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| **STUDIES ON HEALTHY SKIN** | | | | | | | | | | | | |
|  | | **CRS**  **measurements** | | | **Biophysical measurements** | | | **Volunteers** | | **Results CRS** | **Results Biophysical Methods** | |
| [31]  B (65.6%) | | wavelength: 671 nm  step size: 4 µm  depth: 48 µm  #scans/site: 10  body site: volar forearm  SC thickness: measured from water profile.  Diffusion constant -D: measured from Fick’s first law of diffusion.  SC gradient: slope of straight line in SC.  AUC in SC: integral water profile from 0 µm to SC thickness.  AUC below SC: integral water profile from SC thickness to 20 µm deeper. | | | *TEWL*  (DermaLab, Cortex)  *Capacitance*  (Corneometer CM825, Courage & Khazaka)  body site: volar forearm | | | Healthy (n = 14, all women): mean age 49.9y, range 19-65y. | | SC gradient vs. AUC in SC: r = -0.87  SC gradient vs. AUC below SC: r = 0.50  SC gradient vs. SC thickness: r = -0.84  AUC in SC vs. SC thickness: r = 0.97 | TEWL vs. SC gradient: r = 0.08  TEWL vs. SC thickness: r = -0.35  TEWL vs. –D: r = 0.92  Capacitance vs. AUC in SC: r = -0.45  Capacitance vs. AUC below SC: r = 0.55  Capacitance vs. SC thickness: r = -0.49  Capacitance vs. SC gradient: r = 0.62 | |
| [37]  B (71.3%) | | wavelength: 671 nm and 785 nm  step size: 4 µm  depth: 32 µm (671 nm), 24 µm (785 nm)  #scans/site: 10  body sites: cheek, dorsal forearm, inner arm  SC thickness: measured from water profile.  AUC in SC (water, ceramides, cholesterol): integral depth profile from 0 µm to normalized SC thickness.  Lipid/protein ratio: I2820-2900/I2910-2965  Lipid compactness: (I1055-1070 + I1120-1140)/I1080-1090 | | | *TEWL*  (VapoMeter, Delfin)  *Conductance*  (Skicon 200EX, IBS Company)  body sites: cheek, dorsal forearm, inner arm | | | Healthy (n = 40, all women): equally divided in age groups G1 (18-30y), G2 (30-40y), G3 (40-55y), G4 (55-70y). | | *SC thickness:* thinner in cheek, no differences between arms. Increases with age in:   * Cheek (R2 = 0.104, P = 0.043) * Inner arm (R2 = 0.294, P <0.001) * Dorsal forearm (R2 = 0.276, P = 0.001)   *Lipid/protein ratio*: higher in cheek, different between arms only in G4. Decreases with age in:   * Inner arm (R2 = 0.100, P = 0.046) * Dorsal forearm (R2 = 0.155, P = 0.013)   *Lipid compactness*: different between arms only in G4. Decreases with age in:   * Dorsal forearm (R2 = 0.355, P <0.001)   *Water:* higher in cheek, no differences between arms. Decreases with age in dorsal forearm.  *Ceramides:* higher in cheek, different between arms only in G1. Decreases with age in inner arm and dorsal forearm.  *Cholesterol:* higher in cheek, different between arms. Decreases with age in cheek and dorsal forearm. | *TEWL:* higher in cheek, no differences between arms. Decreases with age in:   * Cheek (R2 = 0.244, P = 0.001) * Inner arm (R2 = 0.197, P <0.05)   *Conductance:* higher in cheek, different between arms in G2, G3. G4. No changes with age. | |
| [50]  B (71%) | | wavelength: 720 nm  step size: 2 µm  depth: 40 µm  body site: inner arm.  SC thickness: measured from water profile.  SC gradient: slope of water profile between 4 and 14 µm.  AUC in SC: integral of water profile between 0 and 20 µm. | | | *TEWL*  (VapoMeter, Delfin)  *Conductance*  (NOVA DPM, NOVA)  body sites: inner and outer arm. | | | Healthy (124 infants, 104 adults): age range 3 months – 4y (infants), 14-73y (adults). | | *Water*: higher concentration between 0 and 26 µm depth in infant skin (3-33 months) than in adult skin (P<0.05). Steeper gradient in infant skin than in adult skin (P<0.005). Higher AUC in infant skin than in adult skin (P<0.0005).  *Exogenous water absorption*: higher amount of water between 0 and 8 µm depth in infant skin (3-12 months) (P<0.05). No differences found in adult skin.  *NMF:* lower amount between 0 and 12 µm depth in infant skin (3-12 months) than in adult skin (P<0.05).  *SC thickness:* thinner in infant skin than in adult skin. | *TEWL*: higher in infant skin (3-12 months) than in adult skin in both the inner and outer arms (P<0.0005). In the outer arm, TEWL was higher in the 3-6 months group than in the 7-12 months group (P<0.01). Higher inter-subject variability in the 3-6 months group than in the 7-12 months group and in the adult group.  *Conductance*: higher in infant skin (3-12 months) than in adult skin in both the inner and outer arms (P<0.0005). Higher inter-subject variability in the infant groups than in the adult group.  *Exogenous water absorption and desorption:* higher rate of change of conductance in infant skin than in adult skin. | |
| [53]  C (58.1%) | | wavelength: 671 nm  step size: 3 µm  depth: 40 µm  #scans/site: 5  body site: forearm  AUC in SC: integral water profile from 0 µm to 3 µm and from 0 µm to 15 µm. | | | *Conductance*  (Skicon 200EX, IBS Company)  body site: forearm | | | Healthy (n = 14, 5 men): age range 23-68y. | |  | Before water application:  Skicon: R2 = 0.11 (AUC 3 µm), R2 = 0.31 (AUC 15 µm)  After water application (1h30min):  Skicon: R2 = 0.36 (AUC 3 µm), R2 = 0.33 (AUC 15 µm) | |
| [54]  B (79%) | | wavelength: 671 nm and 785 nm  step size: 5 µm  depth: 30 µm  body site: volar forearm.  AUC in SC (NMF, lactic acid and urea): integral of depth profiles in the intervals 0-5 µm, 5-15 µm, 15-25 µm, 25-35 µm and 0-25 µm. | | | *TEWL*  (Tewameter TM300, Courage & Khazaka)  *Capacitance*  (Corneometer CM825, Courage & Khazaka)  body site: volar forearm | | | Healthy (n =108): equally divided in full-term newborns (1-15 days), babies (5-6 weeks), babies (6 ± 1 month), children (1-2y), children (4-5y), adults (20-35y). | | *Water:* lower gradient in newborns than in all other groups.  *NMF*: higher content in the 5-15, 15-25 and 0-25 µm intervals in newborns than in all other groups. Lower content in each interval in the 6 ± 1month group than in all other groups.  *Lactic acid*: higher content at the surface and in the 0-25 µm interval in the 6 ± 1month group than in all other groups.  *Urea:* similar to bulk NMF. | *TEWL:* no significant differences between the infants and the adults. Significantly higher in the 1-2y group when compared with the 5-6weeks, 6 ± 1month and the 4-5y groups (P = 0.0011, 0.0468, 0.0105, respectively).  *Capacitance:* significantly lower in newborns than in all other groups. Significantly higher in the 5-6weeks and in the 6 ± 1month when compared with the 1-2y, 4-5y and adults (P<0.0001 each). | |
| [55]  B (68.6%) | | wavelength: 671 nm and 785 nm  step size: 2 µm  #scans/site: 2-3  body sites: cheek, volar forearm  Amount in SC (NMF, lactate, urea, t-UCA, ceramides, cholesterol): mean amount from skin surface to 12 µm (forearm) and from skin surface to 8 µm (cheek). | | | *Capacitance*  (Corneometer CM825, Courage & Khazaka)  body sites: cheek, volar forearm | | | Healthy (n = 27, 14 men): mean age 39y, range 25-53y (men);  mean age 32y, range 22-40y (women). | | *Water:* no differences in depth profile.  *Lactate, urea*: higher in summer in the forearm and in the cheek (P<0.05).  *Ceramides, cholesterol*: trend to higher values in summer in the cheek, lower in summer in the forearm (P<0.05).  *NMF:* no definite trend across seasons. Lower in the cheek all year around (P<0.01).  *t-UCA:* lower in summer in the forearm (P<0.05). | Capacitance in forearm: higher in summer (P<0.05).  Capacitance in cheek: higher in summer and in autumn (P<0.05). | |
| [57]  B (67.5%) | | wavelength: 671 nm  step size: 4 µm  depth: 40 µm  #scans/site: 10  body site: volar forearm | | | *TEWL*  (Tewameter TM300, Courage & Khazaka)  *Conductance*  (Skicon 200EX, IBS Company)  body site: volar forearm | | | Healthy (n = 8, 3 men): age range 17-43y. | | Water profile before and after tape stripping similar only if the skin barrier is minimally damaged by the stripping procedure. | Correlation conductance vs. water content: linear up to 37 mass%, exponential above 37 mass%.  Correlation conductance vs. TEWL: linear up to 12 g/(h m2), exponential above 12 g/(h m2). | |
| [69]  C (59%) | | wavelength: 660 nm  step size: 2 µm  depth: 5 µm  #scans/site: 7  body sites: inner and outer forearm, inner and outer calf | | | *TEWL*  (Tewameter TM210, Courage & Khazaka)  *Capacitance*  (Corneometer CM820, Courage & Khazaka)  body sites: inner and outer forearm, inner and outer calf. | | | Healthy (n = 11, all women): age range 55-65y. | | Good predictive ability of the PLS model to indirectly estimate skin biophysical parameters from Raman spectra (R2 > 0.9 for all predicted vs. true parameters). |  | |
| **STUDIES ON ATOPIC DERMATITIS AND PSORIASIS** | | | | | | | | | | | | |
|  | **CRS**  **measurements** | | **Biophysical measurements** | | | **Volunteers** | | | **Results CRS** | | | **Results Biophysical Methods** |
| [32]  B (72.1%) | wavelength: 671 nm  step size: 2 µm  depth: 40 µm  #scans/site: 15  body site: ventral forearm (lesional and non-lesional skin)  Lipid/protein ratio: I2866-2900/I2910-2966 determined from 4 µm to 10 μm | | *TEWL*  (Tewameter TM210, Courage & Khazaka)  body site: ventral forearm (lesional and non-lesional skin) | | | HealthyFLG: **n = 2**  HealthyNON-FLG: **n = 13**  Healthy (5 men): mean age 25y ± 5.2y.  ADFLG: **n = 14** (n=5 with lesional skin)  ADNON-FLG: **n = 14** (n=6 with lesional skin)  AD (11 men): mean age 25.6y ± 5.6y.  FLG mutations: R501X, 2282del4, R2447X, S3247X | | | *Healthy vs. AD (lesional)*: lower lipid/protein ratio in AD (P<0.001).  *Healthy vs. AD (non-lesional):* lower lipid/protein ratio in AD (P<0.005).  *AD (lesional) vs. AD (non-lesional)*: lower lipid/protein ratio in AD (lesional) (P<0.005).  *ADFLG vs. ADNON-FLG:* no differences.  AD:   * correlation with clinical assessment   (r = -0.52, P=0.005) | | | All volunteers:   * correlation 1/TEWL with SCmass/area   (r = 0.67, P<0.001);   * correlation 1/TEWL with lipid/protein ratio   (r = 0.86, P<0.001) |
| [33]  B (79%) | wavelength: 785 nm  step size: 2 µm  depth: 20 µm  #scans/site: 15  body site: ventral forearm (non-lesional skin)  AUC in SC (NMF): integral depth profile from 4 µm to 8 µm. | | *TEWL*  (Tewameter TM210, Courage & Khazaka)  body site: ventral forearm (non-lesional skin) | | | HealthyFLG: **n = 2**  HealthyNON-FLG: **n = 13**  Healthy (5 men): mean age 25y ± 5.2y.  ADFLG: **n = 14**  ADNON-FLG: **n = 14**  AD (11 men): mean age 25.6y ± 5.6y.  FLG mutations: R501X, 2282del4, R2447X, S3247X.  Clinical assessment:  No significant difference in disease severity (OSCORAD). | | | *Healthy vs. AD:* lower NMF levels in AD (P<0.01).  *ADFLG vs.ADNON-FLG*: lower NMF levels in ADFLG (P<0.005).  All volunteers:   * correlation with levels of short chain CER   (r = -0.611, P<0.01);   * correlation with average CER chain length   (r = 0.456, P<0.01);   * correlation with lipid organization (lamellar and lateral) (r >0.4, P<0.01).   AD:   * correlation with clinical assessment   (r = -0.362, P<0.015) | | | *Healthy vs. AD:* significantly higher TEWL in AD (12.2 ± 6.5 and 6.5 ± 1.7 g/(m2 h), P<0.0005).  *ADFLG vs.ADNON-FLG:* no differences.  All volunteers:   * correlation with levels of short chain CER   (r = 0.738, P<0.01);   * correlation with average CER chain length   (r = -0.528, P<0.01);   * correlation with lipid organization (lamellar and lateral) (r = 0.76, P<0.0001); * correlation with NMF levels (r = -0.643, P<0.01)   AD:   * correlation with clinical assessment   (r = 0.560, P<0.01) |
| [42]  C (59.2%) | step size: 10 µm (thenar), 5 µm (forearm)  depth: 30-50 µm (thenar), 0-20 µm (forearm)  body sites: thenar eminence, volar forearm (non-lesional skin) | | *TEWL*  (Tewameter TM210, Courage & Khazaka)  body site: volar forearm (non-lesional skin) | | | FLG+/- and FLG-/- (carriers):  **n = 16** (4 men): 11 with AD (active or history); mean age 33y, range 20-55y.  FLG+/+ (non-carriers):  **n = 23** (8 men): 7 with AD (active or history); mean age 30y, range 20-61y.  FLG mutations: R501X, 2282del4, R2447X, S3247X  Clinical assessment: dry skin in all carriers and in 11 non-carriers. | | | *Carriers vs. non-carriers*: significantly reduced NMF in both thenar and volar forearm in carriers (P< 0.0001). Less inter-individual variability of NMF in thenar.  *Carriers with history AD vs. non-carriers with history of AD:* significantly reduced NMF in carriers (P<0.0001). | | | *Carriers vs. non-carriers*: significantly higher TEWL in carriers (10.3 ± 2.7 vs. 8.3 ± 2.2 g/(m2 h), P = 0.01)\*.  \*mean ± SD |
| [43]  A (84.8%) | wavelength: 671 nm and 785 nm  step size: 2 µm (671 nm), 4 µm (785 nm)  depth: 40 µm  #scans/site: 5  body site: volar forearm (non-lesional skin)  SC thickness: measured from water profile.  AUC in SC (water, ceramides, cholesterol, NMF): integral depth profile from 0 µm to SC thickness. | | *TEWL*  (Tewameter TM210, Courage & Khazaka)  *Capacitance* (Corneometer CM820, Courage & Khazaka)  body site: volar forearm (non-lesional skin) | | | HealthyFLG: **n = 4**  HealthyNON-FLG: **n = 95**  ADFLG: **n = 10**  ADNON-FLG: **n = 87**  AD (24 men): mean age 30.6y ± 8.2y. Gender and age matched (± 3y) healthy volunteers.  AD participants with mild-to-moderate AD.  FLG mutations: R501X, 2282del4, R2447X.  Clinical assessment:  Significantly higher disease severity in ADFLG than in ADNON-FLG (OSCORAD). | | | *Healthy vs. AD*: thinner SC (P = 0.035) and lower amounts of total NMF (P=0.0336), water (P=0.0461), ornithine (P=0.0456), UCA (P=0.0003) in AD.  *Carriers vs. non-carriers:* thinner SC (P=0.0054), reduced water (P=0.0007), total NMF (P<0.0001), alanine (P<0.0001), glycine (P<0.0001), histidine (P<0.0001), proline (P=0.0048), serine (P<0.0001), PCA (P<0.0001) and UCA (P<0.0001), increased lactate (P=0.0234) in carriers.  Alalnine, histidine and PCA/glycine: 92% specificity to diagnose presence of FLG mutations.  *ADFLG vs.ADNON-FLG:* thinner SC, reduced water, total NMF, alanine, glycine, histidine, proline, serine, PCA and UCA in ADFLG.  Negative correlations in ADNON-FLG between disease severity and total NMF, alanine, histidine, PCA, proline, UCA, cholesterol and ceramides.    *HealthyNON-FLG vs. ADNON-FLG*: lower UCA in ADNON-FLG (P=0.006), trend to lower water content in ADNON-FLG (P=0.082). | | | TEWL:  *Healthy vs. AD:* no differences.  *Carriers vs. non-carriers:* trend to increased TEWL in carriers (P=0.0542).  *ADFLG vs.ADNON-FLG*: increased TEWL in ADFLG. Positive correlation with disease severity in ADFLG (r = 0.64, P=0.0470).  HealthyNON-FLG vs. ADNON-FLG: no differences.  Capacitance:  *Healthy vs. AD:* no differences.  *Carriers vs. non-carriers*: decreased capacitance in carriers (P=0.0139).  *ADFLG vs.ADNON-FLG*: no differences. Negative correlation with disease severity in ADFLG (r = -0.79, P = 0.0065) and in ADNON-FLG (r = -0.24, P=0.0242).  *HealthyNON-FLG vs. ADNON-FLG*: no differences. |
| [44]  A (84.1%) | Same procedure as [45] | | *TEWL*  (Tewameter TM300, Courage & Khazaka)  body site: extensor forearm (non-lesional skin) | | | FLG+/+: **n = 57** (34 males); mean age 8y, range 3-17y.  FLG+/-: **n = 55** (32 males); mean age 7y, range 1-17y.  FLG-/-: **n = 25** (15 males); mean age 8y, range 3-17y.  All participants with moderate-to-severe AD.  FLG mutations: R501X, Y2092X, 2282del4, R2447X, S3247X, R3419X, 3702X, S1040X, G1139X.  Clinical assessment:  No significant difference in disease severity (NESS). | | | Different NMF level in the following comparisons:  *ADFLG (FLG+/- and FLG-/-) vs. ADNON-FLG (FLG+/+)* (P<0.001)  *FLG+/+ vs. FLG-/-* (P<0.001)  *FLG+/+ vs. FLG+/-* (P<0.05)  Negative correlations with cytokine levels (IL--1α, IL-1β, IL-18, IL-1RA). | | | *TEWL:*  *FLG+/+ vs. FLG+/- vs. FLG-/-:* no difference in TEWL between FLG genotypes (12.6 (5.2-47.4), 14.05 (5.3-33.0), 15.9 (8.5-36.1) g/(m2 h) respectively, P=0.22)\*.  Positive correlations with cytokine levels (IL-1β, IL-18, IL-1RA, IL-1RA/IL-1α plus IL-1β).  \*median (range) |
| [45]  A (81.4%) | wavelength: 785 nm  step size: 5 µm  depth: 30-50 µm  body site: thenar eminence  #scans/site: 8 (average)  NMF: average level in the depth 30-50 µm. | | *TEWL*  (Tewameter TM300, Courage & Khazaka)  body site: extensor forearm (non-lesional skin) | | | FLG+/+: **n = 53** (32 males); mean age 8.43y ± 3.76y.  FLG+/-: **n = 55** (32 males); mean age 8.2y ± 4.12y.  FLG-/-: **n = 24** (15 males); mean age 8.83y ± 4.16y.  All participants with moderate-to-severe AD.  FLG mutations: R501X, 2282del4, R2447X, S3247X, 3702delG, Y2092X, R3418X, G1138X, S1040X, 10085delC, L2933X.  Clinical assessment:  No significant difference in disease severity (NESS). | | | *FLG+/+ vs. FLG+/- vs. FLG-/-:* significantly different NMF level in each pairwise comparison (P<0.0001).  *ADFLG (FLG+/- and FLG-/-) vs. ADNON-FLG (FLG+/+):* 0.95 AUC on ROC analysis (sensitivity 98.73%, specificity 86.89%, optimal cutoff NMF value 1.07 a.u.).  *FLG+/- vs. FLG-/-:* 0.85 AUC on ROC analysis (sensitivity 96%, specificity 66.77%, optimal cutoff NMF value 0.767 a.u.). | | | *FLG+/+ vs. FLG+/- vs. FLG-/-:* no difference in TEWL between FLG genotypes (15.54 ± 9.34, 15.59 ± 6.72, 17.35 ± 7.37 g/(m2 h) respectively, P=0.70)\*.  \*mean ± SD |
| [56]  B (69.4%) | step size: 2 µm  depth: 20 µm (lesional skin + high severity), 10 µm (lesional skin + low severity, non-lesional)  #scans/site: 2-5  body site: forearm (lesional and non-lesional skin)  SC thickness: measured from water profile.  Amount in SC (water, NMF, lactate, urea, t-UCA, ceramides, cholesterol): mean amount from surface to 10 µm or to 20 µm. | | *Capacitance* (Corneometer CM825, Courage & Khazaka)  *Conductance*  (Skicon 200, IBS Company)  body site: forearm (lesional and non-lesional skin) | | | Psoriasis (**n = 6**, all men): mean age 39y, range 23-53y.  Clinical assessment:  Differences in disease severity (n = 4 high severity, n = 2 low severity) based on indices of infiltration, erythema and scaling. | | | *Lesional vs. non-lesional skin:* lower ceramides (P<0.1) in lesional skin. Trend to lower water, NMF and t-UCA in lesional skin. | | | *Lesional vs. non-lesional skin:* lower conductance (P<0.1) and capacitance (P<0.01) in lesional skin. |
| **STUDIES ON MOISTURIZERS EFFECT AND SKIN IRRITATION** | | | | | | | | | | | | |
|  | | **CRS**  **measurements** | | **Biophysical measurements** | | | **Volunteers** | | **Results CRS** | | | **Results Biophysical Methods** |
| [34]  B (79.7%) | | body site: lower legs (non-lesional skin)  Amount in SC (NMF, PCA, ceramides): measurements at 5 µm and at 10 ± 1 µm depth.  AUC in SC (water): integral water profile in three equally spaced compartments. | | *TEWL*  (Dermalab, Cortex)  *Capacitance*  (Corneometer CM825, Courage & Khazaka)  body site: lower legs (non-lesional skin) | | | AD (n = 20, 4 men):  mean age 40.9y, range 18-65y. | | *Ceramides:* increase from baseline in treated site at both depths (+54% at 5 µm, + 40% at 10 µm, P < 0.05 vs. untreated).  *NMF, PCA:* trend to higher content from baseline in treated site at both depths.  *Water*: trend to higher content from baseline in treated site in the deepest SC compartment. | | | *TEWL:* reduction from baseline in treated site (-30%, P = 0.002 vs. untreated).  *Capacitance*: increase from baseline in treated site (+118%, P < 0.001 vs. untreated). |
| [35]  B (78.9%) | | wavelength: 671 nm  step size: 2 µm  depth: 40 µm  #scans/site: 8  body site: volar forearm  SC thickness: measured from water profile.  AUC in SC: integral water profile from 0 µm to SC thickness. | | *Capacitance*  (Corneometer CM820, Courage & Khazaka)  body site: volar forearm | | | Healthy (n = 14, 7 men): mean age 32y, range 23-55y. | | *SC thickness*: increase at 2 weeks of product use (P = 0.0121) and at 1 week following last product application (P = 0.0162) for the moisturizer containing niacinamide.  *Water*: increase at 2 weeks of product use (P = 0.0275) and at 1 week following last product application (P = 0.0435) for the moisturizer containing niacinamide. | | | *Capacitance:* increase throughout the two weeks of product application for all three moisturizers. |
| [36]  B (71.2%) | | wavelength: 671 nm and 785 nm  step size: 2 µm (671nm), 4 µm (785nm)  depth: 40 µm  #scans/site: 8  body site: volar forearm  SC thickness: measured from water profile. | | *TEWL*  (Aquaflux AF103, Biox Systems)  body site: volar forearm | | | Healthy (n = 20, 5 men): mean age 24y, range 21-28y. | | *SC thickness*: increase after 28 days of bi-daily application of a commercial formulation containing 5% niacinamide with respect to baseline (P < 0.001). | | | *TEWL*: during tape stripping: lower values in the site in which the commercial niacinamide formulation was applied compared to baseline, to the untreated site and to the site in which only the vehicle was applied (P < 0.05). Before tape stripping: no differences. |
| [51]  B (78.4%) | | wavelength: 785 nm  step size: 2 µm  depth: 24 µm (carotenoids), 35 µm (water)  body site: volar forearm | | *TEWL*  (Tewameter TM300, Courage & Khazaka)  *Capacitance*  (Corneometer CM825, Courage & Khazaka)  body site: volar forearm | | | Healthy (n = 7, 4 men): mean age 42.4y, range 27-53y. | | *Water:* reduction in water content up to a depth of 24 µm, effect more important at the skin surface (30% reduction on average).  *Carotenoids:* significant reduction in carotenoid content at the skin surface (70% reduction approximately), lower reduction in the deeper SC. | | | *TEWL:* average increase of 50% after TTP application.  *Capacitance:* significant decrease after TTP application (from 46.4 ± 6.5 to 34.4 ± 4.8, P < 0.0001). |
| [64]  C (56.7%) | | wavelength: 671 nm  depth: 20 µm  #scans/site: 5  body site: volar forearm | | *TEWL*  (VapoMeter, Delfin)  *Capacitance*  (Corneometer, Courage & Khazaka)  body site: volar forearm | | | Healthy (1 woman, 27y). | | *Water:* higher water for certain topicals tested and time points. | | | *TEWL:* lower for each topical tested and in each time point.  *Capacitance:* higher for each topical tested and in each time point. |
| [66]  B (76.6%) | | *NMF, ceramides*:  step size: 2 µm (0-30 µm), 5 µm (30-50 µm), 25 µm (50-100 µm).  *Water*:  step size: 2 µm (0-100 µm)  #scans/site: 7  body site: volar forearm  SC thickness: measured from water profile.  AUC in SC (water, NMF, ceramides): integral water profile from 0 µm to SC thickness. | | *TEWL*  (Tewameter TM300, Courage & Khazaka)  body site: volar forearm | | | Healthy (n = 20, all women): age range 18-65y. | | *Water:* at the vehicle site, increase in total content only immediately after patch removal with respect to the SLS site. At day 1 and 2, the effect was reversed with an increase at the SLS site with respect to the vehicle site (P < 0.001).  *NMF*: Histidine pH7, lactate, ornithine, urea different between SLS and vehicle sites only immediately after patch removal. Alanine, glycine, histidine pH4, PCA, serine, t-UCA pH4 and t-UCA pH8 different up to 6 days after patch removal. No changes in proline. Lactate, ornithine and urea higher immediately after patch removal, while other NMF components lower.  *Ceramides:* increase immediately after patch removal in the SLS site compared to the vehicle site.  *Cholesterol:* no changes. | | | *TEWL:* significantly higher at the SLS site than at the vehicle site immediately after and up to 6 days following patch removal (P < 0.01). |

*AD = atopic dermatitis, a.u. = arbitrary units, AUC = Area Under the Curve, CER = ceramides, CRS = confocal Raman Micro-Spectroscopy, FLG = filaggrin, NESS = Nottingham Eczema Severity Score, NMF = Natural Moisturizing Factor, PCA = pyrrolidone-5-carboxylic acid, PLS = Partial Least Squares, OSCORAD = Objective Severity SCOring of Atopic Dermatitis, r = Pearson’s correlation coefficient, R2 = squared correlation coefficient, ROC = Receiver Operating Characteristic, SC = stratum corneum, SLS = sodium lauryl sulphate, TEWL = transepidermal water loss, TTP = tissue tolerable plasma, t-UCA = trans-urocanic acid.*