ejpmr, 2025, 12(3), 21-27

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

EFFICACY AND ENDURANCE OF HIGH DOSES OF ORAL VITAMIN D3 IN THE TREATMENT OF PSORIASIS VULGARIS

Roula Baddour[1], Yousef Zrek[2] and Marah Aldali[3]*

[1]Professor-Department of Dermatology and Venerology, Faculty of Medicine, Latakia University, Latakia, Syria.
[2]Assistant Professor-Department of Laboratory, Faculty of Medicine, Latakia University, Latakia, Syria.
[3]PhD Student-Department of Dermatology and Venerology, Faculty of Medicine, Latakia University, Latakia, Syria.

***Corresponding Author: Marah Aldali**

PhD Student-Department of Dermatology and Venerology, Faculty of Medicine, Latakia University, Latakia, Syria.

Article Received on 07/01/2025 **Article Revised on 28/01/2025** **Article Published on 18/02/2025**

ABSTRACT

Background There are limited randomized controlled trials of oral vitamin D supplementation in psoriasis, especially in Asia, and the results are inconclusive. **Objective:** To investigate the clinical effect of oral vitamin D supplementation on psoriasis. **Methods:** A study was conducted on 50 patients who were given vitamin D at a dose of 60,000 IU every two weeks for 6 months. Serum vitamin levels was measured. The disease was evaluated clinically using the area and severity index. **Results:** Giving oral vitamin D to psoriasis patients leads to an increase in the level of the vitamin in the serum after 3 and 6 months (average vitamin D 17.2 - + 5.3, and after 3 and 6 months 24.15 - + 4.5 and 40.1 - + 10.8, respectively) in addition to clinical improvement with a decrease in the PASI index after 3 and 6 months (average PASI 8.6 - +3.2 and after 3 and 6 months 6.1 - +2.5 and 3.7 - +2.8 respectively) and no significant side effects were recorded. **Conclusion:** Oral vitamin D supplementation in patients with psoriasis increased the serum vitamin D level and significantly improved the treatment outcome without increasing adverse events.

KEYWORDS: psoriasis, serum levels of vitamin D.

INTRODUCTION

Psoriasis is a common, chronic, relapsing inflammatory disease that affects approximately 1-3% of the population. It manifests as erythematous, scaly plaques on the scalp, knees, elbows, and lower back, most commonly. There are many hypotheses proposed to explain the mechanism of the disease, including genetic and immunological theories, and one of the most important theories is that it is a T-cell-mediated disease.

The main disorder in psoriasis is a disorder of keratinocyte proliferation, but the presence of a mixed inflammatory infiltrate of leukocytes in psoriatic skin has implicated the immune system in the pathogenesis, as the interaction between keratinocytes, immune cells, and cytokines secreted by these cells, including cells of the innate immune system (plasma dendritic cells producing IFN-a, myeloid dendritic cells producing TNF-a, IL-23, and IL-12, macrophages, and neutrophils), cells of the adaptive immune system (CD4+ T cells, especially their Th17 subsets producing IL17A in addition to IL-17F, IL-21, IL-6, and TNF-a, and Th1 producing IFN-y and IL-2, and regulatory T cells) and vascular changes may contribute to the initiation and maintenance of the dermatitis characteristic of psoriasis. The main source of vitamin D is through exposure to sunlight and its production in the skin, while foods and nutritional supplements are secondary sources of the vitamin. Vitamin D itself is not biologically active, so it must be metabolized to reach its active form, which is 1-25 dihydroxyvitamin D.

Vitamin D is metabolized by hydroxylation at the 25-site in the liver and the 1a-site in the kidney through cytochrome oxidase p450 enzymes.

Vitamin D receptors (VDR) are found in the skin, bone, colon, breast, prostate, muscle, vessels, brain, and immune cells, which explains its wide-ranging effects on the body and its contribution to many inflammatory and immune diseases and cardiovascular disorders.

Many recent studies have indicated the importance of the role of vitamin D in the pathogenesis of psoriasis, as it is an immune modulator that affects the proliferation of keratinocytes, as it inhibits the genes responsible for the proliferation of keratinocytes, in addition to its role in regulating the synthesis of glucosylceramide, which is necessary for the integrity of the skin barrier, as well as interfering with the innate and acquired immune response through its effect on T cells and the production of inflammatory cytokines. Therefore, changes in the

level of vitamin D create changes at the level of the skin barrier.

Importance of the research

The importance of the research comes from the existence of many recent global studies that have shown low serum levels of vitamin D in psoriasis patients, and therefore its oral replacement may have a role in treating this disease or reducing its severity, which may make it a proposed treatment for psoriasis or a support for other traditional treatments.

Research objective

- Primary objective: Evaluating the effectiveness of oral vitamin D in treating psoriasis vulgaris (Decrease in PASI index with high serum levels of vitamin D)
- Secondary objectives: Studying the side effects of vitamin D in treated patients.

MATERIALS AND METHODS

Type of study Before & After study

Research sample

The studied sample consisted of patients in Tishreen University Hospital in Lattakia during the period between 2021-2023 who met the study conditions and their number was 50 patients.

Acceptance criteria

- Plaque psoriasis patients over 18 years of age who have low serum levels of vitamin D.

Exclusion criteria

- Patients with renal and hepatic failure
- Patients with malabsorption
- Patients with high calcium
- Patients with a history of kidney stones
- High parathyroid hormone
- Ineligible patients
- Pregnant and lactating women
- Those taking immunosuppressants
- Those taking certain medications such as thiazides, antiepileptics, anticoagulants or bisphosphonates.
- Those currently taking vitamin D or during the previous two months at a dose greater than 1000 IU per day.
- Those currently undergoing ultraviolet radiation therapy or during the previous month.

The patients were examined, diagnosed and informed consent was obtained for their entry into the treatment plan.

The Psoriasis Severity Index (PASI) was calculated and divided as follows

The Psoriasis Severity Index (PASI)	
PASI < 7	Mild psoriasis
PASI 7-12	Moderate psoriasis
PASI > 12	Severe psoriasis

Patients were questioned about the following information

- Age & Gender
- Skin color and Fitz-Patrick classification
- Current or past medications and treatments

Evaluation was done at the first meeting, then after 3 months, and after 6 months.

Patients were replaced with a dose of 120,000 IU monthly (60,000 IU every 2 weeks) for 6 months.

Serum vitamin D levels were measured and classified as follows:

Serum levels of vitamin D	
< 20 ng/ml	Severe deficiency
21-29ng/ml	Insufficiency
30-100ng/ml	Sufficiency
>100ng/ml	Toxicity

Patients were followed up and evaluated at each visit for any side effects such as thirst, constipation, nausea and vomiting.

Patients were contacted regularly in case of more serious symptoms such as cardiac arrhythmia, loss of appetite, weight loss and polyuria.

Statistical study

The data was processed using the SPSS program, version 26, according to the appropriate statistical methods for the data. A descriptive study of the sample was conducted and then an analytical study that served the research objectives. The statistical methods used include the Student test for independent samples, a one-way analysis of variance test, pivot tables, and a study of the relative risk factor.

RESULTS

Distribution of the sample according to gender, age, and skin tone

The study included 26 females (52%) and 24 males (48%), and The mean age of the sample was 13.9+- 40.5, with the largest number of patients aged between 26-35 (30%), The number of patients with skin color III according to Fitzpatrick classification was 28 patients (56%).

Table 1: Distribution of the sample according to gender, age, and skin tone.

			Frequency	Percent	Valid Percent	Cumulative Percent
Gender	valid	Male	26	52.0	52.0	52.0
		Female	24	48.0	48.0	100.0
		Total	50	100.0	100.0	
Age	valid	≤25	9	18.0	18.0	18.0
		26-35	15	30.0	30.0	48.0
		36-45	6	12.0	12.0	60.0
		46-55	11	22.0	22.0	82.0
		>55	9	18.0	18.0	100.0
		Total	50	100.0	100.0	
Skin Tone	valid	Fitzpatrick III skin tone	28	56.0	56.0	56.0
		Fitzpatrick IV skin tone	22	44.0	44.0	100.0
		Total	50	100.0	100.0	

Changes in vitamin D and PASI values during treatment

The table shows a gradual increase in vitamin D values during period until six months of the treatment, which is consistent with the nature of the treatment through the vitamin doses taken. The table also shows a gradual decrease in PASI values during period until six months of the treatment, which is consistent with the nature of the study that shows improvement in patients through a decrease in PASI values with the vitamin doses taken.

Table 2: Changes in vitamin D and PASI values during treatment.

		N	Mean	Std. Deviation	Std. Error	Min	Max
PASI	Initial examination	50	8.6620	3.29817	.46643	3.00	15.20
	After 3 months	50	6.1500	2.51057	.35505	2.80	12.20
	After 6 months	50	3.7460	2.82895	.40007	0.00	10.10
Vitamin D	Initial examination	50	17.2658	5.32024	.75240	10.10	26.40
	After 3 months	50	24.1500	4.55874	.64470	12.50	29.60
	After 6 months	50	40.1000	10.89473	1.54075	10.00	62.80

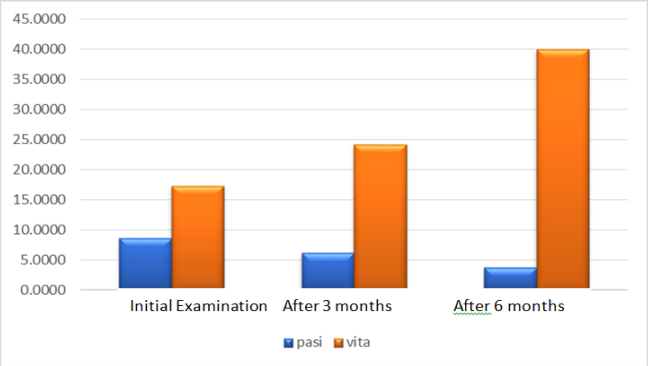

Figure 1: Changes in vitamin D and PASI values during treatment.

Study of the correlation between vitamin D and PASI values during the treatment period

The sig value is less than 0.05, which means that there is a significant correlation between vitamin D values and PASI values during the treatment period, and the Pearson correlation coefficient value was equal to -0.514, which means that there is a moderately strong inverse correlation between vitamin D values and PASI values for the sample during the treatment period.

Table 3: Correlations between vitamin D and PASI values during treatment.

		PASI	Vitamin D
PASI	Pearson Correlation	1	-.541**
	Sig. (2-tailed)		.000
	N	150	150
Vitamin D	Pearson Correlation	-.541**	1
	Sig. (2-tailed)	.000	
	N	150	150
****. Correlation is significant at the 0.01 level (2-tailed).**			

CONCLUSION

The increase in vitamin D values has a direct relationship with the decrease in PASI values in the studied sample during the treatment period.

Study of the correlation between response to treatment and skin tone

The test of differences for two independent samples was relied upon, and the results were as follows:

Table 4: ANOVA correlation of response and treatment and skin tone.

Improvement rates After 6Months Of Treatment	Levene's Test for Equality of Variances		t-test for Equality of Means				
	F	Sig.	T	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
Equal variances assumed	1.527	.223	.187	48	.852	.01568	.08366
Equal variances not assumed			.183	39.8	.856	.01568	.08587

According to Table 4, the sig value was greater than 0.05, which means that there are no significant differences between the improvement rate as a result of treatment and the skin tone pattern of the third or fourth degree, as shown in the following Table 5:

Table 5: Descriptives correlation of response and treatment and skin tone.

Skin tone		N	Mean	Std. Deviation	Std. Error Mean
Improvement rates After 6 Months Of Treatment	Fitzpatrick skin tone III	28	.5529	.26408	.04991
	Fitzpatrick skin tone VI	22	.5372	.32776	.06988

Table 5 shows the statistical descriptions of the improvement rate for each sample member based on the color pattern at the beginning of treatment, not exceeding 0.015, which means there is no difference in improvement based on the skin tone, and thus we can conclude that there is no correlation of the skin tone at the beginning of treatment on the improvement rate for the sample members.

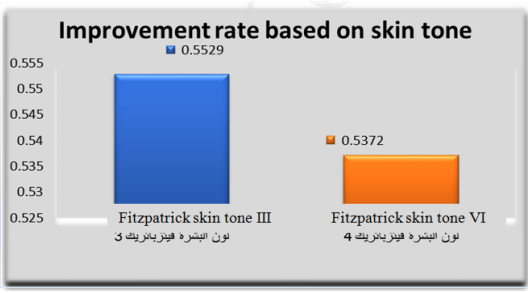

Figure 2: Comparison of the average percentage of improvement based on skin color.

The figure shows the great convergence in the average percentage of improvement for the sample members after 6 months of treatment, and it was divided on the basis of skin tone (Fitzpatrick classification) upon the initial examination at the beginning of treatment.

Note: (The improvement rate of 70% corresponds to 0.7 and the improvement rate of 50% corresponds to 0.5 ..... and so on in the statistical table).

Study of the correlation between response to treatment, patient age, and severity of illness at admission

Table 6 shows that the sig value is greater than 0.05, which means that there is no effect of age on the level of response to treatment in the studied sample, Table 7 also shows that the sig value is greater than 0.05, which means that there are no significant differences between the average percentage of improvement in patients according to the level of severity of the injury at the initial examination (PASI).

Table 6: ANOVA correlation between response to treatment and patient age; Improvement rate after 6 months.

	Sum of Squares	df	Mean Square	F	Sig
Between Groups	.498	4	.124	1.537	0.208
Within Groups	3.644	45	.081		
Total	4.142	49			

Table 7: ANOVA correlation between response to treatment and severity of illness; Improvement rate after 6 months.

	Sum of Squares	df	Mean Square	F	Sig
Between Groups	.216	2	.108	1.295	0.283
Within Groups	3.926	47	.084		
Total	4.142	49			

Comparison of the average improvement rate based on the severity of the disease upon admission

Table 8 shows a comparison of the average rate of improvement as a result of treatment among the sample members after dividing them based on the severity of the disease at the initial examination. The figure shows that there is an increase in the level of improvement with the increase in the severity of the disease from the beginning of treatment.

Table 8: Descriptives of the relationship between response to treatment and severity of disease upon admission; Percentage of improvement after 6 months.

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max
					Lower Bound	Upper Bound		
Mild	15	.4525	.22652	.05849	.3270	.5779	.00	.72
Moderate	24	.5667	.32890	.06714	.4278	.7056	.00	1.00
Severe	11	.6285	.26815	.08085	.4483	.8086	.31	1.00
Total	50	.5460	.29074	.04112	.4634	.6287	.00	1.00

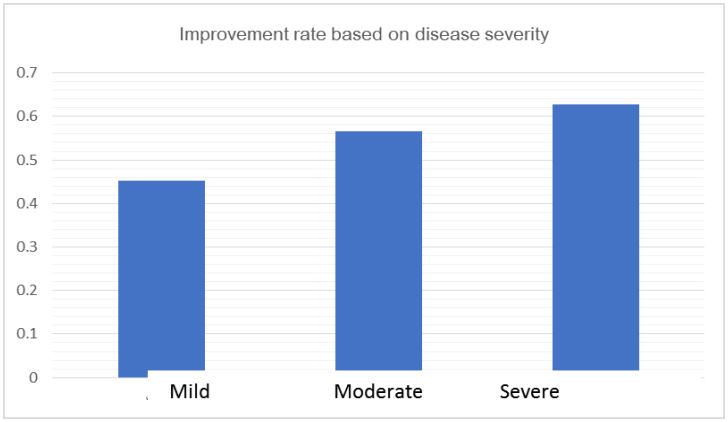

Figure 3: Comparison of mean percentage of improvement based on disease severity at admission.

The chart shows a comparison of the average percentage of improvement due to treatment among the sample members after dividing them based on the severity of the disease at the initial examination at admission. The chart shows that there is an increase in the level of improvement with the increase in the severity of the disease from the beginning of treatment, as the greatest improvement was for individuals who had a high severity of the disease, while the lowest percentage of improvement was for patients who had a mild disease at the beginning of treatment.

DISCUSSION

This study included 50 patients with plaque psoriasis and vitamin D deficiency and the results were as follows

- The study included 26 females (52%) and 24 males (48%).
- The mean age of the sample was 13.9+- 40.5, with the largest number of patients aged between 26-35 (30%).
- The number of patients with skin color III according to Fitzpatrick classification was 28 patients (56%).
- The mean PASI at admission was 3.2+- 8.6, after 3 months of treatment 2.5+- 6.1, after 6 months of treatment 2.8 -+ 3.7.
- The mean vitamin D at admission was 5.32+- 17.26, after 3 months 4.55+- 24.15, and after 6 months 40.10+- 10.89.

Thus, we conclude that the increase in vitamin D has a direct relationship with the decrease in PASI values during the treatment period

- 30-50% improvement occurred in 19 patients (38%).
- 50-80% improvement occurred in 17 patients (34%).
- 100% improvement, i.e. complete recovery, occurred in 9 patients (18%).
- The number of patients who did not achieve any improvement (no recovery) was 5 patients (10%).
- There was no relationship between response to treatment and skin color or patient age.
- There was no relationship between response to treatment and severity of disease upon admission.

- No significant side effects were recorded, and two side effects, nausea and constipation, were mentioned in 14 patients (28%).

By comparing results of this study with global studies

- In the study of Finamor et al… [8] conducted in Hungary in 2013 and included 9 patients at a dose of 35 thousand IU/day for 6 months, the results were as follows: All patients achieved an improvement rate of +3 and +4 without significant side effects.
- In the study of Hata et al.. [9] conducted in Brazil in 2014 and included 16 patients at a dose of 4000 IU/day for 6 months, the results were as follows: No change in PASI was recorded (i.e. no improvement).
- In the study of Jarret et al… [10] conducted in the United States in 2018 and included 65 patients at a dose of 100 thousand IU monthly (3300 IU/day) for 4 years, the results were as follows: The results did not specify the use of vitamin D3 at a monthly dose of 100 thousand IU as a treatment for mild psoriasis in ages over 50 years.
- In the study by Ingram et al…[11] conducted in New Zealand in 2018 and included 101 patients with a dose of 200,000 IU monthly initially and then 100,000 IU monthly for 11 months, the results were that there was no benefit from the treatment.
- In the study by Disphanurat et al…[12] conducted in Thailand in 2019 and included 45 patients with a dose of 20,000 IU every two weeks for 6 months, the results were as follows:

PASI improved moderately after 3 and 6 months and no side effects were recorded.

Psoriasis Area and Severity Index (PASI)

0	no improvement
+1	mild improvement in psoriasis index up to 25%
+2	moderate improvement between 26 to 50%
+3	noticed improvement between 51 to 75%
+4	more than 75% improvement to cure

Limitations and disadvantages of the study

- Not following up with patients after the proposed treatment period to study their relapse due to financial obstacles and difficulty communicating with patients and their commitment to the proposed treatment due to the long study period extending for 6 months.
- Not studying other clinical forms of psoriasis such as pustular psoriasis and erythroderma psoriasis due to the long study period and considering these patterns as emergency cases that need rapid medical intervention.

CONCLUSIONS

- Vitamin D is a good treatment option for plaque psoriasis patients at a dose of 120,000 international units monthly, where 18% of patients achieved complete recovery, 38% of patients achieved an improvement rate between 30-50%, and 34% of patients achieved an improvement rate between 50-80%, while 10% of patients did not achieve any improvement.
- The increase in vitamin D levels during treatment has an inverse correlation with the PASI index.
- There is no correlation between the response to treatment and each of the severity of the disease at admission, the patient's age, and skin color.
- No significant side effects were recorded, and two side effects were mentioned, which are nausea and constipation, in 28% of patients.

Recommendations

- Oral vitamin D is considered a good treatment option for treating plaque psoriasis in those who have low levels of it in the laboratory.
- Do not fear the serious side effects of vitamin D, as it is a safe and tolerable treatment with studied doses and duration and with appropriate patient selection.
- Conducting future joint interventional therapeutic studies that include vitamin D with other known traditional therapeutic options for treating psoriasis, such as ultraviolet radiation or methotrexate in small doses or other topical treatments that enhance the combined benefit, which will be positively reflected on the clinical side.
- Conducting future comparative studies between the effectiveness of vitamin D as a therapeutic option and other proposed treatments for psoriasis.
- Conducting future studies that include different doses of vitamin D, whether more or less than the dose studied in this research, with different treatment durations, and studying the results of this change on the clinical improvement of the disease and on the potential side effects of oral vitamin D.

DECLARATION

Ethical Statement

All methods were carried out in accordance with relevant guidelines and regulations. Ethical approval for the current study has been obtained from the institutional review board of Latakia University with the ethical number: (IRP:GDDS6545). We confirm that all experiments were performed in accordance with the Declaration of Helsinki

ACKNOWLEDGMENT: None.

Consent to publish: Written informed consent for publication was obtained from all authors.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Funding and financial support were not obtained from any individual, institution, agency, drug industry, or organization.

Conflict of Interest: The authors reported no potential

conflicts of interest.

Transparency statement: I affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Author's contribution

Conceptualization, Methodology, Validation, Formal analysis, Data curation, Writing original draft preparation, Visualization: **Marah Aldali**

Writing review and editing, Supervision: **Roula Baddour, Yousef Zrek**

All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. *Immunocompetent cells in psoriasis. In situ immunophenotyping by monoclonal antibodies.* Bos JD, Hulsebosch HJ, Krieg SR, et al., Arch Dermatol Res., 1983; 275: 181.
2. P*athophysiology of psoriasis*. Blauvelt A, Ehst BD, *uptodate, 2017. https://www.uptodate.com/contents/pathophysiology-of-psoriasis*
3. *Vitamin D Metabolism, Mechanism of Action, and Clinical Applications. Bikle, Daniel D., Chem Biol., 2014; 21: 319–329.*
4. *Stimulation versus inhibition of keratinocyte growth by 1,25 dihydroxyvitamin D3: dependence on cell culture conditions. Gniadecki R., J. Invest Dermatol., 1996; 106: 510–516.*
5. *A pilot study assessing the effect of prolonged administration of high daily doses of vitamin D on the clinical course of vitiligo and psoriasis. Danilo C, et al., Dermato – Endocrinology, 2013; 5(1).*
6. *Vitamin D analogs in the treatment of psoriasis. Reichrath J, et al., Dermato – Endocrinology, 2011; 3(3).*
7. *Psoriasis, vitamin D and the importance of the cutaneous barrier's integrity: an update. Mattozzi C, et al., 2016; The Journal of Dermatology, 43(5): 507-514.*
8. Finamor, D.C.; Sinigaglia-Coimbra, R.; Neves, L.C.; Gutierrez, M.; Silva, J.J.; Torres, L.D.; Surano, F.; Neto, D.J.; Novo, N.F.; Juliano, Y.; et al. A pilot study assessing the effect of prolonged administration of high daily doses of vitamin D on the clinical course of vitiligo and psoriasis. Dermatoendocrinology, 2013; 5: 222–234. [Google Scholar] [CrossRef] [Green Version]
9. Hata, T.; Audish, D.; Kotol, P.; Coda, A.; Kabigting, F.; Miller, J.; Alexandrescu, D.; Boguniewicz, M.; Taylor, P.; Aertker, L.; et al. A randomized controlled double-blind investigation of the effects of vitamin D dietary supplementation in subjects with atopic dermatitis. J. Eur. Acad. Dermatol. Venereol, 2014; 28: 781–789. [Google Scholar] [CrossRef] [Green Version]
10. Jarrett, P.; Camargo, C.A., Jr.; Coomarasamy, C.; Scragg, R. A randomized, double-blind, placebo-controlled trial of the effect of monthly vitamin D supplementation in mild psoriasis. J. Dermatolog. Treat., 2018; 29: 324–328. [Google Scholar] [CrossRef]
11. Ingram, M.A.; Jones, M.B.; Stonehouse, W.; Jarrett, P.; Scragg, R.; Mugridge, O.; von Hurst, P.R. Oral vitamin D3 supplementation for chronic plaque psoriasis: A randomized, double-blind, placebo-controlled trial. J. Dermatolog. Treat., 2018; 29: 648–657. [Google Scholar] [CrossRef
12. Disphanurat, W.; Viarasilpa, W.; Chakkavittumrong, P.; Pongcharoen, P. The clinical effect of oral vitamin D2 supplementation on psoriasis: A double-blind, randomized, placebo-controlled study. Dermatol. Res. Pract, 2019; 2019: 5237642. [Google Scholar] [CrossRef]