

- Numerous studies have shown that consumers typically under apply product by 1/4 to 1/2 of what should be applied
- Data shows that consumers seldom re-apply after the initial application
- Not all body areas get comprehensive application and coverage

Patients Often Don’t Apply Recommended Amounts of Sunscreen

High-SPF Compensates for Under-Application of Sunscreen

- OBJECTIVE: To measure the actual SPF values of various sunscreens (SPF 30 to 100) applied in the reduced amounts typically used by consumers

Methods

- 4 lotion and 2 spray sunscreens, selected based on formulation similarities
  - (A) - SPF 30 lotion sunscreen (Coppertone Sport 30)
  - (B) - SPF 100 lotion sunscreen (Neutrogena Ultra Sheer Lotion SPF 100)
  - (C) - SPF 100 spray sunscreen (Neutrogena Ultimate Sport Spray SPF 100)
  - (D) - SPF 50 lotion sunscreen (Coppertone Sport 50+)
  - (E) - SPF 50 spray sunscreen (Coppertone Sport 50 Continuous Spray)
  - (F) - SPF 70 lotion sunscreen (Coppertone Sport 70+)

Ouyang et al., J Am Acad Dermatol, 2012
**Methods**

- Application densities: 
  - 0.5, 1.0, 1.5 and 2.0 mg/cm²
- Products applied according to the standard protocol for SPF Testing, on the back of human volunteers

**Actual SPF at different application doses**

<table>
<thead>
<tr>
<th>Application density</th>
<th>Mean SPF at 30</th>
<th>Mean SPF at 50</th>
<th>Mean SPF at 70</th>
<th>Mean SPF at 100</th>
<th>Mean SPF at 20</th>
<th>Mean SPF at 30 spray</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mg/cm²</td>
<td>31.0</td>
<td>12.0</td>
<td>70.0</td>
<td>104.0</td>
<td>58.7</td>
<td>105.3</td>
</tr>
<tr>
<td>1.0 mg/cm²</td>
<td>21.8</td>
<td>43.3</td>
<td>56.4</td>
<td>79.3</td>
<td>36.6</td>
<td>75.0</td>
</tr>
<tr>
<td>1.5 mg/cm²</td>
<td>16.0</td>
<td>26.0</td>
<td>37.1</td>
<td>55.9</td>
<td>25.7</td>
<td>50.1</td>
</tr>
<tr>
<td>2.0 mg/cm²</td>
<td>11.0</td>
<td>19.3</td>
<td>27.1</td>
<td>44.0</td>
<td>12.6</td>
<td>22.4</td>
</tr>
</tbody>
</table>

**Results**

- There was a linear relationship between application density and the actual SPF
- Sunscreens labeled SPF > 50 provided significant protection even when applied at “real world” typical application densities

**Can You Trust the SPF?**

In four years of our sunscreen tests, almost half of the products failed to meet their SPF claim after water immersion—despite the fact that all tested claims of water resistance. And if you think your skin to mineral products, you’re taking a greater chance; the mineral-only sunscreens performed far worse than the chemical formulations.
**BACKGROUND**

- In the 2011 proposed monograph, the US Food and Drug Administration requested additional data stating "there is currently insufficient evidence that there is clinical benefit to the consumer at SPF above 50."
- In real-world settings, consumers apply sunscreens at densities lower than are used to clinically determine SPF and the linear dependence of SPF to application density is well established.
- It is hypothesized that a sunscreen with a higher SPF would provide greater in-use efficacy compared with one currently labeled at the proposed maximum of SPF 50+.
- Objective of this study was to evaluate the difference in sunburn protection provided by different SPF sunscreens during a day of downhill snow skiing.

**METHODS**

- 199 healthy men and women ≥18 years of age participated in a one day split face, randomized, double blind study in Vail, Colorado.
- The difference in sunburn protection provided by two currently available sunscreens (SPF 50+ and SPF 100+) was evaluated.
- Products were supplied in a kit containing two overwrapped tubes of sunscreen marked “right” and “left.” Each subject wore both sunscreens simultaneously, with product application randomized to either the right or left side of the face.
- Subjects utilized the sunscreens as they would normally during ski activities. Diaries were used to record sun exposure time and the frequency and timing of sunscreen re-applications.
- Subjects reported the next morning for clinical evaluation.

**STUDY DESIGN**

- Participants and evaluator were blinded to test product identity. Participants (Fitzpatrick skin type I to III, Erythema Score of 0.5 or less) were randomized to one of two treatment regimens for the face and neck:
  - (SPF 50+ on left & SPF 100+ on right) or (SPF 100+ on left & SPF 50+ on right)
- Products Evaluated
  - Neutrogena® Ultra Sheer® Dry-Touch Sunscreen Lotion Broad Spectrum SPF 100+ (UPC 086800873105)
  - Banana Boat® Sport Performance® with Powerstay Technology Sunscreen Lotion Broad Spectrum SPF 50+ (UPC 079656045130)
- Participants self-applied the pre-weighed study products upon receipt, prior to outdoor sun exposure as they normally would. To address any questions by subjects about product application or usage, subjects were referred to the product study labels which contained the complete sunscreen Drug Facts information without ingredients list.
- Time spent outdoors was captured by the subjects in the provided exposure diary and solar conditions were tracked utilizing a stationary radiometer. An application diary was used to record the frequency and time of any product reapplications.
- Primary and Secondary efficacy endpoints were evaluated by clinical grading the morning after the recreational sun exposure period. At which time study products were also collected and weighed to determine usage.
**STUDY PARTICIPATION AND CONDITIONS**

- Conducted on a sunny day (March 21, 2016) during normal recreational skiing/snowboarding in Vail, Colorado, USA (base elevation approx. 8,200').
- 199 participants (42% women, 37±16 years old); Fitzpatrick skin Type I (16%), Type II (73%), & Type III (11%)
- Participants averaged 6.05 ± 1.29 hours of sun exposure

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**RESULTS**

**Usage**

No differences were observed in usage, application density, or reapplication frequency of the study products.

**Primary Endpoint**

SPF 100+ sunscreen was significantly more effective at protecting against sunburn than was SPF 50+ sunscreen.

**Secondary Endpoint**

Erythema was significantly lower on the SPF 100+ protected side of the face, and erythema progression was observed to be more than twice as severe on the SPF 50+ protected side.

**Post-Hoc Analysis**

The number of sunscreen reapplications was not observed to diminish the enhanced protection benefit of the SPF 100+ product.
RESULTS

Post Hoc Analysis

SPF 100+ sunscreen was significantly more effective at protecting against sunburn in all examined skin types.

CONCLUSIONS

• Product usage data confirms that consumers apply sunscreen at densities far less than that utilized to determine the SPF value listed on the product label.
• In this real-world, actual usage study, the SPF 100+ sunscreen was significantly more effective in protecting against sunburn than the SPF 50+ sunscreen.
• Reapplication data confirms that consumers typically reapply the product less frequently than recommended on product label and that reapplication is observed to preserve but not enhance sunscreen efficacy.

CONCLUSIONS

• The SPF 100+ sunscreen was significantly more effective in protecting against sunburn than the SPF 50+ sunscreen for all skin types evaluated.
• These findings demonstrate that there is a need for sunscreens labelled with SPFs greater than 50+ to provide consumers with better choices for sunburn protection.

SUMMARY

• The SPF 100+ sunscreen was significantly more effective in protecting against sunburn than the SPF 50+ sunscreen for all skin types evaluated.
• These findings demonstrate that there is a need for sunscreens labelled with SPFs greater than 50+ to provide consumers with better choices for sunburn protection.

CALLING FOR A SUNSCREEN REVOLUTION

Dermatologists’ Perceptions Recommendations and Usage of Sunscreen

N = 156

Farber et al., JAMA Dermatol. 2016
Dermatologists’ Perceptions, Recommendations, and Usage of Sunscreen

Dermatologists’ Beliefs

- 97% of dermatologists were comfortable recommending sunscreens with an SPF of 50 or higher.
- 83% agree high SPF sunscreens (SPF 50+) provide an additional margin of safety at real-life application levels.
- 98% recommend at least SPF 30 or higher to patients planning to be outdoors in summer.
- 35% recommend SPF 50+.
- 100% choose SPF 30+ for themselves and family.
- 62% choose SPF 50+.

99% believe patients under-apply sunscreen.

Recommend the High SPF Sunscreens You Choose for Yourself and Your Family

<table>
<thead>
<tr>
<th>SPF Recommendation by Years in Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
</tr>
<tr>
<td>70+ SPF</td>
</tr>
<tr>
<td>50-69 SPF</td>
</tr>
<tr>
<td>30-49 SPF</td>
</tr>
<tr>
<td>15-29 SPF</td>
</tr>
<tr>
<td>SPF &lt;15</td>
</tr>
</tbody>
</table>

High SPF is proven to offer clinically significant benefits in real-world settings and actual use scenarios.

- Recommend sunscreen to all patients – not just those perceived to be at higher risk.
- Discuss value of High SPF sunscreens for:
  - Patients who under-apply
  - Acute and long-term exposure
  - Extended outdoor activity

More Years in Practice, More Likely to Recommend High SPF
Photoprotection - Key Patient Concepts

Roger I. Ceilley, M.D.
Clinical Professor of Dermatology
The University of Iowa

DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY

- Ferndale Healthcare
- Galderma Laboratories
- LEO Pharmaceuticals

Sunscreens -- Why?

- Sun avoidance, protective clothing and hats are not always practical/possible, or desirable
- Prevention of sunburn
- Prevention of skin cancer
- Protection from photoaging
- Protection for those with photosensitivity (drug, connective tissue disease, porphyria)

Do Sunscreens Prevent Skin Cancers?

- Consistent Sunscreen Use Has Been Shown to Prevent Some Skin Cancers
  - Squamous cell carcinoma of the skin/AK
  - Melanoma?

NMSC

- 1,383 Australians 4.5 years

- Daily sunscreen vs. no sunscreen
  - No change in BCC incidence
  - SCC decreased with sunscreen usage
    1,115 vs. 1,832 per 100,000 stat sig

Green et al, Lancet 1999

NMSC

- 120 transplant recipients
  - All informed about sun protection. Half provided SPF > 50 sunscreens for daily application
  - 24 months
    - Invasive SCC
      - 0 sunscreen vs. 8 control
    - BCC
      - 2 sunscreen vs. 9 control

Jurgensen et al, BJD 2009
The Changing Impact of Sunscreens in the Prevention of Melanoma

- Meta-analyses of observational case-control studies have demonstrated - no protective benefit of sunscreens and the development of malignant melanoma.
- Sunscreens prevalent at the time of study, and how sunscreen is used and applied have failed to find any association between use and risk of melanoma.
- Modern high SPF, broad spectrum sunscreens can be expected to be an effective measure compared to sunscreens used 10 – 20 years ago.

Sunscreens as a preventative measure in melanoma: an evidence-based approach or the precautionary principle?

- Significant numbers of melanomas might be avoided by regular sunscreen use during recreational summer sun exposure

Sunscreen Use and Nevi

- RCT of sunscreen in 307 children
- Age 6 or 7 years
- Followed for 3 years
- Sunscreen children had fewer nevi on the trunk

Reduced Melanoma After Regular Sunscreen Use: Randomized Trial Follow Up

Participants and Methods
- In 1992, 1,621 randomly selected residents in Australia, age 25 – 75 years were randomly assigned to daily or discretionary sunscreen application to head and arms.
- Treated for 5 years then followed for 10 years

Reduced Melanoma After Regular Sunscreen Use: Randomized Trial Follow Up

- 10 year follow-up post study
  - Melanoma total
    • 11 sunscreen vs. 22 control
  - Melanoma invasive
    • 3 sunscreen vs. 11 control

  Melanoma may be preventable by regular sunscreen use in adults.
Prevention of Melanoma with Regular Sunscreen Use

- Since exposure to UV radiation (UVR) is the only known modifiable cause of melanoma, this study is a potential “game changer” for the primary prevention of melanoma.

Robinson et al, JAMA, July 20, 2011 Vol 306, No 3

Sunscreens May Fail to Meet SPF Claims on Product Labels

- Unprotected sun exposure is the most preventable risk factor for melanoma and other nonmelanoma skin cancers. Proper sun protection should include seeking shade; wearing protective clothing; and using a broad-spectrum, water-resistant sunscreen with a sun protection factor (SPF) of 30 or higher.

Cutis, July 13, 2016

Sunscreens May Fail to Meet SPF Claims on Product Labels

- New data from Consumer Reports indicate that 48% of all sunscreens tested (N=104) over 4 years did not provide the sun protection factor (SPF) promised on product labels, leaving consumers with insufficient sun protection, which could lead to long-term sun damage including wrinkles or skin cancer. Furthermore, 42% of chemical sunscreens (n=85) and 74% of mineral sunscreens (n=19) did not meet their SPF claims.

Cutis, July 13, 2016

40% of Sunscreens Don’t Adhere to AAD Guidelines

- In a cohort of highly-rated sunscreen products, a significant proportion did not adhere to the AAD guidelines, mostly attributable to a lack of water resistance. The most striking variation was price, which varied 3000%. Researchers evaluated 65 of 6,500 products from the Amazon.com online catalog characterized as sunscreens.
  - Of the total number of products evaluated, the median price was $3.32 (range $0.68 to $23.47).
  - 40% did not adhere to AAD guidelines (broad spectrum, SPF >30, and water resistant for sunscreens).
  - Cosmetic elegance was the most cited feature 198 of 325, followed by product performance 146 of 325 and skin type compatibility 78 of 325.

Xu, Kwa, et al; JAMA Dermatology; epub 2016 Jul
Study: Many people use sunscreen incorrectly

AAD recommends protection by:
- Seek shade
- Wearing protective clothing
  - Long sleeves
  - Wide brimmed hat
  - Sunglasses
- Apply broad-spectrum
- Water-resistant
- SPF of 30 or higher
- Apply to cover all exposed skin; about 1 oz
- Apply 15 min before exposure and reapplied every 2 hours, or after swimming or sweating

JAAD, May 11, 2016

Underusage of Sunscreen
- Large variation in sunscreen application
  - many use less than recommended 2 mg/cm²
- Users received a mean SPF of 20 – 50% of expected due to inadequate application
- Underprotection due to inadequate application might explain why sunscreen use has been reported in some studies as a risk factor for melanoma

Stokes et al, Photodermatol Photoimmuno Photomed, 1997

Sunburn and sun-protective behaviors among adults with and without previous nonmelanoma skin cancer: A population-based study

Fischer et al; JAAD, August 2016

After Skin Cancer, Sun Protection is Still Spotty
- Even though people may be more careful in the sun after skin cancer, having had a malignancy still doesn’t convince everybody to take basic precautions like wearing hats or sunscreens.
  – JAAD, May 2016
- “It is critical for physicians to counsel skin cancer patients on the importance of proper sun protection,” Martin, who wasn’t involved in the study, said by email.
  – JAAD 2016

Sunscreens Safe in Babies, Children
- Despite what some popular online media outlets report, sunscreens are safe in children and can even be used on infants under 6 months of age when sun avoidance – best approach to protecting babies from the damaging effects of the sun – is not possible.

**Relationship between SPF and amount of sunscreen applied in-vivo**

- SPF typically determined at 2mg/cm² application
- 4 areas were treated with a sunscreen SPF 4 at 0.5, 1, 2 and 4 mg/cm²
- Relationship between amount applied and the SPF provided was most likely to follow exponential growth ($r^2 = 0.903$)
- **Conclusion:**
  - Application of 1mg/cm² or 0.5mg/cm² makes the SPF fall as the square or fourth root, respectively, and 4mg/cm² results in an almost squared SPF.

Faurschou et al, Br J Dermatol, 2007

**Sunscreen SPF vs. Application Concentration**

![Graph showing the relationship between Sunscreen SPF and Application Concentration](image)

**Are We Winning the War Against Sun Damage?**

![Image of two people in swimsuits]

**Sun Protection in Children of Melanoma Survivors Still Lacking**

- The researchers concluded that while melanoma survivors may have a heightened awareness of the importance of their children’s sun protection, their children are not routinely protected.

**Compliance with sunscreen advice in a survey of adults engaged in outdoor winter recreation at high-elevation ski areas**

David B. Bullock, PhD; Peter A. Anderson, PhD; Barbara J. Wallace, PhD; Michael J. Scott, PhD; Julie A. Malon, MD; Mark R. Flanary, PhD; and Greg R. Conner, PhD

Golden and Denver, Colorado; San Diego and Ashburn, California; Lexington, Kentucky; and Birmingham, Alabama

**Background:** Adults are advised to use sunscreen with a sun protection factor (SPF) of 15 or higher, apply it 15 minutes before exposure, and reapply it every 2 hours to reduce exposure to ultraviolet radiation in sunlight for the prevention of skin cancer.

- Applying SPF 15 or higher (50%)
- Applying 30 min before skiing (73%)
- Re-applying every 2 hrs (20%)

JAAD Dec 2012
What's new that can we offer our patients…

Better UVA Protection

High SPF Formulation More Effective During Intense UV Exposures
- New SPF 85 photostabilized formulation tested vs. SPF 50
- 56 subjects applied sunscreen to face while skiing at Vail, Colorado 1/13/08
  - 1 application only at start of day
  - Average hours exposed 5.0 hours
  - Noon Sun 22 minutes = 1 MED
  - 7/28 sunburned SPF 50 vs. 1/28 SPF 85 (p=0.02)
- Conclusion:
  - SPF 85 formulation more effective than SPF 50 in protecting from sunburn with a single application in a high UV test environment

Multiple Benefits of High SPF Sunscreens
- High SPF helps compensate for consumer under-application. SPF protection is directly proportional to the amount applied
- Consumers typically apply 1/2 to ¼ of the amount used in SPF test.
- Schalka et al. Photodermatology, Photobiology & Photomedicine 25, 175-181
- High SPF slows down chronic cumulative damage
- High SPF is appropriate for most vulnerable individuals and for use in high sun exposure conditions
SPF 85 sun screen provides significantly more sunburn protection than SPF 50

“The current FDA proposal to cap SPF labeling at 50+ may deprive consumers of the ability to accurately select the higher SPF formulations that may be needed at high-UV environments.”

Russak et. al. JAAD Feb 2010

UV Radiation only accounts for 5% of sunlight

Visible and Infrared Radiation are the other 95%

Solar Radiation Spectrum

Visible light is emitted by objects at a very high temperature.
Infrared light is emitted by all objects at ordinary temperatures

Infrared Radiation and Skin

1/3 of the solar energy reaching the earth surface is IR-A
As much as 50% of the free radicals may be produced by the Sun's visible light

"Convolution of the action spectrum with sunlight spectral irradiance showed that 50% of the total skin oxidative burden was generated by visible light."


Visible light induced ROS damages DNA in vitro

Visible Light Induces MMP Expression

Visible Light Can Induce Inflammation

Visible light induced ROS damages DNA in vitro

DNA modifications result from direct modifications - cyclobutane pyrimidine dimers, and indirect oxidative DNA modifications

Base modifications sensitive to Epg (8-hydroxyguanine and formamidopyrimidines) has secondary peak sensitivity in the visible region between 400 and 500nm.
IR + Visible enhances UVB photocarcinogenesis?

UVB (FS), UVA (Xe)

UVB (FS), UVA (Xe)

UVB (FS)

Schroeder et al., J Invest Dermatol 2008

IR Damage can be prevented with Topical Antioxidants – In Vivo

Infrared Radiation-Induced Matrix Metalloproteinase

Figure 4: IRA radiation-induced erythrocyte reduction in human skin through topical application of antioxidants. Mouse healthy.

Junkins-Hopkins et al., J Invest Dermatol 2008

Summary Conclusions

- In addition to UV, both IR and visible light can have damaging effects on skin
  - Dermal matrix degradation
  - Pigmentation effects
  - DNA damage and potentially enhancement of UV photocarcinogenesis

- Free radicals are also generated by visible and IR radiation and contribute to this damage

- The proportion of this damage relative to UV damage is estimated to be as much as 10 to 20%

Protection against non-UV ROS damage can be best accomplished with effective levels of anti-oxidants in and on the skin.

Non-Sunscreen Photoprotection: Antioxidants Add Value to a Sunscreen


- A SPF 25 sunscreen with AOX was tested for UV protection
- AOX showed no effect on Langerhan’s cell numbers but had effect in MMP-1 expression.

Sun Protection and Antioxidants

- Vitamin E
- Vitamin C
- Polyphenols (Green tea) epigallocatechin-3-gallate (EGCG)
- Genistein (soybeans)
- Resveratrol (grape skins, peanuts, and red wine)
- Lycopene (an isomer of beta carotene – red fruits and vegetables, such as tomatoes, watermelons)
- Combinations may be synergistic

Topical Antioxidants in Sunscreens

- Many used vitamin E and C
- Green Tea extract
- Polypodium leucotomos
- Data is most extensive for Green Tea polyphenols
- Most improve the protective value slightly
- Stability, activity in intact skin, etc

Junkins-Hopkins et al, JAAAD 2010

1JAAD 2003 Lin, 2JAAD 2001 Elmets, 3JAAD 2004, Middlekamp-Hop

Protection against non-UV ROS damage can be best accomplished with effective levels of anti-oxidants in and on the skin.
Take Home Message:

IR damages human skin
Damage includes skin aging and likely more skin cancer
IRA protection is necessary and possible (sunscreens & daily photoprotection, topical anti-oxidants & ? oral)

Commercially Available Systemic Photoprotection

- “Sunpill” – a mix of antioxidants
  - Unpublished data showing an increase in the SPF when used alone or with sunscreen
- “Heliocare” – Polypodium Leucotomos Extract.
  - Polypodium Leucotomos is a natural extract from tropical fern leaves with potent antioxidant properties
  - Tanew JAAD Jan 2012

Polypodium Leucotomos (PL)

- Decreases psoralen-UVA induced phototoxicity, pigmentation and damage¹
- Decreases UV induced damage of human skin¹
- Inhibits UVB radiation-induced immunosuppression²
- Inhibits Langerhans cell depletion induced by UVB/UVA radiation³

¹Middelkamp-Hup et al, JAAD 2004
²Siscovick et al, Photodermatology, Photoimmunology & Photomedicine 2008
³Mulero et al, Experimental Dermatology 2008

Polypodium Leucotomos

- May prevent UVA induced photodamage by preventing UVA dependent mitochondrial DNA damage¹
- Beneficial in preventing PLE²
- Photoprotective activity provides safe and effective treatment for photoprotection with idiopathic photodermatoses³
- Prevents PMLE⁴

¹JAAD 2010
²Tanew et al, JAAD 2010
³Caccialanza et al, Ita/Derm/Venereol 2011
⁴JAAD Jan 2012

Polypodium leucotomos

- Polypodium leucotomos extract (PLE) is used in over 25 countries worldwide as Heliocare™ or Fernblock®
- PLE has been safely used in humans, both topically and orally, for over 25 years

PLE: ORIGIN & DEVELOPMENT

- Polypodium leucotomos is a fern originating in Central America
- Originally an aquatic plant, it adapted to life on land, developing its own natural protective mechanisms against UV radiation
- Used for centuries by native Americans as an anti-inflammatory agent in the treatment of dermatological conditions such as psoriasis and atopic dermatitis
PLE: ORIGIN & DEVELOPMENT

- Extract is obtained from selected plants under carefully controlled conditions
- No pesticides or chemicals
- Strict laboratory procedures according to pharmaceutical quality standards are employed to ensure complete safety and efficacy

PLE: ORIGIN & DEVELOPMENT

PLE is composed of:

- **POLYPHENOLS**
- **MONOSACCHARIDES**
  - fructose, mannose, & glucose
- **FLAVONOIDS**

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<th>Anti-Oxidant Activity</th>
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<td>Value</td>
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Recommended application of sunscreen

- Two coats or about 1 full teaspoon of sunscreen should be applied to each body part prior to going outside
- Head, neck, and ears; front of trunk, back of trunk, each arm, dorsum of hand, and shoulder; and each lower leg, upper leg, and dorsum of foot
- The leg needs to be divided into upper and lower segments with each getting 1 teaspoon.

Current Sunscreen Controversies: A Critical Review

Methods
- We analyzed studies surrounding the safety and toxicity of oxybenzone, retinyl palmitate, and nanoparticles of zinc oxide (ZnO) and titanium dioxide (TiO₂).

Results
- Research revealed that topical use of sunscreen protects against squamous cell carcinoma, does not cause vitamin D deficiency/insufficiency.
- Has not demonstrated to adversely affect the health of humans.

Conclusions:
- The use of sunscreens remains an important part of an overall photoprotective strategy.
- With increased usage of sunscreen by the public, continuous and vigilant monitoring of the overall safety of the future products is also needed.
SPF Cap 50+

- Cons
  - Higher SPFs have better protection at "real world" application concentrations
  - 50+ - Is it 51 or 100?
  - What will be the incentive to develop a better sunscreen if there is no way to reflect that on the label?

Sun Protection and Anti-oxidants

- Generation of reactive oxygen species (ROS) and other free radicals by UV radiation is counteracted by antioxidants to prevent oxidative stress
- Lead to genetic alterations that include DNA damage, mutations and genomic instability
- Antioxidants scavenge free radicals but also have other anticarcinogenic properties, which include modulating signal transduction pathways such as nuclear factor-kappa beta and beta-catenin

Junkins-Hopkins et al, JAAD 2010

New Sun Cream Compound Offers Unprecedented Protection Against UVA Radiation

The researchers from the University of Bath, working with colleagues at Kings College London, hope to see the mitoiron claw compound added to sunscreens and skin care products within 3-4 years.
Free iron concentration is particularly high within mitochondria, the batteries of the cell, where it is needed for several vital functions.


New Sun Cream Compound Offers Unprecedented Protection Against UVA Radiation (Con’t)

However, UVA exposure in sunlight, excess free iron acts as a catalyst for the production of toxic reactive oxygen species (ROS), damaging cell components such as DNA, fat and proteins thereby increasing the risk of cell death and cancer.
However this custom-designed iron chelator (a molecule that binds to an iron atom like a claw) moves directly to mitochondria where it safely binds the excess free iron, preventing it from reacting upon exposure to UVA rays.