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The effect of glycerol, propylene glycol and polyethylene glycol 400 on the partition coefficient of benzophenone-3 (oxybenzone)

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Sunscreen products are widely used to protect the skin from sun-related deleterious effects. The objective of the study was to investigate the potential effect of glycerol, propylene glycol and polyethylene glycol 400 on dermal absorption of oxybenzone by studying their effects on its partition coefficient. The partition coefficient was evaluated in a chloroform-water system at room temperature. It was found that glycerol and propylene glycol decreased the partition coefficient of oxybenzone, while an increase in partition coefficient was observed with polyethylene glycol 400. The findings suggest that polyethylene glycol 400 in contrast to glycerol and propylene glycol has the potential of increasing the vehicle-skin partition coefficient of oxybenzone when cosmetic products containing such an UV absorber are topically applied to the skin.

1. Introduction

Benzophenone-3 (common name, oxybenzone), [2-hydroxy-4-methoxyphenyl]phenyl methanone, is an ultraviolet radiation filter at wavelengths between 270 and 350 nm (Benda and Steinberg 2000). Due to its ability to protect the body against sunburn arising from UVB absorption and some absorption into the short wave (UVA) region, oxybenzone is formulated into dermatological products either alone or more often in combination with other sunscreens. Cosmeceutical products (balms, creams, gel creams, lotions, sprays, sticks) containing oxybenzone may also have glycerol, propylene glycol and polyethyleneglycol 400 incorporated into their formulations. These vehicles are in cosmetic or pharmaceutical formulations to serve as co-vehicles, humectants or dermal permeation enhancers. For instance, propylene glycol has been reported to enhance the skin permeability of estradiol (Mollsaard and Hoelgaard 1983), methotrexate (Vaidyanathan et al. 1985), diazepam and midazolam maleate (Toniton 1986), steroids (Ostrenga 1971; Woodford and Barry 1982) and metronid (Mollsaard and Heolgaard 1983). Due to highly lipophilic nature of the UV absorbers (sunscreens), dermal absorption after topical application has been reported (Hayden et al. 1997; Jiang et al. 1999). Other reports have also shown that skin permeation of UV absorbers can be influenced by cosmetic formulations (Aghazarian et al. 1999; Kuruf and Hekimeglu 2001). Futhermore, potential bioaccumulation and systemic toxicity of sunscreens (including oxybenzone) after topical application have also been reported (Hagedorn-Leweke and Lippold 1995; Schlumpf et al. 2001). The aim of the study was to investigate the influence of these vehicles on the partition coefficient of oxybenzone. It is envisaged that understanding the actions of the vehicles on the partition coefficient of oxybenzone will provide some knowledge on their potential effect on dermal absorption of oxybenzone. Potts and Guy (1992) have shown the dermal permeability coefficient to depend on the partition coefficient and molecular weight of chemical substances. Bunge and Cleek (1995) have found that partition coefficient can be used to evaluate dermal absorption of chemical substances. Nevertheless, to our knowledge, no previous study on how the lipophilicity of oxybenzone can be affected by these vehicles is available and in this paper, we report on the effect of glycerol, propylene glycol and polyethylene glycol 400 on the partition coefficient of oxybenzone.

2. Investigations, results and discussion

The calibration graph of oxybenzone was linear in the range of 8.0–40.0 μg/ml. Peak area versus concentration relationship is described by regression equation: $A = 29.7964\ C - 1.1602$ ($R = 0.9999$). The effect of glycerol, propylene glycol and polyethylene glycol 400 on the partition coefficient of oxybenzone was studied in a chloroform-water system at room temperature and the results obtained are given in the Table. Glycerol and propylene glycol decreased the partition coefficient of oxybenzone. Propylene glycol showed a stronger decreasing effect on the partition coefficient of oxybenzone than glycerol at the same concentration level. The decreasing effect was observed as the concentration of the vehicle was increased. However, polyethylene glycol 400 was found to increase the partition coefficient of oxybenzone and this effect occured at increasing concentration. For instance, at the maximum concentration studied (25% w/v), the logarithm partition coefficients of oxybenzone produced by glycerol, propylene glycol and polyethylene glycol 400 are 3.499, 3.308 and 4.404 respectively. The difference between the effect of glycerol and propylene glycol on the partition coefficient of oxybenzone may be related to the polarity of both solvents. Glycerol being more polar than

Table: Effect of glycerol, propylene glycol and polyethylene glycol 400 on the partition coefficient of oxybenzone and the estimated permeability coefficient

Covehicle conc. (% w/v)	Glycerol		Propylene glycol		Polyethylene glycol 400	
	log P	log K_p (cm/h)	log P	log K_p (cm/h)	log P	log K_p (cm/h)
0	3.7754	−1.4117	3.7754	−1.4117	3.7554	−1.4117
5	3.7496	−1.4300	3.6068	−1.5314	4.0199	−1.2381
10	3.6777	−1.4811	3.5273	−1.5879	4.0830	−1.1933
15	3.6238	−1.5194	3.4746	−1.6253	4.1327	−1.1580
20	3.6046	−1.5330	3.3782	−1.6937	4.3003	−1.0390
25	3.4913	−1.6134	3.3083	−1.7434	4.4043	−0.9652

propylene glycol interacts more with water molecules through hydrogen bonding. This in turn increases the ability of glycerol-water vehicles to squeeze out oxybenzone molecules into the organic phase. Futhermore, an increase in dielectric constant of glycerol-water vehicles when compared to propylene glycol-water vehicles could also explain the different effects on the partition coefficient of oxybenzone. The observed increase in partition coefficient of oxybenzone with polyethylene glycol 400 may be explained by assuming the polyethylene glycol-oxybenzone complex having more affinity for the organic phase than the aqueous phase, thus the partitioning of oxybenzone out of water layer and into the chloroform layer. A plot of concentration of each covehicle versus the observed logarithm partition coefficient is shown in Fig. 1 for glycerol and propylene glycol and Fig. 2 for polyethylene glycol 400. In Fig. 1, the graphs illustrate that both vehicles decreased the partition coefficient of oxybenzone and this effect decreases as the concentration is increased. However, in Fig. 2 an increase in the partition coefficient of oxybenzone was observed with increasing concentration of polyethylene glycol 400. Also in both plots, a close linear relationship was obtained, with correlation coefficients of −0.9787, −0.9841 and 0.9771 for glycerol, propylene glycol and polyethylene glycol 400 respectively. The observed logarithm partition coefficient values were used to estimate the permeability coefficient of oxybenzone through the skin at various concentrations and the results are given in the Table. The dermal permeability coefficient was calculated using a previously reported equation (Potts and Guy 1992):

$$\log K_p\,(\mathrm{cm/h}) = -2.7 + 0.71 \log P - 0.0061\ \mathrm{MW} \quad (1)$$

where log K_p is the logarithm dermal permeability coefficient; log P is the observed logarithm partition coefficient for oxybenzone; MW is the molecular weight of oxybenzone. An earlier report (Korinth et al. 2005) has indicated the permeability coefficient (K_p) to be a useful parameter in evaluating percutaneous absorption. A comparison of the K_p values of oxybenzone in glycerol-water, propylene glycol-water and polyethylene glycol 400-water vehicles at a concentration level of 25% w/v, showed polyethylene glycol 400-water vehicles ($K_p = 0.1083$ cm/h) with factors of about 6 and 4 much higher than propylene glycol-water ($K_p = 0.0181$ cm/h) and glycerol-water ($K_p = 0.0244$ cm/h) vehicles respectively.

The study indicates that glycerol and propylene glycol decreased the partition coefficient of oxybenzone in a chloroform-water system. Propylene glycol was observed to produce a stronger decreasing effect than glycerol. Polyethylene glycol 400 was found to increase the partition coefficient of oxybenzone and thus has the potential of increasing its dermal absorption. As dermal absorption of UV absorbers should be avoided, the study suggests that glycerol and propylene glycol are better co-vehicles than polyethylene glycol 400 in the formulation of cosmetic products containing oxybenzone.

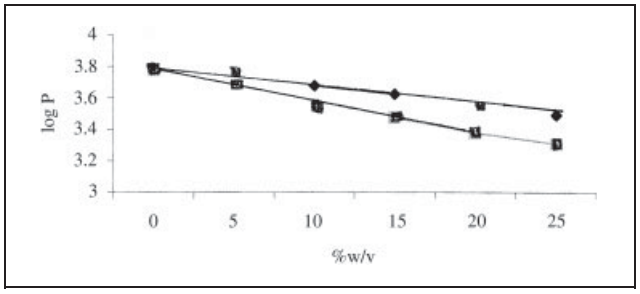

Fig. 1: Plot of concentration of glycerol-water and propylene glycol-water vehicles versus logarithm partition coefficent of oxybenzone

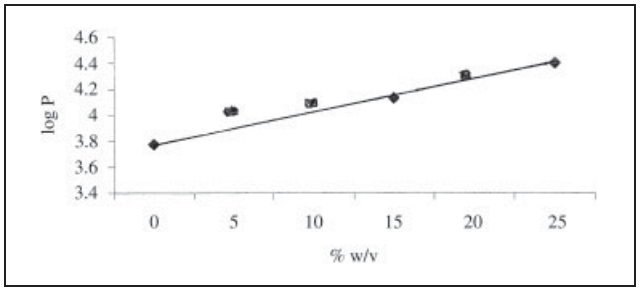

Fig. 2: Plot of concentration of polyethylene glycol 400-water vehicles versus logarithm partition coefficient of oxybenzone

3. Experimental

3.1. Materials

Benzophenone-3 (oxybenzone), glycerol, propylene glycol and polyethylene glycol 400 were purchased from Sigma-Aldrich (USA). Chloroform was purchased from Fisher Scientific (USA).

3.2. Apparatus

All separations were carried out with Hitachi LC 6200 pump and AS 2000 autosampler, Kratos spectroflow 783 detector. A Zorbax analytical column C_{18}, 150 mm × 4.6 mm, 3.5 μm was used.

3.3. Chromatographic procedure

The mobile phase consisted of methanol and water (84 : 16). The flow rate was 1 ml/min at 35 °C. The injection volume was 10 μl and detection was effected at 254 nm.

3.4. Standard solution

Stock solution of oxybenzone (80 μg/ml) was prepared in methanol. Aliquots (8.0–40.0 μg/ml) of the standard stock solution were pipetted into a 10 ml volumetric flask diluted to volume with methanol.

3.5. Partition coefficient measurement

The partition coefficient of oxybenzone was determined in a chloroform-water system. To 5 ml chloroform solution containing 100 mg of oxybenzone 15 ml aqueous solution of different concentrations of glycerol, propylene glycol and polyethylene glycol 400 were added. The flasks were stoppered and agitated at room temperature for 2 h to achieve complete equilibration. Both phases were analysed by a chromatographic method for oxybenzone content and its concentration was calculated from a preconstructed calibration gragh. The partition coefficient of oxybenzone was calculated using the following equation (Johansen 1980a),

$$P = \frac{C_o V_w}{C_w V_o} \quad (2)$$

where, P = partition coefficient
C_o = concentration of oxybenzone in the organic phase
C_w = concentration of oxybenzone in the aqueous phase
Vw = volume of the aqueous phase
Vo = volume of the organic phase

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