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LC analysis of benzophenone-3: II application to determination of 'in vitro' and 'in vivo' skin penetration from solvents, coarse and submicron emulsions

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Abstract

The aim of this study was to determine the skin penetration of benzophenone-3 in vitro and in vivo in order to investigate a possible influence of formulation. Six different vehicles, three solvents and three different emulsion types were evaluated in vitro and in vivo. Each vehicle was applied to the skin model at 2 mg cm^{-2}. First, histological studies on ear pigskin and human skin were evaluated. In vitro measurements were performed with static diffusion cells using pigskin at 1, 2, 4, and 8-h. In vivo, benzophenone-3 concentration in stratum corneum was evaluated by the stripping method after 30-min application on forearm of volunteers. It was shown that ear pigskin and human skin appear similar and in both experiments significant differences between vehicles were noticed. The six vehicles could be ranked in the same order of benzophenone-3 skin concentration. At 8-h, the highest concentration of benzophenone-3 in skin was obtained with propylene glycol, and O/W submicron emulsion. On the contrary, the two oily solvents, W/O emulsion and O/W coarse emulsion restrain the concentration of this UV-filter in the skin. At each time, permeability in vitro and in vivo were well correlated. Low concentrations were measured in the receptor fluid suggesting that percutaneous absorption of this UV-filter across the skin would be minimal. The in vitro and in vivo skin penetration capacity of benzophenone-3 from six vehicles was confirmed and quantified. A satisfactory relationship between binary in vitro and in vivo was established.

Keywords: Percutaneous penetration; Sunscreens; Stripping method; Submicron emulsions

1. Introduction

Of all the properties studied during the formulation of sunscreen preparations, the most important seems to be the impact of the formulation on skin penetration. Benzophenone-3 or oxybenzone

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is currently used in many cosmetic formulations on the market, such as lipcares, sunscreen lotions or emulsions, shampoos and hair sprays, despite this large use there is few but recently published data to the potential skin penetration. Some literature describes oil in water or water in oil emulsions, gels, lotions or hydroalcoholic formulation which were investigated in vivo or in vitro [1–5]. These preparations contained a combination of various ingredients and in these cases, it is difficult to extrapolate findings from one to all preparations. The vehicle used is a factor influencing percutaneous absorption: it may enhance or block the movement of the UV-filter through the skin. According to the literature, mineral solvents are preferentially used in this field (petrolatum jelly, paraffin, liquid paraffin) [6,7] but benzophenone-3 is poorly soluble in these products [8–10]. To prevent crystallization of the active sunscreens, the vehicles used must be carefully selected. In this field, solubility and penetration of benzophenone-3 from a range of solvent (50% saturated solution) was investigated by Jiang et al. [11]. In our study, all vehicles used to deliver oxybenzone to the skin surface were non-polar or semi-polar solvents used in dermatology: coconut oil (natural oil), capric-caprilic triglyceride (neutral oil, with high skin compatibility), and propylene glycol. Both oily phases were used to formulate two types of vehicle: oil/water and water/oil emulsions, with different sizes of droplets.

The purpose of the present investigation was to examine in vitro and in vivo the vehicle effect on skin penetration of benzophenone-3. In a first step, in vitro experiments were performed using a static diffusion Franz cell. Pigskin and particularly pig ear resembles human skin morphologically and functionally, and percutaneous permeation rates appear to be similar [12]. Furthermore, this model is useful for its availability and ease of preparation, in contrast to using human skin obtained from surgery or cadavers, which is normally not frequently available and which is quite often already damaged. In the present study, four times were investigated, 1, 2, 4, 8 h according to recent works in this field [1,4,11].

Stratum corneum is an important lipophilic barrier to the permeation of drug but it also acts as a reservoir for topically applied chemicals. In the second step, in vivo experiments were performed and the amount of benzophenone-3 present in the stratum corneum after 30 min application time was determined, according to the stripping technique developed by Rougier et al. [13–15]. Half an hour was also investigated by Treffel et al. [1], and by Marginean Lazar et al. [16] and Oliva et al. [17] in tape stripping method with sunscreens and other drugs. Thus, this short time is representative of the stratum corneum reservoir function.

2. Experimental

2.1. Reagent and chemicals

Oxybenzone or Benzophenone-3 (2-hydroxy-4-methoxybenzophenone), was used without further purification (stated purity 99.5%, Sigma, St Louis, MO). Saline solution was prepared with 9‰ (W/W) NaCl (Merck, Darmstadt, Germany). Methyl alcohol (99.9%, Carlo Erba RS HPLC, Farmaitalia, Milano, Italy), for HPLC. Extractions were performed with hexane, ethyl acetate (Normapur, Prolabo, Fontenay s/bois, France), Silica gel disposable extraction cartridges (6-ml, 500 mg, SDS, Valdonne, France) were used for chromatography. Ethyl alcohol absolute (99.7%, Carlo Erba RPE-ACS, Farmaitalia, Milano, Italy). The solvents chosen were capric-caprilic triglycerides (Miglyol 812, Condea), Coconut oil (Laboratory CPF, Melun, France) and Propylene Glycol (Prolabo, Fontenay s/bois France). Surfactants used were sorbitan stearate (Dehymuls SMS, Henkel, Düsseldorf, Germany), Polyoxyethylen-20 sorbitan monooleate (Emulgin SMO-20, Henkel, Düsseldorf, Germany), Methoxy PEG-22/dodecyl glycolpolymer (Elfacos E200, Akzo, Compiègne, France), Polyglyceryl-2 dipolyhydroxystearate (Dehymuls PGPH, Henkel, Düsseldorf, Germany), Cetearyl glucoside (Montanov 68, Seppic, Paris, France), polyacrylamide and isoparaffin and laureth-7 (Sepigel 305, Seppic, Paris, France). Water was freshly redistilled for emulsion formulations and sterile (versol, Lyon, France) for droplet size analyses.

2.2. Apparatus

Formulations were performed at 24 ± 1°C with an homogenizer at 400-rpm (Turbotest 33/300, Rayneri). An Ultra Turrax (Ika-Tron labortechnik) was used for extraction. The HPLC system consisted of a Beckmann 344 System with a variable wavelength detector (set at 287 nm). The chromatograph was equipped with a Merck Lichrosph 60 RP select B (250 mm × 5 μm) column. The mobile phase was isocratic methanol-water (92:8, v/v) with a flow rate of 0.75 ml min^{-1}. The injection volume was always 20 μl. Franz glass diffusion cells were used. The area for diffusion was 0.785 cm^2 and the receptor chamber volume varied from 10.2 to 10.8 ml. Measurements of droplet sizes were made with a Zetasizer 3000 (Malvern instrument, Malven, UK) operating at 633 nm. Data were collected at a scattering angle of 90°C. A Leitz orthoplan with dyective magnitude 4, 10, was used for microscopic analysis.

2.3. Emulsions formulations

Three different emulsions were formulated under the following conditions. Water and other components were heated separately at 75 ± 2°C. Under agitation at 400-rpm the aqueous phase was added to the other components in 1 min and cooled to room temperature over 45 min. All emulsions were stored at 25 ± 1°C before further observations were made.

For oil/water submicron emulsions the dispersed phase consisted of a mixture of coconut oil and capric-caprilic triglyceride (25%) Dehymuls SMS (6%) Emulgin SMO (9%) Sepigel 305 (1%). The amount of distilled water was 60%. The dispersed phase of oil/water coarse emulsions consisted of a mixture of coconut oil and capric-caprilic triglyceride (25%), Montanov 68 (10%). The amount of distilled water was 65%. For water/oil emulsions the dispersed phase was a mixture of coconut oil and capric-caprilic triglyceride (25%), Elfacos E200 (15%), Dehymuls PGPH (7.5%). The amount of distilled water was 52.5%. In each case the same emulsion was also formulated with 3% of benzophenone-3. At first, the droplet size was measured by microscopy. In a second stage only photon correlation spectroscopy (PCS) measurements were made on submicron emulsions. In each case, analyses were performed in triplicate. Three stability methods were performed with two accelerated tests. The first accelerated test concerned stability at elevated temperatures, (15 days at 50°C), and the second concerned stability under centrifugation, 15 min at 5000 rpm. The last test included long term stability at 25 ± 1°C.

2.4. Liquid chromatography

The aim of a previous work was to develop an easy and adapted HPLC analytical method and validation procedure for the determination of oxybenzone levels in pig-ear skin and saline solution. This method was applied to determine the amounts of oxybenzone from 'in vitro' and 'in vivo' transdermal experiments, and this method was extensively described in a previous work [18].

2.5. Skin and microscopic sample preparations

Pig ears were obtained from a slaughterhouse from freshly-killed animals (within 4 h of death). After cold water cleaning and shaving, full thickness skin (about 1 ± 0.1 mm) was removed with a scalpel from the cartilage of the outer region, and the subcutaneous fat removed. Only intact skin discs with 3-cm inner diameter were kept and sealed in plastic bags then stored at -20°C until use, for period not exceeding 6 weeks.

Skin samples were fixed in Bouin liquor and then cut vertically into 5-mm wide strips from the skin surface of the central region. Each section was embedded in paraffin wax. Tissues were divided into small pieces (about 5 μm in thickness) and stained with hematoxilin and eosin and then Masson's trichrome.

2.6. Permeation studies using excised pig-ear skin

The diffusion of benzophenone-3 across excised pig-ear skin was studied using a static diffusion cell based on the Franz design. The diffusion cell consists of donor and receptor chambers between

which the skin is positioned [19]. A portion of pigskin (3 cm^2) was placed as a barrier between the two halves of a horizontal skin permeation system. The dermis side of the skin was in contact with the receiver compartment and stratum corneum with the donor compartment. The area available for diffusion was 0.785 cm^2 which corresponded to 0.208 ± 0.052 g of skin and the receptor chamber volume varied from 10.2 to 10.8 ml. The receptor chamber was maintained at 37.0 ± 0.5°C throughout the experiment. And the contents were continuously agitated by a small bar magnet. Receptor fluids must not adversely affect the barrier properties of the skin or the physicochemical properties of oxybenzone. Physiological saline solution was used for this work. Oxybenzone under these conditions is readily soluble in the receptor fluid (4.7 ± 0.2 μg ml^{-1} ($n = 6$)). The diffusion cell was prepared and allowed to equilibrate for 1 h before application of the oxybenzone formulation. Oxybenzone was applied to the surface at 2 mg cm^{-2}, the product being spread uniformly over the whole area using a digital pipette. At the end of each application time the receptor fluid was removed, and the skin surface was washed four times with 5-ml ethanol, 5-ml distilled water, 5-ml ethanol, 5-ml distilled water. Analyses were performed on the exposed skin area and only on this part.

2.7. In vivo experiments

The anatomical site chosen was the inner forearm. Volunteers (six per group) were Caucasians aged 37.3 ± 7.7 years and were free of dermatological disorders. The subjects were required to read and sign a human experimentation consent form. The vehicles were applied to the surface of the skin at 2 mg cm^{-2} and were spread uniformly over the whole area. An open circular cell, fixed with adhesive tape, delimited this area (1-cm^2). The application time was 30 min. After this time the excessive substance on the applied area was quickly eliminated, by lightly cleaning with a cotton swab and washing and rinsing twice with 500 μl ethanol followed by distilled water (500 μl) and finally a light drying with a cotton swab. At the end, the stratum corneum of the treated area was removed by seven successive tape strippings using '3 M' invisible adhesive tape. Strippings were applied under controlled conditions over 10 s. The first sample was discarded and the six following strippings were pooled and deposited in a 50-ml vessel with 5-ml of methanol and then stirred with a magnetic bar for 30 min. Levels of benzophenone-3 were analyzed by HPLC.

2.8. Statistical analysis

Stat Graphic Plus software [20] was used to performed statistical analysis on the data. In all case, Log-Anova test was checked to determine the homogeneity of variance. An ANOVA was reported and whenever analysis of variance on data showed significant differences. Newman–Keuls's test was used to determine which means are significantly different from which others. When the homogeneity of variances was rejected the Kruskal–Wallis test was employed, then to determine which medians are significantly different from which others a Box-and-Whisker Plot was used.

3. Results and discussion

3.1. Histological appearance of skin

The skin separated from the subcutaneous fat layer was kept for histopathological analysis and microscopic examination. In a first step, unstored skin samples of pig ear and woman breast were compared (Figs. 1 and 2). Both epidermises were moreover histologicaly comparable for thickness and cellular structure. In the dermis layers differences were solely due to the number of hair follicles and sebaceous glands. In woman mammalian skin this number is reduced. The histological appearance of pig-ear skin after frozen storage is presented in Figs. 3 and 4. The epidermis and dermis layers showed no damage although a low temperature (-20°C) was applied for 1 and 5 weeks, respectively.

This observation has been corroborated by other investigators who concluded that percutaneous permeation rates appear to be similar

[21,22]. Furthermore this model is useful for its availability and ease of preparation, in contrast to using human skin obtained from surgery or cadavers, which is normally not frequently available and which is quite often already damaged. No skin damage was found either during the freezing process, and the maximum storage time under these conditions to ensure maintenance of skin integrity could be evaluated at 1.5 months. It is nowadays desirable to replace human skin with animal skin, and pig epidermal membrane is a relevant model for in vitro percutaneous absorption studies [23–26].

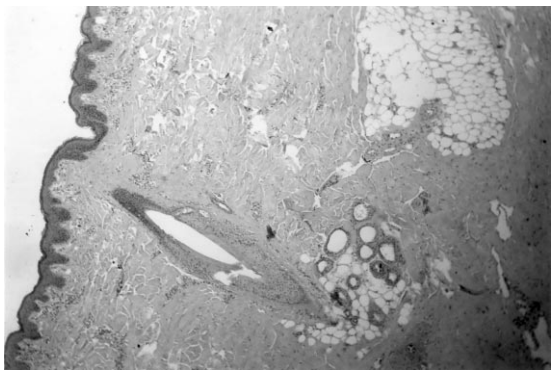

Fig. 1. Histological appearance of pig ear skin obtained without storage (4 × 10).

Fig. 2. Histological appearance of woman mammalian skin obtained without storage (4 × 10).

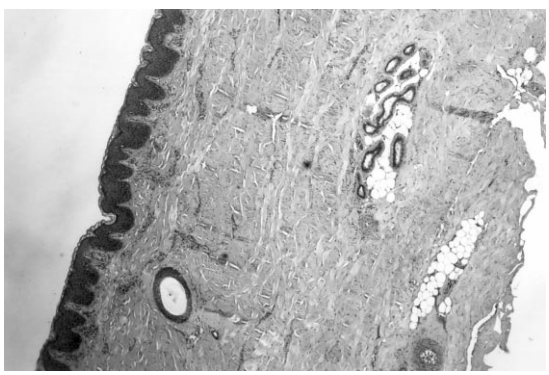

Fig. 3. Histological appearance of pig ear skin obtained after 1 week of storage (− 18°C).

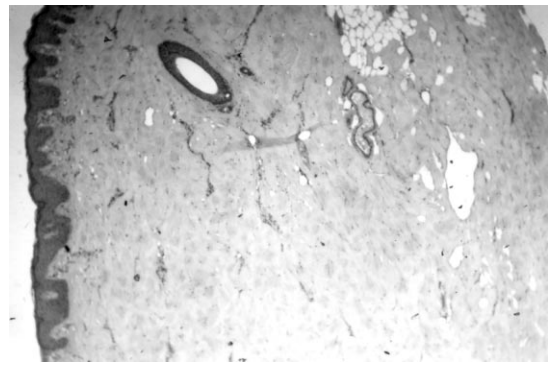

Fig. 4. Histological appearance of pig ear skin obtained after 5 weeks of storage (− 20°C).

3.2. Emulsion formulations

The three different emulsions were made with the same oily phase, only the surfactants to induce W/O or O/W were differents. The different emulsions did not shown signs of macroscopic or microscopic instability with accelerated tests and with the long-term stability test (at 25°C for 8 months). The O/W coarse emulsion was obtained with alkyl polyglucoside surfactant and the droplet size (2–40 μm) was microscopically observed. The submicron emulsions obtained were characterized by their particle size distribution, one of the most important characteristics of an emulsion. The PCS method is considered the most appropriate for studying droplets < 1 μm, in this work the selected candidate points. Appropriately diluted samples (10-μg in 100-ml sterile water) were analyzed (in triplicate). In the international standard, two parameters describe particle size distribution, the average PCS mean diameter and

the polydispersity index (PI). PI is a dimensionless measure of the broadness of size distribution. For submicron emulsions with and without benzophenone-3, the mean diameter was 228.0 and 203.3 nm, respectively. Both emulsions had the same PI: 0.08.

3.3. In vitro skin penetration

In the present study it seemed inappropriate to investigate 48 h exposure to a sunscreen. Indeed, long applications of sunscreen formulations were not realistic. Independent samples (skin and receptor phase) were analyzed in triplicate at 1, 2, 4 and 8-h. The exposure time must reflect in-use conditions. Just 8 h were investigated, so the slope of the linear portion of the curve could not be estimated and the steady state flux was not obtained.

Fig. 5 shows the distribution of benzophenone-3 in skin from various vehicle. The highest concentration of benzophenone-3 in pigskin was obtained with propylene glycol where the concentration was near that of the saturated solution (31.21 ± 1.15 g l^{-1}, 4 h agitation at 37°C). It can be regarded as a penetration enhancer. High concentrations were also obtained with submicron emulsion, which acts as penetration enhancers. We did not find any difference between the two oily phases, capric-caprilic triglycerides and coconut oil, and the two other emulsions. In all emulsions, the same proportion of capric-caprilic and coconut oil was formulated with the same percentage of oxybenzone. The results indicated that the submicron systems increase more than 3-fold the oxybenzone concentration in the skin at 8 h post-application. The different vehicles: coconut oil, capric-caprilic triglyceride, emulsions and propylene glycol enabled respectively 12.5, 14, 3 and 3% Benzophenone-3 to be dissolved. By comparing the maximum solubility of benzophenone-3 to the penetration value, the solubilities in the vehicle apparently play a role. But although the lowest penetration in skin was obtained with the vehicle in which benzophenone-3 was most soluble, the opposite conclusion is not always true. In all emulsions, the Benzophenone-3 in the oily phase was at nearly saturated concentration, but although greatest penetration in skin was obtained with submicron emulsion, coarse emul-

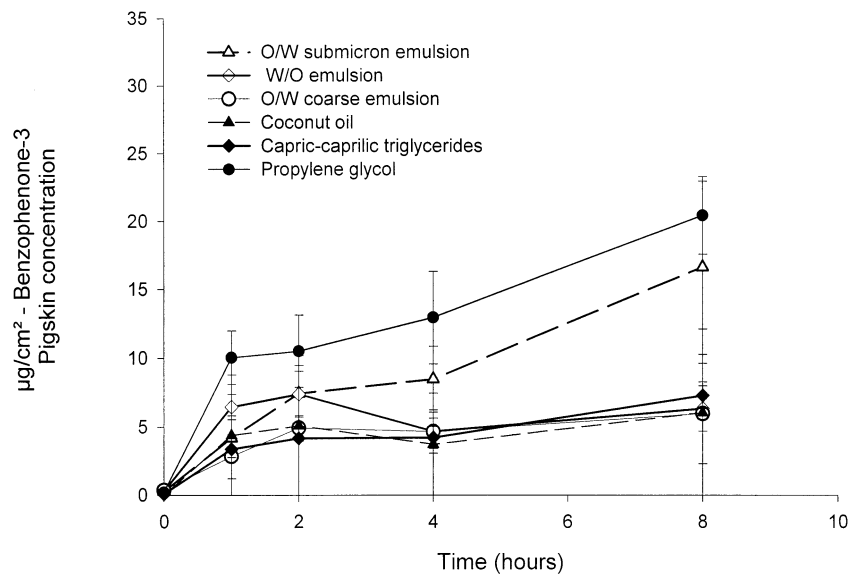

Fig. 5. Benzophenone-3 concentration in pig skin, expressed as µg cm^{-2} (mean ± SE), from various vehicles ($n = 3$, with two or three injections). Time 0 correspond to a point where the solvent (without benzophenone-3) was added with 4 h of contact. Area available for diffusion was 0.785 cm^2, which correpond to 0.217 ± 0.056 g of skin.

Table 1
ANOVA, table for Benzophenone-3 concentration in pig skin by vehicle, time 8 h

Source	Sum of square	Df	Mean square	*F*-ratio	*P*-value
Between groups	1757.86	5	351.57	29.84	0.0000
Within groups	530.23	45	11.78		
Total	2288.09	50			

sion and W/O emulsion produced low concentrations of benzophenone-3. A one way analysis of variance was performed (Table 1) and the *P*-Value of the *F*-test is less than 0.05, there is a statistically significant difference between the vehicle at the final time (8 h). With the Newman–Keuls multiple comparison procedure, three homogenous groups were identified (Table 2). It is interesting to note that time had a moderate influence with four vehicles (where no differences were discriminate among the means) and an enormous affect for propylene glycol and submicron emulsion (vehicles which act as enhancers).

Table 2
Newman–Keuls multiple comparison procedure (95%)[a]

Vehicles	Count	Mean	Homogeneous groups		
			1	2	3
O/W coarse emulsion	9	5.97	X		
Coconut oil	6	6.06	X		
W/O emulsion	9	6.34	X		
Capri-caprilic TG	9	7.56	X		
O/W submicron emulsion	9	16.62		X	
Propylene glycol	9	20.43			X

[a] Multiple range test for Benzophenone-3 concentration in pig skin by vehcle, time 8 h. This table applies a multiple comparison procedure to determine which means are significantly different from which others. Three homogeneous are identified using columns of X's.

Profiles of absorption for benzophenone-3 show that significant amounts of this UV-filter were found in the saline solution. However the low levels of benzophenone-3 found, did not support the hypothesis that the total amount of oxybenzone present in skin after application corresponds to the dose which finishes by passing into the blood. At the final time (8 h), the concentration of benzophenone-3 in saline solution were significantly different ($P < 0.05$), Table 3. Using Newman–Keuls test two homogeneous groups were identified (Table 4) and the highest percutaneous penetration was obtained with all three emulsions, even if the skin concentration of each formulation was very different at this time. Curiously, the three solvents had the same concentration at 8 h in saline solution. Propylene glycol was also in the same range and the solvents produces concentrations in benzophenone-3 twice as low as those for formulations (Fig. 6). These low concentrations measured in the receptor fluid suggest that percutaneous absorption of this UV-filter is minimal across the skin. It seems that the filter incorpo-

Table 3
ANOVA table for Benzophenone-3 concentrationin saline solution by vehicle, time 8 h

Source	Sum of square	Df	Mean square	*F*-ratio	*P*-value
Between groups	8.86	5	1.77	11.57	0.0000
Within groups	5.98	39	0.15		
Total	15.84	44			

Table 4
Newman–Keuls multiple comparison procedure (95%)[a]

Vehicles	Count	Mean	Homogeneous groups	
			1	2
Capri-caprilic TG	9	0.42	X	
Coconut oil	9	0.47	X	
Propylene glycol	6	0.47	X	
O/W coarse emulsion	6	1.12		X
W/O emulsion	6	1.24		X
O/W submicron emulsion	9	1.48		X

[a] Multiple range test for benzophenone-3 concentration in saline solution by vehicle, time 8 h. This table applies a multiple comparison procedure to determine which means are significantly different from which others. Two homogeneous groups are identified using column of X's.

rated in different vehicles was absorbed in the inner compartment after application at low rates in all cases. The skin acts as a compartment in which the concentration of benzophenone-3 was more elevated and dependent on the vehicle.

The results achieved here show the importance of vehicle effect on the skin penetration of benzophenone-3. The two oily solvents, the W/O emulsion and O/W coarse emulsion restrain the concentration of this UV-filter in the skin, whereas propylene glycol and submicron emulsion allow a greater penetration. This confirm the results of Gupta et al. [5] where benzophenone-3 and octyl methoxycinnamate skin penetration were investigated in two different vehicles. Minimal penetration of UV-filters is best archived with oily vehicle and maximal with hydroalcoholic formulation. Jiang et al. [11] showed an very interesting relationship between penetration of benzo phenone-3 and solubility parameter of vehicle. The nature of membrane influence the degree of skin retention of benzophenone-3. With human skin they conclude that ethanol had the greatest effect on epidermal flux followed by semipolar emollient.

From the results obtained in the study it can be deduced that the use of submicron emulsion improves the penetration of oxybenzone in skin when compared with classical W/O and O/W

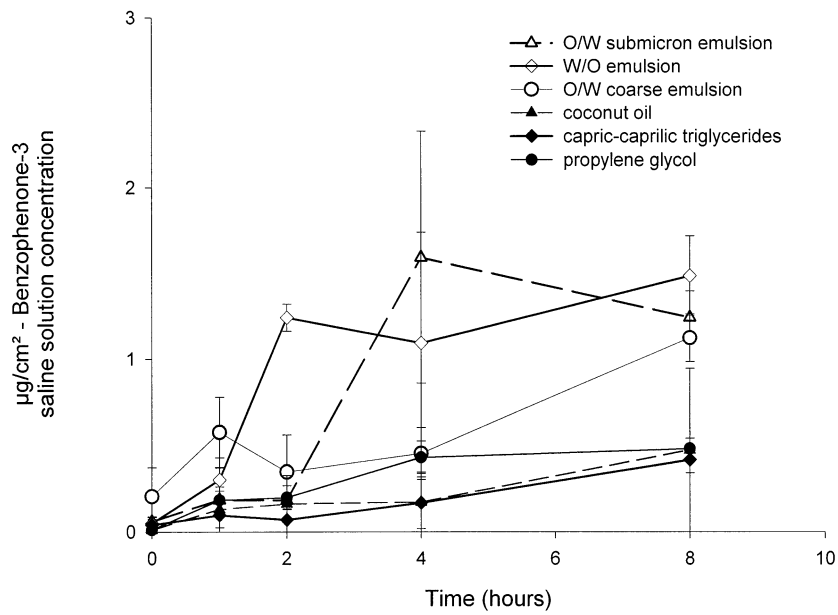

Fig. 6. Benzophenone-3 concentration in saline solution (receptor fluid) expressed as µg/cm^2 (mean $\pm$ SE), from various vehicles ($n = 3$, with two or three injections). Time 0 correspond to a point where the solvent (without benzophenone-3) was added with 4 h of contact. Area available for diffusion was 0.785 cm^2 which correspond to 10.5 $\pm$ 0.3 ml of saline solution.

Table 5
Kruskal–Wallis test, in vivo evaluation, stripping at 30 min ($n = 6$, three injections)[a]

Vehicles	Sample size	Average rank
O/W submicron emulsion	18	74.78
W/O emulsion	18	52.00
O/W coarse emulsion	18	28.44
Propylene glycol	18	87.94
Coconut oil	18	32.78
Capric-caprilic triglycerides	18	51.06

[a] Test statistic = 49.52, P-value, 2 10^{-9}.

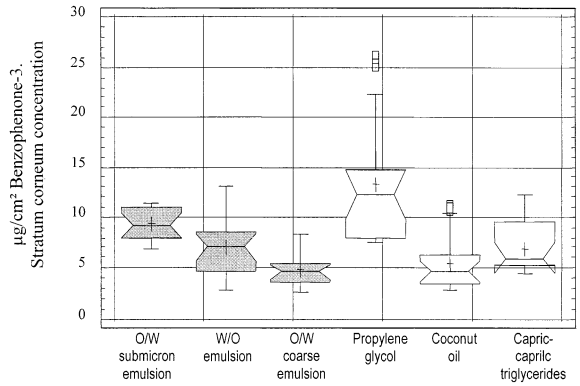

Fig. 7. Box-and Wisker Plot, with median notch. Data from stripping method ($n = 6$, with three injections) following application for 30 min, from various vehicles. Data are expressed as µg cm^{-2}.

emulsions. Submicron emulsions are novel vehicles of oil-in-water type dispersion and can be used as drug carriers, as suggested or reported recently by several authors [27–30]. The effect observed in this study also shows that occlusion with oily vehicles does not increase the skin penetration of benzophenone-3.

3.4. In vivo stratum corneum penetration

Tape stripping method is a useful technique for selectivity in removing the skin's outermost layer, the stratum corneum. This method is considered a mildly invasive technique, with a short period of immobilization and brief skin exposure. The amounts recovered range from 4.82–13.26 µg cm^{-2} of benzophenone-3. The concentration in benzophenone-3 for each vehicle was compared and the Kruskal–Wallis test was performed. This test tests the null hypothesis that the median within each of the six vehicles is the same. In our study, the P-value was less than 0.05 (Table 5), thus there is a statistically significant difference between the medians at 95% confidence level. The Box-and Whisker plot (Fig. 7) is a useful tool to determine which medians are significantly different from which others. In this work the greatest concentration of benzophenone-3 in stratum corneum was also obtained with propylene glycol and submicron emulsion. We did not find any difference between capric-caprilic triglycerides and W/O emulsion and the lowest levels were found with coconut oil and O/W coarse emulsion. These results confirm that under the operating conditions of our study benzophenone-3 has a high affinity to stratum corneum, but in vivo or in vitro penetration of benzophenone-3 is strictly dependent on the selected vehicle.

Fig. 8 clearly shows that in vivo and in vitro skin concentrations were in both cases of the same order of magnitude. Only the amount that penetrated in an 8-h period was more elevated. For the 30-min application the total amount of benzophenone in the stratum corneum presented the best correlation (0.96) with the amount in vitro after 4-h which suggests that in vivo the penetration delay time is short. It is self-evident that in vivo investigations are preferable to the in vitro method. Nevertheless, in vitro experiments with pigskin were well correlated with the in vivo experiments and would make it easier to screen different solvents and new formulations to predict their pharmacological effect. All methods are only approximate for quantifying percutaneous absorption, but pigskin could serve as a good model membrane in transdermal delivery system studies for sunscreens and the extrapolation of the in vitro test results (4-h) to the in vivo situation might be reasonable. This assumption is useful as a basis for vehicle comparison.

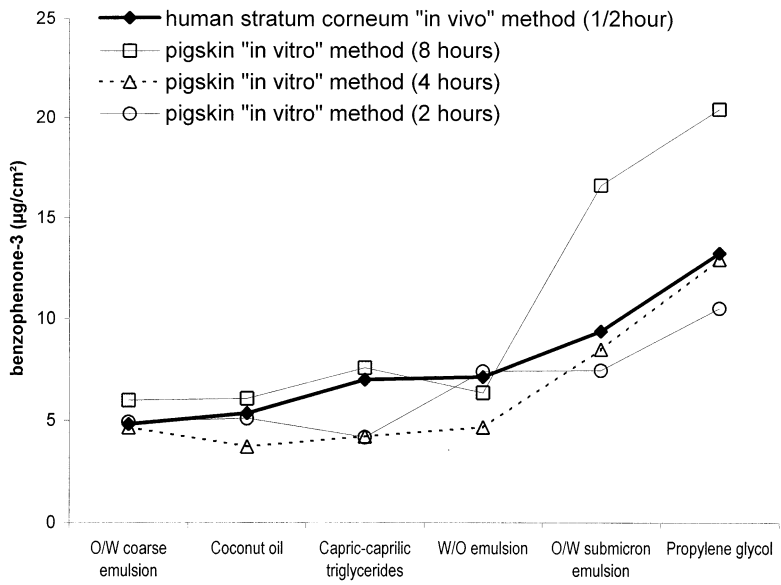

Fig. 8. Correlation between in vivo and in vitro method. Data from stripping at 30 min and 2, 4, and 8 h skin contact.

4. Conclusions

In our study the six vehicles were ranked in the same order of skin concentration for both the in vivo and in vitro methods. It may be also concluded that cutaneously applied oxybenzone is able to penetrate the skin but in this case the major part remains on the skin. The reservoir function of the stratum corneum for benzophenone-3 was assessed by stripping method, and confirmed with the levels found in pig skin by in vitro technique. It has been confirmed in this work that the skin concentration and consequent systemic distribution of this sunscreen may occur at significant levels, and the extent of this concentration will vary depending on the solvent and formulation used. The most important aspect of sunscreen vehicles is now to resist skin damage. They may also limit the percutaneous penetration with an adapted formulation. Based on these arguments, it is believed that submicron emulsions are of little interest for sunscreen formulations. The capric-caprilic triglycerides and coconut oil appear to be interesting solvents for sunscreen formulations that limit percutaneous penetration. If a cosmetic or dermatological preparations are necessary, W/O formulations which are water proofing or classical O/W emulsions look the better choice to limit higher oxybenzone skin concentration.

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