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AARS News

AARS 2023 Research Scholar Award Provided to Christopher G. Bunick, MD, PhD

The AARS is pleased to announce that the 2023 Research Scholar Award has been provided to Christopher G. Bunick, MD, PhD, of Yale University. The award will fund research aimed at identifying novel antibiotic compounds for the treatment of acne.

Tetracyclines account for the majority of antibiotics used in dermatology,¹ including first-generation (tetracycline) and second-generation (doxycycline; minocycline) broad-spectrum agents, as well as a third-generation narrow-spectrum agent (sarecycline) approved for the treatment of acne in 2018. However, antibiotic use is associated with the risk for antibiotic resistance, which has been deemed a global public health threat.²

Dr. Bunick and colleagues at the Bunick laboratory previously showed how sarecycline interacted with *Cutibacterium acnes* (*C. acnes*) on a molecular level, expanding application of its mechanism of action. With the Research Scholar Award funding, Dr. Bunick and his team propose to elucidate fundamental mechanisms of action of more than 20 additional tetracycline-class compounds. Their goal is to identify a highly selective agent for that has greater efficacy and less risk of antibiotic resistance than currently used antibiotic therapies. Specifically, inspired by their findings related to the molecular interaction of sarecycline with the *C. acnes* bacterium, they will investigate the molecular actions of other antibiotics to determine which show the greatest potential efficacy against the bacterium.

C. acnes is a commensal organism that resides on human skin. An over-abundance of *C. acnes* and subsequent accumulation of its inflammatory byproducts is a primary contributor to the development of acne.

The AARS Research Scholar Award is conferred on an annual basis to support promising research aimed at improving the care of patients with acne, rosacea, and hidradenitis suppurativa. Awards are conferred based on a rigorous application and review process, in which the grant committee assesses the feasibility of the study, its potential to expand understanding of acne, rosacea, hidradenitis suppurativa, and related diseases, and the likely practical impact of research findings.

“We are pleased to be able to support Dr. Bunick’s research on novel tetracycline compounds that could be used to treat acne,” says Andrea Zaenglein, MD, president of the AARS. “Acne is a common disease that can have a significant impact on affected individuals. While oral antibiotics are an important tool in our treatment armamentarium, we take concerns for antibiotic resistance seriously and understand the role that dermatologists play in reducing the risks. The potential to target *C. acnes* more efficiently with reduced risk for resistance is certainly appealing.”

1. Del Ross J.Q., Webster G.F., Rosen T. Status report from the scientific panel on antibiotic use in dermatology of the American Acne and Rosacea Society: part 1: Antibiotic prescribing patterns, sources of antibiotic exposure, antibiotic consumption and emergence of antibiotic resistance, impact of alterations in antibiotic prescribing, and clinical sequelae of antibiotic use. *J. Clin. Aesthet. Dermatol.* 2016;9:18.

2. Antibiotic resistance. Web: <https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance>. Accessed August 18, 2023.

AARS Signs on to Joint AADA/APA Comment Regarding REMS Program Administration

The American Acne and Rosacea Society (AARS) continues to advocate for greater transparency and stakeholder participation in the design and management of Risk Evaluation and Mitigation Strategies or REMS. AARS has joined 14 other medical specialty groups to co-sign a letter sent to FDA by the American Academy of Dermatology

Association (AADA) and the American Psychiatric Association (APA) urging meaningful changes to the REMS modification process.

AARS is particularly concerned about the administration of the iPLEDGE REMS program for isotretinoin. Administrative changes to the iPLEDGE REMS system in 2021 resulted in digital access limitations and call center failures that led to major disruptions in patient access. AADA, APA, and its cosignatories maintain that problem arise because manufacturers who sponsor REMS programs and the companies that administer them are not required to seek input from physicians, pharmacists, patients and other stakeholders when considering modifications to REMS administration. Furthermore, sponsors and administrators may not provide timely notice of pending changes.

The letter has been submitted to the FDA in response to the agency's call for comment.

"The AARS is pleased to have been invited to cosign this letter and appreciates the opportunity to cooperate with the AADA. We are proud to represent the needs of patients with moderate to severe acne who are candidates for isotretinoin therapy, as well as the dermatologists who treat them," says AARS President Andrea Zaenglein, MD. "We affirm the importance of the iPLEDGE program to assure safe use of isotretinoin. However, we feel strongly that stakeholders such as prescribers, pharmacists, and patients can add invaluable insight into the development and modification of REMS programs and must receive transparent, timely, and comprehensive communication about intended modifications."

REMS programs are required by FDA and sponsored by the manufacturers and marketers of affected drugs. Most REMS programs are administered by third party vendors. In the case of iPLEDGE, the program is sponsored by the Isotretinoin Product Manufacturers Group (IPMG) and administered by Syneos. Modifications to the administration of a REMS, such as changes to a website or call center availability, do not currently require open public comment and may be made with little or no advance notice. Changes to REMS requirements must be approved by FDA and typically require committee meetings and open comment periods.

AARS has also recently participated in FDA meetings regarding proposed modifications to iPLEDGE requirements; many of the changes supported by AARS were ultimately recommended by the committee. ([Read more on our blog.](#)) However, committee recommendations are non-binding, and FDA has yet to issue a final ruling.

Industry News

Ortho Recognizes 6 Honorees in Aspire Higher Scholarship Program. July 27, 2023.

<https://ir.bauschhealth.com/news-releases/2023/07-27-2023>

Ortho Dermatologics has selected six students who have been treated for a dermatologic condition to each receive a scholarship of up to \$10,000 to pursue their undergraduate or graduate degrees. The awards are part of the 2023 [Aspire Higher Scholarship](#) program. Honorees, selected from 216 applications, were recognized in part due to their essays that provided an overview of their educational journeys while living with dermatologic conditions and the role a health care professional played in treating the condition. "This year marks the 10-year anniversary of the Aspire Higher Program. Over the last decade, Ortho Dermatologics and our Aspire Higher Scholarship program have supported 75 students who have been affected by dermatologic conditions by helping them achieve their higher education goals," said Don Pearl, senior vice president, Ortho Dermatologics, in a statement. "We are thrilled to announce the 2023 recipients and were deeply moved and inspired by their personal stories. We are truly honored to

have the opportunity to help them pursue their academic aspirations through this scholarship, and we also thank the health care providers who had a critical hand in helping to treat their conditions.”

The 2023 Aspire Higher Scholarship Program recipients are:

Undergraduate Scholar Awards

- Serena Goyal, Clarksville, Maryland – Virginia Commonwealth University
- Arianna Kaas, Pewaukee, Wisconsin – University of Wisconsin Madison
- Elle Tondo, Denton, Texas – University of New Haven

Graduate Scholar Awards

- Erynn Taylor, McDonough, Georgia – Georgia College and State University
- Matthew Kaczynski, Providence, Rhode Island – Warren Alpert Medical School of Brown University
- Katrina Hertz, Glenn Heights, Texas – University of Pennsylvania

New Medical Research

Discovery and characterization of a novel bacteriocin HA2-5 that strongly inhibits propionibacterium acnes.

Peng Z, He M, Yang X, et al. *J Agric Food Chem*. 2023 Aug 30;71(34):12741-12748. doi: 10.1021/acs.jafc.3c04617. Epub 2023 Aug 16. <https://pubmed.ncbi.nlm.nih.gov/37587448/>

Increased drug resistance has significantly reduced the effectiveness of antibiotics used in the treatment of *Propionibacterium acnes*. Therefore, there has been a trend toward the development of new antimicrobial agents to circumvent drug resistance. In this study, we isolated and purified a novel bacteriocin, HA2-5, from *Bacillus haynesii* HA2, which effectively killed *P. acnes* through membrane disruption at a minimum inhibitory concentration (MIC) of 8 µg/mL. HA2-5 with 2× MIC was able to kill 99.9% of *P. acnes* within 24 h. HA2-5 shows excellent stability and tolerance to temperature, pH, proteases, chemical reagents, UV radiation, and metal ions, with almost no loss of inhibitory activity after treatment. In addition, the very low hemolytic activity and cytotoxicity suggest that HA2-5 is biosafe. Notably, HA2-5 exhibits preferred antibacterial activity against gram-positive pathogens with an MIC of 16-32 µg/mL. In conclusion, this study shows that bacteriocin HA2-5 has the potential to be used as an alternative to antibiotics for acne treatment.

Isotretinoin-associated acne fulminans: A multicenter, retrospective study of the European Academy of Dermatology and Venereology Task Force on Acne, Rosacea and Hidradenitis Suppurativa.

Dessinioti C, Dréno B, Bettoli V, et al. *J Eur Acad Dermatol Venereol*. 2023 Aug 29. doi: 10.1111/jdv.19477. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/37643921/>

Background: Acne fulminans (AF) is a rare severe acne entity. Although occasionally reported, it is unclear whether AF development is associated with oral isotretinoin treatment. Objectives: To investigate the occurrence of isotretinoin-associated AF, clinical characteristics and prognosis at follow-up. Methods: An international, multicenter, retrospective study was performed in 8 hospitals following the call of the EADV Task Force on Acne, Rosacea and Hidradenitis suppurativa (ARHS). Characteristics of patients treated with isotretinoin before the development of AF (isotretinoin-associated acne fulminans, IAF) were compared with non-IAF (NAF). Results: Forty-nine patients diagnosed with AF from 2008 to 2022 were included (mean age 16.4 years, SD: 2.9, 77.6% male). Arthralgias/arthritis occurred in 11 patients (22.9%). AF occurred without any previous acne treatment in 26.5% of the patients. Overall, 28 patients (57.1%) developed AF after oral isotretinoin intake (IAF group), while the remaining 21 patients (42.9%) developed AF without previous oral isotretinoin administration (NAF group). IAF occurred after a median duration of isotretinoin treatment of 45 days (IQR: 30, 90). Patients with IAF were more frequently male compared to patients

with NAF (89.3% vs 61.9%, respectively, $p=0.023$). There were no differences in patients with IAF versus NAF in patient age, the duration of pre-existing acne, a family history of AF, the distribution of AF lesions or the presence of systemic symptoms or arthralgias. Regarding the management of AF, patients with IAF were treated more frequently with prednisolone (96.2%) compared to those with NAF (70%) ($p=0.033$) and less frequently with isotretinoin (32.1%) compared to NAF (85.7%) ($p<0.001$). At a median follow-up of 2.2 years, 76.4% of patients were free of AF and scarring was present in all patients. Conclusions: No specific clinical or demographic characteristics of IAF when compared with NAF could be detected, a fact that does not support IAF as a distinct clinical entity.

Nanotechnology and narasin: A powerful combination against acne. Abid F, Savaliya B, Parikh A, et al. *Nanoscale*. 2023 Aug 25;15(33):13728-13739. doi: 10.1039/d3nr01789c. <https://pubmed.ncbi.nlm.nih.gov/37577823/> Acne vulgaris is widely regarded as the most prevalent skin disorder characterized by painful, inflammatory skin lesions that are primarily attributed to the pathogenic actions of *Cutibacterium acnes* (*C. acnes*). To improve the clinical management of this disease, there is a pressing clinical demand to develop innovative antibacterial therapies that utilize novel mechanisms. The current research aimed to discover the antibacterial efficacy of narasin (NAR), a polyether ionophore, against drug-resistant acne bacteria. In addition, the study aimed to formulate self-nanomicellizing solid dispersions (SNMSD), utilizing Soluplus® (SOL), as a drug delivery system to incorporate NAR and selectively target the lipophilic *C. acnes* abundant environments within the skin. Furthermore, the study aimed to investigate the *ex vivo* deposition and permeation of NAR into the various layers of the skin using full-thickness porcine ear skin as a model skin. By encapsulating NAR within spherical polymeric micelles ($dn < 80$ nm) aqueous solubility was significantly increased by approximately 100-fold (from $<40 \mu\text{g mL}^{-1}$ to $4600 \mu\text{g mL}^{-1}$). Following optimization, the micelle solution was integrated into a gel formulation (containing 0.2% w/v NAR) and evaluated for stability over 4 weeks at room temperature (drug content $>98\%$). Results from drug deposition and permeation experiments demonstrated that the deposition of NAR from the NAR-micelle solution and its gel formulation into the lipophilic stratum corneum ($19\,835.60 \pm 6237.89 \text{ ng cm}^{-2}$ and $40\,601.14 \pm 3736.09 \text{ ng cm}^{-2}$) and epidermis ($19\,347 \pm 1912.98 \text{ ng cm}^{-2}$ and $18\,763.54 \pm 580.77 \text{ ng cm}^{-2}$) was superior to that of NAR in solution, which failed to penetrate any skin layers. In conclusion, the outcomes of this study provide evidence that NAR exhibits promising activity against antimicrobial resistant strains of *C. acnes* (MIC range ≤ 0.008 - 0.062) and that micelle nanocarriers can improve the aqueous solubility of poorly water-soluble drugs. Furthermore, our results highlight the ability of nanomicelles to enable selective and targeted drug delivery to the lipophilic skin layers.

Efficacy and safety of microencapsulated benzoyl peroxide cream, 5%, in rosacea: Results from two phase III, randomized, vehicle-controlled trials. Bhatia ND, Werschler WP, Baldwin H, et al. *J Clin Aesthet Dermatol*. 2023 Aug;16(8):34-40. <https://pubmed.ncbi.nlm.nih.gov/37636253/>

Objective: A new formulation of benzoyl peroxide (E-BPO cream, 5%) entraps benzoyl peroxide (BPO) in silica microcapsules. This study assesses the efficacy, safety, and tolerability of E-BPO cream, 5%, in rosacea in two Phase III clinical trials. Methods: In two 12-week, randomized, double-blind, vehicle cream-controlled Phase III trials, 733 subjects at least 18 years old with moderate to severe rosacea were randomized (2:1) to once-daily E-BPO cream, 5%, or vehicle. Results: In Study 1, the proportion of subjects achieving IGA clear/almost clear at Week 12 was 43.5 percent for E-BPO cream, 5%, and 16.1 percent for vehicle. In Study 2, the respective values were 50.1 percent and 25.9 percent. In Study 1, the decrease in lesion count from baseline to Week 12 was -17.4 for E-BPO cream, 5%, versus -9.5 for vehicle. In Study 2, the respective values were -20.3 and -13.3 (all $P<0.001$). The difference was also significant at Week 2. There were no treatment-related serious adverse events; 1.4 percent of subjects (1.8% E-BPO cream, 5%, 0.4% vehicle) discontinued due to adverse events. Assessed local tolerability was found to be similar

among subjects in both E-BPO and vehicle. E-BPO was not compared with unencapsulated BPO. Conclusion: E-BPO is an effective and well tolerated treatment for rosacea.

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Long-term efficacy and safety of microencapsulated benzoyl peroxide cream, 5%, in rosacea: Results from an extension of two phase III, vehicle-controlled trials. Werschler WP, Sugarman J, Bhatia N, et al. *J Clin Aesthet Dermatol.* 2023 Aug;16(8):27-33. <https://pubmed.ncbi.nlm.nih.gov/37636251/>

Objective: We sought to assess the long-term safety and tolerability of microencapsulated benzoyl peroxide cream, 5% (E-BPO cream, 5%), in subjects with rosacea. Efficacy and tolerability have been previously demonstrated in two 12-week, randomized, double-blind, vehicle-controlled Phase III trials. Methods: In this open-label extension study (NCT03564145; clinicaltrials.gov), all subjects from the initial placebo-controlled Phase III trials could receive E-BPO cream, 5%, for up to an additional 40 weeks, up to a total of 52 weeks of E-BPO cream, 5%, exposure. If a subject was assessed at study visits as "clear" or "almost clear" using the 5-point Investigator Global Assessment (IGA) scale (IGA 0 or 1), E-BPO cream, 5%, was not dispensed. If a subject was assessed as "mild to severe" (IGA 2+), E-BPO cream, 5%, was applied daily until they reached "clear" or "almost clear." Results: The safety and tolerability profile for E-BPO cream, 5%, was similar to that reported in the Phase III studies. Five subjects (0.9%) discontinued study drug due to treatment-related adverse events, and 17 subjects (3.2%) experienced an adverse event considered related to study drug. IGA success after 40 weeks of active treatment was 66.5 percent for subjects continuing from the Phase III vehicle group (n=172) and 67.6 percent for subjects who continued Phase III E-BPO cream, 5% (n=363). The study ended early in accordance with the protocol. Limitations: Safety and tolerability of E-BPO were not compared with those of unencapsulated BPO. Conclusion: E-BPO cream, 5%, showed a favorable safety and tolerability profile during this 40-week, open-label extension study.

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Combining superpulse dynamic CO2 laser and supramolecular salicylic acid in the treatment of dense comedones with higher clearance in a shorter time: A prospective, randomized, split-face clinical trial. Yang MY, Liu J, Ning DC, et al. *Lasers Surg Med.* 2023 Aug 15. doi: 10.1002/lsm.23717. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/37582350/>

Objectives: Dense comedones are common in patients with acne vulgaris, and promoting treatment can prevent the progression of acne lesions. However, the efficacy-time conflict makes the treatment challenging and the medication options are limited by the side effects. Materials and methods: Thirty-five patients with symmetrical dense comedones were enrolled and the two sides of the face were randomly assigned to receive 30% supramolecular salicylic acid (SSA) combined with CO2 laser or CO2 laser monotherapy at an interval of 2 weeks for six treatment sessions. Comedones count, porphyrin index (PI), texture index (TI), melanin index, erythema index, hydration index (HI), transepidermal water loss (TEWL), and side effects were recorded at each visit till the 12th week. Results: Thirty-one patients completed the study. Comedones on the combined-SSA side were reduced more after six treatments, that the mean reduction rate of the combined-SSA side was 85.76%, and that of the CO2 laser-treated side was 62.32% (P between < 0.001). Combining SSA also showed a better effect on reducing PI and TI than CO2 laser singly (P between < 0.001). TEWL and HI between the two sides showed no significant differences after treatments. No permanent or severe side effects were observed on both side. Conclusions: The treatment combined CO2 laser with 30% SSA dealt with the efficacy-time conflict while significantly reducing comedones and improving skin texture in 12 weeks and no serious adverse reactions occurred. Limitations: It is a single-center study and the number of subjects was small.

Ameliorative effect of lactobacillus plantarum CCFM8661 on oleic acid-induced acne: Integrated the gut microbiota link to the acne pathogenesis. Ai J, Ma W, Pan Z, et al. *J Sci Food Agric.* 2023 Aug 13. doi: 10.1002/jsfa.12921. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/37574818/>

Background: Acne vulgaris is an inflammatory disease of the pilosebaceous unit of the skin that has serious adverse effects on the physical and mental health of patients. Probiotics are extensively employed in dermatology and could be an alternative option for acne therapy. Here, we evaluated the effect of oral ingestion of live and inactivated *Lactobacillus plantarum* CCFM8661 on oleic acid-induced acne using a mouse model. Results: Results found that live *L. plantarum* CCFM8661 suppressed the skin inflammation and serum hormone (insulin and testosterone) production in acne mice. Parallely, live *L. plantarum* CCFM8661 effectively reduced the formation of skin lipids (TG and NEFA), and normalized the expression of skin lipid metabolism-related genes (PPRA- γ , SREBP-1c, ACC α , FASN, PPRA- α , ACOX1, HSL and ATGL). In comparison, inactivated *L. plantarum* CCFM8661 had no effect on skin inflammation or serum hormone secretion, but decreased the skin TG and normalized the expression of skin lipid metabolism-related genes (PPRA- γ , SREBP-1c, FASN and ATGL) in acne mice. Both live and inactivated *L. plantarum* CCFM8661 raised the richness of gut microbiota, reduced the ratio of Bacteroidetes: Firmicutes, and decreased the relative abundance of *Staphylococcus* in the feces of acne mice. Conclusion: Oral ingestion of *L. plantarum* CCFM8661, particularly live cells, could alleviate acne by suppressing skin inflammation, normalizing the metabolism of hormones and skin lipids, which may be achieved by improving the gut microbial ecosystem.

Efficacy and safety of topical flutamide 1% gel as an adjunctive therapy in the treatment of patients with acne vulgaris. Nassar A, Sayed AE, Samy A, Essam R. *J Cutan Med Surg.* 2023 Aug 11;12034754231191475. doi: 10.1177/12034754231191475. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/37571839/>

Background: Acne vulgaris is a worldwide dermatological condition that has a complex pathophysiology in which androgens play an important role. Flutamide is a first-generation non-steroidal antiandrogen that can be used for acne treatment. Aim: To evaluate the potential therapeutic efficacy and safety of topical flutamide in the treatment of acne vulgaris. Methods: A randomized controlled study included two equal groups, each had 27 patients, with a total of 54 patients with mild to moderate acne vulgaris having inflammatory (papules and pustules) and non-inflammatory (comedones) lesions. For eight weeks, Group (A) received 1% Flutamide topical gel on the face twice daily, whereas Group (B) served as the control group. Result: After 8 weeks of topical Flutamide 1% gel application twice daily, there was a significant reduction in papules count, and a highly significant reduction in pustules number from baseline. Limitations: We recommend that topical Flutamide 1% gel be tried on a larger number of patients with acne vulgaris, for longer therapeutic duration and follow up periods after treatment. Conclusion: Patients with acne vulgaris may find topical Flutamide 1% gel to be a viable, efficient, and safe solution with few adverse effects.

Modified red light 5-aminolevulinic acid photodynamic therapy versus low dose isotretinoin therapy for moderate to severe acne vulgaris: A prospective, randomized, multicenter study. Zhang L, Yang Y, Wang B, et al. *J Am Acad Dermatol.* 2023 Aug 7;S0190-9622(23)02417-9. doi: 10.1016/j.jaad.2023.07.1023. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/37558093/>

Background: Modified 5-aminolevulinic acid photodynamic therapy (M-PDT) and isotretinoin (ISO) are effective treatments for moderate to severe acne vulgaris. Objective: To evaluate the efficacy and adverse effects of M-PDT and ISO for moderate to severe acne vulgaris. Methods: A multicenter, randomized clinical trial was conducted with participants randomly assigned to the M-PDT group (up to 5 weekly sessions following manual comedone extraction) or the ISO group (oral isotretinoin, 0.5 mg/kg/d for 6 months) and followed up to six months post-therapy. Results: Totally 152 patients were allocated. The overall effective rates in the M-PDT group were significantly higher than the ISO group at one month (67.74% vs. 10.26%), while the opposite was the case one month after treatment (75.81%

vs. 97.44%). Time to achieve 50% lesion improvement in the M-PDT group was significantly less than the ISO group (1 vs. 8 weeks). 70.67% of the ISO group patients experienced systemic side effects such as hepatotoxicity while side effects were skin-limited in the M-PDT group. Limitations: Limitations of this study included relatively low numbers of participants and high withdrawal rate. Conclusion: M-PDT offers a more rapid onset of improvement, comparable overall efficacy, good tolerability, and comparable durability of response compared with ISO.

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Lysine-dendrimer, a new non-aggressive solution to rebalance the microbiota of acne-prone skin. Leignadier J, Drago M, Lesouhaitier O, et al. *Pharmaceutics*. 2023 Aug 3;15(8):2083. doi: 10.3390/pharmaceutics15082083. <https://pubmed.ncbi.nlm.nih.gov/37631297/>

Acne is a chronic inflammatory skin disease that affects the quality of life of patients. Several treatments exist for acne, but their effectiveness tends to decrease over time due to increasing resistance to treatment and associated side effects. To circumvent these issues, a new approach has emerged that involves combating the pathogen *Cutibacterium acnes* while maintaining the homeostasis of the skin microbiome. Recently, it was shown that the use of a G2 lysine dendrimer (G2 dendrimer) could specifically decrease the *C. acnes* phylotype (IAI) involved in acne, compared to non-acne-causing *C. acnes* (phylotype II) bacteria. In the present study, we demonstrate that the efficacy of this technology is related to its 3D structure, which, in contrast to the linear form, significantly decreases the inflammation factor (IL-8) linked to acne. In addition, our in-vitro data confirm the specific activity of the G2 dendrimer: after treatment of bacterial cultures and biofilms, the G2 dendrimer affected neither non-acneic *C. acnes* nor commensal bacteria of the skin (*Staphylococcus epidermidis*, *S. hominis*, and *Corynebacterium minutissimum*). In parallel, comparative in-vitro and in-vivo studies with traditional over-the-counter molecules showed G2's effects on the survival of commensal bacteria and the reduction of acne outbreaks. Finally, metagenomic analysis of the cutaneous microbiota of volunteers who applied a finished cosmetic product containing the G2 dendrimer confirmed the ability of G2 to rebalance cutaneous acne microbiota dysbiosis while maintaining commensal bacteria. These results confirm the value of using this G2 dendrimer to gently prevent the appearance of acne vulgaris while respecting the cutaneous microbiota.

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Comparative efficacy between intense pulsed light narrow spectrum and broad spectrum in the treatment of post-acne erythema (PAE). Al-Quran L, Li G, Liu Z, et al. *Clin Cosmet Investig Dermatol*. 2023 Aug 1;16:1983-1996. doi: 10.2147/CCID.S419743. eCollection 2023. <https://pubmed.ncbi.nlm.nih.gov/37547541/>

Purpose: Post-acne erythema (PAE) is one of the most common physical sequelae of acne regression, PAE can resolve spontaneously, but in some patients it may last for years. This study aimed to evaluate the efficacy and safety of narrow and broad spectrum filters of intense pulsed light (IPL) for the treatment of PAE. Patients and methods: This prospective study evaluated 60 patients with PAE for at least 6 months, assigned equally to three groups: 1st group received narrow-spectrum with vascular filter (530-650 nm and 900-1200 nm), 2nd group received broad-spectrum with (560/590-1200 nm) filters, the appropriate adjustments were made according to patient's skin color. Every patient received four sessions one month apart. 3rd group is blank control group did not receive any treatment. CAT (CEA (Clinical Erythema Assessment), Area, and Telangiectasia) used to grade clearance of PAE before and after treatment, Investigators Global Assessment (IGA) used to assess the improvement score after the treatment, and Cardiff Acne Disability Index (CADI) used to evaluate the impact of PAE on patients' Quality of Life (QoL). Self-satisfaction scale completed at the follow-up. Adverse events and acne relapse were recorded. Results: A significant decrease of CAT score in vascular group ($P < 0.05$). IGA scale showed significant improvement after vascular treatment. A significant decrease in CADI ($P < 0.05$) after vascular treatment. Patient satisfaction was higher in vascular

group than control and blank control groups. Acne relapse observed in control and blank control groups (40% and 15%, respectively). 10% of patients showed pigmentation, 15% had blisters after 590 nm treatment. Conclusion: IPL vascular filter (530-650 nm and 900-1200 nm) have efficacy in the treatment of PAE. CADI score, patient satisfaction, and acne relapse were significantly better after vascular narrow spectrum treatment than broad-spectrum treatment.

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Efficacy of FRO on acne vulgaris pathogenesis. Kim JE, Han H, Xu Y, et al. *Pharmaceutics*. 2023 Jul 4;15(7):1885. doi: 10.3390/pharmaceutics15071885. <https://pubmed.ncbi.nlm.nih.gov/37514071/>

Acne vulgaris is a common skin disease characterized by increased sebum production, inflammation, and *Cutibacterium acnes* (CA: formerly *Propionibacterium acnes*) hyperproliferation in pilosebaceous follicles. This study evaluated the efficacy of FRO, a formula composed of fermented *Rhus verniciflua* Stokes and *Orostachys japonicus*, against acne pathogenesis via antimicrobial assessment and an in vitro analysis. Stimulated model cells treated with hormones, CA, or lipopolysaccharide (LPS) were designed based on the characteristics of acne pathogenesis, including inflammation and sebum hypersecretion. High-performance liquid chromatography, disc diffusion, MTS, and western blotting assays were used to examine potential anti-acne effects. FRO was determined to contain phenolics such as gallic acid, fisetin, quercetin, and kaempferol. FRO exerted antimicrobial activity against CA and inhibited reactive oxygen species production that was otherwise increased by LPS or CA in HaCaT cells. Additionally, FRO exerted anti-inflammatory effects by inhibiting iNOS, TNF- α , IL-6, p-STAT-3, and p-NF- κ B, which were previously upregulated by LPS or CA in THP-1 and HaCaT cells. FRO inhibited lipogenesis induced by steroid hormones and CA by decreasing FAS and SREBP-1 levels in sebocytes. Additionally, FRO down-regulated the androgen receptor, 5 α -reductase, SREBP-1, and FAS levels, which were upregulated by steroid hormone in LNCaP cells. Taken together, our findings suggest that FRO alleviates acne by inhibiting the growth of CA, inflammation, and excess sebum and could be used for functional cosmetics or acne treatments.

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Clinical Reviews

Insights into acne and the skin barrier: Optimizing treatment regimens with ceramide-containing skincare. Schachner LA, Alexis AF, Andriessen A, et al. *J Cosmet Dermatol*. 2023 Aug 21. doi: 10.1111/jocd.15946. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/37605504/>

Introduction: Acne is a common, complex, multifactorial inflammatory skin disease associated with epidermal barrier dysfunction. Beginning in childhood, acne affects many adolescents and adults. Acne is associated with lower self-esteem, anxiety, and depression and may cause scars and pigmentary sequelae. The review explores the relationships between acne and the skin barrier function and discusses nuances in the prevention, treatment, and maintenance of acne and its impact on the skin barrier. Methods: The advisors' previous publications addressed prescription and nonprescription pediatric acne treatment and skincare using cleansers, moisturizers, and a practical algorithm for treatment and maintenance, including skincare recommendations for pediatric acne patients and an algorithm for skin of color patients with acne. Before the meeting, literature was culled on the relationship between the skin barrier and acne and current best practices in acne, addressing prescription and nonprescription acne products and skincare as monotherapy, adjunctive, and maintenance treatment. Results: After discussing 13 draft statements, the advisors applied the selected literature and drew from their clinical knowledge and experience, and agreed on five statements. The follicular epithelial barrier is directly involved with changes that occur during both comedogenesis and in stages of inflammation, especially with follicular rupture compromising the barrier's integrity. In acne-affected skin, sebaceous glands are larger, sebum excretion and filaggrin expression higher, and stratum

corneum lipids are reduced. Educating patients and clinicians about inflammation's central role in acne and measures to reduce inflammation is essential. Skin irritation and xerosis from acne and treatments lead to poor treatment adherence. A skincare regimen should be included in the acne prevention, treatment, and maintenance care regimen and should be ongoing. Maintenance treatment with topical agents and skincare using gentle ceramide-containing cleansers and moisturizers is a recommended strategy after successfully controlling the disease. Conclusions: Epidermal barrier dysfunction contributes to acne exacerbation. Using the appropriate treatment and skincare helps to minimize irritation and inflammation, enhance treatment adherence, and improve patient outcomes.

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Treatment of mild to severe acne with 1726 nm laser: A safe alternative to traditional acne therapies. Goldberg DJ, Andriessen A, Bhatia AC, et al. *J Cosmet Dermatol*. 2023 Aug 18. doi: 10.1111/jocd.15964. Online ahead of print.

<https://pubmed.ncbi.nlm.nih.gov/37596781/>

Introduction: Acne is the most common reason for dermatology consultation in adolescents and young adults. Consultation is often delayed despite unsuccessful self-treatment. Postponing effective treatment places acne sufferers at higher risk for permanent acne scars and post-inflammatory pigment changes. Aim: This review discusses clinical challenges with present therapeutic options for acne treatment and the role of a 1726 nm laser for acne. Methods: Current acne treatment guidelines were reviewed. A literature review was conducted for trials of light-based acne therapy. The selectivity of previous light-based therapies was reviewed. Results: Available acne therapy is effective, but treatment-related side effects are common. Acne treatment guidelines do not include recommendations for light-based treatments. Different types of light-based treatments have been tried but until now no wavelength specifically targeted sebaceous glands. Conclusion: The 1726 nm laser is safe and effective for treating mild to severe acne in all Fitzpatrick skin types. Acne resolution is apparent within the first month and improves for up to 2 years beyond treatment.

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Rosacea in children: A review. Chiriac A, Wollina U. *Eur J Pediatr*. 2023 Aug 9. doi: 10.1007/s00431-023-05083-0. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/37555972/>

Rosacea is a facial inflammatory disorder that shows an increasing incidence with age. While rosacea is common > 60 years of age, pediatric rosacea is uncommon. Diagnostic criteria are based on clinical symptoms. Laboratory investigations and histopathology are only needed to exclude other differential diagnoses. There are several subtypes such as erythematotelangiectatic, papulopustular, periorificial, and granulomatous variants. In contrast to adult rosacea, phymatous subtypes do not belong to pediatric rosacea. A special subtype seen in infants and children is an idiopathic facial aseptic granuloma. Genetic and environmental factors contribute to its pathogenesis. Treatment options are in analogy to adult rosacea classified into topical and systemic drugs. In the case of oral tetracyclines, discoloration of teeth and impairment of enamel are possible adverse events. Conclusion: Pediatric rosacea belongs to the rosacea spectrum but has peculiarities compared to the adult subtype.

Fractional ablative CO2 laser and oral isotretinoin - a prospective randomized controlled split-face trial comparing concurrent versus delayed laser treatment for acne scars. Taleb E, Gallo ES, Salameh F, et al. *Lasers Surg Med*. 2023 Aug 9. doi: 10.1002/lsm.23713. Online ahead of print.

<https://pubmed.ncbi.nlm.nih.gov/37555247/>

Background: Therapeutic dogma has been to treat acne scars with ablative fractional laser no less than 6 months after isotretinoin (ITN) cessation. Objective: To evaluate the safety and efficacy of fractional ablative CO2 laser (FACL) in patients treated concurrently with ITN. Methods: We conducted a prospective split-face randomized control trial in

patients treated with FACL concurrently with ITN versus patients treated with FACL 6 months post-ITN treatment. Patients received 3 monthly sessions of FACL with concurrent ITN treatment on half of the face; the other side of the face received the same FACL treatment regimen 6 months post-ITN cessation. Patients were followed for adverse effects up to 6 months post-FACL treatment. Final cosmesis was scored using the Quantitative Global Acne Scarring Grading System (GASGS) by three independent dermatologists. Results: The GASGS of the concurrent ITN-FACL treated side of the face was significantly lower than the side treated with delayed laser therapy (4.7 ± 2.5 vs. 7.7 ± 2.9 , respectively, $p < 0.001$). Limitations: The laser's settings were standardized, and not adjusted per patient skin type. Conclusion: Per our prospective trial, concurrent treatment of FACL -ITN is superior to delayed FACL treatment 6 months post-ITN cessation. Fractional ablative laser treatment is effective in improving acne scars, which persist despite isotretinoin therapy.

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A systematic review to evaluate the efficacy of azelaic acid in the management of acne, rosacea, melasma and skin aging. King S, Campbell J, Rowe R, et al. *J Cosmet Dermatol*. 2023 Aug 7. doi: 10.1111/jocd.15923. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/37550898/>

Background: Topical azelaic acid (AA) is indicated for acne and rosacea, but there is some evidence for its use for other dermatological conditions. Aims: To assess the effectiveness and safety of topical AA for acne vulgaris, rosacea, hyperpigmentation/melasma, and skin aging. Methods: RCTs of at least 6 weeks' treatment duration were eligible for inclusion. Databases including MEDLINE, Embase, CINAHL, and ClinicalTrials.gov were searched up to December 2022. Two reviewers were involved in all stages of the systematic review process. Results: Forty-three RCTs met the inclusion criteria. Meta-analyses within 20 rosacea studies demonstrated that erythema severity, inflammatory lesion counts, overall improvement, and treatment success (achieving skin clarity) were significantly improved with AA compared with vehicle after 12 weeks. AA was more effective than metronidazole 0.75% for improved erythema severity, overall improvement, and inflammatory lesion counts. Sixteen acne studies suggest that AA is more effective than vehicle for improving global assessments and reducing acne severity. AA 20% also significantly reduced more lesions than erythromycin gel. Within seven melasma studies, AA 20% was significantly better than vehicle for both severity and global improvement. AA 20% demonstrated significantly better results compared with hydroquinone 2% for global improvement. Very few significant differences between AA and comparators were observed for commonly reported adverse events. No eligible RCTs were found that evaluated skin aging. Conclusions: AA is more effective than vehicle for rosacea, acne and melasma. Comparisons between AA and other treatments were often equivalent. Where there is equivalence, AA may be a good option for some clinical situations. RCT evidence is needed to evaluate the effectiveness of AA on skin aging.

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Comparative efficacy of pharmacological treatments for acne vulgaris: A network meta-analysis of 221 randomized controlled trials. Huang CY, Chang IJ, Bolick N, et al. *Ann Fam Med*. 2023 Jul-Aug;21(4):358-369. doi: 10.1370/afm.2995. <https://pubmed.ncbi.nlm.nih.gov/37487721/>

Purpose: Acne is an extremely common skin disease with an estimated global prevalence of 9.4%. We aim to provide comprehensive comparisons of the common pharmacological treatments for acne. Methods: Randomized controlled trials comparing the efficacy of pharmacological therapies for acne vulgaris in patients of any age and sex and with a treatment duration of >2 weeks were included. PubMed and Embase databases were searched from inception until February 2022. Our prespecified primary end points were mean percentage reduction in total, inflammatory, and noninflammatory lesions. Treatment ranking was determined by P values. Results: There were 210 articles describing 221 trials and 37 interventions included in the analysis. Our primary analysis of percentage reduction in total lesion

count had 65,601 patients enrolled. Across all trials, the mean age was 20.4 years. The median duration of treatment was 12 weeks. The median total, inflammatory, and noninflammatory lesion counts were 72, 27, and 44, respectively. The most effective treatment was oral isotretinoin (mean difference [MD] = 48.41; P = 1.00), followed by triple therapy containing a topical antibiotic, a topical retinoid, and benzoyl peroxide (BPO) (MD = 38.15; P = .95) and by triple therapy containing an oral antibiotic, a topical retinoid, and BPO (MD = 34.83; P = .90). For monotherapies, oral or topical antibiotics or topical retinoids have comparable efficacy for inflammatory lesions, while oral or topical antibiotics have less effect on noninflammatory lesions. Conclusion: The most effective treatment for acne is oral isotretinoin, followed by triple therapies containing a topical retinoid, BPO, and an antibiotic. We present detailed comparisons of each intervention to serve as a practical database.

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Physiological and Psychological Effects of Isotretinoin in the Treatment of Patients with acne: A narrative review. Ding RL, Zheng Y, Bu J. Clin Cosmet Investig Dermatol. 2023 Jul 18;16:1843-1854. doi: 10.2147/CCID.S416267. eCollection 2023. <https://pubmed.ncbi.nlm.nih.gov/37483471/>

Isotretinoin (ISO) is a powerful vitamin A derivative that offers the potential for treatment of permanent remission of acne; however, its potential side effects on both physiological and psychological aspects limit its application. This article reviews the side effects of ISO from physiological and psychological aspects in detail, to better screen the suitable population of ISO and improve the efficiency of clinical treatment. Our findings indicate that ISO may cause teratogenicity, skin reactions, ocular reactions, changes in blood indicators, and occasional acne fulminans. To optimize clinical treatment, more attention should be paid to identifying the specific conditions under which these reactions occur, how severe they are, and how they subside to alleviate patient concerns. Regarding the controversial issue of psychological side effects caused by ISO, researchers should shift their focus to the psychological problems that acne itself may cause.

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Obstacles to early diagnosis and treatment of hidradenitis suppurativa: Current perspectives on improving clinical management. Snyder CL, Chen SX, Porter ML. Clin Cosmet Investig Dermatol. 2023 Jul 17;16:1833-1841. doi: 10.2147/CCID.S301794. eCollection 2023. <https://pubmed.ncbi.nlm.nih.gov/37483473/>

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition that can progress to significant tunnels and scars that affect quality of life, especially if diagnosis and treatment are delayed. Average delay after initial presentation of HS symptoms can range from 3 to 10 years in adults and 1 to 2 years in children. Factors associated with diagnostic delay include female gender, non-white race, and greater disease severity at diagnosis. Contributing factors include misdiagnoses, difficulty accessing a dermatologist, hesitation in seeking care due to the stigmatizing nature of the disease, and lack of awareness among providers and patients. While efforts to increase awareness include academic talks at conferences and by foundations geared toward HS, social media offers the opportunity to reach young audiences. Many patients report dissatisfaction with their HS treatments. Better understanding of HS pathophysiology and implementation of clinically focused phenotypes and endotypes can lead to development of more targeted and efficacious therapies. FDA approval of medications for HS beyond adalimumab will increase access to a wider selection of therapies, and implementation of therapeutic drug monitoring may maximize the use of biologics for HS.

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