



Literature List Veterinary & Zoology

*J.-H. Wang, S.-J. Hwang, S.-K. Lee, Y. Choi, C.K. Byun, C.-G. Son, **Anti-Melanogenic Effects of Fractionated Cynanchum atratum by Regulation of cAMP/MITF Pathway in a UVB-Stimulated Mice Model**, Cells 2023, 12*

Abstract: Based on traditional pharmacological applications and partial in vitro data, *Cynanchum atratum* (CA) is proposed to act on skin whitening. However, its functional evaluation and underlying mechanisms have yet to be identified. This study aimed to examine the anti-melanogenesis activity of CA fraction B (CAFB) on UVB-induced skin hyperpigmentation. Forty C57BL/6j mice were exposed to UVB (100 mJ/cm², five times/week) for eight weeks. After irradiation, CAFB was applied to the left ear once a day for 8 weeks (the right ear served as an internal control). The results showed that CAFB significantly reduced melanin production in the ear skin, as indicated by the gray value and Mexameter melanin index. In addition, CAFB treatment notably decreased melanin production in α -MSH-stimulated B16F10 melanocytes, along with a significant reduction in tyrosinase activity. Cellular cAMP (cyclic adenosine monophosphate), MITF (microphthalmia-associated transcription factor), and tyrosinase-related protein 1 (TRP1) were also noticeably downregulated by CAFB. In conclusion, CAFB is a promising ingredient for treating skin disorders caused by the overproduction of melanin and its underlying mechanisms involving the modulation of tyrosinase, mainly mediated by the regulation of the cAMP cascade and MITF pathway.

*A. Idée, M. Mosca, D. Pin, **Skin Barrier Reinforcement Effect Assessment of a Spot-on Based on Natural Ingredients in a Dog Model of Tape Stripping**, Vet. Sci. 2022, 9, 390*

Skin barrier restoration is an important part of atopic dermatitis therapy. We investigated the effect of a spot-on containing plant-based essential fatty acids and essential oils on skin barrier parameters in a dog model of acute skin barrier disruption, using five healthy beagle dogs maintained in a laboratory setting. Four test sites on the dorsum and a control site on the abdomen were defined on each dog. Transepidermal water loss (TEWL) and skin surface hydration (SSH) were measured before and after tape stripping on the first day and then for three consecutive days, over four consecutive weeks. The spot-on was applied at the end of each of the first three weeks. The increase in TEWL after tape stripping was reduced after the spot-on application and reached control values in Weeks 3 and 4. SSH after tape stripping was reduced in Week 4 compared with the baseline. Thus, the ATOP 7[®] spot-on significantly reduced acute skin barrier impairment in a dog model. The use of this product should be further evaluated as a potential treatment for skin barrier defects such as canine atopic dermatitis.

*S.Y. Kim, T. Hong Yoon, J. Na, S.J. Yi, Y. Jin, M. Kim, T.-H. Oh, T.-W. Chung, **Mesenchymal Stem Cells and Extracellular Vesicles Derived from Canine Adipose Tissue Ameliorates Inflammation, Skin Barrier Function and Pruritus by Reducing JAK/STAT Signaling in Atopic Dermatitis**, Int. J. Mol. Sci. 2022, 23, 4868*

Canine atopic dermatitis (AD) is a common chronic inflammatory skin disorder resulting from imbalance between T lymphocytes. Current canine AD treatments use immunomodulatory drugs, but some of the dogs have limitations that do not respond to standard treatment, or relapse after a period of time. Thus, the purpose of this study was to evaluate the immunomodulatory effect of mesenchymal stem cells derived from canine adipose tissue (cASCs) and cASCs-derived extracellular vesicles (cASC-EVs) on AD. First, we isolated and characterized cASCs and cASCs-EVs to use for the improvement of canine atopic dermatitis. Here, we investigated the effect of cASCs or cASC-EVs on DNCB-induced AD in mice, before using for canine AD. Interestingly, we found that cASCs and cASC-EVs improved AD-like dermatitis, and markedly decreased levels of serum IgE, (49.6%, $p = 0.002$ and 32.1%, $p = 0.016$ respectively) epidermal inflammatory cytokines and chemokines, such as IL-4 (32%, $p = 0.197$ and 44%, $p = 0.094$ respectively), IL-13 (47.4%, $p = 0.163$, and 50.0%, $p = 0.039$ respectively), IL-31 (64.3%, $p = 0.030$ and 76.2%, $p = 0.016$ respectively), RANTES (66.7%, $p = 0.002$ and 55.6%, $p = 0.007$) and TARC (64%, $p = 0.016$ and 86%, $p = 0.010$ respectively). In addition, cASCs or cASC-EVs promoted skin barrier repair by restoring transepidermal waterloss, enhancing stratum corneum hydration and upregulating the expression levels of epidermal differentiation proteins. Moreover,

cASCs or cASC-EVs reduced IL-31/TRPA1-mediated pruritus and activation of JAK/STAT signaling pathway. Taken together, these results suggest the potential of cASCs or cASC-EVs for the treatment of chronic inflammation and damaged skin barrier in AD or canine AD.

Y.-J. Kim, J.O. Lee, S.-Y. Kim, J.M. Lee, E. Lee, J. Na, K.-H. Yoo, S.-J. Park, B.J. Kim, **Effect of A. polygama APEE (Actinidia polygama ethanol extract) or APWE (Actinidia polygama water extract) on wrinkle formation in UVB-irradiated hairless mice**, J Cosmet Dermatol, March 2022

Background: Actinidia polygama (silver vine) is considered a medical plant which has been used in oriental medicine. It has been used for the treatment of pain, gout, rheumatoid arthritis, and inflammation. Few studies reported on the effect of Actinidia polygama (silver vine) on skin photoaging. Objective: To evaluate the anti-photoaging effect of the ethanol and water extracts of A. polygama (APEE and APWE, respectively) in UVB-irradiated hairless mice. Methods: SKH-1 hairless mice were exposed to UVB irradiation (30~60 mJ/cm), following orally APEE or APWE oral administration for 10 weeks. We examined the effect on wrinkle improvement by a measuring Fullscope, PRIMOS, Craniometer and Cutometer. Furthermore, we analyzed histological changes in mouse dorsal skin through hematoxylin and eosin (H&E) and Masson's trichrome (MT) staining. The expression of matrix metalloproteinase (1, 3, and 9) expression was analyzed by immunoblotting. Results: Oral administration of APEE or APWE at 100 or 200 mg/kg in UVB-irradiated mice alleviated the symptoms of skin aging, such as wrinkling, epidermal hyperplasia, and water loss. In addition, the APEE or APWE oral administration increased skin elasticity by enhancing the production of type I collagen, elastin, and hyaluronic acid synthase and downregulating matrix metalloproteinase (1, 3, and 9) expression. Conclusion: Based on results for our study, APEE or APWE could protect the UVB-mediated skin wrinkle and is new target for the developing anti-wrinkle cosmetics.

H.R. Yun, S.W. Ahn, B. Seol, E.A. Vasileva, N.P. Mishchenko, S.A. Fedoreyev, V.A. Stonik, J. Han, K.S. Ko, B.D. Rhee, J.E. Seol, H.K. Kim, **Echinochrome A Treatment Alleviates Atopic Dermatitis-like Skin Lesions in NC/Nga Mice via IL-4 and IL-13 Suppression**, Mar. Drugs 2021, 19, 622

Atopic dermatitis (AD) is a chronic inflammatory skin disease in which skin barrier dysfunction leads to dryness, pruritus, and erythematous lesions. AD is triggered by immune imbalance and oxidative stress. Echinochrome A (Ech A), a natural pigment isolated from sea urchins, exerts antioxidant and beneficial effects in various inflammatory disease models. In the present study, we tested whether Ech A treatment alleviated AD-like skin lesions. We examined the anti-inflammatory effect of Ech A on 2,4-dinitrochlorobenzene (DNCB)-induced AD-like lesions in an NC/Nga mouse model. AD-like skin symptoms were induced by treatment with 1% DNCB for 1 week and 0.4% DNCB for 5 weeks in NC/Nga mice. The results showed that Ech A alleviated AD clinical symptoms, such as edema, erythema, and dryness. Treatment with Ech A induced the recovery of epidermis skin lesions as observed histologically. Tewameter[®] and Corneometer[®] measurements indicated that Ech A treatment reduced transepidermal water loss and improved stratum corneum hydration, respectively. Ech A treatment also inhibited inflammatory-response-induced mast cell infiltration in AD-like skin lesions and suppressed the expression of proinflammatory cytokines, such as interferon- γ , interleukin-4, and interleukin-13. Collectively, these results suggest that Ech A may be beneficial for treating AD owing to its anti-inflammatory effects.

K.J. Vanderwolf, C.J. Kyle, P.A. Faure, D.F. McAlpine, C.M. Davy, **Skin pH varies among bat species and seasons and between wild and captive bats**, Conservation Physiology, Volume 9, 2021

Skin is a key aspect of the immune system in the defence against pathogens. Skin pH regulates the activity of enzymes produced both by hosts and by microbes on host skin, thus implicating pH in disease susceptibility. Skin pH varies inter and intra-specifically and is influenced by a variety of intrinsic and extrinsic variables. Increased skin alkalinity is associated with a predisposition to cutaneous infections in humans and dogs, and inter-specific and inter-individual variation in skin pH is implicated in differential susceptibility to some skin diseases. The cutaneous pH of bats has not been characterized but is postulated to play a role in susceptibility to white-nose syndrome (WNS), a fungal infection that has decimated several Nearctic bat species. We used non-invasive probes to measure the pH of bat flight membranes in five species with differing susceptibility to WNS. Skin pH ranged from 4.67 to 8.59 and varied among bat species, geographic locations, body parts, age classes, sexes and seasons. Wild *Eptesicus fuscus* were consistently more acidic than wild *Myotis lucifugus*, *Myotis leibii* and *Perimyotis subflavus*. Juvenile bats had more acidic skin than adults during maternity season but did not differ during swarming. Male *M. lucifugus* were more acidic than females during maternity season, yet this trend reversed during swarming. Bat skin was more acidic in summer compared to winter, a pattern also reported in humans. Skin pH was more acidic in captive than wild *E. fuscus*, suggesting environmental impacts on skin pH. The pH of roosting substrates affects skin pH in captive bats and may partially explain seasonal patterns in wild bats that use different roost types across seasons. Future research on the influence of pH on microbial pathogenic factors and skin barrier function may provide valuable insights on new therapeutic targets for treating bat skin conditions.

A. Cekiera, J. Popiel, M. Siemieniuch, Z. Jaworski, M. Slowikowska, N. Siwinska, A. Zak, A. Niedzwiedz, **The examination of biophysical parameters of the skin in Polish Konik horses**, PLoS ONE 16(6), June 2021

This study aimed to assess the biophysical parameters of the skin in Polish Konik horses (Polish primitive horses). According to the authors, this is the first assessment performed on such a wide scale in this group of animals. The evaluation carried out is innovative both with regards to the breed of the animals and the wide scope of the physicochemical skin assessment. The study group comprised mares, stallions and geldings, and the evaluations concerned transepidermal water loss, corneometry, pH, skin temperature assessment and mexametry. These parameters were assessed in five skin regions: the lips, the right ear, the prosternum, the right side of the neck and the chest. The measurements were taken after spreading the hair apart, with the use of a Multiprobe Adapter System (MPA®) and dedicated probes (Courage + Khazaka electronic GmbH, Cologne, Germany). The measurements revealed statistically significant differences in the values of transepidermal water loss in the lips in mares compared with stallions ($P = 0.023$) and also in stallions compared with geldings ($P = 0.009$). Corneometry showed significantly higher results in the neck region in mares compared with stallions ($P = 0.037$) and the prosternum areas in mares and geldings compared with stallions ($P = 0.037$ and $P = 0.018$). Skin pH measurement on the right side of the neck rendered significantly higher values in stallions than in mares ($P = 0.037$). In geldings, the skin temperature was significantly higher than in stallions ($P = 0.049$). Once the appropriate physicochemical values for specific animal species and breeds are determined, non-invasive methods of skin examination in many diseases and also methods of evaluation of the efficacy and/or adverse effects of applied medications can be established.

W. Rungseevijitprapa, B. Yingngam, C. Chaiyasut, **Improvement of Biophysical Skin Parameters of Topically Applied Fermented Soybean Extract-Loaded Niosomes with No Systemic Toxicity in Ovariectomized Rats**, Pharmaceutics 2021, 13, 1068

Despite the known beneficial impacts of estrogen used as hormone replacement therapy to ameliorate signs of skin aging in postmenopausal women, its compliance rates are low. A significant amount of estrogen may be absorbed into the blood circulation and can lead to systemic actions. Soy isoflavone exhibits biological activities similar to synthetic estrogen because it is a heterocyclic phenolic compound. The disadvantage of most topical ingredients based on isoflavone is that they contain biologically inactive glycoside forms, which must be converted to a readily absorbed aglycone for the topical application. The purposes of this study were to develop niosomes-loaded *Aspergillus oryzae*-fermented soybean extract (FSE) to enhance skin absorption with proven systemic side effect compared to estrogen application. Skin hydration and viscoelasticity of 75 days post-ovariectomized (OVX) Wistar rats following 84-day topical treatment with various tested gel formulations containing fermented soybean extract (FSE) were evaluated. The tested formulations were gel + FSE nanoniosomes, gel + FSE microniosomes, gel + FSE (200 μg FSE/9 cm^2 /rat), gel + blank nanoniosomes (a negative control), and gel + 17 β -estradiol (E2) nanoniosomes (a positive control, 20 μg E2/9 cm^2 /rat). Changes in vaginal cornifications and weights of uteri, livers, and kidneys in the OVX rats and signs of primary skin irritation in the rabbits were evaluated for their toxicities. Results showed that FSE-loaded nanoniosomes improved the skin hydration and viscoelasticity better than gel + FSE microniosomes and gel + FSE, respectively, but lower than those of gel + E2 nanoniosomes ($p < 0.05$). Unlike all gel + E2 nanoniosomes, the FSE formulations showed no changes in vaginal cells and weights of uteri, livers, and kidneys and no signs of skin irritation. In conclusion, The FSE niosomebased gels should be promising candidates for delivering phytoestrogens against signs of skin aging with no systemic toxicities.

H. Heo, J. Madhavan, S. Eun, H. Jung, H. Lee, **Pre-Clinical Evaluation of Proprietary Lutein, Zeaxanthin, and Rosemary Formulation for Its Dermal Protective Activity in Male Swiss Albino Mice**, Prev. Nutr. Food Sci. 2021;26(4): p. 425-433

This study aimed to evaluate the efficacy of the proprietary lutein, zeaxanthin, and rosemary formulation for its dermal protection against ultraviolet (UV) irradiated skin dehydration. A total of 48 male Swiss albino mice of 8~12 weeks of age were divided into eight groups of 6 mice: mice in group 1 (G1) were considered the normal control, without treatment and without skin shaving; mice in G2 had their skins were shaved, but did not receive treatment; mice in G3 were the pathological control; mice in G4 were treated as standard (hyaluronic acid); mice in G5~G8 were treated with low and high doses of 2 different test substances, respectively. Mice were anaesthetized and then depilatory was applied on the dorsal skin area (2 $\text{cm} \times 2 \text{ cm}$) on alternate days, then UV/blue light irradiation was carried out for 15 min for 6 weeks. Collagen type 1 gene expression was determined via densitometric analysis, skin elasticity was assessed, and stratum corneum water contents were measured using a cutometer and corneometer. Skin hydration was assessed through transepidermal water loss, and several serum biochemical parameters (collagenase, hydroxyproline, hyaluronic acid, and ceramide levels) were determined to assess the skin moisturizing activity of the product. Images for assessing photoaging were considered between different groups on day 42. All these subjective parameters reached

statistical significance ($P < 0.05$) in groups treated with the proprietary lutein and rosemary formulation compared with the placebo-treated group. In conclusion, the proprietary lutein, zeaxanthin, and rosemary formulation showed better protection of skin subjected to UV irradiated skin dehydration.

D.J. Son, J.C. Jung, Y.M. Choi, H.Y. Ryu, S. Lee, B.A. Davis, Wheat Extract Oil (WEO) Attenuates UVB-Induced Photoaging via Collagen Synthesis in Human Keratinocytes and Hairless Mice, *Nutrients* 2020, 12, 300

The efficacy of wheat extract oil (WEO), standardized to glucosylceramides, for protecting against ultraviolet B (UVB)-induced damage of skin barrier function was assessed using the SHK-1 hairless mouse model and two human skin cell lines, namely, CCD-986sk and HeCaT. The ability of repeated oral administration of 30, 60, and 120 mg of WEO/kg/day for 12 weeks to prevent skin damage of SKH-1 hairless mice induced by UVB irradiation was evaluated. The results demonstrated that UVB-induced water evaporation (transepidermal water loss, TEWL) was significantly decreased by WEO. Similarly, UVB-induced losses in moisture and skin elasticity were improved by WEO supplementation. WEO attenuated the tissue procollagen type I, hyaluronic acid (HA), and ceramide reductions induced by UVB treatment as well. Collagen concentrations in skin tissue were increased in the WEO-treated mice, while UVB-induced epidermal thickening was reduced. In vitro studies using HeCaT human keratinocytes confirmed increased HA and collagen synthesis in response to WEO treatment. This may occur via WEO suppression of matrix metalloproteinase-1 (MMP-1), since its induction by UVB treatment was diminished in treated CCD-986sk cells. Oral administration of WEO improves skin barrier function in UVB-irradiated mice by attenuating damage typically observed in photoaging. This research further clarifies the clinical benefits previously observed by dietary WEO consumption.

E. Sofrona, L.-A. Tziveleka, M. Harizani, P. Koroli, I. Sfiniadakis, V. Roussis, M. Rallis, E. Ioannou, In Vivo Evaluation of the Wound Healing Activity of Extracts and Bioactive Constituents of the Marine Isopod Ceratothoa oestroides, *Mar. Drugs* 2020, 18, 219

Wound healing is a fundamental response to tissue injury and a number of natural products has been found to accelerate the healing process. Herein, we report the preparation of a series of different polarity (organic and aqueous) extracts of the marine isopod *Ceratothoa oestroides* and the in vivo evaluation of their wound healing activity after topical administration of ointments incorporating the various extracts on wounds inflicted on SKH-hr1 hairless mice. The most active extract was fractionated for enrichment in the bioactive constituents and the fractions were further evaluated for their wound healing activity, while their chemical profiles were analyzed. Wound healing was evaluated by clinical assessment, photo-documentation, histopathological analysis and measurement of biophysical skin parameters, such as transepidermal water loss (TEWL), hydration, elasticity, and skin thickness. The highest levels of activity were exerted by treatment of the wounds with a fraction rich in eicosapentaenoic acid (EPA), as well as myristic and palmitoleic acids. Topical application of the bioactive fraction on the wounds of mice resulted in complete wound closure with a skin of almost normal architecture without any inflammatory elements.

S.P. Saunders, A. Floudas, T Moran, C.M. Byrne, M.D. Rooney, C.M.R. Fahy, J.A. Geoghegan, Y. Iwakura, P.G. Fallon, C. Schwartz, Dysregulated skin barrier function in Tmem79 mutant mice promotes IL-17A-dependent spontaneous skin and lung inflammation, *Allergy*, 2020;75: p. 3216–3227

Background: Atopic dermatitis (AD) is associated with a dysregulation of the skin barrier and may predispose to the development of secondary allergic conditions, such as asthma. *Tmem79^{ma/ma}* mice harbor a mutation in the gene encoding Transmembrane Protein 79 (or Mattrin), which has previously been associated with AD. As a result of the *Tmem79* gene mutation, these mice have a defective skin barrier and develop spontaneous skin inflammation. In this study, *Tmem79^{ma/ma}* mice were assessed for the underlying immunological response in the development of spontaneous skin and lung inflammation. Methods: Development of spontaneous skin and lung inflammation in *Tmem79^{ma/ma}* mice was analyzed. We further investigated susceptibility to cutaneous *Staphylococcus aureus* infection. *Tmem79^{ma/ma}* were crossed to IL-17A-deficient mice to address the contribution of IL-17A to spontaneous skin and lung disease. Results: *Tmem79^{ma/ma}* mice developed IL-17A-dependent spontaneous AD-like inflammation and were refractory to *S aureus* infection. Mutant mice progressed to airway inflammation subsequent to the occurrence of dermatitis. The progression from skin to lung disease is dependent on adaptive immunity and is facilitated by cutaneous expansion of Th17 and TCR $\gamma\delta$ T cells.

S.P. Loureiro Luna, A. Schoen, P. H. Esteves Trindade, P. Barreto da Rocha, Penetration Profiles of a Class IV Therapeutic Laser and a Photobiomodulation Therapy Device in Equine Skin, *J Equine Vet Sci*, Feb 2020

Photobiomodulation therapy (PBMT) effects depend on the energy settings and laser penetration. We investigated the penetration time profiles of two different light therapy devices, at the dark and light skin regions

in horses. Six light skin and six dark skin adult clinically healthy Arab and Quarter horses were used. A cutometer was used to measure the width of the skin fold from both sides of the cervical area, followed by three measurements of the thickness of the same skin fold by transversal and longitudinal ultrasonography (US). The depth of light penetration was compared based on the percentage of penetration versus power, between a portable PBMT device versus a class IV laser device. The laser mean power output was measured with an optical power meter system for 120 seconds after penetrating the skin. Skin width and laser penetration were compared among equipment by paired "t" test. There was no difference in the width of the skin fold between measurements acquired by the cutometer against either longitudinal or transversal US or between the US measurements at cervical versus metacarpus area. Light penetration was greater in both kinds of skins in the PBMT (0.01303 ± 0.00778) versus class IV laser ($0.00122 \pm \text{SD } 0.00070$) ($P < .001$). The PBMT device provided a greater energy penetration than the class IV laser in unclipped light and dark skin, suggesting that the former may produce a better therapeutic effect. The color of the skin changes penetration profiles of PBMT.

M.P. Szczepanik, P.M. Wilkoł ek, Ł.R. Adamek, G. Kalisz, M. Goł yński, W. Sitkowski, I. Taszkun, Transepidermal water loss and skin hydration in healthy cats and cats with non-flea non-food hypersensitivity dermatitis (NFnFHD), Pol J Vet Sci. 2019 Jun; 22(2): p. 237-242

Allergic skin diseases in cats are amongst the most prevalent dermatological conditions in this species. The objectives of this study were to evaluate different types of skin barrier measurements in healthy cats and cats with non-flea non-food hypersensitivity dermatitis (NFnFHD). 24 clinically healthy and 19 NFnFHD cats were included in this clinical trial. In each animal, the transepidermal water loss (TEWL) and skin hydration (SH) were assessed on six clipped body sites by VapoMeter SWL 4605 and Corneometer® CM 825, respectively. Results of TEWL measurement were, significantly higher in one of the six examined body sites, namely on the lumbar area ($p=0.0049$). Furthermore, a statistically significant difference was found between the average TEWL values ($p=0.019$). Statistically notable differences were measured at least in one certain body site for SH: in the groin ($p=0.02$), where the values in the affected cats were lower than in the healthy individuals. These results may suggest that in NFnFHD cats transepidermal water loss is higher than in healthy cats. Skin hydration is, at least, in certain body sites, lower in atopic feline patients than in healthy individuals.

D. Cobiella, L. Archer, M. Bohannon, D. Santoro, Pilot study using five methods to evaluate skin barrier function in healthy dogs and in dogs with atopic dermatitis, Vet. Dermatology, January 2019

Background: Atopic dermatitis is associated with skin barrier defects. In people, noninvasive techniques are used to quantify the skin barrier functionality. In dogs, transepidermal water loss (TEWL), stratum corneum hydration and pH have been used to assess skin barrier function. However, few studies have determined their repeatability. Objective: To assess the repeatability of measurements of skin hydration, TEWL, pH, skin absorbance and erythema in healthy and atopic dogs. Animals: Fifteen healthy and 15 atopic privately owned dogs. Methods and materials: Three repeated measurements using Corneometer®, Skin-pH-Meter®, Colorimeter® and VapoMeter® were obtained from inguinal, axilla, pinna and interdigital space by three investigators. Intra- and interobserver variability (coefficient of variation, correlation coefficients and intraclass correlation coefficients) and difference between the two groups (*t*-test or Mann–Whitney U-test) were determined. Results: High repeatability and low variation were observed both intra- and interobservers for all devices except the VapoMeter®. The most repeatable device was the Skin-pH-Meter®, whereas the VapoMeter® was the device with the highest intra- and interobserver variability. Atopic dogs had a significantly increased pH (inguinal $P = 0.03$; axilla $P = 0.02$) and erythema (inguinal $P = 0.01$; axilla $P = 0.02$) compared to healthy dogs. No differences between the two groups were detected using the Corneometer®, VapoMeter® or Colorimeter® (tartrazine absorption). Conclusion and clinical significance: The results of this pilot study support the use of Corneometer®, Skin-pH-Meter® and Colorimeter® in the assessment of skin barrier function in dogs; further investigations to optimize measurements and confirm these results are needed.

I. Popa, A.L. Watson, A. Solgadi, C. Butowski, D. Allaway, J. Portoukalian, Linoleate-enriched diet increases both linoleic acid esterified to omega hydroxy very long chain fatty acids and free ceramides of canine stratum corneum without effect on protein-bound ceramides and skin barrier function, Archives of Dermatological Research (2018) 310: p. 579–589

Few studies have investigated the influence of increased amounts of dietary linoleic acid on the epidermal lipid biochemistry and TEWL in healthy subject. The influence of dietary linoleic acid on canine stratum corneum (SC) lipids was studied by feeding two groups of five dogs differential amounts of linoleic acid (LA) for three months. SC was harvested by tape stripping and lipids were analyzed by thin-layer chromatography and mass spectrometry. The dogs that were fed the higher concentration of LA showed high increases in the contents of both linoleic acid and free ceramides in the SC, whereas the protein-bound ceramide content was unchanged. Acylacids that represent the esterified form of linoleic acid in omega hydroxyl very long chain fatty acids (ω -OH VLCFA) accounted for most of the elevation of LA, whereas the concentration of the free form

was not significantly changed. Corroborating the absence of change in the protein-bound ceramides content of healthy dogs SC, TEWL was nearly unaffected by the linoleic acid-enriched diet.

*K. Nomoto, Y. Itaya, K. Watanabe, T. Yamashita, T. Okazaki, Y. Tokudome, **Epidermal permeability barrier function and sphingolipid content in the skin of sphingomyelin synthase 2 deficient mice**, Exp Dermatol, 2018 Jan*

Sphingomyelin synthase (SMS) is an enzyme that generates sphingomyelin (SM) from ceramide (CER) and phosphatidylcholine. SM in the epidermis is a precursor of CER, an important lipid for epidermal permeability barrier function. However, the physiological role of SMS in skin is unclear. To uncover the function of SMS in skin, we investigated sphingolipid metabolism enzyme activity in skin, SM content in the epidermis, CER content in the stratum corneum (SC) and transepidermal water loss (TEWL) as an indicator of barrier function in SMS2-knockout (KO) mice. The activities of sphingolipid metabolism enzymes in skin homogenates were measured using a fluorescently labelled substrate. Enzymatic reaction products were detected by high-performance liquid chromatography (HPLC). Lipids in the epidermis or SC were extracted and quantified by high-performance thin layer chromatography (HPTLC). TEWL was measured using a Tewameter TM300. In SMS2-KO mice, SMS activity in skin homogenates, epidermal SM content and SC CER content were significantly decreased relative to wild-type (WT) mice. The TEWL of SMS2-KO mice was significantly increased compared to WT mice. Our data indicate that SMS2 generates SM in the epidermis and contributes to epidermal permeability barrier function and will support understanding of SM-related metabolic disorders.

*M. Held, J.R. Rothenberger, J. Schiefer, W.P. Petersen, A.R.S. Rahmanian-Schwarz, H.E. Schaller, A. Daigeler, **Alteration of biomechanical properties of burned skin**, Poster Presentation, 17th European Burn Association Congress EBA, Barcelona, September 2017*

Background: The prevalence of burns in the general population is high. Despite new research findings, skin burns and its resulting tissue damage are still not entirely understood. In particular, little is known about the depth-dependent alteration of skin biomechanical properties of these wounds.

Methods: Thirty-six burn wounds with six different depths were generated on the abdomen of six Göttingen minipigs. The alteration of skin biomechanical properties was evaluated objectively after 15 and 360 min using a Cutometer device. Biopsies for histological evaluation were taken and the depth of burn was correlated with biomechanical properties.

Results: Firmness of skin (R0), overall elasticity (R8) and calculated elasticity (Ue) demonstrated a continuous decrease with an increasing depth of burn 15 min after wound generation. Gross elasticity (R2), net elasticity (R5) and amount of elasticity of the whole curve (R7), however, showed an increase of values with increasing depth of injury. A further decrease of elasticity was demonstrated 360 min after wound generation. Conclusion: The alteration of skin biomechanical properties is a function of damaged tissue structures. The presented results demonstrate a depth-dependent decrease of principal elastic parameters with an increasing depth of burn and the results indicate progressive tissue damage over the time.

M.P. Szczepanik, P.M. Wilkołak, Ł.R. Adamek, M. Zajaczk, M. Gołynski, W. Sitkowski, I. Taszkun, **Evaluation of the correlation between Scoring Feline Allergic Dermatitis and Feline Extent and Severity Index and skin hydration in atopic cats**, Veterinary Dermatology September 2017*

Background: Evaluation of the severity of clinical signs of cats with allergic skin diseases has used two scoring systems: Scoring Feline Allergic Dermatitis (SCORFAD) and the Feline Extent and Severity Index (FeDESI). The integrity of the cutaneous barrier can also be evaluated by measuring skin hydration. A correlation between the clinical score and skin hydration has been observed in humans and dogs with atopic dermatitis (AD). Hypothesis: To demonstrate a correlation between the clinical score and skin hydration of cats affected with presumed AD. Animals: European short hair cats (n = 18): 11 females and seven males with a confirmed diagnosis of AD. Methods: SCORFAD and FeDESI scores were calculated and the measurements of skin hydration were assessed from seven body sites using corneometry. The correlation between the SCORFAD and FeDESI systems and skin hydration of each site, and the average skin hydration was calculated. Results: There was a positive correlation between the SCORFAD score and skin hydration for the axilla, thorax and forelimb; for FeDESI and axilla and lumbar sites. There was a negative correlation between the FeDESI and skin hydration for the pinna (r = 0.47). Conclusions and clinical importance: Measurements of skin hydration could be a useful tool for the evaluation of allergic cats. There is limited evidence of any useful correlation between clinical scoring systems and measurements of hydration. The pinna may be a suitable region for the assessment of skin barrier function in normal and allergic cats.

*M. Held, A.S. Enaelke, P.S. Tolzmann, A. Rahmanian-Schwarz, H.E. Schaller, J. Rothenberaer, **Biomechanical Skin Property Evaluation for Wounds Treated With Synthetic and Biosynthetic Wound Dressings and a Newly Developed Collagen Matrix During Healing of Superficial Skin Defects in a Rat Models**, Wounds, 2016 Sep;28(9): p. 334-340*

Introduction: There is a high prevalence of superficial wounds such as partial-thickness burns. Treatment of these wounds frequently includes temporary application of wound dressings. The aim of this study was to compare a newly developed collagen matrix with commonly used temporary skin dressings for treatment of partial-thickness skin defects. Materials and Methods: Through a skin dermatome, 42 standardized superficial skin defects were generated on the back of 28 adult male Lewis rats. The wounds were treated with a synthetic wound dressing (Suprathel, Polymedics Innovations Inc, Woodstock, GA) (n = 14), a biosynthetic skin dressing (Biobrane, Smith & Nephew, Hull, UK) (n = 14), or a newly developed bovine collagen matrix, Collagen Cell Carrier (Viscofan BioEngineering, Weinheim, Germany) (n = 14). Biomechanical properties of the skin were determined and compared every 10 days over a 3-month period of using the Cutometer MPA 580 (Courage + Khazaka Electronic GmbH, Cologne, Germany). Results: As opposed to healthy skin, statistically significant differences were detected between days 10 and 30, and between days 60 and 80, for calculated elasticity (Ue), firmness of skin (R0), and overall elasticity (R8). After 3 months, no statistically significant differences in skin elasticity were detected between the different wound dressings. Conclusions: The presented results give an opportunity to compare the wound dressings used for treatment with respect to skin elasticity and reveal the potential of the bovine collagen matrix in the treatment of superficial skin defects; therefore the results facilitate further evaluation of collagen matrix in surgical applications and regenerative medicine.

C.W. Bradley, D.O. Morris, S.C. Rankin, C.L. Cain, A.M. Misic, T. Houser, E.A. Mauldin, E.A. Grice, Longitudinal evaluation of the skin microbiome and association with microenvironment and treatment in canine atopic dermatitis, J Invest Dermatol, 2016 June; 136(6): p. 1182–1190

Host-microbe interactions may play a fundamental role in the pathogenesis of atopic dermatitis (AD), a chronic relapsing inflammatory skin disorder characterized by universal colonization with *Staphylococcus*. To examine the relationship between epidermal barrier function and the cutaneous microbiota in AD, this study employed a spontaneous model of canine AD (cAD). In a cohort of 14 dogs with cAD, the skin microbiota was longitudinally evaluated with parallel assessment of skin barrier function at disease flare, during antimicrobial therapy and posttherapy. Sequencing of the bacterial 16S ribosomal RNA gene revealed decreased bacterial diversity and increased proportions of *Staphylococcus* (*S. pseudintermedius* in particular) and *Corynebacterium* in comparison to a cohort of healthy control dogs (n=16). Treatment restored bacterial diversity with decreased *Staphylococcus* proportions, concurrent with decreased cAD severity. Skin barrier function, as measured by corneometry, pH, and transepidermal water loss (TEWL) also normalized with treatment. Bacterial diversity correlated with TEWL and pH, but not corneometry. These findings provide insights into the relationship between the cutaneous microbiome and skin barrier function in AD, the impact of antimicrobial therapy on the skin microbiome, and highlight the utility of cAD as a spontaneous non-rodent model of AD.

M. Held, J. Rothenberger, D. Tolzmann, W. Petersen, H.-E. Schaller, A. Rahmanian-Schwarz, Alteration of Biomechanical Properties of Skin During the Course of Healing of Partial-thickness Wounds, Wounds 2015; 27(5): p. 123-128

The incidence of partial-thickness wounds is high and, until recently, little was known about the alteration of the biomechanical properties of the skin in these wounds during the course of healing. The aim of this study was to demonstrate the biomechanical changes in skin elasticity. Materials and Methods: Fourteen standardized skin defects were created on the back of fourteen adult male Lewis rats (Charles River Laboratories International, Inc, Wilmington, MA) using a skin dermatome. Biomechanical properties of the skin were determined every 10 days over a period of 3 months using a skin elasticity measurement device (Cutometer MPA 580, Courage and Khazaka, Cologne, Germany). Calculated elasticity (UE), firmness of skin (R0), and overall elasticity (R8) were assessed. In addition, histological evaluation was performed in regard to quality of skin. Results: After an initial decrease of UE, R0, and R8 until 30 days after surgery, the values of R0 and R8 increased between day 50 and day 60. Starting on day 60, a further decrease of values was indicated. Conclusion: The alteration of biomechanical properties of skin is a function of tissue structure. The presented results demonstrate the complex changes of skin biomechanical properties in the course of healing of partial-thickness wounds. This study could serve as a model to compare the effectiveness of different wound dressings in regard to skin elasticity. Acute trauma, burn injuries, and chronic diseases often lead to skin defects. Partial-thickness skin defects play an important role in wound management because of their high incidence. These wounds are commonly treated with a broad range of wound dressings¹⁻⁶ that protect the wound from further damage, promote healing, improve functional and aesthetic outcomes, and reduce hospitalization time and medical costs.⁷ Wound dressings imitate important features of natural skin, such as the releasing of water vapor, acting as a microbial barrier, and providing elasticity⁸ to accelerate epithelialization and wound healing while avoiding dehydration of the wounds. Every type of wound, whether acute, chronic, dry, or moist, requires a specific kind of dressing.⁹ Synthetic as well as biological substances, such as collagen, are used for wound coverage.¹⁰ The choice of the best wound dressing is still challenging and an objective determination of the outcomes is difficult. Skin elasticity and skin plasticity are indicators for biological age of skin. Changes in

biomechanical properties of skin may be due to trauma, ultraviolet light, mechanical and chemical strain, nicotine, alcohol, genetic predispositions, diseases, and others. Stiff and clustered networks of collagen and elastic fibers may influence skin quality.¹¹ Many factors may influence wound healing, and thus also influence the quality of newly formed skin. The authors think choice of wound dressing is a major factor that influences skin quality. In this context, the aim of the present study was to demonstrate the process of changes in biomechanical properties of skin during the course of healing of partial-thickness wounds.

*J.Y. Kim, O.S. Lee, S. Ha, J.H. Kim, G. Park, J.K. Kim, C.H. Oh, **In vivo assessment of the effect of taxifolin glycoside on atopic dermatitis-like skin lesions using biomedical tools in NC/Nga mice**, Clin Exp Dermatol, 2015 Jul;40(5): p. 547-555*

Background: Noninvasive methods of assessment are widely used in clinical trials. However, such methods have not been established in atopic dermatitis (AD), which is a chronic inflammatory skin disease. Aim: To demonstrate, using biomedical tools, the benefits of a new substance, taxifolin glycoside (TAX), in an AD model, the NC/Nga mouse. Methods: We evaluated the efficacy of topical TAX for AD by measuring clinical skin severity score, cytokine expression and serum IgE level, and by using biomedical measures (vapometry and corneometry). Topical TAX was applied to AD-induced NC/Nga mice for 3 weeks. The anti-inflammatory effects of this compound were demonstrated noninvasively using biomedical tools and immunological assays. Results: Our method of AD assessment using biomedical tools is more objective and accurate than visual inspection. The results obtained using the biomedical tools were identical to those obtained using immunological assays. Conclusions: In vivo biomedical tools are useful for diagnosing and monitoring treatment effects in AD.

*M. Zajęc, M. Szczepanik, P. Wilkótek, Ł. Adamek, Z. Pomorski, **The influence of non-specific anti-pruritus treatment with cyclosporine A on transepidermal water loss (TEWL) in natural atopic dermatitis in dogs**, Polish Journal of Veterinary Sciences Vol. 18, No. 2 (2015), p. 415–424*

Atopic dermatitis is a common allergic skin disease in dogs. Monitoring the progress of treatment and the assessment of the severity of disease symptoms are crucial elements of the treatment procedure. One of the common means of assessing the severity of the clinical signs of the disease is the CADESI 03. Research studies have pointed to a possibility of assessing the severity of skin lesions by means of measuring biophysical skin parameters such as TEWL, skin hydration and erythema intensity. The aim of the study was the assessment of changes in TEWL and CADESI values measured in ten different body regions during non-specific anti-pruritus treatment. The examination was performed on ten dogs with atopic dermatitis (age from 2.5 years to 7 years, mean age 3.8 years). The measurements were performed in the following body regions: the lumbar region, the right axillary fossa, the right inguinal region, the ventral abdominal region, the right lateral thorax region, the internal surface of the auricle, interdigital region of the right forelimb, cheek, bridge of nose and the lateral site of antebrachium. A statistically significant decrease in CADESI values was reported starting from the second week of treatment. In the case of the mean TEWL values, a fall was observed after one week of treatment in the ventral abdominal region and the interdigital region, after two weeks of treatment in the axillary fossa and the inguinal region, and after three weeks in the cheek and the lateral thorax region. There was no statistically significant decrease in TEWL values in the course of treatment in four other regions.

*M. Zajęc, M.P. Szczepanik, P.M. Wilkótek, Ł.R. Adamek, Z.J.H. Pomorski, W. Sitkowski, M. Gołyński, **Assessment of a correlation between Canine Atopic Dermatitis Extent and Severity Index (CADESI-03) and selected biophysical skin measures (skin hydration, pH, and erythema intensity) in dogs with naturally occurring atopic dermatitis**, The Canadian Journal of Veterinary Research, 2015*

Atopic dermatitis is a common allergic skin disease in dogs. The aim of this study was to examine the possibility of a correlation between biophysical skin variables: skin hydration (SH), skin pH, and erythema intensity measured in 10 different body regions and both total Canine Atopic Dermatitis Extent and Severity Index (CADESI-03) and CADESI measured in a given region (CADESI L). The study was conducted using 33 dogs with atopic dermatitis. The assessment of the biophysical variables was done in 10 body regions: the lumbar region, right axillary fossa, right inguinal region, ventral abdominal region, right lateral thorax region, internal surface of the auricle, interdigital region of right forelimb, cheek, bridge of nose, and lateral site of antebrachium. Positive correlations were found between SH and CADESI L for the following regions: the inguinal region ($r = 0.73$) and the interdigital region ($r = 0.82$), as well as between total CADESI and SH on digital region ($r = 0.52$). Also, positive correlations were reported for skin pH and CADESI L in the lumbar region ($r = 0.57$), the right lateral thorax region ($r = 0.40$), and the lateral antebrachium ($r = 0.35$). Positive correlations were found in the interdigital region between erythema intensity and the total CADESI-03 ($r = 0.60$) as well as the CADESI L ($r = 0.7$). The results obtained suggest that it may be possible to use skin hydration, pH, and erythema intensity to assess the severity of skin lesion but positive correlation was only found in < 13.3% of possible correlations and usage of these measures in dogs is limited.

G. Imokawa, K. Ishida, **Biological Mechanisms Underlying the Ultraviolet Radiation-Induced Formation of Skin Wrinkling and Sagging I: Reduced Skin Elasticity, Highly Associated with Enhanced Dermal Elastase Activity, Triggers Wrinkling and Sagging**, *Int. J. Mol. Sci.* 2015, 16, p. 7753-7775

The repetitive exposure of skin to ultraviolet B (UVB) preferentially elicits wrinkling while ultraviolet A (UVA) predominantly elicits sagging. In chronically UVB or UVA-exposed rat skin there is a similar tortuous deformation of elastic fibers together with decreased skin elasticity, whose magnitudes are greater in UVB-exposed skin than in UVA-exposed skin. Comparison of skin elasticity with the activity of matrix metalloproteinases (MMPs) in the dermis of ovariectomized rats after UVB or UVA irradiation demonstrates that skin elasticity is more significantly decreased in ovariectomized rats than in sham-operated rats, which is accompanied by a reciprocal increase in elastase activity but not in the activities of collagenases I or IV. Clinical studies using animal skin and human facial skin demonstrated that topical treatment with a specific inhibitor or an inhibitory extract of skin fibroblast-derived elastase distinctly attenuates UVB and sunlight-induced formation of wrinkling. Our results strongly indicated that the upregulated activity of skin fibroblast-derived elastase plays a pivotal role in wrinkling and/or sagging of the skin via the impairment of elastic fiber configuration and the subsequent loss of skin elasticity.

A. Tuzuner, S. Akdagli, T. Sen, et al., **An objective analysis of sebum, pH and moisture levels of the external ear canal skin**, *American Journal of Otolaryngology* (2015) 424-428

Objective: To determine sebum, pH and moisture levels of external ear canal skin, and compare the patients who complain of ear itching and the normal population for these parameters. And evaluate the improvement subjectively in the ones given dexamethasone sodium phosphate (DSP) cream or placebo-water in oil emulsion type cream, and to determine the changes in sebum, pH and moisture levels after the treatment. Methods: 32 females with the complaint of isolated external ear canal itching and 42 healthy women were included in this randomized prospective controlled study. The sebum, pH and moisture levels of ear skin of the patients and the controls were determined from baseline and following treatment. Patients used DSP in their right and the placebo in their left ears for 15 days. Subjective analysis of itching level was measured at baseline, and on 15th and 30th days using visual analog scale (VAS).

M. Gołyński, M. Szczepanik, K. Lutnicki, Ł. Adamek, M. Gołyńska, P. Wilkołek, W. Sitkowski, Ł. Kurek, P. Dębiak, **Biophysical parameters of rats' skin after the administration of methimazole**, *Bull Vet Inst Pulawy* 58, p. 315-319, 2014

The paper describes the influence of oral administration of methimazole on biophysical skin parameters. Wistar rats of different sex (220–260 g) were used in the experiment. Biophysical skin parameters, such as transepidermal water loss (TEWL), corneometry, and pH were examined at seven-day intervals. Significant changes in the parameters were observed on the 7th d of methimazole administration. The changes were observed in both sex but males appeared to be less sensitive in that respect. Changes in the parameters in the females showed rapid mechanisms, which normalised transepidermal water loss and skin hydration, as well as restored skin barrier functions. TEWL, skin hydration, and skin pH measurements allow an early assessment of skin barrier dysfunction after administration of this drug.

M. Zajęc, M.P. Szczepanik, P.M. Wilkołek, Ł.R. Adamek, Z.J.H. Pomorski, W. Sitkowski, M. Gołyński, **Assessment of the relationship between transepidermal water loss (TEWL) and severity of clinical signs (CADESI-03) in atopic dogs**, *Vet Dermatol* 2014; 25: p. 503–583

Background: Atopic dermatitis (AD) is a common allergic skin disease of dogs. Objective documentation of disease severity is important for the assessment of responses to therapeutic interventions. One common means of assessing the severity of clinical signs is the Canine Atopic Dermatitis Extent and Severity Index (CADESI)-03. In addition, studies of the biophysical parameters of the skin suggest that assessment of transepidermal water loss (TEWL) may also have value for estimation of disease severity. Hypothesis/Objectives: The aim of the present study was to verify the correlation between TEWL and CADESI-03 measured at 10 different body sites. Animals: Twenty-six dogs with AD (age range 1–7 years, median age 3 years). Methods – The assessment was performed at the following 10 body sites: the lumbar, inguinal, ventral abdominal, interdigital regions, axillary fossa, lateral thorax, lateral aspect of the antebrachium, concave surface of the auricle, cheek and bridge of the nose. Results: Positive correlations were found between TEWL and the total CADESI-03 for the auricle ($r = 0.59$), bridge of nose ($r = 0.62$) and interdigital skin ($r = 0.47$). Positive correlations were also observed between TEWL and local CADESI-03 scores for the axillary fossa ($r = 0.73$), inguinal region ($r = 0.55$) and interdigital skin ($r = 0.77$). Conclusions and clinical importance: The results indicate that it may be possible to use measurement of TEWL to assess the severity of skin lesions, but a positive correlation was found in only five of 10 body regions examined.

M. Gołyński, M. Szczepanik, K. Lutnicki, Ł. Adamek, M. Gołyńska, P. Wilkołek, W. Sitkowski, Ł. Kurek, P. Dębiak, **Biophysical parameters of rats' skin after the administration of methimazole**, Bull Vet Inst Pulawy 58, p. 315-319, 2014

The paper describes the influence of oral administration of methimazole on biophysical skin parameters. Wistar rats of different sex (220–260 g) were used in the experiment. Biophysical skin parameters, such as transepidermal water loss (TEWL), corneometry, and pH were examined at seven-day intervals. Significant changes in the parameters were observed on the 7th d of methimazole administration. The changes were observed in both sex but males appeared to be less sensitive in that respect. Changes in the parameters in the females showed rapid mechanisms, which normalised transepidermal water loss and skin hydration, as well as restored skin barrier functions. TEWL, skin hydration, and skin pH measurements allow an early assessment of skin barrier dysfunction after administration of this drug.

M. Wagh, **Skin Deep: Exploring the Hidden World of Dogs (and Humans)**, Bellwether Magazine, Volume 1, Number 80, Fall 2013

By current estimates, the human body contains 10 times more microbial cells than human cells. Acting in ways both beneficial and harmful, the microorganisms living on the surface of the skin, as well as in the gut and other organs, constitute a complex ecosystem known to influence digestion, allergies, and a variety of diseases.

M.P. Szczepanik, P.M. Wilkołek, M. Pluta, Ł.R. Adamek, M. Gołyński, Z.J.H. Pomorski, W. Sitkowski, **The examination of biophysical skin parameters (transepidermal water loss, skin hydration and pH value) in different body regions in Polish ponies**, Polish Journal of Veterinary Sciences Vol. 16, No. 4 (2013), p. 741–747

The purpose of this study was to evaluate transepidermal water loss, skin hydration and skin pH in normal Polish ponies. Twelve ponies of both sexes were examined in the study. Measurements were taken from seven different sites: the neck region, the shoulder, thorax, lumbar, inguinal, lip region and the pinna. In each of the regions transepidermal water loss (TEWL), skin hydration and skin pH were measured. For transepidermal water loss, the lowest values were observed in the pinna (10.54 g/hm²), while the highest values were observed in the lip region (30.98 g/hm²). In the case of skin hydration the lowest values were observed for the thorax region (1.96 CU), and the highest for the lip region (48.28 CU). For skin pH, the lowest results were obtained in the pinna (7.03), and the highest in the lumbar region (8.05).

M. Tarutani, K. Nakajima, Y. Uchida, M. Takaishi, N. Goto-Inoue, M. Ikawa, M. Setou, T. Kinoshita, P.M. Elias, S. Sano, Y. Maeda, **GPHR-Dependent Functions of the Golgi Apparatus Are Essential for the Formation of Lamellar Granules and the Skin Barrier**, Journal of Investigative Dermatology (2012) 132, p. 2019–2025

Organelles located in secretory and endocytotic pathways are known to acidify their lumens, and therefore they are called acidic organelles. Compromising the acidic environments of those organelles using compounds such as monensin, bafilomycin, and ammonium chloride, which do not specifically affect the Golgi apparatus, causes marked effects on trafficking, processing, and glycosylation of proteins and lipids (Weisz, 2003), although the mechanisms by which those processes are regulated by the acidic pH are largely unknown. Recently, we identified a new anion channel named Golgi pH regulator (GPHR) (Maeda et al., 2008). GPHR functions as a counterion channel and is critical for Golgi acidification. The loss of GPHR function results in increased luminal pH, which in turn causes impaired transport, disrupted glycosylation, and abnormal Golgi morphology; thus, GPHR is indispensable for normal Golgi functions (Maeda et al., 2008). As GPHR is localized in the Golgi, increased pH and impaired functions are observed in the Golgi selectively among acidic organelles (Maeda et al., 2008). Lamellar granules include lipids, proteases, protease inhibitors, and proteins (Elias et al., 1998; Madison, 2003; Ishida-Yamamoto et al., 2004; Elias and Choi, 2005) that are needed to generate the skin barrier (Odland and Holbrook, 1981), and functional defects in these factors lead to impaired barrier formation. The origin of lamellar granules has been thought to be the trans-Golgi network (TGN; Elias et al., 1998), but direct evidence for that has not been reported. If the origin of lamellar granules is the Golgi apparatus, impairing Golgi functions should result in the degeneration of lamellar granules. Here we show that skin-specific knockout of GPHR function markedly impairs the formation of lamellar granules, supporting the fact that they originate from the Golgi apparatus. The results further show that GPHR has a critical role in the skin barrier function, as well as in the development of other tissues.

M.P. Szczepanik, P.M. Wilkołek, Ł.R. Adamek, Z.J.H. Pomorski, **The examination of biophysical parameters of skin (transepidermal water loss, skin hydration and pH value) in different body regions of normal cats of both sexes**, Journal of Feline Medicine and Surgery (2011) 13, p. 224-230

The purpose of this study was to evaluate transepidermal water loss (TEWL), skin hydration and skin pH in normal cats. Twenty shorthaired European cats of both sexes were examined in the study. Measurements were taken from five different sites: the lumbar region, the axillary fossa, the inguinal region, the ventral

abdominal region and the left thoracic region. In each of the regions, TEWL, skin hydration and skin pH were measured. The highest TEWL value was observed in the axillary fossa (18.22 g/h/m²) and the lowest in the lumbar region (10.53 g/h/m²). The highest skin hydration was found in the inguinal region (18.29 CU) and the lowest in the lumbar region (4.62 CU). The highest skin pH was observed in the inguinal region (6.64) and the lowest in the lumbar region (6.39). Statistically significant differences in TEWL were observed between the lumbar region and the left side of the thorax region (P $\frac{1}{4}$ 0.016), the axillary fossa (P $\frac{1}{4}$ 0.0004), the ventral region (P $\frac{1}{4}$ 0.005), and the inguinal region (P $\frac{1}{4}$ 0.009). There were significant differences in skin hydration between the lumbar region and the left thorax (P $\frac{1}{4}$ 0.000003), the axillary fossa (P $\frac{1}{4}$ 0.002), the ventral abdomen (P $\frac{1}{4}$ 0.03), and the inguinal region (P $\frac{1}{4}$ 0.0003) as well as between the thorax and the ventral abdomen (P $\frac{1}{4}$ 0.005). TEWL was higher in females (15 g/h/m²) than in males (4.57 g/h/m²). Skin hydration was higher in females (13.89 CU) than in males (12.28 CU). Significant differences were not found between males and females for TEWL and skin hydration. Skin pH was higher in males (6.94) than in females (6.54), which was significant (P $\frac{1}{4}$ 0.004).

A.M. Ewert, Interferometrie, Meibometrie und biochemische Analyse der Lipidschicht des Tränenfilms beim Hund, Dissertation an der Klinik und Poliklinik für kleine Haustiere des Fachbereichs Veterinärmedizin der Freien Universität Berlin, 2011

Ein gesunder und stabiler Tränenfilm (TF) stellt einen entscheidenden Faktor für die Aufrechterhaltung der Augengesundheit dar. Er ernährt die avaskuläre Hornhaut, schützt sie mechanisch und immunologisch vor diversen Umwelteinflüssen und optimiert die Lichtbrechung an der Augenoberfläche [1]. In der Humanmedizin ist schon lange bekannt, dass ein Defizit der wässrigen Anteile des dreischichtigen präkornealen TF nicht ausschließlich für eine unzureichende Befeuchtung des Auges und das daraus resultierende Krankheitsbild des „trockenen Auges“ verantwortlich gemacht werden kann. Unumstritten ist in diesem Zusammenhang die Relevanz einer intakten Lipidschicht (LS) für den funktionsfähigen TF und somit für die Augengesundheit. Ein „trockenes Auge“, welches trotz ausreichender Produktion der wässrigen Phase auftritt, wird als evaporatives „trockenes Auge“ bezeichnet (syn. Evaporative dry eye; EDE). Das EDE ist durch eine erhöhte Verdunstung und Instabilität des TF u.a. aufgrund einer mangelnden bzw. unzureichenden LS charakterisiert und kann sich klinisch ähnlich einer Keratokonjunktivitis sicca (KCS) präsentieren. Von den Meibom Drüsen (MD) am Lidrand gebildet und sezerniert (hier Meibom Sekret, MS), gewährleistet eine physiologische LS die Stabilität des gesamten TF und somit eine ausreichende Befeuchtung der Augenoberfläche. Die LS ist nur wenige Mikrometer dünn und eine komplexe Komposition verschiedener polarer und nicht polarer Fette. Die logische Schlussfolgerung ist, dass kleinste Veränderungen in der Zusammensetzung oder ein quantitatives Defizit der LS großen Einfluss auf die Funktionalität des TF haben können.

G. Fahrgruber, Biophysical Characterization of Lesions of Acute and Subchronic Allergic Contact Dermatitis in Domestic Pigs, Dissertation at the University of Veterinary Medicine of Vienna, Austria, May, 2010

Allergic contact dermatitis (ACD) or contact hypersensitivity is a common eczematous skin reaction in sensitized individuals (WEEDON and STRUTTON, 2002; BAKER(a),2006; NOSBAUM et al., 2009). Very familiar are contact allergic reactions to nickel sulfate containing jewelry or occupational diseases of hair dressers, health care persons or construction workers who experience cutaneous hypersensitivity reactions after repeated contact with particular ingredients of hair dyes or chemicals in latex gloves or in building materials (MOWARD and MARKS, 2003; GERAUT et al., 2009). Urushiol is a very potent allergen in leaves of genus Toxicodendron, a plant native in North America. Farmers, workers in forestry or hikers suffer from ACD after incidental repeated contacts with these plants (GLADMAN, 2006). They are, therefore, named poison ivy, poison oak or poison sumac.

J. K. Kim, J. H. Cho, Change of external auditory canal pH in acute otitis externa, Annals of Otolaryngology & Laryngology 118 (11); 769-772, 2009

Abstract: Objectives: We investigated (1) the correlation between the degree of acute otitis externa (AOE) and a change of pH and (2) the recovery of pH after acidification compared to an antibiotic otic solution in AOE. A change of pH in the external auditory canal (EAC) is very important for the pathogenesis of otitis externa. Therefore, not only an antibiotic otic solution, but also acidification, is known to be a good treatment for AOE. However, pH has only been investigated in chronic otitis externa, and not in AOE. Methods: This was a prospective randomized control study. Forty adult patients (56 ears) with AOE and 40 normal control subjects (80 ears) participated in this study. The severity of disease was graded as mild, moderate, or severe. The pH of each EAC was then measured. The patients were randomly assigned into 2 groups: one for vinegar irrigation and the other for topical antibiotics. The pH of the diseased ears was measured at 1 and 2 weeks after the treatment.

P. Benz, A. Tichy, B. Nell, Review of the measuring precision of the new Meibometer MB 550 through repeated measurements in dogs, Vet Ophthalmol. 2008 Nov-Dec;11(6): p. 368-74

A meibometer is a device to measure the delivery rate of lipids on the eyelid margin. The aim of this study is to determine the measuring precision of the new Meibometer MB550 (Courage-Khazaka electronic GmbH, 50829, Cologne, Germany), linked to a computer, by means of repeated measurements in dogs by different examiners. **PROCEDURE:** Two investigators measured the lipid rate on the eyelid margin in 10 healthy dogs for 10 days. One examiner measured the right eye (OD) and the other measured the left eye (OS) for 5 days. After 5 days, the eyes to be measured were switched between the examiners. The new device was able to record all measurement values as charts and curves in comparison to the previous Meibometer, which displayed only one value.

*J.W. Fluhr, K.R. Feingold, P.M. Elias, **Transepidermal water loss reflects permeability barrier status: validation in human and rodent in vivo and ex vivo models***, *Experimental Dermatology* 2006, p 483 – 492

Permeability barrier function is measured with instruments that assess transepidermal water loss (TEWL), either with closed- or open-loop-systems. Yet, the validity of TEWL as a measure of barrier status has been questioned recently.

*R. Ofri, K. Orgad, P.H. Kass, S. Dikstein, **Canine meibometry: Establishing baseline values for meibomian gland secretions in dogs***, *The Veterinary Journal* (2006)

Meibomian lipid secretions are essential in preventing tear evaporation. Disorders of the meibomian glands may therefore play an important role in the pathogenesis of some forms of keratoconjunctivitis sicca (KCS). Until now, meibomian lipid secretions have never been quantitatively evaluated in dogs.

und soll in dieser Studie mit dem NLS-Test weiter untersucht werden.

*M. Schunck, C. Neumann, E. Proksch, **Artificial Barrier Repair in Wounds by Semi-Occlusive Foils Reduced Wound Contraction and Enhanced Cell Migration and Reepithelization in Mouse Skin***, *J Invest Dermatol* 125: p. 1063 –1071, 2005

The repair of the permeability barrier to prevent the entry of harmful substances into the body is a goal in wound healing. Semi-occlusive foils, which provide an artificial barrier, are commonly used for the treatment of wounds. We examined the effects of foils on wound contraction, cell migration, and reepithelization. Full-thickness skin wounds in mice were covered with occlusive latex foils or semi-occlusive water vapor-permeable hydrocolloid foils for either the entire, the first half, or the second half of the wound-healing period. We found that application of foils for the entire healing period initially reduced wound healing during the first week of treatment, whereas healing was enhanced during the second week. Foils were found to reduce wound contraction, but enhanced reepithelization during the second week of wound healing because of increased proliferation and migration of keratinocytes. These effects were also noted when the hydrocolloid foils were applied for the second part of the healing period, only. The fully occlusive latex foil led to irritation of the skin, whereas less irritation occurred under semi-occlusive conditions. In summary, we found that artificial barrier repair with semi-occlusive foils in wounds reduced wound contraction and enhanced cell migration and reepithelization without irritation.

*U. Kappes, S. Schliemann-Willers, L. Bankova, C. Heinemann, T.W. Fischer, M. Ziemer, H. Schubert, J. Norgauer, J.W. Fluhr, P. Elsner, **The quality of human skin xenografts on SCID mice: a noninvasive bioengineering approach***, *Br J Dermatol*, 2004 Nov;151(5): p 971-976

Background: Animal models are important tools for studies in skin physiology and pathophysiology. Due to substantial differences in skin characteristics such as thickness and number of adnexa, the results of animal studies cannot always be directly transferred to the human situation. Therefore, transplantation of human skin on to SCID (severe combined immunodeficiency) mice might offer a promising tool to perform studies in viable human skin without the direct need for human volunteers. Objectives: To characterize the physiological and anatomical changes of a human skin transplant on a SCID animal host. Methods: In this study human skin was transplanted on to 32 SCID mice and followed for 6 months. Barrier function was assessed by transepidermal water loss (TEWL; tewametry) and moisture content of the stratumcorneum was studied by measurement of electrical capacitance (corneometry). Results: The results showed considerable deviations of TEWL values and skin hydration between the grafts and human skin in vivo. The human skin showed epidermal hyperkeratosis and moderate sclerosis of the corium 4 and 6 months after transplantation on to SCID mice. Conclusions: Our results indicate that human skin does not completely preserve its physiological and morphological properties after transplantation on to SCID mice. Therefore, results from experiments using this model system need to be discussed cautiously.

*K. Matsumoto, K. Mizukoshi, M. Oyobikawa, H. Ohshima, H. Tagami, **Establishment of an atopic dermatitis-like skin model in a hairless mouse by repeated elicitation of contact hypersensitivity that enables to conduct functional analyses of the stratum corneum with various non-invasive biophysical instruments***, *Skin Research and Technology* 2004, 10, p. 122-129

Pathogenesis of atopic dermatitis (AD) has been studied in animal models such as the NC/Nga mouse strain or Balb/C mice that are repeatedly treated with 2,4,6-trinitro-1-chlorobenzene (TNCB). These mice exhibit features of chronic contact dermatitis, including an intensified early type skin reaction, increased number of mast cells and elevated serum IgE levels with a shift of cutaneous cytokine expression from a type 1 to type 2 profile.

S.L. Hester, C.A. Rees, R.A. Kennis, D.L. Zoran, K.E. Bigley, A.S. Wright, N.A. Kirby, J.E. Bauer, Evaluation of Corneometry (Skin Hydration) and Transepidermal Water-Loss Measurements in two Canine Breeds, The American Society for Nutritional Sciences J. Nutr. 134:2110S, August 2004

Mammalian skin is a highly dynamic organ that is constantly adapting to changes in its environment. It provides structural, sensory, immunologic, and physiologic functions and contributes an essential barrier function against potential environmental insults.

S. Kim, B. Young Kang, S. Yong Cho, D. Suk Sung, 20-O-β-D-Glucopyranosyl-20 (S)-Protopanaxadiol (Compound K) Induces Expression of Hyaluronan Synthase 2 Gene in Transformed Human Keratinocytes and Fibroblasts and Increases Hyaluronan in Hairless Mouse Skin, IFSCC Magazine, Vol. 7, No. 3, 2004

Ginsenosides, the major active ingredients of ginseng, show a variety of biomedical efficacies such as anti-aging, anti-oxidation and anti-inflammatory activities. To understand the effects of 20-O-β-D-glucopyranosyl-20 (S)-protopanaxadiol (compound K) – one of the major metabolites of ginsenosides – on the skin, we assessed the expression level of approximately 100 transcripts in compound K-treated HaCaT cells using cDNA microarray analysis.

S. Hansen, Influence of environmental and pulsation factors on teat skin condition and teat tissue with regard to mastitis, Dissertation Tierärztliche Hochschule Hannover, 2002

Milking and non-milking influences on teat skin and tissue parameters were examined in a series of trials in New Zealand at the Dairying Research Corporation, Hamilton and on farms within a 100 km radius of Hanover, in Germany. In New Zealand, identical twins were available for six short-term trials and one long-term trial, involving 10 twin sets. In Germany, one main trial was carried out, with 304 unrelated cows located on five participating dairy farms. The determination of the teat skin parameters pH and moisture was possible, with the Corneometer CM 820 and Skin-pH-Meter PH 900 (Courage and Khazaka electronic GmbH, Cologne, Germany). The teat skin moisture was determined in arbitrary units. The test of repeatability resulted in a coefficient of variation (cv) of 25.6 per cent for moisture and 6.07 per cent for pH. The reproducibility over time resulted in similar cvs. Teat skin moisture and pH were not significantly correlated. The average teat skin pH of New Zealand cows varied from 6.44 to 6.88 for lactating cows and from 7.06 to 7.26 for dry cows. German lactating cows had a mean teat skin pH of 7.19 to 7.26. In New Zealand, the teat skin moisture of lactating cows fluctuated between 23.9 and 39.8, and between 23.0 to 57.5 for dry cows. The average teat skin moisture of German lactating cows ranged from 46.6 to 47.8. The teat skin moisture was correlated with the environmental temperature on a low level. The teat skin pH correlated with the environmental temperature and the relative humidity. The milking interval did not have any influence on teat skin moisture or pH. The application of a post milking teat sanitiser, containing iodine and a mixture of glycerine and sorbitol, increased the moisture of teat skin significantly. This increase was observable up to 16 h, but after 24 h, the effect had deteriorated. The low pH of the sanitiser solution (3.3) had a very strong, decreasing influence on the teat skin pH. Six different teat sanitiser formulations were tested regarding their teat conditioning properties. The level of glycerine in the sanitiser influenced the moisture level on the skin. Products without emollient did not moisturise the teat skin as well as products with emollient. Disinfectant solutions with a pH around neutral did not change the teat skin pH whilst treatments with the same pH (3.5) resulted in approximately the same decrease in teat skin pH. The influence of the treatments on the teat skin flora was tested, taking rinsing samples. The teat skin flora observed on untreated skin was similar to the microflora reported in the literature. However, no effect of the sanitiser treatment on the number of teats colonised with a particular group or genus of bacteria could be found. Ten twin sets were used to compare two different pulsation modes in a long-term trial. The group, treated with the 'fast' milking mode exhibited significantly higher teat thickness changes than the 'slow' group. Yet, the pulsation treatment had no significant effect on teat skin moisture or pH. The udder health of 253 German cows was compared with teat skin moisture and pH. No significant correlation of these parameters was observed. Analysis of the data indicated that time, farm and individual cow factors influenced the teat skin parameters to a greater extent than the udder health on quarter basis.

L.A. Young, J.C. Dodge, K.J. Guest, J.L. Cline, W.W. Kerr, Age, Breed, Sex and Period Effects on Skin Biophysical Parameters for Dogs Fed Canned Dog Food, American Society for Nutritional Sciences, J. Nutr. 132: 1695S–1697S, 2002

Noninvasive skin biophysical methods have been used in clinical and experimental dermatology for humans (1). The application of some of these methods has also been investigated for companion animals (2–9). Skin biophysical measurements have been reported to be affected by age, breed, sex, site of measurement, animal excitement, evaluation (time) period or season, gonadal status and even coat color (9). The objective of this study was to look at the effect of age, breed, sex and time period on skin biophysical parameters for dogs fed a nutritionally complete and balanced canned food for adult dogs.

T.-H. Oh, J.-H. Jeong, K.-H. Jang, The Comparison of Shampoos for Skin Hydration by Measurement of Epidermal Capacitance in Normal Canine Skin, J Vet Clin 18(3): p. 206-210, (2001)

Various commercial shampoos were frequently prescribed for dermatologic therapy in small animal practice. Skin hydration affected by the shampoos, however, was not evaluated routinely. In order to evaluate the skin hydration for the exact prescription of shampoos method to measure skin hydration of shampoos are needed. This study was undertaken to evaluate the skin hydration effect of shampoo on canine skin using Comeometer. Five healthy dogs were applied with 7 commercial shampoos: Humilac, Sebocalm, Sebolytics, Etiderm, Benzoyl peroxide, HyLyt and Zn-7 Derm. Skin hydrations were evaluated by measurement of electrical capacitance by Comeometer. A statistically significant increase in skin hydration was found 17(p< 0.05) and 77 minutes (p<0.01) after application of Humilac indicating a humidifying effect of this product. A statistically significant decrease in skin hydration was found for the Benzoyl peroxide after 77 minutes (p < 0.05). No statistically significant differences between the other shampoos were found. None of the products tested had any negative effect on the skin barrier function. The Comeometer was found useful for detecting skin hydration to shampoos and considered as a simple and useful tool for prescription of various shampoos routine practice.

T. Ajito, K. Suzuki, J. Okumura, N. Hatano, Skin pH of Domestic Animals (study in Japanese), J.jp J. Large Anim. Clinics 24(1): p. 9-12, 2001

Skin pH was examined using skin sebumeter, corneometer and pH-meter...

F.L. Ruedisueli, N.J. Eastwood, N.K. Gunn, T.G.D. Watson, Skin pH in Dogs of Different Breeds, Skin Research and Technology, Vol. 2, No. 1, February 1996

Normal skin pH in humans ranges from pH 5.4-5.9, but can vary between anatomical sites. No such pH data are known for dogs. In this study skin pH was measured in dogs of different breeds, demonstrating variation between measuring sites, breeds, sex, and coat colour. All animals were fed the same commercial dry dog food. Skin pH was measured with a flat membrane skin pH meter (Courage and Khazaka, Germany) on the head, pinna, flank, axillar and inguinal region. All sites were clipped except head and pinna. The mean pH for 12 Labradors, measured over 5 days, for flank, head, and pinna were (mean \pm SE) 7.48 ± 0.04 , 8.10 ± 0.06 and 6.11 ± 0.03 , respectively. Inguinal and axillar measurements showed day-to-day variability. For interbreed comparison skin, pH on the flank was measured on three male and three female Miniature schnauzers 7.25 ± 0.17 , Springer spaniels 6.65 ± 0.08 , Yorkshire terriers 7.71 ± 0.13 , and Labrador retrievers 7.13 ± 0.10 . The overall data showed effects of site (p<0.001), sex (p<0.001; males>females<9, neutering (p<0.01; neutered>entire), colour (p<0.01; black>yellow) and breed(p<0.01) and a sex effect within breeds. These findings demonstrate that skin pH measurements are possible in dogs and that the variability due to site, sex, breed, and coat may be important in the aetiology and management of dermatological disorders in relation to susceptibility, hypersensitivity, and treatment response.