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New Medical Research

Systemic isotretinoin has an impact on hemoglobin, ferritin, urea, ceruloplasmin, albumin, uric acid levels and neutrophil to lymphocyte ratio in acne patients. Hareedy MS, Tawfik KM. J Cosmet Dermatol. 2022 Jun 29. doi: 10.1111/jocd.15199. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35770307/>

Background: Patients suffering from moderate to severe acne are commonly treated with systemin isotretinoin, however, a great controversy about its safety had been raised. The aim of the present study is to evaluate effects of isotretinoin on hepatic, renal and hematologic functions and to evaluate the potential oxidative stress in relation to isotretinoin therapy. Methods: Fifty-three female patients, treated from moderate-severe acne with isotretinoin (0.5mg/kg/day), were included. Blood samples were taken for measuring low density lipoprotein (LDL), triglycerides, hemoglobin, erythrocyte sedimentation rate (ESR), bilirubin, total protein, albumin, globulin, blood urea nitrogen, ferritin, uric acid, creatinine, C- reactive protein (CRP), ceruloplasmin, alanine transaminase (ALT), aspartate transaminase (AST) levels, and Red Blood Cells (RBC), White Blood cells (WBCs), and Platelet counts before starting isotretinoin treatment and six months later. Results: Isotretinoin was associated with increased levels of triglycerides, LDL, ESR, CRP, uric acid, and ferritin after 6 months of therapy ($p < 0.0001$), Blood urea levels were significantly elevated from 3.681 ± 0.91 to 3.838 ± 0.877 ($p = 0.014$), ALT, AST, Hemoglobin, globulin, and total proteins were significantly elevated after 6 months. Platelets, WBCs, albumin, albumin/globulin ratio, copper, ceruloplasmin, and neutrophil/lymphocyte ratio were significantly decreased after 6 months. Conclusion: Isotretinoin therapy could be associated with oxidative stress and hepatic, lipid, and blood abnormalities in patients with acne. Serum ferritin was elevated while serum ceruloplasmin was decreased. isotretinoin could also affect immune regulation (decreasing neutrophil to lymphocyte ratio), isotretinoin was associated with a possible positive nitrogen balance (increasing proteins) and with elevations of blood urea nitrogen and uric acid levels.

Efficacy of alpha hydroxy acid combined with intense pulsed light in the treatment of acne vulgaris: A meta-analysis. Huang Q, Chen D, Pan S, et al. J Cosmet Dermatol. 2022 Jun 28. doi: 10.1111/jocd.15186. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35763391/>

Background: Acne patients frequently receive combination therapy. However, there has been no rigorous review of the efficacy of combining alpha hydroxy acid with IPL for acne vulgaris treatment. Objective: Assessing the effectiveness and safeness of alpha-hydroxy acids in combination with IPL in the treatment of people with acne vulgaris. Methods: A computer search of common biomedical databases, including PubMed, Web of Science, Cochrane Library, Embase, Wanfang, CNKI, SinoMed, and VIP, was extensively conducted to identify previous studies on randomized controlled trials of alpha hydroxy acid combined with IPL in the management of acne vulgaris. Results: A total of 18 publications were included (1435 patients with common acne met the inclusion criteria). The meta-analysis showed that alpha hydroxy acid (AHA) combined with IPL had higher overall efficacy than the control group (OR = 4.24; 95% CI 2.66~6.74; $P < 0.01$). In the case of acne vulgaris, AHA combined with IPL and the AHA alone showed a remarkable difference in total efficiency (OR = 4.10; 95% CI 2.12~7.91; $P < 0.01$); and AHA combined with IPL were more effective than IPL alone (OR = 4.02; 95% CI 2.25~7.16; $P < 0.01$). In addition, the occurrence of adverse reactions that occurred in AHA combined with IPL and control groups did not differ (OR = 0.86; 95% CI 0.46~1.60; $P = 0.64$). Conclusion: AHA combined with IPL therapy was superior to other therapies. Although it was slightly more expensive, it was effective and had a wide range of applications.

Integrative skincare trial of intense pulsed light followed by the phyto corrective mask, phyto corrective gel and resveratrol BE for decreasing post-procedure downtime and improving procedure outcomes in patients with rosacea. Barbarino SC, Bucay VW, Cohen JL, Gold MH. *J Cosmet Dermatol.* 2022 Jun 28. doi: 10.1111/jocd.15189. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35765796/>

Background: Rosacea is a chronic inflammatory skin condition of varying severity that can significantly impact patient quality of life. Intense pulsed light (IPL) is an established treatment for rosacea-associated telangiectasia, inflammation, and erythema. This study assessed whether application of a phyto-corrective mask, gel, and resveratrol antioxidant serum after IPL treatment can improve outcomes and reduce procedure-related adverse effects. Methods: In a prospective, open-label, split-face, 3-month study, 10 subjects with moderate to severe facial rosacea underwent IPL treatment on both sides of the face. The following were applied to the right side of the face only: phyto corrective mask once weekly starting immediately after IPL; phyto corrective gel twice daily; and resveratrol antioxidant treatment at night. Both sides of the face were treated with sunscreen. Subjects were assessed on Day 1, 1 and 3 months after IPL by three, independent evaluators using the 5-point Global Aesthetic Improvement Scale (GAIS). All subjects rated skin redness, hydration and overall improvement on Day 1 and completed a patient satisfaction questionnaire at the 1- and 3-month visits. Results: Ten women were enrolled, aged 44-72 years old, with moderate (n=6) to severe (n=4) rosacea. IPL was effective at reducing symptoms with rosacea classified as absent in 5 women and mild in 5 at the final 3-month visit. GAIS scores also revealed improvements on both sides of the face, but the skincare treated side showed continuous improvement over 3 months with all patients remaining at least 'Improved', whereas there appeared to be a waning effect after 1 month following with IPL alone. On Day 1 after IPL, all women reported less redness, improved hydration and improved skin appearance on the right side of the face. Patient satisfaction was consistently rated higher on the right side of the face. Conclusion: Application of a phyto-corrective mask, gel, and resveratrol antioxidant serum may complement IPL treatment for rosacea by enhancing treatment outcomes and reducing procedure-related symptoms.

Treatment opportunities and technological progress prospective for acne vulgaris. N Chauhan P, Sharma A, Rasheed H, et al. *Curr Drug Deliv.* 2022 Jun 23. doi: 10.2174/1567201819666220623154225. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35747981/>

A frequent inflammatory pilosebaceous disorder that affects 80-90% of teenagers, acne vulgaris is still a concern for dermatologists and other doctors in the field of medicine. Acne has a significant psychosocial impact and is responsible for a bigger worldwide burden of disease than psoriasis, cellulitis, and melanoma, as measured by age-standardized disability-adjusted life years. Patients may experience psychological problems as well as severe skin scars as a result of the condition. The pathogenesis process of acne lesion is complex, so it is myriad of available treatment. Acne is caused by a combination of four different pathological causes, including an increase in sebum production, irregular follicular desquamation, *P.acnes* proliferation, and inflammation of the afflicted skin. Synthetic, hormonal, and herbal treatments, as well as their efficacy in treating acne vulgaris, are discussed in this article. The laser and light treatment for acne vulgaris available within a specific wavelength range that stimulates type I and III collagen and elastic fibres is described in relation to radiation therapies. The innovative drug delivery techniques are covered here such as particle, vesicular, and colloidal delivery systems as a prospective therapy. We will present a practical method to acne management in this article and discuss how to assess acne, how to use topical therapies, and how systemic therapy can be used to treat acne. This review will inform readers on the most recent advances in our understanding of acne treatment-related technological potential, with a particular emphasis on developing treatment alternatives and creative ways that can assist improve patient results. Acne has been the subject of substantial research, both in terms of disease mechanism and therapeutic approaches. However, as *Propionibacterium acnes* develops resistance to current medications there is a requirement for novel therapeutic

modalities. Additionally, the absence of required data regarding the efficacy of complementary and alternative medicine (CAM) therapies need greater investigation into these treatment choices.

Combined use of energy-based interventions with low-dose isotretinoin for the treatment of inflammatory acne: A retrospective cohort analysis. Kim J, Jongudomsombat T, Lee Y, et al. *J Cosmet Dermatol.* 2022 Jun 20. doi: 10.1111/jocd.15171. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35723897/>

Background: The combined use of oral isotretinoin with energy-based interventions including fractional microneedle radiofrequency, pulsed dye laser, and ablative fractional laser is an effective way to treat moderate-to-severe inflammatory acne lesions. However, studies regarding its efficacy and safety are limited. Aims: This study aimed to assess the efficacy and safety of a treatment using low-dose isotretinoin with energy-based interventions for inflammatory acne. Patients and methods: This retrospective cohort study included 126 patients who were diagnosed with inflammatory acne and were treated with systemic isotretinoin for at least 3 months. Patients were divided into EBD (energy-based intervention) (n=82) and non-EBD groups (n=44). Clinical outcomes of both groups were assessed using medical records and digital photographs. Results: After treatment, the modified Global Acne Grading Score of the EBD and non-EBD groups decreased by 35.1 ± 17.2 and 25.6 ± 10.1 , respectively. The improvement in acne severity was significantly greater in the EBD group than in the non-EBD group. Cumulated isotretinoin dose and frequency of drug-related side effects were significantly higher in the non-EBD group than in the EBD group. Conclusion: Combined treatment with low-dose isotretinoin and energy-based intervention is well tolerated and associated with positive responses in patients with inflammatory acne.

Increased prevalence of minocycline-resistant staphylococcus epidermidis with tet(M) by tetracycline use for acne treatment. Nakase K, Koizumi J, Fukumoto S, et al. *Microb Drug Resist.* 2022 Jun 20. doi: 10.1089/mdr.2021.0319. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35723664/>

Staphylococcus epidermidis, a major skin bacterium, can cause opportunistic infections. Use of antimicrobial agents against *Cutibacterium acnes* for acne treatment becomes a risk factor for emergence of antimicrobial-resistant skin bacteria. In this study, the impact of antimicrobial treatment of acne vulgaris on *S. epidermidis* antimicrobial resistance was assessed. A total of 344 *S. epidermidis* strains isolated from patients with acne vulgaris who visited hospital (165 strains) and dermatological clinics (179 strains), respectively, were analyzed. Except for doxycycline, the resistance rates were higher in strains isolated from patients who had used antimicrobials for acne treatment than in those isolated from patients who had not used antimicrobials. The prevalence rates of strains with erm(C) from patients who used macrolides and clindamycin (hospital, 78.0%; clinics, 61.3%) and those of strains with tet(M) from patients who used tetracyclines (hospital, 27.5%; clinics, 42.4%) were significantly higher than those of strains from patients who did not use antimicrobials ($p < 0.05$). All strains with erm(A) (8/8) and 91.7% strains with erm(C) (156/170) showed high-level resistance to macrolides and clindamycin (MIC ≥ 256 $\mu\text{g/mL}$). Furthermore, almost all strains with tet(M) showed resistance to minocycline. Our results showed that the use of antimicrobials for acne treatment may lead to an increased prevalence of antimicrobial-resistant *S. epidermidis*. In particular, the emergence of minocycline-resistant strains with tet(M) owing to the use of tetracyclines (doxycycline and minocycline) is a critical issue. Appropriate antimicrobial use for acne treatment may be an important strategy to prevent the emergence of antimicrobial-resistant skin bacteria.

Celastrol inhibits LL37-induced rosacea by inhibiting Ca²⁺/CaMKII-mTOR-NF- κ B activation. Zeng Q, Yang J, Yan G, et al. *Biomed Pharmacother.* 2022 Jun 16;153:113292. doi: 10.1016/j.biopha.2022.113292. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35717785/>

Rosacea is a common chronic facial inflammatory disease that affects millions of people worldwide. Due to the unclear

etiology of rosacea, effective treatments are limited. Celastrol, a plant-derived triterpene, has been reported to alleviate inflammation in various diseases. However, whether celastrol exerts protective effects in rosacea remains to be elucidated. In this study, weighted gene co-expression network analyses (WGCNA) were performed. Hub modules closely related to rosacea clinical characteristics were identified and found to be involved in inflammation- and angiogenesis-related signaling pathways. Then, the pharmacological targets of celastrol were predicted using the TargetNet and Swiss Target Prediction databases. A GO analysis indicated that the biological process regulated by celastrol highly overlapped with the pathogenic biological processes in rosacea. Next, we showed that celastrol ameliorated erythema, skin thickness and inflammatory cell infiltration in the dermis of LL37-treated mice. Celastrol suppressed the expression of rosacea-related inflammatory cytokines and inhibited the Th17 immune response and cutaneous angiogenesis in LL37-induced rosacea-like mice. We further demonstrated that celastrol attenuated LL37-induced inflammation by inhibiting intracellular-free calcium ($[Ca^{2+}]_i$)-mediated mTOR signaling in keratinocytes. Chelating intracellular Ca^{2+} with BAPTA/AM potentiated celastrol-induced repression of LL37-induced p-S6 elevation. The mTOR agonist MHY1485 dramatically reinforced LL37-induced rosacea-like characteristics, while celastrol attenuated these outcomes. Moreover, celastrol inhibited LL37-activated NF- κ B in a mTOR signaling-dependent manner. In conclusion, our findings underscore that celastrol may be a rosacea protective agent by inhibiting the LL37-activated Ca^{2+} /CaMKII-mTOR-NF- κ B pathway associated with skin inflammation disorders.

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Isotretinoin laboratory monitoring in acne treatment: A Delphi consensus study. Xia E, Han J, Faletsky A, et al. *JAMA Dermatol.* 2022 Jun 15. doi: 10.1001/jamadermatol.2022.2044. Online ahead of print.

<https://pubmed.ncbi.nlm.nih.gov/35704293/>

Importance: Although isotretinoin may rarely be associated with laboratory abnormalities such as hypertriglyceridemia, the optimal approach to laboratory monitoring is uncertain, and there is wide variation in clinical practice. Objective: To establish a consensus for isotretinoin laboratory monitoring among a diverse, international cohort of clinical and research experts in acne. Design, setting, and participants: Using a modified electronic Delphi process, 4 rounds of anonymous electronic surveys were administered from 2021 to 2022. For laboratory tests reaching consensus ($\geq 70\%$ agreement) for inclusion, questions regarding more time-specific monitoring throughout isotretinoin therapy were asked in subsequent rounds. The participants were international board-certified dermatologist acne experts who were selected on a voluntary basis based on involvement in acne-related professional organizations and research. Main outcomes and measures: The primary outcome measured was whether participants could reach consensus on key isotretinoin laboratory monitoring parameters. Results: The 22 participants from 5 continents had a mean (SD) time in practice of 23.7 (11.6) years and represented a variety of practice settings. Throughout the 4-round study, participation rates ranged from 90% to 100%. Consensus was achieved for the following: check alanine aminotransferase within a month prior to initiation (89.5%) and at peak dose (89.5%) but not monthly (76.2%) or after treatment completion (73.7%); check triglycerides within a month prior to initiation (89.5%) and at peak dose (78.9%) but not monthly (84.2%) or after treatment completion (73.7%); do not check complete blood cell count or basic metabolic panel parameters at any point during isotretinoin treatment (all $>70\%$); do not check gamma-glutamyl transferase (78.9%), bilirubin (81.0%), albumin (72.7%), total protein (72.7%), low-density lipoprotein (73.7%), high-density lipoprotein (73.7%), or C-reactive protein (77.3%). Conclusions and relevance: This Delphi study identified a core set of laboratory tests that should be evaluated prior to and during treatment with isotretinoin. These results provide valuable data to guide clinical practice and clinical guideline development to optimize laboratory monitoring in patients treated with isotretinoin.

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Low-dose versus conventional-dose oral isotretinoin regimens: A systematic review on randomized controlled comparative studies of different regimens. Legiawati L, Fahira A, Taufiqurrachman I, et al. *Curr Drug Saf.* 2022 Jun 13. doi: 10.2174/1574886317666220613162225. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35702787/>

Background: The effectiveness of Isotretinoin is superior compared to other acne therapies, particularly in reducing acne lesion counts. Concerns, however, arise relating the most optimal dosage regimen with the best efficacy and lesser side effect Objective: We intend to review existing randomized controlled comparative studies of isotretinoin in different regimens Methods: PubMed, Cochrane, Scopus, and ScienceDirect were searched. The inclusion criteria is RCT article. Full-text reading excluded articles that did not use GAGS as the method of measurement. The Out of 921 articles electronically searched, 6 RCTs were extracted and summarized descriptively. After full-text reading, 4 RCTs were included. We then conducted risk of bias assessments for the selected studies using The Cochrane Risk of Bias Tool. Results: Across all trials, low-dose regimens were preferable in all types of acne-owing to its similar efficacy to conventional dose but with fewer occurrence of side effects as well as better patients' satisfaction and compliance. Furthermore, a continuous low-dose regimen had the best efficacy in comparison to other regimens of low-dose treatment. Discussion: The limitations of our study include a slight difference of dosage between selected studies. Other limitations are that some studies did not explain the side effects and relapse rate thoroughly and did not state the compliance scoring method used. Conclusion: This review recommends continuous low-dose treatment as the chosen regimen for acne vulgaris. However, further evaluation regarding relapse rate compared to the conventional dose is needed.

Fibrous palygorskite clays as versatile nanocarriers for skin delivery of tea tree oils in efficient acne therapy. Zhang Z, Zhang X, Fu Z, et al. *Int J Pharm.* 2022 Jun 11;623:121903. doi: 10.1016/j.ijpharm.2022.121903. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35697203/>

This paper presents a facile approach to develop palygorskite (Pal), a fibrous clay mineral, as a delivery system of tea tree oil (TTO) for topical acne therapy. The obtained TTO-Pal composite showed an efficient loading of TTO (27.4%) with a selective accumulation of terpine-4-ol and 1,8-cineole (two major antimicrobial TTO constituents), sustained release of TTO at skin physiological conditions (pH5.4, 32 °C) and superior skin sebum (2.2 g/g) absorbability. In vitro toxicological assessments showed that the Pal incorporation strategy significantly reduced the acute contact toxicity of TTO. The antimicrobial results revealed a preferable bacteriostatic effect for the TTO-Pal system towards opportunistic dermal pathogens (*Escherichia coli*, *Staphylococcus aureus* and *Propionibacterium acnes*) over the beneficial bacterium (*Staphylococcus epidermis*). Moreover, TTO-Pal based formulations exhibited pronounced clinical therapeutic efficacy in treating facial acne by rapidly reducing inflamed lesions, modulating skin sebum overproduction and restoring barrier function. This is the first report of using fibrous clay as a biocompatible nanocarrier system for topical delivery of essential oils in efficient management of facial acne with both in vitro and in vivo evidences, which may open perspectives for fibrous clay-drug delivery system in topical application and expand the high added value development of this mineral resource in the advanced healthcare fields.

Biomarkers of tretinoin precursors and tretinoin efficacy in patients with moderate to severe facial photodamage: A randomized clinical trial. Chien AL, Kim DJ, Cheng N, et al. *JAMA Dermatol.* 2022 Jun 8;e221891. doi: 10.1001/jamadermatol.2022.1891. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35675051/>

Importance: Topical formulations of tretinoin precursors (retinol and its ester derivatives) are widely available over the counter and may offer similar clinical benefits to those of tretinoin for treatment of photoaging. However, which of the many purported molecular effects of retinoids most strongly drives clinical improvements in tretinoin-treated skin remains unclear. Objectives: To evaluate the clinical efficacy of topical tretinoin precursors (TTP) vs tretinoin (RA) in

treating moderate to severe facial photodamage and to identify potential biomarkers that correlate with clinical efficacy. Design, setting, and participants: This randomized, double-blind, single-center, parallel-arm study of 24 patients with moderate to severe facial photodamage was conducted at an academic referral center from November 2010 to December 2011, with data analysis performed from January 2012 to December 2021. Interventions: Daily topical application of 0.02% RA or 1.1% TTP formulation containing retinol, retinyl acetate, and retinyl palmitate for 24 weeks. Main outcomes and measures: Photoaging and tolerability were assessed by dermatologist evaluations and patient-reported outcomes. Target gene expression was assessed by real-time quantitative polymerase chain reaction of biopsied tissue from treated areas. Results: A total of 20 White women were ultimately analyzed (9 randomized to TTP, 11 randomized to RA). At week 24, there was no significant difference in Griffiths photoaging scores among patients receiving TTP vs RA (median, 4 vs 5) (TTP - RA difference: -1; 95% CI, -2 to 1; P = .27). Treatment with TTP was associated with erythema 6 times less frequently than RA (11% vs 64%) (TTP - RA difference: -0.53; 95% CI, -0.88 to -0.17; P = .01). Target gene analysis showed significant CRABP2 messenger RNA (mRNA) induction (confirming retinoic acid receptor signaling) but no significant changes in procollagen I or MMP1/3/9 mRNA in TTP-treated samples. Instead, MMP2 mRNA, which encodes a type IV collagenase, was significantly reduced in TTP-treated samples (week 24 - baseline mRNA difference: -5; 96% CI, -33 to 1.6; P = .02), and changes in MMP2 were strongly correlated with changes in fine wrinkles ($r = 0.54$; 95% CI, 0.12 to 0.80; P = .01). Interestingly, patients with severe baseline wrinkles exhibited greater improvements ($r = -0.74$; 95% CI, -0.89 to -0.43; P < .001). This trend was mirrored in MMP2 mRNA, with initial expression strongly predicting subsequent changes ($r = -0.78$; 95% CI, -0.89 to -0.43; P < .001). Conclusions and relevance: In this randomized clinical trial, there was no significant difference in efficacy between this particular formulation of TTP and tretinoin 0.02%. However, the results of these mechanistic studies highlight MMP2 as a possible mediator of retinoid efficacy in photoaging.

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Serum level of brain-derived neurotrophic factor (BDNF) associated with depression in patients with rosacea: A candidate predictive biomarker. Wang T, Liu F, Jia X, et al. Clin Cosmet Investig Dermatol. 2022 Jun 2;15:1029-1036. doi: 10.2147/CCID.S367545. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35677222/>

Background: The biomarker to predict the depression in patients with rosacea was absent. Objective: We aimed to explore the potential association between BDNF and depression in patients with rosacea, and also to determine whether serum BDNF level is a potential biomarker for identifying depression in patients with rosacea. Methods: The patients with rosacea, rosacea with depression and healthy control were included, clinical evaluation (DLQI, RSSs, BDI-II) and serum BDNF levels detection were performed on subjects, the comparisons and correlation analysis of the obtained data were performed. Results: In clinical evaluation, whether DLQI or RSSs, rosacea with depression group was significantly higher compared to rosacea group. Besides, we found the serum BDNF levels were lower in patients with rosacea and rosacea with depression compared to healthy controls, also in the rosacea with depression group, serum BDNF levels were lower than in rosacea patients. Whatever in rosacea or rosacea with depression group, the statistical significance of serum BDNF levels between the different subtypes like the ETR and PPR was not found. In further correlation analysis, we found no correlation between serum BDNF and RSSs in patients with rosacea whatever the subtype of ETR or PPR. Interestingly, we found a negative correlation between serum BDNF levels and BDI-II in rosacea with depression group, the decreased serum BDNF levels were associated with the increased BDI-II, also the ROC confirmed it can evaluate the depression in patients with rosacea. Conclusion: Serum BDNF level is a potential biomarker for identifying depression in patients with rosacea.

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Profiling the effects of systemic antibiotics for acne, including the narrow-spectrum antibiotic sarecycline, on the human gut microbiota. Moura IB, Grada A, Spittal W, et al. *Front Microbiol.* 2022 May 31;13:901911. doi: 10.3389/fmicb.2022.901911. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35711781/>

Treatment for moderate-to-severe acne vulgaris relies on prolonged use of oral tetracycline-class antibiotics; however, these broad-spectrum antibiotics are often associated with off-target effects and negative gastrointestinal sequelae. Sarecycline is a narrow-spectrum antibiotic treatment option. Here, we investigated the effect of prolonged sarecycline exposure, compared with broad-spectrum tetracyclines (doxycycline and minocycline) upon the colonic microbiota. Three in vitro models of the human colon were instilled with either minocycline, doxycycline or sarecycline, and we measured microbiota abundance and diversity changes during and after antibiotic exposure. Significant reductions in microbial diversity were observed following minocycline and doxycycline exposure, which failed to recover post antibiotic withdrawal. Specifically, minocycline caused a ~10% decline in Lactobacillaceae and Bifidobacteriaceae abundances, while doxycycline caused a ~7% decline in Lactobacillaceae and Bacteroidaceae abundances. Both minocycline and doxycycline were associated with a large expansion (>10%) of Enterobacteriaceae. Sarecycline caused a slight decline in bacterial diversity at the start of treatment, but abundances of most families remained stable during treatment. Ruminococcaceae and Desulfovibrionaceae decreased 9% and 4%, respectively, and a transient increase in Enterobacteriaceae abundance was observed during sarecycline administration. All populations recovered to pre-antibiotic levels after sarecycline exposure. Overall, sarecycline had minimal and transient impact on the gut microbiota composition and diversity, when compared to minocycline and doxycycline.

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Clinical Reviews

Pro and contra: Is synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) a spondyloarthritis variant? Furer V, Kishimoto M, Tomita T, et al. *Curr Opin Rheumatol.* 2022 Jul 1;34(4):209-217. doi: 10.1097/BOR.0000000000000884. Epub 2022 Jun 9. <https://pubmed.ncbi.nlm.nih.gov/35699334/>

Purpose of review: The purpose of this review is to present the up-to-date evidence on the epidemiology, pathogenesis, musculoskeletal manifestations, and imaging of the synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome and to discuss its relationship with spondyloarthritis (SpA). Recent findings: SAPHO is a rare inflammatory disorder of bone, joints, and skin, with a worldwide distribution that predominantly affects the middle-age adults. The hallmark of the syndrome is a constellation of sterile inflammatory osteitis, hyperostosis, and synovitis involving the anterior chest wall, associated with acneiform and neutrophilic dermatoses, such as palmoplantar pustulosis and severe acne. The axial skeleton, sacroiliac, and peripheral joints can be involved in a similar fashion to SpA. The pathogenesis of the syndrome is multifactorial. The diagnosis is mainly based on the clinical and typical radiological features. The treatment approach is based on the off-label use of antibiotics, bisphosphonates, disease-modifying antirheumatic drugs, and anticytokine biologics. Summary: The SAPHO syndrome shares common features with SpA-related diseases, yet also shows some unique pathogenetic and clinical features. The nosology of SAPHO remains a subject of controversy, awaiting further research into the pathogenetic and clinical aspects of this syndrome. A better understanding of these aspects will improve the diagnostics and clinical care of patients with SAPHO.

Endo-radiofrequency subcision for acne scars treatment: A case series study. Nilforoushzadeh MA, Heidari-Kharaji M, Fakhim T, et al. *J Cosmet Dermatol.* 2022 Jun 29. doi: 10.1111/jocd.15195. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35770321/>

Background: Acne scars have important psychosocial suffering for patients. Several interventions have been utilized to treat acne scars, that have different degrees of efficacy and side effect. Multimodal method can attain better results

to improving the physical appearance of the patients that can significantly increase the quality of life. Subcision is a recognized treatment procedure particularly for rolling acne scars, but it needs modification to increase the effect of procedure. Aims: To assess the efficacy and safety of Endo-Radiofrequency (Endo-RF) subcision in acne scars treatment. Methods: In this study, 9 adult patients with atrophic acne scars were enrolled. The patients receive Endo-RF subcision one time and followed up for 6 months. Outcome was measured using biometric assessment by Visioface 1000 D, Mexameter and skin ultrasound imaging system, post-treatment photographs and patient's satisfaction. Results: the results showed that patients had significant improvement from baseline according to the reduction of the number of skin fine and large pore ($P < 0.05$), and spots ($P < 0.05$). Also the density and thickness of the dermis and epidermis were significantly increased ($P < 0.05$). Conclusions: Endo-RF subcision modality can consider as a safe and effective method for acne scar treatment.

A case of 5-aminolevulinic acid photodynamic therapy (ALA-PDT) combined with surgery for the treatment of acne conglobate. Wu QY, Zhang Q, Bu WB, et al. Photodiagnosis Photodyn Ther. 2022 Jun 24;102986. doi: 10.1016/j.pdpdt.2022.102986. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35760351/>

We report the case of a 20-year-old man with acne conglobata (AC) who was treated with 5-aminolevulinic acid photodynamic therapy (ALA-PDT) sequentially to derroofing, and finally used fractional carbon dioxide laser for aesthetic requirements, achieving satisfying results. AC is a severe form of acne vulgaris that can lead to significant scarring and has serious negative effects on a patient's psychological well-being and quality of life. Some cases are likely resistant to currently available treatments. This report describes a promising, and effective method for the treatment of AC.

The increasing importance of the gut microbiome in acne vulgaris. Siddiqui R, Makhlof Z, Khan NA. Folia Microbiol (Praha). 2022 Jun 16. doi: 10.1007/s12223-022-00982-5. Online ahead of print. <https://pubmed.ncbi.nlm.nih.gov/35711021/>

Acne is a frequently presented dermatological condition brought about by an interplay among inflammation, increased sebum production, hyperkeratinisation, and predominantly Propionibacterium acnes (renamed as Cutibacterium acnes) proliferation, leading to debilitating psychological scars. However, it has been shown that it is the loss of microbial diversity in the skin and the imbalance among C. acnes phylotypes that brings about acne rather than the C. acnes species as a whole. Interestingly, recent evidence suggests that other microorganisms may be implicated, such as the fungi Malassezia and the bacteria Cutibacterium granulosum. A plethora of scientific evidence suggests that the gut microbiome is implicated in the overall health and physiology of the host; studies show that the gut microbiome of acne patients is distinct and depicts less microbial diversity compared to individuals without acne. Herein, using the key terms: acne, C. acnes, IGF-1, sebum, and gut microbiome, we carried out a review of the literature, using Google Scholar and PubMed, and discussed the role of the gut and skin microbiome in relation to acne, as a narrative review. The role of hormones, diet, sebum, and stress in relation to the gut microbiome was also investigated. Therapeutic implications and the use of pre-/postbiotics are also deliberated upon. In this light, future research should investigate the relationship between the gut microbiome and the agreed upon factors of acne pathology, potentially leading to the discovery of novel acne treatments with milder side effects.

The role of herbal medicine in the treatment of acne vulgaris: A systematic review of clinical trials. Proença AC, Luís Â, Duarte AP. Evid Based Complement Alternat Med. 2022 Jun 15;2022:2011945. doi: 10.1155/2022/2011945. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35754694/>

Over the past few decades, interest in medicinal plants and phytochemicals for the treatment of skin disorders, including acne vulgaris, has progressively increased. Acne vulgaris is a chronic inflammatory disease of the

pilosebaceous unit, which mainly occurs in adolescents and young adults. The treatment focuses on the four main factors involved in its pathogenesis: increased sebum production, hyperkeratinization, overgrowth of Cutibacterium acnes, and inflammation. The treatment includes topical retinoids, benzoyl peroxide, antibiotics, and oral isotretinoin. In this regard, the use of herbal medicine as a complementary and alternative medicine is a promising strategy. The main objective of this study was to systematically evaluate the efficacy and safety of medicinal plants and phytochemicals in the treatment of acne vulgaris. Three scientific databases (PubMed, Web of Science, and Scopus) were searched from inception to January 2021. Clinical trials comparing herbal therapies with placebo or other medicines for the treatment of acne vulgaris were included and analyzed. Outcome measures of interest comprised acne lesions (inflammatory and noninflammatory), sebum production, acne severity, and quality of life. The risk of bias in the included randomized controlled trials (RCTs) was assessed using the Cochrane risk-of-bias tool. A total of 34 clinical trials involving 1753 participants met the inclusion criteria for this systematic review. Most trials showed that herbal medicine significantly reduces inflammatory and noninflammatory acne lesions and has a relevant effect on acne severity. Some medicinal plants revealed equal or higher efficacy to standard treatments. No significant difference between groups in sebum production and quality of life was observed and no severe adverse events were reported. This systematic review provides evidence that medicinal plants and phytochemicals are promising treatments for mild to moderate acne vulgaris. However, more quality of evidence and standardized methodologies are needed to support their effectiveness and safety claims.

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Innovative use of negative air ions as an alternative therapy for acne vulgaris: A report of three cases. Han HS, Jeong GJ, Lee HW, et al. *Ann Dermatol.* 2022 Jun;34(3):216-220. doi: 10.5021/ad.2022.34.3.216. Epub 2022 May 20. <https://pubmed.ncbi.nlm.nih.gov/35721339/>

Acne vulgaris is a universal skin disease with multifactorial pathogenesis. Although an extensive range of treatment options exist for acne, a substantial number of patients are still struggling for an optimal treatment option due to the side effects or contraindications to the conventional acne treatment. Negative air ions (NAIs) are electrically charged molecules that naturally exist in the atmosphere. Since they are natural component of air, there are no known side effects and contraindications to their application. Furthermore, among the identified benefits of NAIs, certain mechanisms are related to acne pathogenesis, allowing them to be attractive candidates for acne treatment. Here, we describe three patients with acne who showed considerable clinical improvement after NAI therapy. All of the patients had failed to tolerate traditional acne treatment options. In all three cases, considerable improvement was observed in acne severity and the number of total lesions. Based on the three cases and a review of literature underlying the effects of NAIs, we suggest that NAIs may be a safe and effective alternative therapeutic option for acne vulgaris.

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Dermatology: How to manage rosacea in skin of color. Maliyar K, Abdulla SJ. *Drugs Context.* 2022 May 31;11:2021-11-1. doi: 10.7573/dic.2021-11-1. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35720055/>

Rosacea is a common inflammatory skin disorder affecting the face. Common cutaneous symptoms include papules, pustules, persistent centrofacial erythema, telangiectasias, recurrent flushing, phymatous changes and a variety of ocular manifestations. Previous epidemiological studies have demonstrated that the incidence of rosacea is much lower in people with darker Fitzpatrick phototypes compared to fair-skinned individuals. In patients with darker skin, the centrofacial erythema can be masked and difficult to appreciate, impacting the ability for providers to make diagnoses and leading to misdiagnoses. Thus, it is difficult to say with certainty that the disparities in prevalence in rosacea amongst fair-skinned and darker individuals are true. The primary aim of this article is to raise awareness

that rosacea is a global disease and to provide healthcare professionals with strategies to identify and manage rosacea amongst individuals with skin of color.

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Adverse events in isotretinoin therapy: A single-arm meta-analysis. Kapala J, Lewandowska J, Placek W, Owczarczyk-Saczonek A. *Int J Environ Res Public Health*. 2022 May 26;19(11):6463. doi: 10.3390/ijerph19116463. <https://pubmed.ncbi.nlm.nih.gov/35682048/>

Isotretinoin (ISO) is an oral prescription-only retinoid, well known for its acne-treating effect. However, it affects a substantial number of human cell types, causing a broad spectrum of adverse effects. The purpose of this study is to establish the isotretinoin therapy adverse events among human clinical trials and their prevalence. Two authors (J.K., J.L.) systematically performed the literature review and assessment from December 2021-February 2022. Three databases (PubMed, ClinicalTrials, and Cochrane Library) were searched using the following terms: "isotretinoin acne vulgaris" for published studies in English from 1980-2021. Finally, 25 randomized controlled clinical trials (RCTs) and five open-label clinical trials provided 3274 acne vulgaris suffering patients. Isotretinoin therapy affects almost all of the systems in the human body, causing numerous adverse events. However, they mainly concern mild mucocutaneous conditions (severe cases are rare) and represent individual responses to a drug. In addition, all adverse events are reversible and can be avoided by specific preparations.

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Acne fulminans induced by lymecycline in a patient with hidradenitis suppurativa: A case report. Trave I, Micalizzi C, Molle M, et al. *Case Rep Dermatol*. 2022 May 9;14(2):112-116. doi: 10.1159/000523799. eCollection May-Aug 2022. <https://pubmed.ncbi.nlm.nih.gov/35702372/>

Acne fulminans (AF) is a rare and severe form of inflammatory acne that typically occurs in male adolescents with acne vulgaris and is characterized by the sudden onset of painful, bleeding, and ulcerated lesions. It has been described very rarely in association with hidradenitis suppurativa (HS). Its onset may be induced by drugs, particularly isotretinoin. We present a case of a 16-year-old patient with HS who developed AF following initiation of antibiotic therapy with lymecycline. In the literature, only 2 patients who developed a coexistence of AF and HS have been reported, and there are only 2 other similar cases of AF induced by doxycycline and lymecycline. We consider our case to be of particular interest not only because of the very rare concomitant presence of AF and HS but also because AF was induced by lymecycline, a drug commonly used to treat both acne and HS and described only once as a drug responsible for AF, so it is an aspect that deserves to be considered by the clinician dealing with similar conditions.

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Dermatology: How to manage acne in skin of color. Chiang C, Ward M, Gooderham M. *Drugs Context*. 2022 May 31;11:2021-10-9. doi: 10.7573/dic.2021-10-9. eCollection 2022. <https://pubmed.ncbi.nlm.nih.gov/35720053/>

Acne vulgaris is a prevalent dermatological condition worldwide but is especially challenging to treat in individuals with skin of color (SOC). Corresponding to Fitzpatrick skin phototypes III-VI, people of African, Asian, Middle Eastern and Hispanic ethnicity are considered to have SOC. With the additional risk of postinflammatory hyperpigmentation (PIH) as a consequence of inflammatory acne or its respective treatment, managing acne in this population holds significant importance. PIH adversely impacts self-esteem and quality of life and, thus, is usually the patient's priority of treatment. Available acne treatments are similar for all skin types. However, some are more beneficial for individuals with SOC, in particular by targeting both active acne lesions and PIH. The acne treatment literature was searched for topical and systemic treatments that were specifically studied in the SOC population. These treatments included topical agents, such as retinoids and azelaic acid, in addition to topical antibiotics and benzoyl peroxide. Newer

formulations and combined regimens reported effective in reducing lesions are less likely to induce PIH and may treat pre-existing PIH. Moisturizer use, titrating doses and patient education are strategies to minimize irritation and improve adherence. In addition, systemic therapies, including oral antibiotics, isotretinoin, oral contraceptives and spironolactone, are efficacious for refractory acne or more severe cases but specific studies in SOC are lacking. Chemical peels may improve acne and target PIH directly. Overall, based on limited evidence, topical and systemic therapies are well tolerated in the SOC population, but efficacy should be balanced with the risk of adverse effects. This narrative review aims to highlight formulations and combination therapies that are effective and safe for treating acne and PIH in patients with SOC.

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