Studies of Sunscreens: Percutaneous Absorption of Benzophenone-3 and Photostability

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Helena Gonzalez
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Docent Berit Berne
Uppsala Universitet

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I H Gustavsson Gonzalez, A Farbrot and O Larkö. Percutaneous absorption of benzophenone-3, a common component of topical sunscreens. *Clinical and Experimental Dermatology 2002; 27, 691-94.*

II H Gonzalez, A Farbrot, O Larkö and A-M Wennberg. Percutaneous absorption of the sunscreen benzophenone-3 after repeated whole body applications - with and without UV irradiation. *British Journal of Dermatology 2006; 154, 337-40.*

III H Gonzalez, C-E Jacobson, A-M Wennberg, O Larkö and A Farbrot. Solid-phase extraction and HPLC: application to study the urinary excretion pattern of benzophenone-3 and its metabolite 2,4-dihydroxybenzophenone in human urine. *Submitted for publication.*

IV H Gonzalez, N Tarras-Wahlberg, B Strömdahl, A Juzeniene, J Moan, O Larkö, A Rosén and A-M Wennberg. Photostability of commercial sunscreens upon sun exposure and irradiation by ultraviolet lamps. *Submitted for publication.*

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Helena Gonzalez
Department of Dermatology and Venereology
Institute of Clinical Sciences
The Sahlgrenska Academy at Göteborg University
Göteborg, Sweden

Abstract

Aim: To learn more about percutaneous absorption of the photoactive compound benzophenone-3 (BZ-3) and to study the excretion pattern of BZ-3 and its metabolite dihydroxy benzophenone (DHB). We also got the opportunity to develop a reverse-phase HPLC method to analyze BZ-3 and DHB. The photostability of seven commercial sunscreens was also studied.

Material and methods: *Paper I:* 11 participants applied a sunscreen, 2 mg/cm^2, containing 4% BZ-3. They collected urine for 48 hours after the application. *Paper II:* 26 participants applied a sunscreen, 2 mg/cm^2, containing 4% BZ-3 morning and night for five days. Half of the participants were exposed to UV radiation (UVR). They collected urine for the five days the sunscreen was applied and an additional five days after the last application. *Paper III:* The assay uses: solid-phase extraction with C8 columns; a Genesis C18 column (4.6 mm x 150 mm); a gradient acetonitrile-water mobile phase; a UV-detector set at 287 nm. *Paper IV:* Seven commercial sunscreens were studied with absorption spectrophotometry. Sunscreen product, 0.5 mg/cm^2, was placed between plates of silica. The area under the curve (AUC) in the spectrum was calculated for the different UV regions. AUC before (AUC_{before}) and after (AUC_{after}) artificial UV exposure and before and after natural UV exposure were calculated. If the AUC Index (AUCI), defined as $AUCI=AUC_{after}/AUC_{before}$, was > 0.80, the sunscreen was considered photostable.

Results: *Paper I:* The average total amount excreted was 11 mg, median 9.8 mg, which is approximately 0.4% of the applied amount BZ-3. *Paper II:* The volunteers excreted 1.2-8.7% BZ-3 of the total applied amount. The mean value found was 3.7%. There was no significant difference between the two groups; $p<0.99$. *Paper III:* The assay was linear r^2 >0.99, with detection limits for BZ-3 and DHB of 0.01 µmol/l and 0.16 µmol/l respectively. Relative standard deviation was less than 10% for BZ-3 and less than 13% for DHB. The excretion pattern varied among the human volunteers, different patterns were discerned among the individuals. *Paper IV:* Three sunscreens were unstable after 90 min of natural UV, in the UVA range the AUCI was between 0.41 and 0.76. In the UVB range, one of these sunscreens was unstable with an AUCI of 0.75 after 90 min. Three sunscreens were photostable after 120 min of natural UV, in the UVA range the AUCI was between 0.85 and 0.99 and in the UVB range between 0.92 and 1.0.

Conclusions: *Paper I:* BZ-3 is absorbed by the skin and excreted in the urine after one topical application of a sunscreen containing 4% BZ-3. There are individual differences in the amount excreted and in the excretion pattern. *Paper II:* Repeated topical applications of a sunscreen containing 4% BZ-3 lead to a higher excretion of BZ-3. There was no statistical difference after exposure to UVR. *Paper III:* The developed reverse-phase HPLC-method was reliable and suitable to handle a large number of samples. BZ-3 and DHB were excreted in a similar pattern. *Paper IV:* Three of the seven investigated sunscreens were photounstable in the UVA region. The combination ethylhexyl methoxycinnamate and butyl methoxydibenzoylmethane was unstable regardless of which other photoactive compound that was included in the sunscreen.

Key words: benzophenone-3, dihydroxy benzophenone, sunscreens, UV radiation, reverse-phase HPLC, photostability