Clinical Nutrition & Supplements For Rosacea and Acne

Original | Clinical Research White Paper

December 2021 | Saju Jospeh MD FACS, Devan A. Patel PharmD, Teri A. Standridge B.S., Malini M. Patel

Introduction to Clinical Nutrition for Rosacea and Acne Sufferers

Introduction

In the United States, acne is the most common skin condition, affecting up to 50 million Americans annually.¹ Typically, acne begins in puberty and affects many adolescents. However, acne can occur at any age, and in adults, it can continue to persist into the 30s and 40s.² The prevalence of adult acne has been increasing over the last seven years, reaching 15% percent of all women.¹ Adult female acne (AFA) affects women over the age of 25 and may persist continuously or intermittently from adolescence or manifest for the first time in this period.³ Adult acne presents characteristics and multiple etiopathogenic factors that make managing it more complex.

Acne vulgaris is a chronic skin disorder in which dead skin cells, bacteria, and oil block hair follicles, causing blemishes on the skin. Furthermore, acne is characterized primarily by inflammation. There are certain factors that can trigger or worsen acne, including hormonal changes, certain medications, diet, and stress. There is no cure for acne; however, it can be successfully treated and controlled with the proper treatment and dietary changes.

According to the American Academy of Dermatology, rosacea is also a highly common skin condition affecting 16 million Americans annually.² It is a chronic skin disorder that can affect people of all ages and races but is predominantly present in those between the ages of 30 and 60, those with a family history of rosacea, those with fair skin, and women, especially during menopause.⁴

Rosacea is a skin disorder that causes red, irritated skin, flushing over the face, and inflammatory lesions. It mainly affects the central areas of the face, such as the cheeks and nose. It can make the skin thicker as well as cause eye problems such as redness, dryness, or itchiness.⁴ Additionally, symptoms such as burning, stinging, and increased skin sensitivity are common. There are various trigger factors known to cause rosacea flare-ups, including spicy foods, emotional stress, alcohol, ultraviolet exposure, and hot baths. However, some research has found that an increase in cathelicidins is a potential cause of the skin bumps as well as the flushing and the visible blood vessels. Cathelicidins are antimicrobial molecules that are part of the innate immune system's strategy for fighting threats. In a different form, cathelicidins are more abundant in rosacea patients compared to those without the condition. Even though the leading cause of rosacea is still under research, excess inflammation and dysregulation of the immune system could be possible causes.⁶ There is no cure for rosacea, but there are treatments to improve the symptoms. It is important to note that if rosacea is left untreated, it may worsen over time. Taking early action can help manage the condition and prevent flare-ups.

Ultimately, rosacea and acne are widespread skin conditions affecting many Americans, especially women. Without a cure for either disorder, treating and controlling the symptoms through medications and diet can help improve both skin conditions.

Understanding the Burden of Rosacea and Acne

Similar to many chronic conditions, rosacea and acne inflict a heavy burden on most patients, often resulting in low self-esteem and decreased social interactions. In a recent survey, the top five emotions patients reported feeling included embarrassment, discomfort, low self-esteem, frustration, and low confidence.⁷ Beyond the visible manifestations of acne and rosacea, there are significant implications for patients, such as detriment to their mental health and well-being.⁸ A study examining data from the 2002-2012 US National Inpatient Sample, consisting of about 20 percent of pediatrics and adults, revealed that patients with acne and rosacea had increased odds of mental health disorders. Both acne and rosacea were associated with a higher risk of mood, anxiety, impulse control, and personality disorders.⁹

These chronic skin conditions significantly impact quality of life as well. In a recent survey,⁷ patients were significantly more likely to avoid daily lifestyle habits because of their disease. This included sun exposure, drinking alcohol, eating hot or spicy foods, having hot drinks, and using make-up.

Both acne and rosacea involve substantial costs that can be significant for both the patient and the health care system. Skin disorders and diseases account for \$75 billion in medical, preventative, and prescription/non-prescription drug costs for the U.S. healthcare system. The total medical costs for acne and rosacea in 2013 were \$846 million and \$165 million, respectively. Depending on the severity of a patient's acne or rosacea, their condition can intrude into other parts of their lives, including their career. Not only is there a potential activity impairment, but there is also a financial impact. Individuals may miss work, school, or university due to possible impairment, medical appointments, or low self-esteem. The lost productivity due to acne and rosacea was \$398 million and \$78 million, respectively. Without a cure for conditions like rosacea or acne, ongoing maintenance treatments might be necessary for years, adding more burden financially. Nonetheless, through diet and lifestyle changes, there are ways to mediate the inflammation, redness, and appearance of these skin conditions.

Along with the psychological and financial impact of these chronic skin disorders, there have also been indications that these patients are at a higher risk for gastrointestinal conditions. A study involving over 13,000 adolescents revealed that those with acne were more likely to experience gastrointestinal symptoms such as constipation, halitosis, and gastric reflux. In a cohort study pertaining to rosacea, there was a direct correlation between rosacea occurrence and gastrointestinal conditions such as bacterial overgrowth, celiac disease, Crohn's disease, and stomach cancer. Yet another possible burden of these skin conditions is weight gain resulting from gastrointestinal problems. However, with a few alterations in diet, these problems can be mitigated.

The Gut-Skin Connection

Hippocrates, the father of medicine, once said, "all disease begins in the gut." The gut microbiome, containing about 300 to 500 different species of naturally occurring bacteria, comprises more than 80% of the body's immunity. ¹³ While some bacteria are harmful to our health, many are immensely beneficial and even necessary to a healthy body. This microbiome is found in the intestines and can influence overall health and skin.

The connection between the gut and skin is an intriguing topic. Numerous studies have shown that these organs are uniquely related by purpose, function, and maintaining homeostasis. ¹⁴ Systemic and local inflammation is regulated through communication between the gut and the skin. If the gut microbiome becomes unbalanced, it can cause leaky gut and inflammation, negatively affecting the skin. ¹⁴ An altered gut flora can promote the release of substance P in the gut and skin, promoting inflammation. Substance P is a neuropeptide produced in the gut, as well as the brain and skin. ¹⁵ The gut microbiota plays a significant role in many inflammatory disorders of the skin. For example, an impaired intestinal barrier can result in intestinal bacteria entering the bloodstream, which can accumulate in the skin and disrupt the skin microbiome. ¹⁴

Research suggests that there is a potential role of a gut-skin connection in rosacea, particularly Helicobacter pylori. Helicobacter pylori are gram-negative bacteria found in the stomach and small intestine, which may cause chronic gastritis, ulcers, and even some stomach cancers. In a recent cohort study, patients with rosacea that had gastrointestinal conditions such as celiac disease, Crohn's disease, and irritable bowel syndrome were higher among patients with rosacea when compared to controls. Since the microbiome plays a key role in the host's innate and adaptive immune system, it can be responsible for the effects of rosacea. Excess inflammation due to an imbalance of gut flora can trigger rosacea outbreaks as well.

As for acne, the gut microbiome can play a key role in the progression and severity of the skin condition. Acne is a multifarious condition where stress can be one of the factors. Emotional stress can impair the gut microbe, particularly Lactobacillus and Bifidobacterium species. Psychological stress can cause gut microbes to produce neurotransmitters that can enter the bloodstream through the intestinal barrier, leading to systemic inflammation.¹⁹

Current Management for Rosacea and Acne

Currently, there is no cure for rosacea, as stated before. There are medications such as skin creams, systemic antibiotics like doxycycline, topical anti-inflammatory medications like metronidazole, azelaic acid, sodium sulfacetamide, and ivermectin, prescription eye drops, and even glycolic peels.^{5,21} Traditionally, topical and oral antibiotics are also the mainstay in acne treatment. Even though this approach is effective for both acne and rosacea patients, it comes with risks such as antibiotic resistance and disruption of the microflora. Also, there are possible side effects involved with taking tetracycline (like doxycycline), which is typically used in both

rosacea and acne patients.²⁰ There is a potential of permanent tooth discoloration in individuals developing teeth and thus should be avoided in children as well as during pregnancy.^{20,21}

Aside from conventional treatments like topical and oral treatments, patients should consider avoiding certain foods when managing these conditions. Some triggers that can exacerbate rosacea include hot drinks, spicy foods, caffeine, and alcohol. Additional non-food triggers include exercise, stress, sun, and extreme hot and cold weather. Other methods of managing rosacea include laser treatments or electrosurgery to shrink blood vessels, surgery or dermabrasion to treat scarring of the nose, and overall skin protection measures, such as using sunscreen and sunglasses. 5,18,21

Sometimes, rosacea and acne need to be managed for many years, or even indefinitely. Even though symptoms can improve with the use of medications like topical and oral antibiotics, these are only temporary treatments, and stopping these medications can result in symptoms returning or even worsening. Physicians should consider GI microbes as a source for rosacea and acne flairs and consider dietary modifications in this patient population.²¹

The Role of Diet in Managing Rosacea

Conventional treatments for rosacea fail to address the potential underlying cause. As stated before, anecdotally that certain foods may act as rosacea triggers, but research has suggested that certain foods and dietary modifications can be essential components of rosacea therapy. There is sufficient research to indicate that the microbiome represents an important therapeutic target, given the evidence for gut-skin connection.^{5,22}

Promoting a healthy gut consists of multiple dietary measures. These include consumption of a fiber-rich diet, prebiotics, probiotics, and specific dietary nutrients. Researchers have found that a 2-week increase in fiber intake can alter a person's gut microbiome significantly. Once metabolized by bacteria, fiber promotes a healthy gut microbiome and increases the species of bacteria that break down the fiber. 22 In contrast, a lack of fiber has been linked to damaging effects on the gut flora and the gut itself.18 In a 2016 study, mice were fed a fiber-deficient diet which resulted in a proliferation of pathogenic bacteria. Subsequently, these bacteria began to digest the protective gut mucus. When the mice were given a diet rich in fiber, it supported the growth of beneficial microbiomes.²³ Research has suggested that probiotics may be helpful in skin conditions like rosacea. As mentioned previously, an imbalance of gut microbiota has been linked to many chronic GI conditions that are prominently associated with rosacea in patients. Probiotics may impact the skin barrier, improving the function and reducing sensitivity.¹⁸ Prebiotics stimulate the growth, diversity and activity of beneficial GI microbiota. 18 There are some limited studies that have also promoted specific dietary nutrients to alleviate some of the symptoms of rosacea. These beneficial microbes have been shown to support gut health and skin health in numerous ways.18

Dietary modifications and interventions can provide an avenue for treating skin conditions like rosacea and acne, chronic gastrointestinal conditions, and overall health. The gut-skin connection has been studied for quite some time, indicating the gut microbiota control the skin's health with the immune system. Further research is still needed; however, key nutrients can support those suffering from rosacea and acne.

Key Nutrients to Support Rosacea and Acne

Vitamin A

Vitamin A, also known as retinyl acetate, is a lipid-soluble essential nutrient that supports the skin, eye, reproductive health, and immune function. Vitamin A is known as an anti-inflammatory vitamin because of its crucial role in enhancing the immune system. It has wound healing properties, allowing the skin to heal and regenerate. Through intricate processes, vitamin A regulates sebum production, promotes skin to proliferate, resulting in the reduction of bumps and pimples on the skin and reducing redness. Deficiencies in vitamin A have been linked to an increased susceptibility to skin infection and inflammation. This susceptibility has suggested an integral role for vitamin A in promoting immune function in the skin. ²⁶

Vitamin A modulates the immune response and maintains the homeostasis of epithelial tissues and mucosa through its metabolite, retinoic acid, and is involved in the formation of the epithelial and mucous tissues. This means it functions as the "front line' of defenses against pathogen invasion. Skin is a major retinoid-responsive tissue. The epidermis and dermis contain proteins and receptors that mediate the biological effects of the metabolites of vitamin A in the skin.²4 Retinoic acid controls gene expression through these retinoic acid receptors. This essential nutrient is an integral part of the mucus layer in both the respiratory and intestinal systems. Vitamin A promotes mucus secretion, improving the non-specific immunity function of these tissues, thus increasing the integrity of the intestinal mucus. Having intestines with increased integrity can help maintain resistance against foreign pathogens and promote a barrier function, thus protecting the mucus of the intestines and supporting the growth of essential microbiota.²5 These processes are intricately involved in the homeostasis of the skin microbiome and may induce the processes that regulate hair follicle immunity.²6

Vitamin C (ascorbic acid)

Vitamin C is a water-soluble essential vitamin linked to numerous health benefits. It is involved in the formation of the skin barrier and collagen in the dermis and plays a physiological role in the skin in cell signal pathways of cell growth and differentiation. Additionally, it works against skin oxidation and aging. Vitamin C status in individuals with skin inflammation such as rosacea and acne have lower levels compared to unaffected individuals.²⁹

Vitamin C is a powerful antioxidant that can strengthen the body's immune system, an important additional benefit. Antioxidants boost the immune system by protecting cells from free radicals.²⁷ Having an accumulation of free radicals can put the body in oxidative stress, which has been linked to many chronic diseases such as cancer, inflammatory diseases, asthma, and more. Inflammation impedes the skin's renewal process. Because antioxidants protect tissues from damage, they prevent unwanted inflammatory responses from occurring and allow the skin to repair itself and correct visible damage.

Vitamin C can also stimulate collagen growth, which is vital for youthful skin.²⁷ Collagen is an important component in the connective tissue of the basement membrane and blood vessels, and vitamin C is essential for collagen synthesis. The redness in rosacea is believed to be caused by blood vessels that dilate too easily. The anti-inflammatory bioflavonoids found in Vitamin C help support weakened blood vessels, and strengthening these blood vessels can help reduce redness and inflammation.²⁸

Vitamin C is a beneficial nutrient alone, but it can also be added to adjuvant therapies for skin diseases such as acne. In patients with acne, the adjunctive agent can aid against clarithromycin-resistant p. acnes. When patients are on clarithromycin, it can improve skin hardness, smoothness, and post-inflammatory pigmentation after micro-needling.³⁰

Vitamin C is an antioxidant with numerous benefits, including improving one's immunity and acting as an anti-inflammatory. Rosacea symptoms triggered by inflammation and weakened blood vessels can be improved with dietary modifications and supplementation of vitamin C. This nutrient can be consumed through brightly colored fruits and vegetables and in supplement form.

Vitamin K (Menaquinone-7)

Vitamin K is a fat-soluble vitamin that aids in reducing inflammation with its antioxidant properties. It also improves the natural barrier of the skin.³¹ It can protect the skin against environmental aggressors like free radicals and UV rays of the sun, preventing rosacea from triggering.^{5,31} Along with Vitamin C, Vitamin K can help with collagen production, which can help maintain the elasticity and capillary integrity of the skin. This also helps with redness and inflammation in rosacea.

A study found that a sufficient amount of Vitamin K can produce a protein that lowers vascular proliferation and mineralization, resulting in halted development of varicose veins. These veins can be prominent in patients with rosacea. Vitamin K also has the ability to improve the elasticity of blood vessels, which can help the area look less irritated.31

Consuming foods like fresh, leafy greens, Brussels sprouts, cabbage, fish, and eggs can increase Vitamin K consumption along with fermented foods. Vitamin K can synergistically work with

Vitamin C to bring antioxidant properties to the body and skin. The anti-inflammatory properties and collagen production can help reduce the symptoms of rosacea, such as redness, pimples, and bumps.³¹

Niacin (Niacinamide)

Niacinamide is a multifunctional nutrient that is a water-soluble derivative of niacin, or vitamin B3, found in meat, fish, and wheat.^{32,33} Along with the many benefits of niacinamide, such as lowering cholesterol, easing arthritis, and boosting brain function, it has many benefits for skin care. It acts as an antioxidant while possessing biological activities, making it an important cosmetic ingredient.³³ Firstly, it has anti-inflammatory and skin-lightening properties that can improve inflammatory skin conditions like acne and rosacea. It can also decrease the production of sebum.³³ A study published in the International Journal of Dermatology showed that 4 percent niacinamide gel used twice daily significantly decreased acne in 8 weeks. Another benefit of niacin is that it can support the barrier function of the skin, which is important in patients with rosacea as it is easily susceptible to irritation. Niacinamide increases the production of ceramides, which are skin lipids responsible for maintaining the barrier function of the skin and keeping it hydrated. In patients with rosacea, this can prevent water loss in compromised skin. Niacinamide has anti-aging properties, such as slowing down the appearance of wrinkles by increasing the production of collagen.³²

Many studies have shown how efficacious niacinamide is in treating skin conditions. One particular study treated patients with a formulation consisting of niacinamide, zinc, copper, and folic acid while comparing it to the conventional treatment of oral antibiotic therapy. The percentage of patients who received the formulation alone had a significant improvement, 79 percent of patients, while oral antibiotic monotherapy showed significant improvement. The study concluded that this formulation was effective for treating patients with acne and rosacea and should be considered as an alternative or adjunct to therapy.³³

Zinc

Zinc is a mineral and one of the many essential nutrients your body needs for proper growth and maintenance. Zinc is mainly known for protecting the immune system by fighting off harmful bacteria.³⁴ It happens to be one of the most widely studied forms of treating rosacea and acne. This mineral can help with redness, irritation, and inflammation that is caused by skin conditions like rosacea and acne.

Zinc can act as an anti-inflammatory by assisting with the metabolism of omega-3 fatty acids.³⁵ Additionally, zinc can act as an antibacterial and reduce the effect the bacteria has on the skin.

Zinc can assist with reducing clogging of the pores by breaking down substance P, resulting in reduced sebum production. It can also help with reducing keratinocyte activation. Keratinocytes

produce keratin, which helps bind the skin cells together. Having an excessive amount of keratin can prevent cells from separating, leading to blocked pores. By reducing the amount of keratin produced, zinc helps keep the skin pore more open. Zinc can also aid in apoptosis which can help with the skin renewing itself. If someone has a deficiency in zinc, it can delay apoptosis, resulting in the skin sticking together instead of dying, which can cause the pores to be clogged.³⁴

In a double-blind study, zinc decreased the severity of rosacea by approximately 75 percent, while the placebo group displayed no improvement.³⁵ It also reported no significant side effects. Zinc is a high-performance mineral that promotes the body's immunity, the normal functioning of the skin, absorption, and opening of the pores.

Copper

Copper is one of the nine minerals that are recognized as essential nutrients for humans. Copper is naturally found in many food sources such as meats, vegetables, and grains. Two properties that copper possesses make it desirable for skin treatment. Firstly, it has potent biocidal properties that can kill harmful bacteria in the gut and the skin. Secondly, it is involved in numerous physiological and metabolic processes that are essential for just about all the tissues in the body, including the skin. In the skin, copper helps stimulate proliferation of dermal fibroblasts, regulates matrix production, promotes angiogenesis, and upregulates collagen and elastin. The properties that copper possesses can help the appearance of the skin, reduce redness and even accelerate the healing process for patients who have acne or rosacea.

A study concluded that low serum copper levels were a possible cause of acne. In the study, 50 females that suffered from acne were matched with 50 healthy females without acne, and their copper levels were measured in the serum. The results showed that the serum copper levels were lower in affected patients compared to healthy patients. In another study, supplementation of copper with zinc helped prevent zinc-induced copper deficiency.³⁵

Manganese (Manganese Sulfate)

Manganese is a trace element that is important for a healthy body, as it is necessary for development, metabolism, and the antioxidant system.³⁷ Manganese also activates several enzymes systems and helps the body use various vitamins such as vitamin C, E, other B-vitamins, and biotin.³⁸ These vitamins, and their role in patients with chronic skin conditions, were previously mentioned. Because manganese increases the activity of an antioxidant called superoxide dismutase (SOD), it assists in preventing the superoxide free radicals from damaging cellular components. By neutralizing free radicals, SOD can reduce and help prevent some acne damage.³⁷ Manganese is needed to produce the amino acid proline, which is essential for collagen formation.³⁸ This can help support the existing vessels and surrounding structure, helping with skin redness and smoothness. A study was performed to determine the effect of

manganese level concentration in acne patients. The results revealed statistically decreased manganese levels in acne patients.³⁷ Inflammation, redness, and irritation can be reduced amongst patients with acne and rosacea.

Organic Turmeric Root Powder

Turmeric is a common spice used throughout the world and is best known for its active component, curcumin. It has exhibited anti-inflammatory, antimicrobial, antioxidant, wound healing, and chemopreventive properties.^{33,39} Turmeric and its active components also have been shown to mediate dilation and constriction of peripheral arterioles, which helps with skin redness.⁴⁰ A systematic review revealed that the majority of the studies that meet inclusion involving turmeric and the skin had noted a statistically significant improvement in skin disease severity in turmeric treatment groups compared to the controls. Along with the improvement of the skin, the majority of the studies indicated no adverse effects, making it a safe alternative for assisting in inflammation and redness in chronic skin conditions.

Along with the direct effect on the skin, turmeric can also play a role in the gut microbiome.⁴¹ Curcumin in the gut favors the growth of beneficial bacteria while reducing pathogenic strains. Several studies have reported how curcumin reduces intestinal inflammation, thus modulating the homeostasis of the gut-skin axis. As previously stated, the gastrointestinal tract plays an immunoregulatory role, and maintaining a healthy gut detoxifies the skin.⁴¹ When the balance of the gut microbes is restored, they have an anti-inflammatory effect which ultimately eliminates skin inflammation.⁵

Organic Apple Cider Fruit Vinegar Powder

Apple cider vinegar is essentially a vinegar made from apples during the cider fermenting process. It has many beneficial properties, including improving digestion, supporting the immune system, lowering blood sugar, aiding in weight loss, improving the heart, and improving skin health. Another benefit of apple cider vinegar is the nutrients it contains, including manganese and iron, whose benefits were previously stated.⁴² Vinegar has polyphenolic antioxidants that can help reduce free radicals in the body and apple cider vinegar, in particular, is high in pectin, a polysaccharide that occurs in apples and can play a role in improving the skin's barrier.⁴³

Consuming apple cider vinegar can help with gastrointestinal problems. It has antimicrobial activity, which can reduce pathogenic bacteria while promoting beneficial bacteria resulting in homeostasis between the skin and gut. Along with the antimicrobial activity, apple cider vinegar can promote a balance of pH levels in the stomach, which can help the pH of the skin.⁴⁴ When the skin has optimal pH level, it improves the skin barrier function and moisture retention and

reduces scaling. Apple cider vinegar has many benefits for the stomach and skin and can assist in the inflammation of the skin, irritation, and redness for rosacea or acne.⁴⁵

Organic Ginger Root Powder

Ginger is a globally-known spice that has a long history of medicinal uses. It has been proven to possess anti-inflammatory, antioxidant, antitumor, and antiulcer effects. 46 Many people use it for alleviating symptoms of nausea and vomiting. In relation to the skin, studies are limited for the direct correlation. However, with its anti-inflammatory, antioxidant, antitumor, and antiulcer effects in the stomach, it can correlate to better skin health. Even though there are studies proving it as a gastroprotective agent, more extensive studies on ginger are needed to further demonstrate its efficacy. 46

Broccoli Sprout Extract

Following a limited diet lacking in nutrients can trigger symptoms of rosacea. Superfoods such as broccoli sprouts, specifically the extract, are beneficial for the skin. Broccoli sprout extract contains sulforaphane which has been indicated in studies to reduce skin redness and inflammation. Researchers have found that sulforaphane has anti-cancer, anti-inflammatory, anti-viral, and detoxifying abilities along with a host of other important health benefits. Sulforaphanes can support liver function, making it easier to detoxify both internal and external substances. In the case of acne and rosacea, hormones in excess would lessen, resulting in a decrease since excess estrogen has been linked to increased sebum.⁴⁷

Broccoli sprout extract also benefits gut health. It has been shown to reduce inflammation associated with both colitis and ulcers and combat infections from a pathogenic organism, Helicobacter pylori, by inhibiting its growth and colonization.⁴⁸ Broccoli sprout extract is an excellent nutrition source. It is high in vitamins A, B, and C, dietary fiber, and folic acid, all of which are necessary for healthy skin, hair, and anti-aging benefits.⁴⁹

Probiotics

Probiotics are live microorganisms that benefit the host. There has been an abundance of evidence suggesting probiotics can benefit your skin just as they benefit the gut. Evidence has indicated that by maintaining a balanced gut of bacteria, probiotics can reduce inflammation that can cause skin irritation, sensitivity, and redness in skin conditions. Orally consumed probiotics have been shown to reduce systemic markers of inflammation and oxidative stress, both of which are elevated locally in those with acne. In one study, acne patients were given a lactobacillus-fermented drink over a 12-week period. The researchers found a significant improvement in these patients as well as decreased oiliness.⁵⁰ In a clinical study, patients who

received oral Lactobacillus species in conjunction with antibiotics experienced a significantly greater decrease in acne lesions compared to those who were on antibiotics alone.⁵¹

Two specific Lactobacillus species, Lactobacillus acidophilus complex and Lactobacillus paracasei, are probiotics that are generally used to improve normal microbial flora of the gut and maintain skin health.⁵ A study that gave Lactobacillus paracasei to mice found that the probiotic induced T regulatory cells and inhibited CD4+ T-cell proliferation while increasing the secretions of anti-inflammatory cytokines. This same effect can be exhibited in humans, as it has been shown to reduce inflammation and improve immunity.⁵² In another study, when Lactobacillus paracasei was orally administered, secretions of substance P decreased. Lower systemic levels of substance P enhanced skin barrier function and decreased local skin inflammation. In relation to acne and rosacea, as substance P increases, sebum production occurs more.⁵³ Probiotic supplementation signifies a promising approach to treating acne and rosacea as an alternative or even adjunctive treatment.⁵¹

Green Tea Leaf Extract

Aside from the antioxidant and anti-inflammatory effects of green tea, studies have also demonstrated that it is a natural alternative for photoprotection and could also be a treatment for UV-induced rosacea.³³ A study evaluated a combination of antioxidants, including green tea polyphenols, caffeine, and resveratrol. The combination concluded that it reduced facial redness in most patients who participated in the study by 6 weeks.⁵⁴ Treatment with green tea extracts may benefit patients with skin conditions that present with redness and telangiectasia, which are dilated small blood vessels on the skin, by directly minimizing the appearance of these vessels and minimizing disruption of the skin barrier.

Neem Leaf Powder

Neem leaf has many medicinal properties and has remarkable effects on chronic skin conditions.⁵⁵ The medicinal properties include immunomodulatory, anti-inflammatory, anti-hyperglycemic, antiulcer, antimalarial, antifungal, antibacterial, antiviral, antioxidant, antimutagenic, and anti-carcinogenic properties. In a study, a formulation containing green tea and neem leaf extract as well as bitters, licorice, and basil was investigated for antibacterial activity and physio-chemical parameters. This formula displayed significant efficacy in controlling acne induced by bacteria.⁵⁶ Neem leaf extract combined with other nutrients and herbs can help with skin inflammation, redness, irritation and can help control the bacteria in rosacea and acne patients.

Organic Spirulina

Spirulina is an alga containing many antioxidants. Studies have shown antiaging and anti-inflammatory effects. Spirulina also contains high content of vitamin A, vitamin B, vitamin E, calcium, iron, and phosphorus, all of which are vital for your skin's health. Spirulina may also have an impact on gut health, resulting in less inflammation of the gut and skin. Spirulina also works wonders on dull skin as it may increase growth factors in dermal fibroblast cells, which are the cells responsible for creating collagen. It can also act on congested skin as it gently detoxifies and encourages cell renewal. Another benefit of spirulina is that it improves the epidermis structure and acts as a hydration booster. This assists with skin barrier function, particularly skin protection, antiaging, and oil control. Spirulina's moisturizing effect can help with irritation in rosacea and acne patients.⁵⁷ With the antioxidant and anti-inflammatory effects, it can also improve redness and inflammation.

Organic Chlorella

Chlorella is another type of algae with antioxidant and anti-inflammatory properties. Chlorella has significant inhibitory activity reducing inflammatory cell damage. ⁵⁸ Chlorella has been shown to significantly reduce reactive oxygen species (ROS), which can help reduce cell damage that may occur during acne and rosacea inflammation, reduce irritations, and keep the integrity of the skin barrier. Aside from the direct benefits to the skin, chlorella also boosts the presence of probiotics. In particular, it stimulates the growth of Lactobacillus acidophilus, which is one of the specific probiotics used to improve normal microbial flora of the gut and maintain skin health. Both spirulina and chlorella can synergistically work together by reducing inflammation, reducing the appearance of acne and rosacea, preventing oxidative stress, preventing flare-ups, and from getting worse over time. ^{57,58}

Organic Maqui Berry

Maqui berry is a nutrient-rich berry with a wide variety of benefits. Unlike other berries, Maqui berries have three times more antioxidants. As stated before, antioxidants can protect the skin's surface from oxidative damage caused by free radicals. Many studies have also demonstrated the anti-inflammatory effects of Maqui berries. In one study, Maqui berry supplement showed improvement in inflammation in blood vessels compared to no supplementation. Along with its antioxidant and anti-inflammatory effects, Maqui berries help promote a healthy gut, which is important in patients who have rosacea and acne. Studies have shown that the components of maqui berries increased the number of good bacteria helping keep the gut-skin axis in check. Maqui berries have shown great antioxidant activity and anti-inflammatory effect and could be a useful superfood in treating rosacea and acne.

Conclusion

Rosacea and acne are common skin conditions affecting both men and women. They are visible and relapsing conditions that involve periods of flare-ups in patients. Because everyone's experience of these conditions ranges, it makes it difficult to treat these complex conditions. There are conventional treatments that help manage these chronic skin conditions, but in a survey, only 14% of patients rated themselves as 'clear' of symptoms, highlighting the extent of the unmet need. Despite the many therapeutic options available for the treatment of rosacea acne, there are none that are curative. The available treatments provide inconsistent results, varying success, and side effects such as antibiotic resistance and disruption of the microflora. Patients are increasingly turning to alternative products containing natural ingredients since these ingredients have shown impactful results. Having a better understanding of these skin conditions and making dietary changes can make a powerful difference.

The evidence for a gut-skin connection can provide an avenue to intervene by making a tailored approach to a patient's diet. Avoiding triggers that cause flare-ups, taking all the vitamins and minerals mentioned above, and ultimately establishing gut health may be effective in providing better outcomes for these patients. These vitamins and minerals can help keep symptoms at bay while providing an overall healthy body and immune system. Addressing factors beyond the visibility and appearance of the skin, like the gut-health, can help with the underlying issues associated with these chronic skin conditions and result in healing and reducing flare-ups, redness, inflammation, and irritation.

References

- 1. Bickers DR, Lim HW, Margolis D, Weinstock MA, Goodman C, Faulkner E et al. The burden of skin diseases: 2004 a joint project of the American Academy of Dermatology Association and the Society for Investigative Dermatology. Journal of the American Academy of Dermatology 2006;55:490-500.
- Skin conditions by the numbers. American Academy of Dermatology. https://www.aad.org/media/stats-numbers. Accessed September 3, 2021.
- 3. Bagatin E, Freitas THP, Rivitti-Machado MC, et al. Adult female acne: a guide to clinical practice [published correction appears in An Bras Dermatol. 2019 Mar-Apr;94(2):255. Machado MCR [corrected to Rivitti-Machado MC]]. An Bras Dermatol. 2019;94(1):62-75. doi:10.1590/abd1806-4841.20198203
- 4. Rosacea. National Institute of Arthritis and Musculoskeletal and Skin Diseases. https://www.niams.nih.gov/health-topics/rosacea#tab-risk
- 5. Patel D. Best Rosacea Diet Tips To Improve Your Gut Health. Zen Nutrients. https://zennutrients.com/blogs/news/best-rosacea-diet-tips-follow-these-tips? pos=1& psq=rosacea& ss=e& v=1.0. Accessed September 2021.
- 6. What your doctor may not tell you about rosacea + how to fix it. HAPPY GUT®. https://www.happygutlife.com/what-your-doctor-may-not-tell-you-about-rosacea-and-how-to-fix-it/. Published March 24, 2021. Accessed September 2021.
- 7. Sittampalam A. Rosacea and psoriasis of the face: Looking beyond the visible. https://congress-galderma.com/eadv/2020/assets/documents/Rosacea%20and%20psoriasis%20of%20the%20face.pdf . Accessed September 2021.
- 8. Huynh TT. Burden of Disease: The Psychosocial Impact of Rosacea on a Patient's Quality of Life. Am Health Drug Benefits. 2013;6(6):348-354.
- 9. Singam V, Rastogi S, Patel KR, Lee HH, Silverberg JI. The mental health burden in acne vulgaris and rosacea: an analysis of the US National Inpatient Sample. Clin Exp Dermatol. 2019;44(7):766-772. doi:10.1111/ced.13919
- 10. Acne by the numbers. J Am Acad Dermatol . 2017.
- 11. Rosacea by the numbers. J Am Acad Dermatol . 2017.
- 12. Gunnars K. Does all disease begin in your gut? the surprising truth. Healthline. https://www.healthline.com/nutrition/does-all-disease-begin-in-the-gut . Published February 27, 2019. Accessed September 2021.
- 13. Dix M. 7 signs of an unhealthy gut and 7 ways to improve gut health. Healthline. https://www.healthline.com/health/gut-health#signs-and-symptoms . Published August 25, 2020. Accessed September 2021.
- 14. The gut-skin axis. The Secret Life Of Skin.

 https://thesecretlifeofskin.com/2019/09/23/gut-skin-axis/. Published August 21, 2020.

 Accessed September 2021.

- 15. Mashaghi A, Marmalidou A, Tehrani M, Grace PM, Pothoulakis C, Dana R. Neuropeptide substance P and the immune response. Cell Mol Life Sci. 2016;73(22):4249-4264. doi:10.1007/s00018-016-2293-z
- 16. Gravina A, Federico A, Ruocco E, et al. Helicobacter pylori infection but not small intestinal bacterial overgrowth may play a pathogenic role in rosacea. United European Gastroenterol J. 2015;3(1):17-24. doi:10.1177/2050640614559262
- 17. Salem I, Ramser A, Isham N, Ghannoum MA. The Gut Microbiome as a Major Regulator of the Gut-Skin Axis. Front Microbiol. 2018;9:1459. Published 2018 Jul 10. doi:10.3389/fmicb.2018.01459
- 18. Weiss E, Katta R. Diet and rosacea: the role of dietary change in the management of rosacea. Dermatol Pract Concept. 2017;7(4):31-37. Published 2017 Oct 31. doi:10.5826/dpc.0704a08
- 19. Bowe WP, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis back to the future?. Gut Pathog. 2011;3(1):1. Published 2011 Jan 31. doi:10.1186/1757-4749-3-1
- 20. Baldwin H. Oral Antibiotic Treatment Options for Acne Vulgaris. J Clin Aesthet Dermatol. 2020;13(9):26-32.
- 21. Rosacea. Cedars. https://www.cedars-sinai.org/health-library/diseases-and-conditions/r/rosacea.html. Accessed September 2021.
- 22. Short-term increase in fiber alters gut microbiome. Medical News Today. https://www.medicalnewstoday.com/articles/short-term-increase-in-fiber-alters-gut-microbiome#Microbiome-composition. Accessed September 2021.
- 23. Desai MS, Seekatz AM, Koropatkin NM, et al. A Dietary Fiber-Deprived Gut Microbiota Degrades the Colonic Mucus Barrier and Enhances Pathogen Susceptibility. Cell. 2016;167(5):1339-1353.e21. doi:10.1016/j.cell.2016.10.043
- 24. Vitamin A and skin health. Linus Pauling Institute.

 https://lpi.oregonstate.edu/mic/health-disease/skin-health/vitamin-A . Published January 1, 2021. Accessed September 2021.
- 25. Huang Z, Liu Y, Qi G, Brand D, Zheng SG. Role of Vitamin A in the Immune System. J Clin Med. 2018;7(9):258. Published 2018 Sep 6. doi:10.3390/jcm7090258
- 26. Illuminating the Role of Vitamin A in Skin Innate Immunity and the Skin Microbiome: A Narrative Review Fritzlaine C. Roche 1,2 and Tamia A. Harris-Tryon 1,3,
- 27. Raman R. 7 impressive benefits of vitamin C supplements. Healthline.

 https://www.healthline.com/nutrition/vitamin-c-benefits#6.-Boosts-immunity-.

 Published February 19, 2020. Accessed September 2021.
- 28. Is vitamin C the perfect fix for rosacea symptoms? Dermatology on Bloor. https://dermonbloor.com/vitamin-c-perfect-fix-rosacea-symptoms/. Published March 29, 2019. Accessed September 2021.
- 29. Pullar JM, Carr AC, Vissers MCM. The Roles of Vitamin C in Skin Health. Nutrients. 2017;9(8):866. Published 2017 Aug 12. doi:10.3390/nu9080866
- 30. Wang K, Jiang H, Li W, Qiang M, Dong T, Li H. Role of Vitamin C in Skin Diseases. Front Physiol. 2018;9:819. Published 2018 Jul 4. doi:10.3389/fphys.2018.00819

- 31. Mehmet S. This is why midlife women should be adding vitamin K to their diet and skincare routine. Woman and Home Magazine.

 https://www.womanandhome.com/us/beauty/benefits-vitamin-k-diet-skincare-328176/. Published July 25, 2019. Accessed September 2021.
- 32. Wnek D. Everything You Need to Know About Niacinamide, According to Skincare Pros. Good Housekeeping. https://www.goodhousekeeping.com/beauty/anti-aging/a32191645/what-is-niacinamide-for-skin/. Published March 13, 2021. Accessed September 2021.
- 33. Emer J, Waldorf H, Berson, D. Botanicals and Anti-Inflammatories: Natural Ingredients for Rosacea. Semin Cutan Med Surg. 30:148-155.
- 34. Sieradzan E. Zinc for acne and rosacea and any skin problem. Essence of Beauty. https://essenceofbeauty.ca/zinc-for-acne-and-rosacea-and-any-skin-problem/. Published February 27, 2020. Accessed September 2021.
- 35. Acne Rosacea (Holistic). PeaceHealth. https://www.peacehealth.org/medical-topics/id/hn-1001000. Accessed September 2021.
- 36. Borkow G. Using Copper to Improve the Well-Being of the Skin. Curr Chem Biol. 2014;8(2):89-102. doi:10.2174/2212796809666150227223857
- 37. Abdulsahib AA, Al-Aly RA. Evaluation of Manganese (Mn+2) in Serum of Acne Patients. journal of kerbala university. 2009;7(4):140-143.
- 38. Goodson A. 10 evidence-based benefits of manganese. Healthline.

 https://www.healthline.com/nutrition/manganese-benefits. Published August 31, 2018.

 Accessed September 2021.
- 39. Vaughn AR, Branum A, Sivamani RK. Effects of Turmeric (Curcuma longa) on Skin Health: A Systematic Review of the Clinical Evidence. Phytother Res. 2016;30(8):1243-1264. doi:10.1002/ptr.5640
- 40. Vaughn AR, Pourang A, Clark AK, Burney W, Sivamani RK. Dietary supplementation with turmeric polyherbal formulation decreases facial redness: a randomized double-blind controlled pilot study. J Integr Med. 2019;17(1):20-23. doi:10.1016/j.joim.2018.11.004
- 41. Di Meo F, Margarucci S, Galderisi U, Crispi S, Peluso G. Curcumin, Gut Microbiota, and Neuroprotection. Nutrients. 2019;11(10):2426. Published 2019 Oct 11. doi:10.3390/nu11102426
- 42. Kwan N, Mukherjee T, Lawler M, et al. The skin benefits of Apple Cider Vinegar (ACV): Everyday health. EverydayHealth. https://www.everydayhealth.com/skin-beauty/apple-cider-vinegar-good-your-skin/. Accessed September 2021.
- 43. Suh DC, Kim Y, Kim H, et al. Enhanced In Vitro Skin Deposition Properties of Retinyl Palmitate through Its Stabilization by Pectin. Biomol Ther (Seoul). 2014;22(1):73-77. doi:10.4062/biomolther.2013.094
- 44. Barrett H. 9 benefits of apple cider vinegar with 'the mother': <a href="https://www.hollandandbarrett.com/the-health-hub/vitamins-and-hub/vitamins-hub/vi

- <u>supplements/supplements/apple-cider-vinegar-supps/5-benefits-of-apple-cider-vinegar-with-the-mother/</u>. Published September 22, 2021. Accessed September 2021.
- 45. Ali SM, Yosipovitch G. Skin pH: from basic science to basic skin care. Acta Derm Venereol. 2013;93(3):261-267. doi:10.2340/00015555-1531
- 46. Nikkhah Bodagh M, Maleki I, Hekmatdoost A. Ginger in gastrointestinal disorders: A systematic review of clinical trials. Food Sci Nutr. 2018;7(1):96-108. Published 2018 Nov 5. doi:10.1002/fsn3.807
- 47. Hodges RE, Minich DM. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. J Nutr Metab. 2015;2015:760689. doi:10.1155/2015/760689
- 48. Yanaka A, Fahey JW, Fukumoto A, et al. Dietary sulforaphane-rich broccoli sprouts reduce colonization and attenuate gastritis in Helicobacter pylori-infected mice and humans. Cancer Prev Res (Phila). 2009;2(4):353-360. doi:10.1158/1940-6207.CAPR-08-0192
- 49. Zuzka Light Broccoli Sprouts A Rising Superfood Comments.

 https://zuzkalight.com/nutrition/broccoli-sprouts-a-rising-superfood/. Accessed September 2021.
- 50. Bowe, W.P., Logan, A.C. Acne vulgaris, probiotics and the gut-brain-skin axis back to the future? Gut Pathog 3, 1 (2011). https://doi.org/10.1186/1757-4749-3-1
- 51. Salem I, Ramser A, Isham N, Ghannoum MA. The Gut Microbiome as a Major Regulator of the Gut-Skin Axis. Front Microbiol. 2018;9:1459. Published 2018 Jul 10. doi:10.3389/fmicb.2018.01459
- 52. Benyacoub J, Bosco N, Blanchard C, Demont A, Philippe D, Castiel-Higounenc I, et al. Immune modulation property of lactobacillus paracasei NCC2461 (ST11) strain and impact on skin defences. Beneficial Microbes. 2014;5(2):129-136
- 53. Lee WJ, Jung HD, Lee HJ, Kim BS, Lee SJ, Kim DW. Influence of substance-P on cultured sebocytes. Archives of Dermatological Research. 2008;300(6):311-316
- 54. Ferzli G, Patel M, Phrsai N, Brody N. Reduction of facial redness with resveratrol added to topical product containing green tea polyphenols and caffeine. J Drugs Dermatol. 2013;12(7):770-774.
- 55. Kumar VS, Navaratnam V. Neem (Azadirachta indica): prehistory to contemporary medicinal uses to humankind. Asian Pac J Trop Biomed. 2013;3(7):505-514. doi:10.1016/S2221-1691(13)60105-7
- 56. Rasheed A, Shama SN, Joy JM, Reddy BS, Roja C. Formulation and evaluation of herbal anti-acne moisturizer. Pak J Pharm Sci. 2012;25:867–70.
- 57. Ragusa I, Nardone GN, Zanatta S, Bertin W, Amadio E. Spirulina for Skin Care: A Bright Blue Future. Cosmetics. 2021; 8(1):7. https://doi.org/10.3390/cosmetics8010007
- 58. Sibi G. Inhibition of lipase and inflammatory mediators by Chlorella lipid extracts for antiacne treatment. J Adv Pharm Technol Res. 2015;6(1):7-12. doi:10.4103/2231-4040.150364

- 59. Piazza S, Fumagalli M, Khalilpour S, et al. A Review of the Potential Benefits of Plants Producing Berries in Skin Disorders. Antioxidants (Basel). 2020;9(6):542. Published 2020 Jun 20. doi:10.3390/antiox9060542
- 60. Watson RR, Schönlau F. Nutraceutical and antioxidant effects of a delphinidin-rich maqui berry extract Delphinol®: a review. Minerva Cardioangiol. 2015;63(2 Suppl 1):1-12.
- 61. Overall J, Bonney SA, Wilson M, et al. Metabolic Effects of Berries with Structurally Diverse Anthocyanins. Int J Mol Sci. 2017;18(2):422. Published 2017 Feb 15. doi:10.3390/ijms18020422
- 62. Faria A, Fernandes I, Norberto S, Mateus N, Calhau C. Interplay between anthocyanins and gut microbiota. J Agric Food Chem. 2014;62(29):6898-6902. doi:10.1021/jf501808a
- 63. Galderma Global Study reveals true burden of rosacea and encourages healthcare professionals to look 'beyond the visible'. Galderma.

 https://www.galderma.com/news/galderma-global-study-reveals-true-burden-rosacea-and-encourages-healthcare-professionals-look . Published June 1, 2018. Accessed September 2021.