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AARS News

10th Annual AARS Scientific Symposium Registration is live! We encourage you to register now for our free luncheon symposium to be held in person on Wednesday, May 18, 2022 from 11:00 AM – 1:00 PM at the Oregon Convention Center. Co-chaired by AARS Past Presidents J. Mark Jackson and Lawrence Eichenfield, it's sure to be a great afternoon of acne, hidradenitis suppurativa, and rosacea research highlights. This annual event is held in conjunction with the Society for Investigative Dermatology meeting and is a great chance to network with AARS members and researchers! Free registration to reserve your spot: [Click Here to Register!](#)

AARS BoD Member Emmy Graber invites you to earn free CME! AARS Members are invited to attend two free CME meetings on acne, rosacea and acne scarring. These will be held in person on Friday, June 24, 2022 and virtually on Tuesday, October 18, 2022. For further details and to register online and view more information, proceed to this website today: <https://armmeeting.com/>

Industry News

Phase 3 data: Sun Pharma's Winlevi is safe and effective acne Tx. March 26, 2022. DermWire, Practical Dermatology. <https://practicaldermatology.com/news/phase-3-data-sun-pharmas-winlevi-is-safe-and-effective-acne-tx?c4src=news-landing:feed>

The new data supports therapeutic rationale for first-in-class androgen receptor inhibitor. Results from two Phase 3 pivotal clinical trials showed favorable safety and efficacy data for Winlevi (clascoterone) cream 1% in patients with acne aged 12 years and older. The findings were presented at the American Academy of Dermatology (AAD) 2022 Annual Meeting in Boston. The two multicenter, randomized, double-blind pivotal Phase 3 trials enrolled more than 1440 subjects with moderate-to-severe acne vulgaris who received either WINLEVI or placebo for 12 weeks. The primary efficacy endpoints were 1) the proportion of patients achieving "success," defined as an Investigator Global Assessment (IGA) score of 0 ("clear") or 1 ("almost clear"), with at least a 2-point reduction in IGA score from baseline; and 2) absolute change from baseline in non-inflammatory lesion counts (NILC) and inflammatory lesion counts (ILC) at Week 12. Safety was assessed from local skin reactions (LSRs) and treatment-emergent adverse events (TEAEs) through Week 12 (measured at baseline and at Weeks 4, 8, and 12). In the two studies, 18.8 percent and 20.9 percent of Winlevi-treated patients achieved success based on IGA at Week 12, compared with 8.7 percent and 6.6 percent of patients receiving placebo ($P < 0.01$). The mean absolute change from baseline in NILCs at Week 12 was -20.4 and -19.5 for patients treated with Winlevi, versus -13.0 and -10.8 for placebo-treated patients ($P \leq 0.0001$). The mean absolute change from baseline in ILCs at Week 12 was -19.3 and -20.1 in the Winlevi groups, compared to -15.4 and -12.6 in the two studies' placebo groups ($P < 0.01$). The safety profile of Winlevi was similar to that of placebo in the two studies. TEAEs occurred in 38 (11.1%) and 41 (11.2%) of Winlevi-treated patients and in 41 (11.7%) and 50 (13.8%) of those who received placebo. No severe or serious TEAEs occurred in any patient treated with Winlevi. The most frequently reported TEAEs were nasopharyngitis (1.8% and 3.7% for Winlevi, 1.1% and 1.9% for placebo), headache (0.6% and 0.3% for Winlevi, 1.1% and 0.8% for placebo), and oropharyngeal pain (0.6% and 0.3% for Winlevi, 1.1% and 1.1% in both placebo arms). In both studies, the frequencies of each LSR were similar between treatment groups, and the majority of patients did not experience each reaction. The most frequent LSRs were erythema (redness) and scaling/dryness, with the majority of reactions characterized as minimal or mild. "The data presented at AAD 2022 add to the growing body of evidence supporting the use of Winlevi as a foundational acne treatment," says Nicholas Squitieri, MD, Associate Vice President of Medical Affairs at Sun Pharma, and co-author

of the AAD poster presentation, in a news release. "We look forward to further exploring its clinical utility as we conduct more studies and data analyses." "Before Winlevi became available, there was no topical medication available that was able to reduce sebum production, which is a major cause of acne," adds Hilary Baldwin, MD, Medical Director of the Acne Treatment and Research Center in Brooklyn, NY, and past president of the American Acne and Rosacea Society (AARS). "It is therefore encouraging to see favorable efficacy and safety data results from the latest analysis of the Winlevi Phase 3 clinical trials. This data should also provide dermatologists with confidence that they can use Winlevi to treat both females and males with acne."

Dermwire exclusive: FDA clears Cutera's AviClear acne device. March 25, 2022. DermWire, Practical Dermatology. <https://practicaldermatology.com/news/dermwire-exclusive-fda-clears-cuteras-aviclear-acne-device?c4src=news-landing:feed>

Cutera's AviClear is the first energy device to receive a nod for the treatment of mild, moderate, and severe acne. The U.S. Food and Drug Administration has cleared granted 510(k) clearance to Cutera's AviClear acne device. This is the first energy device to receive a nod for the treatment of mild, moderate, and severe acne. AviClear targets acne at the source by selectively targeting the sebocytes and suppressing sebum production. In addition to reducing existing acne, clinical trials show that future breakout episodes are shorter, less intense, and more infrequent following the AviClear procedure. Further, acne clearance results continue to improve over time, demonstrating the long-term efficacy of this novel treatment. Importantly, no pain mitigation was utilized or required by any clinical study participant. "AviClear significantly shifts the treatment paradigm for acne by offering a safe, drug-free, and effective alternative to what is currently available," David Goldberg, MD, JD clinical-trial investigator for AviClear, tells Dermwire. "I am excited about this device because it has an easy user interface and no significant adverse events were observed in the clinical trials, similarly, I know my patients will be thrilled about this new treatment because it can be performed on all skin types, any time of year, and the results are long-lasting." "Existing device treatments for acne are neither long-lasting nor particularly effective," says Jeffrey S. Dover, MD, FRCPC, board-certified dermatologist and Cutera advisory board member in a news release. "Topical therapies yield temporary results and oral medications present several challenges. AviClear offers patients a safe, well-tolerated, drug-free approach with durable results, which significantly shifts the treatment paradigm for acne." "Physicians and patients have long sought a modern alternative to the acne pills, peels and topicals that have been static for nearly 30 years," adds David Mowry, CEO of Cutera. "Developed with extensive physician and patient input, AviClear was created to redefine the treatment of acne – all without a prescription." AviClear is expected to be made available to physicians throughout the United States over the course of 2022. Doctors and consumers are encouraged to visit www.AviClear.com and sign up for updates on product availability and local treatment providers.

Galderma launches Twyneo in the US. March 25, 2022. DermWire, Practical Dermatology. <https://practicaldermatology.com/news/galderma-launches-twyneo-in-the-us?c4src=news-landing:feed>

Galderma has launched Twyneo (tretinoin and benzoyl peroxide) Cream, 0.1%/3% in the US. The launch takes place during the annual meeting of the American Academy of Dermatology (AAD) Annual Meeting. Twyneo Cream features patented microencapsulation technology that allows the delivery of two ingredients that have not been previously combined and enables their controlled release. It is the first and only 0.1% tretinoin and 3% benzoyl peroxide (BPO) 2-in-1 combination proven to rapidly treat moderate to severe facial acne. "Effective prescription acne treatments currently involve multi-step regimens because there is rarely a single treatment option that addresses the multiple causes of the skin condition. These routines can often result in low adherence, especially among boys," says Caroline Robinson, MD, FAAD, Founder of Tone Dermatology. "TWYNEO Cream may help teens with acne—especially the boys—struggling with generic tretinoin or adhering to complex treatment routines, since it's a once-daily, potent

combination that can be used any time of day.” In clinical trials, some people saw results in as little as two weeks of using Twyneo Cream, and their skin continued to clear over time. These studies demonstrated a 25 percent decrease in pimples at two weeks and a 58–66 percent decrease at 12 weeks. In all, 27–41 percent of people achieved clear or almost clear skin by the end of the trial. More than half of people who used Twyneo Cream were satisfied at two weeks and by 12 weeks of treatment, 8 in 10 subjects were satisfied with their results. Twyneo Cream was well tolerated, and side effects were mild to moderate and decreased over time. The most common side effects occurring in >2% of persons using TWYNEO Cream were application site pain, dryness, erythema (redness), and exfoliation. “Twyneo Cream is a novel and exciting medical advance because its microencapsulation technology enables the combination of BPO with the highest concentration of tretinoin available. While these two treatments can be difficult to tolerate in high concentrations, Twyneo Cream was well tolerated,” says Hillary Baldwin, MD, Medical Director of Acne Treatment & Research Center and principal investigator for the Twyneo Cream clinical trials. “The patented microencapsulation technology in Twyneo Cream segregates and envelopes the active ingredients in silica core shells that keep both crystals separate and stable while gradually releasing onto the skin.” “As a regimen in a bottle that combines two of the most trusted first-line treatments for acne, Twyneo Cream is truly a breakthrough for teens and their parents looking for an acne treatment that fits within a simple skincare routine and provides rapid, noticeable results,” says Heather Chase, Head of Rx Marketing and Customer Experience, Galderma US. “Twyneo Cream is another example of Galderma’s commitment to providing cutting-edge treatments to advance dermatology for every skin story.” Twyneo Cream will be available throughout the US by prescription in Q2. A month’s supply of Twyneo Cream costs \$0 for commercially covered patients or \$60 for uninsured patients with the Galderma CAREConnect savings card. Twyneo Cream may cost less than generic tretinoin alone when using the Galderma CAREConnect savings card.

New Medical Research

Adjunctive treatment for acne vulgaris by tranexamic acid. Charoenwattanayothin A, Saiwichai T, Chaichalotornkul S. *J Cosmet Dermatol.* 2022 Apr 7. doi: 10.1111/jocd.14972. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35388589/>

Background: Acne is a chronic, inflammatory skin disorder of pilosebaceous units. Tranexamic acid (TXA) acts as a plasmin inhibitor to reduce blood loss and is also used to treat rosacea due to its anti-inflammatory effects. Some parts of the pathogenesis of rosacea are similar to inflammatory acne. Objectives: The study aimed to evaluate the efficacy of 10% TXA serum in treating acne and its adverse effects. Methods: A randomized, double-blind, placebo-controlled, split-face study was performed on 18 mild to moderate acne patients. Patients applied 10% TXA serum on one side of the face and placebo on another side twice daily for 8 weeks. Acne lesion counts and adverse effects were evaluated every 2 weeks. Results: Significant differences in total inflammatory acne counts were observed between TXA and placebo since week 4 ($p = 0.008$). TXA mainly reduced papules and pustules, as papule counts significantly decreased since the 8th week ($p = 0.046$) and pustule counts significantly reduced since week 8 ($p = 0.033$). Moreover, physicians also found that TXA serum reduced the redness of the skin, corresponding with the imaging from VISIA® Skin Analysis. The anti-inflammatory effect of TXA resulted in less PIE and PIH. Adverse effects, including erythema and scaling, were treated by applying any moisturizing cream. Conclusion: Topical 10% TXA can reduce inflammatory acne effectively. Adverse effects were minor and treat easily.

The efficacy of probiotic-derived lotion from lactobacillus paracasei MSMC 39-1 in mild to moderate acne vulgaris, randomized controlled trial. Sathikulpakdee S, Kanokrungeee S, Vitheejongjaroen P, et al. *J Cosmet Dermatol.* 2022 Apr 5. doi: 10.1111/jocd.14971. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35384257/>

Background: Probiotics provide benefits for reducing acne. Previous studies showed an anti-inflammatory effect of *Lactobacillus paracasei*. However, the clinical evidence of topical probiotic lotion and acne treatment is still lacking. **Objective:** To evaluate the efficacy and safety of probiotic-derived lotion compared to 2.5 % benzoyl peroxide in the treatment of mild to moderate acne vulgaris. **Methods:** Topical probiotic-derived lotion was formulated from cell-free supernatant of *L. paracasei* MSMC 39-1. In vivo study showed the ability of the supernatant to inhibit both antibiotic-resistance and susceptibility strains of *C. acnes* and inhibit tumor necrosis factor- α . The patients with mild to moderate acne vulgaris on the face were randomized to receive topical probiotic-derived lotion or 2.5 % benzoyl peroxide. Acne lesion counts, erythema index, and side effects were assessed after 2 and 4 weeks of treatment. **Results:** One hundred and four acne vulgaris patients were enrolled. After four weeks of treatment, the inflammatory acne lesion counts and erythema index significantly decreased compared to baseline in both the probiotic lotion group and 2.5 % benzoyl peroxide group ($p < 0.001$ in both groups) without statistically significant difference between the two groups ($p > 0.05$). However, the comedones were not affected in both groups. Four patients (7.69%) treated with probiotic-derived lotion and 14 patients (26.92%) treated with 2.5% benzoyl peroxide reported treatment-associated side effects. **Conclusion:** Probiotic-derived lotion is safe and effective for treating mild to moderate acne vulgaris, a comparable outcome with 2.5% benzoyl peroxide. It could be an alternative treatment of acne with more minor side effects.

Multi-transcriptomic analysis and experimental validation implicate a central role of STAT3 in skin barrier dysfunction induced aggravation of rosacea. Wang Y, Wang B, Huang Y, et al. *J Inflamm Res.* 2022 Mar 31;15:2141-2156. doi: 10.2147/JIR.S356551. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35392024/>

Objective: Rosacea is a chronic inflammatory skin disease with high morbidity. Previous studies have described the contribution of skin barrier dysfunction (SBD) in the progression of rosacea, but the specific mechanism remains unclear. In this study, we aim to investigate the key genes that may involve SBD-mediated rosacea aggravation. **Methods:** In this study, we evaluated the SBD patterns of rosacea based on the expression of 23 skin barrier-related genes (SBRGs) using a consensus clustering analysis and revealed the SBD-mediated immune cells infiltration in rosacea using GSE65914 dataset. The key genes associated with SBD and rosacea progression were identified using WGCNA analysis and then verified in rosacea mice model. **Results:** Two distinct SBD patterns (moderate- and high-SBD patterns) were determined in rosacea. GO, KEGG and GSEA analysis revealed the differently immune-related signal pathways between two SBD patterns in rosacea. The XCell immune cell assays showed that the increased immune infiltration with SBD. Subsequently, the WGCNA analysis identified STAT3 as the hub gene related to rosacea and SBD, and correlation analysis revealed that STAT3 could contribute to the progression of rosacea partly by dysregulating immune infiltration via activating the cytokine/chemokines signal. Finally, the up-regulated STAT3 was verified in the epidermis of rosacea tissues and correlated with SBRGs expression using IHC and epidermal transcriptome data of rosacea. The vivo experiment showed that tape stripping-induced SBD evidently induced the expression of STAT3 and increased CD4+ T cell infiltration in LL37-induced rosacea-like skin lesion in mice. **Conclusion:** In conclusion, our results showed that the destruction of the skin barrier aggravates the inflammation levels and immune infiltration of rosacea partly by activating STAT3-mediated cytokine signal pathways in keratinocytes.

Triple steps acne scar revision technique a new combination therapeutic modality for atrophic acne scars. Mohammed GF, Al-Dhubaibi MS. *J Cosmet Dermatol.* 2022 Mar 29. doi: 10.1111/jocd.14944. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35348282/>

Background: Atrophic acne scarring is an unfortunate, permanent complication of acne vulgaris, associated with significant psychological distress. **Objective:** A new complementary treatment of atrophic acne scars using subcision

and injection of hybrid cooperative complexes of high and low molecular weight hyaluronan (hybrid H-HA/L-HA). Methods: This study included eighty-two patients divided into two groups with predominantly atrophic acne scarring. Group 1 received subcision with saline injection, while group 2 received Triple steps acne scar revision technique (TSASRT). After topical anesthesia, the procedure of combining subcision and hybrid H-HA/L-HA technique was done in which the first step started using subcision technique done to release fibrous cords at the dermal or deep dermal, subcutaneous plane using Nokor needles-18g. The second step is to inject the scar's atrophic dermal component with a 29g needle, applying an average amount of hybrid H-HA/L-HA (0.02-0.1mL) to the dermal component. The third step was to fill the subcised space with hybrid H-HA/L-HA (0.02-0.1 mL) using a 25g cannula. Results: Clinical improvement was achieved in both groups. There were statistically significant improvements in the TSASRT versus subcision ($p \leq 0.05$) in acne scar severity index and qualitative scarring grading system. Conclusion: The triple step acne scar revision technique appears to be a safe and effective way to treat atrophic acne scars on the face.

Efficacy of a one-session fractional picosecond 1064-nm laser for the treatment of atrophic acne scar and enlarged facial pores. Puaratanaarunkon T, Asawanonda P. *J Cosmet Laser Ther.* 2022 Mar 23;1-5. doi: 10.1080/14764172.2022.2055079. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35318885/>

A picosecond-domain laser reportedly elicits positive treatment outcomes for acne scar and enlarged pores, but multiple sessions are often required. We sought to evaluate the efficacy of one-session fractional picosecond 1064-nm laser in treating atrophic acne scar and conspicuous pores. Fifty-nine acne scar patients with skin phototypes III and IV were treated with picosecond 1064-nm laser with microlens array (MLA) (8 mm spot, 0.8 J/cm², 10 Hz) for one session. The efficacy of acne scar was evaluated by Antera® 3D CS, whereas facial pore counts and diameter were evaluated by VISIA-CR and dermoscopic images, respectively. All measurements were performed at baseline, weeks 1, 2, 4 and 6. Acne scar volume and facial pore counts showed a statistically significant reduction at 1 week and subsequent follow-up period when compared to baseline (weeks 1-6; $P < .001$). The volume of acne scars and the number of enlarge pores decreased by 22.03% and 15.13%, respectively. Of note, there was no significant change in diameter of facial pores. The adverse events, including erythema and folliculitis, were mild and short-lived. A single session of picosecond 1064-nm laser with MLA was safe and effective in improving atrophic acne scar and the number of enlarged pores.

Microbotox: A prospective evaluation of dermatological improvement in patients with mild-to-moderate acne and erythematotelangiectatic rosacea. Calvisi L, Diaspro A, Sito G. *J Cosmet Dermatol.* 2022 Mar 21. doi: 10.1111/jocd.14692. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35312149/>

Background: Botulin toxin (BTX) is a potent neurotoxin produced by the bacterium *Clostridium botulinum*, since its approval by FDA in 2002 for cosmetic purpose has been widely used. Recent studies indicate that it exerts its activity on various type of skin cells and can be used in some dermatological disease. Objective: The aim of the study was to demonstrate how to use a peculiar dilution of botulinum toxin type A in the treatment of some dermatological disease like mild-to-moderate acne vulgaris and erythematotelangiectatic rosacea. Material and methods: 50 patients were enrolled, 35 with mild-to-moderate acne and 15 with erythematotelangiectatic rosacea. Both group of patients were treated with a specific dilution of Onabotulinum toxin A called Microbotox. Patient images were taken before and 4 weeks after the treatment. Results: The authors and patients were extremely satisfied with their treatments. There were no immediate or delayed complication in none of both group of patients. Conclusion: Botulinum toxin shows a great promise either in dermatological disease like mild-to-moderate acne vulgaris and erythematotelangiectatic rosacea. Microbotox appears to be a valid, long-lasting, and a standardized approach to treat these kind of two disease.

Microneedle fractional radiofrequency for atrophic acne scars: In vivo evaluation of results by 3D analysis and reflectance confocal microscopy. Fusano M, Bencini PL. *Dermatol Ther.* 2022 Mar 16:e15454. doi: 10.1111/dth.15454. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35297143/>

The efficacy of microneedle fractional radiofrequency (MFR) for the treatment of atrophic acne scars has been recently described, but accurate in vivo microscopic documentation of the processes occurring has never been reported. The aim of this study is to describe in vivo morphological atrophic acne scars' variations after treatment with MFR by means reflectance confocal microscopy (RCM) and three-dimensional (3D) imaging. A total of 11 patients requiring treatment for atrophic facial acne scars were treated with four monthly sessions of MFR. 3D imaging and RCM were assessed at baseline and 1 month after last session. Clinical improvement, according to Global Assessment Improvement Scale, and patients' satisfaction were evaluated. Clinical improvement was observed in all the treated patients, although better results were obtained for boxcar scars ($p = 0.043$). 3D imaging revealed a significant improvement in terms of mean scars' depth ($p < 0.001$). Otherwise, RCM highlighted collagen remodeling with restoration of a reticular structure. Our study confirms the efficacy and safety of MFR in acne scars' treatment and provides the microscopic description of the results using RCM.

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Bee venom and its major component melittin attenuated cutibacterium acnes- and IGF-1-induced acne vulgaris via inactivation of Akt/mTOR/SREBP signaling pathway. Gu H, An HJ, Gwon MG, et al. *Int J Mol Sci.* 2022 Mar 15;23(6):3152. doi: 10.3390/ijms23063152. <https://pubmed.ncbi.nlm.nih.gov/35328573/>

Acne vulgaris is the most common disease of the pilosebaceous unit. The pathogenesis of this disease is complex, involving increased sebum production and perifollicular inflammation. Understanding the factors that regulate sebum production is important in identifying novel therapeutic targets for the treatment of acne. Bee Venom (BV) and melittin have multiple effects including antibacterial, antiviral, and anti-inflammatory activities in various cell types. However, the anti-lipogenic mechanisms of BV and melittin have not been elucidated. We investigated the effects of BV and melittin in models of Insulin-like growth factor-1 (IGF-1) or Cutibacterium acnes (C. acnes)-induced lipogenic skin disease. C. acnes or IGF-1 increased the expression of sterol regulatory element-binding protein-1 (SREBP-1) and proliferator-activated receptor gamma (PPAR- γ), transcription factors that regulate numerous genes involved in lipid biosynthesis through the protein kinase B (Akt)/mammalian target of rapamycin (mTOR)/SREBP signaling pathway. In this study using a C. acnes or IGF-1 stimulated lipogenic disease model, BV and melittin inhibited the increased expression of lipogenic and pro-inflammatory factor through the blockade of the Akt/mTOR/SREBP signaling pathway. This study suggests for the first time that BV and melittin could be developed as potential natural anti-acne agents with anti-lipogenesis, anti-inflammatory, and anti-C. acnes activity.

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Evaluation of therapeutic effect and prognosis of danzhi xiaoyao powder combined with photodynamic therapy in the treatment of rose acne. Yu X, Zhang N, Jin J, et al. *Comput Math Methods Med.* 2022 Mar 11;2022:1636839. doi: 10.1155/2022/1636839. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35309844/>

Background: Rose acne is a chronic inflammatory skin disease that can cause paroxysmal flushing, persistent erythema, papules or papules on the face, and pustules, and it has a greater impact on the life of patients, so it is important to treat it. Objective: To investigate the effect of Danzhi Xiaoyao Powder combined with photodynamic therapy (PDT) on the curative effect evaluation and prognosis of patients with rose acne. Patients and Methods. The clinical data of 110 rose acne patients who were treated in our hospital from January 2019 to January 2021 were selected as the subject of this retrospective study. They were divided into a control group and a treatment group according to the random residue grouping method. The new crown epidemic, loss to follow-up, etc. fell out of 5 cases

in each group, and finally, 50 cases in each group were left. Among them, the control group was treated with PDT, and the treatment group was combined with Danzhi Xiaoyao Powder on the basis of the control group. Then we observe and compare the effects of skin lesion scores and clinical symptom scores and differences in clinical efficacy between the two groups. Results: The comparison of the clinical symptom scores of the two groups of patients before treatment was not statistically significant ($P > 0.05$), while the burning score, tingling score, dryness score, and pruritus score of the treatment group after treatment were significantly different. The internal comparison after treatment was lower than before treatment, and the comparison between the treatment groups was significantly higher than the control group, which was statistically significant ($P < 0.05$). There was no statistically significant difference in the skin lesion scores of the two groups before treatment ($P > 0.05$), while the papules score, pustule score, erythema score, and telangiectasia score of the treatment group after treatment were significantly different and compared within the group. After treatment, the treatment group was significantly higher than the control group, and the comparison was statistically significant ($P < 0.05$). The effective rate of 98.00% in the treatment group was significantly higher than the 76.00% in the control group, and the difference was statistically significant ($P < 0.05$). The clinical efficacy of the two groups of patients showed that the rash, chest tightness, nausea, and diarrhea of the treatment group were significantly lower than those of the control group, and the difference was statistically significant ($P < 0.05$). Conclusion: Danzhi Xiaoyao Powder combined with PDT to treat rose acne is effective, can quickly control inflammatory papules and inflammatory erythema, effectively improve the clinical symptoms of patients, and reduce adverse reactions.

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Antibacterial activity of the essential oil from litsea cubeba against cutibacterium acnes and the investigations of its potential mechanism by gas chromatography-mass spectrometry metabolomics. Chen J, Zhang J, Zhu L, et al. Front Microbiol. 2022 Mar 2;13:823845. doi: 10.3389/fmicb.2022.823845. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35308342/>

Cutibacterium acnes (*C. acnes*) is an anaerobic Gram-positive bacterium generally considered as a human skin commensal, but is also involved in different infections, such as acne and surgical infections. Although there are a variety of treatments, the side effects and the problem of bacterial drug resistance still limit their clinical usage. In this study, we found that essential oil (EO) distilled from fresh mature *Litsea cubeba* possessed promising antibacterial activity against *C. acnes*. In order to elucidate its potential mechanism, bacteriostatic activity test, Live/Dead kit assay, scanning electron microscope (SEM), transmission electron microscope (TEM), and metabolomics were employed. In addition, the content of adenosine triphosphate (ATP) in bacterium and the activities of key enzymes involved in critical metabolic pathways were detected using a variety of biochemical assays. The results showed that EO exhibited significant antibacterial activity against *C. acnes* at a minimum inhibitory concentration (MIC) of 400 $\mu\text{g/mL}$ and a minimum bactericidal concentration (MBC) of 800 $\mu\text{g/mL}$, and EO could destroy *C. acnes* morphology and inhibit its growth. Moreover, results from our study showed that EO had a significant effect on the *C. acnes* normal metabolism. In total, 86 metabolites were altered, and 34 metabolic pathways related to the carbohydrate metabolism, energy metabolism, amino acid metabolism, as well as cell wall and cell membrane synthesis were perturbed after EO administration. The synthesis of ATP in bacterial cells was also severely inhibited, and the activities of key enzymes of the glycolysis and Wood-Werkman cycle were significantly affected (Pyruvate Carboxylase, Malate Dehydrogenase and Pyruvate kinase activities were decreased, and Hexokinase was increased). Taken together, these results illustrated that the bacteriostatic effect of EO against *C. acnes* by breaking the bacterial cell morphology and perturbing cell metabolism, including inhibition of key enzyme activity and ATP synthesis. The results from our study may shed new light on the discovery of novel drugs with more robust efficacy.

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Sarecycline demonstrated reduced activity compared to minocycline against microbial species representing human gastrointestinal microbiota. Ghannoum MA, Long L, Bunick CG, et al. *Antibiotics (Basel)*. 2022 Feb 28;11(3):324. doi: 10.3390/antibiotics11030324. <https://pubmed.ncbi.nlm.nih.gov/35326788/>

Prolonged use of broad-spectrum tetracycline antibiotics such as minocycline and doxycycline may significantly alter the gut and skin microbiome leading to dysbiosis. Sarecycline, a narrow-spectrum tetracycline-class antibiotic used for acne treatment, is hypothesized to have minimal impact on the gastrointestinal tract microbiota. We evaluated the effect of sarecycline compared to minocycline against a panel of microorganisms that reflect the diversity of the gut microbiome using in vitro minimum inhibitory concentration (MIC) and time-kill kinetic assays. Compared to minocycline, sarecycline showed less antimicrobial activity indicated by higher MIC against 10 of 12 isolates from the Bacteroidetes phylum, three out of four isolates from Actinobacteria phylum, and five of seven isolates from the Firmicutes phylum, with significantly higher MIC values against *Propionibacterium freudenreichii* (≥ 3 dilutions). In time-kill assays, sarecycline demonstrated significantly less activity against *Escherichia coli* compared to minocycline at all time-points ($p < 0.05$). Moreover, sarecycline was significantly less effective in inhibiting *Candida tropicalis* compared to minocycline following 20- and 22-h exposure. Furthermore, sarecycline showed significantly less activity against *Lactobacillus paracasei* (recently renamed as *Lacticaseibacillus paracasei* subsp. *paracasei*) ($p = 0.002$) and *Bifidobacterium adolescentis* at 48 h ($p = 0.042$), when compared to minocycline. Overall, sarecycline demonstrated reduced antimicrobial activity against 79% of the tested gut microorganisms, suggesting that it is less disruptive to gut microbiota compared with minocycline. Further in vivo testing is warranted.

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Clinical Reviews

Gut microbiota modulation and gold nanoparticle-mediated photothermal therapy for treatment of recalcitrant acne. Seo J, Roh HJ, Jung JY. *Clin Case Rep*. 2022 Mar 24;10(3):e05642. doi: 10.1002/ccr3.5642. eCollection 2022 Mar. <https://pubmed.ncbi.nlm.nih.gov/35356183/>

Recent studies highlight that gut dysbiosis, an imbalanced state of intestinal microbiota, exacerbates skin inflammation. Here, we showed the presence of gut microbiota alterations in two patients with recalcitrant acne and investigated the impact of its therapeutic modulation together with gold nanoshell-mediated photothermal therapy (gold PTT).

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Blue-grey hyperpigmentation in acne after vandetanib therapy and doxycycline use: A case report. Perlmutter JW, Cogan RC, Wiseman MC. *SAGE Open Med Case Rep*. 2022 Mar 22;10:2050313X221086316. doi: 10.1177/2050313X221086316. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35341100/>

Vandetanib is an oral tyrosine kinase inhibitor with cutaneous adverse effects that include the development of acne. We present a patient who underwent vandetanib therapy for stage IV medullary thyroid cancer in conjunction with the use of doxycycline for acne that developed. After vandetanib use, blue-grey pigmentation developed in the acne on his face, chest, back, and arms, which darkened after the use of doxycycline. We review the literature to report that this blue-grey hyperpigmentation was likely vandetanib-induced but may have been the result of both drugs being used in combination.

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Demodicosis imitating acne vulgaris: A case report. Paichitrojjana A. Clin Cosmet Investig Dermatol. 2022 Mar 19;15:497-501. doi: 10.2147/CCID.S358000. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35340734/>

Demodicosis is caused by Demodex mite infestation and can present with a variety of clinical manifestations, including pityriasis folliculorum type, rosacea-like type, folliculitis-like type and perioral dermatitis-like type. Therefore, this skin condition is often misdiagnosed or underdiagnosed. This report presents a 19-year-old woman with a history of pityriasis folliculorum type demodicosis and successful treatment with oral ivermectin. After one year of remission, the patient began to develop a dry, itchy rash on her face for one month before multiple small edematous papules and pustules gradually appeared on both cheeks. The patient was first diagnosed as acne vulgaris and treated with doxycycline for 2 weeks, but the clinical symptoms did not show any signs of improvement. After reassessment based on clinical presentation and laboratory examination that found multiple Demodex mites from pustules and rash on both cheeks, the patient was diagnosed with folliculitis-like type demodicosis. However, this patient still had a very good response to oral ivermectin and metronidazole gel, and all clinical symptoms disappeared within 4 weeks after treatment. This is a case report of demodicosis imitating acne vulgaris and the first report demonstrating a change in clinical manifestations of demodicosis from pityriasis folliculorum type to folliculitis-like type.

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MicroRNA cross-involvement in acne vulgaris and hidradenitis suppurativa: A literature review. Borgia F, Peterle L, Custurone P, et al. Int J Mol Sci. 2022 Mar 17;23(6):3241. doi: 10.3390/ijms23063241. <https://pubmed.ncbi.nlm.nih.gov/35328662/>

Acne Vulgaris (AV) and Hidradenitis suppurativa (HS) are common chronic inflammatory skin conditions that affect the follicular units that often coexist or are involved in differential diagnoses. Inflammation in both these diseases may result from shared pathways, which may partially explain their frequent coexistence. MicroRNAs (miRNAs) are a class of endogenous, short, non-protein coding, gene-silencing or promoting RNAs that may promote various inflammatory diseases. This narrative review investigates the current knowledge regarding miRNAs and their link to AV and HS. The aim is to examine the role of these molecules in the pathogenesis of AV and HS and to identify possible common miRNAs that could explain the similar characteristics of these two diseases. Five miRNA (miR-155 miR-223-, miR-21, and miRNA-146a) levels were found to be altered in both HS and AV. These miRNAs are related to pathogenetic aspects common to both pathologies, such as the regulation of the innate immune response, regulation of the Th1/Th17 axis, and fibrosis processes that induce scar formation. This review provides a starting point for further studies aimed at investigating the role of miRNAs in AV and HS for their possible use as diagnostic-therapeutic targets.

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Ocular manifestations of systemic isotretinoin in patients with acne: A systemic review and meta-analysis. Elubous KA, Toubasi AA, Elubous A, et al. Cutan Ocul Toxicol. 2022 Mar 16;1-10. doi: 10.1080/15569527.2022.2050747. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35296199/>

Purpose: To examine the effects of systemic isotretinoin treatment on the eye using several ocular examination parameters. Methods: We conducted a systemic review for literature published up to June 2021 in both PubMed and Web of Science databases. We included prospective observational or interventional studies evaluating ocular manifestations of isotretinoin in acne patients. The primary outcome measures were anaesthetized and non-anaesthetized Schirmer test, tear break-up time (TBUT), central corneal thickness (CCT), average retinal nerve fiber layer (RNFL) thickness, ganglion cell-inner plexiform layer (GC-IP) thickness, subfoveal choroidal thickness, axial length, ocular surface disease index (OSDI), meibomian gland expression (MGE) and conjunctival stain. The National Institute of Health (NIH) quality assessment tools were used to assess the data quality. The effect size used to analyze the included studies was the weighted mean difference (WMD) and its related confidence intervals (95% CIs). Results:

Twenty-one publications involving 1105 eyes of 842 participants met the inclusion criteria. Isotretinoin use was significantly associated with reduction in the scores of anaesthetized Schirmer (WMD = -2.23, 95%CI: -3.28 to -1.18), non-anaesthetized Schirmer (WMD = -3.74, 95%CI: -4.23 to -3.25), TBUT (WMD = -3.47, 95%CI: -5.09 to -1.86), and CCT (WMD = -7.39, 95%CI: -13.91 to -0.88). Isotretinoin use was significantly associated with increase of OSDI (WMD = 18.29, 95%CI: 7.54-29.03), MGE (WMD = 1.02, 95%CI: 0.70-1.33) and conjunctival stain scores (WMD = 0.61, 95%CI: 0.47-0.76). No significant change was noted in RNFL thickness (WMD = -0.64, 95%CI: -1.80 to 0.51); GC-IP thickness (WMD = 0.42, 95%CI: -1.08 to 1.92); subfoveal choroidal thickness (WMD = -1.80, 95%CI: -6.69 to 3.09), and axial length (WMD = 0.08, 95%CI: -0.19 to 0.35). A significant heterogeneity was found between the study estimates in each of anaesthetized Schirmer, TBUT, MGE, OSDI, and conjunctival stain tests. Conclusion: Isotretinoin use results in a statistically significant reduction of the central corneal thickness, TBUT, and Schirmer test scores. A statistically significant increase in MGE, OSDI and conjunctival stain scores was found. No statistically significant change of average RNFL, GC-IP thickness, subfoveal choroidal thickness, or axial length was observed. Further well-designed studies should evaluate the long-term effect of isotretinoin on the eye and reach a firmer conclusion.

Microbiome and probiotics in acne vulgaris-a narrative review. Chilicka K, Dzieńdziora-Urbińska I, Szyguła R, et al. *Life (Basel)*. 2022 Mar 15;12(3):422. doi: 10.3390/life12030422. <https://pubmed.ncbi.nlm.nih.gov/35330173/>

Acne vulgaris is a chronic disease characterized by the appearance of eruptions such as whiteheads, blackheads, pustules, papules, and cysts. Among factors that cause acne vulgaris are the abnormal keratinisation of the sebaceous canal, bacterial colonization (*Cutibacterium acnes*), increased sebum production, genotypic factors, and hormonal disorders. Treatment is often long and tedious and can lead to a reduction in quality of life and social isolation. The intestinal microbiota is greatly important in the formation of acne lesions. It is also responsible for the proper immunity of the organism. Acne is a disease that can be related to the condition of the digestive tract and its microbiome. Research shows that the use of probiotics may reduce skin eruptions. The probiotic supplementation and cosmetics markets are very dynamically developing. The use of internal supplementation and probiotic-containing cosmetics gives hope for the improvement of the skin condition of people with acne.

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Effective intense pulsed light protocol in the treatment of moderate to severe acne vulgaris of the chest and back. Piccolo D, Kostaki D, Dianzani C, et al. *J Clin Aesthet Dermatol*. 2022 Mar;15(3):22-25. <https://pubmed.ncbi.nlm.nih.gov/35342499/>

Background: Acne is defined as a chronic inflammatory disease of the pilosebaceous units, mainly affecting the face of young adults, but the chest and back can be involved as well. Oral antibiotics, topical retinoids, azelaic acid, benzoyl peroxide, and isotretinoin represent the most common treatment used for the treatment of acne, but several adverse effects and a lack of durable remission, with poor adherence by the patients, have been reported thus far. Lasers have been shown to be effective and safe to treat acne; intense pulsed light (IPL) demonstrates high efficacy rates, minimal discomfort, rapid recovery times, and excellent cosmetic and therapeutic outcomes. Objective: In this prospective study, we assessed the efficacy, safety, and reproducibility of a novel IPL protocol as a monotherapy in the treatment of acne of the chest and back. Methods: We included patients (N=50) aged 14 to 30 who presented with moderate papulopustular acne sited on the chest and back (Cook's Acne Grading Scale method 4-6, Pillsbury Scale III-IV). We performed four IPL sessions at two-week intervals on each patient. Results: An excellent outcome was achieved in 50 percent of the patients and a good outcome in the 35 percent of the patients. Patients experienced light erythema and mild burning as the most common side effects, which spontaneously resolved within 24 to 96 hours. Conclusion: Consistent with previous reports, our study demonstrated IPL to be a safe and effective treatment for severe cases of acne on the chest and back, providing excellent aesthetic and therapeutic results in 85 percent of

treated patients.

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A combination of non-ablative laser and hyaluronic acid injectable for postacne scars: A novel treatment protocol. Akerman L, Mimouni D, Nosrati A, et al. *J Clin Aesthet Dermatol.* 2022 Mar;15(3):53-56. <https://pubmed.ncbi.nlm.nih.gov/35342506/>

Background: Postacne facial scars are often associated with significant patient distress. Energy-based devices, including non-ablative lasers, are commonly used for the treatment of postacne scarring. There is relatively limited data regarding the combination of non-ablative lasers with hyaluronic acid injections for postacne scarring. Objective: We aimed to evaluate the efficacy of a non-ablative 1,540-nm erbium:glass laser combined with a hyaluronic acid injectable for the treatment of postacne scars. Methods: This was a retrospective analysis of 12 patients who underwent the full treatment protocol. A before and after blinded clinical evaluation was performed independently by two dermatologists and graded on a scale from 0 (indicating a worsening of scarring) to 4 (indicating a 76-100% improvement in scarring). Pain perception, adverse effects, and patient satisfaction were evaluated. Results: A mean correct blinded before and after evaluation by two dermatologists was 96 percent. Patients demonstrated mild to moderate improvement as assessed by a quartile scale of improvement (25-50%). Mild transient pain was reported by most patients. The satisfaction level of the patients was high (4 out of 5). Limitations: The limitations of our study include the small cohort, retrospective design, and lack of a histological correlation. Conclusion: Our results suggest that this combination treatment using 1,540-nm fractional erbium:glass laser and hyaluronic acid injections is both safe and effective for patients with postacne facial scars.

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The role of skin immune system in acne. Firlej E, Kowalska W, Szymaszek K, et al. *J Clin Med.* 2022 Mar 13;11(6):1579. doi: 10.3390/jcm11061579. <https://pubmed.ncbi.nlm.nih.gov/35329904/>

Acne vulgaris is a skin disease that often occurs in adolescence and in young adulthood. The main pathogenic factors are hyperkeratinization, obstruction of sebaceous glands, stimulation of sebaceous gland secretion by androgens, and bacterial colonization of sebaceous units by *Cutibacterium acnes*, which promotes inflammation. Little is known about the role of skin immune cells in the development of acne lesions. The aim of the study was to try to understand the role of skin immune cells in the course of acne. Recent studies have shown that there are at least four major pathways by which *Cutibacterium acnes* interacts with the innate immune system to induce inflammation: through TLRs, activating inflammasomes, inducing the production of matrix metalloproteinases (MMPs), and stimulating antimicrobial peptide (AMP) activity. Cells of adaptive immune response, mainly Th1 and Th17 lymphocytes, also play an important role in the pathogenesis of acne. It is worth emphasizing that understanding the role of the skin's immune cells in the pathogenesis of acne may, in the future, contribute to the application of modern therapeutic strategies that would avoid addiction to antibiotics, which would alleviate the spectrum of resistance that is now evident and a current threat.

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