Safety of Oxybenzone: Putting Numbers Into Perspective

Oxybenzone, an organic UV-B and short-wave UV-A filter, has been available for over 40 years[1]; it is widely used in sunscreens and other consumer products in the United States.[2] The Centers for Disease Control and Prevention has estimated the prevalence of oxybenzone exposure in the general US population to be 96.8%.[3] In the past few years, oxybenzone has received increasing attention as a potentially harmful compound. Initial concerns arose when a report demonstrated systemic absorption of oxybenzone in humans at a rate of 1% to 2% after topical application.[4] Similar or higher rates of cutaneous absorption in human subjects have been observed.[5-9] The potential for biological effects, however, were first published in a study by Schlumpf et al[10] demonstrating uterotropic effects in immature rats after oral administration of oxybenzone; it should be noted that the estrogenic effect detected was less than 1 million-fold of estradiol, the positive control used. Nonetheless, this study has served as the basis for considerable concern among the public.

In assessing the potential for hormonal disruption in humans, we decided to place into perspective the doses of oxybenzone used by Schlumpf et al[10] to achieve the 23% increase in uterine size reported in immature rats. We performed 2 calculations: (1) we determined the equivalent amount of sunscreen required to be used topically in humans to achieve the effective cumulative amount of oxybenzone orally administered to immature rats; and (2) we determined the number of years of daily application required to obtain the equivalent levels of oxybenzone that the experimental animals were exposed to.

Methods. The oral dose of oxybenzone used by Schlumpf et al[10] was 1525 mg/kg/d over a 4-day period. The effective cumulative dose was 6100 mg/kg. To calculate an equivalent amount of sunscreen, the following assumptions were applied to the formula: (1) the weight of an average woman in the United States was assumed to be 74.6 kg[11]; (2) the absorption rate of topically applied oxybenzone, 10%, was assumed to be approximately 2%[4-9]; and (3) the maximum concentration of oxybenzone in sunscreen sold within the United States was assumed to be 6% (wt/vol), or 60 mg/mL.[12]

([6100 mg of Oxybenzone/kg × 74.6 kg]/2%) × (1 mL of Sunscreen/60 mg of Oxybenzone) = 379 217 mL

We then calculated the number of years of daily application that would be required to apply 379 217 mL of sunscreen under 3 different scenarios:

Scenario 1: 100% body surface area (BSA) coverage at a standard dose of 2 mg/cm^2 would require 30 mL (10 950 mL/y with daily application).

Scenario 2: 100% BSA coverage at a dose of 1 mg/cm^2 would requires 15 mL (5475 mL/y).

Scenario 3: 25% BSA coverage at a dose of 1 mg/cm^2 would require 3.75 mL (1369 mL/y).

Table. Years of Daily Sunscreen Application Required by an Average US Woman to Reach Systemic Levels of Oxybenzone per Unit of Body Mass Equivalent to Those Given to Immature Rats[10]

Characteristic	Scenario 1	Scenario 2	Scenario 3
Body surface area covered, %	100	100	25
Application dose, mg/cm^2/d	2	1	1
Application amount required, mL/d	30.00	15.00	3.75
Time required, y	34.6	69.3	277.0

For the purposes of this estimation, a generous in-use dose of 1 mg/cm^2 was used,[13-16] and it was assumed that coverage of 25% of the human BSA was limited to the face, neck, hands, and arms.[17]

Results. The numbers of years of daily application required to obtain the equivalent amount of sunscreen under the 3 scenarios are listed in the **Table**.

Comment. Our results indicate that both the application regimens and time periods required to obtain systemic levels of oxybenzone equivalent per unit of body mass are essentially unattainable. Our assumption is more conservative. For instance, the bioavailability of the oxybenzone-containing rat chow used by Schlumpf et al[10] may not have been 100%, and we did not take into account the excretion of oxybenzone in humans. In fact, oxybenzone has not been demonstrated to accumulate in the plasma even after several days of topical application.[6,9,18] Most relevant to this discussion, however, is that in a human study, oxybenzone did not demonstrate significant endocrine disruption, even with application of a formulation containing 10% oxybenzone.[6] In fact, after 40 years of use, we are not aware of any published study that demonstrates acute toxic effects in humans with systemic absorption of oxybenzone.

We do not intend for this exercise to serve as a basis from which to legitimize the extrapolation of data from immature rats to humans. In fact, basic scientific principles regarding the complexities of each respective biological system preclude this. Nonetheless, we hope that this analysis helps to place into perspective the doses reported by the in vivo study from which inappropriate conclusions have been drawn and considerable controversy has developed.

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Accepted for Publication: November 30, 2010.
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Author Contributions: All authors had full access to all of the data in the study and take responsibility for the

integrity of the data and the accuracy of the data analysis. *Study concept and design:* Wang and Burnett. *Acquisition of data:* Wang and Burnett. *Analysis and interpretation of data:* Burnett and Lim. *Drafting of the manuscript:* Wang and Burnett. *Critical revision of the manuscript for important intellectual content:* Wang, Burnett, and Lim. *Statistical analysis:* Lim. *Study supervision:* Wang and Lim.
Financial Disclosure: None reported.

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Open Pores With Plugs in Porokeratosis Clearly Visualized With the Dermoscopic Furrow Ink Test: Report of 3 Cases

Porokeratosis is an autosomal dominantly inherited disorder characterized by brown annular lesions with scaling ridges, which histopathologically corresponds to the cornoid lamella. Several dermoscopic findings of porokeratosis have been reported, including a whitish peripheral rim, brown globules and/or dots, red dots and/or red lines, and scarlike structures in the center of the lesions.[1] Herein, we report 3 cases of porokeratosis of Mibelli dermoscopically clearly showing multiple pores.

Report of 3 Cases. *Case 1*. An 88-year-old man presented with a 30-year history of multiple brown plaques. No family history of porokeratosis was reported. Clinical examination revealed that brown, round, sharply demarcated annular plaques up to 3 cm in size were widespread on the trunk and extremities (**Figure 1**). Dermoscopic evaluation of the lesions showed a brown rim along on periphery of the lesions (**Figure 2**A). The fine pigment network, dots and/or globules, and the small shining white or brown spots were mainly observed within the brown band.

Staining of the skin surface with whiteboard marker (the *furrow ink test*) clearly revealed the rims along the inside and outside of the peripheral band and multiple open pores with keratotic plugs (Figure 2B). Furthermore, the furrow ink test highlighted the differences in texture on the skin surface in some lesions. The texture was diminished and flattened in the periphery and finer in the central portion of the lesions compared with normal skin. Some pores corresponded to hair openings, which were confirmed pathologically (**Figure 3** and **Figure 4**). Although the pores were observed in almost all lesions, the number and distribution varied in each lesion.

Case 2. An 89-year-old man presented with a 2-year history of multiple brown plaques. Clinical examination revealed brown, sharply demarcated annular plaques up to 2 cm in size on the extremities. Dermoscopically, the multiple small brown spots were observed in the central area. Pathologic findings showed a column of compact hyperkeratosis with parakeratosis in the part corresponding to acrosyringium as well as typical cornoid lamella in the periphery of the lesion.

Case 3. A 52-year-old man presented with a 1-year history of multiple brown plaques. Clinical examination revealed light-brown, round, sharply demarcated plaques on the extremities. Dermoscopic findings were similar to those in cases 1 and 2, except with fewer pores.

Comment. Dermoscopic examination in our cases showed that the multiple pores seemed to correspond to hair openings and sweat pores. Porokeratosis of Mibelli was originally believed to involve columns of parakeratosis, the cornoid lamella, emerging only from the ostia of eccrine ducts. However, Reed and Leone[2] later proposed that the cornoid lamella did not originate from the ostia of ec-

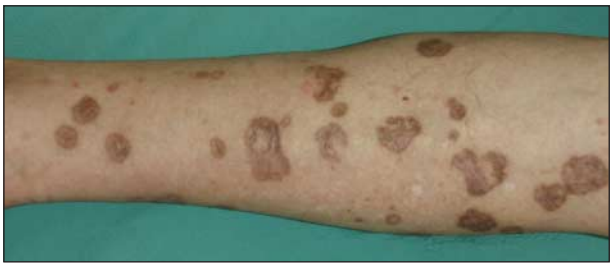

Figure 1. Case 1. Brown, round, sharply demarcated plaques on the leg.