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REVIEW ARTICLE

The role of nutrition in inflammatory pilosebaceous disorders: Implication of the skin-gut axis

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ABSTRACT

Nutrition plays a critical role in the manifestation and management of inflammatory pilosebaceous disorders. There is rich potential for insight into the impact of dietary effects on the pathophysiology of inflammatory pilosebaceous disorders including acne vulgaris, hidradenitis suppurativa, rosacea, and the closely related seborrhoeic dermatitis. Acne vulgaris and hidradenitis suppurativa are thought to have similar diet-modulating pathogenic pathways. Western diet influences Acne vulgaris and hidradenitis suppurativa by increasing insulin and modulating FOX01/mTOR, resulting in over-expression of cytokeratins, hyperproliferation of keratinocytes, and hypercornification of the follicular wall. Key receptors in rosacea are alternatively activated by UV radiation, hot beverages, spicy foods, vanilla, cinnamon, caffeine, alcohol, cold temperatures, and niacin- and formalin-containing foods, to increase oedema and flushing, resulting in erythema, telangiectasia, and warmth, characteristic features of the condition. Seborrhoeic dermatitis, while not a follicular disorder, is closely related, and can be modulated by dietary influences, such as biotin and probiotics. This overview summarizes the role that nutrition plays on these disorders, and identifies dietary modifications as potential adjunctive therapies.

Key words: acne, hidradenitis suppurativa, inflammation, nutrition, pilosebaceous disorder, rosacea, seborrhoeic dermatitis.

WHAT THIS RESEARCH ADDS

- The 'skin-gut axis' concept proposes an inherent link between the gastrointestinal microbiome and the skin, which, when aberrantly modulated, can result in inflammatory pilosebaceous disorders, such as acne vulgaris, hidradenitis suppurativa, rosacea, and seborrhoeic dermatitis.
- Dependent on the pathways that provoke such disease states, modulation of specific diets may help to prevent or reverse the incidence and severity of the disease.

INTRODUCTION

There is currently a wealth of emerging evidence supporting the influence of nutrition on dermatologic disorders. Much of the progress comes from investigating the role of nutritional regulation in oxidation-reduction reactions, inflammation, and hormonal changes,[1,2] and the suggested impact from alteration to the gut microbiome and the skin-gut axis.[3,4]

The human microbiome describes an ecosystem of microorganisms that has been referred to in sum as an 'invisible organ', suggesting its critical contributions to physiologic processes such as digestion and immunity.[3] The 'skin-gut axis' concept historically proposed a theory linking alterations of the gastrointestinal (GI) microbiome to increased intestinal permeability, systemic inflammation, and the subsequent development of acne vulgaris. More recent studies of skin-gut connection suggest that the contribution of gut microbiome to regulation of systemic inflammation also influences oxidative stress, glycaemic control, and tissue lipid content.[4] Due to the breadth of individual variability in the microbiome and the complexity of the skin-gut axis, it is not surprising that these systems are suspected to contribute to a wide variety of cutaneous disorders.

In addition to acne vulgaris interesting parallels are observed in related dermatoses associated with pilosebaceous unit disruption, such as hidradenitis suppurativa,

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rosacea, and seborrhoeic dermatitis. This overview aims to provide a summary of the literature depicting the effect that nutrition has on follicular disorders and to address the dietary management of these disorders.

Acne vulgaris

Acne vulgaris is caused by a constellation of events including follicular hyperkeratinization, increased sebum production, and *Propionbacterium acnes* overgrowth, with subsequent follicular rupture and inflammation.[5,6] Acne generally starts during puberty, coinciding with sex hormone surge, and usually resolves by the third decade of life. However, acne may present or persist into adulthood, most commonly in women with hormonal dysregulation.[7]

Classic theories about the impact of Western Diet on acne continue to gain credibility over time, and parallel more recent notions about effects of alteration to the gut microbiome and the skin-gut axis. A Western diet is one that includes increased consumption of foods with high glycaemic index, red meat, dairy, and egg protein.[8] This diet increases sebogenesis, providing an optimal environment for *P. acnes* and other microorganisms to thrive, resulting in acne formation.[4]

Western diet and optimal cutaneous conditions during puberty converge to enhance the actions of insulin and insulin-like growth factor-1 (IGF-1). Such elevated growth factors downregulate FOX01, a nuclear transcription factor that typically suppresses activation of the androgen receptor, transcription of key cell proliferation genes and inflammatory cytokines, and lipid biosynthesis. FOX01 inhibition results in pilosebaceous unit androgen receptor stimulation, which causes the sterol regulatory element-binding protein to modulate gene transcription, increasing sebaceous function and keratinocyte proliferation[9] (Fig. 1).

The standard American diet is one that is high in linoleic acid, mostly found in vegetable oils, nuts, seeds, and animal products.[10] Similar to high-glycemic index foods,

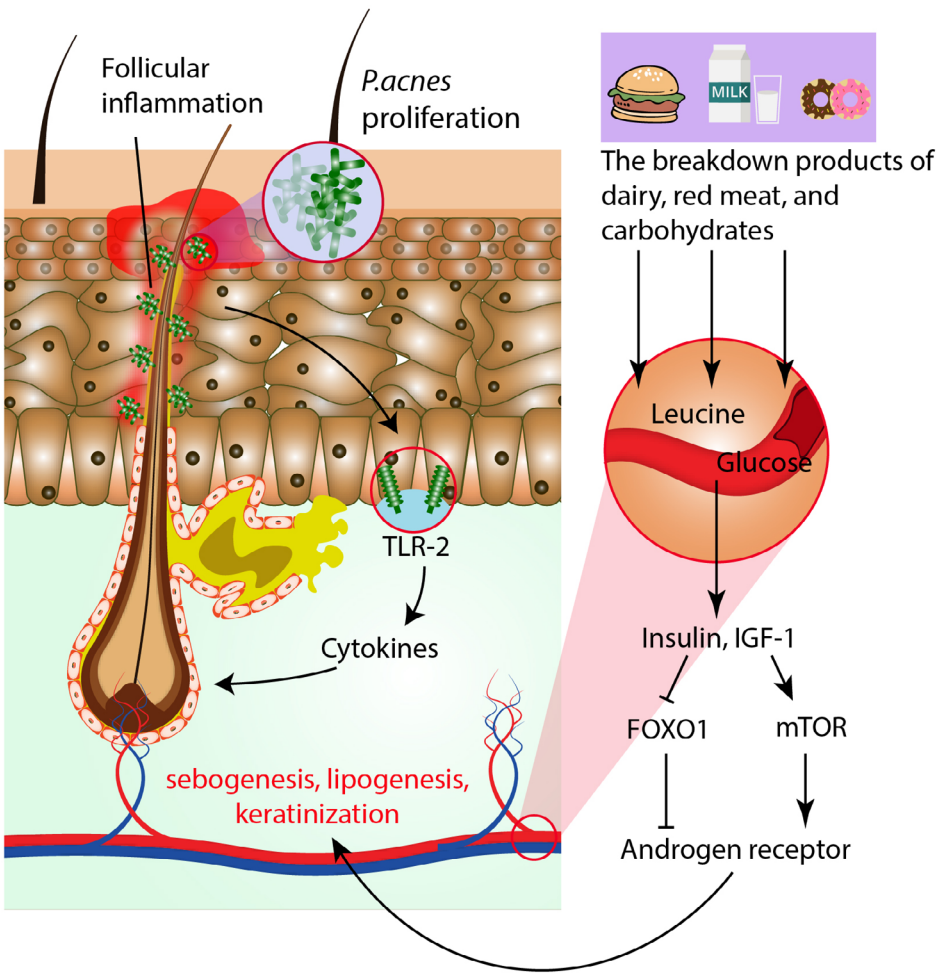

Figure 1 The breakdown products of dairy, red meat, and carbohydrates enhance insulin and IGF-1 production, which attenuates FOX01 signal transduction while increasing mTOR activation. Both pathways increase keratinocyte desquamation and sebaceous lipogenesis, driving the pathogenesis of both acne vulgaris and hidradenitis suppurativa. Additionally, proliferation of *Propionbacterium acnes* in acne induces TLR-2 (and TLR-4) to increase follicular inflammation.

linoleic acid has a role in acnegenesis. Linoleic acid is a ligand of nuclear peroxisome proliferator-activated receptors-gamma, which potently prompts sebocyte lipogenesis and follicular keratinocytic differentiation[9] (Fig. 1).

Additionally, pubertal and dietary growth factors activate basal keratinocytes to release interleukin (IL)-1 to stimulate the over-expression of cytokeratins, resulting in keratinocyte hyperproliferation and follicular wall hypercornification. This is the precursor event to comedone formation. Proliferation of *P. acnes* induces cytokine (IL-6, IL8, and IL-12) production via Toll-like receptor (TLR)-2, resulting in follicular inflammation and lipogenesis[9] (Fig. 1).

To date, the most compelling evidence involving diet and skin is the link between acne and carbohydrates. In a cohort study involving 50 patients with mild to severe acne and 36 healthy controls, 12-h fasting blood samples of acne patients had significantly higher mean glycaemic index (47.42 *vs* 44.52, $P = 0.022$) and glycaemic load (79.04 *vs* 63.36, $P = 0.001$) compared to controls. Serum adiponectin inversely correlated with glycaemic index ($r = -0.212$, $P = 0.049$), and was significantly lower in the acne group (9.93 *vs* 11.28 ng/mL, $P = 0.015$).[11] In a case–control study involving 44 acne patients and 44 controls, acne patients had significantly higher dietary glycaemic load compared to controls (175 *vs* 122, $P < 0.001$), with higher milk and ice cream consumption.[12]

Secondary to foods high in glycaemic index, dairy and red meat also play a role in acne vulgaris. Dairy and red meat contain high levels of the branched chain amino acids, such as leucine.[13] Leucine stimulates mammalian target of rapamycin complex 1 (mTORC1), a major transcription factor that controls sterol-regulatory element-binding protein, to augment lipogenesis within sebaceous glands, causing acne. In addition to stimulating increased androgen hormone secretion, mTORC converts leucine into components necessary for sebaceous lipid synthesis[14] (Fig. 1).

The modern controversy on the effect dairy has on acne questions which dairy products are most egregious.[15,16] In 2017, a longitudinal questionnaire-based study of Norwegian adolescents demonstrated that high intake of full-fat dairy products (≥2 glasses of milk per day) correlated with acne incidence in both males (OR 4.81, 1.59–14.56) and females (OR 1.80, 1.02–3.16).[17] Other studies investigating adolescents show conflicting evidence, suggesting that consumption of low-fat or skim milk, but not full-fat milk, contained high bioactivity that was positively associated with acne.[15,18,19] This is due to the whey content in processed milk that is proposed to be the most acnegenic. Although whey, a milk protein, is found in lower fractionated quantities in 1% milk when compared to whole milk or 2% milk,[20] whey protein is often added to skim/reduced fat milk to match the caloric content.

In addition to its presence in milk, whey is a popular nutritional supplement among athletes and body builders. In a case series of five healthy adult men who had been consuming whey protein 3–7 times per week to increase muscle bulk, moderate to severe facial and truncal acne developed within 5.6 ± 1.8 months. One of the five patients who agreed to discontinue ingesting whey protein concentrates had complete clearance of acne lesions within 6 weeks, without additional treatment.[21] In a case series of five healthy adolescent men ingesting whey protein daily, eruptions of cystic acne, inflammatory papules, pustules, and closed comedones occurred within 2 weeks to 1 month of ingestion. Four of the patients' acne improved with discontinuation of whey supplement, while one patient's acne cleared following discontinuation of whey in combination with isotretinoin.[22] Although the aforementioned studies include small cohorts, they support the negative role that milk and whey protein have on the mTOR pathway and acne.

Alternate theories expound on the influence of gut microbiota alteration on glycemic control, oxidative stress, and tissue lipid content. The literature estimates that 40% of patients with acne have concurrent hypochlorydia, and this may encourage migration of bacteria from the colon toward the small intestine, causing alterations in intestinal microflora, and development of small intestinal bacterial overgrowth (SIBO). Small intestinal bacterial overgrowth is defined as the overabundance of excessive colonic bacteria within the small intestine. Small intestinal bacterial overgrowth patients have a compromised ability to absorb proteins, fats, carbohydrates, B vitamins, and other micronutrients, and this environment encourages bacterial overgrowth, causing direct injury to the intestinal epithelial lining, bacterial migration, and subsequent systemic inflammation,[23] that may have cutaneous manifestations. The fine-tuned balance of these physiological systems are all players in the pathogenesis of acne and are disrupted by Western Diet, thus compromising the pivotal regulatory functions of the gut microbiome.[4,23] The evidences on the role prebiotics, probiotics, and others, have on the development of acne are well described, but are out of the scope of this review.[4,23]

Hidradenitis suppurativa

Similar to acne vulgaris, high glycaemic load diets and dairy intake have been identified as contributors in the pathogenesis of hidradenitis suppurativa (Fig. 1). Hidradenitis suppurativa is a chronic follicular disease characterized by occlusion, inflammation, and scarring of the folliculo-pilo-sebaceous unit in the axillae, groin, perianal, perineal, and inframammary skin regions.[24]

Hidradenitis suppurativa usually presents between puberty and 40 years old, and is more often seen in women, although men typically have more severe disease.[24] In addition, hidradenitis suppurativa is frequently associated with a variety of comorbidities such as metabolic syndrome and inflammatory bowel diseases (IBD), and is worsened by nicotine use. As a result of hormone dysregulation and nicotine stimulation, increased ductal keratinocyte proliferation from the follicular epithelium cause follicular hyperkeratosis and plugging, resulting in follicular occlusion.[24] Leakage of microscopic antigens stimulates the adaptive and innate immune systems to release pro-inflammatory mediators.[25]

Evidence of an association between hidradenitis suppurativa and metabolic syndrome suggests the negative impact that Western Diet has on the condition, whereas an association with IBD suggests that these patients may have disrupted gut microbial and immune milieu. Taken together, a link between hidradenitis suppurativa and gut-skin axis disruption is undeniable. A 2016 meta-analysis suggests that 12.8% of hidradenitis suppurativa patients have comorbid IBD (95% CI: 11.7–13.9%),[26] which is four times greater than the general northern European population (0.41–0.74%).[27] Eppinga and colleagues[28] reported *Escherichia coli* overgrowth and *Faecalibacterium prausnitzii* depletion (7.46 log10copies/g, $P = 0.001$) in patients with IBD and concomitant hidradenitis suppurativa, compared to healthy controls, while no significant change in the presence of these bacterium was observed in hidradenitis suppurativa alone (*F. prausnitzii*: 8.50 log10copies/g, $P = 0.10$), challenging the alternative theory that the concomitance of hidradenitis suppurativa and IBD was due to a concerted alteration to the gut microbiota.

In a pilot study by Brocard and colleagues,[29] involving 22 patients with recalcitrant Hurley Stage I or II (failed prior treatment with antibiotics, isotretinoin, surgery, or anti-androgens), zinc gluconate monotherapy (90 mg of zinc gluconate daily for 4 months) resulted in complete and partial remission in 36% and 63% of the cohort, respectively. The authors conducted a similar study to examine changes in lesional innate immunity markers in 12 patients with Hurley stage I or II who were treated with zinc gluconate (90 mg/day of zinc gluconate for 3 months). The treatment significantly decreased ($P < 0.001$) lesional and nonlesional skin expression of cutaneous markers involved in innate immunity (TLR 2, 3, 4, 7, and 9; ICAM-1; IL-6; TNF; α-MSH; TGF-β; β-defensin-2 and 4; IGF-1). Down-regulation of these markers was significantly stronger in lesional skin compared to nonlesional skin, except for TNF.[30] Hessam and colleagues[31] were interested in the impact that the combination of 90 mg/day oral zinc gluconate and 2% topical triclosan twice per day for 3 months had on 66 patients with Hurley stage I and II HS. Improvement in the modified hidradenitis suppurativa score (32.5–25, $P < 0.0001$) and the Dermatology Quality of Life Index ($P = 0.0386$) was significant, with a noticeable decrease in the number of inflammatory nodules (7.3 ± 5.1 to 5 ± 4.4, $P < 0.001$), new boils or flare-ups (3–1, $P = 0.0009$), and erythema scores (2–1, $P = 0.0001$).

In a prospective study, 12 hidradenitis suppurativa patients with serology-proven allergy to *Saccharomyces cerevisiae* (brewer's yeast) and purulent axillary and perineal fistulas who underwent surgical excision or localized treatment, brewer's yeast elimination diet for 12 months resulted in immediate stabilization of clinical symptoms and subsequent increase in their reported quality of life, including return of the patients' daily and sexual activities. Hidradenitis suppurativa recurrence occurred immediately following accidental or voluntary consumption of foods containing wheat or brewer's yeast, such as beer, wine, bread and other bakery products. Although no control group was prospectively studied to compare the response to dietary exclusion, there appears to be a strong association of the inflammatory potential of this yeast.[32]

Diets high in dairy and/or glycaemic index, such as those containing casein, whey, bovine placenta and mammary gland components, as well as the breakdown products of sugar and flour, have been shown to cause sebaceous gland plugging and subsequent folliculo-pilosebaceous unit rupture.[33] In addition, leucine, the same amino acid implicated in worsening of acne and found in high concentration in red meat and dairy products, stimulates the insulin/IGF-1 pathways via activation of the mTORC pathway[13] (Fig. 1). Monfrecola and colleagues[34] identified upregulation of mTOR in lesional and nonlesional hidradenitis suppurativa skin, and direct correlation with lesion severity.

Rosacea

Rosacea is broadly associated with erythema and papule or pustule formation with transient or non-transient erythema, papules and pustules, and/or telangiectasia. Rosacea differs from the aforementioned follicular disorders in that it lacks pilosebaceous unit plugging and comedone formation. Barrier dysfunction characteristic of rosacea skin is associated with altered sebaceous lipid profile.[35] However, there are skin-gut parallels that can be made between rosacea and acne or hidradenitis suppurativa. When compared to the general public, patients with rosacea have a greater hazards ratio of coeliac disease (1.46), Crohn disease (1.45), ulcerative colitis (1.19), and irritable bowel syndrome (1.34). Additionally, small intestinal bacterial overgrowth is 2–20 times greater in rosacea patients than the general public.[36]

To understand the role small intestinal bacterial overgrowth has in rosacea, Parodi and colleagues[37] randomized 52 rosacea patients with small intestinal bacterial overgrowth and three healthy controls with small intestinal bacterial overgrowth to receive the standard treatment antibiotic, rifaximin (1200 mg/day for 10 days), or placebo. Rifaximin is non-absorbable, and thus, can be used to control overgrowth because it exerts a localized action on the intestinal bacteria. Following its use, cutaneous lesions cleared in 20/28 patients, and greatly improved in 6/28 patients, while patients in the placebo group experienced no change (18/20) or worsened lesions (2/20) ($P < 0.001$). When the placebo patients were switched to receive the treatment, small intestinal bacterial overgrowth was eradicated in 17/20 cases, with complete resolution in 15 patients.

Gravina and colleagues[38] performed a prospective study to assess the prevalence of *Helicobacter pylori* and/or small intestinal bacterial overgrowth in 90 patients with rosacea and 90 controls, and whether treatment led to resolution. In their cohort, *H. pylori* was present in 49% of rosacea patients and 27% of controls, while small intestinal bacterial overgrowth prevalence was comparable between the two groups (10% *vs* 7.8%, respectively, $P = 0.6$). Ten weeks following treatment with clarithromycin for *H. pylori* or rifaximin for small intestinal bacterial overgrowth,

there was substantial reduction in rosacea lesions for both groups (97% and 86%, respectively). Emerging evidence suggests that gut dysbiosis is closely associated with rosacea.

Nam and colleagues reported that Korean women with rosacea had significantly increased gut concentrations of *Acidaminococcus* ($P < 0.05$) and decreased concentration of *Peptococcaceae* ($P < 0.05$), compared to healthy controls. The increased intestinal *Acidaminococcus* is intriguing, as this bacterium consumes intestinal glutamate—an amino acid that plays a critical role in barrier function, amino acid metabolism, and nitrogen balance. *Peptococcaceae* is involved in butyrate synthesis, which provides energy necessary for maintenance and preservation of gut epithelium.[39] Whether or not diet can influence the dysbiosis phenomenon has not been elucidated. However, it is recognized that changes in the gut microbiome result in cutaneous manifestation.

While the evidence on altered gut microbiome's effect on rosacea is debatable, the characteristic neurogenic inflammation is currently understood to be the predominant trigger. Transient receptor potential ankyrin receptor 1 (TRPA1) is located in perivascular sensory neurons in the dermis, and is activated by cold temperatures and formalin-containing foods (i.e., crustacean, wet noodle, tofu, dried shitake mushroom). Transient receptor potential vanilloid 1 (TRVP1), also known as the capsaicin receptor, is located on sensory nerves and keratinocytes, and is activated by UV radiation, hot beverages, spicy foods, vanilla, cinnamon, caffeine, and alcohol.[40] When activated, these receptors release substance P and calcitonin gene-related peptide. These mediators induce an exuberant, yet transient, inflammatory response: while calcitonin gene-related peptide dilates arterioles, Substance P particularly affects post-capillary venules, resulting in flushing and edema[41] (Fig. 2).

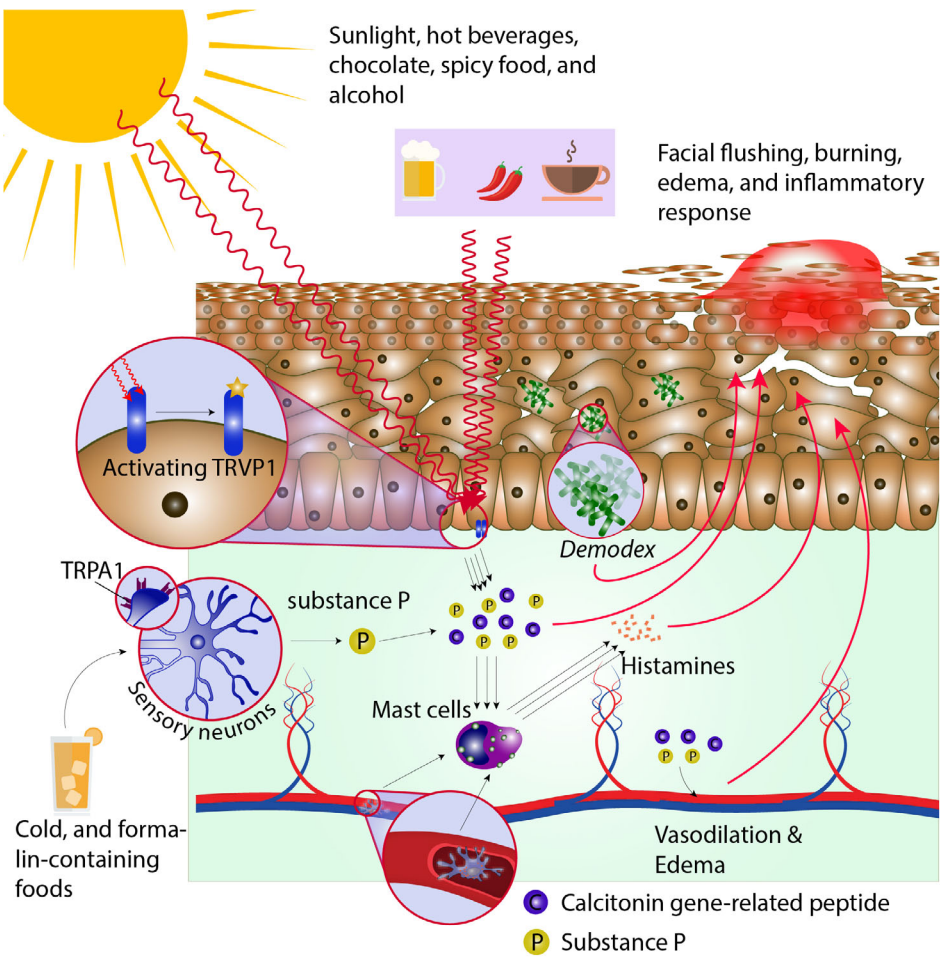

Figure 2 Sunlight, hot beverages, chocolate, spicy food, and alcohol, among others activate transient receptor potential vanilloid 1 (TRVP1) on keratinocytes, while cold, and formalin-containing foods (i.e., tofu, wet noodles) activate transient receptor potential ankyrin receptor 1 (TRPA1) on sensory neurons, stimulating the release of substance P and calcitonin gene-related peptide. These two mediators dilate the arterioles (calcitonin gene-related peptide) and post-capillary venules (Substance P). The resulting facial flushing, burning, edema, and inflammatory response associated with rosacea.

Niacin is another well-known flush trigger in rosacea. Niacin activates niacin receptor G protein-coupled receptor 109A in dermal Langerhans cells to release prostaglandins around the capillaries to promote erythema, skin warmth, and occasional stinging and itching.[42] Thus, rosacea patients should be counseled on strategic avoidance of niacin-containing foods, such as turkey, peanut, tuna, liver, chicken breast.

In addition to the vasodilatory effects for the aforementioned dietary triggers, *Demodex folliculorum* modulate TLR signaling to induce production of IL-7, IL-12, TNF-α, and IL-1. These mediators in turn recruit Th1 or Th17 cells that signal for T cell-derived cytokines, such as IL-17 and IL-22. Along with UV radiation, these cytokines activate keratinocytes to produce CXCL1 and CXCL8, chemokines that recruit neutrophils to the site of inflammation. IL-17 also promotes angiogenesis via vascular endothelial growth factor and other angiogenic mediators (CCL2, CXCL1, or CXCL8) to cause telangiectasia that are characteristic of rosacea.[43]

Acetaldehyde and acetone are major breakdown products of alcohol. Following alcohol consumption, these metabolites cause histamine release, which is believed to instigate dermal vasomotor instability to cause facial flushing edema. However, alcohol does have significant opiate-like effects, and thus the discovery that flushing following alcohol is also mediated by endogenous opiate peptides is not completely alarming. Bernstein and Soltani demonstrated that endogenous opioid peptides (encephalin and endorphin) are key molecular triggers of the vascular reactivity that results in flushing after alcohol consumption. In their study, subcutaneous naloxone hydrochloride (0.8 mg in 2 mL saline) but not oral sustained release chlorpheniramine maleate (12 mg) prior to the imbibition of 360 mL of beer containing 6% ethanol, was effective in inhibiting facial flushing and increase in mean forehead skin temperature.[44]

Seborrhoeic dermatitis

Seborrheic dermatitis is a chronic inflammatory process of hairy regions due to *Malassezia* yeast overgrowth that affects 3–5% of the population, with a predilection in the immunocompromised population. It has a bimodal-age distribution that typically presents in children and middle-aged to elderly adults. Its eruption following increased sebaceous gland activity hints to a dietary relation that mimics the process in acne. Like acne, the literature reports few cases of increased glucose tolerance in the blood and skin of patients with seborrhoeic dermatitis. However, Dowlati and colleagues[45] reported no difference in insulin concentrations between a group of 20 seborrhoeic dermatitis patients and 20 healthy controls ($P = 0.13$). Thus, unlike acne and other hyperproliferative disorders, there is no association between hyperinsulinism and seborrhoeic dermatitis.

Table 1 Diets causing flare-ups of inflammatory pilosebaceous disorders and alternative recommendations

Disease	Dietary pathogenesis	Pro-inflammatory diet	Recommended diet
Acne vulgaris	Western diet increased insulin levels and downregulates FOX01, which increases androgen receptor activity and mTOR, resulting in over-expression of cytokeratins, hyperproliferation of keratinocytes, and hypercornification of the follicular wall	• Diets with high mean glycemic index[11–15] • High intake of dairy products and casein[15,17–19] • Whey protein[21,22] • Foods high in leucine (dairy and red meat)[15]	• Reduce foods with high mean glycemic index[11–15] • Reduce intake of dairy products and casein[15,17–19] • Discontinue use of whey protein[21,22] • Reduce foods high in leucine (dairy and red meat)[15]
Hidradenitis suppurativa	See above	• Diets with high mean glycemic index[24,33] • High intake of dairy products[24,33] • All bakery products (e.g., pizza, bread, cakes, etc.), vinegar, black tea, soy sauces, beer, wine, fermented cheese, mushrooms[32]	• Daily 90 mg zinc gluconate[29–31] • Vegetables and fresh fruit, cereals that do not contain yeast (e.g., rice or corn cakes made with puffed cereals), white meats, eggs, vegetables, green tea, coffee[32] • Discontinuation of diets with high *Saccharomyces cerevisiae* (beer, wine, bread, and other bakery products)[32]
Rosacea	TRPA1 (cold temperatures and formalin-containing foods) and TRVP1 (UV radiation, hot beverages, spicy foods, vanilla, cinnamon, caffeine, and alcohol) release substance P and calcitonin gene-related peptide to induce flushing and inflammation	• Hot beverages, spicy foods, caffeine, vanilla, cinnamon, niacin- (i.e., turkey, peanut, tuna, liver, chicken breast) and formalin-containing foods (i.e., crustacean, wet noodle, tofu, dried shitake mushroom), alcohol[50]	• Following rosacea-promoting diets, patients may use 0.8 mg SC naloxone hydrochloride to reduce the side effects[44]
Seborrhoeic dermatitis			• Biotin supplements (preliminary).[46] • Linoleic acid diet (preliminary).[48] • Kombucha tea ethyl acetate, 80 mg/mL (*in vivo* studies needed)[49]

Biotin is essential for glucose and fatty acid synthesis. Biotin deficiency is commonly implicated in hair and nail disorders, including seborrhoeic dermatitis. Humans cannot synthesize biotin and obtain it through diet and synthesis from normal microflora that reside in the large intestine. In a retrospective study by Trueb involving 541 female patients, 35% of the cohort had suboptimal (100–400 ng/L) or deficient (<100 ng/L) serum biotin levels, which resulted in a seborrhoeic-like dermatitis. None of the patients with optimal (>400 ng/L) serum biotin levels developed seborrhoeic dermatitis.[46] In contrast to these findings, in a double-blind placebo-controlled study of infants suffering from flexural seborrhoeic dermatitis, daily oral biotin supplementation (5 mg) for 2 weeks yielded no significance in clearance of flexural seborrhoeic dermatitis, with a mean illness duration of 1.3 months versus 1.4 months in biotin and placebo groups, respectively.[47] Although these studies investigated biotin levels in two distinct populations, this literary discrepancy may be enough to prompt the exploration of the role biotin plays in seborrhoeic dermatitis.

Linoleic acid, and its metabolic products gamma-linolenic acid and arachidonic acid, are crucial dietary components of fat that ensure maintenance of proper epidermal barrier. Additionally, linoleic acid is a substrate for inflammatory mediators, such as prostaglandins and leukotrienes.[48] As previously mentioned, linoleic acid is commonly found in vegetable oils, nuts, seeds, and animal products. However, in a cohort study investigating serum linoleic acid levels in 20 infants with seborrhoeic dermatitis, no associations could be made between infantile seborrhoeic dermatitis and essential linoleic acid deficiency.[47] In a later study involving 30 children with infantile seborrhoeic dermatitis, results demonstrated that those affected with seborrhoeic dermatitis had elevations in serum essential fatty acids ($P < 0.01$) and decreased linoleic acid ($P < 0.001$) compared to healthy controls, suggesting that alterations in fatty acids may play a role in the development of seborrhoeic dermatitis.[48] The incongruence between these studies warrants further research into the impact that fatty acids have on the development of seborrhoeic dermatitis.

Probiotics are live bacteria and yeast that interact beneficially with the digestive system. Kombucha, a fermented tea, contains probiotics that may have positive therapeutic implications for resolution of seborrhoeic dermatitis. Mahmoudi and colleagues examined the effect that kombucha tea ethyl acetate fraction had against *Malassezia* species isolated from 19 patients with seborrhoeic dermatitis. The group identified that kombucha tea ethyl acetate fraction has *in vitro* dose-dependent antifungal activity against *Malassezia* strains (10, 40, 80 mg/mL: 33%, 59%, 96% inhibition, respectively and 0%, 0%, and 79% fungicide activity, respectively). Topical ketoconazole, one of the first line treatments for seborrhoeic dermatitis, inhibits 100% of the *Malassezia* strains, but has only 57% fungicidal efficacy.[49] Thus, it appears that kombucha tea ethyl acetate fraction has more effective antifungal function than topical ketoconazole, and its ability to inhibit *Malassezia in vivo* should be explored.

CONCLUSION

While historically controversial, the plethora of evidence to date linking inflammatory follicular disorders and diet is undeniable. This overview provides a framework for the deleterious effects of the Western diet in both acne and hidradenitis suppurativa, recognizes the long-standing association between rosacea and spicy foods and alcohol, and acknowledges the novel evidence of micronutrient deficiencies in patients with seborrhoeic dermatitis. We now have mechanistic explanation for the century old tale of dietary triggers for the pilosebaceous conditions. While mTOR/FOX01 triggers acne and hidradenitis suppurativa following ingestion of meat, dairy, carbohydrates, and dairy, TRVP1/TRPA1/M109R activates flares of rosacea with UV radiation, hot beverages, spicy foods, formalin- and niacin-containing foods, vanilla, cinnamon, caffeine, and alcohol. Most poignantly, the current landscape sets the stage for fruitful exploration of the gut microbiomes' effect on skin health regulation, and an opportunity to elucidate more fully the skin-gut axis with specific implications for inflammatory dermatologic conditions.

With these promising directions in mind for future investigations, there is enough evidence to date to warrant consideration of some individualized recommendations for dietary interventions against common follicular disorders (Table 1). Most prudent would be the reduction in glycaemic load, red meat, and dairy intake for patient's managing acne vulgaris and hidradenitis suppurativa, with the added modification of eliminating brewer's yeast and zinc-based supplementation in cases of hidradenitis suppurativa. Future investigations are needed to further elucidate the mechanisms in which spicy foods and alcohol contributes to rosacea flare. In cases of seborrhoeic dermatitis, the consideration of the potential link between the gut microbiome and this inflammatory condition should be seriously considered and addressed, especially among populations where this is more common, such as people with HIV and those with neuropsychiatric disorders. Elucidating the possibility of dietary deficiency driving the gut-skin connection may yield further insight into whether social determinants that lead to compromised dietary intake could be predisposing some populations to cutaneous dysfunction.

Because the gut microbiome is a relatively young area of research, and most of the findings to date suggest a complex composition that differs between and within individuals, optimizing dietary management on an individual basis may be advised until more comprehensive recommendations are available. Studies are also needed on how dietary components may cause the 'leaky gut syndrome', in which intestinal dysbiosis leads to permeability of the intestinal layer. Such disruption causes inflammatory changes in distance organs, including the skin. There is a plethora of opportunity for future discovery of the interface of

nutrition and follicular disorders, with huge potential to positively impact patient care.

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