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Effects of Oral Epigallocatechin Gallate Supplementation on the Minimal Erythema Dose and UV-Induced Skin Damage

H.Y. Jeon J.K. Kim W.G. Kim S.J. Lee

Food Research Institute, Amorepacific Corporation R&D Center, Yongin, Korea

Key Words
Epigallocatechin gallate · Systemic photoprotection · Minimal erythema dose · Transepidermal water loss

Abstract
Background/Aims: Excessive exposure to UV radiation causes acute adverse effects like sunburn and photosensitivity reactions and is involved in the induction and development of skin cancer. It has been reported that antioxidants have photoprotective effects against solar UV radiation. We investigated the effect of oral epigallocatechin gallate (EGCG), a powerful antioxidant in green tea, on the minimal erythema dose (MED) and UV-induced skin damage. ***Method:*** Female HWY/Slc hairless rats were fed the normal diet supplemented with 1,500 ppm EGCG for 8 weeks; then, the MED was determined and visual scores and transepidermal water loss were assessed to evaluate the severity of UV-induced skin damage. ***Results:*** At week 8 of the study, the use of dietary EGCG significantly increased MED. UV-radiation-induced sunburn severity and alterations in epidermal barrier function were also attenuated by the supplementation of EGCG. ***Conclusion:*** Regular intake of EGCG strengthens the skin's tolerance by increasing MED and thus prevents UV-induced perturbation of epidermal barrier function and skin damage. These results suggest that EGCG is a potent candidate for systemic photoprotection.

Introduction

The skin is continuously exposed to harmful environments which cause various adverse effects on the structure and function of the skin. Among those environmental influences, solar UV radiation is of considerable importance in the pathobiochemistry of specific types of skin cancer, premature aging of the skin, photosensitivity disorders and sunburn [1]. Solar UV radiation is subdivided into UVA (320–400 nm), UVB (290–320 nm) and UVC (<290 nm) [2]. The ozone layer efficiently absorbs UVC so that the wavelengths of solar UV radiation that damage the skin are UVA and UVB. UVA penetrates into the deeper layer of the skin where it breaks up the elastin and collagen fibers, causing premature photoaging of the skin. UVB radiation is 1,000 times more genotoxic and strongly absorbed by DNA, causing sunburn and skin cancer [3, 4].

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Sang Jun Lee, PhD
Food Research Institute, Amorepacific Corporation R&D Center
314-1, Bora-dong, Giheung-gu
Yongin-si, Gyeonggi-do 446-729 (Korea)
Tel. +82 31 280 5810, Fax +82 31 281 8392, E-Mail leesjun@amorepacific.com

The conventional sun-protective behavior is applying a sunscreen to the skin. Sunscreens contain chemicals that absorb UV rays, thereby protecting the skin [5]. Since sunscreens can be removed by perspiring or swimming, for best results, a sunscreen should be applied 30–60 min before venturing into the sun. Although sunscreen use is still the first-line strategy of preventing UV damage to the skin, it is helpful in avoiding photodamage only to a certain extent.

Oral supplementation has gained considerable attention for protecting the skin from a harmful environment such as sunlight and pollutants and restoring it. In view of the growing interest in systemic photoprotection, many compounds have been assessed for their ability to provide photoprotection after oral administration. Since reactive oxygen species formed upon solar radiation play a central role in initiating and driving the detrimental signaling events, antioxidant supplementation is thought to provide a photoprotective effect against UV radiation [6]. Dietary botanical agents, which possess anti-inflammatory, immunomodulatory and antioxidant properties, are among the most promising groups of compounds that can attenuate the adverse effects of overexposure to UV radiation [7].

The present study was designed to test whether epigallocatechin gallate (EGCG) supplementation has a protective effect against UV radiation. EGCG is a powerful antioxidant thought to be responsible for the significant benefits of green tea on skin. Studies have recently shown that oral administration of green tea polyphenols in the drinking water of mice results in significant protection against UV-induced damage and photocarcinogenesis. The photoprotective effect of green tea polyphenols is mediated by inhibition of UV-induced immunosuppression through a cytokine interleukin-12-dependent DNA repair mechanism [8, 9]. Moreover, oral administration green tea polyphenols also inhibit UVB-induced oxidative damage and expression of matrix metalloproteinases [10]. Since EGCG comprises approximately 59% of the total of catechins and is assumed to be the source of most of the biological activity of tea, oral administration of EGCG may provide a promising strategy to counteract solar UV radiation [11, 12].

Materials and Methods

Materials

EGCG (>94%) was obtained from DSM Ltd. All other chemicals were available products of analytical grade or HPLC grade.

Animals

Female HWY/Slc hairless rats (9 weeks old) weighing 190–210 g were obtained from SLC Inc. (Shizuoka, Japan). The animals were acclimatized for 1 week in the animal facility prior to the experiments and housed under controlled conditions. All care and treatment of rats were in compliance with the guide for care and use of laboratory animals and local institutional guidelines.

Experimental Design

Twenty-five female HWY/Slc hairless rats were randomly divided into 5 groups: 2 groups, normal control and EGCG-treated group, for minimal erythema dose (MED) measurement and 3 groups, nonirradiated control, UV-irradiated control and UV-irradiated+EGCG-treated group, for the assessment of UV-induced skin damage. Each group of 5 rats was housed in a cage.

The rats of the UV-irradiated group were exposed to UVB lamps (Waldmann UV800; Villingen-Schwenningen, Germany; 285–350 nm, peak at 310–315 nm) 3 times a week. The intensity of irradiation was gradually increased from 97 mJ/cm^2 (equivalent to 1 MED) to 194 mJ/cm^2 (equivalent to 2 MED) to achieve the total dose of 3,492 mJ/cm^2 (equivalent to 36 MED) over the 8 weeks. The normal, nonirradiated and UV-irradiated control groups were fed a commercial rat food that contained protein (approx. 20%) and fat (approx. 7%). The EGCG-treated groups were fed the normal diet supplemented with 1,500 ppm EGCG (Feedlab Korea Corp., Seoul, Korea). Food and water were provided ad libitum. Food consumption and body weight were recorded during the experimental period.

MED Measurement

After 8 weeks of supplementation with EGCG, the MED was determined visually by using 12 incremental exposures of 51.7–194.0 mJ/cm^2. The lowest dose causing a sharply circumscribed homogenous erythema 24 h after UVB exposure was defined as the MED.

UV-Induced Skin Damage Assessment

Visual Score Assessment. Visual scoring of skin condition was performed to evaluate the skin condition. The visual score was recorded by one investigator who had been trained in its use in a series of pilot tests with the consultant dermatologist. The extent of skin scaling and damage was scored according to a scale ranging from 0 to 5, with 0 representing normal skin and 5 representing extensive cracking with widespread reddening or occasional bleeding.

Transepidermal Water Loss. Transepidermal water loss (TEWL) was measured as a marker of epidermal barrier function using a wireless vapometer (Delfin Technologies Ltd., Kuopio, Finland). The measurement was carried out 48 h after the final irradiation to allow a recovery from the acute UV effect.

Statistical Analysis

The results are presented as means ± SD. Statistical analysis was performed using the SPSS program (SPSS 12.0). MED and TEWL data were analyzed by t test and one-way ANOVA with Duncan's multiple range tests, respectively. Nonparametric data and visual scores were analyzed by the Friedman repeated measures test with ANOVA on ranks.

Results and Discussion

MED Measurement

Erythema dose responses are displayed in figure 1. The normal-diet group showed MEDs ranging from 90.5 to 103.5 mJ/cm^2, with a mean value of 99.2 mJ/cm^2. A significant ($p < 0.01$) increase was observed after supplementation of EGCG for 8 weeks; the MED ranged from 129.3 to 155.2 mJ/cm^2, with a mean value of 144.9 mJ/cm^2 (fig. 1).

Visual Score Assessment

UV exposure significantly increased visual scores when compared to normal control. Three rats out of 5 showed widespread reddening or occasional bleeding, and the others showed redness with moderate intensity. However, EGCG-treated rats showed markedly low visual scores with a mean value of 2.5 (fig. 2). Each picture of rat dorsal skin is a representative of each group of 5 rats.

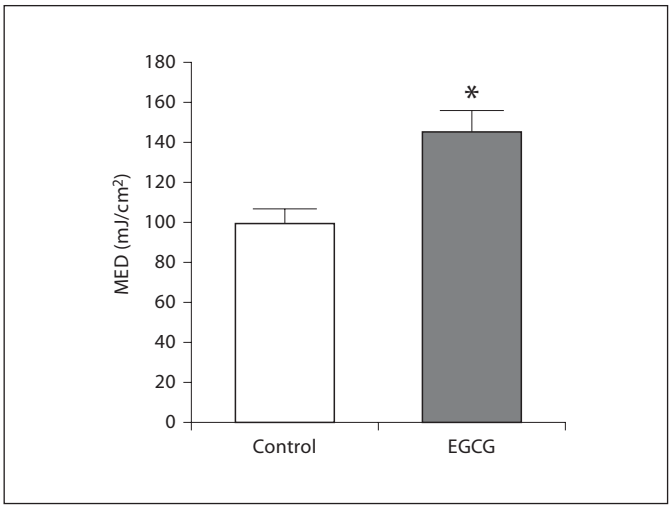
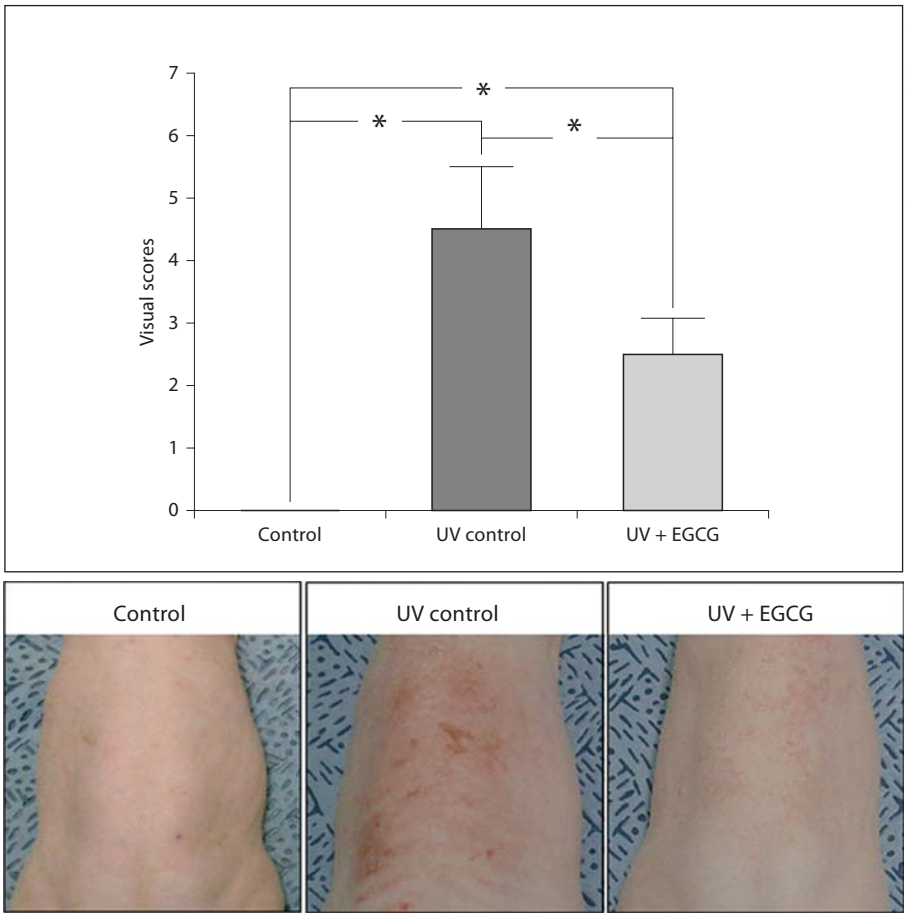


Fig. 1. Effect of dietary EGCG on MED. After 8 weeks of supplementation of EGCG, the MED was determined based on the erythema that occurred after simulated UV radiation. Each column represents the mean ± SD. * $p < 0.01$, compared with controls.



Color version available online

Fig. 2. Effect of dietary EGCG on UVB-induced skin damage. Hairless rats were exposed to UVB 3 times a week to induce skin damage. At the end of an 8-week oral administration of EGCG, visual scores were assessed to evaluate the severity of skin damage. Each column represents the mean ± SD. * $p < 0.01$, compared with controls or UV-irradiated controls, respectively.

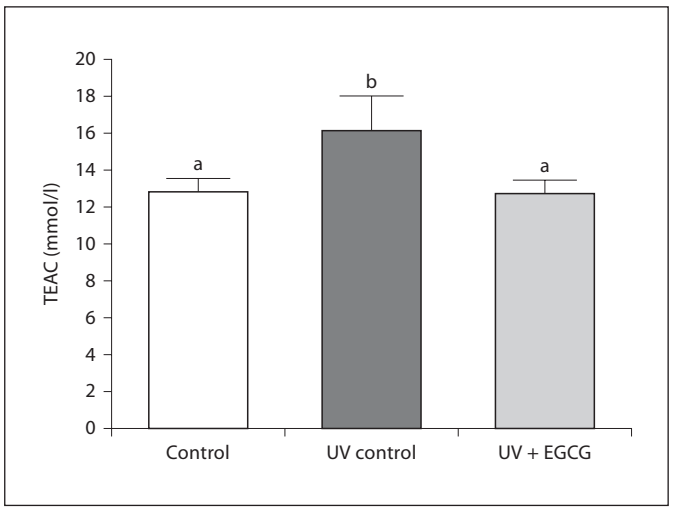


Fig. 3. Effect of dietary EGCG on the UVB-induced perturbation of skin barrier function. Hairless rats were exposed to UVB 3 times a week. At the end of an 8-week oral administration of EGCG, TEWL was measured as a marker of skin barrier function. Each column represents the mean ± SD. Values not sharing the same letter are significantly different, with $p < 0.01$.

Transepidermal Water Loss (TEWL)

UVB irradiation markedly increased TEWL to 16.1 ± 1.9 g/m^2/h when compared to the normal control, 12.8 ± 0.8 g/m^2/h; however, the EGCG-treated group remained at a control level of 12.7 ± 0.8 g/m^2/h (fig. 3). No adverse effect was observed during the study period.

The present results show the significant increase in MED by the supplementation of EGCG. The MED is a measure of the ability of a sunscreen to protect against erythema, which is thus primarily a measure of UV protection. This suggests that EGCG supplementation increases the MED which might indicate a consequent reduced risk for UV-induced skin damage. Oral EGCG, with its strong antioxidant capacity, provides a strategy to combat the excess generation of reactive oxygen species in response to UV radiation and hence strengthens the skin's defense capacity against UV radiation [10]. Although sunscreen use is a valuable method of sun protection, it cannot completely block the UV rays. Besides, some body areas are frequently missing when applying the sunscreen [13]. Oral sunscreens can improve the currently used means of photoprotection.

We also observed that EGCG consumption significantly attenuated the UV-induced sunburn severity and perturbation of epidermal barrier function. Dermatohistological specimens at 48 h after the last irradiation showed no distinct histological differences other than epidermal thickening in UV-irradiated controls (data not shown). This observation is consistent with results of previous studies in which UV irradiation induced a progressive thickening of the epidermis [14]. Even though morphological changes showed little similarity to human sunburn, these experimental results can be transposed to humans.

The amount of EGCG given to the animals was roughly equal to about one third to one cup of green tea per day [15]. Although the dosage of EGCG used in this study is too high to be physiologically relevant, this result indicates that several cups of green tea a day may help sustain the skin's natural ability to deal with UV-radiation-related effects and aging. However, some discouraging and unexpected side effects were often observed in the case of the application of antioxidant supplements. There are several possible explanations for these contradictory findings. Extra antioxidants may interfere with some essential defensive mechanism by eliminating free radicals. Also, the human population is heterogeneous and the diversity of initial antioxidant levels is hardly exceptional [16, 17]. Nevertheless, there are some clear tendencies concerning the systemic application of EGCG. Taking into consideration all the available literature and the results of the present study, EGCG is a potent antioxidant that works as an oral photoprotector.

Conclusions

In conclusion, the present study shows that the regular intake of EGCG markedly increases the MED and thus strengthens the skin's tolerance to the UV radiation. The conclusion is supported by the observation that EGCG supplementation attenuated the UV-induced perturbation of epidermal barrier function and skin damage. EGCG, with its demonstrated efficacy to protect the skin from solar UV radiation, is an ideal candidate as a product for systemic photoprotection. However, long-term studies using a low dose are required to provide additional supportive evidence. Nevertheless, this study serves as a good point of departure to accelerate the development of new photoprotective strategies based on the endogenous protective response to UV light.

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