Skin Research and Technology 2009; 15: 392–398
Printed in Singapore · All rights reserved
doi: 10.1111/j.1600-0846.2009.00376.x

Skin Research and Technology

Measuring transepidermal water loss: a comparative *in vivo* study of condenser-chamber, unventilated-chamber and open-chamber systems

Sara Farahmand, Lilian Tien, Xiaoying Hui and Howard I. Maibach

Department of Dermatology, School of Medicine, University of California, San Francisco, CA, USA

Background/aims: Two main systems have been utilized for measuring transepidermal water loss (TEWL): open chamber and closed chamber. Yet, further validation and standardization studies may be necessary to reveal the sensitivity, precision, and robustness of these instruments.
Methods: Three instruments are compared for their applicability to assess TEWL: unventilated chamber, open chamber and condenser chamber. The comparative study was performed on human forearm skin ($n=6$), in the normal condition (baseline), and after (1) 10 tape strippings on both arms, (2) moisturizer cream (Eucerin®) and petrolatum application for 1 h, and (3) 1% sodium lauryl sulfate (SLS) aqueous solution and distilled water (as control) application for 20 min.
Results: The condenser-chamber system, was the only device among these three that could show the effect of tape stripping on TEWL values as compared with baseline ($P<0.001$). The effect of moisturization, in terms of % change of TEWL values after application of cream and petrolatum, did not show significant difference between devices ($P>0.05$). However, only the values obtained from condenser-chamber device revealed a highly significant change as compared with baseline ($P<0.001$). Condenser-chamber system could also discriminate between the effect of moisturizer and petrolatum on TEWL values ($P<0.05$). The change of TEWL values after SLS application was shown to be significant by unventilated and condenser-chamber systems ($P<0.05$). However, none of the devices differentiated between the effect of water and 1% SLS solution applied for 20 min. The values obtained from all three instruments correlate well with each other ($P<0.001$).
Conclusion: Our results highlight the differences between two closed-chamber TEWL measurement instruments, which are designed based on different measurement principles. This may provide insights to find the best practice to improve the quality, precision and sensitivity of the measurements.

Key words: TEWL – human skin – barrier function – comparative study

Accepted for publication 15 May 2009

TRANSEPIDERMAL WATER LOSS (TEWL) refers to the total amount of water loss through the skin: liquid water passing the stratum corneum by passive diffusion and water vapor loss as a result of sweating (1, 2). However, when determinations are made below the thermal sweating threshold, contributions of eccrine sweat evaporation should be minimal (2). TEWL is a frequently used non-invasive method for elucidation of skin structure and water barrier function (3, 4). When the skin water barrier is damaged, TEWL increases. Even subtle changes in barrier integrity might be detected by measuring TEWL (5). As TEWL measures total vapor loss, another application of TEWL measurement may be to assess the degree of sweating (1).

Interestingly, there are no methods for measuring TEWL directly; In fact, TEWL is being inferred from water vapor flux evaporating from the skin. If TEWL is the only source of water reaching the skin surface and the skin surface remains dry, then the measured vapor flux equals TEWL (6). *In vivo*, TEWL can be measured according to different approaches: (i) closed-chamber method, which measures the increase of relative humidity (RH) in a closed air chamber, (ii) the ventilated chamber method, which measures water picked up by a gas passing through the chamber, (iii) open-chamber method, which utilizes an open capsule, and estimates the vapor pressure gradient from the difference in vapor pressure at the two fixed heights of measurement. All these methods have inherent drawbacks, as they interfere with the microclimate overlying the surface of the skin. The main problem with open-chamber systems is their vulnerability to disturbance from ambient air movements. The major concern with the closed-chamber method is its inability to perform continuous measurements, as the accumulated water vapor needs to be purged after every reading. A different approach in closed-chamber systems has been introduced by Imhof (6), where a condenser is used to remove water vapor from the closed measurement chamber, thus enabling continuous flux measurement to be made without purging (7).

Recently, we compared the efficacy of a closed-chamber, a condenser-chamber and an open-chamber TEWL measurement system, in an *in vitro* human skin study, where we evaluated the correlation of skin permeability and TEWL. Our results documented the same pattern of TEWL measurements for all the instruments, furthermore, TEWL values measured by open and condenser-chamber devices, demonstrated a significant correlation with tritiated water flux (8).

This study compares the sensitivity and efficacy of those TEWL measurement instruments by means of paired *in vivo* measurements on normal and altered skin.

Materials and Methods

Instruments

Unventilated-chamber system

VapoMeter™ *SWL-2* (instrument A) (Delfin Technologies Ltd, Kuopio, Finland), is a portable and battery-operated device containing a Honeywell humidity sensor HIH 3605-B in a closed chamber. The closed-chamber conditions are created upon skin contact with surface area of 1 cm diameter. Measuring time is between 7 and 12 s. The instrument has to rest for at least 20 s between the measurements to allow the elevated RH and temperature inside the closed chamber to return to ambient (5, 9).

Condenser-chamber system

AquaFlux AF200 (instrument B) (Biox systems Ltd, London, UK), has a closed chamber equipped with a condenser cooled to below the freezing point of water ($-7.65\,^{\circ}C$), which acts as a sink for water vapor. With the aid of a humidity sensor (with inbuilt calibration), water vapor flux is determined using Nilsson's diffusion gradient principle. No recovery time is necessary before starting the next measurement, because of the controlled microclimate (10, 11).

Open-chamber system

Tewameter® TM210 (instrument C) (Courage+Khazaka Electronic, Köln, Germany) is based on the diffusion gradient principle in an open chamber. The water vapor pressure gradient is indirectly measured by two pairs of a combined thermistor and hygrosensor, mounted at two different heights inside a hollow cylinder (height 2 cm, diameter 1 cm). The probe head is placed horizontally on the skin at a constant pressure. After probe equilibration, measuring time was set to be 45 s. During the whole experiment, determinations were performed according to published standardized protocols (2, 3, 12).

Volunteers

Six healthy volunteers [four female and two male; three Caucasians and three Asian; age range 27–72 (mean age 46 ± 16)] were enrolled after providing informed consent. Subjects had no skin disorders and underwent an evaluation of skin of both forearms, being subdivided into different measuring zones as described in the experimental design. Subjects were instructed not to apply topical products on the test sites.

Experimental design

A comparative study including parallel *in vivo* measurements with three devices was performed on forearm skin. Three sites on the inner sides of the volar forearms were selected for measurements: site 1 just above the wrist, site 2 was in the middle and site 3 just below the cubital fossa. These skin areas are relatively hairless preventing hairs or particles touching the sensors (5).

The study was conducted during winter in a room with daily ranges of RH $45.1 \pm 3.21\%$ and temperature range $22.1 \pm 1\,^{\circ}C$. All volunteers were adapted to this condition at least 15 min before starting the measurements.

At all three mentioned sites ($3\,cm^2$) with these devices, the following measurements were performed: (a) baseline TEWL values (expressed in g/m^2h) on left and right arm on two different days and (b) effect of single topical application of a cosmetic moisturizing cream ($10\,mg/cm^2$, Eucerin® Calming cream, Beiersdorf Inc., Wilton, CT, USA) on the left arm and petrolatum (purified grade, Fisher scientific, Fair Lawn, NJ, USA) on the right arm. The products were applied gently with a cotton swab, and after 1 h were gently wiped off with paper towel. After 30 min, TEWL measurements with the devices were started. (c) Effect of mild chemical barrier disruption with sodium lauryl sulfate (SLS) application on left arm (1% w/v SLS in water, Sigma, St Louis, MO, USA, 99% purity). The detergent solution (300 μL) was applied through a small occlusive patch (Hill Top Chamber®, diameter 25 mm, Hill Top Research, Miamiville, OH, USA) and remained for 20 min. The corresponding test sites on the other forearm were identically treated with a water patch as control. After removal of the occlusive chambers, forearms were rinsed with lukewarm tap water and gently dried with a paper towel. TEWL measurements were started after 15 min.

Just on site 3 of the left and right arms, the effect of mild barrier damage induced by tape stripping was also determined (10 tape strips, D-squame®, Cuderm Corporation, Dallas, TX, USA). The tape disc was pressed onto the skin using a roller. The roller was then removed and the tape peeled from the skin with forceps. TEWL measurements were immediately started thereafter.

All the measurements were performed three times and the mean values reported.

Statistical analysis
Statistical analysis was performed using SPSS software (SPSS 11.5, SPSS Science, Chicago, IL, USA). Normal distributions were tested by Kolmogrov–Smirnov test of normality before performing comparisons with a paired *t*-test. When three experimental groups were compared, ANOVA analyses were performed, followed by a pairwise *post hoc*, Tukey test. The correlations between TEWL values obtained with three devices were determined by calculating the Pearson's correlation coefficient.

The level of significance was $P < 0.05$.

Results

Baseline values
Before evaluating the effects of variables, the baseline values of all test sites were measured (Table 1). The first day results showed that, TEWL values measured on site 1 were significantly different with sites 2 and 3 in both arms, as recorded by instruments A and B, whereas, no significant difference between sites was detected by instrument C ($P > 0.05$). Inter-day variations of results were observed for instruments A (unventilated chamber) and B (condenser chamber): On day 2, according to B, the sites 1 and 2 showed a significant difference on left arm, whereas on right arm, site 1 was significantly different with sites 2 and 3. Instrument A's (unventilated chamber) measurements on day 2, proved no significant difference between sites on both arms. No statistically significant variation was shown between corresponding sites on the left and right arm, as measured by three instruments (Table 1).

TABLE 1. Baseline TEWL values measured by three devices at three sites on left and right forearm

	Left arm			Right arm		
	Site 1	Site 2	Site 3	Site 1	Site 2	Site 3
Open-chamber*						
Day 1	8.87[†] [44.5]	9.97 [60]	7.65 [37.5]	9.58 [30.4]	6.65 [33.7]	7.92 [19.5]
Day 2	8.94 [17.3]	6.96 [18.4]	7.56 [22.1]	8.74 [46]	6.82 [19.4]	7.42 [33]
Unventilated-chamber						
Day 1[‡]	8.37 [17.6]	6.4 [14.81]	6.63 [17.2]	11.84 [20.1]	6.23 [11.5]	6.77 [15]
Day 2*	15.8 [45]	7.83 [37.2]	8.73 [49.6]	12.98 [53]	8.64 [30.6]	7.74 [42]
Condenser-chamber						
Day 1[‡]	14.66 [17.7]	11.12 [22]	9.68 [20]	14.78 [31.1]	9.7 [17.9]	9.5 [20.5]
Day 2[§]	13.3 [31.1]	8.34 [9.3]	9.13 [21]	13.4 [24.4]	8.58 [4.8]	8.46 [16.8]

*No significant difference in TEWL values was detected between sites in both arms (one-way ANOVA: P-value > 0.05).
[†]Each number represents mean (coefficient of variation %) of TEWL values measured three times on six subjects.
[‡]On both arms, TEWL values of site 1 are significantly different with sites 2 and 3 (one-way ANOVA, P-value < 0.001).
[§]On the left arm, the difference between TEWL values of sites 1 and 2 was significant, and on the right arm.
TEWL values of site 1 are significantly different with sites 2 and 3 (one-way ANOVA, P-value < 0.05).

Tape stripping effect
Instrument B (condenser chamber) was the only device that showed the effect of tape stripping on TEWL as compared with the baseline. (Fig. 1a).

No significant difference was detected between left and right arm values, as measured by three devices ($P > 0.05$).

Effect of moisturizing cream and petrolatum
The effect of moisturization, in terms of % change of TEWL values after application of cream and petrolatum on all sites, did not show significant inter-device variation ($P > 0.05$). However, only the values obtained from device B (condenser chamber) revealed a highly significant change as compared with the baseline ($P < 0.001$). Figure 1b presents this trend for site 3.

Device B also discriminated between the effect of cream and petrolatum on TEWL values of sites 2 and 3 ($P < 0.05$).

Percent change of TEWL compared with baseline values, were not significantly different between three sites. The values determined for site 3 are shown in Table 2.

Effect of detergent (SLS 1% aqueous solution)
The change of TEWL values after SLS application on all three sites was shown to be significant by unventilated-chamber and condenser-chamber systems ($P < 0.05$). Figure 1c illustrates this pattern for site 3.

However, no device differentiated between the effect of water and 1% SLS aqueous solution applied for 20 min (Table 2).

No statistically significant inter-device or inter-site variation was observed in percent change of TEWL after SLS or water application. The values determined for site 3 are shown in Table 2.

Interdevice correlations
TEWL values measured by three instruments are correlated significantly ($P < 0.001$) (Fig. 2). Pearson's correlation coefficient is 0.58 for B (condenser chamber) and A (unventilated chamber),

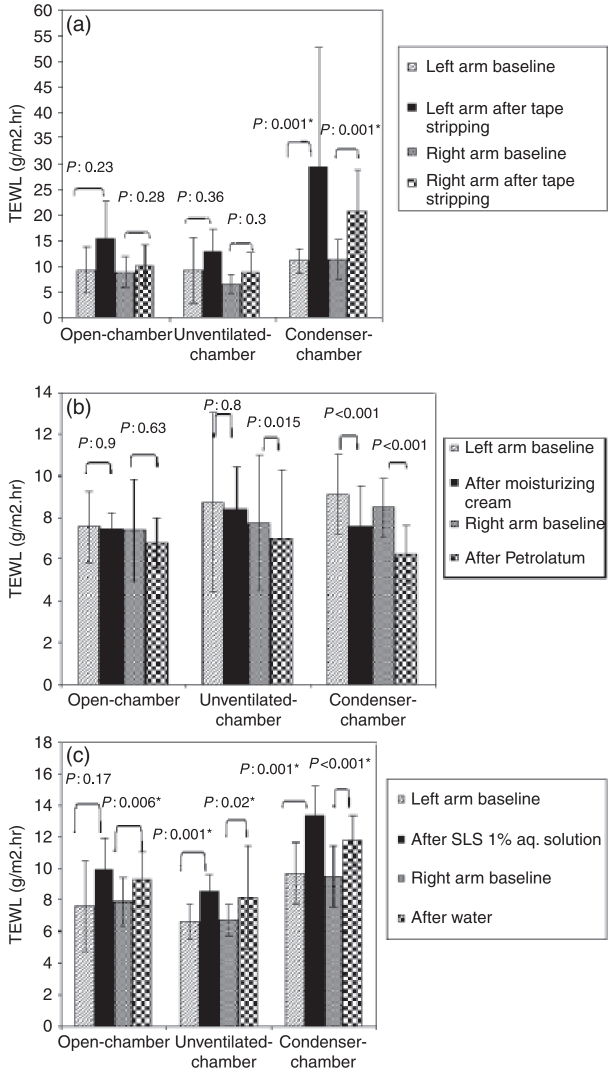

*Fig. 1. Comparison of three devices in detecting (a) tape stripping effect on TEWL (b) moisturization effect on TEWL and (c) detergent effect on TEWL. *The mean difference is significant at 0.005 level.*

TABLE 2. % Change of TEWL values compared to baseline after different treatments on forearm as measured by three devices

	Tape stripping*		Moisturizing		Detergent†	
Device/parameter	Left arm	Right arm	Eucerin® cream‡	Petrolatum‡	SLS 1%	Control (water)
Open-chamber‡	16.4	14.4	2.7§	– 1.9	53.8	18.3
Unventilated-chamber	76.3	53.1	– 10.6§	– 9.9	32.9	17.8
Condenser-chamber	167.1	81.6	– 17.2¶	– 26.4	45.5	25.6

*No significant difference was detected between left and right arm values, as measured by three devices (*t*-test, $P > 0.05$).
†None of the devices could prove a significant difference between SLS 1% solution and water treatment effect (*t*-test, $P > 0.05$).
‡No significant difference was seen between devices (*t*-test, $P > 0.05$).
§No significant difference between effect of cream and petrolatum was observed (*t*-test, $P > 0.05$).
¶The effect of cream and petrolatum was significantly different (*t*-test, $P < 0.05$).

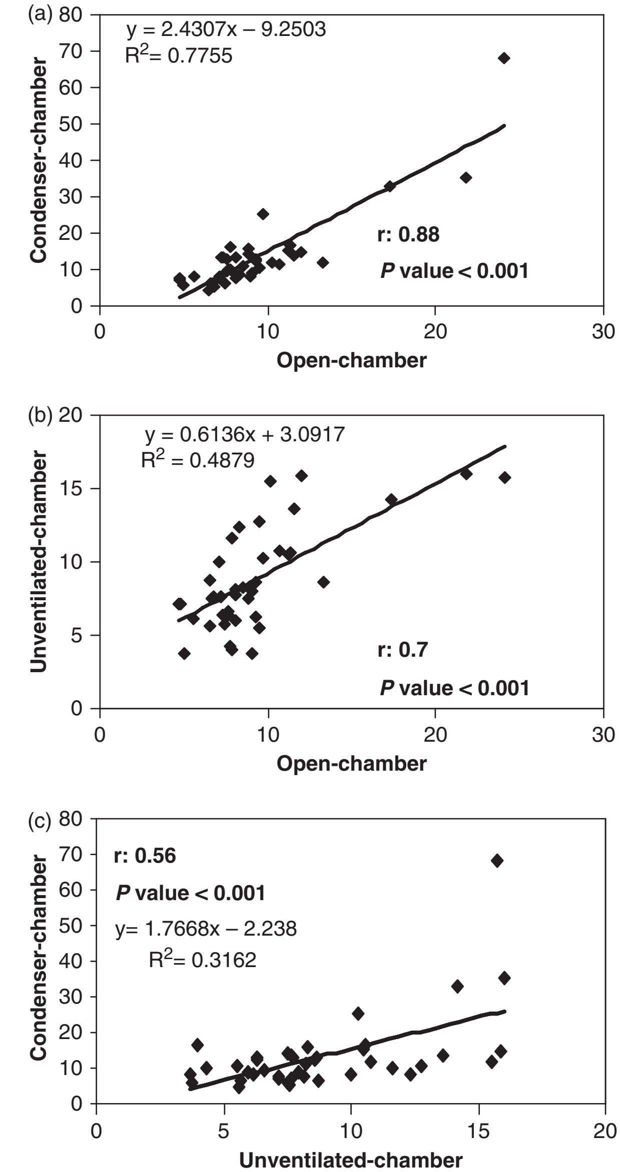

Fig. 2. Correlations between TEWL measurements under various experimental conditions (baseline, tape stripping, detergent and moisturizer application). (a) Open-and condenser-chamber, (b)open- and unventilated-chamber, (c) condenser-chamber and unventilated-chamber.

0.70 for A (unventilated chamber) and C (open chamber), and 0.88 for B (condenser chamber) and C (open-chamber).

Discussion

Wilson provides an in-depth overview of TEWL technology (13). The open and closed-chamber techniques for TEWL assessment are well established and the results obtained from the instruments correlate well with each other (5, 9, 14–16). This comparative *in vivo* study compared the sensitivity of two conventional open and closed-chamber devices with a recently developed condenser-chamber system.

The first part of the study investigated the baseline values of corresponding test areas, three on each forearm. As a consequence of different measurement and calibration principles, results obtained with different methods cannot be directly compared with accuracy (1). However, data shown in Table 1, demonstrates similarities between values measured by different devices. As a diffusion gradient measurement method, TEWL measurement can be modeled using Fick's first law. Therefore, a molecular diffusion coefficient for water vapor is defined. Diffusion resistance might be considered to be the sum of the stratum corneum (SC) barrier resistance, and the diffusion resistance imposed by open or close cylinder of TEWL measurement instrument. When the skin is not disrupted, the SC diffusion resistance is large compared with that of the measurement chamber. Therefore, differences in TEWL measurement chambers have little influence on measurements and similar readings of TEWL are expected, provided the instruments are correctly calibrated (1, 6). This explains the similarities of baseline values measured by different devices.

A similar pattern is observed for unventilated-chamber and condenser-chamber systems in measuring baseline values, as they both indicate a significant difference of site 1 (located closer to the wrist) with sites 2 and 3. This contrasts with studies, which found more variability for the areas closer to the elbow (5, 17). Our possible explanation for this finding is the higher probability of skin perturbations at site 1, as this area is highly exposed to frequent washing, and rubbing. The variabilities observed by other studies for the sites around cubital fossa, might be related to sweat gland activities interference with TEWL readings. The physiological unequivalence of different sites on the forearm demonstrates the need for careful selection of test sites and corresponding control areas for TEWL studies.

Inter-day variation of results should also be considered as a possible source of error in concluding the parameters effect on TEWL. The unventilated-chamber device readings show the highest inter-day variation (Table 1), and open-chamber system readings present the lowest. Further validation studies in terms of robustness and ruggedness may confirm this finding.

The second part investigated the effect of mild skin barrier disruptions (10 tape strippings, short-term dilute detergent application), and moisturization (O/W cream and petrolatum application) on TEWL, and the sensitivities of devices in detecting these effects have been compared.

After tape stripping, the condenser-chamber instrument was the only device that showed the increase of TEWL values compared with the baseline. As mentioned earlier, when the SC barrier resistance is decreased, the diffusion resistance of the measurement heads can no longer be neglected. Therefore, instruments show different results as their cylinders have different dimensions. The diffusion resistance is 900 S/m for condenser-chamber and 1000 S/m for open-chamber system (6). Meanwhile, the condenser acts as a sink for water vapor and controls the chamber microclimate humidity independently of ambient humidity. That could provide more sensitivity and reliability for the condenser-chamber device, in detecting the changes in skin barrier function. Nevertheless, the skin barrier resistance after 10 strips is still huge compared with chamber diffusion resistance. Thus, another explanation for this observation could be the heterogeneity of the stripping effect. Stripping is known to produce uneven results, with patches of high damage surrounded by relatively undamaged stratum corneum. The local flux from areas of high damage could be high enough to cause local RH to approach saturation level of 100%, even when the average over the measured area is much lower. The open chamber has, in any case, a much higher skin surface RH for a given flux than the condenser chamber. Therefore, the lower sensitivity of the open chamber in this test could be due to localized saturation (R. E. Imhoff personal communication).

After chemical disruption of the skin barrier with SLS (as an anionic surfactant which can remove epidermal barrier lipids), almost all the devices could prove the significant TEWL increase. Percent change of TEWL values was not significantly different between devices, although as presented in Table 2, percentage change measured by condenser chamber > unventilated chamber > open chamber. Higher sensitivity of condenser-chamber technique, environment-related variables (for open-chamber system), blocking of normal skin evaporation (for unventilated-chamber system) or inter-individual variations could be some of the reasons for this observation.

Following moisturizer application, in 10–15 min, water contained in the product evaporates and a lipidization phase starts. Lipids on the skin surface usually occlude the stratum corneum and impair water evaporation. In fact, no change, a slight or a more important decrease of TEWL may be detected during the lipidization phase, depending on the formulation applied on the skin: a lotion containing 80% water in the first case, a cream in the second and petrolatum in the third (3). We wiped-off the cream or petrolatum after 1 h, when presumably lipidization phase was started and no interference between product water evaporation and TEWL was expected. Our results (Table 2) agree with this fact, despite that for open-chamber system there is 2.7% increase in TEWL. Furthermore, the difference between cream and petrolatum effect could just be revealed by condenser-chamber system. This highlights the chief limitation of open-chamber devices, as they are extremely sensitive to any variation in the microclimate (due to the instrument, environment or individual), which can affect the accuracy of the results obtained from them.

Nevertheless, the measurements of all instruments show strong correlations with each other, in spite of differences in values, which are attributed to different calibration methods. Interestingly, the correlation of condenser-chamber and open-chamber readings seems to be stronger (r: 0.88) than condenser-chamber and unventilated-chamber systems ($r = 0.56$). Because of closer calibration and the fact that latter instruments are both categorized as closed-chamber systems, a stronger correlation of their values was expected. This could be attributed to the lack of reproducibility in measurements (as is observed for the unventilated chamber), or to vapor saturation in the chamber, which can cause inaccurate determinations.

Conclusion

Our results suggest that condenser-chamber method offers important advantages as it conquers the limitations of conventional closed and open-chamber systems: tendency to skin occlusion, and sensitivity to ambient conditions, respectively.

However, the measurements performed by all systems are significantly correlated.

Further validation and comparative studies, including ventilated-chamber systems, with large sample sizes, are necessary to confirm these findings. Meanwhile, standardization of TEWL calibration method would improve the comparability of different TEWL measurement instruments.

Taken together, this highly valuable technology will benefit from further comparisons as well as prudent clinical interpretations of the data from any instrument.

Acknowledgements

We thank Dr Robert E. Imhof and Biox Systems Ltd for their technical support and helpful discussions.

References

1. Tupker RA, Pinnagoda J. Measurement of transepidermal water loss by semi open systems. In: Serup J, Jemec GBE, Grove GL, eds. Handbook of non-invasive methods and skin, 2nd ed. Boca Raton: CRC-Taylor and Francis, 2006: 382–392.
2. Rogiers V., EEMCO group. EEMCO guidance for the assessment of Transepidermal water loss in cosmetic science. Skin Pharmacol Appl Skin Physiol 2001; 14: 117–128.
3. Gabard B. Testing the efficacy of moisturizers. In: Elsner P, Berardesca E, Maibach HI, eds. Bioengineering of the skin: water and the stratum corneum, 1st ed. Boca Raton: CRC Press, 1995: 147–154.
4. Beradesca E, Maibach HI. Stratum corneum water content and TEWL. In: Baran R, Maibach HI, eds. Text book of cosmetic dermatology, 2nd ed. London: Martin Dunitz, 1998: 529–535.
5. De Paepe K, Houben E, Adam R, Wiesemann F, Rogiers V. Validation of VapoMeter, a closed unventilated chamber system to assess transepidermal water loss vs. the open-chamber Tewameter. Skin Res Technol 2005; 11: 61–69.
6. Imhof RE. Invited Lecture, Intensive Course in Dermato-cosmetic Sciences, Vrije Universiteit, Brussels, 2007. Available at http://www.biox.biz/Downloads/PDFs/Imhof-Dermato-Cosmetic-Notes-2007.pdf (accessed 5 June 2008).
7. Imhof RE. Method and equipment for measuring water vapor flux from surfaces. US Patent 6439028, 2001.
8. Elkeeb R, Hui X, Chan H, Tien L, Maibach HI. Correlation and transepidermal water loss with skin barrier properties in vitro: comparison of three evaporimeters. Skin Res Technol (In press).
9. Zhai H, Dika E, Goldovsky M, Maibach HI. Tape-stripping method in man: comparison of evaporimetric methods. Skin Res Technol 2007; 13: 207–210.
10. Imhof RE. TEWL and skin barrier. Invited Lecture, 6th Annual Meeting of the Skin Forum, Winchester, 2005. Available at http://www.biox.biz/Support/ConfContribDetails09.htm (accessed 5 June 2008).
11. Nilsson GE. Measurement of water exchange through skin. Med Biol Comput 1977; 15: 209–218.
12. Pinnagoda J, Tupker RA, Agnar T, Serup J. Guidelines for transepidermal water loss (TEWL) measurement. A report from the standardization group of the European Society of Contact Dermatitis. Contact Derm 1990; 22: 164–178.
13. Wilson D, Maibach H. A review of transepidermal water loss. In: Maibach HI, Boisitis EK, eds. Neonatal skin: structure and function, 1st ed. NewYork: Marcel Dekker, 1982: 83–100.
14. Grove GL, Grove MJ, Zerweck C, Pierce E. Comparative metrology of the evaporimeter and the Dermalab® TEWL probe. Skin Res Technol 1999; 5: 1–8.
15. Fluhr JW, Feingold KR, Elias PM. Transepidermal water loss reflects permeability barrier status: validation inn human and rodent *in vivo* and *ex vivo* models. Exp Dermatol 2006; 15: 483–492.
16. Tagami H, Kobayashi H, Kikuchi K. A portable device using a closed-chamber system for measuring transepidermal water loss: comparison with the conventional method. Skin Res Technol 2002; 8: 7–12.
17. Chilcott RP, Farrar R. Biophysical measurements of human forearm skin *in vivo*: effect of site, gender, chirality and time. Skin Res Tech 2000; 6: 64–69.

Address:
Sara Farahmand
90 Medical Center Way
Surge 110, Box 0989
San Francisco, CA 941143-0989
USA
Tel:+1 415 476 4997
Fax:+1 415 753 5304
e-mail: farahmands@derm.ucsf.edu, farahmand.s@gmail.com