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AARS Announcements

Register Now for Our 15th Annual AARS Networking Reception

Please join us for our 15th Annual AARS Member Networking Reception co-hosted with *Practical Dermatology* on Friday, March 20, 2020 from 6:30 PM – 8:30 PM at the Ellie Caulkins Opera House in the Chambers Grant Salon. It's only a one-minute walk from the convention center! Participation is open to all! Come to learn more about the upcoming **AARS Global Research Summit** activities in May 2020! Register now for free as space is limited to see this fabulous venue and spend time with your friends and colleagues! Click Here to Register!

Industry News

Acne pipeline watch: Dermata Therapeutics completes enrollment in phase 2b trial of once-weekly topical DMT310 for acne. February 11, 2020. DermWire, Dermatology Times. https://practicaldermatology.com/news/acne-pipeline-watch-dermata-therapeutics-completes-enrollment-in-phase-2b-trial-of-once-weekly-topical-dmt310-for-acne?c4src=news:feed

Dermata Therapeutics, LLC completed enrollment of patients in its Phase 2b clinical trial evaluating the safety, tolerability and efficacy of DMT310 in moderate to severe acne patients. The Phase 2b trial enrolled 182 patients randomly in two groups, DMT310 or placebo, at 14 sites across the United States. "Today's completion of enrollment marks a significant milestone for Dermata and our DMT310 program as we advance this unique product for the treatment of acne," states Christopher Nardo, PhD., Dermata's SVP, Development, in a news release. "DMT310 offers a new approach to the treatment of acne with its once-weekly application and combination of mechanical and biological mechanisms of actions that is 100% natural. We are very pleased with the positive feedback we have received from both physicians and patients, and we look forward to top-line results in June 2020." DMT310-003, is a 12-week, multi-center, double-blind, randomized, placebo-controlled trial designed to evaluate the safety, tolerability and efficacy of once-weekly dosing of DMT310 in 182 moderate-to-severe acne patients, defined as a grade 3 or 4 on the Investigator Global Assessment (IGA) five-point scale with at least 20 inflammatory and 20 non-inflammatory lesions on the face. The trial contained two arms: (1) DMT310 + H2O2; and (2) Placebo + H2O2. The primary endpoint is the absolute change from baseline in inflammatory lesion count at week 12. The secondary endpoints are absolute change from baseline in non-inflammatory lesion count and the IGA treatment success at week 12, defined as percentage of patients with at a two-point reduction on IGA compared to baseline. The trial also uses a HIPAA compliant smartphone application on patients' mobile devices to document treatment compliance. During the study, patients will record a10-second video, which is then reviewed by clinic staff, to ensure complete and timely application of the product. DMT310 is a natural product derived from a rare variant of freshwater sponge that is harvested under specific environmental conditions and then processed into a powdered. The powder is mixed with hydrogen peroxide immediately prior to application and only needs to be applied once per week. The product's multiple mechanisms of action can treat the several clinical and aesthetic skin conditions.

Sun Pharma's new ad campaign raises awareness of acne and its impact. February 10, 2020. DermWire, Dermatology Times. https://practicaldermatology.com/news/sun-pharmas-new-ad-campaign-raises-awareness-of-acne-and-its-impact-1?c4src=news:feed

Sun Dermatology, a division of Sun Pharmaceutical Industries, Inc., USA, launched Take on Acne – a new advertising campaign designed to raise awareness of the profound impact of acne on everyday life, particularly among teenagers and young adults (roughly 12-25 years of age). Acne affects more than 85% of adolescents and, depending on its severity, persistence and other factors, is highly correlated with psychosocial problems and low self-esteem. The Take on Acne ads depict the disruptive nature of powerful and painful acne breakouts that often seem to come out of nowhere. Featuring strong, empowering messages such as, “You are not your acne” and “Take back your face,” the campaign emphasizes the biological and genetic causes of acne, while dispelling misperceptions that the condition is always caused by poor hygiene or diet. “Take on Acne is meant to empower people with acne to re-gain control as their lives are interrupted by breakouts that can feel uncontrolled and overwhelming,” says Andy Nelson, Vice President, Sales and Marketing, Medical Dermatology, Sun Pharma. “By showing what adolescents with acne are going through, our aim is to give rise to the voice of the patient in a meaningful way, underscoring our commitment to these patients and the dermatology professionals who serve them.” The ad concept is the result of research Sun Pharma conducted to understand how acne impacts teens and young adults, and how they experience this condition in their own words. The research uncovered common themes through personal expressions of psychosocial angst, hopelessness, and isolation. Research participants reported viewing themselves through a distorted lens, as if defined by their condition, and admitted to self-retreating to avoid being judged. “Adolescence is a highly vulnerable life-stage for anyone, and the vulnerability is often magnified for those suffering from the more severe forms of acne,” said Nicholas Squittieri, MD, chief medical officer of Sun Pharma. “Take on Acne intentionally uses provocative imagery to urge people with acne to seek earlier intervention, which can not only prevent formation of physical scars, but also lifelong psychosocial scars. It’s also important that people know that some forms of acne are medical conditions that require clinical intervention.” The Take on Acne campaign will run in a variety of online digital, video, audio, gaming, and social media outlets, as well as on digital billboards across the US. Individuals seeking more information can visit TakeOnAcne.com to assess if and when to take action and to opt-in to receive acne-related materials.

New Medical Research

Effect of isotretinoin (13-cis-retinoic acid) on levels of soluble VEGF receptors (sVEGFR1, sVEGFR2, sVEGFR3) in patients with acne vulgaris. Ayhan E, Aslan Ö, Araç E. J Dermatolog Treat. 2020 Feb 11:1-19. doi: 10.1080/09546634.2020.1729331. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32043381

Background/Aim: The effect of isotretinoin on soluble VEGFRs has not been previously investigated. This study evaluate the effects of isotretinoin (13-cis-retinoic acid) on soluble VEGFR1 (sVEGFR1), soluble VEGFR2 (sVEGFR2) and soluble VEGFR3 (sVEGFR3).Methods: The study included 38 patients (28 females, 10 males) receiving systemic isotretinoin treatment and 38 healthy individuals (28 females, 10 males) with similar age and gender characteristics. The blood samples of the patient group at third months and blood samples of the control group were compared in terms of sVEGFR1, sVEGFR2 and sVEGFR3 concentrations. Results: It was significant that sVEGFR1 was low and sVEGFR3 was high in patients receiving isotretinoin (p: 0.038, p: 0.021, respectively). There was no significant change in sVEGFR2 levels between the groups (p: 0.519). Conclusions: We think that the effect of isotretinoin on

sVEGFR1, sVEGFR2 and sVEGFR3 may be secondary to its effects on the VEGF family. However, after clarifying the effect of isotretinoin on the VEGF family, we think that it can be used in some tumors and vascular diseases.

Efficacy of modified qufeng runmian powder () on acne vulgaris with syndromes of dampness and blood stasis: A multicenter, randomized, double-blind, placebo-controlled clinical trial. Zhang TB, Bai YP, Yang HY, et al. Chin J Integr Med. 2020 Feb 11. doi: 10.1007/s11655-020-3214-4. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32048170

Objective: To evaluate the efficacy and safety of a Chinese medicine (CM) Modified Qufeng Runmian Powder (, MQFRMP) for the treatment of acne vulgaris with CM syndromes of dampness and blood stasis. Methods: In this multicenter, randomized, double-blind, placebo-controlled clinical trial, 220 acne vulgaris patients with CM syndrome of dampness and blood stasis were included and randomly assigned using a central area group random design to receive either MQFRMP or the placebo, with 110 cases in each group. MQFRMP or a placebo at 145 g/bag were administered once daily for 4 weeks, respectively. The primary index of efficacy was the effective rate according to the acne severity score (ASS). The secondary indices of efficacy included the changes in the dermatology life quality index (DLQI) score, VISIA scores (spots, pores, brown spots, porphyrins and red areas) and skin assessment (skin pH, sebum amount and hydration) according to a SOFT skin multianalyzer. Results: (1) Follow-up: a total of 204 patients completed the follow-up, with 103 in the treatment group and 101 in the control group. (2) Effective rate: the total effective rate of the treatment group was significantly higher than the control group [83.5% (86/103) vs. 31.7% (32/101), P<0.01)] with 95% confidence interval of 39.3%-66.4%. (3) DLQI: DLQI scores were significantly decreased the treatment and control groups (both P<0.01), but the treatment group was more obvious than the placebo group (P<0.01). (4) VISIA scores: the scores of spots, brown spots and red areas in the treatment group decreased compared with baseline (P<0.05). In the control group, the scores of brown spots and pores decreased compared with baseline (P<0.05). The improvement was more obvious in the treatment group than in the control group for all items (P<0.05). (5) Skin assessment: the pH and sebum score in the both groups decreased drastically compared with the baseline (all P<0.01), however, the improvement was more obvious in the treatment group than in the control group (P<0.01). The hydration amount in the two groups showed no statistically significant difference compared with the baseline (both P>0.05). (6) Safety: two cases of mild drug allergy were observed in the treatment group. Conclusion: MQFRMP was effective and safe for the treatment of acne vulgaris with syndromes of dampness and blood stasis. (No. ChiCTR1900020479).

Effect of serum 25 hydroxy vitamin d level on isotretinoin-induced musculoskeletal symptoms: A cross-sectional study. Mülkoğlu C, Karaosmanoğlu N. Sci Rep. 2020 Feb 10;10(1):2245. doi: 10.1038/s41598-020-59167-0. https://www.ncbi.nlm.nih.gov/pubmed/32042004

Isotretinoin (ISO) is a drug which is used for the treatment of severe and refractory acne vulgaris (AV), over the last few decades. The drug has various musculoskeletal side effects. The aim of this study was to investigate relationship between serum 25 hydroxy (OH) vitamin D levels and the ISO-induced musculoskeletal side effects in patients with AV. We included 87 patients receiving ISO and had musculoskeletal symptoms as adverse effect (AE) group. Another 90 patients receiving ISO for AV and had any musculoskeletal complaints were recruited as control (C) group. Locomotor system examination of the patients was performed by the same clinician. Serum 25 OH vitamin D levels of the all participants were measured. Patients in the AE group were divided into three subgroups by serum 25 OH vitamin D levels. Patients with serum 25 OH vitamin D level lower than 10 ng/ml was classified as Group I, the ones between 10-20 ng/ml as Group II and those higher than 20 ng/ml were classified as Group III. AE and C groups were

similar in terms of age and sex ($p > 0.05$). There was no statistically significant difference in the mean serum vitamin D levels between two groups ($p = 0.17$). Also, there was no significant difference in number of arthralgia ($p = 0.30$), myalgia ($p = 0.29$), low back pain ($p = 0.10$) and sacroiliitis ($p = 0.17$) between three subgroups in AE group. In addition, we found no statistically significant correlation between the serum vitamin D levels and age, cumulative dose of ISO, arthralgia, myalgia and sacroiliitis parameters in AE group ($p > 0.05$). Serum 25 OH vitamin D levels between the AE and C groups were similar. We also found that no significant difference in musculoskeletal adverse events between AE subgroups. Therefore, it can be concluded that vitamin D deficiency has no effect on the musculoskeletal adverse events in patients receiving ISO.

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Association of race/ethnicity and sex with differences in health care use and treatment for acne. Barbieri JS, Shin DB, Wang S, et al. JAMA Dermatol. 2020 Feb 5. doi: 10.1001/jamadermatol.2019.4818. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32022834

Importance: Our understanding of potential racial/ethnic, sex, and other differences in health care use and treatment for acne is limited. Objective: To identify potential disparities in acne care by evaluating factors associated with health care use and specific treatments for acne. Design, setting, and participants: This retrospective cohort study used the Optum deidentified electronic health record data set to identify patients treated for acne from January 1, 2007, to June 30, 2017. Patients had at least 1 International Classification of Diseases, Ninth Revision (ICD-9) or International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) code for acne and at least 1 year of continuous enrollment after the first diagnosis of acne. Data analysis was performed from September 1, 2019, to November 20, 2019. Main outcomes and measures: Multivariable regression was used to quantify associations between basic patient demographic and socioeconomic characteristics and the outcomes of health care use and treatment for acne during 1 year of follow-up. Results: A total of 29 928 patients (median [interquartile range] age, 20.2 [15.4-34.9] years; 19 127 [63.9%] female; 20 310 [67.9%] white) met the inclusion criteria for the study. Compared with non-Hispanic white patients, non-Hispanic black patients were more likely to be seen by a dermatologist (odds ratio [OR], 1.20; 95% CI, 1.09-1.31) but received fewer prescriptions for acne medications (incidence rate ratio, 0.89; 95% CI, 0.84-0.95). Of the acne treatment options, non-Hispanic black patients were more likely to receive prescriptions for topical retinoids (OR, 1.25; 95% CI, 1.14-1.38) and topical antibiotics (OR, 1.35; 95% CI, 1.21-1.52) and less likely to receive prescriptions for oral antibiotics (OR, 0.80; 95% CI, 0.72-0.87), spironolactone (OR, 0.68; 95% CI, 0.49-0.94), and isotretinoin (OR, 0.39; 95% CI, 0.23-0.65) than non-Hispanic white patients. Male patients were more likely to be prescribed isotretinoin than female patients (OR, 2.44; 95% CI, 2.01-2.95). Compared with patients with commercial insurance, those with Medicaid were less likely to see a dermatologist (OR, 0.46; 95% CI, 0.41-0.52) or to be prescribed topical retinoids (OR, 0.82; 95% CI, 0.73-0.92), oral antibiotics (OR, 0.87; 95% CI, 0.79-0.97), spironolactone (OR, 0.50; 95% CI, 0.31-0.80), and isotretinoin (OR, 0.43; 95% CI, 0.25-0.75). Conclusions and relevance: The findings identify racial/ethnic, sex, and insurance-based differences in health care use and prescribing patterns for acne that are independent of other sociodemographic factors and suggest potential disparities in acne care. In particular, the study found underuse of systemic therapies among racial/ethnic minorities and isotretinoin among female patients with acne. Further study is needed to confirm and understand the reasons for these differences.

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Prediction of neonatal acne based on maternal lipidomic profiling. Wang H, Wang J, Zhou M, et al. J Cosmet Dermatol. 2020 Feb 6. doi: 10.1111/jocd.13320. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32027074

Background: Neonatal acne occurs in the first few weeks after birth. Some lesions are more serious and leave scars. Maternal surface skin lipids (SSL) have a strong correlation with SSL of infants. The establishment of prediction rank model based on maternal SSL is essential to the prevention and treatment of neonatal acne. Method: Surface skin lipids samples were collected from the mothers (M) of 56 neonatal acne patients and the mothers (HM) of 19 healthy infants. Surface skin lipids from the right forehead were collected using a noninvasive method. UPLC-QTOF-MS was applied to detect SSL. Partial least squares discriminant analysis and receiver operating characteristic (ROC) analysis were performed to screen and validate potential lipids. Random forest (RF) and ROC analysis were used to establish a prediction model and evaluate its accuracy. Results: Sixteen altered potential lipids belonging to fatty acids, sphingomyelins, and glycerides were associated with M. M had less lipids than HM. Spearman's correlation of 16 lipids revealed 9 with high correlation. They were chosen as characteristic values of the RF prediction model. And the model showed an average accuracy of 98% in the validation set. Conclusion: We have established an RF model for predicting neonatal acne and have shown that high skin barrier-related lipids were markers for predicting neonatal acne.

Efficacy and safety comparison of combination of 0.04% tretinoin microspheres plus 1% clindamycin versus their monotherapy in patients with acne vulgaris: A phase 3, randomized, double-blind study. Dogra S, Sumathy TK, Nayak C, et al. J Dermatolog Treat. 2020 Feb 5:1-9. doi: 10.1080/09546634.2020.1720579. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32020824

Background and objectives: There is an unmet need for topical treatments with good tolerability in management of acne vulgaris. The present study aimed to evaluate efficacy and safety of a novel tretinoin (microsphere, 0.04%) formulation in combination with clindamycin (1%) gel for treatment of acne vulgaris.Materials and methods: This phase 3 randomized, double-blind study included patients with moderate-to-severe acne. Patients were treated with tretinoin (microsphere, 0.04%) + clindamycin (1%) or one of the monotherapies (tretinoin, 0.025%; clindamycin, 1%). Key endpoints included percent change in lesion counts, and improvement in Investigator's Static Global Assessment (ISGA) score.Results: 750 patients were randomized (combination, n = 300; tretinoin and clindamycin, each n = 150). At week 12, reductions in inflammatory (77%), non-inflammatory (71%) and total lesions (73%) were significantly greater with combination treatment versus either monotherapy ($p < .03$). Proportion of patients rated 'clear' or 'almost clear' with ≥2-grade ISGA improvement was higher with combination (46%) versus monotherapies ($p < .02$). Adverse events occurred in 20 patients, most were mild-moderate; no deaths or serious adverse events were reported. The discontinuation rates due to adverse events with combination therapy were low (≤1%).Conclusion: The once-daily, microsphere-based formulation was generally tolerable with a positive impact on therapeutic outcomes and patients' compliance. ClinicalTrial Registration No.: CTRI/2014/08/004830.

Sebocyte differentiation as a new target for acne therapy. An in vivo experience. Ottaviani M, Flori E, Mastrofrancesco A, et al. J Eur Acad Dermatol Venereol. 2020 Jan 30. doi: 10.1111/jdv.16252. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31999869

Background: Acne, a disease of the sebaceous gland with multifactorial pathogenesis, affects more than 85% of adolescents. A better deepening of the mechanisms underlying the disease is needed to define effective and

mechanism-targeted treatments. Objective: To understand whether the sebocyte differentiation process could be involved in the pathogenesis of the disease. Methods: Protein expressions were evaluated by Western blot analysis and ELISA; mRNA levels by Real time RT-PCR; lipid analysis and lipid peroxidation were performed by gas-chromatography, mass spectrometry and spectrophotometric assay. Results: In vitro, low differentiated SZ95 sebocyte expressed an up-modulation of genes involved in sebogenesis and a higher level of insulin receptor respect to differentiated cells, resulting in an increased response to insulin and in the production of acne like sebum. The induction of SZ95 sebocytes differentiation by the Peroxisome Proliferator Activated Receptor γ (PPARγ) modulator NAC-GED0507 reduced the response to insulin normalizing the sebum production and decreasing the release of proinflammatory mediators. In vivo treatment of acne patients with NAC-GED0507 1% gel ameliorated clinical manifestations and induced in sebum the expression of PPARγ, associated with the decrease of mTOR activation and levels of inflammatory molecules, confirming the results obtained in vitro. Conclusions: The study provides relevant insight into acne pathogenesis, identifying an alteration of sebocyte differentiation as pathogenetic basis of the disease and the induction of the differentiation process as a therapeutic target in acne therapy interfering with all pathogenic mechanisms.

The effect of silymarin on liver enzymes in patients taking isotretinoin: A randomized clinical trial. Mirnezami M, Jafarimanesh H, Rezagholizamenjany M, et al. Dermatol Ther. 2020 Jan 30:e13236. doi: 10.1111/dth.13236. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31997509

The aim of the present study was to investigate the effect of silymarin (Livergol) on liver enzymes in patients taking isotretinoin (Roaccutane). In this double-blind clinical trial, 74 patients with acne and taking isotretinoin were randomly assigned into intervention (N = 37) and control (N = 37) groups. The intervention group received a 140 mg Livergol capsule per day for 30 days. The control group received a starch-containing capsule as a placebo once a day for 30 days. Liver enzyme levels were measured before and after the intervention. The data were analyzed using chi-square test, Independent t test, paired sample t test and analysis of covariance (ANCOVA). The results showed no statistically significant difference between the intervention and control groups at the beginning of study in levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) ($p > .05$). At the end of the study, a statistically significant difference was observed between the two groups in levels of AST and ALT ($p < .05$). Livergol prevented liver enzymes from increasing, so it can be used as an effective, low-cost, and low-complication treatment for the problem of increased levels of liver enzymes following the use of isotretinoin.

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Psychosocial aspects of adult acne: Data from 13 European countries. Altunay IK, Özkur E, Dalgard FJet al. Acta Derm Venereol. 2020 Jan 29. doi: 10.2340/00015555-3409. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31993670

The link between acne and psychiatric morbidities has been demonstrated in many studies; however, large scale studies aiming to reveal the psychosocial impact of acne are rare. The aim of this study was to assess the psychological burden of adult acne patients. This analysis was based on a multicenter study including 213 acne patients and 213 controls from 13 European countries. The Hospital Anxiety and Depression Scale (HADS), Dermatology Life Quality Index, and EuroQol 5 dimensions 3 levels scores of the patients with acne were analyzed. Patients with acne (n = 213) had higher HADS scores for anxiety (mean ± standard deviation 6.70 ± 3.84) and depression (3.91 ± 3.43) than the controls ($p < 0.001$ for both). For patients with acne, 40.6% reported that they were

very concerned about their skin disease, 12.3% had suicidal ideation, and, among those, 10 (4%) patients implied that acne was the cause of their suicidal thoughts. After adjusting for other variables, patients who had suicidal ideation ($p = 0.007$, and adjusted odds ratio 3.32 [95% confidence interval (CI): 1.39–7.93]) and stressful life events ($p < 0.001$, and adjusted OR 5.85 [95% CI: 2.65–12.86]) had a greater chance of fulfilling the HADS criteria for anxiety. This study highlights the need for a psychotherapeutic approach in order to recognize the concerns of acne patients and optimize their treatment.

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Development and initial validation of a multidimensional acne global grading system integrating primary lesions and secondary changes. Bernardis E, Shou H, Barbieri JS, et al. JAMA Dermatol. 2020 Jan 29. doi: 10.1001/jamadermatol.2019.4668. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/31995147

Importance: The qualitative grading of acne is important for routine clinical care and clinical trials, and although many useful systems exist, no single acne global grading system has had universal acceptance. In addition, many current instruments focus primarily on evaluating primary lesions (eg, comedones, papules, and nodules) or exclusively on signs of secondary change (eg, postinflammatory hyperpigmentation, scarring). Objectives: To develop and validate an acne global grading system that provides a comprehensive evaluation of primary lesions and secondary changes due to acne. Design, setting, and participants: This diagnostic study created a multidimensional acne severity feature space by analyzing decision patterns of pediatric dermatologists evaluating acne. Modeling acne severity patterns based on visual image features was then performed to reduce dimensionality of the feature space to a novel 2-dimensional grading system, in which severity levels are functions of multidimensional acne cues. The system was validated by 6 clinicians on a new set of images. All images used in this study were taken from a retrospective, longitudinal data set of 150 patients diagnosed with acne, ranging across the entire pediatric population (aged 0-21 years), excluding images with any disagreement on their diagnosis, and selected to adequately span the range of acne types encountered in the clinic. Data were collected from July 1, 2001, through June 30, 2013, and analyzed from March 1, 2015, through December 31, 2016. Main outcomes and measures: Prediction performance was evaluated as the mean square error (MSE) with the clinicians' scores. Results: The scale was constructed using acne visual features and treatment decisions of 6 pediatric dermatologists evaluating 145 images of patients with acne ranging in age from 0 to 21 years. Using the proposed scale to predict the severity scores on a new set of 40 images achieved an overall MSE of 0.821, which is smaller than the mean within-clinician differences (MSE of 0.998). Conclusions and relevance: By integrating primary lesions and secondary changes, this novel acne global grading scale provides a more clinically relevant evaluation of acne that may be used for routine clinical care and clinical trials. Because the severity scores are based on actual clinical practice, this scoring system is also highly correlated with appropriate treatment choices.

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Cosm-nutraceutical nanovesicles for acne treatment: Physicochemical characterization and exploratory clinical experimentation. Amer SS, Nasr M, Abdel-Aziz RTA, et al. Int J Pharm. 2020 Jan 28;577:119092. doi: 10.1016/j.ijpharm.2020.119092. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32004681

The full exploration of the 'nutraceuticals' therapeutic potential in cosmetics has been hindered by their poor stratum corneum permeation. Therefore, the aim of the present study was to formulate a nutraceutical; quercetin, in novel

vitamin C based nanovesicles (aspasomes), and to explore their beneficial effects in the treatment of acne. Aspasomes were characterized for their particle size, zeta potential, entrapment efficiency (EE%), 3-months storage stability, skin deposition/permeation, antioxidant potential, and morphology. Aspasomes antibacterial efficacy on Propionibacterium acnes using the zone of inhibition assay was also tested, whilst their safety on skin fibroblastic cells was assessed in vitro using 3T3 CCL92 cell lines. An exploratory clinical trial was conducted in acne patients, and the percentage reduction of inflammatory, non-inflammatory and total acne lesions was taken as the evaluation criterion. Results revealed that quercetin-loaded aspasomes displayed a desirable nanometer size (125-184 nm), negative charge with good storage stability, and high skin deposition reaching 40%. Aspasomes managed to preserve the antioxidant activity of quercetin, and exhibited a significantly higher antibacterial effect (15 ± 1.53 mm) against Propionibacterium acnes than quercetin alone (8.25 ± 2.08 mm), and were safe on skin fibroblastic cells. Upon clinical examination in 20 acne patients (14 females, 6 males), quercetin aspasomes exhibited reduction percentages of 77.9%, 11.8% and 55.3% for inflammatory lesions, comedones and total lesions respectively. This opens vast applications of the presented formulation in the treatment of other oxidative skin diseases and delineates the nutraceuticals and nanoformulations prepared from natural materials as promising dermatological treatment modes.

Minocycline 1.5% foam for the topical treatment of moderate-to-severe papulopustular rosacea: Results of two phase 3, randomized, clinical trials. Gold LS, Del Rosso JQ, Kircik L, et al. J Am Acad Dermatol. 2020 Jan 28. pii: S0190-9622(20)30127-4. doi: 10.1016/j.jaad.2020.01.043. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32004648

Background: Efficacious topical medications for rosacea are needed. FMX103 1.5% is a novel, topical minocycline foam that may have therapeutic benefits in treating rosacea, while minimizing systemic side effects due to its topical route of delivery. Objective: Determine the efficacy, safety, and tolerability of 12 weeks of treatment with FMX103 1.5% topical minocycline foam for papulopustular rosacea. Methods: Two 12-week, Phase 3, randomized, multicenter, double-blind, vehicle-controlled, 2-arm studies were performed in patients with moderate-to-severe papulopustular rosacea. Results: Subjects who received FMX103 1.5%, vs vehicle-treated controls, exhibited a significantly greater reduction in the number of inflammatory lesions (FX2016-11: -17.57 vs -15.65; P=.0031; FX2016-12: -18.54 vs -14.88; P<.0001) and higher rates of Investigator Global Assessment treatment success (FX2016-11: 52.1% vs 43.0%; P=.0273; FX2016-12: 49.1% vs 39.0%; P=.0077). No serious treatment-related treatment-emergent adverse events occurred. Limitations: The generalizability of these data from a controlled clinical trial should be examined in a real-world setting. Conclusion: FMX103 1.5% was efficacious for moderate-to-severe papulopustular rosacea, while maintaining a favorable safety profile.

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Susceptibility of cutibacterium acnes to topical minocycline foam. Sutcliffe J, McLaughlin R, Webster G, et al. Anaerobe. 2020 Jan 28;62:102169. doi: 10.1016/j.anaerobe.2020.102169. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32058277

FMX101 4% minocycline foam (FMX101 4%) is a novel, topical minocycline formulation for treatment of acne vulgaris. We report that FMX101 4% had an MIC90 of 0.25 μg/ml and was ≥4-fold more active than comparator antimicrobials against a panel of 98 clinical Cutibacterium acnes isolates. The panel was diverse by clonal complex and sequence type, having 20 novel multi-locus sequence types including clonal complexes and sequence types associated with acne (CC1, CC3, and CC4; ST1 and ST3). Some isolates were phenotypically resistant to clindamycin (6.1%),

erythromycin (14.3%), and tetracycline (2.0% intermediate resistance). Six isolates (6.4%) carried a mutation in the quinolone resistance-determining region of gyrA. With C. acnes, spontaneous resistance to FMX101 4% occurred at frequencies ranging from ≤5 × 10-9 to <1 × 10-8; mutations were identified in rpsJ, a gene encoding 30S ribosomal protein S10. No mutant exhibited a minocycline MIC above 0.5 µg/ml. No second-step mutation in previously isolated mutants or strains containing rpsJ ± 16S rRNA mutations was detected following minocycline challenge. Minocycline retained antibacterial activity against C. acnes over 15 multiple passages; thus, no selective growth advantage for minocycline-resistant mutants occurred under the experimental conditions. FMX101 4% has the potential to retain the favorable resistance profile of minocycline in diverse C. acnes isolates while providing the benefits of a topical formulation for treatment of acne vulgaris.

Tazarotene 0.045% lotion for the once-daily treatment of moderate-to-severe acne vulgaris in adult males. Cook-Bolden FE, Gold MH, Guenin E. J Drugs Dermatol. 2020 Jan 1;19(1):78-85. doi: 10.36849/JDD.2020.3979. https://www.ncbi.nlm.nih.gov/pubmed/32023013

Background: There has been an increasing interest in gender differences both in the pathogenesis and treatment of acne vulgaris (acne). However, while acne prevalence among adolescents is comparable across sexes, acne is much more common in adult women than in adult men which has been largely ignored. Acne is likely less common in adult men because of the declining rate of sebum secretion observed with increasing age, and yet it can be more severe than in adult women. In addition, adherence to topical medications is especially poor in adult men where tactile and sensory perceptions are low. The first lotion formulation of tazarotene was developed using polymeric emulsion technology to provide an important alternative option to treat these acne patients, especially those who may be sensitive to the irritant effects of other tazarotene formulations. Objective: To evaluate the efficacy and safety of a new tazarotene 0.045% lotion formulation based on polymeric emulsion technology in treating adult male subjects with moderate or severe acne, in comparison with adolescent males treated with the same tazarotene 0.045% lotion. Methods: Post hoc analysis of two multicenter, randomized, double-blind, vehicle-controlled phase 3 studies in moderate-or-severe acne. Subjects (aged 10 and older, N=1614) were randomized (1:1) to receive tazarotene 0.045% lotion or vehicle, once-daily for 12 weeks. Efficacy assessments included changes in baseline inflammatory and noninflammatory lesions and treatment success (at least 2-grade reduction in Evaluator's Global Severity Score [EGSS] and clear or almost clear). Quality of Life was assessed using the validated Acne-QoL scale. Safety, adverse events (AEs) were evaluated throughout; cutaneous tolerability (using a 4-point scale where 0=none and 3=severe) at each study visit. Results: A total of 268 male subjects (85≥18 years old and 183<18 years old) were treated with tazarotene 0.045% lotion once-daily for 12 weeks. At week 12, percent reductions in inflammatory and noninflammatory lesions with tazarotene 0.045% lotion were 62.3% and 59.5% in the adult male population, compared with 49.4% (P=0.001) and 49.5% (P=0.016) in the adolescent male population. Treatment success was achieved by 33.0% of adult male subjects treated with tazarotene 0.045% lotion, compared with 21.6% in the adolescent male population (P=0.059). Quality of life (as assessed by Acne-QoL domain scores) was better in adolescent males at baseline. Improvements in QoL domain scores were similar to those seen in the overall study population, with greater absolute change in domain scores in the adult males. Improvement in acne symptom scores was significantly greater in adult males (P=0.029). Tazarotene 0.045% lotion was well-tolerated. The number of subjects reporting any AE in the adult male population was 11 (13.6%) compared with 39 (21.4%) in the adolescent male population. There was only one (1.2%) treatment-related AE (application site pain) reported in the adult males compared with 11 (6.0%) in the adolescent males, where the most common treatment-related AEs were application site pain (3.3%), dryness (1.1%), and erythema (1.1%). Mean scores for hyper- and hypopigmentation were very low at baseline in both groups with no appreciable change with treatment. Conclusions: Tazarotene 0.045% lotion provides greater efficacy and

better tolerability in adult males (above 18 years old) than the adolescent male population with moderate-to-severe acne patients.

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Acne vulgaris in an undergraduate population in Nigeria. Ayanlowo O, Ariyo M, Adekanmbi A. West Afr J Med. 2020 Jan-Mar;37(1):62-66. https://www.ncbi.nlm.nih.gov/pubmed/32030714

Background: Acne vulgaris is a chronic inflammatory disease of the pilo-sebaceous unit. It affects teenagers and young adults. Factors which can provoke or aggravate acne include cosmetic agents, medications, and sunlight. Acne has been associated with intense emotional and psychological distress. Aims: This study aimed to describe predisposing factors, clinical characteristics and the quality of life of students with acne in an undergraduate community. Methods: This is a cross sectional descriptive study of students of Babcock University, located in the South-Western Nigeria. Data was collected at the residential halls using structured questionnaire which consists of students' demographic data, symptoms, predisposing factors, previous treatment, Cardiff Acne Disability Index; and examination findings to document the presence of acne and clinical characteristics. Results: Acne vulgaris was documented in 391 students (88.5%). Age range of respondents was between 15 and 35, and mean age was 19.51 + 2.25 years. The mean duration of symptoms was 47.46 + 38.27 months. Factors perceived to precipitate acne include food, stress, cleansers and sugary drinks. The mean CADI score for all respondents was 3.27 +3.07 which represents a mild effect on the quality of life. There was no significant difference in the severity of acne in males and females. Conclusion: This study documents a high prevalence of acne, although it has only a mild effect on the quality of life of the students. In view of the high percentage of students with acne, it should be penned down for public health intervention to prevent mismanagement, progression and complications.

Clinical Reviews

Platelet-rich plasma in noninvasive procedures for atrophic acne scars: A systematic review and meta-analysis. Long T, Gupta A, Ma S, Hsu S. J Cosmet Dermatol. 2020 Feb 15. doi: 10.1111/jocd.13331. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32061047

Background: The use of platelet-rich plasma (PRP) combined with noninvasive, nonenergy procedures for atrophic acne scars has shown promise. To date, there has not been a systematic review or meta-analysis of the effectiveness of this therapy. Aims: To use meta-analysis to compare Goodman and Baron qualitative scores, patient satisfaction outcomes, and adverse effects in patients undergoing combination procedures with PRP, combination procedures without PRP, and noninvasive monotherapy without PRP in the treatment of patients with atrophic acne scars. Patients/methods: The Pubmed and Cochrane library databases were searched for relevant studies published before May 1, 2019. PRISMA guidelines were utilized. Studies that compared the use of PRP in combination with a noninvasive procedure and therapies without PRP for the treatment of atrophic acne scars were included. Cochrane's handbook was utilized to assess the individual biases of the included studies. Publication bias was assessed. Results: A total of 311 participants (153 whole-face participants and 158 split-face participants) were reviewed across eight included studies. Quantitative analysis of 241 participants across six included studies showed a statistically significant

reduction in scar severity scores in favor of microneedling or subcision with PRP (P < .001). Combination therapy with intradermal or topical PRP was significantly more effective than monotherapy alone and combination therapy with an adjunct other than PRP (P < .001 and .001, respectively). Conclusion: This systematic review and meta-analysis demonstrated that microneedling or subcision with PRP produced statistically significant improvement in validated outcomes over microneedling or subcision alone.

The role of the cutaneous microbiome in hidradenitis suppurativa: Light at the end of the microbiological tunnel. Langan EA, Recke A, Bokor-Billmann T, et al. Int J Mol Sci. 2020 Feb 11;21(4). pii: E1205. doi: 10.3390/ijms21041205. https://www.ncbi.nlm.nih.gov/pubmed/32054085

The development of next generation sequencing, coupled with advances in bio-informatics, has provided new insights into the role of the cutaneous microbiome in the pathophysiology of a range of inflammatory skin diseases. In fact, it has even been suggested that the identification of specific skin microbial signatures may not only be useful in terms of diagnosis of skin diseases, but they may also ultimately help inform personalized treatment strategies. To date, research investigating the role of microbiota in the development of inflammatory skin diseases has largely focused on atopic eczema and psoriasis vulgaris. The role of the microbiome in Hidradenits suppurativa (HS)-also known as acne inversa-a chronic auto-inflammatory skin disease associated with significant morbidity, has received comparatively little attention. This is despite the fact that antimicrobial therapy plays a central role in the treatment of HS. After briefly outlining the clinical features of HS and current treatment strategies, we move on to review the evidence of microbial dysbiosis in HS pathophysiology. We conclude by outlining the potential for metagenomic studies to deepen our understanding of HS biology but more importantly to identify novel and much needed treatment strategies.

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New herbal biomedicines for the topical treatment of dermatological disorders. Hoffmann J, Gendrisch F, Schempp CM, Wölfle U. Biomedicines. 2020 Feb 8;8(2). pii: E27. doi: 10.3390/biomedicines8020027. https://www.ncbi.nlm.nih.gov/pubmed/32046246

Herbal extracts and isolated plant compounds play an increasing role in the treatment of skin disorders and wounds. Several new herbal drugs, medicinal products and cosmetic products for the treatment of various skin conditions have been developed in recent years. In this nonsystematic review, we focus on herbal drugs that were tested in controlled clinical studies or in scientifically sound preclinical studies. The herbal biomedicines are intended to treat atopic dermatitis (St. John's wort, licorice, tormentil, bitter substances, evening primrose), psoriasis (araroba tree, lace flower, barberry bark, indigo, turmeric, olibanum, St. John's wort), actinic keratosis (birch bark, petty spurge), herpes simplex (lemon balm, sage and rhubarb), rosacea (green tea, licorice, tormentil) and acne vulgaris (tea tree oil, green tea, hop), or to improve photo protection (green tea, Dyer's weed, cocoa tree, carotinoids, licorice), aesthetic dermatology (licorice, pine bark, gotu kola) and wound healing (birch bark, onion).

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Evaluating FMX-101 as a promising therapeutic for the treatment of acne. Valente Duarte de Sousa IC. Expert Opin Pharmacother. 2020 Feb 8:1-6. doi: 10.1080/14656566.2020.1721461. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32037906

Introduction: Oral minocycline is a mainstay of therapy for moderate-to-severe acne; however, systemic side effects which include hepatotoxicity, lupus-like syndrome, drug hypersensitivity syndrome, autoimmune hepatitis, polyarteritis nodosa, gastrointestinal side effects and skin hyperpigmentation are of concern. Topical antibiotics commonly used in acne, such as erythromycin and clindamycin, present high P. acnes resistance rates which has opened the market for new topical antibiotics. FMX-101 is a novel topical minocycline foam that has shown promising results in phase I, II and III trials for the treatment of moderate-to-severe acne with a better safety profile than oral minocycline. Areas covered: The author provides an overview FMX-101 including its clinical efficacy and safety. The author then provides their expert opinion on this treatment and its potential for the treatment option for acne. Expert opinion: The topical foam formulation of FMX-101 has been shown to reduce both inflammatory and non-inflammatory lesions and to improve IGA scores in patients with moderate-to-severe acne without significant systemic absorption thus limiting associated side effects. Overall, the proven efficacy and safety profile of FMX-101, together with the low systemic absorption, high skin tolerability and cosmetically acceptable foam formulations render this novel therapy an important addition to the acne treatment armamentarium.

Low dose of isotretinoin: A comprehensive review. Abdelmaksoud A, Lotti T, Vojvodic A, et al. Dermatol Ther. 2020 Feb 5:e13251. doi: 10.1111/dth.13251. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32022958

Isotretinoin is a first-generation retinoid initially approved for treatment of sever cases of acne vulgaris (nodulocystic acne). Due to its broad anti-inflammatory and immunomodulatory properties, it has been used beyond its initial approval in a myriad of other indications. Adverse effects of isotretinoin vary from xerosis to teratogenicity. Herein, we reviewed the literature, through date-unlimited Pubmed search, from inception till December 2019, using the following search terms: 'low-dose Isotretinoin' & 'Dermatology', "isotretinoin & safety", "isotretinoin, off-label uses", "isotretinoin& male fertility", "isotretinoin, iPLEDGE system", aiming to deliver a therapeutic update relevant to clinical practice. All English-language articles were considered with no limitation based on the articles' type. Low dose isotretinoin is not limited to old and novel dermatological conditions, but also showed promising results in the field of infertility and safety in the field of gastroenterology. We also highlight on the safety profile of the drug and experts' recommendations to enhance safety measures to decrease fetal risk while on isotretinoin.

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Standard management options for rosacea: The 2019 Update by the National Rosacea Society Expert Committee. Thiboutot D, Anderson R, Cook-Bolden F, et al. J Am Acad Dermatol. 2020 Feb 6. pii: S0190-9622(20)30166-3. doi: 10.1016/j.jaad.2020.01.077. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32035944

In 2017 a National Rosacea Society expert committee developed and published an updated classification of rosacea to reflect current insights into rosacea pathogenesis, pathophysiology, and management. These developments suggest that a multivariate disease process underlies the various clinical manifestations of the disorder. The new system is consequently based on phenotypes that link to this process, providing clear parameters for research and diagnosis, as well as encouraging clinicians to assess and treat the disorder as it may occur in each individual. Meanwhile, a range of therapies has become available for rosacea, and their roles have been increasingly defined in clinical practice as the disorder has become more widely recognized. This update is intended to provide a

comprehensive summary of management options, including expert evaluations, to serve as a guide for tailoring treatment and care on an individual basis to achieve optimal patient outcomes.

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When bugs and drugs conspire: Driving acneiform skin toxicity. Billi AC, Sarkar MK, Gudjonsson JE. J Clin Invest. 2020 Feb 4. pii: 133787. doi: 10.1172/JCI133787. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32015232

Therapy with antineoplastic agents that inhibit EGFR and MEK is frequently limited by cutaneous adverse reactions, most commonly acne-like eruptions. In this issue of the JCI, Satoh et al. define a mechanism for acneiform skin toxicity wherein EGFR/MEK inhibitors cooperate with the skin commensal Cutibacterium acnes to induce IL-36γ in keratinocytes via the combined actions of Krüppel-like factor 4 and NF-κB transcription factors at the IL-36γ promoter, resulting in neutrophil recruitment. In addition to elucidating why EGFR/MEK inhibitor-induced rashes are often pustular and folliculocentric, this mechanism provides justification for the long-standing practice of management with antibiotic therapy.

Psychosocial burden of hidradenitis suppurativa patients' partners. Włodarek K, Głowaczewska A, Matusiak Ł, Szepietowski JC. J Eur Acad Dermatol Venereol. 2020 Jan 31. doi: 10.1111/jdv.16255. [Epub ahead of print] https://www.ncbi.nlm.nih.gov/pubmed/32003871

Background: Hidradenitis suppurativa is a debilitating disease related to a great psychosocial burden in affected patients and subsequently also people around them. Patients' partners as caregivers may indirectly experience wide range of devastating effects of the disease on their emotional and social life. Objective: The purpose of this study was to determine the QoL impairment in HS patients' partners and to identify its aspects that are affected the most. Correlation between QoL burden and disease severity, duration, sex, age and smoking was also assessed. Methods: 50 HS sufferers were assessed according to disease severity and their partners' QoL was determined using the Family Dermatology Life Quality Index questionnaire. Results: The mean FDLQI for patients' partners was 8.7 ± 6.8 points, indicating generally a moderate effect of HS on their life. Quality of partners' life correlated significantly with disease severity but no correlation was found according to other factors. Conclusion: HS is a highly psychologically devastating disease not only for patients but also for their partners. It occurred to diminish partners' QoL mostly by increasing daily expenditure but also other problems were often reported. Clinicians should be aware of these psychosocial implications, in order to provide optimal therapy of HS affected families by a multidisciplinary specialized management addressing both, patients and their cohabitants simultaneously.

Coupled blue and red light-emitting diodes therapy efficacy in patients with rosacea: Two case reports. Sorbellini E, De Padova MP, Rinaldi F. J Med Case Rep. 2020 Jan 28;14(1):22. doi: 10.1186/s13256-019-2339-6. https://www.ncbi.nlm.nih.gov/pubmed/31992343

Background: Rosacea is a common inflammatory skin condition affecting approximately 5% of the world population. Therapeutic approaches to rosacea are focused on symptom suppression by means of anti-inflammatory agents. More recently, photodynamic therapy, especially light-emitting diodes, has been introduced as a valid alternative to conventional therapy. Case presentation: In the present work, we reported the efficacy and safety of light-emitting diodes therapy combining blue (480 nm) and red (650 nm) light for the treatment of two patients with papulopustular

rosacea: a 22-year-old Caucasian woman and a 68-year-old Caucasian man. Conclusions: This kind of treatment could represent an effective, safer, and well-tolerated approach for the treatment of such conditions.

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The theranostics role of mast cells in the pathophysiology of rosacea. Wang L, Wang YJ, Hao D, et al. Front Med (Lausanne). 2020 Jan 28;6:324. doi: 10.3389/fmed.2019.00324. eCollection 2019. https://www.ncbi.nlm.nih.gov/pubmed/32047752

Rosacea is a chronic inflammatory cutaneous disorder that adversely affects patient's health and quality of life due to the complex course and the need for repeated treatment. The exact molecular mechanisms of rosacea are unclear. Mast cells are innate immune cells that can be found in virtually all tissues. Recently, increasing evidence has indicated that mast cells have important effects on the pathogenesis of rosacea. In this review article, we describe recent advances of skin mast cells in the development of rosacea. These studies suggested that mast cells can be an important immune cell that connected innate immunity, nerves, and blood vessels in the development of rosacea. Moreover, we review the inhibition of mast cells for the potential treatment of rosacea.

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