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Report

Feasibility of daylight-mediated photodynamic therapy for actinic keratosis throughout the year in Central and South America: a meteorological study

Beni Grinblat[1], MD, Gaston Galimberti[2], MD, Gonzalo Pantoja[3], MD, Gloria Sanclemente[4], MD, Miguel Lopez[5], MD, Daniel Alcala[6], MD, Luís Torezan[1], MD, Delphine Kerob[7], MD, Thierry Pascual[8], MSc, and Edgardo Chouela[9], MD

[1]Department of Dermatology, Hospital das Clínicas, University of São Paulo, São Paulo, SP, Brazil, [2]Department of Dermatology, School of Medicine, Hospital Italiano, Buenos Aires, Argentina, [3]Biomer SA, Santiago, Chile, [4]Group of Investigative Dermatology (GRID), School of Medicine, University of Antioquia, Medellín, Colombia, [5]Cirugía Dermatológica y Oncología Cutánea Department, Hospital Militar Dr Carlos Arvelo, Central University of Venezuela, Caracas, Venezuela, [6]Centro Dermatológico Dr Ladislao de la Pascua, Mexico City, Mexico, [7]Galderma International, Paris, France, [8]Galderma R&D SNC, Sophia Antipolis, France, and [9]Centro de Investigaciones Dermatologicas, Buenos Aires, Argentina

Correspondence
Beni Grinblat, MD
Departamento de Dermatologia
Hospital das Clínicas da Universidade de São Paulo
Avenida Dr Eneas de Carvalho Aguiar 255
3 Andar
São Paulo
SP 05403-900
Brazil
E-mail: bgrinblat@gmail.com

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Summary

Background Daylight-mediated photodynamic therapy (DL-PDT) is an efficacious treatment option for thin actinic keratosis (AK) that offers advantages over conventional PDT in terms of tolerability, treatment duration, and cost. A clinical study conducted in Australia determined the mean irradiance during a 2-hour exposure to be 305.8 W/m^2 (range: 40–585 W/m^2). The protoporphyrin IX light dose is influenced by latitude, weather conditions, and time of year. A recent study of meteorological data concluded that DL-PDT can be performed effectively throughout the year in Australia.

Objectives Based on the same hypothesis and applying the same methodology, the present study investigated the suitability of daylight to perform DL-PDT in Central and South America.

Methods Solar radiation and weather data were gathered and analyzed to assess daylight irradiance (light intensity) throughout a full year across 32 geographical locations in Central and South America.

Results The minimum average daily solar irradiance reported was above 305.8 W/m^2 in all locations investigated throughout the year. Annual averages of daily irradiance ranged from 578 W/m^2 in Chihuahua, Mexico, to 321 W/m^2 in Puerto Montt, Chile.

Conclusions Daylight-mediated PDT for AK can be performed effectively throughout the year in Central and South America given that weather conditions permit a comfortable 2-hour direct exposure to daylight.

Introduction

Actinic keratoses (AK) are precancerous lesions caused by prolonged exposure to ultraviolet radiation and are linked to the development of non-melanoma skin cancer.[1] Prevalence of AK worldwide ranges from approximately 13–15% in South America and Europe to 60% in Australia.[2–4] In Colombia, AK and non-melanoma skin cancer are among the first nine causes for dermatological consultation.[5]

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Daylight-mediated photodynamic therapy (DL-PDT) with methyl aminolevulinate (MAL) cream and a 2-hour exposure is an efficacious treatment option for thin AK on the face and scalp.[6,7] This treatment offers advantages over conventional photodynamic therapy (c-PDT) in terms of tolerability, treatment duration, and cost, as shown in European studies.[8–12] In 2014, a direct comparison of DL-PDT with c-PDT in an Australian clinical study corroborated these findings, with DL-PDT leading to high patient satisfaction and improved tolerability.[13] In addition, this study determined mean irradiance during a 2-hour exposure to daylight to be 305.8 W/m² (range: 40–585 W/m²).[13] More recently, this comparison was repeated in five European countries at different latitudes, reiterating the non-inferior efficacy of DL-PDT compared with c-PDT, improved safety profile, reduced treatment pain, and high patient satisfaction.[14]

In South America, recent evidence from São Paulo, Brazil, corroborated the findings of the previous DL-PDT studies. Results showed high cure rates irrespective of the light dose received, with good responses observed even in patients treated during the winter.[15]

Weather conditions and abundance of daylight vary among locations throughout the year. An important shortcoming of the European and Australian DL-PDT studies refers to the limited period of the year during which they were conducted, and thus these studies do not provide information on the feasibility of treatment throughout the year. Wiegell *et al.* recently demonstrated that the light dose required to activate protoporphyrin IX (PpIX) is influenced by latitude, weather conditions, and time of year.[16]

To address these important concerns, Spelman *et al.* conducted a meteorological study assessing the suitability of daylight to perform DL-PDT throughout an entire year in eight locations in Australia.[17] This study concluded that DL-PDT can be performed effectively throughout the year as long as weather conditions permit exposure to daylight for 2 hours.[17] Based on the same hypothesis and applying the methodology used by Spelman *et al.*,[17] in this meteorological study we investigated the suitability of using daylight to to perform DL-PDT throughout an entire year across Central and South America.

Materials and methods

Similarly to the Australian meteorological study conducted by Spelman *et al.*,[17] our investigation used solar radiation and weather data to assess daylight irradiance (light intensity) throughout a full year across 32 geographical locations at different latitudes (Table 1) in Central and South America, including Mexico (MX), Colombia (CO), Venezuela (VE), Brazil (BR), Chile (CI), and Argentina (AR) (Fig. 1), between 1986 and 2005.[18] Meteorological data software (METEONORM; Meteotest, Bern, Switzerland) was used to generate data. Based on these data, the minimum irradiance that induced a clinical benefit (MICB) after 2 hours of exposure to daylight was determined. The theoretical basis and methodology of this data analysis are described in full detail in Spelman *et al.*[17]

Results

According to Rubel *et al.*, mean irradiance during a 2-hour exposure was 305.8 W/m² (range: 40–585 W/m²).[13] The investigators reported no correlation between solar irradiance and clinical benefit, and hence the MICB is equal to the lowest average irradiance (40 W/m²). The high response rate of AK irrespective of light dose was corroborated by a more recent Brazilian study.[15]

In our meteorological study, the minimum average daily solar irradiance reported was above 305.8 W/m² in all locations investigated. The highest annual averages of daily irradiance were observed in Chihuahua (MX) (578 W/m²), Guadalajara (MX) (571 W/m²), and Barquisimeto (VE) (553 W/m²), whereas the lowest were observed in Puerto Montt (CI) (321 W/m²) and Cali (CO) (325 W/m²) (Fig. 2).

Average daily irradiance of below 305.8 W/m² was sporadically observed in certain locations. However, none of the reported values were below the MICB (40 W/m²). The lowest levels were observed in Puerto Montt (CI) during May (152 W/m²), June (112 W/m²), and July (134

Table 1 Geographical locations and latitudes investigated in this study

Mexico	Colombia	Venezuela	Brazil	Chile	Argentina
Chihuahua (28.70°)	Barranquilla (11.00°)	Maracaibo (10.73°)	Natal (−5.80°)	Antofagasta (−23.67°)	San Miguel de Tucuman (−26.78°)
Monterrey (25.70°)	Cartagena (10.40°)	Caracas (10.54°)	Brasilia (−15.90°)	La Serena (−29.90°)	Cordoba (−31.33°)
Mérida (21.00°)	Bucaramanga (7.13°)	Valencia (10.23°)	Rio de Janeiro (−22.90°)	Santiago (−33.50°)	Mendoza (−32.80°)
Guadalajara (20.70°)	Medellín (6.25°)	Barcelona (10.13°)	São Paulo (−23.60°)	Concepción (−36.83°)	Buenos Aires (−33.00°)
Mexico City (19.40°)	Pereira (4.78°)	Barquisimeto (10.05°)	Porto Alegre (−30.00°)	Puerto Montt (−41.47°)	Rosario (−34.67°)
	Bogota (4.63°)				
	Cali (3.40°)				

Figure 1 Geographical locations in Central and South America for which meteorological data were investigated

W/m²), which represent winter months in Chile. During this 3-month period, levels below 305.8 W/m² were also observed in various other cities in the southern hemisphere, including Porto Alegre (BR), La Serena (CI), Cordoba (AR), Mendoza (AR), Buenos Aires (AR), Santiago (CI), Rosario (AR), and Concepcion (CI) (Fig. 2). In the northern hemisphere, such levels were reported only in Monterrey (MX) during December (297 W/m²).

Discussion

This is the first study to investigate the suitability of using daylight to perform DL-PDT in Central and South America based on weather and seasonal conditions. Although several studies have demonstrated the efficacy and advantages of this treatment, no previous study has examined weather conditions in Central and South America.

Grinblat *et al.*[15] previously confirmed that there is no relationship between irradiance and treatment efficacy. The average irradiance levels reported in this meteorological study conducted in Central and South America exceeded the MICB reported in the Australian DL-PDT clinical study.[13]

In accordance with previous recommendations, a 2-hour exposure to daylight should be ensured for effective treatment. It is also advisable to avoid treatment on

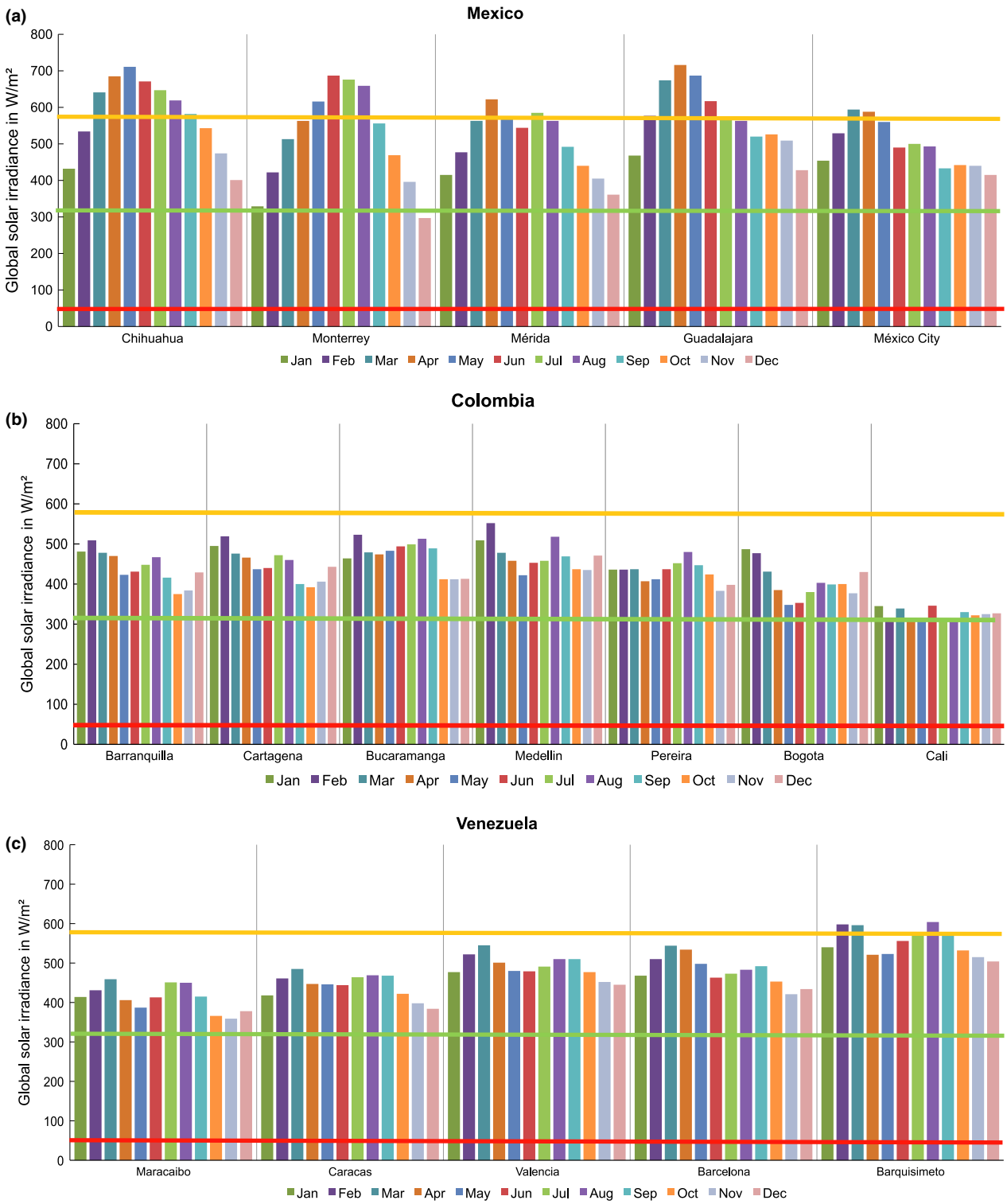

Figure 2 Modeled daily average global radiation for each month (METEONORM data 1986–2005[18]) for (a) Mexico, (b) Colombia, (c) Venezuela, (d) Brazil, (e) Chile, (f) Argentina. Horizontal lines indicate the light intensity levels established in the Australian study of daylight-mediated photodynamic therapy[13] (red: minimum, 40 W/m²; green: average, 305.8 W/m²; orange: maximum, 585 W/m²)

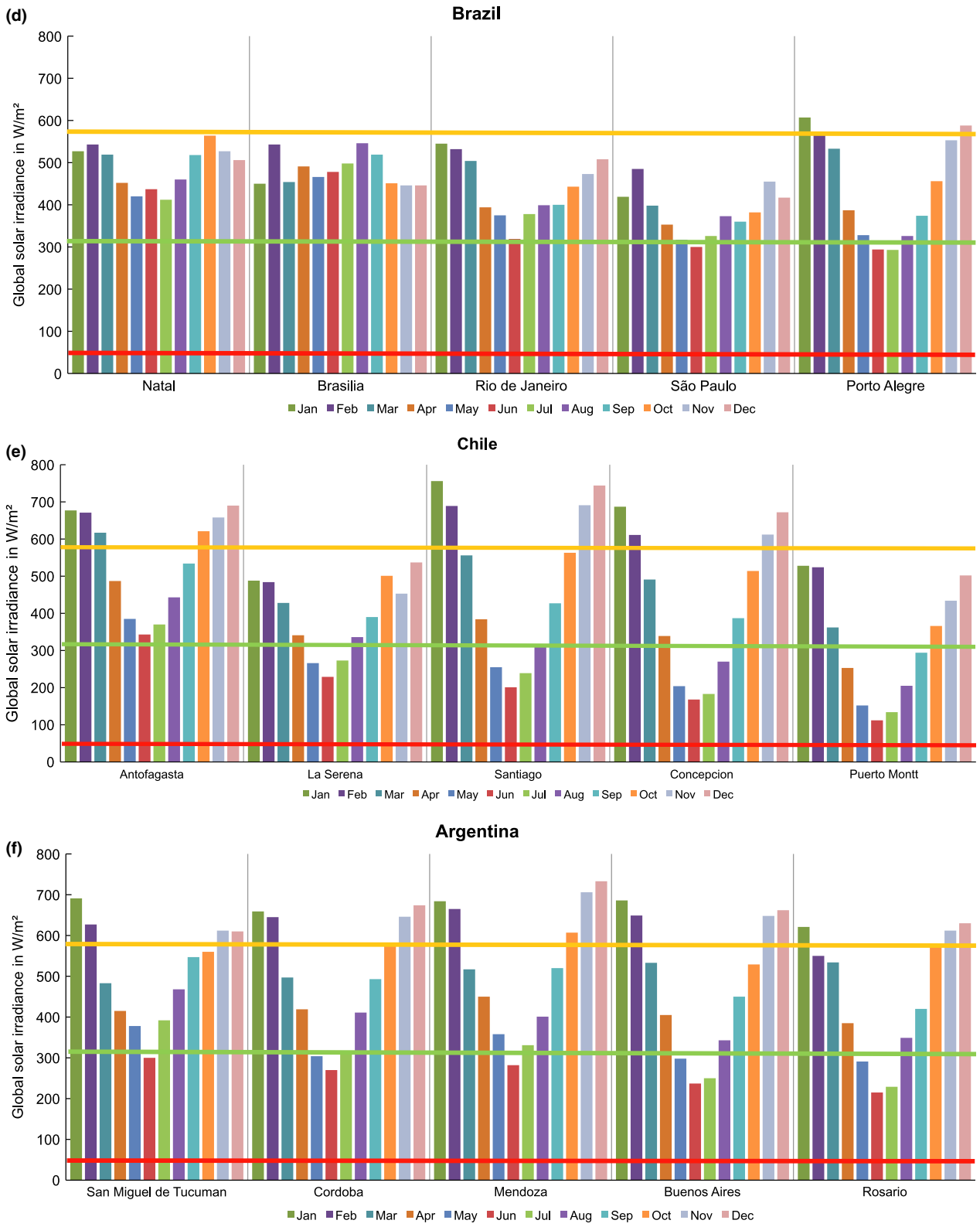

Figure 2 continued

rainy days for patient convenience. In regions closer to the South Pole, such as Puerto Montt in Chile, with low outdoor temperatures (< 10 °C) and a low level of average irradiance during May, June, and July, patients may not accept a 2-hour outdoor exposure, and therefore it may be difficult to perform DL-PDT under these conditions. Moreover, studies have shown that PpIX cannot be activated at cold temperatures, and thus DL-PDT should be avoided in those areas during winter.

In countries closer to the Equator (Colombia, Venezuela and parts of Brazil), DL-PDT appears to be feasible throughout the year, even during winter.

As Lacour *et al.* recently concluded, DL-PDT may be considered a treatment of choice to meet the needs of patients with mild or moderate facial and scalp AK.[14] The outcome of our meteorological study mirrors the conclusions of the meteorological study conducted in Australia.[17] We conclude that DL-PDT for AK can be performed effectively throughout the year in Central and South America, given that weather conditions permit a comfortable 2-hour direct exposure to daylight.

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