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# Studies on the lipophilicity of vehicles (or co-vehicles) and botanical oils used in cosmetic products

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The lipophilic character of five vehicles (or co-vehicles): diethylhexylmaleate, dimethicone, light mineral oil, octyldodecanol and oleyl alcohol and eight botanical oils: *Aloe vera* oil, coconut oil, extra virgin olive oil, grape leaf oil, grape seed oil, hazelnut oil, jojoba oil and safflower oil was determined by partitioning esters of *p*-hydroxybenzoic acid (parabens) between them and phosphate buffer (pH 7.4). The results were compared to those obtained with 1-octanol. The most lipophilic effects were observed with octyldodecanol and oleyl alcohol for the vehicles (or co-vehicles), coconut oil, jojoba oil and safflower oil for botanical oils. Light mineral oil showed the least lipophilic effect. With butylparaben, it was observed that oleyl alcohol, octyldodecanol, coconut oil and jojoba oil were 0.94, 0.91, 0.74 and 0.68 times as lipophilic as 1-octanol respectively. The study indicates that octyldodecanol and oleyl alcohol could be good substitutes for 1-octanol in partition coefficient determination. The estimated permeability coefficients of the parabens suggest that octyldodecanol, oleyl alcohol, coconut oil and jojoba oil could be potential dermal permeation enhancers.

## 1. Introduction

The desire to preserve the skin and bodies in their youthful state has empowered cosmetic chemists to widen the choices of vehicles (or co-vehicles) and botanical oils used in cosmetic manufacturing. The vehicles (or co-vehicles) act as emollients, humectants and plasticizers, while the oils in addition to their moisturizing properties also provide anti-microbial and anti-oxidant effects (Kalemba and Kunicka 2003; Lee and Ghibamoto 2002; Jeffries 2005). Cosmeceutical products for example balms, conditioners, creams, deodorants, lotions, shampoos and wipes containing vehicles (or co-vehicles) and oils occasionally do have bioactives that prevent or treat various skin diseases (Baker et al. 1990; Resh and Stoughton 1976; Varvaresou 2006). The purpose of this study was to investigate the lipophilic character of vehicles (or co-vehicles) and botanical oils used in cosmetic production by partitioning esters of *p*-hydroxybenzoic acid between them and phosphate buffer (pH 7.4). It is hoped that understanding their lipophilicity (measured by partition coefficient), some knowledge could be gained on their potential contribution towards skin absorption of bioactives when cosmetic products containing such bioactives are topically applied to the skin. Previous studies (Bialik et al. 1991; Mollsaard and Hoelgaard 1983; Monti et al. 2002; Stoughton 1982) have reported skin permeation enhancing properties of vehicles (or co-vehicles) and oils used in cosmetic products. Reports (Bungle and Cleek 1995; Hatanaka et al. 1990; Wagner et al. 2002) have also shown that linear correlation exist between permeability coefficient and partition coefficient. Esters of *p*-hydroxybenzoic acid were chosen for the investigation because most cosmetic products contain them as preservatives and also due to differences in their electronic and stereochemical characteristics. A survey of the literature has shown little or no reports on the lipophilicity of the studied vehicles (or co-vehicles) and oils and in this paper, we examine the partitioning of esters of *p*-hydroxybenzoic acid between them and phosphate buffer (pH 7.4).

## 2. Investigations, results and discussion

The regression analysis of the calibration graphs for the parabens gave the correlation coefficients of 0.9994, 0.9994, 0.9994, 0.9995 for methylparaben, ethylparaben, propylparaben and butylparaben respectively. The results on the lipophilicity of the studied vehicles (or co-vehicles) and oils are presented in Tables 1 and 2 respectively. Of the vehicles (or co-vehicles) studied, oleyl alcohol was seen to have the most lipophilic effect on the parabens. This effect was observed to increase with increasing alkyl side chain. For instance using oleyl alcohol as an example, the logarithm partition coefficients observed for methylparaben, ethylparaben, propylparaben, and butylparaben are 1.4243, 1.9225, 2.4746 and 3.2586 respectively. A comparison of the results obtained with 1-octanol, and taking butylparaben as an example, it was observed that light mineral oil, diethylhexylmaleate (Ceraphyl 45), dimethicone (Dow Corning 200 R fluid), octyldodecanol (eutanol G®) and oleyl alcohol (Novol®) were 0.02, 0.10, 0.12, 0.91, 0.94 times as lipophilic as 1-octanol respectively. In Table 2, it was seen that coconut oil exhibited the most lipophilic effect of the oils studied. The increasing effect was also observed as the alkyl side chain increases. The results when compared to 1-octanol, and using butylparaben as an example, showed *Aloe vera* oil,

**Table 1: Lipophilic effects of vehicles (or co-vehicles) on esters of *p*-hydroxybenzoic acid**

| Vehicle (Co-vehicle) | Logarithm partition coefficient | | | |
|---|---|---|---|---|
| | Methylparaben | Ethylparaben | Propylparaben | Butylparaben |
| Diethylhexylmaleate (Ceraphyl 45) | −0.1607 | 0.0128 | 0.1758 | 0.3545 |
| Dimethicone (Dow corning 200 R fluid) | −0.9440 | −0.5519 | −0.0685 | 0.4434 |
| Light mineral oil | −1.8386 | −1.1007 | −0.4927 | 0.0856 |
| Octyldodecanol (Eutanol G) | 0.8689 | 1.6139 | 2.5025 | 3.1760 |
| Oleyl alcohol (Novol) | 1.4243 | 1.9225 | 2.4746 | 3.2586 |
| 1-Octanol | 1.9225 | 2.4746 | 2.9935 | 3.4742 |

**Table 2: Lipophilic effects of botanical oils on esters of *p*-hydroxybenzoic acid**

| Botanical oil | Logarithm partition coefficient | | | |
|---|---|---|---|---|
| | Methylparaben | Ethylparaben | Propylparaben | Butylparaben |
| *Aloe vera* oil | −0.7940 | −0.3732 | 0.1545 | 0.6841 |
| Coconut oil | 0.8215 | 1.2908 | 1.8699 | 2.5558 |
| Extra virgin olive oil | 0.6046 | 1.0662 | 1.5733 | 1.9953 |
| Grape leaf oil | 0.6565 | 1.0934 | 1.5476 | 1.8831 |
| Grape seed oil | 0.6031 | 1.0538 | 1.5663 | 2.0032 |
| Hazelnut oil | 0.5547 | 1.0100 | 1.5124 | 1.9421 |
| Jojoba oil | 0.4218 | 0.9217 | 1.5405 | 2.3527 |
| Safflower oil | 0.6471 | 1.1255 | 1.7271 | 2.2482 |
| 1-Octanol | 1.9225 | 2.4746 | 2.9935 | 3.4742 |

grape leaf oil, hazelnut oil, extra virgin olive oil, grape seed oil, safflower oil, jojoba oil, coconut oil to be 0.20, 0.54, 0.56, 0.57, 0.58, 0.65, 0.68, 0.74 times as lipophilic as 1-octanol respectively. Plots of logarithm partition coefficient of the parabens versus the molecular weight of the alkyl side chain of the parabens are shown in Figs. 1–3. The graphs illustrate that the partition coefficients of the parabens increased as the alkyl side chain increases. The graphs also showed 1-octanol (control) to have the most

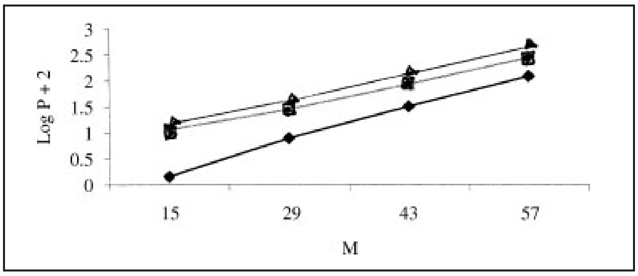


Fig. 1: Plot of logarithm partition coefficient (log P + 2) of parabens versus molecular weight (M) of alkyl side chain of parabens.
◆———◆ Light mineral oil
■———■ Dimethicone (Dow Corning 200 R fluid)
▲———▲ Aloe vera oil

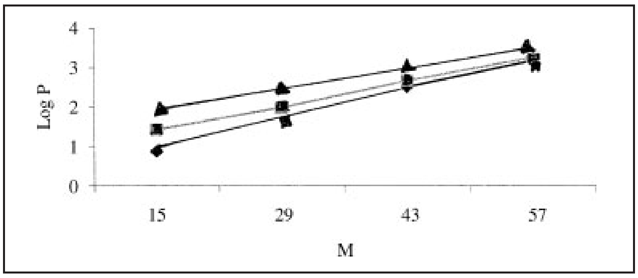


Fig. 2: Plot of logarithm partition coefficient (log P) of parabens versus molecular weight (M) of alkyl side chain of parabens.
◆———◆ Octyldodecanol
■———■ Oleyl alcohol
▲———▲ 1-Octanol

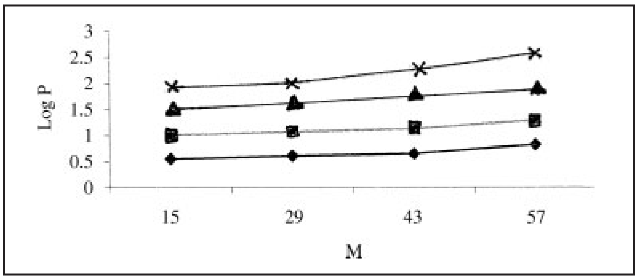


Fig. 3: Plot of logarithm partition coefficient (log P) of parabens versus molecular weight (M) of alkyl side chain of parabens.
◆———◆ Hazelnut oil
■———■ Extra virgin olive oil
▲———▲ Safflower oil
×———× Coconut oil

lipophilic effect on the parabens. In all the plots, a close linear relationship was observed with the following correlation coefficients: light mineral oil (0.9983), diethylhexylmaleate (0.9996), dimethicone (0.9983), octyldodecanol (0.9984), oleyl alcohol (0.9992), *Aloe vera* oil (0.9986), grape leaf oil (0.9980), hazelnut oil (0.9996), extra virgin olive oil (0.9994), grape seed oil (0.9996), safflower oil (0.9994), jojoba oil (0.9941), and coconut oil (0.9965). The observed logarithm partition coefficient values of the parabens in the vehicles (or co-vehicles) and oils that exhibited very significant lipophilic effects were used to estimate the permeability coefficients of the parabens through the skin. The results are presented in Table 3. From the results, the order of dermal absorption enhancing potentials of the vehicles and oils is: oleyl alcohol > octyldodecanol > coconut oil > jojoba oil > safflower oil. An earlier report (Korinth et al. 2005) has shown the permeability coefficient as a useful parameter to evaluate percutaneous absorption. The estimated permeability coefficients of the parabens allowed the study to make some contribution towards previous reports (Byford et al. 2002; Darbre et al. 2004), that implicated parabens in human breast tumours. The reports suggest that local dermal absorption of para-

**Table 3: Estimated permeability coefficients of esters of *p*-hydroxybenzoic acid**

| Vehicle or Botanical oil | Logarithm permeability coefficient (cm/h) | | | |
|---|---|---|---|---|
| | Methylparaben | Ethylparaben | Propylparaben | Butylparaben |
| Octyldodecanol | −2.8438 | −2.5677 | −2.0224 | −1.6298 |
| Oleyl alcohol | −2.6168 | −2.3109 | −1.9096 | −1.5698 |
| Coconut oil | −3.0448 | −2.7971 | −2.4716 | −2.0702 |
| Jojoba oil | −3.3286 | −3.0592 | −2.7054 | −2.2144 |
| Safflower oil | −3.3286 | −2.9145 | −2.5730 | −2.2886 |

bens following application of underarm deodorants and antiperspirants could feasibly be responsible for the breast tumours. The results of the estimated permeability coefficients of the parabens suggest that in addition to the high intrinsic hydrophobicity of the parabens, that the vehicles (or co-vehicles) and other cosmetic product components (for example, botanical oils) in such deodorants and antiperspirants might have contributed to their dermal absorption. Previously reported equation (Potts and Guy 1992): $\log K\rho(\text{cm/h}) = -2.7 + 0.71 \quad \log P - 0.0061\,MW$ was used to calculate the permeability coefficient, where $\log K\rho$, is the logarithm dermal permeability coefficient; $\log P$, is the observed logarithm partition coefficient for the paraben, MW is the molecular weight of the paraben.

The study indicates that octyldodecanol, oleyl alcohol have lipophilic properties comparable to 1-octanol. Light mineral oil showed the least lipophilic effect on the parabens. All the botanical oils studied except *Aloe vera* oil exhibited significant lipophilicity. The lipophilic effects were observed to increase with increasing paraben hydrophobicity. The grape seed oil was noted to have more lipophilic effect than grape leaf oil. Finally, the study indicates that octyldodecanol, oleyl alcohol, could be good substitutes for 1-octanol in partition coefficient measurements and that both vehicles, coconut oil and jojoba oil could be potential percutaneous absorption enhancers.

## 3. Experimental

### *3.1. Materials*

Methylparaben, ethylparaben, propylparaben, light mineral oil, 1-octanol were purchased from Sigma-Aldrich (USA), butylparaben from Protachem Chemicals Inc. (USA), octyldodecanol (eutanol G) from Cognis (USA), diethylhexylmaleate (ceraphyl 45) from ISP Technologies Inc.(USA), dimethicone (Dow Corning 200 R fluid) from Dow Corning (USA), oleyl alcohol (Novol) from Croda Inc. (USA), aloe vera oil from Tri-K Industries Inc. (USA), coconut oil, extra virgin olive oil and hazelnut oil from Natural oils International Inc. (USA), grape seed oil and jojoba oil from Dessert Whale (USA), grape leaf oil D1960 from Carrubba Inc. (USA), safflower oil from Jeen International (USA).

### *3.2. Apparatus*

All separations were carried out with a Hitachi LC 6200 pump and an AS 2000 autosampler, Kratos spectroflow 783 detector. A zorbax SB-CN analytical column, 150 mm × 4.6 mm, 3.5 µm was used.

### *3.3. Chromatographic procedure*

The mobile phase consisted of methanol and 1% aqueous acetic acid (50 : 50). The flow rate was 1 ml/min. The injection volume was 10 µl and detection was effected at 254 nm.

### *3.4. Standard solution*

Stock solution of parabens (100 µg/ml) was prepared in methanol. Aliquots (10.0–50.0 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*

10 ml of each vehicle (or co-vehicle) or botanical oil were added to 10 ml of phosphate buffer (pH 7.4) containing 1 mg of each paraben. However, in the cases of 1-octanol, oleyl alcohol and octyldodecanol, the phosphate buffer contained 20 mg of butylparaben. The flasks were stoppered and agitated at room temperature for 2 h to achieve complete equilibration. The aqueous phase was analysed by a chromatographic method for paraben content and the concentrations were calculated from preconstructed calibration graphs. The partition coefficient of each paraben was calculated using a previously reported equation (Johansen and Bundgaard 1980a).

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