Diet and Psoriasis

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Dietary nutrients can activate the immune system and may lead to the overproduction of pro-inflammatory cytokines.

inflammation immunity nutrients antioxidants

1. Introduction

Chronic inflammation refers to a series of pathophysiological dysregulations which eventually result in a sustained, increased production of pro-inflammatory cytokines and oxidative stress. In recent decades, numerous studies have focused on the association between the inflammatory process and the development of chronic, non-communicable diseases (NCD), such as obesity, diabetes mellitus, cardiovascular diseases, cancer and autoinflammatory diseases such as rheumatoid arthritis and psoriasis [1]. Apart from genetic and environmental factors, nutrition has emerged as a potential modulator of immunological and inflammatory responses [2]. Dietary patterns, such as the Mediterranean diet, which encompass a high intake of fruits and vegetables and a low proportion of fat and sugars, have been proposed to ameliorate chronic inflammation and reduce the incidence of NCD [3]. However, as every diet comprises many different nutrients from different food sources, extensive research has been conducted on the specific nutrients that constitute an everyday dietary regimen, which include macronutrients, namely proteins, fats and carbohydrates, and micronutrients, such as vitamins, trace elements and antioxidants such as polyphenols and carotenoids, which, in turn, can have a different impact depending both on their daily intake and food origin [4].

Psoriasis is one of the most prevalent autoinflammatory diseases worldwide, with an incidence of 2–3% in Europe and North America [5]. Its etiology is considered multifactorial, and it is characterized by the dysregulation of the innate and adaptive immune systems, with the activation of T helper (Th)-1 and Th-17 T cells leading to an increased production of inflammatory cytokines such as interleukins (IL) IL-1, IL-6, IL-23, IL-22, IL-17, and IL-33, tumor necrosis factor alpha (TNF-α), and interferon-gamma (IFN-γ) [6][7]. In this cascade, inflammation plays a cardinal role by promoting hyper-proliferation and angiogenesis, leading to the typical skin lesions and the articular involvement of psoriatic arthritis [8]. Since the report by Späh [9], where the idea of a potential common inflammatory pathway between psoriasis and atherosclerosis was first introduced, the link between psoriasis and chronic inflammation has been highlighted in many studies [10][11][12]. As inflammation is modulated by nutrition, it comes as no surprise that the impact of diet on the incidence and severity of the disease as well as on treatment response has been a matter of extensive research [13].

2. Diet and Psoriasis: Obesity, Dietary Regimens and Promising Therapeutic Targets

Psoriasis is a multifactorial disease, attributed to both genetic and environmental factors. Among the latter, many studies have suggested that nutrition can play a crucial role both in disease pathogenesis and treatment through its effects on chronic inflammation obesity has been recognized as a major risk factor for psoriasis development and progression, and weight loss regimens, together with other dietary interventions such as gluten-free diet or Mediterranean diet seem to offer substantial beneficial results in the course of the disease. Below, research data about the association of psoriasis and different dietary regimens will be discussed, along with possible suggestions and implication for treatment options.

2.1. Obesity

2.1.1. Obesity and Psoriasis: A Bidirectional Association

A growing number of studies have highlighted the association between obesity and psoriasis [14][15][16][17][18][19][20][21][22][23]. The prevalence and incidence of psoriasis is higher among patients with obesity, while obesity is an important predisposing factor for psoriasis onset, progression and severity. Moreover, obesity exerts a negative impact on the treatment of psoriasis and increases the adverse effect of anti-psoriatic drugs [24][25][26][27][28]. A cross-sectional study by Herron et al. pointed out that obesity had a higher prevalence among psoriatic patients compared to the non-psoriatic population and highlighted that body weight was not increased at the onset of the disease but rather during its course, implying that obesity was a consequence rather than a causal factor [14]. The Nurses' Health study was the first large-scale, prospective study which pointed out that increased BMI (Body Mass Index) and weight gain are strongly associated with psoriasis, with a relative risk of 1.63 (95% CI, 1.58–2.61) for BMI ≥ 35.0 compared to controls [20]. A case-control study with 373 patients by Wolk et al. showed that obesity is associated with a two-fold increased risk of psoriasis compared to individuals with normal body weight. In addition, it was the first study investigating BMI as a risk factor for psoriasis severity, indicating that for each one-unit increment in BMI, the risk for psoriasis severity (assessed by Psoriasis Area Severity Index—PASI score) increased by 7% [21]. In accordance with these results, another study by Murray et al. supported that patients with psoriasis and particularly women are more likely to have increased BMI compared to same-gender full siblings, and a positive correlation was demonstrated between obesity and disease severity as determined by body surface area (BSA) and the Physician's Global Assessment (PGA) [17]. Similarly, a case-controlled study by Naldi et al. showed that overweight and obese patients have an odds ratio (OR) of 1.6 and 1.9, respectively, for psoriasis compared to controls [18]. In the more recent HUNT study with 33.734 patients, Snekvik et al. prospectively examined the association between development of psoriasis and BMI, waist circumference, waist-to-hip ratio and 10-year weight gain. Patients with obesity and increased waist circumference have an almost two-fold risk for developing psoriasis, with relative risks being 1.87 and 1.95, respectively. Moreover, subjects with a body weight increase >10 kg had an RR of 1.72 [19]. The same factors were examined in a recent meta-analysis, including 7 prospective studies and 17.637 patients; for each 5 units increase in BMI and for each 5 kg of weight gain, the relative risk of psoriasis increased by 19% and 11%, respectively. Moreover, for each 10 cm increase in waist circumference and

0.1 unit increase in waist-to-hip ratio, the relative risk for psoriasis rose by 24% and 37%, respectively [22]. A previous meta-analysis, including 13 retrospective case-control and 3 prospective case-control studies, showed a relative risk of 1.66 (95% CI 1.46–1.89) for obesity among patients with psoriasis compared with controls and, even more importantly, a hazard ratio of 1.18 (95% CI: 1.14–1.23) for new onset obesity among psoriasis patients, indicating again the double role of obesity both as a cause and a repercussion of psoriatic disease [23].

2.1.2. A Common Inflammatory Pathway

Obesity and psoriasis represent chronic inflammatory states, and many recent studies have focused on the complicated role of visceral fat, which acts as an endocrine organ and releases a number of pro-inflammatory cytokines and adipocytokines resulting in immune dysregulation and low-grade inflammation [29]. Central obesity is associated with increased visceral fat, where activated macrophages stimulate adipocytes to produce pro-inflammatory molecules such as TNF-α, IL-1, IL-6 and IL-8 [30]. Adipocytokines, which are secreted not only by adipocytes but also by macrophages in adipose tissue, contribute equally to the inflammation process [31]. Leptin is an adipocytokine which ameliorates energy expenditure by inducing lipolysis and inhibiting liver lipogenesis [32]. It is well known that obesity is characterized from hyperleptinemia and leptin resistance [32][33][34]. Interestingly, increased leptin levels have also been detected in patients with psoriasis independently of BMI. Apart from aggravating the inflammatory cascade, leptin also induces keratinocyte proliferation, which is a crucial step in the development of the characteristic skin lesions in psoriasis [32][33]; at the same time, it drives T cells toward the Th-1 phenotype. Adiponectin, another adipocytokine which is produced by white adipose tissue (WAT), exerts an anti-inflammatory action by blocking the secretion of TNF-α, IL-6, IL-17 and IL-1, enhancing the secretion of IL-10 and downregulating VCAM-1 and ICAM-1 [35][36]. It should be noted, however, that the evidence regarding the role of adiponectin in psoriasis is inconsistent. A recent meta-analysis of 63 studies, including 2876 psoriasis patients and 2237 healthy controls, showed that patients with psoriasis have decreased levels of adiponectin; on the contrary, another meta-analysis with 521 cases and 482 controls indicated no statistically significant difference in the levels of adiponectin and high-molecular weight adiponectin levels between the two groups [31][37].

Omentin-1 is another adiponectin with anti-inflammatory properties by inhibiting TNF-α. Levels of omentin-1 are decreased in obesity, however, an inverse association with the incidence of psoriasis has not been firmly established [31]. Even more interestingly, consistent results have been shown for resistin, which seems to play a key role in the pathogenesis of the disease through an increase in secretion of pro-inflammatory cytokines such as IL-6, IL-12 and TNF-α via activation of nuclear factor-B signal pathway and is also increased in obesity and other chronic inflammatory states [38][39][40]. In a recent meta-analysis of nine case-control studies, containing 421 psoriasis patients and 348 healthy controls, serum resistin levels were higher in psoriasis patients of both Asian and Caucasian origin [41]. Even more interestingly, a study by Kyriakou et al. indicated diminished blood concentrations of resistin after treatment for psoriasis compared to their initial levels [42].

2.1.3. Obesity and Anti-Psoriatic Treatment

Research data have shown that a high BMI diminishes the effectiveness of pharmacological treatment [24][28]. Obesity can also modify pharmacokinetics of anti-TNF and other biologic agents, leading to increased drug

clearance, shorter half-life and lower serum trough drug concentrations [22]. A cohort study from Italy including patients who received systemic treatment for plaque psoriasis for the first time showed that the percentage of patients achieving reduction of PASI score >75% was 30% lower in obese patients compared to individuals with normal BMI [24]. According to an observational cohort study based on Danish and Icelandic registries, BMI > 30 is associated with higher psoriasis activity at baseline and reduced drug response and treatment adherence (HR:1.85) [25]. In a study by Bardazzi et al., among 33 patients receiving biological agents, patients who put on weight during the 8-month follow-up did not achieve PASI 50, while patients who had a stable weight presented variable response to treatment and those who decreased their weight achieved PASI 90 or PASI 75, even when not responding initially [26]. In a retrospective observational study including 110 patients on anti-TNF-α agents, Di Lernia et al. reported that after two years, the proportion of patients receiving the same treatment was only 42.21%, proposing high BMI as an independent predictor of drug failure and withdrawal [28]. Such results by single studies have been confirmed in a large meta-analysis including 54 studies and 19.372 patients, which showed that obesity is associated with 60% higher odds of inadequate response to anti-TNF treatment as compared to normal BMI; for each unit increment of BMI, there is an augmentation in odds of failure by 6.5% [27].

2.1.4. Effect of Weight Loss Interventions in Psoriasis—A Role for Low-Calorie Diet

During recent years, it has been shown that weight loss through diet and physical exercise reduces oxidative stressors, exerts a positive effect on psoriasis severity and ameliorates the response to pharmacological treatment for psoriasis. In this notion, a significant number of studies have been conducted to investigate the effect of low-calorie diet on psoriasis severity and progression. In a randomized controlled trial with 60 patients, Jensen et al. reported that a 16-week low-energy diet (800–1000 Kcal/day) resulted in significant weight loss (mean change −15.8 Kg compared to −0.4 Kg in control groups), improvements in PASI score (mean change −2.3 vs. −0.3 in control group) and statistically significant amelioration in Dermatology Life Quality Index (a ten-question questionnaire measuring the impact of skin disease on the quality of life) in patients with BMI > 27 compared to control group [43]. These results are in accordance with another RCT by Naldi et al., where a 20-week hypocaloric diet in combination with exercise resulted in a median PASI reduction of 48.0% (95% CI, 33.3%–58.3%) in the intervention group vs. 25.5% (95% confidence intervals-CI, 18.2%–33.3%) in controls. Interestingly, the improvement of psoriasis severity in intervention group was achieved with only a slight weight loss [44]. A recent meta-analysis of six RCTs confirmed that weight loss following lifestyle interventions improves psoriasis compared with controls, with a mean change in PASI score of 2.59. Apart from weight loss per se, such results can be explained also by the effect of physical activity, which upregulates anti-inflammatory molecules such as IL-10 and downregulates TLR expression on monocytes, leading to more favorable immune responses. In addition, bariatric surgery, particularly gastric bypass, reduces the risk of developing psoriasis (HR: 0.52) [45].

Del Giglio et al. conducted a randomized controlled trial to investigate the effect of low-calorie diet on maintenance of psoriasis remission after 12 weeks of methotrexate treatment. After 14-weeks of low-calorie diet, the patients in intervention group did not manage to maintain a statistically significant remission rate, possibly because weight regain was progressively observed in the intervention group after week 24; however, there was a trend towards a slower rebound of psoriasis compared to control group [46]. Similarly, Mutairi et al. conducted a randomized

controlled study to assess the impact of weight loss on the efficacy of biologic agents to obese patients with psoriasis. A diet intervention for 24 weeks resulted in a mean weight reduction of 12.9 ± 1.2 kg in the intervention and 1.5 ± 0.5 kg in the control group, which led to a 84% and 69% improvement in PASI score, respectively [47]. Another prospective study showed that a weight loss >5% is significantly associated with the achievement of minimal disease activity as a response to anti-TNF treatment in obese patients with psoriatic arthritis [48]. A 24-week randomized controlled trial by Gisondi et al. showed that low-calorie diet improves response to cyclosporin treatment in obese patients with moderate-to-severe psoriasis [49]. A possible explanation for the beneficial effect of weight loss on psoriasis progression is the amelioration of obesity-induced inflammation by decreasing the size and the inflammatory activity of hypertrophic adipocytes, the infiltration of adipose tissue by macrophages and the secretion of pro-inflammatory cytokines. Lifestyle intervention and weight loss have been associated with the reduction of TNF-α, IL-8, IL-6, CRP and MCP-1 levels [50]. It becomes evident, therefore, that patients with psoriasis should be encouraged to attempt healthy lifestyle changes in order to maintain normal weight.

2.2. Dietary Patterns and Psoriasis

Apart from low-calorie diets, a number of nutrition strategies and dietary patterns such as gluten-free diet, Mediterranean diet and very-low-carb ketogenic diet have been proposed for weight loss achievement in patients with psoriasis. A diet rich in antioxidants can also be considered a substantial part of a comprehensive treatment regimen along with pharmacotherapy. Despite the lack of large randomized clinical trials to confirm the effect of different diets in patients with psoriasis, an abundance of research data highlights diet as a potential therapeutic target.

2.3. Supplements and Psoriasis

2.3.1. Vitamin D

As mentioned above, apart from being a calcium-regulating vitamin, vitamin D also exerts anti-inflammatory effects. The impact of 1,25(OH)2D3 on keratinocytes by inhibiting proliferation of hyperproliferative cells and increasing differentiation, together with its actions on T-cell activation, has rendered it a possible treatment option for patients with psoriasis [51][52]. According to recent data, patients with psoriasis have decreased vitamin D levels, and this possibly explains why the incidence of psoriatic disease is higher in locations less exposed to ultraviolet light, as this limited exposure leads to decreased vitamin D synthesis, together with the antiproliferative actions of ultraviolet radiation on keratinocytes [53][54]. Similarly, according to a case–control study, patients with psoriasis have lower 25-hydroxyvitamin D (25(OH)D) levels compared to the control group and are more likely to have 25(OH)D deficiency [55]. A possible explanation is that low vitamin D levels lead to the reduction of circulating T-cells and consequently to the dysregulation of immune balance [52]. For this reason, vitamin D and analogues have been proposed as possible treatments in psoriasis [51][56]. Topical therapy with vitamin D as an ointment or cream has been investigated thoroughly and the results indicate that vitamin D and analogues can be utilized either as monotherapy or in combination with a topical corticosteroid, methotrexate or cyclosporine [57][58][59]. The application of calcitriol ointment for eight weeks resulted in improvement of psoriatic lesions in approximately 34% of patients,

compared with 12% to 22.5% of controls [58]. Even more interestingly, vitamin D and analogues have the same efficacy as topical corticosteroids without the adverse effect of skin atrophy, and they are thus suitable for long-term treatment. However, the results regarding the efficacy of oral vitamin D supplementation are inconsistent. A prospective study by Merola et al., including 70,743 female nurses who completed semi-quantitative food frequency questionnaires in 1994, 1998, 2004 and 2006, showed no association between vitamin D intake and the development of psoriasis [60]. Siddiqui et al. conducted a randomized, controlled, double-blinded trial including 50 patients who received 1 μg/day Vitamin D3 supplementation or placebo. No difference between the interventional and control group in psoriasis severity was revealed, implying that Vitamin D3 supplementation is not effective as a treatment for moderate to severe psoriasis [61]. Similarly, a more recent study by Ingram et al. included 101 patients who either received 100.000 IU Vitamin D3/month or placebo and evaluated the relationship between Vitamin D3 intake and psoriasis severity (assessed by PASI score). After three months, there was no significant difference in PASI score between the two groups [62]. In accordance with these results, another RCT with 23 patients who received supplementation with 100.000 IU Vitamin D/month and 42 controls showed that there was no significant difference in any of psoriasis outcome measures (PASI, PGA, PDI) after 12 months [63]. Gaal et al. showed that 0.5 μg/day Vitamin D supplementation had significant immunomodulatory effect in patients with polyarticular psoriasis [64]. Various hypotheses have been made to explain these discrepancies; a main reason is that vitamin D levels are not primarily determined by intake, but rather through sun exposure, a variable which is difficult to ensure in any patient group [62]. In addition, in some studies where no correlation between vitamin D and PASI was found, analysis was limited to only one measurement per person and not on repeated measurements over a follow-up period, while the relationship between PASI and 25(OH)D has not been shown to be linear, either. Lastly, not all patients equally respond to vitamin D administration, a fact which may be attributed to vitamin D receptor (VDR) polymorphisms. In conclusion, according to The Medical Board of the National Psoriasis Foundation, vitamin D supplementation is not recommended in patients with psoriasis and normal serum Vitamin D levels. However, patients with Vitamin D deficiency should receive Vitamin D oral supplements for prevention of psoriasis-related comorbidities [65].

2.3.2. Vitamin B12

Vitamin B12 may have an impact on psoriasis through its contribution to nucleic acid synthesis. In vitro studies supported that Vitamin B12 regulates T-lymphocytes activation and cytokine secretion [66][67]. A few studies have reported an association between psoriasis and Vitamin B12 deficiency [68][69][70]. A retrospective observational study including 98 patients with psoriasis and 98 healthy individuals demonstrated that patients with psoriasis had increased homocysteine levels and lower serum levels of vitamin B12 and folic acid compared to healthy individuals [69]. In another report, the efficacy of vitamin B12 cream with avocado oil was investigated compared to the use of calcipotriol. After 8 weeks, treatment with calcipotriol had a more beneficial impact on psoriasis severity. However, after 12 weeks, no significant differences between the two treatment regimens were demonstrated [70]. Other studies have evaluated the impact of intramuscular administration of Vitamin B12 on the treatment of psoriasis with inconsistent results. Ruedemann et al. reported that the intramuscular administration of vitamin B12 for 10 days led to clinical improvement of psoriasis. In particular, in 11 out of 34 patients, the psoriatic lesions disappeared and 10 out of 34 reached 75% improvement in PASI score [71]. On the contrary, a double-blinded

controlled study by Baker et al. showed that intramuscular administration of vitamin B12 for 3 weeks offered no benefit to psoriatic patients [72]. In general, vitamin B12 is not suggested as a treatment option for psoriasis.

2.3.3. Polyunsaturated Fatty Acids

Research data regarding the effect of n-3 polyunsaturated fatty acids on the treatment of psoriasis are inconsistent. As oils of cold-water fish are rich in EPA and DHA, the effect of fish oil consumption and supplementation has been under investigation [73][74][75][76][77][78]. Collier et al. reported that daily intake of oily fish such as sardines, salmons, herrings and mackerels may promote clinical improvement. More specifically, the study included 18 patients who were advised to initially consume 170 g of white fish daily for 4 weeks and then they were randomized to consume either 170 g of white fish or 170 g of oily fish daily for six weeks; at the end of this second period, the diets were reversed for a further 6 weeks. The consumption of oily fish led to modest significant clinical improvement compared to white fish diet. Moreover, plasma EPA levels increased in patients with oily fish intake [73]. In 80 patients with chronic, stable psoriasis, 34 of whom also had psoriatic arthritis, supplementation with high doses of EPA and DHA for 8 weeks led to decreases in PASI score and a subjective improvement in joint pain [75]. Kragballe et al. reported that the cumulative consumption of 0.9 g/d EPA/DHA in 17 patients with psoriasis for 4 months led to moderate-excellent improvement in 10 of them; in a similar study, the supplementation at the dose of 1.9 g/d showed a significant decrease in PASI score after 4 and 8 weeks. On the contrary, an open study including 26 patients with psoriasis showed that fish oil supplementation did not improve psoriasis outcomes in any of the patients with plaque-type psoriasis except for one, a fact which was attributed to low dosage of EPA and the absence of dietary fat restriction [78].

The outcomes of randomized controlled trials are less encouraging [79][80][81][82]. In an RCT including 28 patients with stable chronic psoriasis, Bittiner et al. observed marked improvement of itching, erythema and scaling after 8 weeks of treatment with 3 g of n-3 fatty acids supplementation compared to olive oil supplementation [79]. On the other hand, two RCTs showed that 1.8 g of EPA for 8 weeks or 10 capsules of fish oil three times daily for three weeks did not achieve clinical improvement compared to olive oil supplementation [80][81]. Again, the unfavorable results can be possible explained by the low doses of EPA (1.8 g and 5.4 g daily) administered, together with the unrestricted dietary fat content, which leads to a lower concentration of EPA in cell membranes due to the competitive action of n-6 PUFAs. Søyland et al. conducted a 4-month double-blinded RCT, including 145 patients with moderate-to-severe psoriasis who were randomly allocated to either 6 g of fish oil daily or to isoenergetic corn oil containing mainly n-6 fatty acids. PASI score did not improve in either group, whereas scaling was reduced in both groups [82]. According to a recent review form Upala et al., including 12 studies, the results regarding the efficacy of n-3 PUFAs supplementation in the severity of psoriasis are still uncertain [83].

2.3.4. Selenium

Apart from the effects on oxidative stress, selenoproteins protect skin from harmful environmental factors such as ultraviolet (UV) rays, preventing keratinocytes apoptosis and increasing the cells' ability to breakdown peroxides [84]. Decreased selenium levels along with the concomitant depressed selenium-dependent enzymatic activity have been observed in patients with psoriasis. Moreover, Serwin et al. reported that low selenium concentration is

associated with increased severity of psoriasis in patients with disease duration more than three years [85]. Several studies have evaluated the efficacy of selenium supplementation in patients with psoriasis. Kharaeva et al. evaluated the efficacy of antioxidant supplementation in 58 hospitalized patients with severe erythrodermic and arthropathic forms of psoriasis. The authors reported that the combination of selenium aspartate, coenzyme Q10 and Vitamin E significantly improved psoriatic manifestations as assessed by PASI and Severity Score (symptom scoring for desquamation of plaques, plaque hyperemia, plaque inflammation, nail dystrophy, and joint pain) compared to placebo. Moreover, the activity of enzymes such as catalase and superoxide dismutase was diminished [86]. Juhlin et al. reported that selenium and Vitamin E supplementation for 8 weeks resulted in the increase of glutathione peroxidase in patients with psoriasis [87]. However, according to an older study in 69 patients, selenium and Vitamin E supplementation for 12 weeks did not reduce psoriasis severity [88]. Similarly, another case-control study, which included 37 patients, showed that selenium supplementation as add-on treatment to narrowband UVB therapy did not significantly improve psoriasis severity (assessed by PASI score) and TNF-R1 and CRP concentrations compared to placebo [89]. The same group examined the effect of selenium supplementation on TNF-R1 levels as add-on strategy to topical treatment with salicylic acid and dithranol ointment. The authors reported that despite the complete remission of skin lesions in both groups, the PASI score was higher in the treatment group, where the increased levels of TNF-R1 were also maintained [90]. These results implied that only inorganic Se compounds with cytostatic and cytotoxic activity may be of benefit to psoriasis patients; in addition, it was suggested that TNF-R1 reflects residual inflammation after clinical improvement of psoriatic lesions and that such high residual levels may be also attributed to the immunomodulating properties of selenium supplementation. As a result, a recommendation for selenium supplementation in patients with psoriasis cannot be established.

2.3.5. Zinc

Only two RCTs have been conducted to investigate the efficacy of oral zinc supplementation in patients with psoriasis. In the study by Clemmensen et al. [91], including 34 patients with psoriatic arthritis, a 24-week zinc supplementation improved joint pain and mobility and alleviated joint swelling. Conversely, Burrows et al. showed that 12 weeks of treatment with zinc sulphate supplementation did not lead to significant differences in psoriasis and severity index in 25 patients with chronic plaque psoriasis [92].

2.3.6. Polyphenols

The best studied phenolic compound regarding psoriasis is curcumin. [93]. Skyvalidas et al. suggested curcumin as a dietary immunosuppressant in patients with psoriasis due to in vitro inhibition of pro-inflammatory IFN-γ and IL-17 [94]. Furthermore, curcumin may enhance the secretion of anti-inflammatory cytokines such as IL-10 [95]. In a study by Antiga et al., curcumin supplementation was evaluated in 63 patients with moderate-to-severe psoriasis treated with topical steroids, who were randomly allocated to 2 g curcumin daily or placebo. After 12 weeks, the intervention group showed a greater improvement in median PASI score, along with a significant reduction in IL-22 serum concentration compared to the placebo group [96]. Bahraini et al. conducted an RCT including 40 patients with moderate-to-severe psoriasis, who were randomized to receive either turmeric tonic twice daily for nine weeks

or placebo. Results demonstrated that turmeric tonic significantly improved erythema, scaling and induration of lesions compared to controls [97]. Another trial indicated that oral curcumin administration in combination with visible light phototherapy can improve moderate to severe plaque psoriasis [98], and a similar result was demonstrated with curcumin as an add-on therapy to acitretin [99]. On the contrary, a study from Kurd et al. showed that 4.5 g/d of oral curcuminoid C3 complex as monotherapy had no effect on any of the disease parameters [100]. In general, curcumin has shown promising results which, however, need to be confirmed by large-scale studies.

Data about other polyphenols is scarce and is mostly based on experimental animal models. In vitro studies have shown that resveratrol, through activating the SIRT1 pathway, can induce apoptosis in the HaCaT keratinocyte cell line and inhibit the production of IL-17 by Th-1 cells [101]. These actions have a favorable effect on psoriatic lesions. In a mouse model of imiquimod-induced psoriasis, resveratrol administration significantly diminished the severity of skin lesions and was associated with beneficial modifications in expression of retinoic acid stimulated genes, and IL-17A and IL-19 mRNA levels [102]. Another polyphenol with remarkable effects on psoriasis is epigallocatechin-3-gallate (EGCG), which is the most abundant catechin in green tea and is known to possess anti-inflammatory, antioxidant and antiproliferative properties [103]. In a study by Zhang et al. in BALB/c mice, which were topically treated with imiquimod for 6 consecutive days, treatment with EGCG attenuated skin inflammation and reduced skin infiltration of T cells, IL-17, IL-22, IL-23 and MDA levels, and increased SOD and CAT bioactivities [104]. Similarly, in mice with flaky skin, treatment with water and green tea extracts led to delayed and milder onset of skin lesions compared to the animals treated with water only [105], and in another mouse model of psoriasis, treatment with a nanoparticle formulation of EGCG led to 20-fold stronger therapeutic effect compared to free EGCG in terms of erythema, scales, infiltratory immune cells and pro-inflammatory cytokines [106]. However, the lack of human studies prevents any recommendation for these polyphenols to be applied as adjuvant treatment for psoriasis.

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