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Industry News

Dermatology has a problem with skin color. By Roni Caryn Rabin. Aug. 30, 2020, New York Times. https://www.nytimes.com/2020/08/30/health/skin-diseases-black-hispanic.html

Common conditions often manifest differently on dark skin. Yet physicians are trained mostly to diagnose them on white skin. In the spring, teenagers started showing up at doctors' offices in droves with angry red and purple blisters on their fingers and toes. The latest unexpected feature of the coronavirus infection fascinated the public, and suddenly photographs of so-called Covid toes were everywhere on social media. But almost all of the images depicted glossy pink lesions on white skin. Though people of color have been affected disproportionately by the pandemic, pictures of Covid toes on dark skin were curiously hard to find. The problem isn't unique to Covid toes or to social media. Dermatology, the medical specialty devoted to treating diseases of the skin, has a problem with brown and black skin. Though progress has been made in recent years, most textbooks that serve as road maps for diagnosing skin disorders often don't include images of skin conditions as they appear on people of color. That's a glaring omission that can lead to misdiagnoses and unnecessary suffering, because many key characteristics of skin disorders — like red patches and purple blotches — may appear differently on people with different complexions, experts say. "Pattern recognition is central to dermatology, and a lot of the pattern recognition is training your eye to recognize certain colors that trigger you to think of certain diseases," said Dr. Jenna Lester, director of the skin of color program at the University of California, San Francisco. "But the color in question is impacted by the surrounding color," she said. "It can look different in darker skin. If you're only trained to look at something in one color, you won't recognize it in another color."

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Cassiopea receives FDA approval for Winlevi® (clascoterone cream 1%), first-in-class topical acne treatment targeting the androgen receptor. August 27, 2020. Cassiopea. https://www.cassiopea.com/2020/08/27/cassiopea-receives-fda-approval-for-winlevi-clascoterone-cream-1-first-in-class-topical-acne-treatment-targeting-the-androgen-receptor/

The approval of WINLEVI brings the first truly new mechanism of action in acne treatment in nearly 40 years. Cassiopea SpA (SIX: SKIN), today announced that the United States Food and Drug Administration (FDA) approved Winlevi® (clascoterone cream 1%) for the treatment of acne in patients 12 years and older. Notwithstanding acne being the most prevalent skin condition in the U.S. affecting up to 50 million Americans annually, the last FDA approval of an acne drug with a new mechanism of action (MOA) occurred nearly 40 years ago. Acne is a multifactorial skin condition, affected by four distinct pathways: excess oil (sebum) production, clogged pores (hyperkeratinization), bacteria growth (C. acnes), and inflammation. Topical treatment options that target androgens, which largely drive sebum production and inflammation, presented a significant unmet need in the acne treatment market until now. "The approval of WINLEVI is an exciting breakthrough in acne treatment. This game-changing topical drug offers a non-antibiotic approach to people with acne, by targeting the androgen receptors directly in the skin. It fills a longstanding gap in acne therapy." said Michael Gold, M.D., Investigator and Medical Director, Gold Skin Care Center and Tennessee Clinical Research Center, see a brief video here. "After 40 years, it provides a much-anticipated, complementary new approach to treat acne." Cassiopea's first-in-class topical androgen receptor inhibitor, WINLEVI, tackles the androgen hormone component of acne in both males and females. Androgen receptor inhibitors act by limiting the effects of these hormones on increasing sebum production and inflammation. In pivotal clinical trials, WINLEVI demonstrated treatment success and reductions in acne lesions and was well tolerated when used twice a day. The most frequently observed local skin reaction was mild erythema. Diana Harbort, CEO of Cassiopea, said: "This milestone approval marks the introduction of a new class of topical medication in Dermatology. Dermatologists

have said targeting androgen hormonal activity in the skin is 'the holy grail' of acne treatment for both males and females. We are proud to bring this new innovation to acne patients. This approval rewards many years of hard work and positions Cassiopea as a leader in Dermatology. Now we look forward to expanding our franchise and advancing our next investigational drug candidate for androgenetic alopecia." WINLEVI is expected to be available in the United States in early 2021. Complete prescribing information is available on www.WINLEVI.com.
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Galderma launches new rosacea public awareness campaign. August 20, 2020. DermWire, Practical Dermatology. https://practicaldermatology.com/news/galderma-launches-new-rosacea-public-awareness-campaign?c4src=news-landing:feed
Face Up to Rosacea offers rosacea patients information to help them navigate their treatment journey, including skincare tips, treatment information, lifestyle hacks, dermatologist advice and stories from other people living with rosacea. Galderma is partnering with rosacea patient and celebrity stylist Brad Goreski for the national awareness campaign, Face Up to Rosacea, to encourage people frustrated with this chronic skin condition to take action by consulting with a dermatologist. Face Up to Rosacea offers rosacea patients information to help them navigate their treatment journey, including skincare tips, treatment information, lifestyle hacks, dermatologist advice and stories from other people living with rosacea. "I want to encourage others to 'Face Up to Rosacea' and stop feeling self-conscious or powerless about their skin," says Goreski in a news release. "Rosacea affected me for a large portion of my life to the point where in the past, I would find myself avoiding photos at work and with my family and friends. Eventually, enough was enough for me, so I spoke with my dermatologist to discuss a treatment plan that was right for me." "While rosacea can be frustrating and unpredictable, it can be effectively managed with prescription treatment," said New York City dermatologist Shereene Idriss, MD. "I'm excited to partner with Galderma and highlight Brad's story to help spread the word about rosacea and the importance of proactive management." "Galderma is committed to providing safe and effective treatment options and educational resources for people with rosacea," adds Matt Gambino, Director, Rosacea Franchise, Galderma Laboratories, L.P. "Through this national awareness campaign, we hope to empower those living with rosacea to understand they are not alone and encourage a discussion with a dermatologist to develop a treatment plan."

New Medical Research

The effects of once-daily tretinoin 0.05% lotion on quality of life in patients with moderate-to-severe acne vulgaris. Tyring SK, Kircik L, Pariser DM, et al. Am J Clin Dermatol. 2020 Sep 4. doi: 10.1007/s40257-020-00559-3. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32886337/
Background: In two phase III clinical trials of patients with moderate-to-severe acne (NCT02932306, NCT02965456), tretinoin 0.05% lotion reduced inflammatory and noninflammatory lesions relative to vehicle lotion, with low potential for cutaneous irritation. Objective: Data from these studies were analyzed post hoc to investigate the effects of tretinoin 0.05% lotion on patient-reported quality of life, as assessed using the Acne-Specific Quality of Life Questionnaire (Acne-QoL). Methods: Mean changes from baseline to week 12 in Acne-QoL scores were analyzed in the pooled intent-to-treat population and a subgroup with treatment success (≥ 2-grade improvement on the Evaluator's Global Severity Scale and rating of "clear" or "almost clear"). Pearson correlations were conducted in the pooled intent-to-treat population to assess the relationship between the Acne-QoL acne symptoms domain and each of the other three domains. Results: In the pooled intent-to-treat population (n = 1640), greater mean improvements were found with tretinoin 0.05% lotion vs vehicle in all four domains: self-perception (mean change: 7.4 vs 6.7); role-emotional (6.8 vs 6.0); role-social (4.8 vs 4.6); acne symptoms (6.5 vs 5.6); all $p < 0.05$. Relative to the intent-to-treat

population, participants who experienced treatment success with tretinoin 0.05% lotion had higher (better) mean Acne-QoL scores at week 12. Correlations between acne symptoms and the other three domains were found at baseline and week 12 ($p < 0.05$). Conclusions: Participants with moderate-to-severe acne reported better quality of life after 12 weeks of treatment with tretinoin 0.05% lotion. Clinical improvements in acne symptoms may have contributed to these outcomes. Trial registration: ClinicalTrials.gov: NCT02932306, NCT02965456.

Effectiveness and safety of 2940nm multifractionaler: YAG laser on acne scars. Cenk H, Sarac G. Dermatol Ther. 2020 Sep 3;e14270. doi: 10.1111/dth.14270. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32882085/
Introduction: Er: YAG laser treatment has been used in resurfacing the acne scars for a long time, however, we could not find any study reporting the recovery rates after each session of the treatment. In this study, we aimed to report the improvement rates after each session. Materials and methods: We retrospectively analyzed the data of 35 patients with acne scars treated with fractional ablative Er: YAG laser. The patients received 1 to 4 sessions of treatment, with 4-week intervals and improvement rates were recorded after each session. Data is available on request from the authors. Results: The improvement rate of the lesions varied between 1% and 25% in 34 patients at the end of the first session, while in one patient, the improvement rate was detected as 26-50%. At the end of the 4th. session, the rate of improvement was 26-50% in 14 out of 24 patients and 51-75% in ten patients. None of the patients showed a 76% -100% improvement at the end of the 4th. session, whereas 48.6% of the patients were satisfied with the treatment. Conclusion: In patients with a high expectation of an excellent improvement, a higher number of sessions of the laser treatment and/or combination treatments with different treatment methods should be planned.
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Efficacy and tolerability of a cream containing modified glutathione (GSH-C4), beta-Glycyrrhetic and azelaic acids in mild-to-moderate rosacea: A pilot, assessor-blinded, VISIA and ANTERA 3-D analysis, two-center study (The "Rosazel" Trial). Dall'Oglio F, Puviani M, Milani M, Micali G. J Cosmet Dermatol. 2020 Sep 3. doi: 10.1111/jocd.13707. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32885541/
Introduction: Rosacea is a very common, chronic inflammatory disease characterized by flushing, erythema and inflammatory lesions. Increased oxidative stress plays a relevant pathogenetic role in Rosacea. Intracellular Glutathione (GSH) is the main scavenger protective mechanism against increased oxidative stress. An altered GSH metabolism in Rosacea has been described. GSH-C4 is a modified GSH molecule characterized by a better intracellular bioavailability and longer half-life. A daily cream (E-AR) containing GSH-C4 (0.1%) with beta-Glycyrrhetic (0.5%) and azelaic acids (10%), with an SPF of 30, is available. Study aim and methods: In a pilot, prospective, two-center, assessor-blinded study we evaluate the efficacy and the tolerability of E-AR cream in subjects with mild to moderate Rosacea treated for 8 weeks. The main outcomes were the Investigator Global Assessment (IGA) 7-point score (from 0, completely clear; to 6, severe) and the clinical and instrumental erythema severity score (ESS) (from 0 to 4) evaluated in a blinded fashion (randomly coded photographs) at baseline, after 4 (only clinical) and 8 weeks (clinical and instrumental). VISIA evaluation for erythema and lesion counts and ANTERA 3D analysis for skin haemoglobin concentration (a parameter associated with inflammation) were also performed at the same time points. Analysis of primary outcomes was performed on an intention-to-treat basis. Tolerability was evaluated at week 4 and 8 recording spontaneously reported side effects. Results: Thirty subjects (22 women and 8 men; mean age 38 years) were enrolled after their written informed consent. Twenty-six (87%) subjects completed the study phases. Four subjects stopped prematurely the trial due to low skin tolerability (n=3) or lost to follow-up (n=1). At baseline, mean (SD) IGA score was 2.6(0.9). At week 4, IGA score decreased (NS) to 2.3(1.2). IGA score decreased significantly ($p=0.0001$) at week 8 to 1.2(1) (mean difference 1.3; 95% CI of the difference from 0.9 to 1.7) in comparison with the baseline. The inflammatory mean (SD) lesion count, evaluated clinically, were 5.1(2.5) at baseline, 2.8(1.9) at week

4, and 1.9 (1.7) at week 8 (p=0.0001; ANOVA Test), representing a 63% reduction. This reduction was confirmed by inflammatory lesions count performed on VISIA pictures (from 4.5 at baseline to 1.7 lesions at week 8). Similar evolution was observed for the clinical and instrumental ESS with a reduction of 56% (clinical) and 48% (VISIA), respectively, at week 8 in comparison with the baseline. ANTERA 3D photographs confirmed the positive evolution observed clinically with a significant reduction (-24%) in hemoglobin content: from 1.88 at baseline to 1.44 at week 8. Conclusion: This new GSH-C4, beta-glycyrrethic and azelaic acids cream has shown to be efficacious in mild to moderate rosacea subjects. Local tolerability is in line with other anti-rosacea treatments.

Efficacy and safety of a new topical gel formulation containing retinol encapsulated in glycospheres and hydroxypinacolone retinoate, an antimicrobial peptide, salicylic acid, glycolic acid and niacinamide for the treatment of mild acne: Preliminary results of a 2-month prospective study. Villani A, Annunziata MC, Cinelli E, et al. G Ital Dermatol Venereol. 2020 Sep 1. doi: 10.23736/S0392-0488.20.06581-5. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32869963/

Background: Acne vulgaris is a common and chronic skin disease that impacts on physical and psychological perceptions. Combination therapy with topical retinoids and antimicrobial agent is considered the preferred approach for most of the subjects affected by mild-to-moderate acne. A correct therapeutic management should include a prolonged treatment to ensure therapeutic success and to prevent recurrences. The aim of this study was to evaluate the efficacy and tolerability of a new topical gel formulation that combines retinol encapsulated in glycospheres and hydroxypinacolone retinoate, associated with an anti-microbial peptide (BIOPEP-15) salicylic acid, glycolic acid, and niacinamide as monotherapy in mild acne vulgaris. Methods: A 2-month prospective study was conducted at the Dermatology Unit of the University of Federico II Naples. Twenty-five patients aged from 14 to 30 years with mild acne of the face (GAGS score≤18) were consecutively enrolled. Each patient was asked to apply the gel formulation once daily in the evening for 8 weeks. The number of acne lesions with VISIA camera system, the Global Acne Grading System (GAGS) score, Trans Epidermal Water loss (TEWL), skin colorimetry (X-rite Spectrocolorimeter), reflectance confocal microscopy exam were evaluated at baseline, after 4 and 8 weeks of treatment for each patient. Tolerability and safety of the product were also evaluated. Results: Twenty-five female patients with a median age of 23.4 were enrolled. Twenty-two (88%) completed the 2-month treatment period visits. At baseline the Total acne lesion number, mean (SD), was 5.5 (4) and the GAG score 9 (4). A significant (p=0.001) reduction in number of total acne lesions was observed at week 4 (-57%) and at week 8 (-80%). All patients presented a significant reduction of the GAGS score values: -42% at week 4 and -78% at week 8, confirming the clinical efficacy of the product. At baseline TEWL was 10.2 g/m2/h (1.3) and 10.7(1.4) at week 8, thus showing that the gel did not impair the skin barrier function. Skin colorimetry was significantly (p=0.0015) reduced by the treatment in comparison with baseline (62 vs. 58) Efficacy of the gel formulation was also confirmed with RCM exams, showing a reduction of dermal inflammation and exocytosis, and an improvement of infundibular hyperkeratinization. We observed that adherence to treatment correlated positively with the improvement of the single parameters. Moreover, side effects such as erythema, dryness, and excessive xerosis were not reported, resulting in a complete adherence to the treatment. Conclusions: Our findings provide favorable evidences of the efficacy and safety of this new product as a first line treatment in patients with mild acne, or, as a maintenance therapy for prolonged periods after the suspension of a systemic treatment. Furthermore, the tolerability of this topical product and the absence of any side effects increased the adherence to the therapy.

Clinical selection criteria in new clinical trials of hidradenitis suppurativa: external validity and implications on the daily clinical practice. Montero-Vilchez T, Salvador-Rodriguez L, Sanchez-Diaz M, et al. Dermatol Ther. 2020 Aug 29;e14254. doi: 10.1111/dth.14254. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32860480/

Background: There are an increasing number of biologic drugs in the pipeline for treating hidradenitis suppurativa

(HS). Clinical trials for these drugs usually share the same clinical selection criteria. Objectives: 1)To describe the clinical profile of HS patients receiving first-line biologic treatment in an HS clinic setting, 2)to assess how this population would meet clinical criteria to participate in a clinical trial and 3)to assess treatment effectiveness at week 16 in eligible vs. non-eligible patients. Methods: Prospective observational study. Patients were grouped according to their eligibility for clinical trials. The effectiveness of adalimumab was assessed by HiSCR, IHS4-category-change and a-50%-reduction on IHS4 at week 16. Results: Thirty-eight patients were included in the study: eight (21.05%) were eligible for clinical trials and 30 (78.95%) were not. The main reason for non-eligibility was not having an AN count≥5. Both groups presented similar number of draining tunnels. Effectiveness at week 16 was lower in non-eligible than eligible patients when evaluated by HiSCR-response but similar if evaluated by the IHS4-category-change or the 50%-reduction in IHS4. Conclusion: In our population, the external validity of current eligibility criteria for clinical trials is low. Most patients receiving adalimumab in real-life setting would not be eligible for clinical trials.
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Efficacy and tolerability of low-dose spironolactone and topical benzoyl peroxide in adult female acne: A randomized, double-blind, placebo-controlled trial. Patiyasikunt M, Chancheewa B, Asawanonda P, et al. J Dermatol. 2020 Aug 28. doi: 10.1111/1346-8138.15559. Online ahead of print.
https://pubmed.ncbi.nlm.nih.gov/32857471/
Effective therapies for adult female acne (AFA) are limited. Oral spironolactone (SPL), 100-200 mg/day, is currently used off-label to treat AFA. However, high-dose SPL results in clinically significant side-effects which prevent widespread use in clinical practice. The efficacy of low-dose spironolactone in AFA is unknown. We examined the efficacy and tolerability of low-dose (25-50 mg/day) oral SPL in Thai women with moderate AFA. A randomized, double-blind, placebo-controlled trial was conducted for 12 weeks. Moderate AFA patients aged between 25 and 45 years received a combination of daily topical benzoyl peroxide (BP) 2.5% plus either SPL 25 mg (SPL25 group), SPL 50 mg (SPL50 group) or placebo. We performed total acne counts and Adult Female Acne Scoring Tool (AFAST) grading at 4-week intervals. The success rate, defined as the proportion of participants achieving a "clear/almost clear" AFAST grade by the end of week 12, was considered as the main outcome. Treatment-related adverse events (TRAE) were recorded. We enrolled 63 participants in the study. The total acne counts decreased significantly in all three groups ($P < 0.05$) as compared with baseline. Participants in the SPL50 group had a significantly higher success rate than those in the placebo group ($P < 0.05$). Serum potassium and creatinine levels showed no significant changes with treatment or between groups. A small number of participants in SPL25 and SPL50 reported mild and temporary TRAE, such as menstrual irregularities, breast tenderness and dizziness. The combination of SPL 50 mg/day and topical BP proved effective in improving moderate AFA in Thai women, with an acceptable side-effect profile. We propose this regimen as an option for treating moderate AFA.

Inhibitory effects of a sargassum miyabei yendo on cutibacterium acnes- induced skin inflammation. Yim MJ, Lee JM, Kim HS, et al. Nutrients. 2020 Aug 27;12(9):E2620. doi: 10.3390/nu12092620.
https://pubmed.ncbi.nlm.nih.gov/32867396/
Acne vulgaris is a chronic inflammatory condition of skin sebaceous follicles. To explore its effects on acne vulgaris, we investigated the antibacterial and anti-inflammatory activities of Sargassum miyabei Yendo (a brown alga) ethanolic extract (SMYEE) on Cutibacterium acnes (C. acnes)-stimulated inflammatory responses, both in vivo and in vitro. To induce inflammation in vivo, C. acnes was intradermally injected into the dorsal skin of mice, to which SMYEE was applied. The antimicrobial activity of SMYEE was evaluated by the determination of minimum inhibitory concentrations (MICs). To explore in vitro anti-inflammatory effects, HaCaT cells were stimulated with C. acnes after treatment with SMYEE. The levels of IL-8 and the underlying molecular effects in C. acnes-stimulated HaCaT cells

were assessed by enzyme-linked immunosorbent assay, Western blotting, and an electrophoretic mobility shift assay. Mouse skin lesions improved after treatment with SMYEE (50 μg/mouse). Neutrophil infiltration was significantly reduced in SMYEE-treated compared to SMYEE-untreated skin lesions. SMYEE reversed the C. acnes-induced increase in IL-8 levels in HaCaT cells and suppressed dHL-60 cell migration. SMYEE also inhibited C. acnes-induced phosphorylation of the extracellular signal-regulated kinase and inhibited activator protein-1 signaling. SMYEE may be a useful treatment for C. acnes-induced acne vulgaris.
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Extracts from cephalaria uralensis (murray) roem. & schult. and cephalaria gigantea (ledeb.) bobrov as potential agents for treatment of acne Vulgaris: Chemical characterization and in vitro biological evaluation. Chrząszcz M, Miazga-Karska M, Klimek K, et al. Antioxidants (Basel). 2020 Aug 26;9(9):E796. doi: 10.3390/antiox9090796. https://pubmed.ncbi.nlm.nih.gov/32859126/
The aim of this study was to compare the chemical composition, as well as antioxidant, anti-inflammatory, antiacne, and cytotoxic activites of various extracts of Cephalaria gigantea and C. uralensis. It is worth underlining that we are the first to characterize the composition and evaluate the biological properties of extracts from Cephalaria gigantea and C. uralensis. Thus, the LC-DAD-MS3 analysis revealed the presence of 41 natural products in studied extracts. The 5-O-caffeoylquinic acid, isoorinetin, and swertiajaponin were the main detected compounds. Among the tested samples, ethanol extract of the aerial parts of C. uralensis (CUE) possessed the most suitable biological properties. It exhibited moderate ability to scavenge free radicals and good capacity to inhibit cyclooxygenase-1, as well as cyclooxygenase-2. Moreover, CUE possessed moderate antibacterial activity against all tested bacterial strains (S. aureus, S. epidermidis, and P. acnes), and importantly, it was non-toxic towards normal skin fibroblasts. Taking into account the value of calculated therapeutic index (>10), it is worth noting that CUE can be subjected to in vivo study. Thus, CUE constitutes a very promising antiacne agent.
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Sarecycline interferes with tRNA accommodation and tethers mRNA to the 70S ribosome. Batool Z, Lomakin IB, Polikanov YS, Bunick CG. Proc Natl Acad Sci U S A. 2020 Aug 25;117(34):20530-20537. doi: 10.1073/pnas.2008671117. Epub 2020 Aug 12. https://pubmed.ncbi.nlm.nih.gov/32817463/
Sarecycline is a new narrow-spectrum tetracycline-class antibiotic approved for the treatment of acne vulgaris. Tetracyclines share a common four-ring naphthacene core and inhibit protein synthesis by interacting with the 70S bacterial ribosome. Sarecycline is distinguished chemically from other tetracyclines because it has a 7-[[methoxy(methyl)amino]methyl] group attached at the C7 position of ring D. To investigate the functional role of this C7 moiety, we determined the X-ray crystal structure of sarecycline bound to the Thermus thermophilus 70S ribosome. Our 2.8-Å resolution structure revealed that sarecycline binds at the canonical tetracycline binding site located in the decoding center of the small ribosomal subunit. Importantly, unlike other tetracyclines, the unique C7 extension of sarecycline extends into the messenger RNA (mRNA) channel to form a direct interaction with the A-site codon to possibly interfere with mRNA movement through the channel and/or disrupt A-site codon-anticodon interaction. Based on our biochemical studies, sarecycline appears to be a more potent initiation inhibitor compared to other tetracyclines, possibly due to drug interactions with the mRNA, thereby blocking accommodation of the first aminoacyl transfer RNA (tRNA) into the A site. Overall, our structural and biochemical findings rationalize the role of the unique C7 moiety of sarecycline in antibiotic action.
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Active pharmaceutical ingredient poly(ionic liquid)-based microneedles for the treatment of skin acne infection. Zhang T, Sun B, Guo J, et al. Acta Biomater. 2020 Aug 25;S1742-7061(20)30483-9. doi: 10.1016/j.actbio.2020.08.023. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32853804/

As an inflammatory skin disease of pilosebaceous follicles, Propionibacterium acnes (P. acnes) can aggravate local inflammatory responses and forms acne lesions. However, due to the skin barrier, various transdermal measures other than antibiotic creams are necessary. Microneedle (MN) patches are emerging platforms for the transdermal delivery of various therapeutics since it can effectively create transport pathways in the epidermis. Herein, we develop an active pharmaceutical ingredient poly(ionic liquid) (API PIL)-based MN patches containing salicylic acid (SA). The PIL-based MNs are simply prepared through photo-crosslinking of an imidazolium-type ionic liquid (IL) monomer in MN micro-molds, and following by anion exchange with salicylic acid anions (SA-). The fabricated SA-loaded PIL-MNs exhibited therapeutic efficiency in the topical treatment of P. acnes infection in vitro and in vivo. These active pharmaceutical ingredient PIL-based MNs can improve acne treatment, demonstrating potential applications for skin diseases. STATEMENT OF SIGNIFICANCE: Microneedle (MN) patches can be used as platforms for transdermal delivery of various therapeutics to treat bacterial infection. Here, a facile strategy was developed to synthesize active pharmaceutical ingredient poly(ionic liquid)-based microneedle patches by anion-exchange with salicylic acid anion (SA-). The fabricated SA-loaded PIL-MNs are active on not only anti-bacteria but also anti-inflammation in P. acnes treated mice, and may have potential applications for skin acne infection.

Clinical and non-invasive instrumental evaluation of the efficacy of a non-steroid anti-inflammatory 8-beta Glycyrrhetinic Acid cream for the treatment of erythema in rosacea. Cameli N, Mariano M, Zanniello R, Berardesca E. Dermatol Ther. 2020 Aug 24;e14224. doi: 10.1111/dth.14224. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32833275/

Background: Rosacea is a very common chronic facial dermatosis characterized by a multiphase evolution. Inflammation is an important compound in rosacea, due to inflammatory reactions to cutaneous microorganisms such as Demodex Follicolorum but also to ultraviolet damage that generates reactive oxygen species. Objective: To evaluate the efficacy and tolerability of a non-steroid anti-inflammatory 18-beta Glycyrrhetinic Acid cream for the treatment of mild rosacea by means of non-invasive methods. Methods: A total of 24 subjects suffering from erythemato-telangiectatic or mild papulo-pustular rosacea were recruited to enter the trial. 12 patient applied an anti-inflammatory cream with 18-beta Glycyrrhetinic acid twice daily for 20 days, 12 patient recruited as control, applied the same formulation without 18-beta Glycyrrhetinic acid. Results: After 10 days treatment, in the patient sample who applied the 18-beta Glycyrrhetinic acid cream a significant reduction of erythema was recorded, the mean change from baseline showed an increase in hydration level of the skin surface but it was not statistically significant. Conclusions: The use of 18-beta Glycyrrhetinic Acid cream can be helpful in managing symptoms and condition of rosacea skin, especially in the management of erythema.

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Clinical Reviews

Antibiotic resistance in acne: Mechanisms, complications and management. Aslan Kayiran M, Karadag AS, Al-Khuzaei S, et al. Am J Clin Dermatol. 2020 Sep 5. doi: 10.1007/s40257-020-00556-6. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32889707/

Antibiotic resistance in acne was first observed in the 1970s, and since the 1980s has become a major concern in dermatologic daily practice. The mechanisms for this type of resistance include biofilm formation that promotes virulence and the transmission of resistant bacterial strains. Genetic mutations with modification of ribosomal RNA,

alteration in efflux pumps, and enzymatic inactivation are able to create resistance to tetracyclines and macrolides. The state of art in acne treatment is no longer to use antimicrobials as monotherapy. There should be a time limit for its use plus the employment of non-antibiotic maintenance. Earlier initiation of oral isotretinoin therapy should be considered in patients with insufficient response to antimicrobials, severe acne, or a history of repeated antimicrobial use. A better understanding of acne pathogenesis, the subtypes of Propionibacterium (also known as Cutibacterium) acnes, homeostasis of the skin microbiota, and the mechanisms of antibiotic resistance would be useful in the selection of narrow-spectrum or species-specific antimicrobials, as well as the non-antimicrobial, anti-inflammatory treatment of acne. A number of novel treatments awaiting clinical proof may include the use of bacteriophages, natural or synthetic antimicrobial peptides, probiotics, and biofilm-targeting agents, as well as the reassessment of phototherapy.

Isotretinoin in the management of acne vulgaris: Practical prescribing. Fallah H, Rademaker M. Int J Dermatol. 2020 Aug 29. doi: 10.1111/ijd.15089. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32860434/
Since it was first approved for use in 1982, isotretinoin has revolutionized the management of acne vulgaris. Despite almost four decades of widespread use, uncertainty still exists regarding the manner in which it is best prescribed. In this review, we provide an update on the pharmacokinetics, mechanism of action, contraindications, interactions, and appropriate dosing schedule of isotretinoin in the treatment of acne. We also discuss the safety of performing concurrent dermatological procedures in patients taking isotretinoin.

Serum zinc levels and efficacy of zinc treatment in acne vulgaris: A systematic review and meta-analysis. Yee BE, Richards P, Sui JY, Marsch AF. Dermatol Ther. 2020 Aug 29;e14252. doi: 10.1111/dth.14252. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32860489/
Background: Oral and topical zinc have been used for the treatment of acne, but there is a lack of definitive evidence for their efficacy. Objectives: To (1) determine if mean serum zinc levels differ between acne patients and controls and (2) to determine the efficacy of zinc preparations in the treatment of acne. Methods: A systematic review and meta-analysis was performed according to recommended PRISMA [Preferred Reporting Items for Systematic Reviews and Meta-Analyses] guidelines. Results: Subjects with acne had significantly lower serum zinc levels compared to controls. Patients who were treated with zinc had a significant improvement in mean inflammatory papule count compared to those who were not treated with zinc. There was no significant difference in the incidence of side effects in zinc supplementation versus comparators. Conclusions: Acne patients have decreased serum zinc levels. Zinc is effective for the treatment of acne, particularly at decreasing the number of inflammatory papules, when used as monotherapy or as an adjunctive treatment.
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Recent advances regarding the therapeutic potential of adapalene. Rusu A, Tanase C, Pascu GA, Todoran N. Pharmaceuticals (Basel). 2020 Aug 28;13(9):E217. doi: 10.3390/ph13090217. https://pubmed.ncbi.nlm.nih.gov/32872149/
Adapalene (ADP) is a representative of the third retinoids generation and successfully used in first-line acne treatment. ADP binds to retinoic acid nuclear receptors. The comedolytic, anti-inflammatory, antiproliferative, and immunomodulatory are the known ADP effects. Its safety profile is an advantage over other retinoids. ADP recently was found to be effective in the treatment of several dermatological diseases and photoaging besides the utility in the treatment of acne vulgaris. New biological effects of adapalene with therapeutic potential are highlighted in this review paper. Thus, adapalene could be a valuable therapeutic drug into the treatment of several types of cancer. Additionally, some neurodegenerative diseases could be treated with a suitable formulation for intravenous

administration. The antibacterial activity against methicillin-resistant Staphylococcus aureus of an analogue of ADP has been proven. In different therapeutic schemes, ADP is more effective in combination with other active substances. New topical combinations with adapalene include ketoconazole (antifungal), mometasone furoate (anti-inflammatory corticosteroid), nadifloxacin (fluoroquinolone), and alfa and beta hydroxy acids. Combination with oral drugs is a new trend that enhances the properties of topical formulations with adapalene. Several studies have investigated the effects of ADP in co-administration with azithromycin, doxycycline, faropenem, isotretinoin, and valganciclovir. Innovative formulations of ADP also aim to achieve a better bioavailability, increased efficacy, and reduced side effects. In this review, we have highlighted the current studies on adapalene regarding biological effects useful in various treatment types. Adapalene has not been exploited yet to its full biological potential.
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Spironolactone in dermatology: Uses in acne and beyond. Searle TN, Al-Niaimi F, Ali FR. Clin Exp Dermatol. 2020 Aug 26. doi: 10.1111/ced.14340. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32844462/
Spironolactone is a synthetic aldosterone receptor antagonist, with a role off-label in various dermatological conditions. Its antiandrogenic properties make it suitable for diseases in which excess androgen production results in unwanted and psychologically distressing manifestations in susceptible females. Treatment with spironolactone aims to attenuate androgen-mediated conditions including acne, hidradenitis suppurativa, female pattern hair loss and hirsutism. We discuss the emerging utility of spironolactone in dermatology, its potential adverse effects and considerations for monitoring.

Sarecycline: A review of preclinical and clinical evidence. Moore AY, Del Rosso J, Johnson JL, Grada A. Clin Cosmet Investig Dermatol. 2020 Aug 13;13:553-560. doi: 10.2147/CCID.S190473. eCollection 2020. https://pubmed.ncbi.nlm.nih.gov/32884318/
Sarecycline is a tetracycline-derived oral antibiotic, specifically designed for acne, and is approved by the Food and Drug Administration (FDA) in 2018 for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris (AV) in patients 9 years of age and older. It has been decades since a novel systemic antibiotic was approved to treat AV, a disease that affects up to 90% of teenagers and young adults worldwide and lasts well into adulthood. Sarecycline holds promise to yield fewer side effects than other commonly used broad-spectrum tetracyclines, including minocycline and doxycycline. The narrower spectrum of antibacterial activity of sarecycline, which specifically targets C. acnes and some Gram-positive bacteria with little or no activity against Gram-negative bacteria, suggests not only the potential for reduced emergence of antibiotic-resistant bacterial strains but also less disruption of the human gut microflora. Here, we review the key preclinical and clinical evidence on sarecycline.
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Doxycycline-induced autoimmune hepatitis. Pan JJ, Promrat K. ACG Case Rep J. 2020 Aug 10;7(8):e00440. doi: 10.14309/crj.0000000000000440. eCollection 2020 Aug. https://pubmed.ncbi.nlm.nih.gov/32821768/
Doxycycline and minocycline are tetracyclines with the potential to cause hepatoxicity. Although autoimmune-like hepatitis from minocycline is well-described, doxycycline-induced autoimmune hepatitis (DIAH) has only been described once. We report a rare case of DIAH with elevated liver enzymes over 5 times the normal upper limit, elevated immunoglobulin G, and high titers of antismooth muscle antibody and antinuclear antibody. By stopping doxycycline, our patient's liver enzymes normalized and immunoglobulin G and autoantibody titers rapidly down trended. As long-term doxycycline therapy becomes more prevalent to treat acne vulgaris and other skin conditions, DIAH may become more prevalent and recognized.
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A meta-analysis of fractional CO 2 laser combined with PRP in the treatment of acne scar. Wu N, Sun H, Sun Q, et al. Lasers Med Sci. 2020 Aug 10. doi: 10.1007/s10103-020-03105-z. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/32827074/

This study aimed to analyze the effectiveness and safety of ablative fractional carbon dioxide laser systems (CO2 AFL) combined with autologous platelet-rich plasma (PRP) in the treatment of acne scars through the retrieval and collection of related literature to further guide the treatment of acne scars. We searched Web of Science, PubMed, Embase, Wanfang Data, Chinese National Knowledge Infrastructure, and VIP Database. All randomized and nonrandomized controlled trials on CO2 AFL combined with PRP in the treatment of acne scars were included, and Revman5.3 systematic review software was used in the meta-analysis. Nine studies were included in this meta-analysis. The data analysis results showed that the CO2 AFL combined with PRP treatment group showed significantly better results than the pure CO2 AFL control group in terms of clinical improvement score, clinical improvement rate, patient satisfaction, and crusting period. The results of this meta-analysis showed that CO2 AFL combined with PRP in the treatment of acne scars is more effective and safer than CO2 AFL alone.

Oral metformin for treating dermatological diseases: A systematic review. Sung CT, Chao T, Lee A, et al. J Drugs Dermatol. 2020 Aug 1;19(8):713-720. doi: 10.36849/JDD.2020.4874. https://pubmed.ncbi.nlm.nih.gov/32845585/

Introduction: Metformin is an antihyperglycemic medication most commonly used to treat Type II Diabetes Mellitus with promising off-label application for the treatment of hidradenitis suppurativa, psoriasis, acne, acanthosis nigricans, and hirsutism. Objective: To comprehensively assess evidence regarding the use of metformin for treating primary cutaneous disorders. Materials and Methods: A systematic literature search was conducted through PubMed, Cochrane, Web of Science, and CINAHL to identify the role of metformin in primary skin disease. Results: Sixty-four studies met inclusion criteria. Metformin demonstrates promising clinical response and favorable safety profile for treatment of HS, with most patients experiencing a decrease in frequency or severity of HS flares, and some experiencing full resolution of HS lesions. Patients with psoriasis treated with metformin experienced quantifiable clinical responses. Application of metformin on polycystic ovarian disease (PCOS) related acne, acanthosis nigricans, and hirsutism yielded mixed clinical results. No serious adverse effects were reported. Conclusion: Metformin is safe and efficacious and may be considered as an adjunctive therapy for the treatment of psoriasis and hidradenitis suppurativa in addition to first line therapies as well as PCOS related acne, acanthosis nigricans, and hirsutism.

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