Comparison of the Minimal Phototoxic Dose in Topical 4,5′, 8-Trimethylpsoralen PUVA Treatment of Caucasian Skin and of Oral Mucous Membrane

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The minimal phototoxic dose values for UVA radiation of psoralen-treated skin and of oral mucous membrane were studied in 16 healthy volunteers. A commercial 0.01% trioxalen ointment was used as the topical photosensitizer. In all 16 persons the radiation dose needed to induce erythema was greater for the buccal mucosa than for the skin, and the average buccal minimal phototoxic dose was 2.3-fold that of the cutaneous minimal phototoxic dose. ***Key words: PUVA-therapy; Phototoxicity; Trioxalen.***

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In 1987 we introduced mouth PUVA, i.e. topical UVA irradiation of oral mucosa after systemic psoralen photosensitization, as an efficacious treatment for recalcitrant oral lichen planus (1), and subsequent studies have confirmed our findings (2, 3).

In PUVA therapy of cutaneous diseases, topical application of the psoralen sensitizers has been used with success (4, 5, 6). In the case of mouth PUVA, topical application would, analogously, be preferable to systemic delivery of the psoralen sensitizer. Whereas the cutaneous phototoxicity of psoralens has been studied in detail (5), corresponding studies in the oral cavity are lacking. We have compared the phototoxicity of topical trimethylpsoralen (TMP) in the skin and oral mucosa of Man.

MATERIAL AND METHODS

Sixteen healthy Caucasians (14 females and 2 males aged 21–30 yr) volunteered for the study. Six of the subjects had

Table I. *Individual MPDs of the volunteers for skin and buccal mucosa*

Person No./sex	Skin type	Cutaneous MPD (J/cm^2)	Mucosal MPD (J/cm^2)	Mucosal/cutaneous MPD MPD
1/F	II	0.6	2.7	4.5
2/F	II	0.6	2.7	4.5
3/F	III	0.6	3.6	6.0
4/F	II	0.9	1.8	2.0
5/F	III	0.9	2.7	3.0
6/F	III	0.9	2.7	3.0
7/F	III	1.2	1.8	1.5
8/F	II	1.2	1.8	1.5
9/M	III	1.2	2.7	2.3
10/F	III	1.2	3.6	3.0
11/M	III	1.2	4.5	3.8
12/F	III	1.5	2.7	1.8
13/F	III	1.5	2.7	1.8
14/F	III	1.8	2.7	1.5
15/F	II	1.8	2.7	1.5
16/F	III	1.8	3.6	2.0

skin type II and 10 had type III (7). A commercial 0.01% TMP ointment (Tripsor®, Orion Ltd, Helsinki) was used for topical sensitization. The ointment was applied for 10 min to the site to be sensitized, and the excess removed with cotton rolls before irradiation. In the case of the oral sensitization, the buccal mucosa was dried and protected from saliva with a dental suction device and cotton rolls. For cutaneous sensitization, the flexor sides of the lower arms were used.

UVA irradiation was carried out with a Blue Point UVA-light device (Dr K. Hönle GmbH, West Germany) equipped with a UVA-transmitting fibre cable, emitting in the 320 to 400 nm range (maximum 362 nm). In the TMP-treated cutaneous or mucosal sites, circular areas, 8 mm in diameter, were irradiated. Skin sites were irradiated in the range of 0.3 to 1.8 J/cm^2, with 0.3 J/cm^2 increments. Mucosal sites were irradiated with 0.45 and 0.9 J/cm^2, and thereafter with 0.9 J/cm^2 increments up to maximally 4.5 J/cm^2. The irradiated sites were inspected at 24 h for signs of erythema.

RESULTS AND DISCUSSION

The cutaneous MPD values varied between 0.6 and 1.8 J/cm^2 with a mean value of 1.2 ($\pm$ 0.4) J/cm^2, while the mucosal MPD values varied between 1.8 and 4.5 J/cm^2 with a mean value of 2.8 ($\pm$ 0.7) J/cm^2 (Table I). In each person, the mucosal MPD was higher than the cutaneous MPD, by a factor of 1.5 to 6 (mean 2.7).

The apparently greater resistance of oral mucosal tissue, in comparison with the skin, to topical psoralen plus UVA-induced inflammation (i.e. higher MPD), is rather surprising. The reason for this disparity is not readily evident, but could relate to differences in penetration of either the radiation or the psoralen into the cutaneous and mucosal tissue. Compared with skin epidermis, human buccal epithelium is up to 10 times thicker (8), and this can be expected to counteract the penetration of UVA into the mucosa because of increased scattering (9). The rate of penetration is, according to the diffusion theory, inversely proportional to epithelial thickness and this might evidently be one reason for a slower or inferior drug absorption in oral mucosa.

The possible differences in the partition coefficients and/or diffusion constants between the oral mucosa and the skin are also unknown (10) and the efficacy of a topically administered psoralen may also be reduced by these factors in oral mucous membrane.

Further studies should be directed towards both psoralen absorption parameters and ultraviolet transmission characteristics of oral mucosal tissue.

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