AARS HOT TOPICS MEMBER NEWSLETTER

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AARS News

Register now for the 11th Annual AARS Scientific Symposium

Learn about some of the latest important research in acne, rosacea, and HS while interacting with some of the brightest young minds in the field and AARS leadership. Plan to join us Wednesday, May 15, 2024 from 11:00 AM – 1:00 PM for the 11th Annual AARS Scientific Symposium at the 81st Annual Meeting of the Society for Investigative Dermatology at the Hilton Anatole in Dallas, Texas. Participation and lunch is complimentary, however space is limited, so we encourage you to register now to reserve your spot! Check our website for more details in the future.
Register Now!

AARS Call for Grant Applications!

The AARS mission is to promote, support, develop and provide an educational forum for the exchange of information related to acne and rosacea and to fund clinical research opportunities for dermatology professionals who strive to improve the care of patients who suffer from acne and rosacea. The deadline to submit applications is Friday, May 31, 2024. Available opportunities are listed below.

AARS CLINICAL RESEARCH AWARD ($10K)

The AARS is proud to offer research grants to advance clinical science, while nurturing new and experienced investigators in the field of acne and rosacea. Dermatology residents, research fellows, and recent graduates are encouraged to apply for clinical research grants. Please refer to the application (downloadable below) for eligibility and application requirements.
AARS Clinical Research Award Grant Application

AARS RESEARCH SCHOLAR AWARD ($75K)

The AARS is excited to invite investigators working at the level of Instructor through Associate Professor in the field of acne or rosacea to apply for the Research Scholar Award. The individual selected for the award must have a strong career goal within the field of dermatology generally and be dedicated to furthering knowledge concerning acne or rosacea specifically. Please refer to the application (downloadable below) for eligibility and application requirements.
AARS Research Scholar Award Grant Application

Response Statement from the American Acne & Rosacea Society to the Valisure Citizen Petition on Benzene in Benzoyl Peroxide Drug Products

On March 5, 2024, Valisure, an independent analytical laboratory located in New Haven, Connecticut, filed a Citizen Petition on Benzene in Benzoyl Peroxide Drug Products. In the petition it states that “Valisure has tested and detected high levels of benzene, a known human carcinogen, in many specific batches of benzoyl peroxide (BPO) products, and the current evidence suggests that on-market BPO products could produce substantial amounts of benzene when stored at above-ambient temperatures, …”.[1] The petition further states that this problem does not appear to be a contamination issue from a specific ingredient, but instead due to the inherent instability of the BPO molecule that can potentially break down to form benzene over the shelf-life of the product, especially after exposure to high temperatures.[1,2] Benzene has become a more recent focus of attention related to safety concerns, with an increase in independent product testing and also updated regulations by the Food and Drug Administration related to benzene.[3]

The American Acne and Rosacea Society (AARS), a society founded by dermatologists years ago to enhance education on acne, fully recognizes that this is a very important issue, especially as benzene exposure is harmful to humans, and takes this petition very seriously. “Public safety is the first priority of the AARS. While we await the FDA review of the information, testing data, and proposal reported in the petition, the AARS is evaluating and researching the details stated in the document in order assure its accuracy and provide guidance based on scientific fact”, stated dermatologist Dr. James Q Del Rosso, President of the AARS.

A very common ingredient found in many over-the-counter (OTC) and prescription acne products, BPO has been widely used in the United States and globally for over 5 decades. It has been classified by the FDA as “generally recognized as safe and effective”, including in The Federal Register Final Rule report (March 4, 2010) and in a Guidance for Industry document (June 2011) “Topical Acne Products for Over-the-Counter Human Use”.[4,5] “This petition came as a surprise to all of us in dermatology as BPO is FDA-approved in many over-the-counter (OTC) and prescription topical products, including a few recently approved prescription products for acne or rosacea” said Dr. Del Rosso. That being said, the data about BPO and benzene exposure is very complex, and the AARS is doing its due diligence to get the best information it can. “Benzoyl peroxide has been a very important part of the treatment of many patients with acne and also some other skin diseases. We want to be sure that any guidance that is given and any decisions that are made are based as much as possible on solid scientific evidence”.

Right now, there are many questions about this issue and we do not yet have all the answers. Until there is further guidance from the FDA and verification of the safety and stability of BPO products, the AARS believes patients should work with their dermatologist or healthcare provider to determine what course to take. There is currently no formal mandate to stop the use of BPO, although switching to another treatment may be a potential option for some. It is important to conscientiously follow storage procedures recommended for the product being used which may minimize the potential for benzene formation. Some products also indicate specific instructions on how long to keep a BPO-containing product until it should be discarded. Other recommendations include discarding expired BPO products and those that have been exposed to temperatures above room temperature. For new BPO products, store at refrigerator temperature which at least theoretically can reduce degradation of BPO to benzene. Replace BPO products every 3 months or as recommended on the specific product.

The AARS regards the potential presence of benzene in BPO and other personal use products as a serious issue that requires more data from well-performed studies. The AARS also hope that manufacturers and regulators will carry out appropriate due diligence and take this opportunity to do the right things and determine what is best for the good of all patients. The AARS is committed to doing its part now and along the way.

References

1. Valisure Citizen Petition on Benzene in Benzoyl Peroxide Products (March 5, 2024), www.valisure.com.
2. Kucera K, Zenzola N, Hudspeth A, Dubnicka M, Hinz W, Bunick CG, Dabestani A, Light DY. Benzoyl peroxide drug products form benzene. Environ Health Perspect. 2024 Mar;132(3):37702. doi: 10.1289/EHP13984. Epub 2024 Mar 14. PMID: 38483533; PMCID: PMC10939128.
3. Guidance for Industry, Reformatting drug products that contain carbomers manufactured with benzene. US Department of Health and Human Services (Food and Drug Administration, Center for Drug Evaluation and Research), December 2023.
4. Federal Register, Vol. 75, No. 42, March 4, 2010, Rules and Regulations. pp 9767-9777.

5. Guidance for Industry, Topical Acne Drug Products for Over-the-Counter Human Use – Revision of Labeling and Classification of Benzoyl Peroxide as Safe and Effective. US Department of Health and Human Services (Food and Drug Administration, Center for Drug Evaluation and Research), June 2011.

New Medical Research

Development of solid lipid microparticles (SLMs) containing asiatic acid for topical treatment of acne: Characterization, stability, in vitro and in vivo anti-acne assessment. Chutoprapat R, Witarat J, Jongpanyangarm P, et al. *Int J Pharm*. 2024 Mar 7:123980. doi: 10.1016/j.ijpharm.2024.123980. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/38460769/

Solid lipid microparticles (SLMs) represent a promising approach for drug delivery in anti-acne applications. In this study, asiatic acid-loaded SLMs (AASLMs) were prepared by melt emulsification method in conjunction with freeze-drying. Comprehensive evaluations comprised particle size, %entrapment efficiency (%EE), %labeled amount (%LA), surface morphology, stability, %release, %skin permeation, and anti-acne activity. The AASLMs exhibited an average particle size ranging from 7.46 to 38.86 μm, with %EE and %LA falling within the range of 31.56 to 100.00 and 90.43 to 95.38, respectively. The AASLMs demonstrated a spherical shape under scanning electron microscopy, and maintained stability over a 3-month period. Notably, formulations with 10 % and 15 % cetyl alcohol stabilized with poloxamer-188 (specifically F6 and F12) displayed a minimum inhibitory concentration (MIC) value of 75 mg/ml against *Cutibacterium acnes.* Furthermore, F12 exhibited a higher %release and %skin permeation compared to F6 over 24 h. In a single-blind clinical trial involving fifteen participants with mild-to-moderate acne, F12 showcased its potential not only in reducing porphyrin intensity and enhancing skin barriers but also in significantly improving skin hydration and brightness. However, further investigations with larger subject cohorts encompassing diverse age groups and genders are necessary to thoroughly establish the performance of the developed AASLMs.

Early and sustained acne lesion reductions with fixed-dose clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel. Harper JC, Kircik LH, Gold M, et al. *J Drugs Dermatol*. 2024 Mar 1;23(3):125-131. doi: 10.36849/jdd.7907. https://pubmed.ncbi.nlm.nih.gov/38443130/

Background: A once-daily, three-pronged approach using an antibiotic, antibacterial, and retinoid may provide faster acne improvement versus monotherapy or dual-combination products. This post hoc analysis compared threshold acne lesion reductions with clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% (CAB) gel - the first FDA-approved triple-combination topical acne product - to its dyads and vehicle. Methods: Phase 2 (N=741; NCT03170388) and phase 3 (N=183; N=180; NCT04214639; NCT04214652), double-blind, 12-week studies randomized participants aged ≥9 years with moderate-to-severe acne to once-daily CAB or vehicle gel; the phase 2 study included three additional dyad gel arms. The pooled percentage of participants achieving ≥33%, ≥50%, and ≥75% reduction in inflammatory and noninflammatory acne lesions was evaluated. Results: As early as week 4 in the phase 2 study, ≥33% reduction in inflammatory lesions occurred in a significantly greater percentage of CAB gel-treated participants (82.7%) than with the 3 dyads and vehicle (61.1-69.8%; P<0.05, all). These early reductions were sustained throughout the study, with significantly (P<0.05) more CAB-treated participants achieving ≥50% reduction in inflammatory lesions versus dyads and vehicle from weeks 4-12. By week 12, CAB led to substantial reductions of ≥75% in significantly more participants than dyads and vehicle (65.8% vs 49.9-51.2% and 21.6%; P<0.05, all). Similar trends were observed for noninflammatory lesions in the phase 2 study and for inflammatory and noninflammatory lesions in the phase 3 studies. Conclusions: Lesion count reductions were significantly greater with CAB versus its dyads and vehicle gel as early as week 4, with substantial reductions observed after 12 weeks of treatment. This

faster-acting and sustained efficacy of CAB gel - coupled with its optimized formulation, once-daily dosing, and tolerability - may positively impact treatment adherence.
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A novel systems-wide approach in addressing acne with a multi-targeting nutraceutical. Burgess C, Gold M, Farris PK, et al. *J Drugs Dermatol*. 2024 Mar 1;23(3):160-167. doi: 10.36849/jdd.8138. https://pubmed.ncbi.nlm.nih.gov/38443131/
Acne vulgaris (AV) is one of the top concerns dermatologists encounter from women. Until now, therapies addressing AV have largely centered around, and have been successful at, targeting the pathophysiological mechanisms that occur at the pilosebaceous unit: sebum hypersecretion, follicular keratinization, over-proliferation of *Cutibacterium acnes*, and a localized immune response. In addition to these, there is good evidence to suggest that other systemic drivers of a generalized inflammatory response may contribute to the development or exacerbation of acne and that addressing these underlying factors may open more opportunities for developing effective treatments. These include psycho-emotional stress, diet and metabolism, hormonal fluctuations, skin and gut microbiome, oxidative stress, and immune response. While there is accumulating evidence that vitamins, minerals, and botanicals may mitigate some of the pro-inflammatory effects from the activation of these underlying systems, their use and recommendations are limited by a lack of quality efficacy and safety evidence. Here, we present the current evidence for the use of individual supplements in addressing the 6 systemic underlying drivers of AV. We also present a clinical study on the safety and efficacy of a nutraceutical combining many of these ingredients in the management of AV in men and women.
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Treatment of erythematous acne scars using 595-nm pulsed dye laser combined with 1565-nm ResurFX nonablative fractional laser. Zhou C, Yao M, Chen W, et al. *J Cosmet Dermatol*. 2024 Mar 1. doi: 10.1111/jocd.16235. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/38426374/
Background: Acne vulgaris is a common inflammatory disease associated with various sequelae after skin lesion remission. Acne erythema has been considered simple erythema or a vascular lesion; however, because the understanding of this disease has improved, acne erythema is currently considered an early scar with erythematous components. Aims: This study evaluated the efficacy of using both a 595-nm pulsed dye laser (PDL) and 1565-nm nonablative fractional laser (NAFL) for the treatment of erythematous scars caused by acne. Methods: Ninety patients with acne scars were equally randomized to two groups. Group A (n = 45) received treatment with the NAFL. Group B (n = 45) received treatment with the PDL and NAFL. Each patient underwent one treatment session and 4 weeks of follow-up. Results: Qualitative ($\chi 2 = 12.415$; $p < 0.05$) and quantitative ($t = 2.675$; $p < 0.05$) scores of Groups A and B were determined using a global scarring grading system and exhibited statistically significant differences. The quantitative score of Group A was higher than that of Group B (6.67 ± 3.46 vs. 4.98 ± 2.44). The erythema areas of the groups differed significantly after treatment, with Group B exhibiting more notable score improvements (5.00 [3.10, 7.10] vs. 2.80 [1.65, 4.60]; $Z = 3.072$; $p < 0.05$). The erythema regression rate of Group B (88.9%) was significantly higher than that of Group A (66.7%) ($\chi 2 = 20.295$; $p < 0.001$). Adverse events, including redness and swelling (86.6%), scabbing (78.8%), and purpura (36.6%), occurred within 7 days for 86.6% of patients. Conclusions: The combined use of the PDL and NAFL is safe and effective for erythematous acne scars.
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Investigating the impact of added profhilo mesogel to subcision versus subcision monotherapy in treating acne scars; a single-blinded, split-face randomized trial. Dastgheib M, Heidari S, Azizipour A, et al. *J Cosmet Dermatol*. 2024 Mar 1. doi: 10.1111/jocd.16258. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/38429946/

Background: Acne scar is an inflammatory condition, which commonly occurs in patients with acne vulgaris, especially in adults. Mesogels have been reported effective in improving atrophic acne scars. Aims: We investigated the efficacy of adding Profhilo (a hyaluronic acid-based filler) to subcision as a new treatment method. Methods: Twelve patients aged 18-45 years with atrophic acne scars on both sides of the face participated in this single-blinded, split-face, randomized controlled trial. Each side of the face was randomly assigned to one of the treatment methods, including subcision alone and subcision + Profhilo. Patients in the Profhilo arm received mesogel (1 cc) in addition to the subcision procedure. Both methods were carried out two times at 1-month intervals. Assessments were done based on the sonographic depth of scars, and two blinded observers examined photographs at baseline and 3 months after the final session and the results were reported based on an exclusively made formula as the total score. The Global Improvement Scale and Visual Analogue Scale (VAS) (for patient satisfaction) were also used. Results: The VAS score of patient satisfaction was statistically significant in the Profhilo arm, with a mean improvement of 528.08 and 219.06 in the subcision arm ($p = 0.02$). No significant difference was seen in total acne scar reduction comparing the two methods (29.74 in the Profhilo arm and 22.27 in the subcision arm, $p = 0.56$). Sonographic depth reduction was also non-significant, with a mean of 29.21 in the Profhilo arm and 28.53 in the subcision arm ($p = 0.4$). The mean global improvement was reported as four in both arms, and no statistical significance was observed ($p = 0.89$). The best response to treatment belonged to the rolling subtype in both methods ($p = 0.029$ for the Profhilo arm and $p = 0.001$ for the subcision arm). Conclusion: Despite no significant difference between the methods, Profhilo is more effective due to a higher satisfaction rate and better physiologic effects.
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Rhizoma paridis saponins attenuate gram-negative bacteria-induced inflammatory acne by binding to KEAP1 and modulating Nrf2 and MAPK pathways. Yang Y, Wang C, Wang J, et al. *J Cell Mol Med*. 2024 Mar;28(6):e18146. doi: 10.1111/jcmm.18146. https://pubmed.ncbi.nlm.nih.gov/38426932/
Acne vulgaris represents a chronic inflammatory condition, the pathogenesis of which is closely associated with the altered skin microbiome. Recent studies have implicated a profound role of Gram-negative bacteria in acne development, but there is a lack of antiacne agents targeting these bacteria. Polyphyllins are major components of Rhizoma Paridis with great anti-inflammatory potential. In this study, we aimed to evaluate the antiacne effects and the underlying mechanisms of PPH and a PPH-enriched Rhizoma Paridis extract (RPE) in treating the Gram-negative bacteria-induced acne. PPH and RPE treatments significantly suppressed the mRNA and protein expressions of interleukin (IL)-1β and IL-6 in lipopolysaccharide (LPS)-induced RAW 264.7 and HaCaT cells, along with the intracellular reactive oxygen species (ROS) generation. Furthermore, PPH and RPE inhibited the nuclear translocation of nuclear factor kappa-B (NF-κB) P65 in LPS-induced RAW 264.7 cells. Based on molecular docking, PPH could bind to kelch-like ECH-associated protein 1 (KEAP1) protein. PPH and RPE treatments could activate nuclear factor erythroid 2-related factor 2 (NRF2) and upregulate haem oxygenase-1 (HO-1). Moreover, RPE suppressed the mitogen-activated protein kinase (MAPK) pathway. Therefore, PPH-enriched RPE showed anti-inflammatory and antioxidative effects in vitro, which is promising for alternative antiacne therapeutic.
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NLRP3 inflammasome activation and NETosis positively regulate each other and exacerbate proinflammatory responses: implications of NETosis inhibition for acne skin inflammation treatment. Kim HJ, Lee YS, Lee BS, et al. *Cell Mol Immunol*. 2024 Feb 26. doi: 10.1038/s41423-024-01137-x. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/38409251/
Inflammasomes are multiprotein complexes involved in the host immune response to pathogen infections. Thus, inflammasomes participate in many conditions, such as acne. Recently, it was shown that NETosis, a type of

neutrophil cell death, is induced by bacterial infection and is involved in inflammatory diseases such as delayed wound healing in patients with diabetes. However, the relationship between inflammasomes and NETosis in the pathogenesis of inflammatory diseases has not been well studied. In this study, we determined whether NETosis is induced in *P. acnes*-induced skin inflammation and whether activation of the nucleotide-binding domain, leucine-rich family, and pyrin domain-containing-3 (NLRP3) inflammasome is one of the key factors involved in NETosis induction in a mouse model of acne skin inflammation. We found that NETosis was induced in *P. acnes*-induced skin inflammation in mice and that inhibition of NETosis ameliorated *P. acnes*-induced skin inflammation. In addition, our results demonstrated that inhibiting inflammasome activation could suppress NETosis induction in mouse skin. These results indicate that inflammasomes and NETosis can interact with each other to induce *P. acnes*-induced skin inflammation and suggest that targeting NETosis could be a potential treatment for inflammasome-mediated diseases as well as NETosis-related diseases.

Interrupting an IFN-γ-dependent feedback loop in the syndrome of pyogenic arthritis with pyoderma gangrenosum and acne. Lee W, Stone DL, Hoffmann P, et al. *Ann Rheum Dis*. 2024 Feb 26:ard-2023-225085. doi: 10.1136/ard-2023-225085. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/38408849/

Objectives: To study the molecular pathogenesis of PAPA (pyogenic arthritis, pyoderma gangrenosum and acne) syndrome, a debilitating hereditary autoinflammatory disease caused by dominant mutation in PSTPIP1. Methods: Gene knock-out and knock-in mice were generated to develop an animal model. THP1 and retrovirally transduced U937 human myeloid leukaemia cell lines, peripheral blood mononuclear cells, small interfering RNA (siRNA) knock-down, site-directed mutagenesis, cytokine immunoassays, coimmunoprecipitation and immunoblotting were used to study inflammasome activation. Cytokine levels in the skin were evaluated by immunohistochemistry. Responsiveness to Janus kinase (JAK) inhibitors was evaluated ex vivo with peripheral blood mononuclear cells and in vivo in five treatment-refractory PAPA patients. Results: The knock-in mouse model of PAPA did not recapitulate the human disease. In a human myeloid cell line model, PAPA-associated PSTPIP1 mutations activated the pyrin inflammasome, but not the NLRP3, NLRC4 or AIM2 inflammasomes. Pyrin inflammasome activation was independent of the canonical pathway of pyrin serine dephosphorylation and was blocked by the p.W232A PSTPIP1 mutation, which disrupts pyrin-PSTPIP1 interaction. IFN-γ priming of monocytes from PAPA patients led to IL-18 release in a pyrin-dependent manner. IFN-γ was abundant in the inflamed dermis of PAPA patients, but not patients with idiopathic pyoderma gangrenosum. Ex vivo JAK inhibitor treatment attenuated IFN-γ-mediated pyrin induction and IL-18 release. In 5/5 PAPA patients, the addition of JAK inhibitor therapy to IL-1 inhibition was associated with clinical improvement. Conclusion: PAPA-associated PSTPIP1 mutations trigger a pyrin-IL-18-IFN-γ positive feedback loop that drives PAPA disease activity and is a target for JAK inhibition.

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Novel antimicrobial peptides against *Cutibacterium acnes* designed by deep learning. Dong Q, Wang S, Miao Y, et al. *Sci Rep*. 2024 Feb 24;14(1):4529. doi: 10.1038/s41598-024-55205-3. https://pubmed.ncbi.nlm.nih.gov/38402320/

The increasing prevalence of antibiotic resistance in *Cutibacterium acnes* (*C. acnes*) requires the search for alternative therapeutic strategies. Antimicrobial peptides (AMPs) offer a promising avenue for the development of new treatments targeting *C. acnes*. In this study, to design peptides with the specific inhibitory activity against *C. acnes*, we employed a deep learning pipeline with generators and classifiers, using transfer learning and pretrained protein embeddings, trained on publicly available data. To enhance the training data specific to *C. acnes* inhibition, we constructed a phylogenetic tree. A panel of 42 novel generated linear peptides was then synthesized and experimentally evaluated for their antimicrobial selectivity and activity. Five of them demonstrated their high potency

and selectivity against *C. acnes* with MIC of 2-4 µg/mL. Our findings highlight the potential of these designed peptides as promising candidates for anti-acne therapeutics and demonstrate the power of computational approaches for the rational design of targeted antimicrobial peptides.
Download Reference Document

Anatomical variants of acne differ in their impact on social perception. Jankowski M, Goroncy A. *J Eur Acad Dermatol Venereol*. 2024 Feb 20. doi: 10.1111/jdv.19798. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/38379351/
Background: Acne negatively affects quality of life, however quality-of-life scores poorly correlate with disease severity scores. Previous research demonstrated existence of facial areas in which skin lesions have greater impact on gaze patterns. Therefore, we hypothesized that anatomical variants of acne may be perceived differently. Objectives: The aim was to investigate effect of anatomical variants of acne on natural gaze patterns and resulting impact on social perception of acne patients. Methods: We tracked eye movements of participants viewing neutral and emotional faces with acne. Images were rated for acne-related visual disturbance, and emotional faces were rated for valence intensity. Respondents of an online survey were asked to rate their perception of pictured individuals' personality traits. Results: All faces with acne were perceived as less attractive and received poorer personality judgements with mid-facial acne presenting smallest deviation from healthy faces. T-zone and mixed acne exhibited the least significant difference in respondents gaze behavior pattern from each other. In addition, there was no significant difference in respondents' grading of acne visual disturbance or ratings for attractiveness, success and trustworthiness. U-zone adult female acne was rated as the most visually disturbing and received the lowest scores for attractiveness. Happy faces with adult female acne were rated as less happy compared to other acne variants and clear-skin faces. Conclusions: Anatomic variants of acne have a distinct impact on gaze patterns and social perception. Adult female acne has the strongest negative effect on recognition of positive emotions in affected individuals, attractiveness ratings and forming social impressions. If perioral acne lesions are absent, frontal lesions determine impact of acne on social perception irrespective of the presence of mid-facial lesions. This perceptive hierarchy should be taken into consideration while deciding treatment goals in acne patients, prioritizing achieving remission in perioral and frontal area.

Anti-bacterial activity of green synthesized silver and zinc oxide nanoparticles against *Propionibacterium acnes*. Al-Momani H, Massadeh MI, Almasri M, et al. *Pharmaceuticals* (Basel). 2024 Feb 16;17(2):255. doi: 10.3390/ph17020255. https://pubmed.ncbi.nlm.nih.gov/38399471/
Propionibacterium acnes plays a critical role in the development of acne vulgaris. There has been a rise in the number of patients carrying *P. acnes* strains that are resistant to antibiotics. Thus, alternative anti-microbial agents are required. Zinc oxide (ZnO-NPs) and silver (Ag-NPs) nanoparticles can be used against several antibiotic-resistant bacteria. The impact of Ag-NPs and ZnO-NPs against two clinical strains of *P. acnes*, P1 and P2, and a reference strain, NCTC747, were investigated in this research. A chemical approach for the green synthesis of Ag-NPs and ZnO-NPs from Peganum harmala was employed. The microtiter plate method was used to examine the effects of NPs on bacterial growth, biofilm development, and biofilm eradication. A broth microdilution process was performed in order to determine minimal inhibitory (MIC) concentrations. Ag-NPs and ZnO-NPs had a spherical shape and average dimensions of 10 and 50 nm, respectively. MIC values for all *P. acnes* strains for Ag-NPs and ZnO-NPs were 125 µg/mL and 250 µg/mL, respectively. Ag-NP and ZnO-NP concentrations of 3.9- 62.5 µg/mL and 15-62.5 µg/mL significantly inhibited the growth and biofilm formation of all *P. acnes* strains, respectively. ZnO-NP concentrations of 15-62.5 µg/mL significantly inhibited the growth of NCTC747 and P2 strains. The growth of P1 was impacted by concentrations of 31.25 µg/mL and 62.5 µg/mL. Biofilm formation in the NCTC747 strain was diminished by a ZnO-

NP concentration of 15 µg/mL. The clinical strains of *P. acnes* were only affected by ZnO-NP titres of more than 31.25 µg/mL. Established P. acne biofilm biomass was significantly reduced in all strains at a Ag-NP and ZnO-NP concentration of 62.5 µg/mL. The findings demonstrated that Ag-NPs and ZnO-NPs exert an anti-bacterial effect against *P. acnes*. Further research is required to determine their potential utility as a treatment option for acne.
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Alcohol promotes lipogenesis in sebocytes-implications for acne. Kleemann J, Cinatl J Jr, Hoffmann S, et all. *Cells*. 2024 Feb 11;13(4):328. doi: 10.3390/cells13040328. https://pubmed.ncbi.nlm.nih.gov/38391942/
The oral consumption of alcohol (ethanol) has a long tradition in humans and is an integral part of many cultures. The causal relationship between ethanol consumption and numerous diseases is well known. In addition to the well-described harmful effects on the liver and pancreas, there is also evidence that ethanol abuse triggers pathological skin conditions, including acne. In the present study, we addressed this issue by investigating the effect of ethanol on the energy metabolism in human SZ95 sebocytes, with particular focus on qualitative and quantitative lipogenesis. It was found that ethanol is a strong trigger for lipogenesis, with moderate effects on cell proliferation and toxicity. We identified the non-oxidative metabolism of ethanol, which produced fatty acid ethyl esters (FAEEs), as relevant for the lipogenic effect-the oxidative metabolism of ethanol does not contribute to lipogenesis. Correspondingly, using the Seahorse extracellular flux analyzer, we found an inhibition of the mitochondrial oxygen consumption rate as a measure of mitochondrial ATP production by ethanol. The ATP production rate from glycolysis was not affected. These data corroborate that ethanol-induced lipogenesis is independent from oxygen. In sum, our results give a causal explanation for the prevalence of acne in heavy drinkers, confirming that alcoholism should be considered as a systemic disease. Moreover, the identification of key factors driving ethanol-dependent lipogenesis may also be relevant in the treatment of acne vulgaris.
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Lack of association of acne severity with depression, anxiety, stress, and eating attitudes: A cross-sectional study. Karaağaç M, Akça HM, Acat Ö. *J Pers Med*. 2024 Jan 23;14(2):133. doi: 10.3390/jpm14020133. https://pubmed.ncbi.nlm.nih.gov/38392567/
Background: this study aimed to investigate the relationship between acne severity and depression, anxiety, stress, and negative eating attitudes in patients with acne vulgaris. Method: This study was conducted with 81 patients with acne vulgaris who applied to the dermatology outpatient clinic of Karaman Training and Research Hospital. The patients were asked to complete a sociodemographic data form, the three-factor nutrition questionnaire (TFEQ-21), and the depression anxiety stress scale (DASS-21). Acne severity was assessed using the global acne grading system (GAGS) by an expert dermatologist. Results: Of the 81 patients, 74.1% were female and the average age of the cohort was 22.86 years. The average body mass index of the patients was 21.78 and the GAGS average score was 24.25. Correlation tests revealed the lack of any relationship between the GAGS score and the DASS-21 and TFEQ-21 scale scores (and their subscales). The DASS-21 depression subscale was correlated with the TFEQ-21 total score, and TFEQ-21 emotional eating and TFEQ-21 uncontrolled eating scores. Additionally, a relationship was identified between the DASS21-stress subscale score and TFEQ-21 uncontrolled Eating and TFEQ-21 total score, as well as between the DASS21-anxiety scale and the TFEQ-21 total score and TFEQ-21 uncontrolled eating subscale score. Conclusions: Although no relationship was found between acne severity and depression, anxiety, or eating disorders, these conditions can increase the risk of eating disorders among acne patients. Therefore, it is critical to take the necessary precautions for the treatment of depression and anxiety disorders in this patient population.

Topical 10% tranexamic acid with and without microneedling in the treatment of erythematotelangiectatic rosacea: A split-face comparative study. Mohamed RR, Mahmoud Mohamed LG, Mansour M, Rageh MA. *J Clin Aesthet Dermatol*. 2024 Feb;17(2):47-51. https://pubmed.ncbi.nlm.nih.gov/38444423/

Objective: Erythematotelangiectatic rosacea (ETR) is recognized by flushing, persistent centrofacial erythema, and telangiectasia. Many lines of topical treatments have been used for ETR with variable outcomes. We aimed to evaluate the efficacy of 10% topical tranexamic acid (TXA) with and without microneedling in treating ETR. Methods: All patients received treatment on both sides of the face, the right side was treated with microneedling combined with 10% topical TXA, and the left side was treated with 10% topical TXA only. All patients received three sessions at two weeks intervals. The final evaluation was done three months after the last treatment session. Results: The study included 45 females. Their age ranged between 20 and 48 years. The duration of the disease ranged from two months to five years. Both sides of the face showed improvement after treatment. There was a clinically and dermoscopic significant improvement in the side treated with microneedling + TXA compared to the side of the face treated with TXA alone. Limitations: The small sample size and the lack of long-term follow-up. Conclusion: This study showed that TXA is an effective and safe treatment modality for ETR. Microneedling can enhance the delivery of TXA and lead to better outcomes regarding erythema and telangiectasia.

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Clinical Reviews

Hidradenitis suppurativa-related autoinflammatory syndromes: An updated review on the Clinics, genetics, and treatment of Pyoderma gangrenosum, Acne and Suppurative Hidradenitis (PASH), Pyogenic Arthritis, Pyoderma gangrenosum, Acne and Suppurative Hidradenitis (PAPASH), Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis (SAPHO), and rarer forms. Maronese CA, Moltrasio C, Marzano AV. *Dermatol Clin*. 2024 Apr;42(2):247-265. doi: 10.1016/j.det.2023.12.004. Epub 2024 Jan 4. https://pubmed.ncbi.nlm.nih.gov/38423685/

Hidradenitis suppurativa (HS) is an autoinflammatory skin disorder of the terminal hair follicle, which can present in sporadic, familial, or syndromic form. A classification has been proposed for the latter, distinguishing cases associated with a known genetic condition, with follicular keratinization disorders or with autoinflammatory diseases. This review focuses on the clinical and genetic features of those entities (i.e., pyoderma gangrenosum [PG], acne and HS; PG, acne, pyogenic arthritis and HS; psoriatic arthritis, PG, acne and HS; synovitis, acne, pustulosis, hyperostosis, osteitis; and so forth) for which the collective term HS-related autoinflammatory syndromes is proposed.

Rosacea: Pathogenesis and therapeutic correlates. Geng RSQ, Bourkas AN, Mufti A, Sibbald RG. *J Cutan Med Surg*. 2024 Mar 7:12034754241229365. doi: 10.1177/12034754241229365. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/38450615/

Rosacea is a chronic inflammatory condition of which there is no cure. The pathogenesis of rosacea is likely multifactorial, involving genetic and environmental contributions. Current understanding suggests that pro-inflammatory pathways involving cathelicidins and inflammasome complexes are central to rosacea pathogenesis. Common rosacea triggers modulate these pathways in a complex manner, which may contribute to the varying severity and clinical presentations of rosacea. Established and emerging rosacea treatments may owe their efficacy to their ability to target different players in these pro-inflammatory pathways. Improving our molecular understanding of rosacea will guide the development of new therapies and the use of combination therapies.

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Management of acne in pregnancy. Rau A, Keri J, Murase JE. *Am J Clin Dermatol*. 2024 Mar 7. doi: 10.1007/s40257-024-00851-6. Online ahead of print. https://pubmed.ncbi.nlm.nih.gov/38453786/

Acne is one of the most common dermatological conditions to affect women of childbearing age, so it is important to consider the safety of long-term acne treatments on women who could become pregnant. In this review article, we clarify what management options are available to treat acne during pregnancy. Topical treatments, typically first-line for acne, such as azelaic acid, clindamycin, erythromycin, metronidazole, benzoyl peroxide, salicylic acid, dapsone, and retinoids, were reviewed. Systemic treatments, such as zinc supplements, cephalexin, cefadroxil, amoxicillin, azithromycin, erythromycin, and corticosteroids, typically second-line for acne, were also reviewed. Alternative treatments such as light therapy and cosmetic procedures were also evaluated. Due to recommendation of sunscreen utilization during acne treatments, sunscreen usage during pregnancy was also assessed. Management of acne during unplanned pregnancy was discussed in further detail regarding safety and adverse effects. Through summarized tables and examples of studies demonstrating safety and efficacy of treatments, the following is a resource for providers and patients to utilize for management of acne during pregnancy.

Atrophic postacne scar treatment: Narrative review. Attia E. *JMIR Dermatol*. 2024 Feb 21:7:e49954. doi: 10.2196/49954. https://pubmed.ncbi.nlm.nih.gov/38381492/

Acne scarring is a frequent complication of acne. Scars negatively impact psychosocial and physical well-being. Optimal treatments significantly improve the appearance, quality of life, and self-esteem of people with scarring. A wide range of interventions have been proposed for acne scars. This narrative review aimed to focus on facial atrophic scarring interventions. The management of acne scarring includes various types of resurfacing (chemical peels, lasers, and dermabrasion); the use of injectable fillers; and surgical methods, such as needling, punch excision, punch elevation, or subcision. Since the scarred tissue has impaired regeneration abilities, the future implementation of stem or progenitor regenerative medical techniques is likely to add considerable value. There are limited randomized controlled trials that aimed to determine which treatment options should be considered the gold standard. Combining interventions would likely produce more benefit compared to the implementation of a single method.

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PCOS stratification for precision diagnostics and treatment. Joshi A. *Front Cell Dev Biol*. 2024 Feb 8:12:1358755. doi: 10.3389/fcell.2024.1358755. eCollection 2024. https://pubmed.ncbi.nlm.nih.gov/38389707/

Globally, polycystic ovarian syndrome (PCOS) affects approximately 10% of fertile women, leading to great health and economic burden. PCOS is a heterogenous illness that can cause infertility, irregular menstrual cycles, acne, and hirsutism, among other symptoms. The clinical diagnosis is primarily a diagnosis of exclusion if one or more of the three primary symptoms, namely, oligo- or anovulation, hyperandrogenism, and polycystic ovarian morphology, are present. Obesity and PCOS are often coexisting disorders that may be bidirectionally causally related. Phenotypic heterogeneity throughout the reproductive lifespan, such as the overlap of PCOS symptoms with regular fluctuations in a woman's menstrual cycle and metabolism during the menarche and menopausal transition, further complicates diagnosis. PCOS etiology is mostly unknown and complex, likely due to the fact that it is a group of disorders with overlapping metabolic and reproductive problems. Evidence-based, common, standardized guidelines for PCOS diagnosis and treatment are urgently needed. Genomics and clinical data from populations across diverse ages and ethnicities are urgently needed to build efficient machine learning models for the stratification of PCOS. PCOS subtype-specific strategies for early screening, an accurate diagnosis, and management throughout life will optimize healthcare resources and reduce unnecessary testing. This will pave the way for women to be able to take the best possible care of their own health using the latest clinical expertise combined with their unique needs and preferences.

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Recent advances in the management of rosacea through natural compounds. Semenescu I, Similie D, Diaconeasa Z, Danciu C. *Pharmaceuticals* (Basel). 2024 Feb 6;17(2):212. doi: 10.3390/ph17020212. https://pubmed.ncbi.nlm.nih.gov/38399428/

Rosacea is a chronic skin disorder that affects more than 5% of the world's population, with the number increasing every year. Moreover, studies show that one-third of those suffering from rosacea report a degree of depression and are less compliant with treatment. Despite being the subject of prolonged studies, the pathogenesis of rosacea remains controversial and elusive. Since most medications used for the management of this pathology have side effects or simply do not yield the necessary results, many patients lose trust in the treatment and drop it altogether. Thus, dermato-cosmetic products with natural ingredients are gaining more and more notoriety in front of synthetic ones, due to the multiple benefits and the reduced number and intensity of side effects. This review is a comprehensive up-to-date report of studies that managed to prove the beneficial effects of different botanicals that may be useful in the short and long-term management of rosacea-affected skin. Based on recent preclinical and clinical studies, this review describes the mechanisms of action of a large array of phytochemicals responsible for alleviating the clinical symptomatology of the disease. This is useful in further aiding and better comprehending the way plant-based products may help in managing this complex condition, paving the way for research in this area of study.

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Acne and pregnancy: A clinical review and practice pearls. Yaghi M, Baboun D, Keri JE. *Cutis*. 2024 Jan;113(1):E26-E32. doi: 10.12788/cutis.0951. https://pubmed.ncbi.nlm.nih.gov/38478945/

Acne vulgaris is a common condition that routinely affects females of childbearing age. Taking into consideration the reproductive journey of women when treating acne is of paramount importance given the safety concerns to both the mother and the fetus associated with certain medications. Therefore, careful consideration of therapeutic choices during pregnancy is crucial. Herein, we summarize the safety of acne treatments during pregnancy and offer practical clinical pearls for routine dermatology practice.