



# Dietary Intervention and Supplements in the Management of Psoriasis: Current Perspectives

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**Abstract:** Nutrition is a complex topic encompassing diet and a variety of supplements including vitamins, fish oil, herbal products, and probiotics. Patients with psoriasis display high interest in understanding the potential impact of nutritional modifications on their psoriasis. In this review, we examine the evidence for nutritional interventions in psoriasis and summarize important concepts. We found that certain diets, such as low-calorie diets for obese patients, gluten-free diets for patients with comorbid celiac disease, and the Mediterranean diet, may have benefits for psoriasis patients. Supplements in general do not show strong evidence of benefit, though more studies are required given the heterogeneity of these trials. Finally, the gut microbiome has drawn considerable interest in recent years, with specific probiotics showing promising results for psoriasis patients and warranting further exploration.

**Keywords:** nutrition, supplements, probiotics, inflammatory skin disease

## Introduction

Psoriasis (PsO) is an immune-mediated inflammatory skin condition affecting approximately 1–2% of the world population.<sup>1</sup> The influence of nutrition and diet on the presentation of disease has been a topic of great interest over many decades. Psoriasis has been linked to an increase in the risk of cardiovascular disease and other metabolic disorders. This encouraged research on the influence of diet on both the cutaneous symptoms and systemic sequelae of disease.<sup>2</sup> Recently, probiotics and their influence on the gut microbiome have also emerged as a potential adjuvant treatment with potential.

Many patients believe that diet impacts the severity of psoriasis presentation. A national survey revealed that psoriasis patients believe their psoriasis improves after removing alcohol, gluten, nightshade plants (tomatoes, eggplant, peppers, paprika, white potatoes), junk foods, and wheat products, among others. Adding fish oil/omega-3 fatty acids, vegetables, and oral vitamin D also improved self-reported skin outcomes.<sup>3</sup> Supplements, including vitamin B<sub>12</sub>, vitamin D, general multivitamins, and folic acid, are popular across studies in different nations.<sup>3–5</sup> Patients often take supplements not only because of the perceived benefits, but also because of inadequate treatment response to medication.<sup>6</sup> This review will summarize findings during the last decade regarding nutrition and psoriasis.

## Methods

We conducted a search of the literature in November 2021 by using PubMed, Embase, and the Cochrane database. Search terms for the Medline database included combinations of the “psoriasis” and “diet”, “nutrition”, or “food” or the related MESH terms (“psoriasis[MeSH Terms]” and “diet, food, and nutrition[MeSH Terms]” or “psoriasis/diet therapy[MeSH Terms]”). Due to an excellent review on nutrition and psoriasis performed by Ford et al<sup>7</sup> up to August 2017, we performed our initial search from 2017 to November 2021. However, to comprehensively cover all areas that may not have been addressed by Ford et al, we also searched the terms “psoriasis” with “microbiome” and related MESH terms (psoriasis[MeSH Terms] and “microbiome[MESH Terms]”, “microbiota[MESH Terms]”, “gastrointestinal diseases/

microbiology[MESH Terms]”, “gastrointestinal tract/microbiology[MESH Terms]”) with no limits to when the articles were published. Embase was searched using the terms “psoriasis AND nutrition” from 2017. A Cochrane database search was conducted with terms “psoriasis” and “diet”, “nutrition”, “food”, and “microbiome” with no limits to publication date. Manual searches of bibliographies from review papers were conducted to identify other relevant studies. Exclusion criteria included topical regimens. Studies included psoriasis patients given nutritional interventions, either through diet or supplementation, with outcome measures of psoriasis area severity index (PASI) scores or meta-analyses that included trials of this type. A total of 34 studies were included.

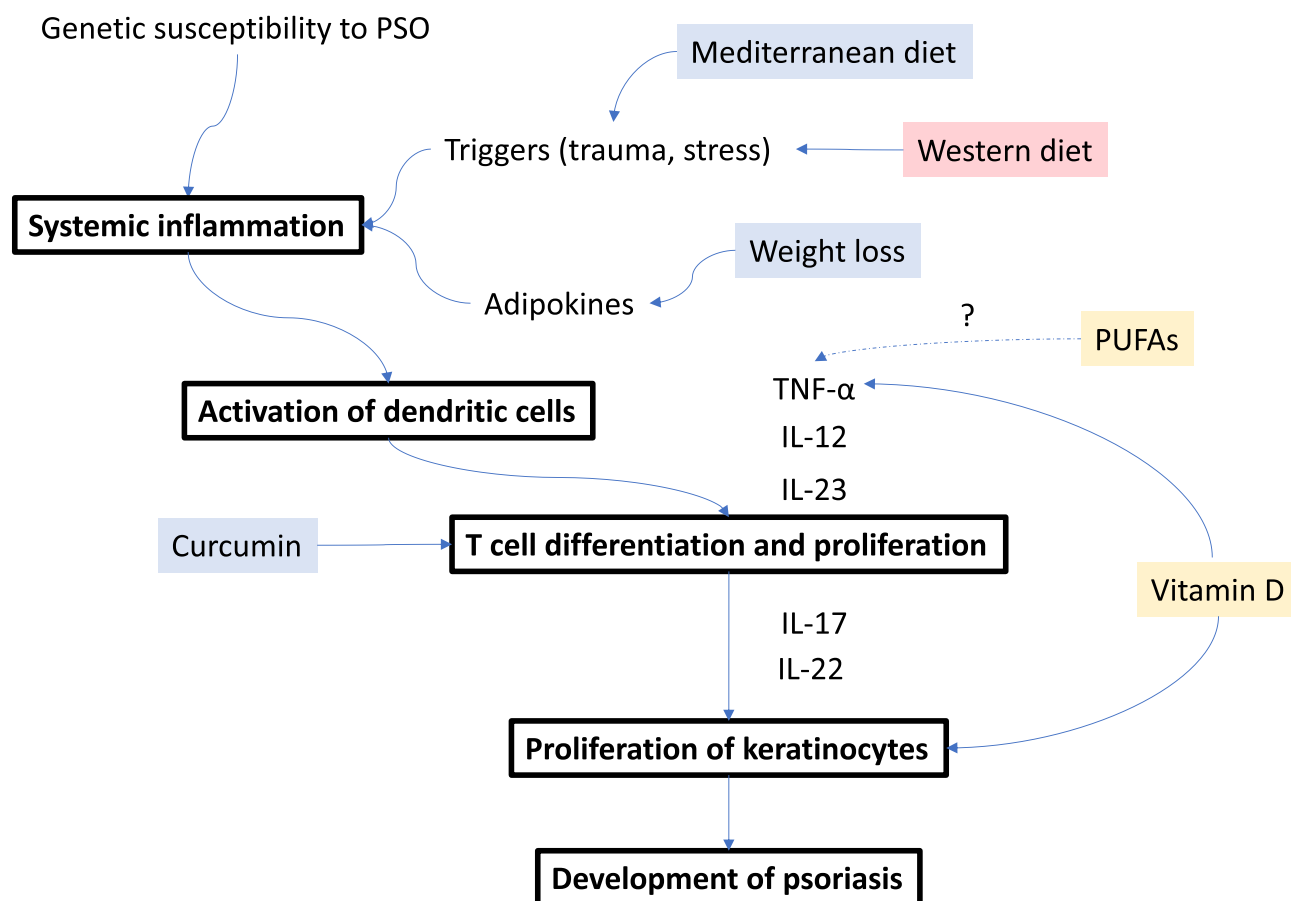
## Results

### Diets

Dietary changes are extremely popular for both patients and for researchers. A summary of the studies included in this review can be found in [Table 1](#). Proposed mechanisms have been illustrated in [Figure 1](#).

#### Low-Calorie Diet

Treatment of psoriasis using low-calorie diets and weight reduction has been examined. A meta-analysis conducted by Mahil et al in 2019 examined 6 RCTs using low-calorie diets, in some cases in combination with psoriasis treatments.<sup>8–13</sup> They found that obese patients receiving a low-calorie diet were significantly more likely to achieve a PASI75 (RR = 1.47, 95% CI: [1.27–1.69]) and have a reduction in mean PASI scores (–2.59, 95% CI: [–4.09, –1.09]). The authors noted that removing two studies that were at a high risk of bias caused the differences in PASI75 to no longer be



**Figure 1** Proposed mechanism of the influence of select diet and nutrients on the pathogenesis of psoriasis. The red-colored diets/supplements are considered to worsen psoriasis outcomes, while the blue diet/supplements improve psoriasis. Yellow supplement are equivocal.

**Table I** Studies on the Effect of Dietary Interventions on Psoriasis Symptoms

Source	Design	Study Population	Intervention	Control	Outcome Summary
<b>Low Calorie Diet</b>					
Mahil et al 2019 <sup>14</sup>	Meta-analysis of 6 RCTs on low-calorie diets with or without lifestyle change (Naldi 2014, Guida 2014, Jensen 2013), established systemic treatment (Al-Mutairi 2014), or with newly initiated treatment (Gisondi 2008, Kimball 2012)	Psoriasis patients with obesity Intervention, n = 382 Control, n = 374	Low-calorie diet	Normal diet (no dietary intervention)	Meta-analysis of 4 trials of risk for patients on lifestyle weight loss intervention achieving PASI75 compared to controls without dietary intervention: 1.47 (95% CI: 1.27 to 1.69) Meta-analysis of 4 trials of mean change in PASI for patients on lifestyle weight loss intervention compared to controls: -2.59 (95% CI: -4.09 to -1.09)
Gisondi et al 2008 <sup>12</sup>	24-week investigator-blinded RCT	Obese patients (BMI ≥30 but <45 kg/m <sup>2</sup> ) greater than 18 years old with moderate to severe psoriasis (BSA ≥10% and PASI ≥10) Intervention: n = 30 Control: n = 31	Low-calorie diet and 2.5 mg · kg <sup>-1</sup> d <sup>-1</sup> cyclosporine A	2.5 mg · kg <sup>-1</sup> d <sup>-1</sup> cyclosporine A	Compared with controls, low-calorie diet group had significantly greater proportion achieving PASI75 (p < 0.001). PASI75 was 66.7% in diet and cyclosporine group compared to 29.0% in cyclosporine alone group. A time-by-treatment interaction was found for PASI scores (p < 0.001) and for body weight (p < 0.001).
Al-Mutairi et al 2014 <sup>10</sup>	24-week clinical trial	Overweight or obese patients (BMI ≥ 25 but < 35) with moderate-to-severe psoriasis currently on biologic therapy (infliximab, etanercept, adalimumab, or ustekinumab) for psoriasis Intervention: n = 131 Control: n = 131	Caloric restriction diet created individually per patient by a dietitian	No diet changes	Weight loss was greater in the intervention group at week 24 (mean 12.9 ± 1.2 kg) while the control group gained weight (mean weight loss -1.5 ± 0.5 kg). PASI75 was achieved by 85.9% of the treatment group compared to 59.3% of the control group (p < 0.001). PASI improvement was statistically different between different systemic medications.
Campanati et al 2017 <sup>15</sup>	24-week clinical trial	Moderate to severe psoriasis patients (BSA >10%, PASI >10, and/or DLQI >10) older than 18 years old Intervention: n = 20 Control: n = 25	Low-carbohydrate low-calorie diet and TNF-alpha inhibitor	TNF-alpha inhibitor only	PASI scores were significantly decreased in the treatment group (mean 3.204 ± 2.57) compared to controls (mean 5.839 ± 3.807), p < 0.05. DLQI scores were also decreased in treatment compared to controls (2.1 ± 1.9 vs 6.7 ± 4.5, respectively, p < 0.05), as did weight (p < 0.05), BMI (p < 0.001), waist circumference (p < 0.0001), total cholesterol (p < 0.05), and serum triglycerides (p < 0.05)
Damiani et al 2019 <sup>19</sup>	1 month observational cohort study	Patients with stable plaque psoriasis older than 18 years n = 108	Fasting during the month of Ramadan	N/A	Decrease in PASI scores after Ramadan fasting (mean difference -0.9 ± 1.2, p < 0.0001). PASI scores at baseline were correlated with BMI (p < 0.05), but were not correlated after Ramadan fasting (p = 0.1415). Change in PASI was correlated with BMI (p < 0.05). Apremilast and mTOR inhibitors were associated with a greater decrease in PASI

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Table 1 (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
Adawi et al 2019 <sup>20</sup>	1 month observational cohort study	Patients with psoriatic arthritis older than 18 years n = 37	Fasting during the month of Ramadan	N/A	Decrease in psoriatic arthritis measures after fasting: DAPSA mean difference -2.35 (95% CI, -3.03 to -1.67, $p < 0.0001$ ), BASDAI mean difference -0.76 (95% CI -1.14 to 0.36; $p = 0.0015$ ), LEI mean difference -0.054 (95% CI, -0.76 to -0.33; $p < 0.0001$ ), DSS mean difference -1.38 (95% CI, -1.91 to -0.86, $p = 0.0001$ ). PASI scores decreased after fasting, with a mean difference of -1.59 (95% CI, -1.87 to -1.32), $p < 0.0001$ . CRP levels decreased significantly, with a mean difference of -1.92 (95% CI, -2.38 to -1.46, $p < 0.0001$ )
<b>Gluten-Free Diet</b>					
Michaëlsson et al 2000 <sup>25</sup>	6 month study, 3-month period of intervention followed by 3 month period of ordinary diet	Patients with psoriasis AGA-positive patients, n = 33 AGA-negative patients, n = 6	Gluten-free diet for 3 months, followed by 3 months of normal diet	N/A	PASI scores decreased after 3 months of GFD in AGA-positive patients, from $5.5 \pm 4.5$ to $3.6 \pm 3.0$ ( $p = 0.001$ ). No change in PASI was seen in AGA-negative patients ( $8.9 \pm 6.4$ to $10.2 \pm 7.9$ , $p = 0.465$ ). Duodenal biopsies of patients with AGA-positivity were unchanged after three months of GFD. During months 3–6 with return to normal diet, 18 of 30 AGA-positive patients could not continue the study due to worsening of disease. None of the AGA-negative patients reported worsening of disease after returning to normal diet.
Michaëlsson et al 2007 <sup>26</sup>	6 months of gluten free diet, follow-up for at least 2 years	Patients with palmoplantar pustulosis n = 123	Gluten-free diet for 6 months	N/A	Patients with elevated AGA or tTG antibodies who adhered to a GFD saw improvement in symptoms and normalization of AGA/tTG. Patients with elevated AGA or tTG antibodies who did not adhere to GFD did not improve in symptoms or antibody elevation.
Kolchak et al 2018 <sup>27</sup>	Cross-sectional case-control cohort study	Psoriasis patients with PASI scores > 2.4 and control patients Psoriasis patients, n = 97 Controls, n = 91	Gluten-free diet for 12 months in patients who had elevated AGA (n = 13)	Healthy patients	Prevalence of elevated AGA was 14% in psoriasis patients. 5% (38% of the AGA-positive group) of those had "strongly positive" AGA > 30.0U/mL. PASI scores were greater in patients with "strongly positive" AGA at baseline. Adherence to GFD for 12 months led to decreases in PASI scores, with greater changes noted for patients in the "strongly positive" AGA group.

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Table 1 (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
<b>Mediterranean Diet</b>					
Barrea et al 2015 <sup>30</sup>	Cross-sectional, case-control cohort study	Patients with mild-to-severe psoriasis, compared to age-, sex-, and BMI-matched controls Psoriasis patients, n = 62 Controls, n = 62	PREDIMED (PREvención con Dieta MEDiterránea) 14-item questionnaire assessing adherence to Mediterranean diet	Healthy patients	A higher percentage of psoriasis patients (30.6%) had poor adherence to a Mediterranean diet compared to controls (4.8%), $p < 0.001$ as well as average adherence (51.7% vs 77.5%, respectively; $p = 0.004$ ); no difference in high adherence was seen (17.7% and 17.7%)  In psoriasis patients, PASI scores were negatively correlated ( $r^2 = 0.599$ ) with adherence to the Mediterranean diet as measured by PREDIMED questionnaire, $p = 0.007$ . Extra virgin olive oil and fish consumption were predictive of lower PASI scores and CRP levels.
Phan et al 2018 <sup>31</sup>	Cohort study	Respondents to the French NutriNet-Santé Psoriasis patients, n = 3557 Patients without psoriasis, n = 27,828	MEDI-LITE (adhesion to a rather anti-inflammatory Mediterranean diet) survey	N/A	Severe psoriasis patients had higher risk of lower adherence to the Mediterranean diet (46%) compared to patients with non-severe psoriasis (36%) and patients without psoriasis (36%).  Psoriasis severity and adherence to Mediterranean diet was inversely associated when controlled for age, sex, BMI, smoking status, physical activity, educational level, and baseline history of cardiovascular disease, diabetes, hypertension, and hypertriglyceridemia. However, when controlling for the above along with depressive symptoms, the association was no longer significant.
Korovesi et al 2019 <sup>32</sup>	Cross-sectional observational study	Patients with mild-to-severe psoriasis without previous exposure to systemic medications and healthy controls Psoriasis patients, n = 69 Controls, n = 69	The Mediterranean Diet Score/ MedDietScore	N/A	Higher adherence to the Mediterranean diet was seen in control patients compared to psoriasis patients. PASI scores in psoriasis patients were inversely related to adherence to Mediterranean diet ( $r = -0.39$ , $p = 0.001$ ). Legumes, fish, and extra virgin olive oil consumption were negative predictors of PASI scores ( $p < 0.05$ ), while dairy consumption was a positive predictor ( $p = 0.002$ ).  Adherence was a negative predictor for PASI scores ( $p = 0.02$ ) after adjusting for age, gender, BMI, and serum high-sensitive CRP.

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**Table I** (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
<b>Ketogenic Diet</b>					
Castaldo et al 2020 <sup>35</sup>	10 week single arm clinical trial	Overweight or obese plaque psoriasis patients older than 18 with a BSA > 10% who have never used systemic treatment n = 37	2 phase weight loss program, with initial 4 week period of protein-sparing, very low-calorie ketogenic diet followed by a 6 week period of hypocaloric, Mediterranean-like diet	N/A	After week 4 (ketogenic diet only), PASI scores were decreased by a mean of -7.2, approximately 50% (95% CI: -8.7 to -5.6). At the end of the 10 week study, PASI scores had decreased by -10.6 (95% CI: -12.8 to -8.4), $p < 0.001$ . BSA involvement, itch severity, DLQI scores, body weight and aorto-mesenteric fat thickness all were decreased at the end of the ketogenic phase (week 4) and end of hypocaloric phase (week 10) compared to baseline. PASI score reduction was independent of baseline weight or baseline disease severity and was not correlated with weight loss reduction.
Castaldo et al 2021 <sup>36</sup>	4 week clinical trial	Overweight patients between the ages of 18 and 65 with plaque psoriasis; healthy control patients without psoriasis. Psoriasis patients, n = 30 Controls, n = 30	Psoriasis patients: 4 weeks of very low-calorie (<500kcal/day) protein-based diet, including whey protein, alkalizing substances, and herbal remedies	Control patients: conventional diet with ordinary food recommended as part of a healthy diet	PASI scores, DLQI, VAS pruritus, VAS pain significantly improved based on variable importance of projection (VIP) score calculated between week 0 and week 4 for psoriasis patients. Prior to diet, psoriasis and control patients had a different metabolome as determined by the multivariate analysis partial least squares-discriminant analysis. Dysmetabolism was noted in psoriasis patients, with specific amino acids including tryptophan, tyrosine, and lysine considered discriminative. At week 4, the metabolome of psoriasis patients changed, with hydroxybutyrate, leucine, pyruvic acid, and choline as discriminative metabolites

**Abbreviations:** AGA, antigliadin antibodies; BSA, body surface area; BMI, body mass index; CRP, C-reactive protein; DLQI, Dermatology Life Quality Index; GFD, gluten-free diet; PASI, Psoriasis Area Severity Index; RCT, randomized clinical trial; tTG, tissue transglutaminase; VAS, visual analog scale.

significant between groups; however, mean PASI scores remained significantly lower in the lifestyle modification group than controls.<sup>14</sup>

Low-calorie diets have been linked to a better response to systemic psoriasis treatment, making it a useful adjunctive treatment. In a randomized study by Gisondi et al, obese psoriasis patients starting cyclosporine, a traditional systemic treatment, had a greater response rate in the low-calorie treatment group (PASI75 response in 66.7%) versus those who received only cyclosporine with no change in diet (29.0%,  $p < 0.001$ ).<sup>12</sup> Al-Mutairi and Nour conducted a study on obese patients beginning biologic therapy for psoriasis (n = 262) randomized to either a low-calorie diet or normal diet control group. Weight loss at week 24 was greater in the diet group, with a significant reduction in waist circumference. The diet group had a significantly greater percentage of people achieving PASI75 of 85.9%, compared to the control group of 59.3% ( $p < 0.001$ ). Though some of the biologic treatments were weight-based (ustekinumab and infliximab), while others were fixed-dose (etanercept and adalimumab), more patients in the low-calorie group achieved PASI75.<sup>10</sup>

Weight loss may also mitigate some negative side effects of certain biologic treatments. An open-label, nonrandomized study on patients using TNF- $\alpha$  inhibitors found that patients who adhered to a low-calorie, low-carbohydrate diet

not only had a greater decrease in mean PASI scores but also did not exhibit increases in BMI and waist circumference associated with TNF- $\alpha$  inhibitors usage, compared to those not on this diet. However, this study was limited in that patients were not randomly assigned to treatment or control group, and patients who did not adhere to the low-calorie diet were excluded from the final analysis.<sup>15</sup>

Though not strictly a low-calorie diet plan, intermittent fasting has been studied as a weight loss diet for its potential benefits, with some promising outcomes in patients with type 2 diabetes mellitus, cardiovascular disease, and inflammatory diseases like multiple sclerosis.<sup>16–18</sup> One observational study investigated the effects of Ramadan fasting in psoriasis patients. Fasting during the month of Ramadan is an important Islamic practice in which Muslims fast during the daylight hours, eating one meal before sunrise and one meal after sunset – essentially a type of intermittent fasting. The 108 patients saw a significant decrease in PASI score after one month, with a mean difference of  $-0.9 \pm 1.2$  ( $p < 0.0001$ ). This effect was correlated with the type of psoriasis treatment – patients on apremilast and mTOR inhibitors (rapamycin) had more significant decreases in PASI score. However, these results may not be solely due to fasting – BMI at the end of the study was not reported. The authors noted that those observing Ramadan often had changes in sleeping patterns by sleeping more in the daytime and working at nighttime, suggesting the benefits may instead be stemming from these sleep modifications.<sup>19</sup> Another study also showed positive effects of intermittent fasting on joint symptoms in patients with psoriatic arthritis.<sup>20</sup>

### Gluten-Free Diet

Avoidance of gluten, a protein found in wheat, barley, and rye, has become a popular diet with the public within the recent decades, with evidence that this practice may benefit certain psoriasis patients.<sup>21</sup> Although gluten intake has not been shown to be a risk factor for psoriasis,<sup>22</sup> a meta-analysis determined an increased risk of psoriasis in patients with celiac disease (OR = 1.8) and increased risk of celiac disease in patients with psoriasis (OR = 2.16).<sup>23</sup> Levels of IgA anti gliadin antibodies, a commonly used diagnostic tool for celiac disease, were also found to be higher in psoriasis patients.<sup>24</sup>

Studies on gluten-free diets in psoriasis patients show benefits only for those who have evidence of gluten sensitivity or celiac disease. Michaëlsson et al demonstrated that psoriasis patients with anti gliadin IgA or IgG showed significant improvements in PASI scores after maintaining a gluten-free diet for three months (PASI reduction from  $5.5 \pm 4.5$  to  $3.6 \pm 3.0$ ); after returning to a regular diet, 60% of patients had deterioration of psoriasis symptoms. Psoriasis patients without these markers did not show improvements with a gluten-free diet or worsening of disease after stopping the diet.<sup>25</sup> The group replicated these results in patients with palmoplantar pustulosis.<sup>26</sup> A study conducted by Kolchak et al followed patients who had elevated anti gliadin IgA for a year on a gluten-free diet. All patients saw an improvement in symptoms, but those with a higher serum anti gliadin IgA of  $>30.0$  U/mL ( $n = 5$ ) had a greater response of PASI decline of 56% compared to those with a lower serum anti gliadin IgA of  $11.5–30.0$  U/mL (PASI decline of 36%,  $n = 8$ ).<sup>27</sup>

### Mediterranean Diet

The Mediterranean diet, with its emphasis on consumption of unsaturated fats like extra virgin olive oil (EVOO), whole fruits and vegetables, legumes, and fish, is one dietary pattern recommended for healthy lifestyle from a variety of organizations, including the United States Department of Agriculture in the Dietary Guidelines for Americans and the American Heart Association.<sup>28,29</sup> Studies have also found the potential to improve psoriasis symptoms with the Mediterranean diet. Barrea et al first published a case–control series of mild-to-severe psoriasis patients ( $n = 62$ ) and found that psoriasis patients were less likely to adhere to the Mediterranean diet (30.6% vs 4.8%), with significantly less EVOO consumption, fruit, fish/seafood, and tree nut consumption compared to controls ( $n = 62$ ). Consumption of EVOO and fish was independently related to PASI scores ( $r = 0.548$  and  $r = 0.139$ , respectively).<sup>30</sup> In 2018, the National Psoriasis Foundation (NPF) weakly recommended a consideration of trialing a Mediterranean diet in psoriasis patients based on this study.<sup>7</sup>

Since publication of the recommendations, additional cross-sectional cohort studies have suggested a dose–response relationship between Mediterranean diet adherence and improvement in psoriasis symptoms. The NutriNet-Santé Cohort, composed of French participants answering web-based questionnaires on health, examined the relationship between



adherence to the Mediterranean diet and psoriasis severity. In the 35,735 responders, 3557 (10.0%) of participants had psoriasis, with 878 (24.7%) having severe psoriasis. 45.5% of patients with severe psoriasis reported a low adherence to the Mediterranean diet, compared to 36.3% of non-severe psoriasis patients and 35.6% of patients without psoriasis ( $p < 0.001$ ). Similar results remained after controlling for sociodemographic variables, in patients with a history of inflammatory bowel disease, and in patients on systemic treatment.<sup>31</sup> A cross-sectional case-control study on 69 Greek mild-to-severe psoriasis patients also showed an inverse relationship between diet adherence and PASI ( $r = -0.39$ ,  $p = 0.001$ ), DLQI ( $r = -0.41$ ,  $p < 0.001$ ), and the inflammatory marker high-sensitivity C-reactive protein (CRP) ( $r = -0.37$ ,  $p = 0.001$ ). The study noted decreases in PASI were notable for increased consumption of legumes, fish, and extra virgin olive oil, while increases in PASI were related to increased dairy product consumption.<sup>32</sup>

### Ketogenic Diet

A ketogenic diet, consisting of a high consumption of fats, moderate consumption of protein, and low consumption of carbohydrates, originally emerged as a treatment for childhood epilepsy but has gained considerable interest in the past decade. A very low-calorie ketogenic diet (VLCKD) has been suggested to promote overall weight loss and reduce oxidative stress and systemic inflammation via production of ketone bodies, with one mouse study specifically noting elevated serum beta-hydroxybutyrate levels.<sup>33,34</sup>

Castaldo et al first investigated this diet with a single-arm trial in overweight or obese psoriasis patients ( $n = 37$ ). Patients were started on a VLCKD diet ( $<500$  kcal per day) for 4 weeks as an initial weight loss induction period, followed by a hypocaloric, balanced Mediterranean-like diet (25–30 kcal per kilogram of ideal body weight per day). Not only did the group have a notable body weight reduction (mean 12.0%,  $-10.6$  kg), but they also had reductions in PASI scores from 13.8 down to 3.2. Improvements in PASI scores were not correlated with the amount of weight loss achieved.<sup>35</sup> A follow-up study on patients with psoriasis ( $n = 30$ ) who followed a VLCKD for 4 weeks replicated clinical improvements in PASI and DLQI scores. In addition, analysis of the biochemical profiles of these patients suggested the diet-induced normalization of abnormal serum metabolites, including calcium, bilirubin, cortisol, LDL, and total cholesterol.<sup>36</sup>

### Inflammatory Diet

In contrast to the diets mentioned above, the “Western” diet could be involved in the worsening of psoriasis. Sometimes referred to as an “inflammatory” or “pro-inflammatory” diet, the Western diet is notable for its high fat and high sugar content.

Patients with psoriasis tend to have worse diets than the general population, especially with increased intakes of high-fat foods and saturated fat along with high alcohol consumption.<sup>38</sup> Psoriasis patients were noted, in comparison to healthy controls to have an overall worse diet measured by the Rapid Eating Assessment for Patients (REAP) questionnaire ( $2.23 \pm 0.31$  for psoriasis and  $2.38 \pm 0.26$  for controls,  $p < 0.01$ ), along with higher consumption of total fat and saturated fat. Overall REAP scores and total fat, though not saturated fat, were correlated with PASI scores.<sup>39</sup> This high-fat, high sugar consumption in psoriasis patients appears to be maintained in many areas of the world: a Thai study found that psoriasis patients had higher instant noodle, pickled food, and coconut milk consumption compared to controls. Among these Thai psoriasis patients, greater psoriasis severities were associated with red meat, belly meat, and instant noodles.<sup>40</sup> Interestingly, a study in Japanese psoriasis patients found that psoriasis patients had a higher BMI and greater intake of sugar/sweeteners like other studies, but Japanese psoriasis patients also had a great seafood intake and lower red meat intake.<sup>4</sup> Regardless of the region or local cuisine tendencies, psoriasis patients appear to have notably different dietary habits than the average population.

However, this relationship does not necessarily indicate a causal effect. One study examining the Nurses’ Health Study II cohort found that this dietary pattern may not be a risk factor for the development of psoriasis. The questionnaire-based cohort study on nurses’ ages 25 to 42 years old did not find a correlation between the amount of “pro-inflammatory” foods (eg processed and red meat, refined grained, high energy beverages like soda) and the hazard ratio of psoriasis development, even after correction for age, race, BMI, smoking, alcohol use, and calorie intake.<sup>37</sup>



**Table 2** Studies on the Effect of Supplements on Psoriasis Symptoms

Source	Design	Study Population	Intervention	Control	Outcome Summary
<b>Fish Oil</b>					
Clark et al 2019 <sup>60</sup>	Meta-analysis	10 RCTs or nonrandomized controlled trials, including Adil 2017, Balbas 2011, Guida 2014, Bittiner 1988, Bjorneboe 1988, Escobar 1992, Grimmer 1993, Gupta 1989, Soyland 1993, Veale 1994; 3 RCTs (Adil 2017, Balbas 2011, Guida 2014) used for quantitative analysis of PASI scoring For PASI scoring Intervention, n = 128 Control, n = 126	PUFAs in various dosages (see individual studies)	Placebo (see individual studies)	PASI scoring mean difference was significantly decreased by -1.56 (95% CI: -2.24 to -0.92). Erythema (8 studies) and scale (5 studies) were also significantly decreased, while itching (5 studies), percent total BSA (4 studies), desquamation (3 studies), and infiltration (3 studies) were not significantly different. Subgroup analysis showed significant differences in improvement when comparing lower dosages of supplementation (<1800 mg/day) to higher dosages (≥ 1800 mg/day). Meta-regression analysis found that higher dosage and lower duration of supplementation was associated with improvements in erythema and scale
Yang and Chi, 2019 <sup>63</sup>	Meta-analysis	13 trials, including Bittiner 1998, Bjorneboe 1988, Danno 1998, Grimmer 1993, Gupta 1989, Gupta 1990, Kristensen 2018, Madland 2006, Mayser 1998, Oliwiecki 1994, Soyland 1993, Strong 1993, and Veale 1994 3 RCTs (Kristensen 2018, Mayser 1998, Soyland 1993) used for quantitative synthesis of PASI scoring For PASI scoring Intervention, n = 172 Control, n = 165	PUFAs in various dosages (see individual studies)	Placebo (see individual studies)	PASI scoring was not significantly different between fish oil supplement groups and controls, with a mean difference of -0.28 (95% CI: -1.74 to 1.19). No differences in incidence of adverse events was noted in 9 trials reporting these outcomes.

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Table 2 (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
Chen et al 2020 <sup>67</sup>	Meta-analysis	18 trials, including Bittiner 1988, Bjorneboe 1988, Stoof 1989, Gupta 1989, Gupta 1990, Escobar 1992, Soyland 1993, Henneicke 1993, Griminger 1993, Strong 1993, Veale 1994, Oliwiecki 1994, Mayser 1998, Danno 1998, Madland 2006, Guida 2014, Kirstensen 2016, and Kristensen 2018 2 RCTs (Soyland 1993 and Kristensen 2018) were used for quantitative synthesis of PASI scoring for fish oil as a monotherapy 2 RCTs (Guida 2014 and Mayser 1998) were used for quantitative synthesis of PASI scoring for fish oil in combination with conventional therapy <u>For monotherapy PASI scoring</u> Intervention, n = 128 Control, n = 125 <u>For combination with conventional therapy PASI scoring</u> Intervention, n = 60 Control, n = 51	PUFAs in various dosages (see individual studies)	Placebo or conventional treatment (see individual studies)	For fish oil monotherapy trials, PASI scoring was not significantly different between treatment and control groups, with a mean difference of 0.43 (95% CI: -0.72 to 1.58), p = 0.47. Lesion area (3 studies) and pruritus score (4 studies) were not significantly different between treatment and control groups. For fish oil used in combination with conventional therapy, PASI scores were significantly different between treatment and controls, with a mean difference of -3.92 (95% CI: -6.15 to -1.69).
Tveit et al 2020 <sup>68</sup>	26 week, double-blind, placebo-controlled RCT	Patients with mild-to-moderate psoriasis (PASI < 10) with stable disease Intervention, n = 32 Placebo, n = 32	10 capsules daily (5 capsules twice daily) of 292 mg herring roe PUFAs with 22% eicosapentaenoic acid and 66% docosahexaenoic acid (2.6g of EPA and DHA daily)	Coconut oil in caprylic acid and capric acid (medium chain triglycerides)	PASI scores improved significantly in the treatment group, with a mean difference of -1.1 (95% CI: -2.2 to -0.03), p = 0.045. DLQI, BSA, PGA, and CRP were not significantly different. 3 patients in the treatment group withdrew during the study compared with 0 in the placebo group. 47% of patients in the treatment group experienced GI events compared to 34% of placebo group

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Table 2 (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
Zhan et al 2021 <sup>69</sup>	Cross-sectional cohort study	Patients responding to the National Health and Nutrition Examination Survey (NHANES) in 2003–2006 and 2009–2014 n = 15,733 Psoriasis patients, n = 414 Controls, n = 15,319			Psoriasis respondents had a higher likelihood of being older and being married/widowed/divorced/separated. Psoriasis respondents were more likely to have a higher BMI and be veterans and smokers. Psoriasis respondents had a significantly lower level of eicosatetraenoic acid (ETA) intake, with psoriasis respondents consuming $0.14 \pm 0.10$ g/day compared to respondents without psoriasis ( $0.16 \pm 0.10$ ), $p = 0.033$ . In comparison, there was no difference between psoriasis respondents and controls in consumption of eicosapentaenoic acid (EPA) ( $0.04 \pm 0.11$ and $0.04 \pm 0.09$ , respectively; $p = 0.131$ ) or docosahexaenoic acid (DHA) ( $0.08 \pm 0.16$ and $0.07 \pm 0.15$ , respectively; $p = 0.319$ ). Dietary intake of ETA trends remained after controlling for gender, age, veteran status, marital status, ratio for family income to poverty, BMI, alcohol intake, and smoking in trend test of association.
<b>Oral Vitamin D</b>					
Theodoridis et al 2021 <sup>79</sup>	Meta-analysis	4 RCTs (Jarrett 2017, Ingram 2018, Disphanural 2019, Siddiqui 1990) of at least 3 months duration using oral vitamin D supplements compared to placebo 3 trials (Jarrett 2017, Ingram 2018, Disphanural 2019) used for quantitative synthesis of PASI Intervention, n = 109 Control, n = 96	Vitamin D in various dosages (see individual studies)	Placebo (see individual studies)	PASI scoring was significantly decreased in the oral vitamin D treatment group, with a mean difference of $-0.92$ (95% CI: $-1.72$ to $-0.11$ ). After applying the Hartung-Knapp adjustment for random effects, PASI scoring was not significantly different between groups ( $-0.92$ , 95% CI: $-2.21$ to $0.38$ ).

(Continued)

Table 2 (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
Prtina et al 2021 <sup>86</sup>	3 month single arm clinical trial	Plaque psoriasis patients over 18 years old with a serum vitamin D level < 25 nmols, normal serum calcium concentration, no use of systemic psoriasis medication or phototherapy for at least 3 months no use of topical vitamin D for at least 3 months n = 40	Vitamin D 5000 IU daily	Placebo	For all severities, PASI scores were significant improved with vitamin D supplementation. At the beginning of the study, 37.5% had mild disease (PASI < 5%), 35.0% had moderate disease (PASI 5–10%), and 27.5% had severe disease (PASI > 10%), whereas the severity distribution at week 12 was 62.5% mild, 25.0% moderate, and 12.5% severe (p < 0.001). Serum vitamin D and vitamin B12 were significantly increased (56.77±14.66 nmol/L to 103.85±32.20 nmol/L and 301.08±95.02 pg/mL to 362.81 ±118.56 pg/mL, respectively), p < 0.001. Serum homocysteine and folate were significantly decreased (12.45 ± 1.92 µmol/L to 10.38 ± 1.66 µmol/L and 8.01±3.88 mg/mL to 6.27±2.60 mg/mL, respectively), p < 0.001. Serum levels of pro-inflammatory markers were decreased with supplementation, while anti-inflammatory markers were increased.
<b>Herbal Medicine</b>					
Luo et al 2021 <sup>87</sup>	Meta-analysis	11 double-blinded RCTs comparing Chinese herbal medicine with non-Chinese herbal medicine interventions with a Jadad quality score ≥4 in efficacy and safety analysis 8 trials (Wang 2003, Zhou 2011, Zhou 2012, Li 2017, She 2017, Lv 2018, Zhang 2018, Mao 2019) were used for quantitative synthesis of PASI scores For PASI scoring Intervention, n = 631 Control, n = 441	Various Chinese herbal medicines (see individual studies)	Placebo, other Chinese herbal medicines, or conventional treatment (see individual studies)	Meta-analysis of PASI scores in treatment groups were significantly lower in the treatment group compared to placebo with a mean difference of -4.02 (95% CI: -6.71 to -1.34). The percentage of patients who achieved PASI50 (5 studies) and PASI90 (2 studies) were not significantly different between groups; however, those who achieved PASI75 was greater in the treatment group (4 studies). DLQI (3 studies) was decreased in the treatment group; however, pruritus (3 studies), recurrence rate (3 studies), and adverse events (11 studies) had no differences between groups.

(Continued)

Table 2 (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
Lv et al 2018 <sup>88</sup>	Meta-analysis	20 RCTs on the Chinese traditional medicinal herb <i>Tripterygium wilfordii</i> 4 RCTs compared it as a combination therapy with acitretin compared to acitretin alone For comparison with acitretin Intervention, n = 50 Control, n = 80	Various preparations of <i>Tripterygium wilfordii</i> (see individual studies)	Placebo, other Chinese herbal medicines, or conventional treatment (see individual studies)	Meta-analysis of odds ratio for achieving PASI60 comparing <i>Tripterygium wilfordii</i> plus acitretin versus acitretin alone was significantly favoring the combination treatment: 0.25 with a 95% CI of 0.10 to 0.63. The addition of <i>Tripterygium wilfordii</i> with other Chinese traditional medicines (glycyrrhizin and compound amino-polypeptide tablet) also achieved greater PASI60 odds ratio compared to the Chinese traditional medicine alone. Adverse events for <i>Tripterygium wilfordii</i> included menstrual disorders, dry mouth, and GI complaints.
Antigua et al 2015 <sup>92</sup>	12 week Phase III, single-dose, double-blind placebo controlled RCT, followed by week 16 follow-up	Patients with chronic mild-to-moderate plaque psoriasis (PASI < 10) Intervention, n = 31 Placebo, n = 32	Topical methylprednisolone aceponate 0.1% ointment once daily and 2g of curcumin (2 tablets of 500mg Meriva (patented bioavailable form of curcumin with lecithin) twice daily)	Topical methylprednisolone aceponate 0.1% ointment once daily and placebo tablet twice daily	PASI reduction was greater in patients in the intervention group (5.6 at baseline to 1.3 at week 12) compared to topical treatment alone (4.7 at baseline to 2.4 at week 16), $p < 0.05$ for difference between groups. IL-17 levels were not decreased between baseline and week 12 in either group. IL-22 levels were significantly decreased at week 12 in the curcumin and topical steroid group ( $p < 0.001$ ), a finding not replicated in the topical steroid only group.
Carrion-Gutierrez et al 2015 <sup>93</sup>	Phase IV double-blind, placebo controlled pilot RCT	Patients with moderate to severe plaque psoriasis based on PGA with plaques able to be treated with phototherapy Intervention, n = 11 Control, n = 10	UVA phototherapy session except on specific experimental plaques, followed by 6 tablets containing 100 mg <i>Curcuma longa</i> extract per day with visible light irradiation (VLRT) on the areas covered during UVA phototherapy	UVA phototherapy session except on specific experimental plaques, followed by 6 tablets containing 100 mg <i>Curcuma longa</i> extract per day with simulated visible light irradiation (VLST) on the areas covered during UVA phototherapy	Specific lesions were used to assess patient response. PGA was lower in the intervention group than controls, with 20% of the intervention group reporting response compared to 0% of controls ( $p < 0.01$ ). Patients who had lesions that responded were group in the intervention group (81%) compared to control (30%), $p = 0.05$ . On places of the body not involved in the experimental area, both groups achieved similar reduction in PASI.

(Continued)

**Table 2** (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
Kurd et al 2008 <sup>94</sup>	16 week Phase II, open label trial	Patients with moderate to severe plaque psoriasis (BSA > 6% and moderate plaque thickness of at least 2 on PASI score) n = 12	3 capsules of 500mg of curcumin three times a day	None	Intention-to-treat analysis showed a 16.7% response rate. Response rate of 25% was found for those who completed the 12 week study (n = 8). Median Skindex 29 score reduction for those who completed the trials was 0.35. At week 12, only 2 patients were classified as "responders" (PASI 75), which was maintained at the week 16 follow-up. 4 patients withdrew, 3 due to lack of efficacy and 1 due to worsening of disease.
<b>Selenium</b>					
Kharaeva et al 2009 <sup>97</sup>	30–35 days, double-blind, placebo-controlled RCT	Hospitalized patients with erythrodermic psoriasis or psoriatic arthritis with age- and sex-matched healthy controls Erythrodermic psoriasis, n = 30 Psoriatic arthritis patients, n = 28 Healthy controls, n = 24	Conventional therapy and 4 capsules/day of supplement with ubiquinone acetate, 50 mg/d (coenzyme Q10), RRR- $\alpha$ -tocopherol, 50 mg/d (vitamin E), and selenium aspartate, 48 $\mu$ g/d dissolved in soy lecithin	Conventional therapy and 4 capsules/day of soy lecithin	Psoriasis severity score were significantly decreased in the treatment group compared to controls for both erythrodermic psoriasis ( $p < 0.001$ ) and psoriatic arthritis patients ( $p < 0.05$ ). PASI scores were similarly lower in treatment groups compared to controls. Serum superoxide levels and granulocyte catalase levels were significantly lower at the end of the trial compared to controls for both erythrodermic psoriasis and psoriatic arthritis patients, as were epidermal CuZnSOD and catalase. Serum CnZnSOD was not significantly difference between treatment and controls.

(Continued)

Table 2 (Continued).

Source	Design	Study Population	Intervention	Control	Outcome Summary
Yousefzadeh et al 2017 <sup>98</sup>	12 week, double blind, RCT	Patients with biopsy-confirmed psoriasis with a PASI score > 10 eligible for methotrexate treatment Intervention, n = 15 Control, n = 15	Methotrexate with once daily proprietary micronutrient supplement	Methotrexate alone	PASI scores were reduced in both groups, but the treatment group showed significantly lower scores ( $31.80 \pm 10.57$ to $5.50 \pm 3.82$ ) compared to controls ( $30.23 \pm 10.87$ to $10.86 \pm 9.84$ ), $p = 0.04$ . Decreases in IL-1 $\beta$ and TNF- $\alpha$ were significant in both groups; the difference between treatment and control groups was also significant ( $p < 0.05$ ).
Serwin et al 2006 <sup>99</sup>	4 week double blind, placebo-controlled, parallel group RCT with follow-up survey 4 weeks after completion of treatment	Hospitalized psoriasis patients without concomitant disease Intervention, n = 19 Control, n = 18	NB-UVB therapy with twice-daily tablets of 100 $\mu$ g of selenium as L-selenomethionine	Narrowband ultraviolet B therapy only	PASI scores were reduced in both groups, but no difference between treatment and controls (baseline $12.37 \pm 4.71$ to $2.34 \pm 1.70$ versus $13.02 \pm 6.25$ to $3.59 \pm 2.27$ , respectively). Serum TNF- $\alpha$ levels and serum CRP levels were significantly decreased in the treatment group at weeks 2, 4, and 8 ( $p < 0.05$ ).
Fairris et al 1989 <sup>100</sup>	12 week double blind, placebo-controlled RCT with a follow-up 12 weeks after treatment end	Moderate-to-severe chronic stable plaque psoriasis with age- and sex-matched healthy control Group 1 (selenium only), n = 22 Group 2 (selenium and Vitamin E), n = 23 Group 3 (placebo), n = 24	Group 1: Tablet of 600 $\mu$ g daily with selenium-enriched yeast Group 2: Tablet of 600 $\mu$ g daily selenium and 600 IU of d-alpha-tocopherol acetate (vitamin E)	Group 3: placebo tablet	No improvement in PASI scores at week 12 compared to baseline for any group. Mean blood and serum selenium levels at week 12 were increased in supplementations groups were increased compared to controls, but skin selenium concentrations were not increased. At week 24, all groups had returned to baseline serum selenium levels.
Harvima et al 1993 <sup>101</sup>	6 week, single arm open label trial	Plaque psoriasis patients with "occasional to widely spread plaques" n = 7	Tablet containing selenomethionine yeast (400 $\mu$ g daily)	N/A	No changes in psoriasis symptom presentation occurred between week 6 and baseline. Blood and selenium levels were increased at week 12. Selenium in protein and tissue of lesional skin was increased, but no changes in selenium-dependent glutathione peroxidase activity was noted.

**Abbreviations:** BSA, body surface area; BMI, body mass index; CRP, C-reactive protein; DLQI, Dermatology Life Quality Index; IL, interleukin; GI, gastrointestinal; NB-UVB, narrowband ultraviolet B; PASI, Psoriasis Area Severity Index; PGA, physician global assessment; PUFA, polyunsaturated fatty acids; RCT, randomized clinical trial; TNF- $\alpha$ , tumor necrosis factor alpha; UVA, ultraviolet A.



## Supplements

Though a popular addition to the diet of many psoriasis patients, supplements have overall not shown robust benefits to patients, as can be seen in summary in [Table 2](#).

### $\omega$ -3 Polyunsaturated Fatty Acids (Fish Oil)

Dietary polyunsaturated fatty acids (PUFAs), which include omega-3 ( $\omega$ -3) and omega-6 ( $\omega$ -6) PUFAs, have been studied to determine the effect of the balance between the two on psoriasis. Seed and vegetable oils, such as palm, soybean, and corn, contain mostly  $\omega$ -6 PUFAs, while cold-water marine fish are a high source of  $\omega$ -3 PUFAs. The ratio between  $\omega$ -6/ $\omega$ -3 PUFAs varies with diet. A lower  $\omega$ -6/ $\omega$ -3 PUFAs ratio, with the majority of PUFAs consumed being  $\omega$ -3, has potential benefits for overall health, including cardiovascular benefits.

Fish oil supplements, which contain  $\omega$ -3 PUFAs, are a popular dietary supplement among patients, though its efficacy remains in doubt. The most recent NPF guidelines on diet do not recommend oral fish oil supplements for psoriasis and psoriatic arthritis.<sup>7</sup> Many studies published in the 1980s and 1990s showed decreases in psoriasis severity after fish oil supplementation; however, many of these trials did not include control groups and had less objective measures of change in disease presentation.<sup>41–45</sup> In controlled trials, the results are more mixed: some report improvements in the clinical picture in the treatment groups on skin or other measures,<sup>46–49</sup> while others show no significant differences.<sup>50–56</sup> Three meta-analyses have attempted to consolidate data from these randomized clinical trials, with only one out of the three findings that  $\omega$ -3 PUFAs made a statistically significant difference in psoriasis outcomes. The trials chosen to conduct the analysis varied greatly among them; all studies emphasized the need for more robust clinical trials to more clearly determine the true effects of  $\omega$ -3 PUFAs.

Clark et al conducted a pooled analysis of 10 randomized clinical trials (RCT) or nonrandomized controlled trials with a treatment group of  $\omega$ -3 PUFAs and a placebo group in patients with psoriasis.<sup>9,46,49,51,54–59</sup> Meta-analysis on PASI scoring reported in three of the trials<sup>9,49,57</sup> showed a statistically significant improvement in the treatment group, with a mean difference of  $-1.58$  (95% confidence interval [CI]:  $-2.24$  to  $-0.92$ ). Other significant reductions included erythema from 8 studies (mean difference:  $-1.66$ ; 95% CI:  $-2.52$  to  $-0.81$ ) and scale from 5 studies (mean difference:  $-0.69$ ; 95% CI:  $-1.26$  to  $-0.13$ ). No significant results were seen in itching, percent total body surface area (BSA) involved, desquamation, or infiltration. The authors conclude that  $\omega$ -3 PUFA offers a promising supplement possibility.<sup>60</sup>

Yang and Chi published a meta-analysis in 2019 using 13 placebo-controlled RCTs on fish oil supplementation for qualitative synthesis.<sup>46–48,50–56,59,61,62</sup> From these, they included 3 RCTs for quantitative synthesis of PASI scores, totaling 337 participants – of note, one of the three involved intravenous  $\omega$ -3 PUFA,<sup>61</sup> while the two others were oral supplements.<sup>50,51</sup> No differences were found between treatment and control groups (mean difference:  $-0.28$ ; 95% CI:  $-1.74$  to  $1.19$ ). However, the authors state that more research is needed, as the heterogeneity of the studies was large, and many of the RCTs they found could not be included in the analysis due to lack of outcome standardization and inadequate data reporting.<sup>63</sup>

Chen et al conducted a meta-analysis with 18 RCTs.<sup>9,46–48,50–56,58,59,61,62,64–66</sup> Inclusion criteria included RCTs with monotherapy or combination therapy using  $\omega$ -3 PUFAs compared with a placebo group or a conventional therapy only group. In studies using  $\omega$ -3 PUFAs as a monotherapy ( $n = 2$ ),<sup>50,51</sup> no differences were determined in the  $\omega$ -3 PUFAs treatment group compared to the placebo group in PASI scores, lesional area, or pruritus scores. However, PASI scores were significantly lower in two trials<sup>9,61</sup> involving patients who received a combination therapy of  $\omega$ -3 PUFAs with conventional treatment (topical or systemic) compared to those on conventional treatment only; the mean difference was  $-3.92$  (95% CI:  $-6.15$  to  $-1.69$ ).<sup>67</sup>

This uncertainty in efficacy has maintained  $\omega$ -3 PUFAs as a highly popular area of study, especially in parsing whether the type of fatty acid affects the efficacy of treatment. One clinical trial investigated the use of herring roe oil, highlighted as containing a 3:1 ratio of docosahexaenoic acid (DHA) to eicosapentaenoic acid (EPA), while other fish oils generally have a 1:1 ratio of these PUFAs. The placebo-controlled, double-blind RCT treated patients with mild-to-moderate psoriasis ( $n = 64$ ) with either herring roe oil capsules or a placebo of coconut oil. At the primary endpoint of 26 weeks, PASI scores were significantly decreased in the treatment group compared with placebo ( $-1.8$  and  $-0.6$ , respectively,  $p < 0.05$ ), though no differences were seen in other measures of disease including DLQI or BSA.<sup>68</sup> A cross-sectional cohort study using the United States National Health and Nutrition Examination Survey (NHANES) examined

a different PUFA, eicosatetraenoic acid (ETA). Comparing the 24-hour dietary recall survey between participants with and without psoriasis showed differences in ETA intake only, not EPA or DHA. Psoriasis patients were not only more likely to eat fewer ETA but also the odds ratio of ETA consumption and psoriasis risk was 0.36, indicating that consumption of ETA may be associated with a decreased risk of psoriasis. Interestingly, this was observed in a dose–effect manner, with greater consumption associated with less reported psoriasis.<sup>69</sup>

## Vitamin D

Vitamin D, an extremely popular supplement and essential for maintenance of an intact skin barrier, has been shown to act as a suppressor of inflammatory cytokines like TNF- $\alpha$ , IL-6, and IL-8, as a mediator in the proliferation of keratinocytes, and as a regulator of skin barrier integrity.<sup>70,71</sup> A multitude of studies have shown an increased prevalence of vitamin D deficiency compared to the general population.<sup>70,72–74</sup> Topical vitamin D analogues like calcipotriol and calcitriol have long been a part of standard dermatological treatment for psoriasis, but the efficacy of oral vitamin D supplementation remains unclear.<sup>75</sup> Although numerous studies have shown vitamin D as a popular supplement for patients,<sup>3,4,6</sup> clinical trial data have shown conflicting evidence, with the most recent NPF guidelines written in 2018 stating that oral vitamin D was not recommended for psoriasis patients.<sup>7</sup> More recent studies and meta-analyses have found similar outcomes—results continue to be mixed on efficacy, though few adverse effects tend to be noted in treatment groups.

A meta-analysis on the three placebo-controlled RCTs<sup>76–78</sup> conducted by Theodoridis et al did not find a favorable effect on psoriasis outcomes for oral vitamin D. Although at 6 months Vitamin D supplementation found an improvement in PASI scores in the treatment group (mean difference [MD] =  $-0.92$ , 95% confidence interval [CI] =  $-1.72$  to  $-0.11$ ), these differences became no longer significant after using the Hartung-Knapp adjustment for random-effects.<sup>79</sup> The authors note that more rigorous studies should be conducted since the studies were few and relatively small, and open-label trials have shown some benefits.<sup>80–85</sup>

Prtina et al in one of the more recent clinical trials studied the efficacy of vitamin D in psoriasis patients with Vitamin D deficiency. In this prospective open-label clinical trial, 40 patients received vitamin D 5000 IU daily for three months. Results of the supplementation showed both improvements in clinical measures of psoriasis severity and changes in numerous serum markers. A statistically significant number of patients in all three severity groups saw improvements in PASI scores. Serum levels of homocysteine, folate, and pro-inflammatory cytokines (hsCRP, IFN- $\gamma$ , TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, and IL-17) were decreased; anti-inflammatory cytokines (IL-10 and IL-5) were increased.<sup>86</sup>

## Herbal Supplements

Herbal medicine, derived from traditional cultural practices, encompasses a large contingent of possible plants used to treat various diseases. A meta-analysis of Chinese herbal medicine as a monotherapy for psoriasis was conducted by Luo et al, finding 11 placebo-controlled, double-blind RCTs using combined 54 herbs. The method of delivery varied, including decoctions (4 trials), particles (4 trials), ointment (1 trial), and capsules (2 trials). Overall PASI scores were decreased in patients using herbal medicines compared (mean difference  $-4.02$ , 95% CI:  $-6.7$  to  $-1.34$ ), though some PASI endpoints were not significant – subgroup analysis found PASI50 and PASI90 had no differences between groups, but PASI75 did. DLQI was also improved in the herbal medicine group.<sup>87</sup> The studies were heterogeneous in both herbal composition and delivery, making it difficult to interpret which compounds are most efficacious; larger scale RCT on specific types of herbal medicine are needed to confirm the findings of these studies and to explore other herbal supplements. A specific herbal supplement, *Tripterygium wilfordii*, was investigated separately in a meta-analysis by Lv et al. The supplement was equally effective in several studies as conventional treatment (cyclosporine and acitretin in one trial each) and helped improve the efficacy of acitretin, with pooled analysis showing that more patients achieved a PASI-60 in the combination group than acitretin alone.<sup>88</sup>

## Curcumin

Curcumin, which occurs naturally in turmeric, has been studied for its anti-inflammatory properties. A number of in vivo studies with human keratinocytes and mice have shown that curcumin acts both to downregulate inflammatory pathways

while stimulating anti-inflammatory ones.<sup>89</sup> Most notable for psoriasis, it has been shown to decrease activity in CD4+ and CD8+ T cells, subsequently decreasing levels of inflammatory cytokines, such as IL-17 and IL-21.<sup>90,91</sup>

Numerous studies on oral curcumin have demonstrated improvements in PASI scores after treatment. Antigua et al conducted a 16-week placebo-controlled RCT on participants with mild-to-moderate psoriasis, comparing the treatment group of oral curcumin and topical steroids treatment with a placebo group using only topical steroid (median PASI at baseline 5.6 and 4.7, respectively). Though at week 16 both groups showed improvements, those taking curcumin had a statistically significant reduction in PASI compared to the placebo group (median PASI of 1.4 and 2.5, respectively), a finding accompanied by a reduction in serum IL-22 in the curcumin group.<sup>92</sup> Curcumin supplementation with phototherapy, specifically real visible light phototherapy, was also shown to be beneficial for patients with moderate-to-severe psoriasis in a placebo-controlled RCT conducted by Carrion-Gutierrez et al.<sup>93</sup> However, these benefits are not assured; Kurd et al conducted an open-label prospective study with 12 patients – 4 of the patients had to withdraw before the end of the trial due to a lack of efficacy of curcumin, and only 2 of the total patients who completed the trial achieved a PASI75 or greater. This trial was conducted with curcumin as a monotherapy, unlike the other two studies.<sup>94</sup>

## Selenium

Research into selenium has focused on its ability to act as an antioxidant, modifying the immune response by allowing increased resistance to oxidative stress and reducing cell proliferation. This property can act in both beneficial and deleterious manners. Selenium can prevent damage from reactive oxygen species but can also catalyze apoptosis in keratinocytes.<sup>95</sup> Studies have found that psoriasis patients have lower selenium levels compared to the general population, with different areas demonstrating different levels. In one meta-analysis, psoriasis patients had higher selenium levels in hair, lower in blood, and equal in serum and plasma.<sup>96</sup>

Studies on selenium supplementation have generally shown mixed effects on psoriasis severity. Kharaeva et al found that, in a randomized double-blind RCT, hospitalized patients with severe erythrodermic psoriasis and psoriatic arthritis had a greater improvement in disease severity scores and PASI when given a mixture of coenzyme Q10, vitamin E and selenium in addition to standard treatment.<sup>97</sup> Yousefzadeh et al conducted a single-blinded RCT on 34 severe psoriasis patients starting MTX. A higher proportion of patients on methotrexate taking a daily micronutrient tablet achieved a PASI75 compared to the methotrexate-only group at week 12, with a concurrent decrease in IL-1 $\beta$  and TNF- $\alpha$  levels. The micronutrient tablet included more than 24 different vitamins and trace minerals (selenium, vitamins B6, B9, B12, and D, among others), making it difficult to parse specific components that may have benefited the patient.<sup>98</sup> However, three studies, including two double-blind RCTs, did not replicate these results; although the treatment groups had an increase in serum selenium, PASI scores were not significantly different between groups.<sup>99–101</sup>

## The Microbiome, Nutrition, and Psoriasis

### Probiotic Supplementation in Clinical Trials

A number of trials have been conducted to examine the effect of probiotics in psoriasis patients (Table 3). Groeger et al conducted one of the first randomized, double-blind RCTs for probiotic use in patients with inflammatory diseases. The 26 patients with mild-to-moderate psoriasis were fed sachets of *Bifidobacterium longum* subsp *infantis* (*B. infantis*) 35264, a probiotic bacteria, for 8 weeks. Serum markers of inflammation, including plasma CRP and TNF- $\alpha$ , were reduced in the treatment group compared to the placebo group, although IL-6 levels were not significantly different. 75% of the treatment group saw decreases in CRP, TNF- $\alpha$  and IL-6, compared to only 7% of the placebo.<sup>102</sup> Another study measured clinical outcomes after administration of a mixture of 3 probiotic strains of bacteria in 90 mild-to-severe psoriasis patients. The double-blind, placebo-controlled RCT by Navarro-Lopez et al found that at week 12, 66.7% of the probiotic group achieved a PASI75 compared to 41.9% of the placebo group ( $p = 0.0317$ ); although not statistically significant, the enterotype distribution was different between treatment and control groups at the end of the treatment period. Six months after the trial ended, a post-study survey found that 20% of the treatment group had a relapse in their psoriasis symptoms, a significantly lower number compared to the placebo group (41.9%,  $p = 0.027$ ), suggesting that the effects of probiotics may be maintained for some time after consumption.<sup>103</sup> Another study, presented as a late-breaking research abstract at the American Academy of Dermatology 2022 Annual Meeting, investigated a non-living strain of

**Table 3** Studies on the Effect of Probiotics on Psoriasis Symptoms

Source	Design	Study Population	Intervention	Control	Outcome Summary
Groeger et al 2013 <sup>102</sup>	8 week, double-blind, placebo-controlled RCT	Patients with psoriasis with a PASI < 16, ulcerative colitis, or chronic fatigue syndrome compared with healthy controls Psoriasis patients, n = 26 Healthy controls, n = 22	Sachets with $1 \times 10^{10}$ CFU viable <i>Bifidobacterium infantis</i> 35264 per day	Placebo sachet of 5 g Maltodextrin per day	At week 8, plasma CRP and TNF- $\alpha$ were significantly reduced in treatment groups compared to placebo (4.47 mg/L to 2.89 mg/L versus 2.68 to 3.55 and 8.20 to 7.67 versus 7.06 to 7.40, respectively), $p < 0.05$ . IL-6 was not reduced in either group. The percentage of patients who saw decreases in plasma CRP, TNF- $\alpha$ , and IL-6 levels was higher in the treatment group (75%) compared to placebo (7%), p-values not reported.
Navarro-Lopez et al 2019 <sup>103</sup>	12 week, double-blind, placebo-controlled RCT with a follow-up during 6 month post-treatment	Mild to moderate plaque psoriasis patients (PASI > 6) Intervention, n = 46 Placebo, n = 44	Topical betamethasone/calcipotriol with daily capsule of 3 probiotic bacteria strains ( <i>Bifidobacterium longum</i> CECT 7347, <i>B. lactis</i> CECT 8145 and <i>Lactobacillus rhamnosus</i> CECT 8361, $1 \times 10^9$ colony-forming units total)	Topical betamethasone/calcipotriol with placebo capsule	At week 12, PASI reduction was seen in a greater proportion of probiotic patients (66.7%) than in the control group (41.9%), $p < 0.05$ . PGA distributions at week 12 were not significantly different between groups. No differences in inflammatory markers (CRP, TNF- $\alpha$ , IL-23, IL-12, IFN- $\gamma$ , IL-1 $\beta$ , IL-6) were noted between groups at week 12. Enterotype distribution was not statistically significant between treatment and placebo groups (enterotype 1: 56.7% vs 46.2%; enterotype 2: 0% vs 42.3% and enterotype 3: 84.6% vs 53.3%, respectively). Follow-up 6 months after trial conclusion saw 20% of treatment group relapsing compared to 41.9% of the placebo group, $p = 0.027$ .

**Abbreviations:** CRP, C-reactive protein; DLQI, Dermatology Life Quality Index; IFN- $\gamma$ , interferon- $\gamma$ ; IL, interleukin; PASI, Psoriasis Area Severity Index; PGA, physician global assessment; PUFA, polyunsaturated fatty acids; RCT, randomized clinical trial; TNF- $\alpha$ , tumor necrosis factor alpha.

*Prevotella histicola* in a proprietary formulation ingested via a capsule. After 16 weeks of treatment, a significantly greater percentage of patients in the treatment arm achieved a PASI50 compared to the placebo arm, concurrently with improvements in DLQI. Interestingly, these results did not show a dose response between those who took one capsule, four capsules, or ten capsules. 24 weeks after the treatment period ended, 60% of responders maintained PASI50, and some even saw further improvements in PASI scores.<sup>104</sup>

## Discussion

The interaction between nutrition and psoriasis is a popular topic of interest to both physicians and patients. Though the literature on the topic abounds, much of the influence of nutrition on psoriasis remains uncertain due to the lack of large, well-controlled studies. Most research supports dietary changes for specific patient populations over the addition of specific supplements, suggesting that changes must be implemented across the entire diet rather than isolated nutrients. Recent research indicates that the changes affected by some of these diets may be in part due to changes in the gut microbiome, suggesting that probiotics may play a role in the future of psoriasis treatment. Nevertheless, it is important to emphasize to patients that diet is an adjuvant treatment to conventional medication.

## Diet

Psoriasis patients may benefit from most guidance on diet given the relative strength of data within specific populations. For some overweight patients, emphasizing a low-calorie diet for weight loss can impart dermatological improvements, not only as a result of weight loss itself but also in addition to increased responsiveness to systemic medications, along with well-established cardiovascular benefits. In conjunction with these findings, intermittent fasting may offer another strategy in patients with difficulties following a low-calorie diet. Though research on this dietary is limited to Ramadan fasting, which adds several confounding factors, the benefits appear to be positive. Possible reasons for improvements with weight loss-focused diets may be due to a decrease in abdominal fat and adiposity, subsequently lowering the level of adipokines and decreasing inflammation on which the psoriatic march relies. Although the relationship between psoriasis severity and various serum adipokine levels is still unclear, Nakajima et al found that adiponectin, a serum adipokine, positively correlated with PASI scores as did IL-22. The mechanism behind obesity exacerbating psoriasis thus may be due to adipokines inducing increasing in Th-17 related cytokines.<sup>105,106</sup> For these recommendations, severe changes in diets should be avoided to prevent nutritional deficiencies. Low-calorie diets and intermittent fasting may be recommended in suitably motivated patients, though difficulties maintaining these dietary plans may make alternatives, such as the Mediterranean diet, more attractive to other patients.

The Mediterranean diet has continually shown positive benefits in both skin and systemic outcomes. RCTs are still limited, but the stronger evidence supporting this diet and its recommendation by academic bodies make this diet quite attractive. Regardless of its effects on psoriasis symptoms, the Mediterranean diet offers benefits for cardiovascular health and decreased mortality. Various mechanisms have been proposed, but because diets consist of a conglomeration of many different foods, exact mechanisms are difficult to parse. High consumption of antioxidants, including red wine and plant-based foods, may impart anti-inflammatory benefits to those following this diet.<sup>107</sup> The consumption of extra-virgin olive oil, with a high polyphenol content compared to other cooking oils, has been shown in healthy patients to reduce gene expression of *IFN $\gamma$*  and *IL7R*, indicating the potential pathway for reduction in inflammation for psoriasis patients.<sup>108</sup> Its promotion to patients should be encouraged for patients who are motivated to change their diet.

Gluten avoidance, while popular, appears to benefit only a subsection of patients with psoriasis who have concomitant gluten sensitivity or celiac disease. The NPF currently strongly recommends a gluten-free diet to psoriasis patients with confirmed celiac disease and a 3-month trial of a gluten-free diet in those with positive antigliadin IgA or IgG antibodies, though it does not encourage screening in psoriasis patients without symptoms or close relatives with celiac disease.<sup>7</sup>

Though the results for the ketogenic diet appear quite positive, the studies examining its effects in patients were extremely restrictive in caloric intake, with patients asked to adhere to a diet of less than 500 kcal a day. This diet may be difficult or even dangerous to follow outside of the close follow-up necessitated by clinical trials, and patients may have difficulties adhering to its extremely restrictive nature even for the relatively short four-week period demonstrated to be effective in the Castaldo trials. Furthermore, some controversy exists regarding the emphasis on high-fat intake in the



ketogenic diet. The Academy of Nutrition and Dietetics caution that the diet objectives generally lower the amount of vitamins and minerals intake, with lower fiber content and higher levels of saturated fat making long-term consequences unclear.<sup>109</sup> Further research must be conducted in more real-world scenarios prior to offering the ketogenic diet as an option for patients.

Although it remains somewhat unclear which aspects of the Western diet are directing the negative outcomes seen in psoriasis patients, the evidence against consuming a high-fat, high-sugar diet is notable. Most studies on this pattern have been limited to case-control cohort studies; however, studies on mice offer possible mechanisms for these observations. High-fat, high-sugar diets in mice induced psoriasiform dermatitis, even without significant weight gain. After only 4 weeks of a Western diet, increased IL-17 producing T-cell localization to the skin was seen. IL-23 receptor expression was also increased in T-cells.<sup>110,111</sup> The exact relationship between what specific foods of the Western diet are responsible for the noted inflammatory consequences has yet to be completely determined – free fatty acids from high-fat diets have been implicated, as has bile acid dysregulation.<sup>112,114</sup> However, one mouse study found that a high-fat diet alone was not enough to induce worsened skin disease. Consuming a diet high in both fat and sugar diets was necessary to cause psoriasiform disease in mice, as the high-fat only diet did not provoke a similar response.<sup>113</sup>

The contrast between observational cohort studies demonstrating a difference between diet in psoriasis patients and findings of the Nurses' Health Study showing no significant differences in hazard ratio for increased Western diet intake may be due to the limitations of the various studies. The Nurses' Health Study cohort is limited to women ages 25 to 40, making generalization more difficult. All studies on the human diet cited in this review were based on subjects' recall and thus may be unreliable. More randomized clinical trials are necessary to elucidate the relationship between the Western diet and psoriasis.

Whether it causes or exacerbates psoriasis, a Western diet has well-established negative effects on the cardiovascular system and overall health. Advising patients against consuming an excess of fat and sugar is essential to global patient care, and working in conjunction with patients to identify healthy alternatives may help psoriasis symptoms, with or without systemic medication.

Specific diets can be recommended for certain patients, but care should be exercised when advising patients on what to pursue.

## Supplements

Most supplements do not show strong evidence supporting their recommendation for patients with psoriasis. Neither  $\omega$ -3 PUFAs and vitamin D, two of the most popular dietary supplements, have convincing evidence to suggest their recommendation. The benefits of oral  $\omega$ -3 PUFAs remain unclear, with most evidence suggesting that they are against the treatment as monotherapy. Even molecular studies have shown conflicting results on whether healthy or diseased patients show a significant decrease in inflammatory markers like CRP, IL-6, and TNF $\alpha$  after consumption of  $\omega$ -3 PUFAs.<sup>115</sup> However, the studies cited in the Clark, Yang and Chi, and Chen meta-analyses tend to be older with inconsistently reported outcomes and less written about the methodology of statistical analysis. Some newer studies on different types of  $\omega$ -3 PUFAs – for example, ETA or DHA instead of EPA – indicate this area still offers opportunities for further study as an adjuvant, especially given that psoriasis patients are particularly partial to the supplement. Pal et al proposed that EPA and DHA, despite both being  $\omega$ -3 PUFAs derived from arachidonic acid that individually decrease inflammation, may have competing effects that limit their efficacy. They point to studies showing different results in EPA only or DHA only studies in mental health as the basis for their conclusions.<sup>116</sup> ETA, another  $\omega$ -3 PUFAs, is less researched than DHA and EPA, especially within psoriasis. Zhan et al in their ETA cohort study note that in in vitro and animal studies, ETA has been suggested to have anti-inflammatory properties potentially. Previous studies have shown a reduction in TNF $\alpha$ , decrease arachidonic acid cell intake, and secretion of the anti-inflammatory cytokine IL-10 in relation to ETA production or consumption.<sup>69</sup> The addition of oral vitamin D similarly has mixed evidence of benefit to patients. Nevertheless, psoriasis patients have higher rates of vitamin D deficiency, and few significant adverse events to vitamin D supplementation have been noted. Vitamin D supplementation should be offered to patients with known vitamin D deficiency.

Herbal supplements, especially *Tripterygium wilfordii* and curcumin, offer promising adjuvant treatment for psoriasis, though their utility as a monotherapy is uncertain. Although unclear what specific herbal supplements are most

efficacious, the positive results in some of the RCTs are encouraging for future study. However, these supplements should not be recommended at this time given their unregulated nature and the unclear potential interaction between some supplements and conventional therapy.

Though there may be benefits to selenium, there are too few clinical trials to make appropriate recommendations at this time, especially since trials showing selenium benefits generally, also included other vitamins or minerals in the treatment groups. Excess selenium intake can cause gastrointestinal concerns, skin lesions, rashes, and muscle weakness,<sup>117</sup> necessitating caution in recommending supplementation.

## Probiotics

Some of the most exciting new directions regarding nutrition and psoriasis stem from research into the gut microbiome. Differences in the gut microbiome between patients with psoriasis and controls are notable, though a consensus on the exact pattern of microbiota changes has yet to be reached.<sup>118</sup> Probiotics have been shown to modify the gut microbiome in a multitude of inflammatory skin diseases. These results appear especially promising because of the specificity of the bacterial strains needed to induce change, as well as a dose–response relationship has seen in a multitude of clinical trials. Additionally, many of these patients appeared to have a maintained response to the probiotic treatment after its withdrawal, suggesting that not only did the treatment alter the gut microbiome, but these alterations were persistent. The nature of this treatment has captured the interest of both patients and researchers as a potentially effective, longer term treatment.

Despite the overall positive results presented in these clinical trials, negative outcomes have been noted. One case study reports a patient with Crohn's disease and palmoplantar psoriasis who experienced a sudden, new onset pustular rash after starting a new over-the-counter probiotic supplement several days before presentation.<sup>119</sup> Although much more research is needed to fully elucidate the benefits, probiotics and the study of the gut microbiome in general offer new prospects for treatment.

Altering the gut microbiome to help treat psoriasis may also reach beyond probiotics in the future – pre-biotics, which are fibers that encourage growth of beneficial bacteria, have been tested separately and in combination with probiotics in patients with atopic dermatitis.<sup>118</sup>

## Conclusion

Diet and nutrition in the context of psoriasis remains a complex topic that can be difficult for both physicians and patients to maneuver. Specific dietary plans, such as a hypocaloric diet promoting weight loss in obese patients, a gluten-free diet for patients with comorbid celiac disease, and a Mediterranean diet emphasizing PUFAs consumption and fresh food, offer promising results. Other diets, like intermittent fasting and a ketogenic diet, are intriguing but lack strong evidence to support their recommendation. Importantly, a Western diet with high-fat and high-sugar intake should be avoided because of its potentially inflammatory properties and overall negative effect on health. Few supplements, including  $\omega$ -3 PUFAs, vitamin D, and selenium, have shown consistent benefits in RCTs; however, some studies suggest that herbal supplements can be safe and somewhat effective as adjuvant treatments. Finally, the gut microbiome is an emerging area of research with significant implications for the effect of nutrition on health. Probiotics may be a potential therapy in the future, but at present must be monitored carefully due to possible negative effects. Overall, nutrition is an essential part of the care of patients with psoriasis. Working with patients to plan the best course of action should be a priority for all physicians.

## Disclosure

Tina Bhutani is a principal investigator for trials sponsored by AbbVie, Castle, CorEvitas, Dermavant, Galderma, Mindera, and Pfizer. She has received research grant funding from Novartis and Regeneron. She has been an advisor for AbbVie, Arcutis, Boehringer-Ingelheim, Bristol Myers Squibb, Janssen, Leo, Lilly, Novartis, Pfizer, Sun, and UCB. Wilson Liao has received research grant funding from AbbVie, Amgen, Janssen, Leo, Novartis, Pfizer, Regeneron, and TRex Bio. The remaining authors have nothing to disclose.



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