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Wound scabs protect regenerating tissue against harmful ultraviolet radiation

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ABSTRACT

Benefits attributed to wound scabs include prevention of blood loss and protection against infection. However, when formation of a wound scab is prevented, the risk of infection is reduced. Moreover, in the absence of a wound scab, wounds heal faster and scar formation is reduced. The question arises why we develop a wound scab. Here we show that wound scabs inhibit transmission of ultraviolet radiation (UVR). We compared the UVR transmittance of human wound scabs to sunscreen by measuring the sun protection factor (SPF) with diffuse transmittance spectroscopy. Three wound scabs showed SPFs of 70, 84, and 300, which is more effective than the most protective commercially available sun block. Because our results demonstrate that a wound scab offers natural protection against UVR, and because no beneficial trait is attributed to wound scabs, we hypothesize that the main function of wound scabs is to limit DNA damage in underlying cells during regeneration of wound tissue exposed to sunlight, thereby reducing the risk of developing skin cancer.

Introduction

Wound healing is a complex interplay between haemostasis, inflammation, formation of new tissue, and tissue remodelling [1–3]. Haemostasis involves formation of a platelet plug, thereby limiting blood loss and reducing the risk of infection. Concurrently, leukocytes are recruited, granulation tissue, new blood vessels and an extracellular matrix are formed, damaged tissue is removed, and tissue remodelling starts that can last for more than a year [1,2]. A hallmark of dermal wound healing is the formation of a dry wound scab, which consists of blood cells such as platelets and erythrocytes, and proteins such as fibrin [4]. Wound scabs contain higher numbers of microorganisms than the underlying tissue [5], suggesting that one of the functions of wound scabs is to trap pathogens, thereby reducing the risk of infection. However, a wound in the oral cavity is not covered by a scab, but usually heals without infection despite the abundant presence of pathogens [6,7]. In fact, when formation of a wound scab is prevented, the risk of infection is reduced, wounds heal faster, and scar formation is reduced [6–10]. Taken together, no beneficial trait is consistently attributed to wound scabs.

Hypothesis

Because no beneficial trait is consistently attributed to wound scabs, and because the skin protects underlying tissue from UVR, we hypothesize that wound scabs, which temporarily replace the skin, inhibit transmission of UVR, thereby reducing the risk of sunlight-induced DNA damage within underlying cells during regeneration of tissue.

Evaluation of the hypothesis

In order to study the UVR protection of wound scabs, we measure their UVR transmittance, calculated their SPF and compared these to values for sunscreen. In vivo, the SPF is defined as the amount of UVR required to produce erythema on protected skin relative to unprotected skin [11]. Fig. 1 shows that erythema of the Caucasian skin induced by solar irradiance is mainly caused by the ultraviolet radiation B (UVB) region of the spectrum (280–315 nm), with a maximum near 305 nm [11–13]. Fig. 1 also shows that erythema is considerably reduced when the skin is protected

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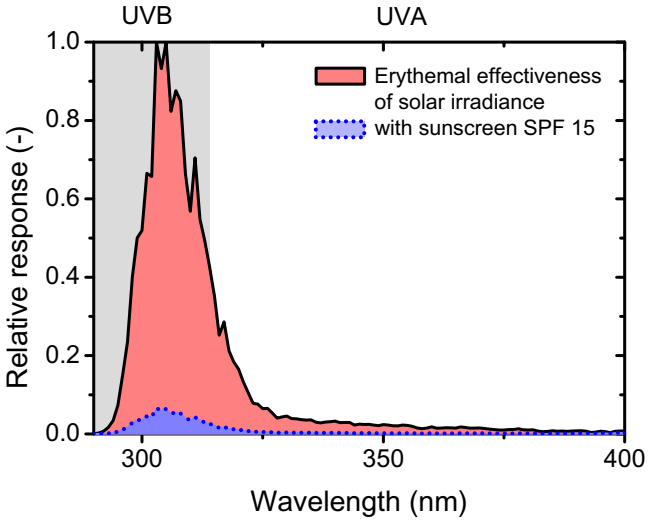

Fig. 1. Erythemal response to solar irradiance. Erythemal spectral effectiveness relative to the reference solar spectral irradiance for the Caucasian skin with and without sunscreen of sun protection factor (SPF) 15. Erythema is mainly induced by ultraviolet radiation B (UVB, grey area) and is considerably reduced for skin protected with SPF 15 sunscreen. UVA: ultraviolet radiation A.

by SPF 15 sunscreen, as measured by diffuse transmittance spectroscopy. In vitro, SPF is defined as the ratio of the areas under the two curves [14].

Sample preparation

By micropipetting, 4 µl·cm^{-2} sunscreen (private label SPF 15 and SPF 50, Etos) was applied between two quartz slides to obtain a spatially homogeneous distribution by capillary attraction. The quartz slides were removed from each other in lateral direction, resulting in two quartz slides coated with 2 µl·cm^{-2} sunscreen each [11], which was immediately covered with medical tape (Transpore, 3 M company) to imitate the texture of human skin [14]. After 30 min, the samples were mounted on an aluminium plate containing a 10.4 mm aperture, with the samples covering the aperture. Wound scabs were collected from healthy individuals and mounted on a plate containing a 3.0 mm aperture.

Diffuse transmittance UVR spectroscopy

The samples were placed in the opening of an integrating sphere (70672, Newport). Light from a fibre-coupled Xenon lamp (E7536, Hamamatsu, Japan) was spectrally filtered (UG11, Schott, U.S.A.) and collimated to a beam with a diameter of 13.0 mm, resulting in an irradiance of 24 W m^{-2}. The output port of the integrating sphere is connected to a fibre, guiding the light to a thermoelectrically CCD (S10141-1108S, Hamamatsu, Japan) mounted on a 284-mm focal length imaging spectrograph (M266, Solar Laser Systems, Russia) with a grating of 2200 grooves mm^{-1}. An Hg(Ar) lamp (6035, Oriel cooperation) was used for spectral calibration. The acquisition time was 3.5 s for SPF 15 sunscreen and 35 s for the other samples. All data are reported as the mean ± standard deviation of 5 measurements. Data processing and data representation were done with MATLAB v.7.14 and OriginPro v.8.0724, respectively. After subtracting the dark current and binning the data (bin width 1 nm), the transmittance $T(\lambda)$ was calculated and used to evaluate the SPF [14]:

$$\mathrm{SPF} = \frac{\int_{290\ \mathrm{nm}}^{400\ \mathrm{nm}} E(\lambda)S(\lambda)d\lambda}{\int_{290\ \mathrm{nm}}^{400\ \mathrm{nm}} E(\lambda)S(\lambda)T(\lambda)d\lambda} \quad (1)$$

where $E(\lambda)$ is the erythemal spectral effectiveness as defined by the International Commission on Illumination [12], $S(\lambda)$ the reference solar spectral irradiance [11], and λ the wavelength of light.

The diffuse transmittance spectra of sunscreen with SPF 15 and SPF 50 and three human wound scabs are shown in Fig. 2. The transmittance spectra of sunscreen with SPF 15 and SPF 50 are the mean transmittance spectra of 5 independent measurements and result in an SPF of 15 ± 4 and 45 ± 11, respectively. Compared to SPF 50 sunscreen, all wound scabs exhibit a decreased transmittance in the UVB region. The estimated SPFs of the studied wound scabs are 84, 70, and 300 for wound scab A, B, and C, respectively. The thickness of wound scab A, B, and C is 0.26 ± 0.03 mm, 0.55 ± 0.06 mm, and 0.93 ± 0.07 mm, respectively.

Fig. 3 shows the erythemal spectral effectiveness of solar irradiance in the absence and presence of wound scab A. In the presence of wound scab A, solar irradiance induces erythema 84 times

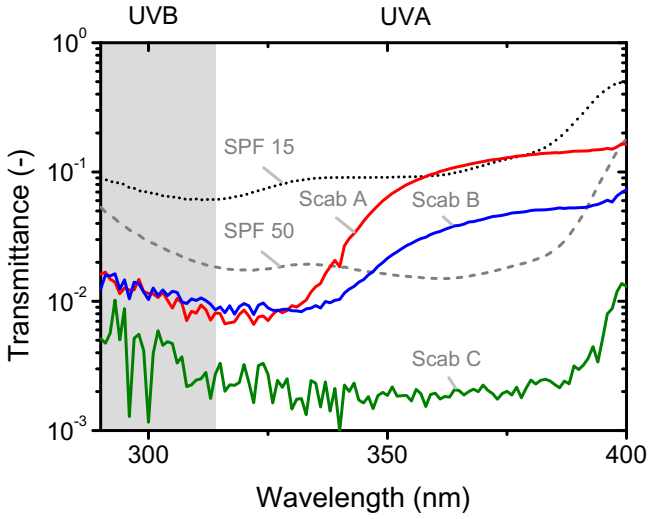

Fig. 2. Ultraviolet radiation (UVR) transmittance of sunscreen and wound scabs. UVR transmittance of sunscreen with SPF 15 and SPF 50 and three wound scabs, revealing that wound scabs effectively attenuate UVR transmission and transmit less UVB radiation than SPF 50 sunscreen.

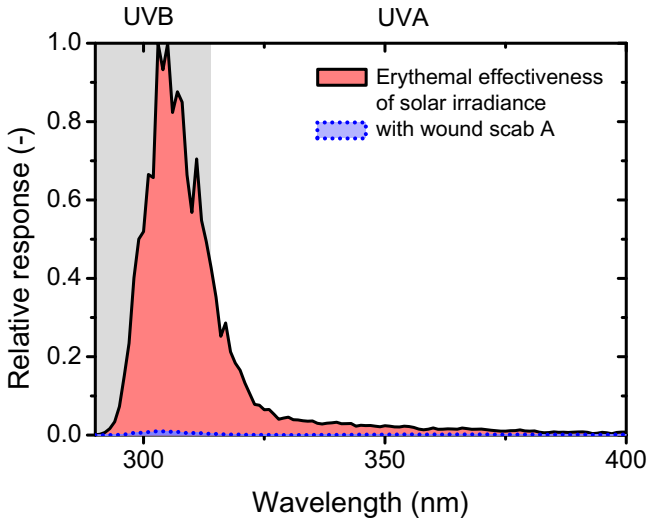

Fig. 3. Erythemal response to solar irradiance of skin covered by a wound scab. Erythemal spectral effectiveness of the reference solar spectral irradiance in the absence and presence of a wound scab. Erythema is inhibited for skin protected by a wound scab.

slower than uncovered skin, illustrating that a wound scab effectively protects underlying regenerating tissue from UVR.

Discussion

We demonstrate that a human wound scab is an excellent sun block against UVR. Exposure of the skin to sunlight results in absorption of UVR, leading to direct UVB-induced DNA damage and indirect ultraviolet radiation A induced DNA damage via generation of reactive oxygen species [15]. Mainly the UVB-induced release of photo-damaged DNA fragments leads to erythema and triggers DNA repair mechanisms [16–18]. When DNA damage is not or insufficiently repaired, the remaining mutations increase the risk of developing skin cancer, including melanoma [18,19]. Because a wound scab effectively inhibits exposure to UVR, coverage of a wound by a scab protects the otherwise exposed cells from UVR-induced DNA damage. Since extensive cell migration, proliferation and differentiation occur in a healing wound, which is not protected from UVR by melanin, inhibition of UVR by a wound scab is essential and is likely to reduce the risk of skin cancer.

Our present finding is supported by two lines of circumstantial evidence. First, after removal of a wound scab the underlying tissue is characterized by hypopigmentation (“white scarring”), illustrating that the newly formed skin is protected from UVR-induced DNA damage and thus lacks melanin production. Second, wounds formed on locations not exposed to UVR, such as wounds within the hand palm or at the underside of the foot, tend not to develop a wound scab.

Taken together, we postulate that a main biological function of human wound scabs is to inhibit the exposure to UVR, thus protecting otherwise exposed cells in a wound from UVR-induced DNA damage. Future research comprises the provision of epidemiological evidence that in the absence of a wound scab people have an increased risk of skin cancer.

Authorship contributions

E.v.d.P. and Y.D.M. conceived the experimental design, performed the experiments, and analyzed the data. E.v.d.P. and R.N. wrote the manuscript with input from all authors. F.A.W.C. participated in data interpretation. T.G.v.L. conceived the experimental design. T.G.v.L., A.S., and R.N. supervised all aspects of the project. R.N. designed the study.

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