Title: The Role of Vitamin D, Omega 3 and Weight Loss in the Management of Psoriasis: a review

Running title: The Role of Vitamin D, Omega 3 and Weight Loss in the Management of Psoriasis

Type: Review article

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Abstract:

Psoriasis is a multi-system, chronic, non-infectious, autoimmune, and inflammatory disorder that mainly affects the skin and has a multifactorial etiology. Nutrition has always been a very important line in the management of multiple diseases, whether dermatological or otherwise. Although it is more important in some diseases than others, nutrition could probably always play a role in augmenting and improving recovery. The advantages of optimizing nutrition and using it as a tool in the management of diseases are many, including cost, knowledge of long-term complications if present and less-to-no side effects compared to newly produced medications. Those nutrients are also likely to benefit one's overall health and not just the pressing condition. Thus, this review aimed at providing an overview of nutrients, such as vitamin D and omega-3 (n-3), and obesity in relation to psoriasis. Using standard search engines, the present study reviewed how vitamin D, n-3 and weight loss can help patients dealing with psoriasis. Evidently, vitamin D and n-3 were found beneficial for alleviating psoriatic symptoms, especially vitamin D, because of its steroid sparing effects. Weight loss in obese individuals with psoriasis was found not only in improving psoriatic lesions as reflected in Psoriasis Area and Severity Index (PASI) but also it protected them against metabolic syndrome. It is important also to note that for patients with psoriasis to use these substances as they could prevent them from developing complications when using conventional medications such as steroids and help them in other areas such as psoriatic arthritis, metabolic syndrome and cardiovascular diseases (CVDs).

Keywords: Psoriasis, vitamin d, omega 3, n-3, obesity, weight loss
1. Introduction

Psoriasis has a prevalence of 2-3% worldwide and is a multi-system, chronic, non-infectious, autoimmune, and inflammatory disorder that mainly affects the skin and affects both males and females equally [1]. Psoriasis has a multifactorial etiology, meaning it includes multiple factors resulting in its development, such as genetics (human leukocyte antigen (HLA) HLA-B13, -B17,-Bw57, and especially HLA-Cw6r) and environmental factors that include physical trauma (known as Koebner phenomenon), infections (e.g. streptococcal pharyngitis), medications (e.g. interferon, β-blockers and lithium) and stress. Psoriasis has a bi-modal age distribution as it could occur as early as 22 years of age or as late as 55 years of age. Early-onset predicts a more severe disease and is a poor prognostic factor [2]. The pathogenesis of psoriasis has several abnormalities that ultimately result in the production of psoriatic lesions. There is alteration of the skin cells “keratinocyte” with shortening of the cell cycle from 311 to 36 hours, causing 28 times the normal production of skin cells. Besides that, there is a presence of the inflammatory CD8+ cytotoxic T cells in the lesions and involvement of inflammatory mediators known as cytokines, which are small secreted proteins with unique interactive effects released by cells, like tumor necrosis factor-alpha (TNF-a) and interleukin (IL)-23 [3]. TNF-a is vital for the maintenance and induction of psoriatic lesions [4]. Another important inflammatory cell involved in psoriasis is the dendritic cell. Langerhans cell is one type of immature dendritic cell that can be activated to potently stimulate the release of said inflammatory cytokines like IL-23, activating
another inflammatory cell, Th17, starting a cascade of reactions (IL-17 and IL-22 release). This, in turn, exacerbates the process of keratinocyte proliferation and inflammation of the layer of the skin known as “the dermis” [5].

Psoriasis can be classified as non-pustular and pustular. The most common form is plaque psoriasis, which is characterized by well-circumscribed salmon-coloured plaques with silvery scales, usually affecting the extensor surfaces like elbows and knees. It is important to note that in various dermatological lesions, differences in skin colour could result in a different clinical presentation to what is classically known about a specific disease. For example: Although the other characteristics are present, the salmon colour in psoriasis is lost in dark-skinned individuals [6]. Another type is guttate psoriasis, which usually affects children following a streptococcal infection [5]. There is also another type of psoriasis more commonly associated with obesity known as inverse or flexural psoriasis, which involves the flexural skin folds such as the inguinal region, gluteal cleft, axilla and external genitalia [7]. A less common but possibly life-threatening type is erythrodermic psoriasis, which is the most common cause of erythroderma and could also be associated with autonomic instability (tachycardia, hypo/hyperthermia) [8].

The management of psoriasis includes topical and systemic treatments. The choice of therapy depends on many factors, such as the severity of psoriasis, the patient's comorbidities (e.g., CVDs), cost, and patient preference. Vitamin D has been used in the management of psoriasis for several years and exists in different forms such as calcipotriol, calcitriol, tacalcitol and maxacalcitol. Another micronutrient of importance in psoriasis is omega 3. Furthermore, weight loss is important in patients who are obese and have psoriasis. Psoriasis clinical outcome is usually assessed in one of two ways, with the more commonly used being PASI score and the second being Dermatology Life Quality Index (DLQI). PASI was introduced to assess response to
retinoids in psoriatic patients. It counts 4 areas (head and neck, upper limbs, the trunk, and lower limbs). The percentage of the skin area affected is given a score. Meanwhile, the 3 plaque signs (erythema, thickness/induration and desquamation/scaling) is assessed on a 5 point scale. The PASI score ranges from 0 to 72 [9]. DLQI measures dermatology patients’ quality of life by asking a few questions about the effect of the disease on one’s life [10].

2. Vitamin D and psoriasis
Vitamin D is a fat-soluble vitamin present in 2 forms, ergocalciferol (vitamin D2) from plants and cholecalciferol (vitamin D3) from animal-based foods. The majority of vitamin D in humans is due to cutaneous synthesis from exposure to sunlight [11]. Vitamin D has been proven to be effective in the management of psoriasis and has been integrated as first-line therapy in clinical settings. There are multiple reasons why vitamin D is thought to be important in the treatment of psoriasis. One reason is that there are many studies that have concluded that psoriatic patients are at higher risk of vitamin D deficiency compared to controls and that it correlated with the severity of the disease. However, it is not significantly associated with the incidence of psoriasis [12-16]. Seasonal variations occur in the serum levels of vitamin D, it is lower during winter, and these seasonal changes coincide with psoriasis symptoms being more severe during fall and winter. Vitamin D is also very beneficial in avoiding the harmful side effects of steroids, as topical use of vitamin D has a “steroid-sparing” effect. Calcitriol ointment is useful in sensitive areas prone to steroid-induced atrophy, such as the face and inguinal region [17]. The long-term application of steroids is complicated by striae, persistent erythema and telangiectasia. When applied over a large body surface area for a prolonged period, it also leads to suppression of the hypothalamic-pituitary axis [17]. Studies have found that in a subgroup of patients where the gene deletion
LCE 3B or 3C in the PSORS4 gene causes psoriasis, vitamin D is effective in the management plan by up-regulating those genes [11].

3. Topical vitamin D analogues

Vitamin D topicals exist in different analogues and can be used as monotherapy or in combination with other modalities, such as narrowband ultraviolet B therapy or steroids. The first produced analog, calcipotriol, was more effective and safer in the treatment of psoriasis over a 6 weeks period than the steroid topical (0.1% betamethasone 17-valerate ointment) (PASI score p <0.001) [18]. One of calcipotriol’s side effects was cutaneous irritation in up to 20% of patients, especially when applied to sensitive areas such as the face and intertriginous areas. Due to that, other analogs such as calcitriol, tacalcitol and the more recent maxacalcitol were developed [17]. Calcitriol is a 3 ug/g dose can be as effective as 50 ug/g calcipotriol and more tolerable in smaller doses (12 weeks long trial) (PASI score p =0.0035) [19]. Meanwhile, maxacalcitol in a 25 ug/g dose can be even more effective than 50 ug/g calcipotriol and, yet again, in a smaller dose (8 weeks long trial) (PASI score p <0.05) [20]. Another merit of the more recent analogs is that tacalcitol and maxacalcitol can be used once daily as opposed to twice daily calcipotriol, which is likely to increase compliance [20-21]. Calcipotriol 50 ug/ml solution over a 4 weeks period alone (p =0.005) or maxacalcitol 25 ug/g over a 16 weeks period in combination with 0.05% betamethasone steroid (PASI score p <0.01) can be used in the management of scalp psoriasis, which is one of the complaints psoriatic patients can present with [22-23]. Another common complaint is nail psoriasis, which poses a challenge to dermatologists as nails respond slowly and are hence difficult to treat. Both calcipotriol 50 ug/g for three months and tacalcitol 4 ug/g for six
months (PASI score p =0.001) ointments are of benefit in nail psoriasis, with calcipotriol being particularly effective in subungual hyperkeratosis, onycholysis and discoloration [24-25].

4. Oral vitamin D in psoriasis and related comorbidities
It has been established that psoriasis is an independent risk factor for CVDs and metabolic syndrome [26]. There is a higher prevalence of metabolic syndrome in psoriasis compared to controls (30.1% vs 20.6% respectively) (PASI score p =0.005) [27]. The exact link between metabolic syndrome, CVDs and psoriasis is poorly understood. However, one postulated mechanism mentioned attributes it to the pathophysiology of both being pro-inflammatory states [26]. Another mechanism could be genetic predisposition because the genes PSORS2, PSORS3 and PSORS4 predisposes to psoriasis and increases the susceptibility for metabolic syndrome and CVDs [28]. Studies have also shown that vitamin D insufficiency (20-29 ng/ml) and deficiency (<20 ng/ml) play a role in insulin action and secretion of which is involved in metabolic syndrome [26]. Vitamin D in metabolic syndrome and CVDs is of great importance, and the proof is that studies demonstrated how serum vitamin D concentrations were inversely associated with the prevalence of metabolic syndrome and the incidence of cardiovascular events [26]. Oral vitamin D (three vitamin D2 capsules 20,000 IU/capsule, every two weeks for six months) has been suggested as a possible adjunctive therapy in the management of psoriasis [29]. This is because of the fact that it was able to improve psoriasis symptoms and (PASI score p =0.039) while also working on the genes mentioned previously [29]. Those findings suggest that the use of vitamin D should not just be limited to ameliorating psoriatic lesions but also could be beneficial in treating psoriasis-related comorbidities. Nevertheless, few studies have shown the efficacy and safety of oral vitamin D in varying doses (0.5-4 pg/day for 36 months (PASI score p <0.001)
and (35,000 IU/day for six months) (PASI score p <0.01) when used for psoriasis, with no serious adverse effects [30-32]. A rare complication when it comes to oral vitamin D is its interference with calcium absorption in the gastrointestinal tract and subsequent hypercalcemia. Thus, it is recommended not to be applied to >30% of body surface area and should not be used for longer than 12 months [33].

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<tr>
<th>Author</th>
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<th>Study type</th>
<th>Dose</th>
<th>Sample size</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Kragballe K et al. [18]</td>
<td>1991</td>
<td>Denmark</td>
<td>RCT</td>
<td>Twice daily 50 µg/g calcipotriol vs. 0.1% betamethasone 17-valerate ointment</td>
<td>345 patients</td>
<td>Calcipotriol treatment was statistically more effective in decreasing erythema, lesions thickness, scaling, and overall PASI score as opposed to 0.1% betamethasone 17-valerate ointment in mild-moderate psoriasis Vulgaris (p &lt;0.001)</td>
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<td>Zhu X et al. [19]</td>
<td>2007</td>
<td>China</td>
<td>RCT</td>
<td>Calcitriol in a 3 µg/g dose vs. 50 µg/g calcipotriol</td>
<td>250 patients</td>
<td>Calcitriol is a 3 µg/g dose can be as effective as 50 µg/g calcipotriol and more tolerable in smaller doses (12 weeks long trial) (PASI score p =0.0035)</td>
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<td>Barker JN et al. [20]</td>
<td>1999</td>
<td>United Kingdom</td>
<td>RCT</td>
<td>25 µg/g of maxacalcitol ointment vs. 50 µg/g calcipotriol</td>
<td>144 patients</td>
<td>25 µg/g of maxacalcitol ointment once daily is more beneficial in reducing erythema and scaling than once daily 50 µg/g calcipotriol ointment (p &lt;0.05)</td>
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<tr>
<td>Study Authors</td>
<td>Year</td>
<td>Country</td>
<td>Study Type</td>
<td>Treatment Description</td>
<td>Patients</td>
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<td>Okubo Y et al. [21]</td>
<td>2014</td>
<td>Japan</td>
<td>RCT</td>
<td>0.05% betamethasone butyrate propionate (BPP) (once daily on weekends) and 25 µg/g maxacalcitrol lotion (MXA) (once daily on week-days)</td>
<td>31 patients</td>
<td>4 and 8 weeks of combination therapy are both statistically significant in decreasing symptoms before switching to MXA mono-therapy (p &lt;0.01). However, study suggests 8-week combination therapy is preferred for severe cases as they had more improvement at the end of the trial (p &lt;0.01)</td>
</tr>
<tr>
<td>Green C et al. [23]</td>
<td>1994</td>
<td>United Kingdom</td>
<td>RCT</td>
<td>50 µg/ml of calcipotriol solution twice daily</td>
<td>49 patients</td>
<td>60% patients showed clearance of psoriatic lesion or marked improvement vs 17% in the placebo group (p &lt;0.001)</td>
</tr>
<tr>
<td>Zakeri M et al. [24]</td>
<td>2005</td>
<td>Egypt</td>
<td>Case study</td>
<td>50 µg/ml of calcipotriol ointment twice daily on nails</td>
<td>24 patients</td>
<td>14 patients showed significant clinical improvement</td>
</tr>
<tr>
<td>Márquez Balbás G et al. [25]</td>
<td>2009</td>
<td>Spain</td>
<td>Clinical trial</td>
<td>Tacalcitol 4 µg/g</td>
<td>15 patients</td>
<td>After 6 months there was significant improvement in nail psoriasis. PASI score (p =0.001)</td>
</tr>
</tbody>
</table>
Table 1: Vitamin D studies

5. Mechanism of action of vitamin D in psoriasis
Vitamin D has been proven to be effective in the management of psoriasis and integrated as a first-line therapy in clinical settings. The efficacy of vitamin D on psoriatic patients was established because of its role in the pathogenesis of psoriasis. Vitamin D decreases inflammation by working on several inflammatory cells, such as plasmacytoid dendritic cells (PDC). Vitamin D receptors are found on pDC and, by disrupting T-cell proliferation and the mediator Interferon-y production, vitamin D can impair the capacity of pDC to induce an inflammatory response. Another inflammatory cell that vitamin D inhibits is Th17, ultimately suppressing Th17’s infiltration.
and the chemo-attractants psoriasin (S100A7) and koebnerisin (S100A15), resulting in less inflammatory cells in psoriatic lesions. Moreover, vitamin D suppresses the pro-inflammatory cytokines IL 12/23 p40, IL-1a, IL-1B, and TNF-a. The aforementioned cytokines and chemo-attractants further exacerbate the inflammation in psoriatic lesions since in psoriasis there is a high degree of inflammation and defective differentiation [11]. Vitamin D promotes proper skin maturation by inducing keratinocyte differentiation by increasing the synthesis of skin proteins, such as keratins, loricrin, involucrin and filaggrin, and enzymes such as transglutaminase [11]. Those anti-inflammatory properties are brought into effect because of the regulatory role of vitamin D on intracellular calcium. Vitamin D results in an increase in intracellular calcium because of rapid hydrolysis of phosphatidylinositol phosphate, affecting keratinization and modulation of inflammation through nuclear and non-nuclear mechanisms [11]

6. Omega 3 and psoriasis
N-3 is the micronutrient that should be taken into consideration in the diet of psoriasis patients, as it could yield improvements clinically. There are three types of n-3, α-linolenic acid, which is plant-derived, eicosapentaenoic acid (EPA) and docosahexaenoic (DHA) acid, both of which are from marine oils [34]. Omega-3 is synthesized by humans from α-linolenic acid, which can be found in green leafy vegetables, marine organisms such as fish and algae, or as oil in canola, linseed and soy [35]. Using fish oil in psoriasis has been recommended many times because of its beneficial effect in multiple different parameters, such as in the DLQI and PASI parameters. Metabolic disease, obesity and CVDs have all been associated with psoriasis [26]. Accordingly,
omega-3 is useful for prophylaxis against different diseases such as metabolic syndrome and obesity, and most notably for CVDs, as per the American Heart Association recommendation [36].

7. Omega 3 clinical trials
In ceaseless clinical trials, omega-3 in varying doses is significantly effective for patients with plaque psoriasis and psoriatic arthritis. N-3 as a combination treatment with other conventional psoriasis treatments was effective in improving the lesion area (15 weeks comparison between fish oil capsule, which has 3.6 g EPA and 2.4 g of DCHA plus UVB versus olive oil, which has 0 g EPA or DCHA plus UVB) (p <0.001) [37], the severity of skin lesions (p <0.0001) [37], and the quality of life in patients with psoriasis (2.6 g/day of n-3 polyunsaturated fatty acids (PUFA) plus biologic drugs like adalimumab versus only biologic for six months) (p <0.001) [38]. However, as monotherapy, a meta-analysis found that omega-3 was not more effective compared to controls like corn oil [36]. Moreover, monotherapy nor a combination of n-3 with other drugs eased pruritus (itching) (p =0.11) [38].

8. Omega 3 and psoriasis-related comorbidities
As mentioned previously, psoriasis is associated with other comorbidities such as obesity, metabolic syndrome and CVDs. Through its different anti-inflammatory pathways, n-3 is able to protect psoriasis patients against such comorbidities. N-3 could be cardioprotective as one study showed that it decreases heart rate, thereby decreasing the stress on the heart (3 g of PUFA, which has 50% of both EPA and DHA vs 3 g of olive oil, which has 80% of oleic acid and 20% linoleic acid for 24 weeks) (p =0.012) [39], indicating its role as a preventative measure for CVDs. In contrast, a meta-analysis suggests otherwise, illustrating that there is no cardioprotective effect [40]. Obesity is another comorbidity associated with psoriasis. One systemic review demonstrated that
n-3 was able to decrease obesity parameters like body weight, body mass index and waist circumference while also reducing triglycerides (fish oil vs placebo) (p <0.05) [36]. Furthermore, plant-derived n-3 (40 g/day of flaxseed) (alpha-linolenic acid) is said to be moderately protective against the development of diabetes mellitus as it improved the marker of insulin resistance (homeostatic model assessment of insulin resistance (HOMA-IR) (p =0.03) [41].

<table>
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<tr>
<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>Study type</th>
<th>Dose</th>
<th>Sample size</th>
<th>Conclusion</th>
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</thead>
<tbody>
<tr>
<td>Gupta AK et al. [37]</td>
<td>1989</td>
<td>United States</td>
<td>RCT</td>
<td>Fish oil capsule, which has 3.6 g EPA and 2.4 g of DCHA plus UVB vs. olive oil, which has 0 g EPA or DCHA plus UVB)</td>
<td>20 patients</td>
<td>Omega 3 significantly improves the lesion area (p &lt;0.001) and the severity of skin lesion (p &lt;0.0001)</td>
</tr>
<tr>
<td>Guida B et al. [38]</td>
<td>2014</td>
<td>Italy</td>
<td>RCT</td>
<td>2.6 g/day of n-3 PUFA plus biologic drugs like adalimumab vs. only biologics</td>
<td>44 patients</td>
<td>Improvement in quality of life in patients with psoriasis (p &lt;0.001) and triglycerides (p &lt;0.05)</td>
</tr>
<tr>
<td>Bloedon LT et al. [41]</td>
<td>2008</td>
<td>United States</td>
<td>RCT</td>
<td>40 g/day of flaxseed while following low fat low cholesterol diet</td>
<td>62 patients</td>
<td>Moderately protective against the development of diabetes mellitus as it improved the marker of insulin resistance (HOMA-IR) (p =0.03)</td>
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</table>

**Table 2:** Omega 3 studies

9. Mechanism of action of omega-3 in psoriasis
There are several mechanisms by which omega-3 brings about the anti-inflammatory properties of which are necessary for battling psoriasis. Though first, one needs to understand the connection between omega-3 on psoriasis and omega 6, which is derived from the oils like the commonly used frying oil of sunflower and soybean [35]. Omega 6 as arachidonic acid is abundantly found in psoriatic lesions. It is metabolized to leukotriene B4 by enzymes called cyclooxygenase or lipoxygenases. This metabolite is a key player in attracting the first line of defense in our body, which are the neutrophils, resulting in inflammation in psoriasis [35]. Marine n-3 (EPA), has a metabolite or a mediator known as leukotriene B5, which is much less potent than the metabolite leukotriene B4 [34]. When n-3 is added to the diet, it inhibits dihomo-y-linolenic acid, thus inhibiting production of arachidonic acid and resulting in an increase in EPA: AA ratio. This increase results in a notable decrease in leukotriene B4, which is a stronger catalyst of inflammation than leukotriene B5. Therefore, the end outcome is less inflammation and consequently improvements in psoriasis symptoms [34]. Resolvins, which are mediators isolated from marine n-3 (EPA), decrease inflammatory cell activity through reducing dendritic cell and neutrophil migration, dermal inflammation and IL-12 production, further reducing inflammation in psoriasis [34]. Another mechanism is that polyunsaturated fatty acids, which include n-3, were found to influence toll-like receptors (TLR). TLRs are found in many inflammatory cells in our bodies, like monocytes, B and T cells. DHA and EPA are natural TLR ligands, meaning they can bind to such receptors such as TLR2 on monocytes, in turn decreasing pro-inflammatory mediators and easing psoriatic lesions [35].

10. Psoriasis and obesity

Obesity is defined as having a body mass index over 30 kg/m2 and its hallmark is abnormal lipid levels in the body. Obesity is more prevalent in psoriatic patients compared
to controls [42] and is associated with higher PASI scores [43], as one study showed that patients who had severe psoriasis (odds ratio 1.79) were more obese than patients with mild psoriasis (odds ratio 1.27) or controls [44]. Obesity is not only a risk factor for psoriasis but also an obstacle in the management of psoriasis as obesity is associated with decreased response to systemic and biological treatments [45]. Because obesity is linked with other diseases such as metabolic syndrome and hepatic steatosis, there could be an increased risk of adverse effects [45]. This raises obesity and psoriasis even more and points towards obesity. Diet control and weight loss are possible management plans in psoriasis. Weight loss could be achieved in different ways, whether through lifestyle modification (diet and physical exercise), pharmacological or surgical approaches.

11. Weight loss through lifestyle modification
Different low calorie diets were explored in clinical trials to see the effect on psoriasis. In one clinical trial, 82 patients with plaque psoriasis were either given a four-week low calorie diet (855 kcal/day) or standard hospital diet (2100 kcal/day) plus topical therapy. The low-calorie diet consisted of 33.9 g/day of proteins, 14.7 g/day of fat, and 149.6 g/day of carbohydrates. The low calorie diet group had significantly better total cholesterol (p <0.01), triglycerides (p <0.001), low density lipoprotein (p <0.01) and a very good clinical outcome (no p-value reported) as opposed to controls [46]. In another randomized controlled trial of 60 patients with BMI above 27 and plaque psoriasis, the patients were subjected to a low-calorie diet (Cambridge diet, which constitutes 8 weeks of 800-1000 kcal/day of meal bars, sachets to make shakes, soups and porridge followed by eight weeks of 1200 kcal/day of regular meals and two formula diet) or routine diet. The low-calorie diet group had a mean loss of 15.4 kg by week 16 (p <0.001). Furthermore, they had better improvement in PASI score (p <0.06) and DLQI
(p =0.02) compared to controls. Adverse effects due to the low-calorie diet included fatigue, mild headaches, constipation, dizziness, cold sensitivity and hunger [46]. Weight loss could also be coupled with exercise, as done in another study where 303 overweight or obese patients with plaque psoriasis, who did not achieve clearance on systemic therapy after 4 weeks, were either given dietary and physical exercise plans or just counselling. In the aforementioned, after 20 weeks, there was a significant improvement in PASI score and psoriasis severity compared to controls (PASI reduction of 48% compared to 25.5%) (p =0.02) [47]. This gives hope for psoriasis patients whom systemic therapy fails to help.

When it comes to dietary weight loss effect on psoriasis, there are three randomized controlled trials reporting statically significant improvements clinically in PASI score after diet control, which achieved at least 5% weight loss (p <0.001). In one of the three randomized controlled trials, there was diet restriction calculated in accordance to each patient by a dietician, with a low-calorie diet consisting of boiled and fresh vegetables, rice, wheat bread, and low-calorie fruits like apples [48]. The other trial used a low energy Cambridge diet with improvement in PASI score (p =0.06) [49]. The third trial included an energy-restricted diet designed to increase consumption of n-3 rich food, also causing an improvement in PASI score (p <0.021) [38]. Other trials did not result in improvements in psoriasis severity after weight loss, which could be due to the fact that they did not reach 5% weight loss or because of low baseline PASI or small sample size [50]. What is currently promising is that weight loss through lifestyle intervention has a dose-response relationship with psoriasis, as the greater the weight loss, the less severe the psoriasis is [50].

12. Pharmacological weight loss
There are limited studies done on the effect of pharmacologically-induced weight loss on psoriasis. The effect of glucagon-like peptide-1 (GLP1) liraglutide and exenatide on obese patients with psoriasis were explored. The study found that the mean weight change was -4.1% to -7.3% [50]. Moreover, there was a significant reduction in PASI score and psoriasis severity compared to baseline PASI reduced from 12 ± 5.9 to 9.2 ± 6.4 (P =0.04) [50]. This effect of GLP1 is possibly only for diabetic patients because, in one study using liraglutide on obese non-diabetic patients vs placebo, liraglutide had no similar findings [50].

**13. Bariatric surgery and psoriasis**
A population-based cohort study examined the effect of various bariatric surgical interventions and the incidence of psoriasis. The study found that gastric bypass (p =0.004) but not gastric banding (p =0.72) decreased the risk of incidence of psoriasis and psoriatic arthritis [50]. This difference in interventions is possible because gastric bypass leads to more weight loss than gastric banding [50].

<table>
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<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>Study type</th>
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<th>Conclusion</th>
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<p>| Pona A et al. [46] | 2019 | N/A | Systemic review | Low-calorie diet (855 kcal/day) or standard hospital diet (2100 kcal/day) plus topical therapy. The low-calorie diet consisted of 33.9 g/day of proteins, 14.7 g/day of fat, and 149.6 g/day of carbohydrates | 82 patients | The low-calorie diet group had significantly better total cholesterol (p &lt;0.01), triglycerides (p &lt;0.001), low-density lipoprotein (p &lt;0.01) and a very good clinical outcome (no p-value reported) as opposed to controls. |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
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<th>Study Design</th>
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<tbody>
<tr>
<td>Naldi L. et al. [47]</td>
<td>2014</td>
<td>Italy</td>
<td>RCT</td>
<td>The dietitian allowed three main meals and a maximum of two snacks (55% carbohydrates, 30% fat and 15% protein). Energy intake set at 0.8 x resting metabolic rate for 12 weeks followed by 1 x resting metabolic rate for eight more weeks plus exercise vs just counselling</td>
<td>303 patients</td>
<td>After 20 weeks, there was significant improvement in PASI score and psoriasis severity compared to controls (PASI reduction of 48% compared to 25.5%) (p =0.02)</td>
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<td>Study Authors and Year</td>
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<tr>
<td>Al-Mutairi N et al. [48]</td>
<td>Kuwait</td>
<td>RCT</td>
<td>Diet restriction calculated in accordance to each patient by a dietician, with a low-calorie diet comprising boiled and fresh vegetables, rice, wheat bread, and low-calorie fruits like apples, plus patients were receiving biological agents</td>
<td>262 patients</td>
<td>Improvement in PASI score (p &lt;0.001)</td>
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<td>Jensen P et al. [49]</td>
<td>Denmark</td>
<td>RCT</td>
<td>Low energy diet consisting of 800-1000 kcal/day for eight weeks followed by eight weeks of normal diet reaching 1200 kcal/day</td>
<td>60 patients</td>
<td>Improvements in PASI score favours low energy group (p =0.06)</td>
<td></td>
</tr>
</tbody>
</table>
Table 3: Weight loss studies

14. Pathogenesis of obesity and psoriasis
There is a complex relationship between obesity and psoriasis. Adipokines, which are mediators released in higher than normal quantities in obese individuals, play a big role in the link between psoriasis and obesity [43]. There are different types of adipokines or hormones. They can be pro or anti-inflammatory. Pro-inflammatory adipokines like leptin, which is able to regulate the proliferation of keratinocytes, and pro-inflammatory cytokines like TNF-a, IL-1B, IL-6 are synthesized and secreted in excess in psoriasis by dysfunctional adipocytes of obesity. Anti-inflammatory adipokines like omentin and adiponectin are decreased in psoriasis and obesity, respectively [43]. This imbalance of pro and anti-inflammatory mediators, which could be due to dyslipidemia in obesity, increases the risk of psoriasis and is the reason why obesity is linked with other diseases such as psoriasis and metabolic syndrome [43].

15. Results
Vitamin D is beneficial in the management of psoriasis, for it does not only improve psoriatic lesions significantly but also has no to very few side effects. Its most advantageous benefit is its steroid-sparing effect, thus allowing patients to use it for longer periods without the concern of using steroids with its major side effects. Psoriasis, which is an independent risk factor for CVDs, illustrates the importance of the usage of vitamin D in psoriasis due to its association with the prevalence of metabolic syndrome and the incidence of cardiovascular events. It also manages to tackle a challenge that dermatologists face by the ability of topical vitamin D to alleviate nail psoriasis. N-3 has been proven to be an effective combination of conventional therapies of psoriasis, not only for alleviating patients symptoms but also as prophylaxis against psoriasis-related diseases like metabolic syndrome, obesity and CVDs. The aforementioned all
shines the light on the importance of such nutrients for psoriatic patients, which poses minimal to no adverse effects, giving it an advantage and appeal for patients. Weight loss, regardless of the method, is an efficient way to help patients suffering from psoriasis. This is especially true for those with psoriatic arthritis. Moreover, weight loss will also protect patients from metabolic syndrome. These researches validate the link between obesity and psoriasis and its role of in its management.

List of Abbreviations:

CVDs: Cardiovascular diseases.
DHA: Docosahexaenoic acid.
DLQI: Dermatology life quality index.
EPA: Eicosapentaenoic acid.
HLA: Human leukocyte antigen.
IL: Interleukin.
N-3: Omega-3.
PASI: Psoriasis area and severity index.
PUFA: Polyunsaturated fatty acids.
RCT: Randomized controlled trial.
TNF-α: Tumor necrosis factor-alpha.

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