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In Vitro Permeation Characterization of the Analgesic Ibuprofen and the Sunscreen Oxybenzone

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Ibuprofen, one of the mostly prescribed nonsteroidal anti-inflammatory drugs (NSAIDs), has been proposed as a topical medication for secondary prevention against skin damage induced by sunburn. The objective of this study was to characterize transmembrane permeation of ibuprofen and sunscreen oxybenzone across poly(dimethyl siloxane) (PDMS) membrane. In vitro diffusion studies were carried out at 37° and 45°C, using a series of ibuprofen and oxybenzone samples, either individually or in combination. Concentrations of ibuprofen and oxybenzone in the receptor compartment for up to 6 h were measured using a high-performance liquid chromatography (HPLC) assay. Ibuprofen and oxybenzone permeated across the PDMS membrane in all diffusion studies. When applied individually, permeation percentages of ibuprofen and oxybenzone ranged from 1.0 to 4.1% and from 13.2 to 25.8%, respectively. When applied in combination, permeation percentages of ibuprofen and oxybenzone were 0.3–1.4% and 7.8–24.3%, respectively. Transmembrane permeation was significantly suppressed when both compounds were present concurrently. High temperature promoted the diffusion process of oxybenzone; a linear correlation was also observed between oxybenzone concentration and its permeation. The proposed permeation enhancement between ibuprofen and oxybenzone was not observed from this study. The potential transdermal interaction and systemic absorption from concurrent application of topical analgesics and sunscreens thus requires further systematic evaluation.

Keywords ibuprofen; oxybenzone; in vitro permeation; concurrent application; PDMS membrane

INTRODUCTION

Ibuprofen is classified as a nonsteroidal anti-inflammatory drug (NSAID) and is one of the most commonly prescribed analgesics for the treatment of pain and inflammation. The anti-inflammatory property of ibuprofen relies on its nonselective inhibition of cyclooxygenase enzymes responsible for the conversion of arachidonic acids to prostaglandins (Godwin, Wiley, & Felton, 2006; Kantor, 1984). Oral administration of ibuprofen and other NSAIDs is frequently accompanied by adverse gastrointestinal symptoms such as nausea, vomiting, and dyspepsia (Beetge, du Plessis, Muller, Goosen, & van Rensburg, 2000; Fugit & Fendrick, 2006; Swart, Breytenbach, Hadgraft, & du Plessis, 2005); chronic oral drug applications can lead to even more serious conditions including decreased gastric cytoprotection, renal impairment, and inhibition of platelet aggregation (Godwin et al., 2006; Lapane, Spooner, & Pettitt, 2001). Topical skin application of ibuprofen or other NSAIDs has proven to be safe and advantageous. A reduced systemic bioavailability of ibuprofen from the skin could minimize the risk of adverse effects encountered with the oral drug administration, whereas effective drug concentrations are also localized on the application site, subsequently reducing drug dose and facilitating drug discontinuation if necessary (Beetge et al., 2000). Numerous studies have explored the applicability of ibuprofen in the treatment of skin inflammation, in particular, secondary prevention against skin damage induced by sunburn through the localized inhibition of cyclooxygenase in the skin and subsequently of inflammatory response (Godwin et al., 2006; Swart et al., 2005).

Ultraviolet (UV) radiation from the sunlight is capable of inducing direct cellular damage to the skin and altering immunological functions of normal skin barrier; it is the primary cause for skin aging, wrinkles, blotchy pigmentation, and skin cancer (Gustavsson Gonzalez, Farbrot, & Larkö, 2002; Olson & Starr, 2006). The relationship between overexposure to sunlight and skin cancer has been widely explored; reduction or avoidance to unhealthy overexposure to sunlight or other sources of UV radiation appears to be clinically essential in protecting the skin from premature damages (Olson et al., 2007; Rivers, Wang, & Marcoux, 2006). Topical sunscreen preparations have been extensively used by the general public as a feasible and economical protective measure against sun exposure for decades. In addition, active sun-blocking agents are now commonly incorporated in a majority of cosmetic and skin-care preparations for regular daily applications. Oxybenzone is one of the active sunscreen components that possess a broad-spectrum efficacy against both UVA and UVB (Gustavsson Gonzalez et al., 2002). To maintain effectiveness

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on the skin surface, sunscreen preparations are to be applied frequently and abundantly. These compounds should exert minimal skin permeation and systemic absorption upon topical administration.

Transdermal characteristics of ibuprofen and oxybenzone have been individually studied. Ibuprofen has demonstrated self-permeation enhancement across various membrane models (Al-Saidan, 2004); percutaneous permeation enhancement is also achieved by using supersaturated solution of ibuprofen and complexation of ibuprofen with cyclodextrin (Godwin et al., 2006; Iervolino, Cappello, Raghavan, & Hadgraft, 2001). The role of oxybenzone as a percutaneous absorption enhancer to some other topically applied substances has also been confirmed (Gupta, Zata, & Rerek, 1999; Pont, Charron, & Brand, 2004). In our laboratory, we have reported a synergistic percutaneous penetration between oxybenzone and insect repellent *N,N*-diethyl-*m*-toluamide (DEET) when commercially available sunscreen and repellent products were applied simultaneously (Gu, Wang, Collins, Kasichayanula, & Burczynski, 2005; Kasichayanula, House, Wang, & Gu, 2005; Wang, Kasichayanula, & Gu, 2006). Concurrent topical use of ibuprofen and oxybenzone could therefore inadvertently alter characteristics of skin permeation of the compounds, subsequently leading to modified skin disposition and therapeutic outcome.

In this study, we investigated the transmembrane permeation of ibuprofen and oxybenzone across the artificial membrane poly(dimethyl siloxane) (PDMS) using an in vitro diffusion model. It was hypothesized that the concurrent use of ibuprofen and oxybenzone would result in enhanced transmembrane permeation of both compounds, similar to what has been found with DEET and oxybenzone, because both possess characteristics of self-permeation or permeation enhancement. The objective of this study was to characterize permeation profiles of ibuprofen and oxybenzone when they were applied individually and in combination. In addition, the effects of application concentration and temperature on the permeation of the two compounds were also evaluated and compared.

MATERIALS AND METHODS

Chemicals and Other Materials

Oxybenzone was purchased from Reidel-de Häen GmbH (Seezle, Germany). Ibuprofen and polyoxyethylene 20-oleyl ether (Brij® 98) were obtained from Sigma-Aldrich Co. (St. Louis, MO, USA). Propylene glycol, sodium hydroxide, potassium phosphate monobasic, acetonitrile, and phosphoric acid were all obtained from Fischer Scientific (Fair Lawn, NJ, USA). Marcelle® Hypo-Allergenic Dermabase® was purchased from Professional Pharmaceutical Corporation (Montréal, QC, Canada). All chemicals used were either high-performance liquid chromatography (HPLC)-grade or Analytical Chemical (AC)-grade. Deionized HPLC-grade water was collected from a Millipore® Milli-Q® Water System (Nepean, ON, Canada) in the laboratory. Synthetic PDMS membrane was purchased from Advanced Biotechnologies Inc. (Silverdale, WA, USA).

Sample Preparation

Seven different combinations of ibuprofen and oxybenzone were tested in the diffusion experiments. Three sample groups contained oxybenzone at an identical concentration with varying concentrations of ibuprofen, and the other four sample groups contained a constant concentration of ibuprofen with varying concentrations of oxybenzone. These selected concentrations of ibuprofen and oxybenzone are commonly found in topical analgesic and sunscreen preparations. We have also used similar oxybenzone concentrations in our previous studies that would facilitate data comparison and correlation. All study groups were tested both individually and in combination. The compositions of the diffusion experiments are listed in Table 1.

To prepare for diffusion samples, ibuprofen was accurately weighed and incorporated into Dermabase® (a blank oil-in-water emulsion lotion base) with a spatula; oxybenzone was carefully weighed and dissolved in propylene glycol, a common pharmaceutical solvent that is also used in many commercially available skin-care preparations. For combined test samples, ibuprofen and oxybenzone were prepared individually as described above and then mixed completely before the diffusion studies.

Diffusion Study

A well-established diffusion setting was used for all experiments, which was composed of fifteen static Franz-style diffusion cells (PermeGear Inc., Bethlehem, PA, USA), a Variomag® multiple-station magnetic stirrer (Daytona Beach, FL, USA), and a thermal water bath (Blue Island, IL, USA). Each diffusion cell consisted of a 2-mL donor compartment and a 3.5-mL receptor compartment, with a 1.1-cm^2 surface area available for drug diffusion.

Before each study, PDMS membrane was cut into small pieces (2 × 2 cm) and soaked in deionized water for preconditioning. Once the membrane was mounted and the diffusion cells assembled, a receptor fluid of phosphate buffer (pH 7.4, 4% Brij® 98, w/v) was carefully placed into the receptor compartments, and the cells were agitated for at least 60 min to achieve equilibrium of the experimental conditions. Use of a surfactant in the receptor medium was able to solubilize the

TABLE 1
In Vitro Diffusion Study Design

	Study Code						
Test Concentration	1	2	3	4	5	6	7
Ibuprofen (%)	1.0	2.5	5.0	5.0	5.0	5.0	5.0
Oxybenzone (mg/mL)	1.0	1.0	1.0	2.5	5.0	10	25

test components in the aqueous solution without affecting membrane or transmembrane diffusion characteristics (Gu, Kasichayanula, Fediuk, & Burczynski, 2004; Gupta et al., 1999; Lazar et al., 1996). Test sample (1 mL of propylene glycol containing oxybenzone, 500 mg of Dermabase® containing ibuprofen, or a combination of both) was then placed in the donor cell; the receptor fluid was stirred continuously at 600 rpm to maintain homogeneity of the diffusion medium throughout the experiment. An aliquat of 100 μL of the receptor fluid was collected from the receptor compartment hourly for 6 h; same volume of fresh, preheated buffer medium was added to the diffusion cells to replenish the test solution after each sampling interval. The diffusion studies were carried out at two temperatures, i.e., 37°C and 45°C; five replicates were used for each diffusion experiment.

HPLC Assay

Concentrations of ibuprofen and oxybenzone in the diffusion samples were analyzed simultaneously, using an HPLC assay developed and validated in our laboratory. The Waters® HPLC system consisted of a 2690 Alliance Solvent Delivery System, a 996 Photodiode Array Detector, a Symmetry® C_{18} column (3.9 × 150 mm, 4 μm), and the data were acquired using a Millennium® 32 Software (Milford, MA, USA). The mobile phase was composed of acetonitrile and water (pH adjusted to 2.5 with acetic acid) at a ratio of 70 : 30 (v/v), and delivered at a flow rate of 1.0 mL/min. Under these chromatographic conditions, ibuprofen and oxybenzone eluted from the column at 2.2 and 2.6 min, respectively. Both compounds were detected at the wavelength of 224 nm; the detection limit was 15 ng for the analytes. Calibration linearity (r^2 = 0.99) was achieved with a range of 25–500 ng for ibuprofen and 25–10,000 ng for oxybenzone. Assay validation and calibration were carried out before and during the drug analysis. All samples were directly injected for drug measurement without pretreatment; no interference was found from other excipients and additives present in the receptor medium.

Data Analysis

The overall permeation percentages of ibuprofen and oxybenzone across the PDMS membrane were calculated based on the ratio of accumulated permeation amount to the actual application amount of the test products in the donor cell. The steady-state permeability coefficients (K_p) of the two compounds were calculated using the following empirical diffusion equation derived from the Fick's First Diffusion Law (Crank, 1975):

$$J_s = K_p C_s \quad (1)$$

where J_s is the steady-state diffusion flux and C_s is the saturated drug concentration. Permeability coefficient is often used to compare permeation profiles for solutes examined under different conditions and related to the rate of diffusion of a solute within a membrane adjusted for differences in membrane thickness and solute concentration.

Statistical analysis was performed using two-way ANOVA and Tukey's test (PC-SAS® Version 8.02, SAS Institute Inc., Cary, NC, USA). The following statistical analyses of the data were conducted: (1) the overall permeation percentages and permeability of ibuprofen and oxybenzone among the seven studies, and (2) the overall permeation percentages of ibuprofen and oxybenzone between the two test temperatures. Differences were considered statistically significant at $p \leq 0.05$. Linear regression was also used to correlate changes between permeation amount and application concentration of the two test compounds.

RESULTS AND DISCUSSION

Concurrent application of various preparations on the surface of the skin, for either therapeutic or cosmetic purposes, has become widely accepted and practiced by the general public. Skin not only offers a highly convenient access to drug administration but also enables localized and systemic drug actions. By selecting appropriate formulation approaches, it is possible to achieve effective systemic drug concentrations through percutaneous drug delivery. Nevertheless, for a majority of topical and consumer care skin products, it is undesirable for the active ingredients to permeate into deeper skin layers or to be absorbed systemically. Although no well-defined boundary has been drawn between systemic and topical drug absorption through the skin, it is clinically important to differentiate drug actions on the surface of the skin. Potential interaction of the preparation on the skin surface can lead to unwarranted pharmacological and toxicological consequences, particularly for topical applications in which percutaneous absorption is generally considered unnecessary and unproductive.

Active sunscreen compounds are extensively incorporated and utilized in various skin care preparations. Percutaneous penetration and systemic absorption of numerous sunscreen ingredients including oxybenzone are undesirable, as this would compromise the use safety of the applications (Gonzalez, Farbrot, Larkö, & Wennberg, 2006; Gu et al., 2005; Hayden, Cross, Anderson, Saunders, & Roberts, 2005; Kasichayanula, House, Wang, & Gu, 2005). Ibuprofen used as a topical antiinflammatory agent should also maintain maximal concentrations in the skin; oral administration of ibuprofen is unlikely to achieve sufficient skin drug concentrations because of extensive systemic distribution and elimination. Formulation approaches including cyclodextrin complexation (Godwin et al., 2006) and supersaturated solution (Cilurzo et al., 2005; Iervolino et al., 2001) have been used to increase skin permeation of ibuprofen. Nevertheless, with simultaneous application of both ibuprofen and oxybenzone and their self-permeating capabilities, penetration characteristics of the two compounds could be altered or modified, which would subsequently result in variable or even undesirable therapeutic outcomes if not dealt with properly.

Transmembrane permeation profiles of ibuprofen and oxybenzone were therefore studied at various concentrations and two different temperatures, by either single component (control) or in combination. These application concentrations represented the realistic dosing ranges of ibuprofen and oxybenzone by the general public; it is also not uncommon to test transdermal permeation of sunscreens at elevated temperature conditions (45°C in this study) because they are designed primarily for summer outdoor applications. Figure 1 shows the overall permeation of ibuprofen with three varying concentrations at the end of a 6-h diffusion study. Compared to its single-component controls, mixing ibuprofen with a constant concentration of oxybenzone at 1.0 mg/mL significantly suppressed the permeation of ibuprofen in all six studies. The reduction in permeation ranged from 190 to 330% among the studies. Similarly, significant permeation suppression was observed for ibuprofen at a constant concentration of 5.0% whereas concentrations of oxybenzone in the mixtures were varied (Figure 2). Compared to its single-component counterparts, the suppression of ibuprofen permeation from these studies ranged from 168 to 274%.

For oxybenzone, its transmembrane permeation was also suppressed in all but three diffusion experiments when ibuprofen was introduced simultaneously; an increase was observed only under higher oxybenzone concentration and temperature conditions. Figure 3 shows permeation profiles of oxybenzone at varying concentrations when concentration of ibuprofen remained constant. Compared to its single-component controls, the suppression percentages of oxybenzone ranged from 7 to 150%, which was smaller than those observed with ibuprofen. Figure 4 shows permeation of oxybenzone at 1.0 mg/mL whereas ibuprofen was introduced at variable concentrations. Similarly, the percentage of suppression ranged from 18 to 69%. Although the increments of oxybenzone permeation were smaller than those of ibuprofen, the overall permeation of oxybenzone at 6 h was much larger than that of ibuprofen; the values were 13.2–25.8% (single oxybenzone), 7.8–24.3% (oxybenzone when combined with ibuprofen), 1.0–4.1% (single ibuprofen), and 0.3–1.4% (ibuprofen when combined with oxybenzone), respectively.

Two temperature conditions were used to evaluate permeation behaviors of ibuprofen and oxybenzone, as the use of sunscreens likely involves high environmental temperatures in the summer. In addition, thermodynamic molecular movement is dependent on temperature and other external parameters, which subsequently enhances drug diffusion and permeation process. Numerous studies have studied the effect of heating

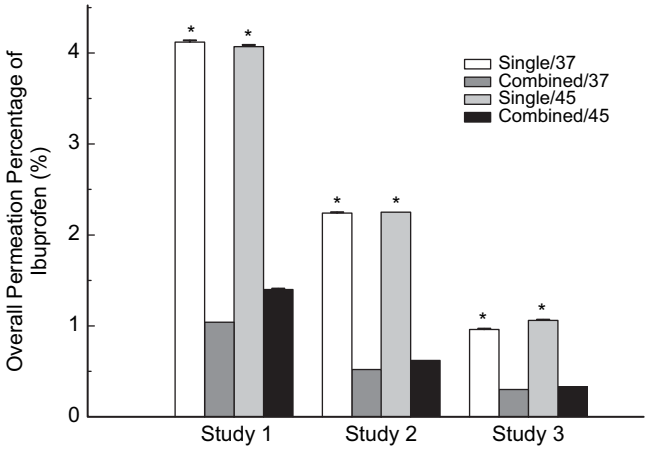

FIGURE 1. Permeation percentages of ibuprofen at 37° and 45°C when oxybenzone concentration was maintained constant at 1.0 mg/mL (*significant difference from combined samples, $p \leq 0.05$, $n = 5$, mean ± *SEM*).

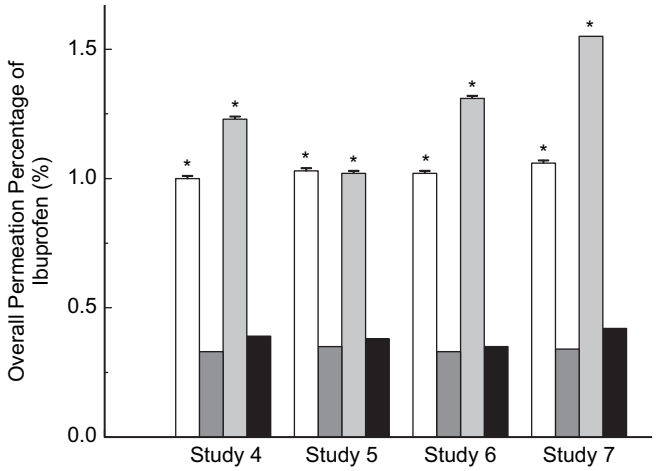

FIGURE 2. Permeation percentages of ibuprofen (5.0%) at 37° and 45°C with variable oxybenzone concentrations (*significant difference from combined samples, $p \leq 0.05$, $n = 5$, mean ± *SEM*, bar legend similar to Figure 1).

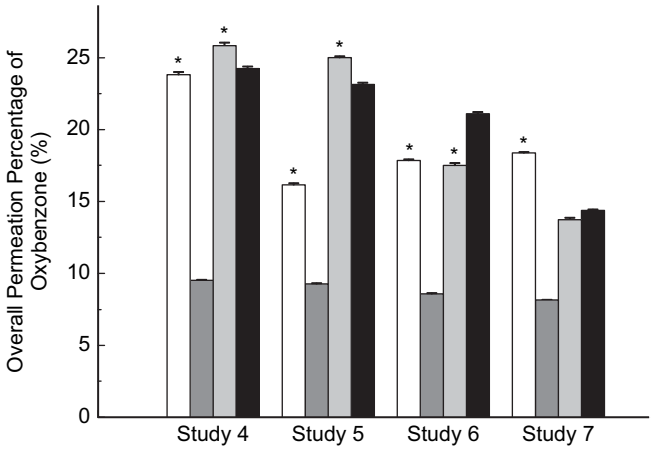

FIGURE 3. Permeation percentages of oxybenzone at 37° and 45°C when ibuprofen concentration was maintained constant at 5.0% (*significant difference from combined samples, $p \leq 0.05$, $n = 5$, mean ± *SEM*, bar legend similar to Figure 1).

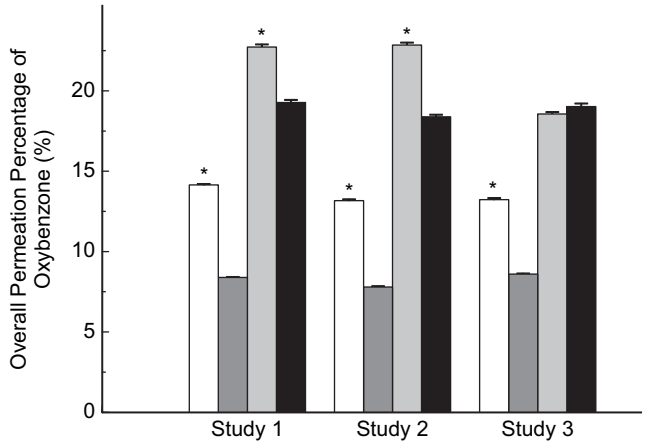

FIGURE 4. Permeation percentages of oxybenzone (1.0 mg/mL) at 37° and 45°C with variable ibuprofen concentrations (*significant difference from combined samples, $p \leq 0.05$, $n = 5$, mean ± *SEM*, bar legend similar to Figure 1).

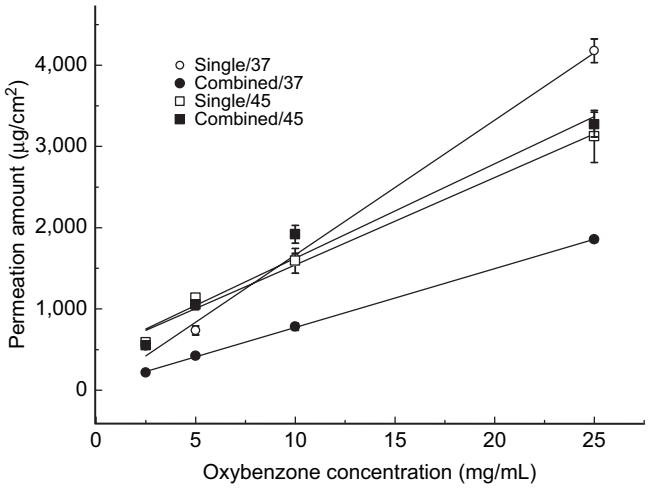

FIGURE 5. Correlation between permeation amount and application concentration of oxybenzone at 37° and 45°C.

on transdermal drug diffusion and absorption, and achieved improvement in drug delivery with various compounds (Akomeah, Nazir, Martin, & Brown, 2004; Merino, Kalia, Delgado-Charro, Potts, & Guy, 2003; Shomaker, Zhang, & Ashburn, 2001). In this study, we found that temperature influenced the permeation of oxybenzone but not that of ibuprofen. This was similar in patterns to our earlier results of oxybenzone with PDMS membrane (Gu et al., 2004). Clarys et al. (2001) have found from an in vivo study in humans that temperature did not significantly alter the adsorption of sunscreens into stratum corneum. In vitro diffusion study might demonstrate slightly different permeation properties than in vivo experiment regarding temperature, as living skin exposed to high environmental temperature will increase blood circulation and sweating, which would consequently facilitate transport of medications from the absorption site. It would be impossible to achieve this simulation from a diffusion experiment in vitro.

Drug concentration available at the site of absorption also influences the rate and extent of transmembrane permeation through the diffusion process. In general, a high concentration gradient would promote molecule diffusion by supplying a constant flow of molecules at the surface of diffusion and creating a "sink condition" within the receptor cell. Various concentrations were tested for this effect on permeation profile. Figure 5 demonstrates the relationship between permeation amount and application concentration of oxybenzone obtained from the study. A linear increase ($r^2 \geq 0.99$) was observed between the permeation amount and the application concentration for oxybenzone. The slopes of the lines were different among the four application approaches at the two test temperatures, indicating the effect of temperature and additional ingredient on diffusion characteristics of oxybenzone. At the first three concentrations tested, high temperature would make more oxybenzone molecules available for diffusion; at 25 mg/mL, however, oxybenzone molecules might have already achieved diffusion equilibrium at 45°C, subsequently resulting in reduced permeation amount in comparison to that of single oxybenzone at 37°C. Figure 6 shows the correlation between the permeation amount and the application concentration for ibuprofen. When ibuprofen was used individually for the diffusion studies, there was no linear relationship found between the two parameters. When oxybenzone was present in the study samples, however, satisfactory linear correlation was observed ($r^2 \geq 0.93$), similar to what was obtained in Figure 5. The effect of study temperature on permeation amount of ibuprofen was not clearly evident with the change of application concentrations.

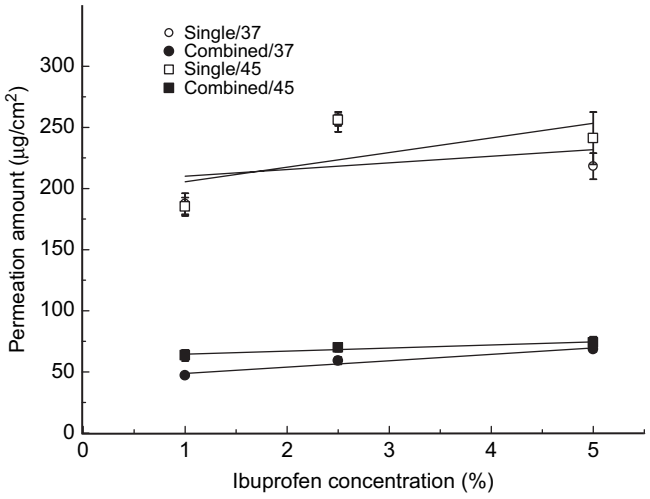

FIGURE 6. Correlation between permeation amount and application concentration of ibuprofen at 37° and 45°C.

Tables 2 and 3 list steady-state permeability coefficient of ibuprofen and oxybenzone across the PDMS membrane from various diffusion experiments, respectively. The values obtained were consistent with the permeation percentages and permeation amounts of the test samples. The permeability of ibuprofen was reduced with the increase of the concentration used, indicating a possible saturation of the diffusion surface by the molecules. When oxybenzone was present in the samples at the same time, the permeability of ibuprofen was further suppressed. No significant difference was observed among the concentrations (studies 4–7) and between the two test temperatures, indicating a satisfactory reproducibility and suitability of the PDMS membrane for the diffusion experiments. For oxybenzone, the trend of decrease in permeability over the concentrations was not clearly obvious. However, there was no significant difference in permeability of the compound when its concentration was maintained constant (studies 1–3). In addition, the effect of temperature change on permeability of oxybenzone was clearly demonstrated in terms of permeability coefficients; 45°C condition produced much higher permeability than 37°C, suggesting that ibuprofen and oxybenzone possessed different permeation behaviors and therefore variable transmembrane characteristics.

Previous references have all indicated transdermal permeation enhancement of ibuprofen and oxybenzone when applied individually. Although no study has yet demonstrated enhancing effect of ibuprofen to other substances, permeation enhancement of numerous substances by oxybenzone has been proven both in our laboratory and by other researchers. That was the primary research hypothesis for this study. On the contrary, this study revealed a permeation suppression between ibuprofen and oxybenzone when both ingredients were simultaneously present in the donor cell, which would definitely require further investigation to understand the interaction mechanism. Transmembrane permeation of ibuprofen observed from this study was significantly lower than that reported for both the single and the combined study designs (Al-Saidan, 2004; Hadgraft, Whitefield, & Rosher, 2003). Several previous studies also showed that ionization of ibuprofen helped

TABLE 2
Steady-State Permeability Coefficient ($\times 10^{-4}$, cm/h) of Ibuprofen

	37°C		45°C	
Study Code	Single	Combined	Single	Combined
Study 1	48.86 ± 3.02	12.47 ± 0.70	48.13 ± 1.93	17.33 ± 1.88
Study 2	29.21 ± 1.19	6.64 ± 0.50	28.56 ± 0.58	8.28 ± 0.51
Study 3	11.99 ± 0.64	3.79 ± 0.16	14.18 ± 1.43	4.49 ± 0.34
Study 4	13.01 ± 0.96	4.45 ± 0.25	16.51 ± 0.78	5.44 ± 0.34
Study 5	13.44 ± 0.95	4.38 ± 0.19	13.36 ± 0.84	5.02 ± 0.42
Study 6	13.62 ± 0.84	4.56 ± 0.24	17.19 ± 0.73	4.63 ± 0.49
Study 7	13.32 ± 0.61	4.36 ± 0.14	21.82 ± 0.47	5.76 ± 0.54

$n = 5$, mean ± *SEM*.

TABLE 3
Steady-State Permeability Coefficient ($\times 10^{-4}$, cm/h) of Oxybenzone

	37°C		45°C	
Study Code	Single	Combined	Single	Combined
Study 1	199.84 ± 9.23	96.51 ± 5.11	313.20 ± 22.61	228.90 ± 27.35
Study 2	189.65 ± 16.52	87.99 ± 8.16	305.59 ± 26.23	236.73 ± 14.62
Study 3	184.29 ± 19.37	92.51 ± 7.70	261.76 ± 16.90	255.78 ± 24.01
Study 4	324.63 ± 28.47	111.14 ± 6.32	333.40 ± 31.26	312.06 ± 12.85
Study 5	201.81 ± 17.83	100.36 ± 6.74	341.42 ± 13.29	294.96 ± 16.10
Study 6	253.45 ± 10.58	103.73 ± 5.50	248.42 ± 20.67	276.20 ± 15.47
Study 7	250.15 ± 9.29	88.40 ± 2.51	200.90 ± 21.88	204.63 ± 11.99

$n = 5$, mean ± *SEM*.

increase its ability to penetrate through the stratum corneum and into the system, a method not utilized in this study (Al-saidan, 2004; Sarveiya, Templeton, & Benson, 2004). Nevertheless, oxybenzone in the single-component samples did yield permeation data comparable to those observed from other studies (Gustavsson Gonzales et al., 2002; Pont et al., 2004; Wang et al., 2006).

The selection of vehicle or solvent to disperse ibuprofen and oxybenzone could affect their release properties and subsequently permeation characteristics across the PDMS membrane. Choice of vehicle can exert significant impact on the permeation of specific compounds, as Hadgraft et al. (2003) have demonstrated in the study of different commercial 5% topical ibuprofen formulations. Dermabase® is an oil-in-water emulsion base that could have retarded release of ibuprofen from the vehicle. Mixing Dermabase® with propylene glycol may have also created a vehicle that institutes an unfavorable condition to the permeation of ibuprofen and oxybenzone. Using artificial PDMS membrane appeared to be suitable for this study in terms of reproducibility and data variation, even though differences in permeation characteristics could still exist, dependent upon other parameters such as solubility, partition coefficient, and preparations (Brain, Green, Dykes, Marks, & Bola, 2006; Wang et al., 2006). Biological skin models would generate experimental results more comparable and relevant to the actual application situations. It appears that more comprehensive studies are required to further understand concurrent use of ibuprofen and oxybenzone.

CONCLUSION

This study demonstrated that transmembrane permeation of the analgesic ibuprofen and the sunscreen oxybenzone was suppressed by a concurrent topical application in vitro, which was different from what had been reported with both compounds when they showed transdermal permeation enhancement used individually. This permeation profile was also contrary to what had been observed with concurrent use of repellent DEET and sunscreen oxybenzone, in which both compounds resulted in synergistic permeation enhancement to each other. The permeation suppression between ibuprofen and oxybenzone was directly associated with the application concentrations but not influenced significantly by the temperature. A combination of ibuprofen and oxybenzone would affect permeation of ibuprofen more than that of oxybenzone.

Topical application of ibuprofen is designed for secondary photoprotection of the skin inflammation. With the coexistence of active sunscreen ingredients such as oxybenzone, skin disposition of ibuprofen could be inadvertently altered, consequently resulting in reduced drug permeation and therapeutic outcome. More systematical experiments are therefore required to further understand the mechanisms of permeation changes and to establish appropriate formulation approaches to deliver drug through the skin efficiently and safely.

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