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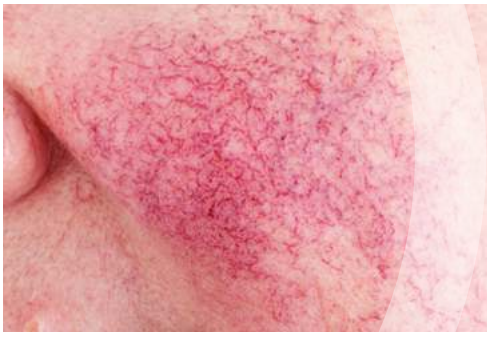
LABORATOIRE DERMATOLOGIQUE



UPDATES ON DERMATOLOGY

EADV 2025

STÉPHANE FAUVERGHE
NAOS Medical Director

Edito

EADV Symposium, Paris – Rosacea Management for a Better Patient Outcome

Rosacea is a complex, multifactorial disease that extends far beyond the skin, impacting self-esteem, social interactions, and overall quality of life. As our understanding of rosacea deepens, so does our commitment to improving patient outcomes through science and empathy.

This special issue brings together four expert perspectives from the EADV symposium in Paris, each offering a unique lens on rosacea management:

- **Prof. Bernard Cribier** explores the evolving pathophysiology of rosacea, highlighting the roles of immune and neurovascular dysregulation, and the promise of targeted therapies.
- **Prof. Brigitte Dréno** examines the interplay between the skin and gut microbiome, challenging old assumptions and pointing to the nuanced effects of microbial communities and the potential of probiotics.
- **Prof. Mark D. Kaufmann** reviews advances in therapeutic strategies, from sub-antimicrobial antibiotics to innovative topical agents, emphasising the importance of anti-inflammatory approaches and maintenance therapy.
- To conclude, I present our ecobiological approach, focusing on both the physical and psychological well-being of patients. Solutions like ROSACTIV™ 2.0 technology included in the SENSIBIO AR+ products, rooted in ecobiology, aim to address the underlying mechanisms of rosacea while respecting the skin's natural balance.

What unites these contributions is a shared vision: to move beyond symptom control and address the root causes of rosacea, integrating cutting-edge research with holistic, patient-centered care. The future of rosacea management lies in personalised, multidisciplinary strategies that honour the complexity of the disease and the individuality of each patient.

I am proud to introduce this collection, which reflects our collective dedication to advancing knowledge and compassion in rosacea care.

SCIENTIFIC PROGRAMME

SPEAKERS
SHORT BIOGRAPHIES

BERNARD CRIBIER

Bernard Cribier is a French dermatologist, **Professor of Universities and Hospital Practitioner (PU-PH)**, and former **Head of the Dermatology Department at the University Hospitals of Strasbourg**.

He is widely recognised for his expertise in **dermatopathology**, emphasising the importance of anatomo-clinical correlation in dermatology education.

Cribier has served as **Editor-in-Chief of the *Annales de Dermatologie*, President of the Dermatopathology Group of the French Society of Dermatology, and Past President of the European Society of Dermatopathology.**

He has authored numerous scientific works, including over **530 indexed publications**, 66 book chapters, and the reference book *Dermatologie. De la clinique à la microscopie*.

His contributions have significantly advanced dermatopathology teaching and research, and he organizes annual seminars dedicated to this field.

BRIGITTE DRENO

Brigitte Dréno is a Dermato-Oncologist. Secretary of the French Academy of Medicine, she is the director of an INSERM INCITE research team.

She is Founding member of the European Association of Dermato-Oncology (EADO), past president of the French Society of Dermatology and of the French college of dermatology teachers.

She is a published author of more than 900 articles.

MARK KAUFMANN

Mark Kaufmann, is a Board-Certified dermatologist and former President of the American Academy of Dermatology (AAD). He is a Clinical Professor in the Department of Dermatology at Mount Sinai Hospital in New York.

After 25 years in private practice in New York City, Dr. Kaufmann became the Chief Medical Officer of Advanced Dermatology and Cosmetic Surgery, overseeing 160 clinics and research sites across the U.S. He also serves on the Board of Directors for the American Society for Dermatologic Surgery and the Florida Academy of Dermatology.

What's New in Rosacea Pathophysiology?

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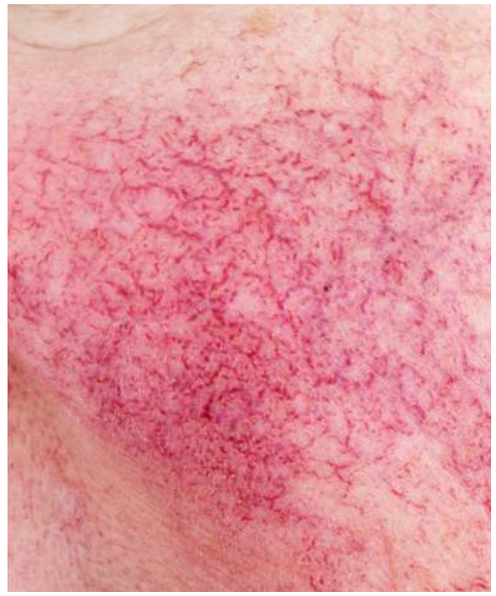
— Pathophysiology of rosacea —



Rosacea is a multifactorial skin disease with phenotypes such as erythema, flushing, telangiectasia, papules, pustules, rhinophyma, ocular signs, burning, oedema, and dryness.[1] Its pathogenesis involves genetic and environmental factors leading to immune and neurovascular dysregulation, vascular changes, microbiome imbalance (notably increased *Demodex*), and inflammation. These contribute to fibrosis, sebaceous gland hypertrophy, and skin barrier dysfunction.[1,2] This complexity supports targeting multiple pathways in future treatments.

A study identified a key link between innate immunity and inflammation in rosacea, showing that increased serine protease activity and cathelicidin levels drive skin inflammation.[3] Individuals with rosacea express abnormally high levels of cathelicidin in facial skin, and the processed forms, such as LL-37, differ from those in healthy individuals. **This discovery enabled the development of a mouse model of rosacea through LL-37 injection.**

— Role of IL-17 and the Th1/Th17 pathway —

Interleukin-17 (IL-17) has emerged as a key mediator of inflammation in rosacea. In an *in vitro* study, rosacea was shown to be associated with activation of the Th1/Th17 pathway.[4] Serum IL-17 levels were found to be elevated in 20 rosacea patients compared to 20 controls, with no correlation with severity, duration or primary features of the disorder.[5] Another study, involving 280 rosacea patients and 70 healthy controls, found increased levels of several pro-inflammatory cytokines in patients, including IL-17, IL-1β, IL-6, IL-8, and TNF-α.[6] **These elevated cytokine levels positively correlated with anxiety and depression, frequently observed in rosacea.**

In the mouse model, treatment with an anti-IL-17 antibody significantly reduced LL-37-induced inflammation.[7] **An exploratory clinical study of IL-17 blockade in papulopustular rosacea showed limited overall benefit. However, the subgroup of 17 patients with severe roasacea improved after 16 weeks of treatments with secukinumab, with marked reductions in papule count and global erythema score.**[8]

Using the LL-37 mouse model offers a possible explanation for the decreased incidence of rosacea with age. The authors compared young (2-month-old) and aged (20-month-old) mice and found that, despite receiving the same dose of LL-37, older mice developed significantly less

symptoms and inflammation.[9] This reduction was linked to altered Th1/Th17 immune organisation: at the molecular level, aged mice showed lower expression of rosacea-related genes, a weakened Th1/Th17 response, and impaired angiogenesis.

— JAK/STAT pathway —

The involvement of the JAK/STAT signalling pathway in rosacea pathophysiology is supported by several mechanisms.[10] This pathway contributes to the generation of matrix metalloproteinase 9 (MMP9) through the cleavage of kallikrein 5 (KLK5), interacts with toll-like receptor 2 (TLR2), and promotes the upregulation of key proinflammatory cytokines such as IL-6, IL-8, and TNF-α. **Among the STAT family members, STAT3 has emerged as a central regulator in both rosacea and skin barrier function. Cases of patients with refractory rosacea and who responded favourably to treatment with JAK1 inhibitors, owing immunomodulatory properties and reduce cytokine production have been reported.**[10] These agents are already used in various dermatologic conditions.

In terms of experimental research, **recent findings highlight the potential role of periostin, an extracellular matrix protein involved in cell adhesion, inflammation, and angiogenesis. Periostin is dysregulated in several inflammatory skin diseases, including cutaneous T-cell lymphoma and atopic dermatitis. In the context of rosacea, periostin may be particularly relevant due to its proangiogenic activity.** A recent study using a periostin-knockdown mouse model of LL-37-induced rosacea demonstrated that suppression of periostin expression led to reduced inflammation and angiogenesis.[11] This effect was evidenced by a decrease in blood vessel density and endothelial cell numbers, and was likely mediated via inhibition of the JAK2/STAT3 and NF-κB pathways. **These findings suggest that periostin may be a promising therapeutic target in rosacea.**

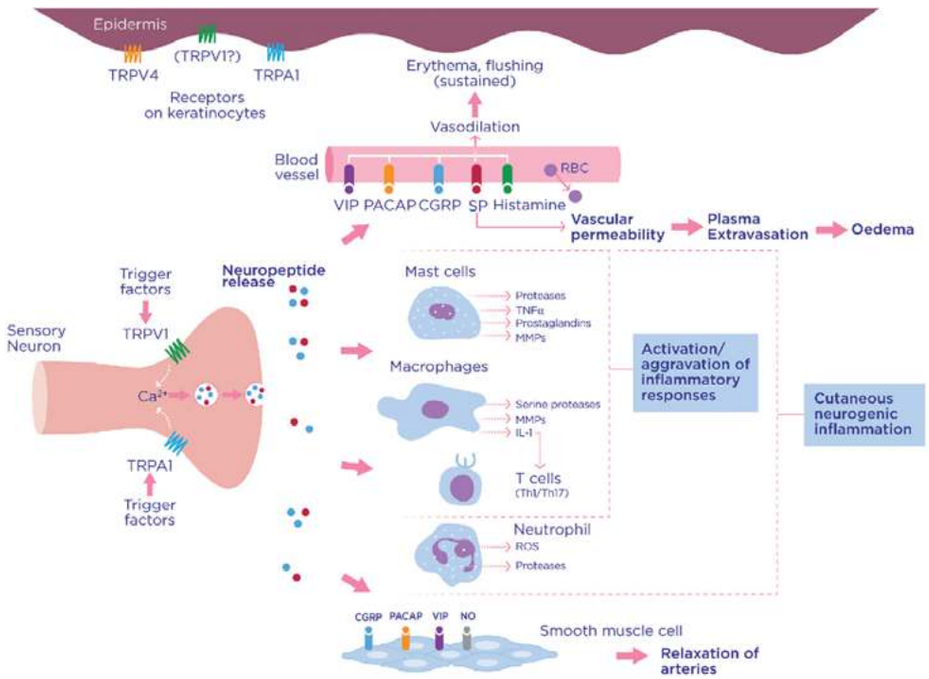
A recent *in vitro* transcriptome study using an LL-37-induced inflammation model in human keratinocytes supports a key role for the JAK/STAT pathway in connection with IL-17 in rosacea.[12] The analysis showed strong upregulation of interferon-stimulated genes, especially *CXCL10, IFIT2, RSAD2, and CXCL11*, while key inflammatory pathways activated included TNF, IL-17, NF-κB, and chemokine signalling. CXCL10 emerged as the most prominently overexpressed chemokine, with its production dependent on JAK1/STAT1 signalling. **These findings highlight the potential of targeting the CXCL10:CXCR3 axis or JAK1/STAT1 pathway to limit T-cell–mediated inflammation in rosacea. A case series of four patients with steroid-induced rosacea treated with an oral JAK1 inhibitor showed improved skin condition without any reported adverse effects.**[13]

— Neurogenic inflammation —

Neurogenic rosacea is characterised by severe neurological symptoms, such as burning and stinging sensations, which can be nearly unbearable. This subtype is frequently resistant to conventional therapies and remains difficult to treat.[14] The underlying mechanisms are illustrated in Figure 1.

A recent proteomic study compared serum samples from 27 rosacea patients and 25 matched healthy controls, identifying 490 differentially expressed proteins.[15] The upregulated proteins were linked to inflammatory (notably IL-17-related), metabolic (especially cholesterol-related), and neuroregulatory pathways, while downregulated proteins were enriched in complement pathways. Cluster analysis revealed two distinct rosacea endotypes: an inflammatory-predominant subtype (n=22) and a neurogenic-metabolic subtype (n=5).
Importantly, specific symptom profiles correlated with molecular signatures: flushing was associated with neutrophil-driven inflammation and lipid metabolism (46 proteins), while burning sensations were linked to neuronal repair and complement activation (120 proteins). These findings position rosacea as a systemic inflammatory condition with distinct endotypes, suggesting the potential for personalised treatment strategies based on neuroimmune and metabolic dysregulation.

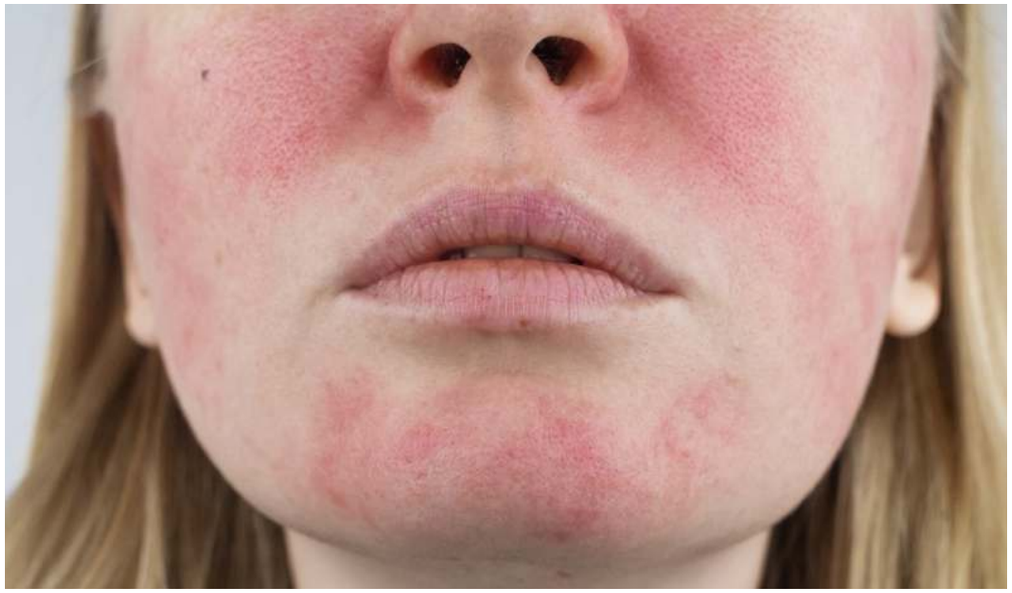
Figure 1. Pathogenic mechanisms of neurogenic rosacea [14]



A proteomic study comparing psoriasis and rosacea revealed distinct proteomic signatures, with psoriasis showing a stronger immune response and marked epidermal hyperplasia, whereas rosacea featured neural and vascular abnormalities.[16] Compared to healthy skin, rosacea skin displayed significant upregulation of inflammation- and axon extension–related proteins, indicating an inflammatory and neuro-hypersensitive microenvironment. In addition, **axon-associated proteins (DPYSL2 and DBNL) correlated with erythema severity, and neutrophil-related proteins (ELANE and S100A family members) correlated with the overall disease severity. SNCA, a marker of neurodegenerative disease, was also positively associated with global severity, suggesting a potential link between rosacea and neurodegenerative comorbidities.**[16] This highlights the complex interactions among vessels, nerves, and inflammation.

In a very recent study, 39 patients with rosacea and 30 healthy controls were examined using corneal confocal microscopy.[17] Patients with rosacea showed a significantly lower nerve fibre density, branch density, and fibre length in the cornea compared with healthy controls. Moreover, those with facial burning symptoms (n = 10) had significantly lower corneal nerve branch density than patients without burning symptoms.

The above findings concerned the peripheral nervous system, but there are also emerging data implicating the central



nervous system in rosacea. In one study, functional PET/CT scans were used to assess network changes in specific brain regions of patients with rosacea (n = 8) compared with healthy controls (n = 10), revealing both increased and decreased signals in defined areas. These results indicate that distinct neural functional alterations occur in rosacea and may contribute to its pathogenesis.[18] This was further supported by a more recent study involving 32 female patients with rosacea and 29 healthy controls, which combined functional magnetic resonance imaging with symptom assessments and psychosocial evaluations.[19] **The study found increased low-frequency fluctuations (reflecting heightened neural activity) mainly in the prefrontal cortex. Notably, these fluctuations were positively correlated with erythema severity, social avoidance, and appearance anxiety scores, suggesting a link between depressive symptoms, cutaneous manifestations, and underlying neural mechanisms in rosacea.**

Repetitive transcranial magnetic stimulation (rTMS) was hypothesised to be a safe, effective treatment for erythemato-telangiectatic rosacea, the most common subtype of rosacea, characterised by persistent facial erythema and flushing, and frequently associated with anxiety and depression. A randomised, double-blind, sham-controlled trial evaluated rTMS in 77 patients with erythemato-telangiectatic rosacea: 39 received active rTMS and 38 sham stimulation.[20] **After 2 weeks, the rTMS group showed significant reductions in erythema and telangiectasia, with improvement in clinical erythema scores of 2 or more points ($p < 0.001$). Depression, anxiety, and sleep quality also improved.**

Finally, a single-cell transcriptomic study generated an atlas of facial skin from female rosacea patients and healthy controls, identifying **11 major cell types being involved in rosacea.**[21] Notable findings include **increased TH1/TH17 lymphocytes, activation of endothelial cells, and a distinct keratinocyte subpopulation with IFNγ-related skin barrier dysfunction unique to rosacea lesions.** Fibroblasts were identified as key producers of pro-inflammatory and vasodilatory signals. **Blocking IFNγ signalling, depleting fibroblasts, or knocking down the gene *PTGDS* (specifically upregulated in fibroblasts) alleviated rosacea-like inflammation and barrier damage in LL-37 mouse models.**

CONCLUSIONS

Scientific interest in rosacea continues to rapidly grow, as shown by the rising number of studies and publications in recent times. The coming years are likely to bring major advances, driven by a deeper understanding of inflammatory mechanisms, including neurogenic inflammation, and new therapeutic technologies. These developments are expected to significantly improve the treatment and management of rosacea.

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The microbiome : a new key player in the management of rosacea?

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INTRODUCTION

In adults, human skin covers an area of approximately 2m². It is the body's largest organ and provides the first line of defence against external agents.[1]
The skin microbiome is a complex ecosystem composed of a multitude of microbial species (microbiota) that interact with the skin barrier and immune cells of the host.[2, 3] In adults, the skin harbours around one trillion bacteria on average (about 50 million/cm²), belonging to more than 500 different species, which represent nearly 3% of the total body mass.[4]

The skin microbiota consists primarily of commensal microorganisms that coexist in homeostasis with the host organism. They help preserve a healthy skin barrier and are mainly represented by *Cutibacterium acnes (C. acnes)*, *Staphylococcus epidermidis (S. epidermidis)*, and *Demodex* species.
A second group of microorganisms includes transient pathogens that temporarily colonise the skin, such as *S. aureus*.[5]
The composition of the skin microbiota varies across different body sites, depending on multiple factors such as pH, humidity, salinity, and sebum content.[6]

— Rosacea, a combination of different etio-pathogenic factors —

Rosacea is a common chronic inflammatory skin disease characterised by erythema, papules, and pustules.[7] The pathophysiology of rosacea remains incompletely understood, but a complex interplay between environmental and genetic factors is believed to trigger an abnormal innate immune response associated with multifaceted neurovascular dysregulation. **Demodex mites, which are normal skin commensals, are considered one of the main triggers in rosacea. They may activate toll-like receptor 2 (TLR2), leading to the overproduction of cathelicidins** – antimicrobial peptides that are part of the innate immune system – which are overexpressed in the skin of patients with rosacea and contribute to exacerbating the characteristic inflammatory processes of the disease.[8, 9]

Moreover, increasing evidence suggests that the gut microbiota plays a significant role in the pathogenesis of rosacea, influencing cutaneous inflammatory responses. Dysbiosis, small intestinal bacterial overgrowth (SIBO), *Helicobacter pylori (H. pilori)* infection, and innate immune system dysregulation may all contribute to the complex pathophysiology of rosacea.[9, 10]

— The diversity of the skin microbiota in rosacea patients—

The skin microbiome in rosacea is not associated with a loss of diversity, but with an even greater number of taxa compared to that of healthy individuals. Studies have shown that the skin microbiome of patients with rosacea exhibits significantly higher alpha diversity ($p \leq 0.0001$) than that of healthy controls.[11] However, compared with healthy individuals, the mean relative abundance of *C. acnes* is significantly lower in rosacea patients (61.8% *vs.* 79.7%, $p=0.014$), while that of *S. epidermidis* is significantly higher (19.64% *vs.* 6.48%, $p=0.036$).[11, 12]

Further research comparing different rosacea subtypes – erythemato-telangiectatic rosacea (ETR) and papulopustular rosacea (PPR) – with healthy skin confirmed that in both subtypes, the relative abundance of *Firmicutes* (e.g., *Staphylococcus* spp.) was increased, whereas that of *Actinobacteria*, mainly *Cutibacterium* spp. was decreased. At a genus level, *C. acnes* abundance was significantly reduced ($p<0.01$) in both ETR (27.3%) and PPR (23.3%) compared with controls (62.6%). Conversely, *Staphylococcus* spp. were significantly increased in patients with ETR (23.0%) compared with controls (7.7%), as were *Streptococcus* spp. (9.6% *vs.* 2.2% in controls).[13] See Figure 1 and Figure 2 for detailed results.

— The impact of skin temperature on rosacea —

Facial skin temperature is higher in patients with rosacea. Papules and pustules may develop because bacteria behave differently at these elevated temperatures. Results from a clinical study showed that *S. epidermidis* isolates from patients with rosacea were consistently β-hemolytic, whereas those from healthy control subjects were non-hemolytic. Bacteria isolated from rosacea patients grew at the same rate and reached the same stationary phase when cultured at either 37°C or 30°C. Moreover, isolates from patients with rosacea secreted a greater number and higher quantities of proteins at 37°C compared with 30°C. In addition, *S. epidermidis* antigens were recognised by TLR-2 in both groups.[14]

Figure 1. Shannon diversity of the bacterial communities in patients with ETR, patients with PPR and healthy controls [13]

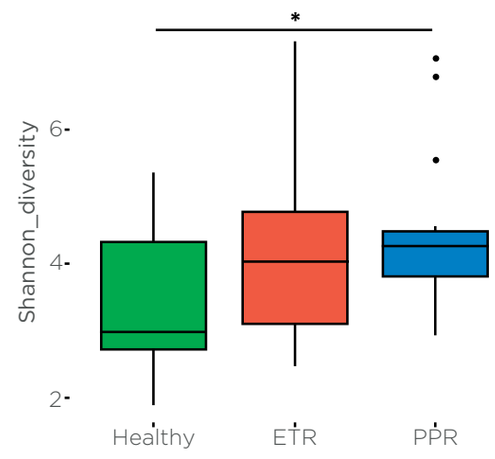
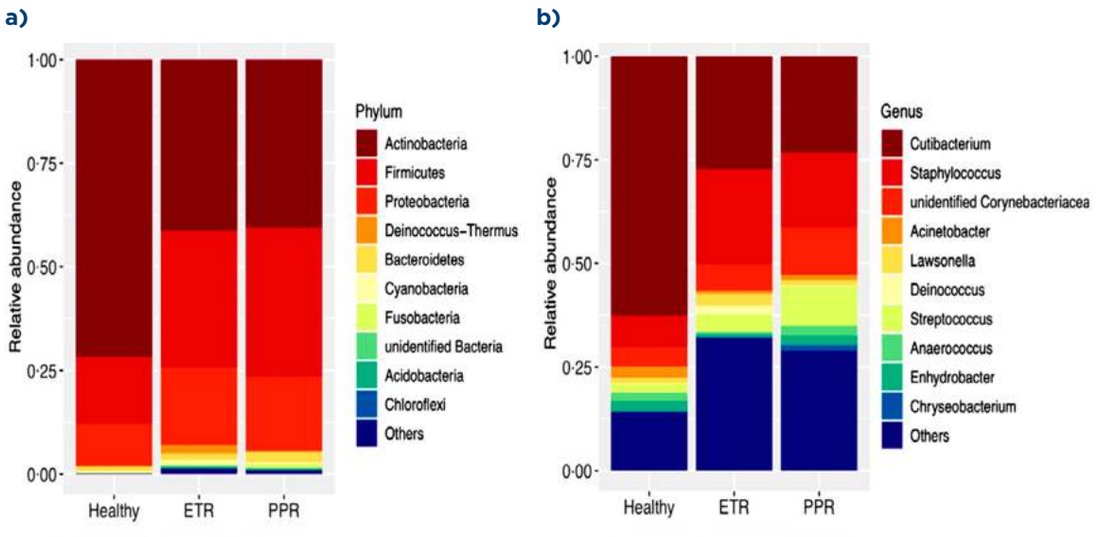


Figure 2. Relative abundances of bacterial taxa at the phylum level (a) and genus level (b) in patients with erythematotelangiectatic rosacea (ETR), patients with papulopustular rosacea (PPR) and healthy controls [13]



— The role of the gut microbiome in rosacea —

The term "gut–skin axis" refers to the complex bidirectional interactions between the gut and the skin, primarily mediated by the regulation of systemic inflammation through intricate mechanisms of immune system modulation.[15, 16]

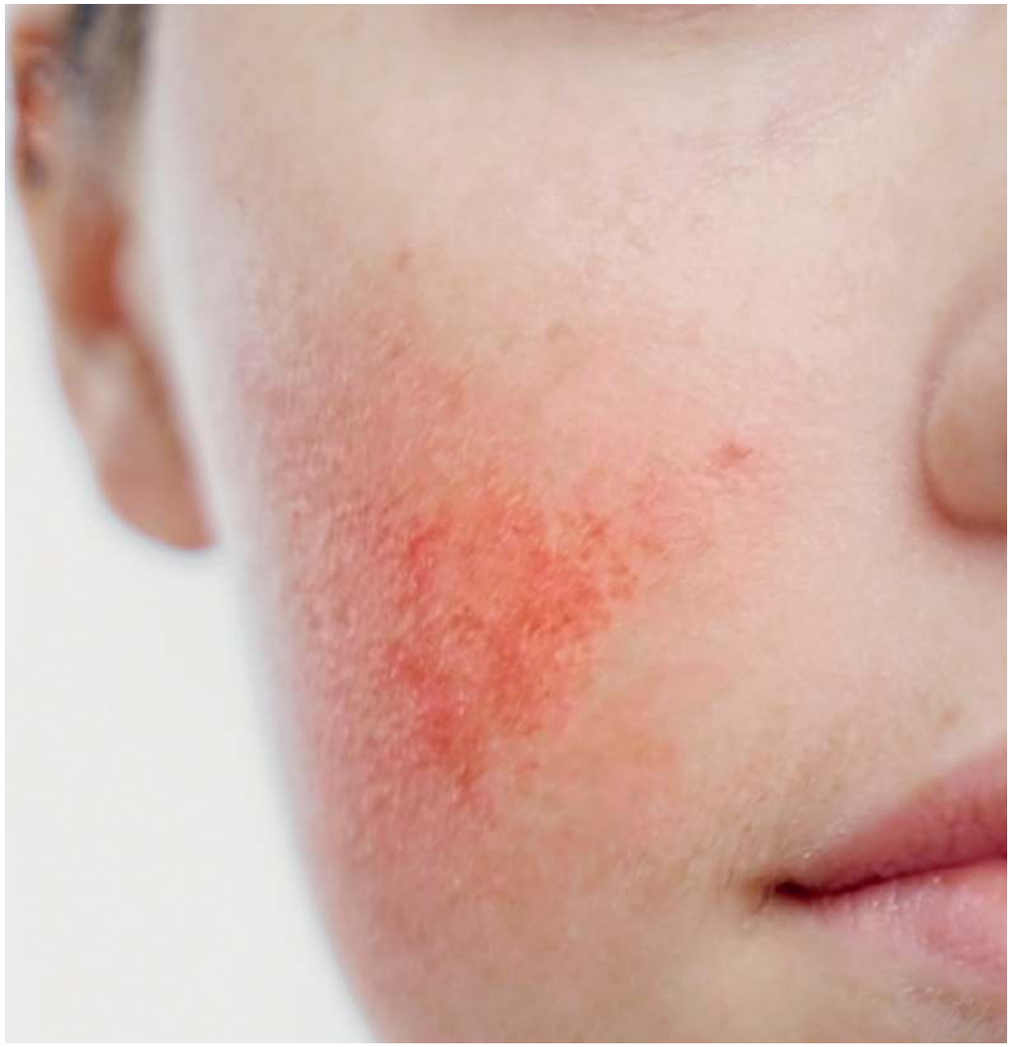
Several gastrointestinal comorbidities, including *H. pylori* infection, have been associated with rosacea, suggesting that an altered gut microbiome may play an important role in its pathogenesis.[17, 18] *H. pylori* exacerbates inflammation by triggering the release of pro-inflammatory cytokines such as TNF-α and IL-8. In addition, it increases nitric oxide (NO) production, promoting vasodilation and further amplifying the inflammatory response. (19) To date, only a few studies have identified specific alterations in the gut microbiota of patients with rosacea, including compositional differences, reduced faecal microbial richness, and distinct microbial community structures.[20, 21]

Emerging evidence suggests that oral probiotics may be beneficial in rosacea management.[22-27] They act on gut dysbiosis to promote a healthier microbial balance, which may help reduce systemic inflammation and improve skin health.[9] **However, further research is needed to confirm their therapeutic potential and to establish evidence-based recommendations for** their use in rosacea.

— Laser therapy and the skin microbiome in rosacea patients —

A clinical study demonstrated that long-pulsed alexandrite laser therapy, used to treat facial redness, alters both the diversity of the skin microbiota and the relative abundance of *Clostridium* spp., *Lawsonella* spp., *Bacteroides* spp., and *Lactobacillus* spp.[28]

The authors recommended the use of specifically adapted dermocosmetic products to help restore the skin microbiome and repair the skin barrier.



— The use of minocycline in rosacea —

Administration of oral minocycline (50 mg) resulted in a notable increase in α-diversity and a structural shift in the skin microbiota. Treatment was accompanied by a reduction in the relative abundance of *Cutibacterium* spp. and *Staphylococcus* spp., indicating negative correlations with enhanced bacterial metabolic pathways such as butyrate synthesis and L-tryptophan degradation. The increased production of butyrate and tryptophan metabolites is thought to contribute to the inhibition of skin inflammation and the promotion of skin barrier repair. In addition, the abundance of skin bacterial genes associated with tetracycline resistance and multidrug resistance increased markedly following antibiotic treatment.[29]

— Ivermectin in rosacea —

In a 12-week open-label study, ten subjects with papulopustular rosacea (PPR) were treated topically with 1% ivermectin cream once daily, applied to both affected and surrounding non-lesional areas. Ten age-matched healthy subjects were enrolled as controls.[30]

After 12 weeks, microbial α-diversity had increased. On lesional skin, the absolute abundance of *S. epidermidis* increased significantly (p=0.039), whereas that of *Demodex* decreased significantly (p=0.002); the abundance of *C. acnes* remained unchanged. No changes were observed on non-lesional skin. Consistent with the increase in *S. epidermidis* DNA, the survival of coagulase-negative *Staphylococcus* increased after treatment on both lesional and non-lesional skin. **These results provide evidence that topical ivermectin decreases *Demodex* density and impacts the bacterial community** (Figure 3).

In a second study involving 41 patients with mild-to-moderate rosacea, ivermectin treatment led to a marked decrease in Demodex density in 87.5% of subjects after one month.[31] Moreover, *Snodgrassella alvi*, a Demodex-associated bacterium, was detected. *Staphylococcus* spp. became significantly dominant and were associated with a decrease in *C. acnes* abundance compared with controls after 30 days of ivermectin treatment.

Clinical improvement during topical ivermectin therapy does not appear to be associated with normalisation of the bacterial microbiome but rather with a reduction in transcriptomic dysregulation and *Demodex density*. **These findings suggest that the skin microbiome plays only a secondary role in rosacea. The inflammatory environment induced by *Demodex* creates a favourable niche for *Staphylococcus* spp., which do not diminish once inflammation has subsided** (Figure 4).

Figure 3. Impact of the abundance of the skin microbiota in rosacea patients [30]

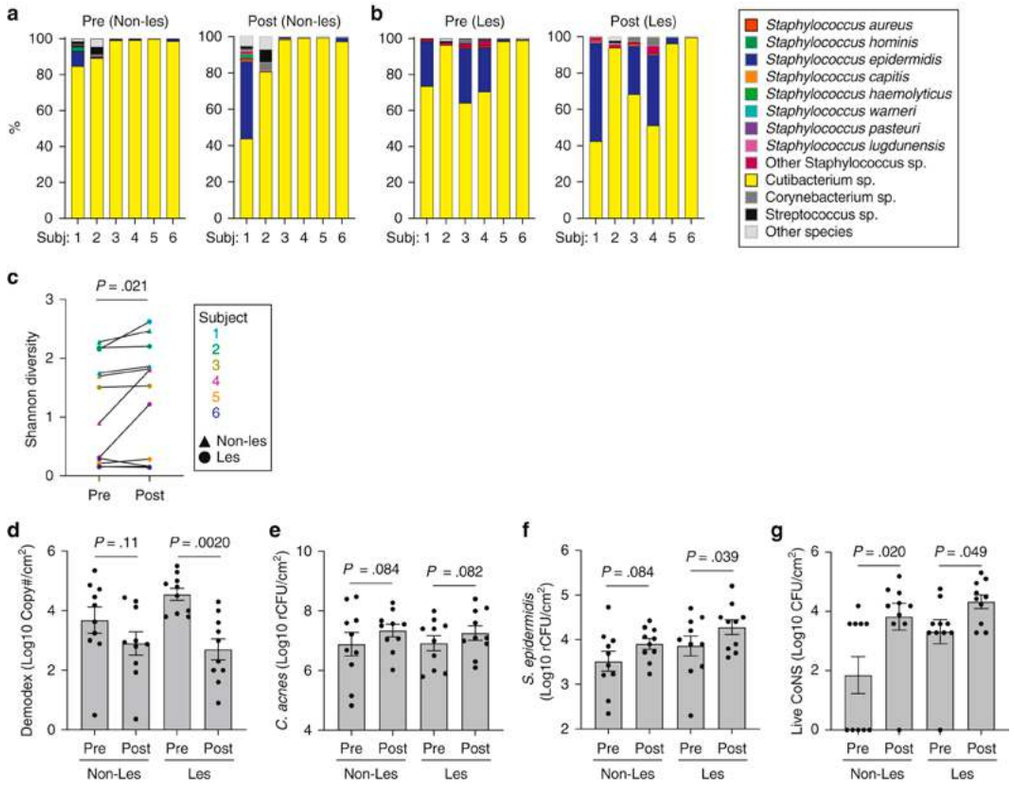
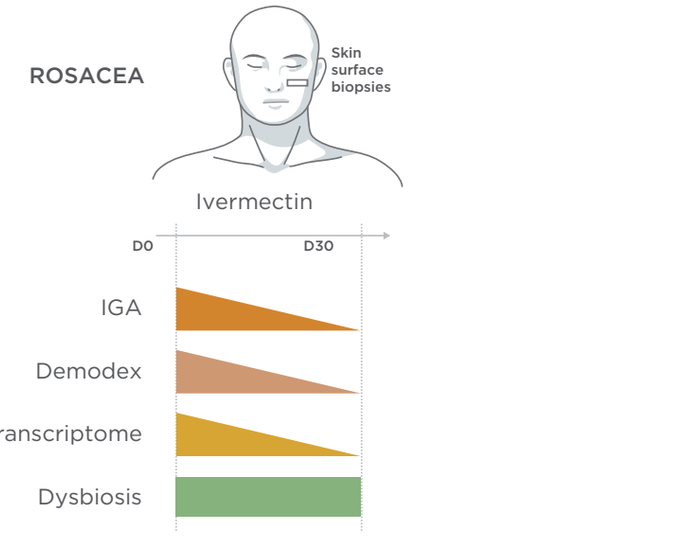


Figure 4. Role of ivermectin in rosacea [31]. Ivermectin given for 30 days, reduces clinical signs (IGA) of rosacea, *Demodex* load and the transcriptome in rosacea lesions. It does not reduce dysbiosis.



CONCLUSION

To date, there is no evidence of dysbiosis in rosacea, with the persistence of microbial diversity suggesting that the skin microbiome does not play a central role in the disease.

Recent data indicate that the skin microbiome is unlikely to play a central role in rosacea. However, in lesional skin, the abundance of *C. acnes* is significantly decreased, while that of *S. epidermidis* is increased. *C. acnes* plays a crucial role in maintaining skin barrier integrity by producing lipids and regulating skin pH. The decrease in its abundance correlates with rosacea severity.

Both the gut and skin microbiomes interact, opening the door to the potential use of oral probiotics. However, clinical trials are needed to confirm their benefit in large patient populations.

Both laser treatments and cyclins, which increase the abundance of genes related to tetracycline resistance, can alter the skin microbiome. Therefore, appropriate skincare - including a cleansing gel with a pH around 5.0 and a repairing moisturiser containing ceramides – should always accompany these therapies.

Ivermectin has both antimicrobial activity against Demodex and anti-inflammatory effects on the skin barrier, which may favour the growth of *S. epidermidis*.

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Rosacea: update on therapeutic strategies

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— Pathogenic mechanisms of Rosacea —

Rosacea is a complex, multifactorial disease. Figure 1 illustrates its pathogenic mechanisms: environmental triggers interact with genetic predisposition, leading to immune and neurovascular dysregulation.[1] This intricate framework mirrors pathways observed in other inflammatory skin diseases, like psoriasis and atopic dermatitis, and supports the rationale for targeting multiple axes of intervention.

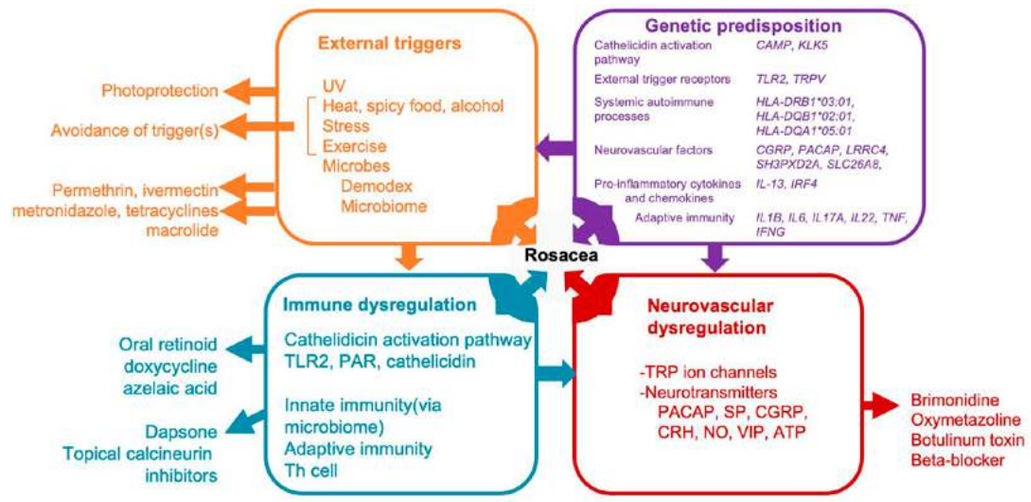
Focusing on immune dysregulation, the role of the microbiome in innate immunity raises important considerations regarding the use of antibiotics with some antibiotic treatments aiming not to target the microbiome directly, but rather to avoid the complications that may arise from its disruption.

— Cyclines: "less is more" —

For a long time, doxycycline has been used in the treatment of rosacea, but a pivotal study in 2007 introduced a paradigm shift showing that "less is more".

In this clinical trial, Oracea®, a novel formulation combining 30 mg of immediate-release and 10 mg of delayed-release doxycycline, demonstrated equivalent efficacy to the conventional 100 mg doxycycline hyclate dose.[2] The reduction of the total number of inflammatory lesions (papules or pustules) was comparable at 4, 8, 12 and 16 weeks. The 100 mg dose of doxycycline did not result in either a stronger therapeutic effect or a faster onset of action compared to Oracea®.

Figure 1. Pathogenic mechanisms of rosacea [1]

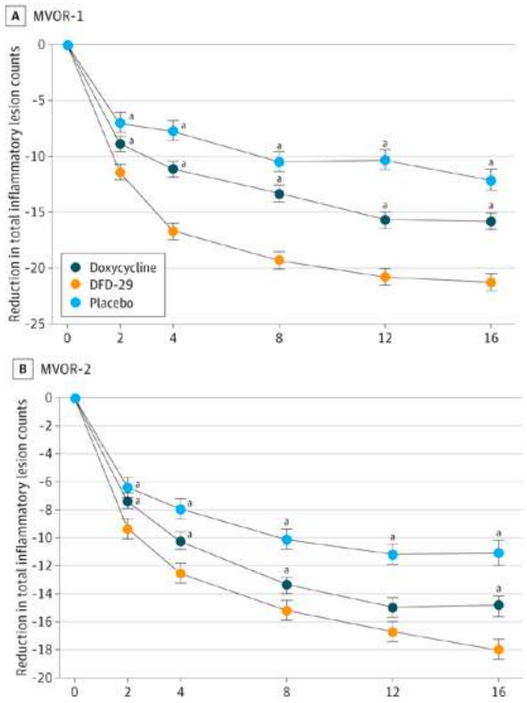


Oracea® delivered a dose even lower than what was previously considered 'low-dose' doxycycline (i.e., 40 mg of immediate-release doxycycline), which has been shown to result in plasma concentrations that do not exceed the antimicrobial threshold and therefore do not exert antibiotic effects.[3] In fact, the U.S. label for Oracea® explicitly states that it should not be used to treat an infection, as the formulation does not reach antimicrobial levels.

This marked the beginning of discussions around the use of sub-antimicrobial antibiotics in rosacea. Why use antibiotics in rosacea if there is no infection? The answer lies in the anti-inflammatory, not antimicrobial properties of doxycycline, which directly address the inflammatory nature of rosacea.

More recently, an article reported the results of 2 double-blind, placebo-controlled, phase 3 randomised clinical trials investigating a low-dose minocycline formulation with reversed release kinetics: 10 mg immediate-release and 30 mg delayed-release.[4] In both trials, this formulation was not only superior to placebo but also significantly more effective and faster than 40 mg low-dose doxycycline in reducing inflammatory lesion counts and improving IGA scores (Figure 2). Across both 16-week studies, adverse events were similar between minocycline and placebo groups, with no cases of pseudotumor cerebri or hyperpigmentation. **This suggests that the new low-dose minocycline is both effective and safe, avoiding the adverse effects typically associated with full-dose cyclins.**

Figure 2. Reduction of inflammatory lesion counts in two double-blind, placebo-controlled, phase 3 randomized clinical trials (MVOR-1 and MVOR-2) comparing DFD-29 (immediate/extended-release minocycline 10mg/30mg), with low-dose doxycycline (40 mg) and placebo [4] (Bhatia 2025)



As for its impact on the microbiome, conclusive data are still lacking. However, an encouraging study presented at the American Academy of Dermatology analysed 40 patients treated with low-dose minocycline and 20 on placebo.[5] After 16 weeks, there were no significant differences in microbiota composition in skin swabs, stool samples, or vaginal swabs: no increase in opportunistic organisms and no disruption of the normal flora. These findings suggest a favourable safety profile for the microbiome, though further studies are needed.

— Topical treatment —

A new topical treatment is currently under investigation, utilising microencapsulated benzoyl peroxide (BPO), a compound traditionally considered too irritating for rosacea-prone skin. In this new formulation, BPO is slowly released, enhancing both efficacy and tolerability. The process involves emulsifying inactive silica monomers with BPO. These monomers migrate to the oil/water interface, forming a silica shell that encapsulates the drug in a controlled manner. Lipids and phospholipids then penetrate this shell to dissolve the BPO, allowing it to leak out gradually over a 24-hour period, rather than being delivered as an immediate bolus to the skin.

A 12-week clinical trial demonstrated that microencapsulated 5% BPO monotherapy was significantly more effective than vehicle control in treating rosacea, based on both investigator global assessment success rates and reduction in inflammatory lesion count.[6] The safety profile of the active treatment was comparable to vehicle alone, with similarly low dryness, scaling, itching, stinging and burning scores.

The exact mechanism of action remains under investigation. It may involve anti-inflammatory effects, anti-Demodex activity, or normalisation of the skin microbiome. **Notably, upcoming data suggest a shift in microbial balance, including an inversion of the ratio between *Cutibacterium acnes* and *Staphylococcus dermatitis*, which may contribute to the clinical benefits observed.**

— Dermocosmetics —

While patients with papulopustular rosacea (PPR) may be treated affectively with antibiotics, sub-antimicrobial dose antibiotics, microencapsulated BPO or a combination of these, additional long-term strategies are necessary once the disease is under control. **Effective maintenance therapy is critical for preventing relapse and managing the chronic nature of rosacea.**

The American Academy of Dermatology recommends that patients adopt a comprehensive maintenance plan to sustain treatment results. This includes not only pharmacologic therapy but also skin care, sun protection, and trigger avoidance (https://www.aad.org/public/diseases/rosacea/triggers/tips).

Key recommendations include:

- Choose rosacea-friendly skin care products
- Test skin care products and makeup before applying them to the face
- Cleanse the face very gently twice a day
- Apply moisturiser after cleansing.
- Protect skin from sun year-round.
- Avoid harsh scrubbing or aggressive treatments
- Use makeup if desired.

CONCLUSION

Scientific interest in rosacea is growing, as reflected by the increasing volume of research and publications in recent years. With a deeper understanding of the underlying inflammatory pathways, the role of the microbiome, and emerging therapeutic technologies, significant advancements in the treatment and management of rosacea are expected. These developments will likely lead to more personalised, effective, and tolerable treatment options for patients.

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A novel ecobiology solution for rosacea-prone skin

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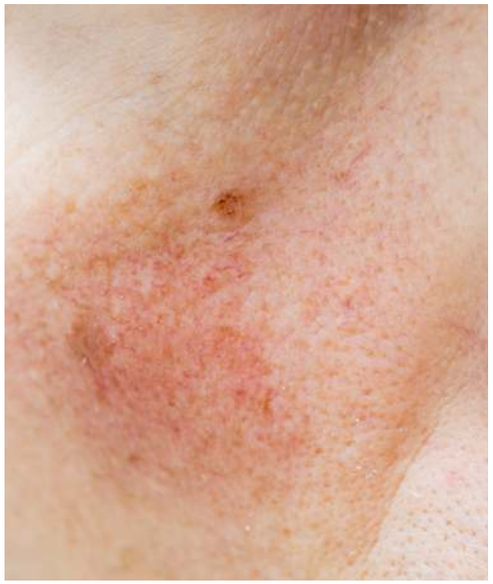
INTRODUCTION

Rosacea is a complex and multifactorial disease that has significant consequences on self-perception, quality of life, relationships, as well as on social and professional life.



— Epidemiology —

In 2016, approximately 5% of the global population was diagnosed with rosacea. An epidemiological study involving 827 individuals with rosacea conducted the same year reported that one-third of participants felt stigmatised because of their condition.[1, 2]

Depression in rosacea patients has been shown to closely correlate with their subjective perception of disease severity.([3, 4]. Additional data collected by BIODERMA indicate that rosacea patients often experience low self-esteem, negative self-image, anxiety about their appearance, and fear of social judgment. Furthermore, 66% of respondents reported lacking information about rosacea, 55% of redness-prone subjects did not use specific anti-redness skincare products, and 40% expressed a need for medical support.

A recent National Rosacea Society survey investigating the emotional and mental impact of rosacea revealed that its effects extend far beyond visible physical symptom. [5] Among 703 respondents, 91% stated that rosacea affected their mental health; 20% reported constant psychological impact, and 28% experienced frequent emotional distress. The most frequently reported emotions were embarrassment (81%) and frustration (72%). More than half of respondents experienced anxiety, 46% felt helpless, 38% reported depression, 30% felt isolated, and 24% expressed anger related to their condition.

These findings highlight the fact that both mental and physical well-being are high priorities for rosacea patients. The survey suggests that discussing emotional health with physicians should be an integral part of ongoing rosacea management.

— Physiopathology —

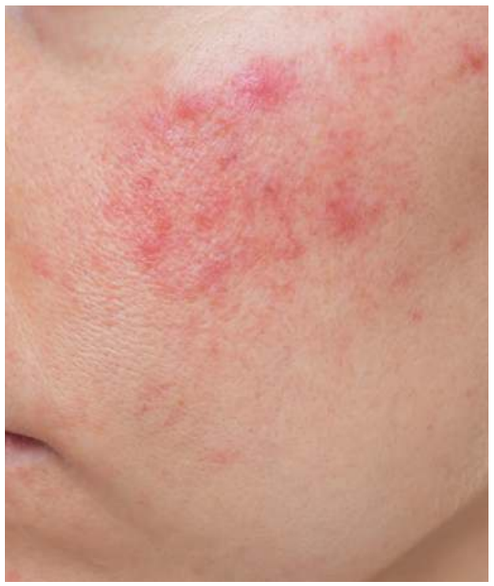
Rosacea arises from a combination of genetic and environmental factors such as emotional stress, UV radiation, spicy food,

hot beverages, alcohol consumption, temperature changes, physical activity, and irritant cosmetics.[6]

Conventional treatments that target only vascular constriction provide only limited and transient efficacy, suggesting that vascular dysregulation is not the sole mechanism underlying rosacea.[7]

In the epidermis of rosacea patients, hypersensitive and hyperreactive nerve endings have been identified, linked to the overexpression of the transient receptor potential cation channel subfamily V member 1 (TRPV1).[8, 9] TRPV1 is a non-selective receptor channel widely expressed in skin tissues, including keratinocytes, peripheral sensory nerve fibres, and immune cells. It is activated by various exogenous and endogenous inflammatory mediators, triggering neuropeptide release and neurogenic inflammation.[10]

Environmental triggers elicit an exaggerated neuronal response, promoting the release of potent vasodilatory neuropeptides such as pituitary adenylate cyclase-activating polypeptide (PACAP) and calcitonin gene-related peptide (CGRP), resulting in inflammation and vasodilation.[11]



Additionally, studies have shown that the innate immune system is altered in rosacea.[12, 13] Toll-like receptors 2 (TLR-2) are overexpressed on the surface of immune cells, and excessively activated by environmental factors.[14, 15] This abnormal activation of an otherwise natural mechanism induces the production of pro-inflammatory and angiogenic molecules, notably kallikrein-5 enzyme (KLK5) and the LL-37 peptide.[16, 17]

As a result, neurovascular dysregulation and immune dysfunction drive excessive angiogenesis and vasodilation, manifesting as flushing, persistent redness, and telangiectasias. These mechanisms also explain the common functional symptoms experienced by patients – discomfort, tightness, tingling, burning, and pain – all of which contribute to a significant reduction in quality of life.

— Innovative care approach with ROSACTIVTM 2.0 technology —

ROSACTIV™ 2.0 was developed to target neurogenic inflammation and regulate innate immunity. It is formulated within BIODERMA's SENSIBIO® AR+ product range.

ROSACTIV™ 2.0 contains creatinine, a neuro-soothing ingredient that reduces hyperreactivity of nerve fibres and neuroinflammation by specifically inhibiting the secretion of vasodilatory neuropeptides PACAP and CGRP, as well as malto-oligosyl glucoside, a soothing polysaccharide that limits excessive activation of innate immune mechanisms by inhibiting KLK5.

Together, these 2 active ingredients reduce inflammation, which in turn decreases excessive vasodilation, angiogenesis, telangiectasia, erythema, skin temperature, and overall skin discomfort.

A proof-of-concept assay using a co-culture model of human microvascular endothelial cells (HMVECs) and normal human dermal fibroblasts (NHDFs) demonstrated that ROSACTIV™ 2.0 significantly inhibited vascular endothelial growth factor (VEGF) production, angiogenesis, and pseudotube formation by 32% ($p < 0.001$), compared with suramin (-24%, $p < 0.01$) (Figure 1). Moreover, ROSACTIV™ 2.0 reduced capsaicin-induced CGRP release by 96% ($p < 0.01$).

In a clinical study, SENSIBIO® AR+ Cream was applied twice daily for 56 days by 40 subjects with mild-to-moderate rosacea significantly improved rosacea severity, as measured by the Investigator's Global Assessment (IGA) (Figure 2). Erythema decreased by 24% ($p < 0.05$) compared with 10% for a neutral cream, with continued improvement up to 29% ($p < 0.05$) two weeks after switching to the neutral cream (Figure 3), confirming an anti-relapse benefit. Additionally, flushing episodes decreased by 18%.

Figure 1. Results of the *in vitro* proof-of-efficacy study of ROSACTIV™ 2.0 on the inhibition of VEGF and angiogenesis

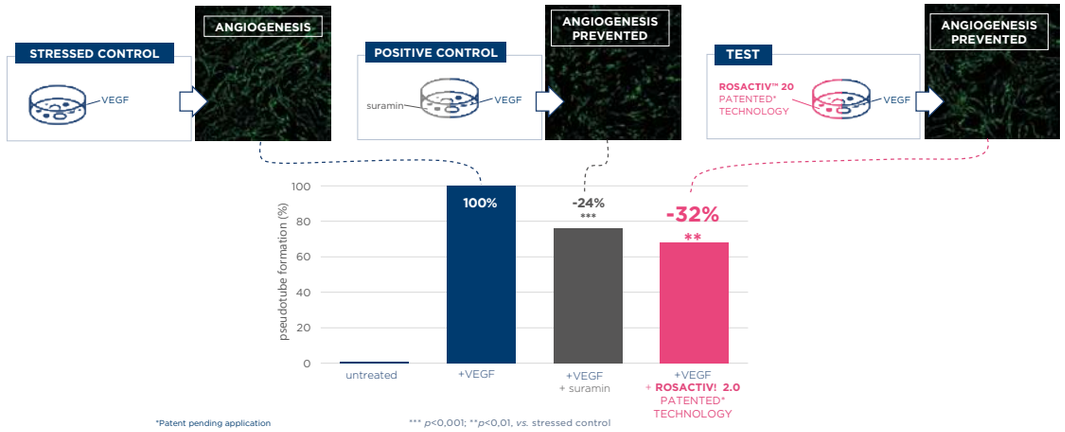
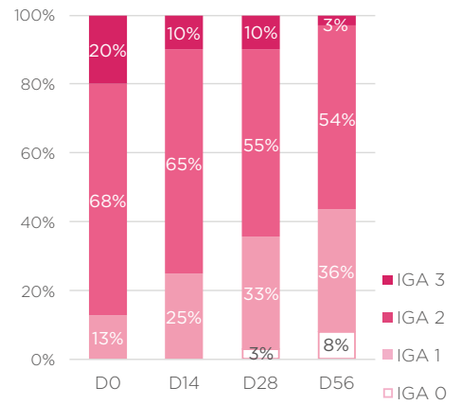
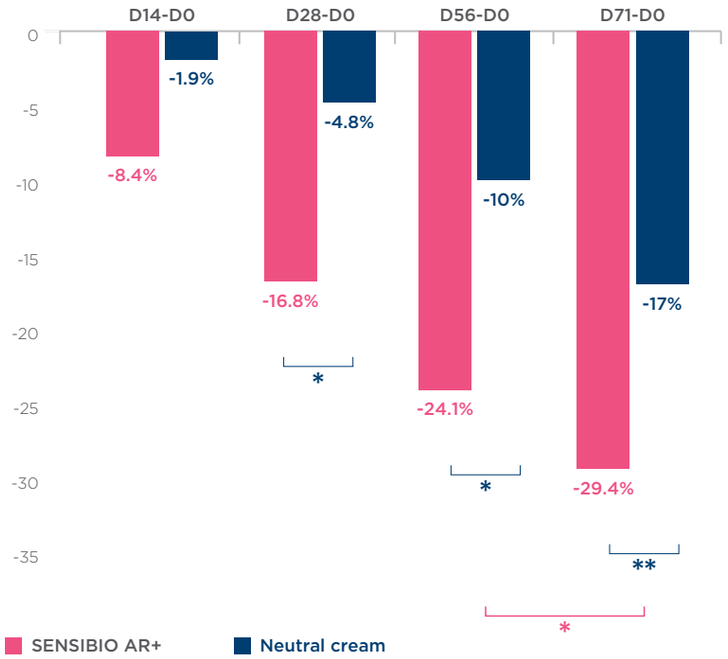


Figure 2. Improvement of rosacea severity



The number of subjects with moderate rosacea decreased by 50% as early as after 14 days of use. After 28 days 41% of the subjects had no or only very mild rosacea compared to baseline (13%).

Figure 3. Evolution of erythema severity over time



*$p<0.05$ **$p<0.05$

Quality-of-life assessment using the RosaQOL questionnaire showed a 30% reduction in patient concerns about rosacea worsening, confirming that **SENSIBIO®AR+ Cream helps to improve both disease management and patient well-being.**

A second clinical study demonstrated that flushing intensity and discomfort sensations were reduced by 35% after just one month of SENSIBIO AR+ Cream application.

— Ecobiological approach of the SENSIBIO® AR+ product range —

The SENSIBIO® AR+ product range adheres to NAOS ecobiology principles, favouring biomimetic ingredients such as ROSACTIV™ 2.0 to support natural skin mechanisms rather than overcorrect them.

CONCLUSION

In conclusion, the biomimetic patented* technology ROSACTIV™ 2.0 acts on key biological pathways mediating vasodilation and angiogenesis—addressing the root causes of redness and discomfort—while respecting NAOS ecobiology principles.

The SENSIBIO® AR+ range provides effective adjuvant care solutions that help improve rosacea symptoms and enhance patients' quality of life.

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NOTES

NAOS ECOBIOLOGY

NAOS, SAS with a capital of € 43,474,650,R.C.S. Aix-en-Provence B535 236 418, 355 rue Pierre-Simon Laplace
13290 Aix-en-Provence. October 24