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NATIONAL SKIN CENTRE

Memorial Sloan Kettering Cancer Center

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Poster 1334

New developments in photoprotection and prevention of photocarcinogenesis

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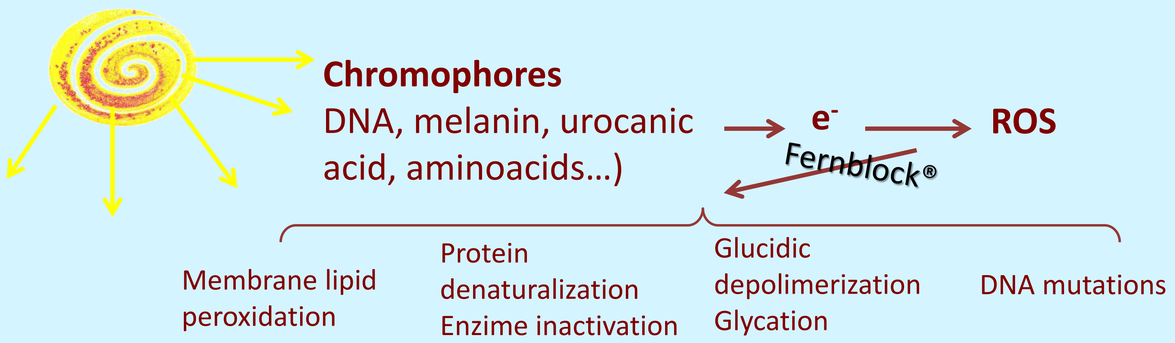
Introduction:

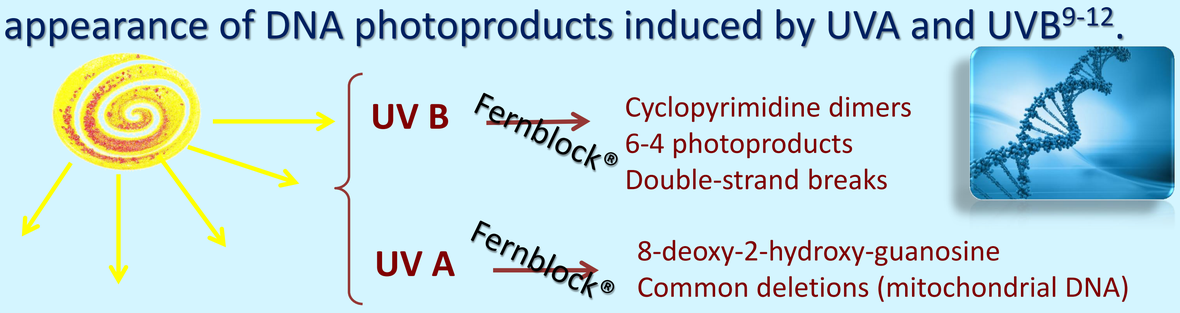
Photoprotection is essential to prevent the deleterious effects of ultraviolet (UV), infrared (IR) and high energy visible (HE-Vis) radiations, including skin cancer, hyperpigmentation, immunosupression and photoaging. Fernblock® is the technology derived from an aqueous extract of *Polypodium leucotomos* (PLE), a tropical fern of the *Polypodiaceae* family native to Central America, which has been demonstrated to contain phenolic compounds with significant antioxidant, immunomodulatory and anti-inflammatory properties. Altogether, these characteristics of Fernblock® make it an excellent photoimmunoprotectant when administered both topically and orally, thus avoiding the detrimental impact of solar radiation on the skin.

Mechanisms of solar photodamage prevented by Fernblock®:

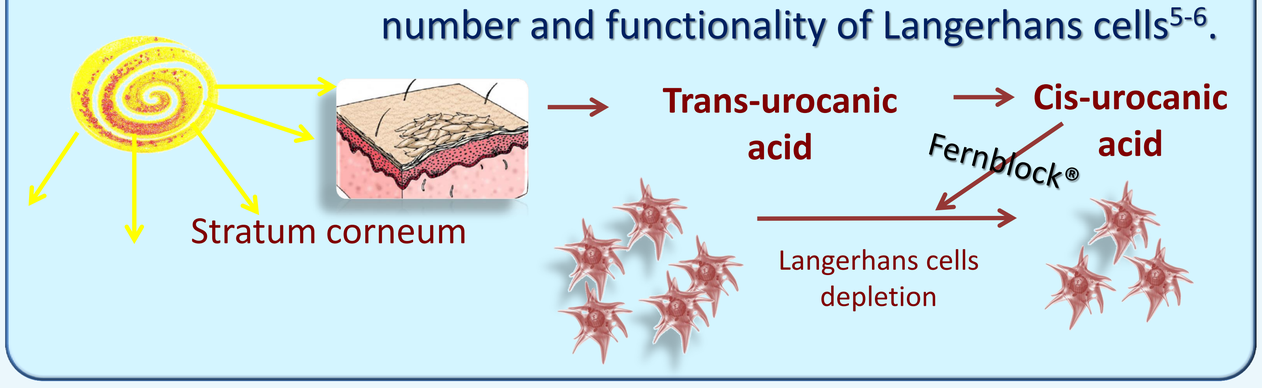
Oxidation: Fernblock® inhibits the production of free radicals and reactive oxygen species (ROS) induced by the UVR[1-4].



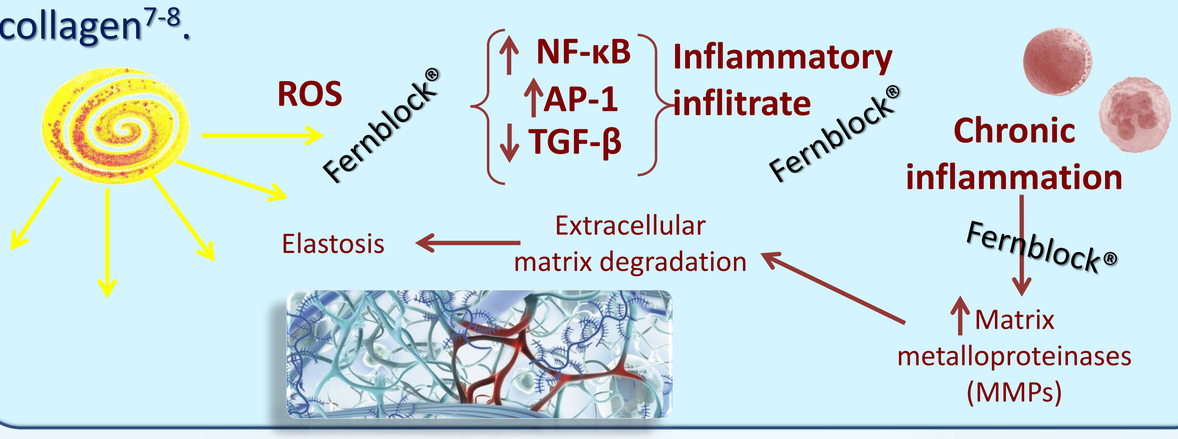
DNA damage: Fernblock® repairs the damage and prevents the appearance of DNA photoproducts induced by UVA and UVB[9-12].



Immunosupression: Fernblock® preserves the morphology, number and functionality of Langerhans cells[5-6].



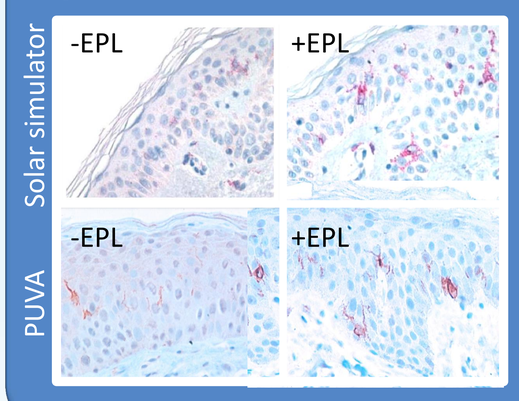
Tissue arquitecture: Fernblock® regulates TGF-ß activity inhibiting MMP-1-2-3, inducing TIMP activity, and increasing the expression of collagen[7-8].



1. González S, 1996; 2. Brieva A , 2002; 3. Philips N , 2003; 4. Mulero M, 2008; 5. Middelkamp MA, 2004; 6. Capote R, 2006; 7. Brieva A, 2003; 8. Alonso-Lebrero JL, 2003; 9. Zattra E , 2009; 10. Villa S, 2010; 11. Rodríguez-Yanes E, 2012; 12. Rodriguez-Yanes E, 2014

Clinical effects of topical or systemic administration of Fernblock®:

PLE preserves morphology, number and function of Langerhans cells, preventing UV-induced immuno-supression. González *et al.* (Photodermatol Photoimmunol Photomed, 1997)



Immunohystochemistry to detect Langerhans cells showing that PLE protected them from UV-induced cytotoxicity, preserving skin immunity.

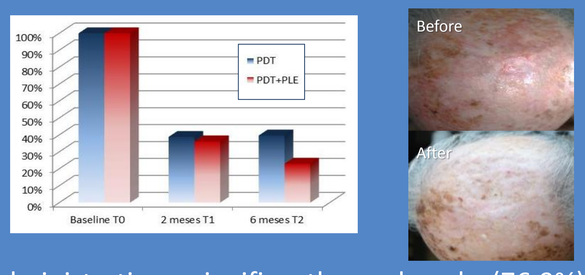
Oral administration of Fernblock® prevents the breakouts of polimorphic light eruption (PMLE). Tanew *et al.* (*JAAD*, 2012, 66:58-62)

- Fernblock® prevented the PMLE symptoms in 30% of patients and significantly increased the number of expositions necessary to induce these lesions.

No. of exposures	Pre-PL	Post-PL
UVA	1.95 ± 1.07	2.62 ± 1.02*
UVB	2.38 ± 1.19	2.92 ± 0.95†

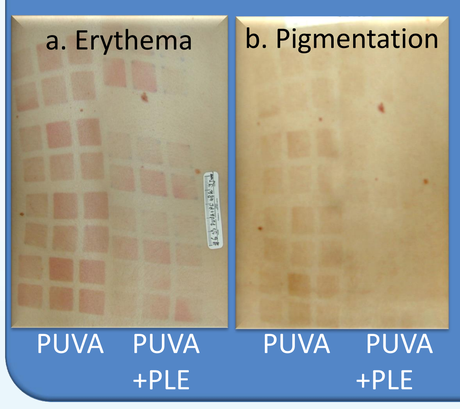
- The 74% of patients treated during the summer time with oral Fernblock ®did not show polymorphic light eruption lesions.

Fernblock® improves the outcome of photodynamic therapy in the treatment of actinic keratoses. Auriemma *et al.* (data on file)



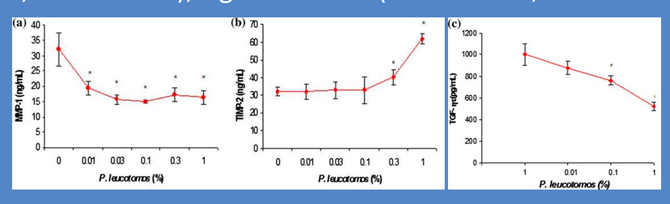
PLE administration significantly reduced (76.9%) the number of AKs following photodynamic therapy (PDT) compared to treatment with PDT alone (60.3%) after a 6-month follow-up (p = 0.04). PLE treatment also decreased the number of PDT sessions needed to achieve optimal results.

Fernblock® diminshes the acute phototoxicity and pigmentation induced by PUVA. Middelkamp-Hup MA *et al.* (J Am Acad Dermatol, 2004, 50: 41-9)



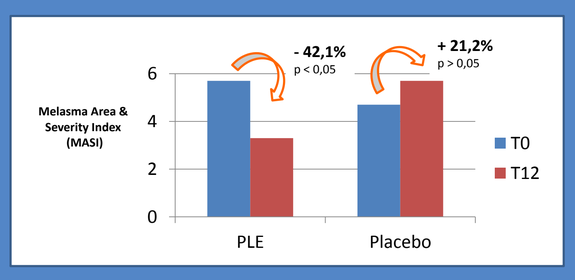
PLE significantly decreased the acute PUVA-induced phototoxic reaction (**fig. a**) and the subsequent cutaneous pigmentary response (**fig. b**). PLE-treated skin sites always showed a statistically significant lower grade of erythema and edema than skin sites exposed to PUVA alone (p = 0.005)

PLE enhances the activity of TIMPs and inhibits MMPs and TGF-β in melanoma cells and reduces sensitivity to UVR in high-risk melanoma patients. Phillips *et al.* (Arch Dermatol Res 2009, 301:487-95); Aguilera *et al.* (JEADV 2013, 27:1095-100).



Effect of PLE on MMP1, TIMP2, and TGF-β expression in melanoma cells incubated with different concentrations of PLE. *$P < 0.05$, relative to control.

PLE reduces severity of melasma Martin L (poster AAD 2012)



21 subjects 18-55 yrs with epidermal melasma, 240mg PLE or placebo twice daily + SPF 45 for 12 weeks

Conclusions:

Oral administration of Fernblock® technology has proven photoprotective activities and has demonstrated to preclude several mechanisms involved in the development of skin cancer. Thereby, Fernblock® emerges as an important treatment on the prevention of skin cancer.