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Psoriasis: Causes, Symptoms, Treatment, Effect on Quality of Life and Future Therapeutic Prospects: A Detailed Review

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Abstract

Objective: *This review's objective is to provide an outline of how psoriasis is caused, what are its symptoms, what are the conventional methods being employed for treatment, and how future prospects can take over the conventional methods. We also aim to put light on how psoriasis is having a huge impact on people's life quality in various fields of life and how this effect can be measured using instruments or questionnaires.* ***Result:*** *It was found that psoriasis can occur in any age group and has an equal effect on males and females. Environmental factors as well as hereditary ones are involved in causing psoriasis. Conventional methods are being used for the treatment and reduction of symptoms but none of the methods have been completely able to cure the disease, hence, there is a hope that nanotechnology can prove efficient. Patients with psoriasis experience substantial limitations in their quality of life affecting their work, social interaction, sexual activity, and confidence.* ***Conclusion:*** *Psoriasis is a non-curable disease but the recent developments in the field of nanotechnology have shown positive results and are expected to work together with topical therapies to cure the disease. Various nanostructures are in use and have proved efficient. But, apart from curing the symptoms, care has to be taken as to how the patients can have a normal life as other individuals and do not have to face social embarrassment as it strongly disturbs their confidence and happiness.*

Keywords: Psoriasis, comorbidities, quality of life, disease burden, psoriasis and depression, QoL Instruments, Nanomedicine

INTRODUCTION

What is Psoriasis

An autoimmune condition called psoriasis can affect the skin and joints. It is a persistent inflammatory condition. It follows an unusual and irregular route. It could be sporadic with brief or prolonged reports of total clearance, or it may be relentless and constantly affected by known or unknown triggers. The Th1-type cytokine profile in skin having lesions, which includes higher levels of interferon, TNF, IL-12, and IL-18, is considered a hallmark of the immune-mediated illness psoriasis. The Th17 pathway has lately emerged as being essential for sustaining the chronic inflammatory process. The CD4+ T cell, which is at the center of this pathway, is kept alive by IL-23 released by dermal dendritic cells which is an example of antigen-presenting cells. These Th17 CD4+ T cells release IL-17 and IL-22, which support and maintain inflammation and the growth of the epidermis [8]. There are several other risks associated with psoriasis. With the rising prevalence of obesity, some psoriatic patients may see a rise in abnormalities in their lipid profile, glucose tolerance, and liver enzymes. Typical risk

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factors for cardiovascular disease, such as elevated levels of cholesterol, hypertension, diabetes, obesity, cigarette use, and a background of prior myocardial infarction, are more prevalent in psoriasis patients. Furthermore, research indicates that myocardial infarction is significantly increased by the presence of psoriasis [1]. Psoriasis is also associated with comorbidity. Psoriasis patients are more likely to acquire other chronic and serious health conditions. Psoriatic arthritis, metabolic syndrome or its elements, cardiovascular illnesses, together with several other conditions like stress and depression, non-alcoholic fatty liver disease, Crohn's disease, and lymphoma, are among the comorbid diseases [9]. All of which together significantly increase morbidity and death. Patients suffering from psoriasis consume significantly more medications than people in general because comorbid condition needs to be managed. Cardiovascular illnesses are the main cause of the significant reduction in life expectancy in psoriasis patients. An elevated risk for cardiovascular death and stroke was identified in people with psoriasis by three recent epidemiological meta-analyses. It has been seen that Type I psoriasis patients experience a more drastic course and a positive family history, but those with a late beginning of the disease (type II psoriasis) do not [10]. Psoriasis is a condition characterized by systemic inflammation. This leads to a series of events which is listed in Figure 1.

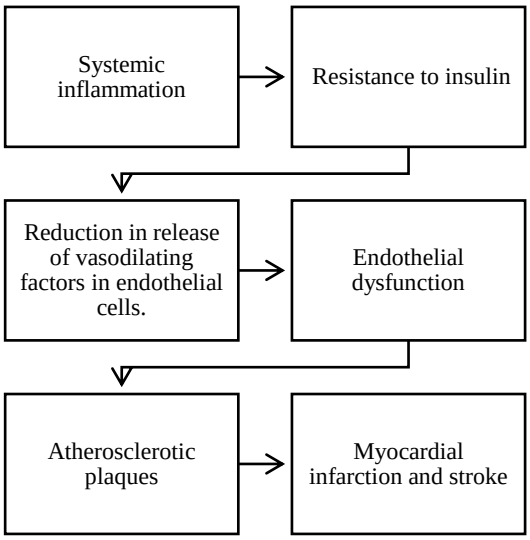

Figure 1. Effect of systemic inflammation in psoriasis [12].

The insulin-sensitizing medication glucagon-like peptide-1 is an successful remedy for the clinical symptoms and indicators of psoriasis. It implies that an important aspect of inflammation is insulin resistance [2]. In psoriasis, the affected patients' physical, emotional, and psychosocial welfare may be significantly harmed. Psoriasis type I and type II clinical manifestations differ by a bimodal age of start. Type I begin at or before the age of 40; Type II starts at or after 40 years old. Type I sickness is present in more than 75% of patients. Individuals with type I psoriasis, or early onset, typically have more relatives that are impacted by the condition and experience more serious symptoms than people with type II psoriasis, or late onset. Psoriasis has an erratic course and progression. There are several genes involved. Papulosquamous psoriasis has a wide range of morphology, location, severity, and course. According to recent research, at least one-third of psoriasis sufferers have pathological concern and anxiety, and all people with the condition experience psychological interpersonal problems. Stress is a significant "trigger" of their illness [11]. It is well-recognized that psychological stress can influence how the immune system responds [3]. Psoriasis patients are more likely to develop several different illnesses depicted in Figure 2 Substantial social morbidity is brought on by psoriasis. The lives of people are negatively impacted by psoriasis due to difficulties with jobs, daily living, and socializing [4]. Psoriasis is a complex inflammatory disease that affects between 0.1 and 3% of the population. Those with minimal clinical manifestations may not seek medical attention, so the true prevalence may be higher [6].

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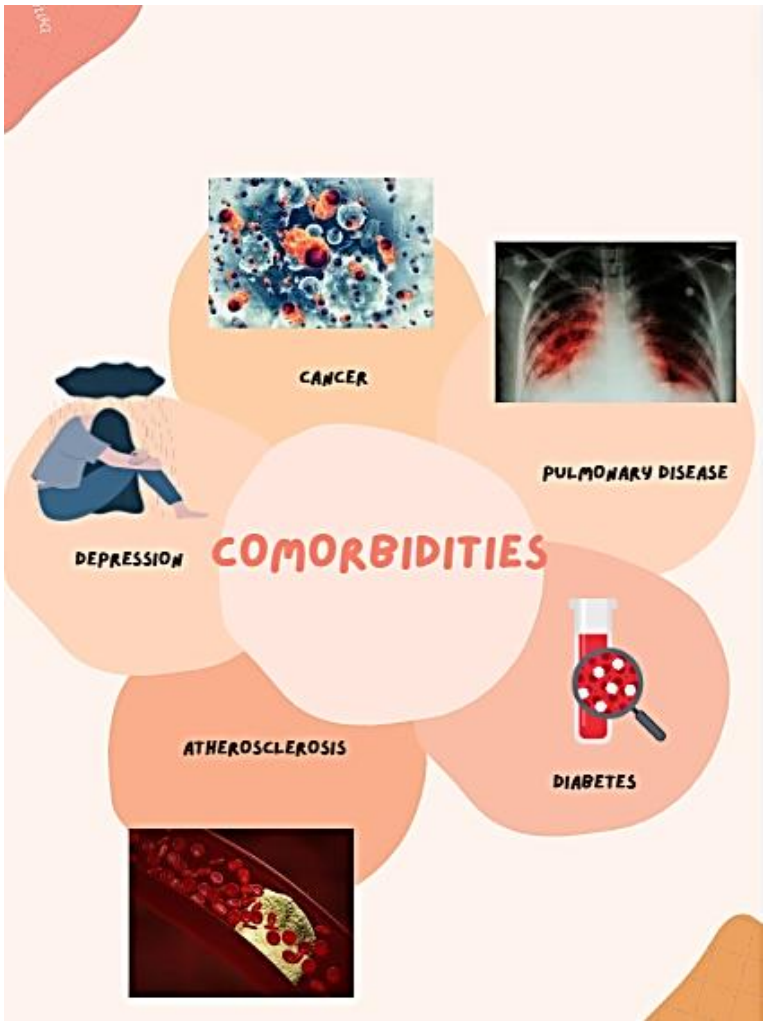

Figure 2. Comorbidities associated with psoriasis.

Epidemiology

About 2% of people in North America and Europe have psoriasis [13]. The prevalence rises essentially linearly over the course of a person's life, from 0.12% at age 1 year to 12% at age 18 [2]. Although psoriasis is widespread, different ethnic groups have variable prevalence rates. Around 2% of the population in the USA is impacted. Psoriasis has been observed to occur at high rates in persons from the Faroe Islands, where 2.8% of the population was found to be affected, according to one research. Psoriasis is uncommon in some ethnic groups, such as the Japanese, and may not exist in Australian aboriginals and South American Indians. Psoriasis can appear at any age; cases of it at birth and in elderly people in their advanced years have been documented. The average age at which psoriasis first manifests itself might range from 15 to 20 years of age, with a second peak occurring between the ages of 55 and 60 [3]. According to estimates, 2% of American adults are affected by psoriasis, and the prevalence is roughly equal for men and women [4]. Psoriasis is present in both sexes; however, women experience it earlier. In children, psoriasis is less common. Although it can manifest at any age, the typical onset age is 28 years old, with ranges between 20 and 50. Psoriasis is more common among Caucasians than in any other racial group, with African-Americans and Asian Americans having prevalence rates that are almost equal to those of Caucasians [6]. The prevalence of psoriasis in various populations ranges from 0% to 11.8%, as per published reports. The prevalence of psoriasis varies with varying regions also. In Denmark, its 2.9%, in the Faroe Islands 2.8%, in the United States 2.2%-2.6%, and in Asia 0.3%. No case of psoriasis was observed in Samonas and South American Indians. East Africans show a higher prevalence than West Africans with 2% and 0.3%

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respectively. Both men and women can develop psoriasis. There is no proof that males and females with psoriasis have different morphologies but age has an effect on the onset of psoriasis. It most commonly appears between the ages of 15 and 30. It's rare for symptoms to appear before the age of 10. Early age of onset is linked to the presence of particular HLA class I antigens, particularly HLA-Cw6. These results prompted Henseler and Christophers to suggest that there are two distinct types of psoriasis: type I, which manifests before the age of 40 and is related to HLA, and type II, which manifests after the age of 40 but lacks HLA correlations [7].

Causes

Many factors play role in causing this disease. The likelihood of developing psoriasis is increased, according to scientific evidence, if a first-degree relative also has the condition [14]. A complex network of molecular pathways that result in clinical disease involves a large number of cytokines, chemokines, and cell surface receptors. Dermal dendritic cells, T cells, neutrophils, and keratinocytes are only a few of the immunologic and skin cells that interact intricately in psoriasis [1]. The climate also shows its effect on the disease. In the winter, psoriasis and psoriatic arthritis worsen, and in the summer, they get better, hence the ultraviolet (UV) index is a helpful variable in the diagnosis and therapy of psoriasis [15]. Psoriasis can be brought on by general triggers like sunlight, chemical irritants, or moderate trauma (scratching, piercings, and tattoos). Systemic medications that can worsen the condition include beta-blockers, lithium, antimalarials, and non-steroidal anti-inflammatory medicines [16]. Psoriasis may also be brought on by HIV infection. Immune-related genes have been identified primarily in DNA-based searches for genes associated with psoriasis, establishing a connection between genetics and immunity [17]. Uncontrolled interactions of innate and adaptive immune system components lead to the development of psoriatic skin lesions. When psoriasis first appears, it stimulates the plasmacytoid dendritic cell to produce interferon α, TNFα, and interleukin 23. TNF α is produced by other cells also such as macrophages, lymphocytes, keratinocytes, and endothelial cells, and then shows its effects on different types of cells. TNF α generates adhesion molecules and secondary mediators, all of which have been linked to psoriatic illness [18]. T-helper 17 and interleukin 23 (IL-23) (TH17), a key immunological mechanism in the pathophysiology of psoriasis illness is the immune axis. Th17 is a subset of T lymphocytes that expresses interleukin 17. Interleukin 23 produced by myeloid cells causes differentiation of Th17 cells. After Th17 cells get activated, it produces factors such as interleukin 17A, 17F, and 22, which enhance the growth of keratinocytes [20]. Keratinocytes release antimicrobial peptides, cytokines, and chemokines that serve as chemo-attractants for immune cells. Hence, in psoriasis, there is a loop of positive feedback between resident epithelial cells and immune system cells. Because the inflammatory environment causes a variety of pro-angiogenic factors to be induced and activated, vascular endothelial cells are also strongly associated with psoriatic illness [21]. Regulatory T cells influence the VEGF-related angiogenic milieu and support epidermal hyperplasia, one of the defining characteristics of psoriasis. VEGF's gene single nucleotide polymorphism may be connected to acute early start of psoriasis [19]. Psoriatic pathophysiological abnormalities are also probably influenced by feedback loops with immune cells and other types of cells, like nerve fibers. It is now recognized that psoriasis is a disease of systemic inflammation rather than a condition that simply affects the skin [2]. One-third of people with psoriasis have a first-degree relative who also has the condition [22]. A multifactorial mode of inheritance is suggested by research. The beginning and exacerbation of the illness are linked to numerous stressful physiologic, psychological, and environmental occurrences. Direct injuries to the skin can cause psoriasis. A streptococcal throat infection can also cause psoriasis or make it worse if it already exists. Infection with the human immunodeficiency virus does not appear to cause psoriasis, but it can worsen an already present condition. Psoriasis frequently gets worse as the infection develops. Psoriasis risk and severity both rise with smoking. Psoriasis is also linked to obesity, and alcohol addiction [4]. Psoriasis has a large genetic component. Psoriasis and other skin conditions including atopic dermatitis share several genes and chromosomal locations. An aberrant activation of the immune system of the skin is a component of the pathogenesis of psoriasis. An inflammatory cascade starts when T cells are activated and release cytokines that cause the target

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tissues to swell and activate more T cells. Psoriasis is made worse by several conditions, including skin injuries, physical and mental stress, cold, alcohol abuse, and medications like beta-blockers and lithium. They discovered that streptococcal infection linked to upper respiratory infections is the most frequent cause of the beginning or progression of psoriasis. It was discovered that psoriasis and obesity are related. Smoking was discovered to be closely related to pustular lesions. Given that a number of immunological mechanisms, both adaptive and innate immune responses, are impacted by nicotine, psoriasis is an immune-mediated condition caused by T-cells. Drugs are also found to exacerbate psoriasis. A few such drugs are- lithium, beta-blockers, synthetic antimalarials, NSAIDs, tetracyclines, interferons, etc. [6].

Symptoms

From the more frequent red scaling raised plaques on the elbows, knees, or scalp to the less common superficial pustules dispersed across the palms or soles, psoriasis can take many different forms. Psoriasis is characterized by raised plaques with red scaling. They are associated with histologically observed aberrant epidermal proliferation and differentiation, swelling of the blood vessels, and inflammation (regular hyperplasia and hyper parakeratosis). A superficial pustule is the second morphologic characteristic., which on histology only exhibits modest epidermal hyperplasia and intraepidermal neutrophil accumulation [1]. Scaling papules and plaque are symptoms of papulosquamous illnesses. The lesions are dry, silvery-white or grey, round papules or plaques with red pigment. The skull, elbows, knees, lumbosacral region, and body folds are typical sites of symmetrical distribution of the lesions. Koebner's phenomenon refers to the possibility of psoriasis developing at the site of trauma or damage. A generalized exfoliative erythroderma can develop from untreated or progressing psoriasis. Involvement of the nails is possible, especially if psoriatic arthritis (PsA) is present. On rare occasions, psoriasis can affect the tongue or the oral mucosa. The dorsal surface of the affected tongue may exhibit strongly outlined, gyrate crimson areas with a whitish-yellow border. The spots could enlarge and spread, altering daily, and may take on distinct circular patterns, it might be a representation of a map, therefore the term "geographic tongue". In terms of appearance, distribution, and severity, psoriasis can vary greatly. Despite the above-mentioned general presentation, the morphology can change and range from microscopic, papules in the shape of tears to pustules. and generalized erythema and scale. Like with other chronic conditions including ischemic heart disease and diabetes, patients suffering from psoriasis experience a decline with respect to their well-being that is comparable to or significantly substandard to that experienced by those patients [3]. 80 to 90 percent of psoriasis patients get nail disease (psoriatic onychodystrophy) during the course of their lifespan. Toenails are less susceptible than fingernails to damage [24]. The areas affected by psoriasis are listed in Figure 3. Hyperkeratosis, onycholysis, and subungual hyperkeratosis are all symptoms of abnormal nail plate growth. Treatment-resistant psoriatic onychodystrophy is a common occurrence. The majority of psoriasis patients have moderate to mild disease, covering a small percentage of the body's surface, less than 5%, and spares the genital area, hands, feet, and face [4]. Many comorbidities, such as cancer, gastrointestinal disorders, chronic obstructive pulmonary disease, and metabolic syndrome, have been linked to psoriasis. Well-being of patients is also known to be considerably reduced by it and has been linked to psychological comorbidities like depression and suicidality. Moreover, behavioral risk factors including Patients with psoriasis are more likely to smoke and drink. Even after adjusting for conventional risk variables, psoriasis has been linked to diabetes, atherosclerosis, myocardial infarction, and stroke independently, according to the study. Compared to the general population, psoriasis patients have higher mortality rates, notably for heart disease, cancer, and liver illness [5]. Most patients with psoriasis describe it as a chronic, recurrent disorder that is frequently itchy and inflammatory. One of the various clinical manifestations of psoriasis may occur; the characteristic psoriatic plaques are erythematous lesions with distinct borders and are typically covered in silvery-gray scaling on the surface. Plaques are typically spread symmetrically, with knees and elbows being the most frequent spots. Patients with psoriasis were more likely than those with urticaria, acne, alopecia, and eczema to report that a stressful experience occurred before the development and worsening of their disease. They came to

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the conclusion that, in contrast to other inciting variables, stress is more likely to be connected to the start of psoriasis. Patients typically say that warmer temperatures and sunlight are good for their psoriasis while cold weather is badFarber and Nall found that 89% of the patients in the Stanford series of 5,600 psoriasis patients stated that their illness deteriorated during cold weather, while 80% of the patients claimed that their psoriasis improved during hot weather and when exposed to sunlight. In a follow-up study of 704 psoriasis patients, the researchers discovered that swimming and sunlight were useful to more than half of the respondents: 10% said in comparison to seawater and sun, fresh water was more efficient, whereas 17% disagreed [6]. Under a microscope, psoriasis shows leukocytic infiltration of the epidermis and papillary dermis, as well as noticeably increased proliferation and insufficient differentiation of the epidermis. Psoriasis is immunologically-mediated, as evidenced by the therapeutic response to immunosuppressive medications, the transmission of the condition via bone marrow transplantation in humans and by purified T-cells in mice with human pre-psoriatic skin, as well as the presence of clonal T-cell receptor (TCR) rearrangements in psoriatic skin [7].

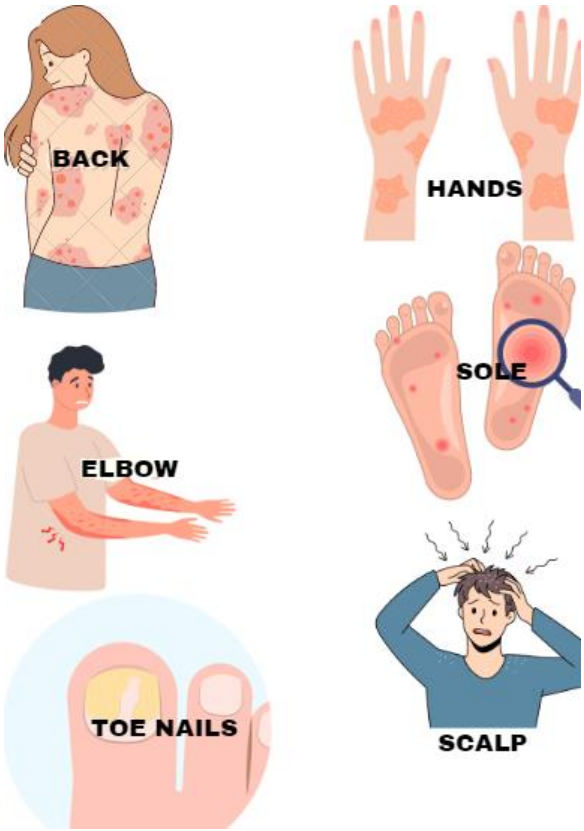

Figure 3. Areas of skin affected by psoriasis.

Treatment

Topical treatments such as glucocorticoids, compounds of vitamin D, or combinations of both are typically sufficient to treat moderate illness (Figure 4). For difficult-to-treat regions like the face topical calcineurin inhibitors are recommended. Corticosteroids are used for scalp treatment. According to a meta-analysis, the most successful treatment for the scalp was corticosteroids and vitamin D3 [23]. Patients with mild-to-severe illness require a mix of phototherapy and systemic therapy. Narrow-band UVB and photochemotherapy using PUVA, are examples of phototherapies (psoralen plus UVA). The two forms of treatment, phototherapy and photochemotherapy, are both quite efficient, but they take a lot of time and are typically only used to control the condition temporarily. PUVA's ability to cause cancer further restricts its long-term use. Psoriasis can be treated with TNF inhibitors etanercept, adalimumab, and infliximab. The growth of Th17 lymphocytes, which are vital effector cells in the inflammation caused by psoriasis, is inhibited by ustekinumab.

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Secukinumab blocks IL-17A. Table 1 lists the common drugs used in the treatment of psoriasis. Since there is no indication of persistent toxicity or pharmacologic interactions, biologics are employed for psoriasis treatment over the long run. The safety profile of biologics is also good, with just a little rise in opportunistic infections. In general, TNF inhibitors are utilized following phototherapy. Although no known cure for psoriasis exists, numerous medicines can lessen or almost completely cease symptoms. The existing treatments are either time-consuming, difficult to use, or don't completely resolve the lesion. Although numerous genetic loci have been linked to psoriasis, the functions of the disease-related variants of these genes are poorly understood. and how they might contribute to the condition. Additionally, it is uncertain how disease-causing signalling pathways interact with one another and how recently found microRNAs affect the progression of the illness. It is still unclear how psoriasis is related to other auto-inflammatory and auto-immune illnesses' pathogenesis. More research is needed on the links between environmental factors, disease burden, and the effects of psoriasis on healthcare resources [2].

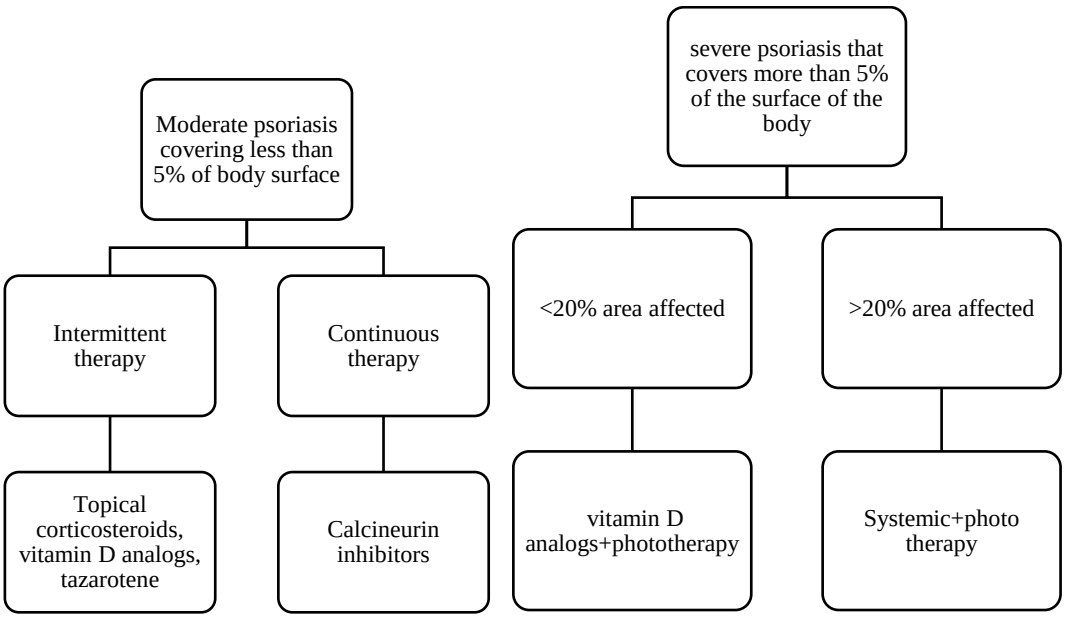

Figure 4. Treatment of psoriasis according to the severity of the disease.

Table 1. List of medications used to treat psoriasis.

Common Drugs Used in Psoriasis [4]
Corticosteroids
Tacrolimus and pimecrolimus
Tazarotene
Vitamin D analogs
Acitretin
Adalimumab
Cyclosporine
Etanercept
Infliximab
Methotrexate

Topical treatments used are calcineurin inhibitors, vitamin D analogs, tazarotene, and corticosteroids. External remedies that are less frequently utilized include salicylic acid, coal tar, and anthralin. Topical corticosteroids are widely used to treat psoriasis. When psoriasis patients have 5 to 20 percent body surface involvement, the vitamin D analogs calcipotriene (Dovonex) and calcitriol

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(Vectical), either alone or alternatively, along with phototherapy, are used to treat the condition**.[25]** Tacrolimus (Protopic) and pimecrolimus (Elidel) are permitted for usage in patients that are over the age of two. Individuals with more severe cases of psoriasis that affect more than 5% of the body's surface, including the hands, feet, and face, or genitalia typically have systemic treatments in addition to phototherapy. Methotrexate, cyclosporine (Sandimmune), acitretin (Soriatane), and biological therapy are examples of systemic treatments. For more than 50 years, psoriatic arthritis has been treated with methotrexate. Folate treatment might lessen side effects. The use of methotrexate in kids with psoriasis has not been authorized. Cyclosporine quickly relieves symptoms, but it has several side effects and prescription combinations that prevent use for a long time. It is commonly employed as a bridging therapy and to address crises. before starting slower-onset maintenance medicines. Children are not permitted to use cyclosporine. Growing numbers of those who suffer from mild to severe psoriasis and those with psoriatic arthritis are being treated with biologic therapy. Adalimumab (Humira), etanercept (Enbrel), and infliximab are examples of inhibitors of tumor necrosis factor used to treat psoriasis and psoriatic arthritis (Remicade). Methotrexate is frequently used with etanercept. Infliximab generates the quickest clinical response among biologic treatments. Infliximab clinical trials show benefits in quality of life and sustained response. Because of the possibility of serious infections, such as tuberculosis, patients on tumor necrosis factor inhibitors must have a baseline and ongoing monitoring [4].

Quality of Life and Psychological Impact

An individual's general well-being is assessed using QoL (Quality of Life). It is intended to include all potential ramifications on someone’s lifestyle, including psychological, social, and physical aspects [55]. According to some authors, quality of life (QoL) refers to an individual’s faith in where they are in life concerning their goals and worldview [56]. Physical impairments, psychological affects, social effects, occupational consequences, everyday hassles, and treatment-related QoL are all factors in psoriasis [57].

Table 2. Percentage effect of psoriasis in different walks of life.

Impact of Psoriasis in Different Fields [36]	**Percentage Affected**
Social functioning	48%
Decreased work efficiency	51.1%
Work distress	62.8%
Life impairment brought on by treatment's side effects	70%
Tense interpersonal relationships and a tense household environment	69.8%
Life constraints brought on by psychological effects	57%
Life-altering effects of social upheaval	55%
Life impairment due to leisure limitations	44%
Impediment to life due to limited daily activities	37%
Decline In sexual activity	40% **[37]**
Limited career progression	555
Reduction in employment status	42%
Reduced earning potential	35%
Work limitation	60%

Having psoriasis is a condition that not only affects a person physically but also psychologically. It greatly impacts the social life and mental well-being of a person. Patients suffering from psoriasis describe limits in their everyday activities, social interactions, and activities that expose their skin, as well as physical discomfort, mental dysfunction, a negative body image, and limitations in their ability to work. Because of these limits, it has an impact on social interactions, emotional health,

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relationships, and work. Group activities, physical activity, hanging out with friends, and going public places were all found to be significantly impacted, as were social relationships and activities with relatives, friends, and neighbors. The ability to form new friendships, social connections, and interactions with family, relatives, and friends appears to be reduced [26]. The percentage effect of psoriasis in different fields of life is listed in Table 2.

It is observed that after one year of illness, interpersonal and professional functioning deteriorated as the psoriasis severity increased. Psoriasis patients reported feeling embarrassed, ashamed, and angry, affecting their behavior overall and causing them to avoid going out in public and less socializing. The connections with family members are also seriously impacted [26]. In one study of psoriasis patients, 89% expressed disappointment and embarrassment about their appearance, 58% experienced anxiety, 42% lacked confidence, and 24% felt depressed [42]. About 50% of those with psoriasis reported that their condition caused them to stop participating in athletic activities, and 26% claimed that their condition created family conflict. Forty-four percent of those who had psoriasis said it caused them serious problems at work [27]. In a poll, more than 40% of patients said their sexual function was negatively impacted by their psoriasis. In this study, a significant connection existed between decreased sexual functioning and joint involvement, increased scaling, increased pruritus, and higher depression scores [43]. Disfigurement is a common side effect of dermatological conditions like psoriasis, which makes the patient's discomfort much worse. The disorder frequently results in relationship problems, emotional distance, social isolation, and depression, all of which influence a person's well-being [28]. A study demonstrated how psoriasis can affect a patient's life in several aspects and to what extent. The findings were that social interaction was affected in 51.5% of patients, work-related issues like decreased efficiency were seen in 62.8% of patients, and relational efficiency was reduced due to a tense environment at home. Sleep disorders and disturbances were seen in 67.4% of the patients especially those who had lesions on the body’s exposed surfaces. Patients having symptoms in the genital area should decrease in sexual functioning in 20.9% of the patients [28]. Increased inclinations for obsessionality, higher levels of external hostility, and higher levels of anxiety and despair have all been discovered in them [29]. A detailed study on several patients with psoriasis was conducted to find out how their lives are getting affected in different fields and to what extent. The results are summarized in Figure 5 [31]**.**

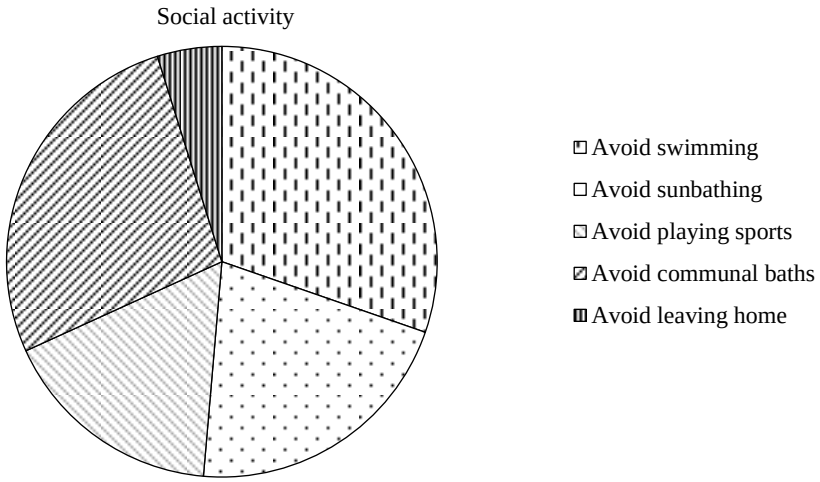

Figure 5. Pie chart depicting activities being affected in a psoriasis patient.

Psoriasis patients frequently endure stigmatization, which has significant psychological and social repercussions. Patients with skin conditions could, as one might anticipate, encounter dread of infection or filth, social rejection, and avoidance of touch. Such incidents drastically lower patients' quality of life [30]. It was found that 11% of psoriasis patients get divorced [32]. Psoriasis also makes it difficult to create and sustain an intimate relationship [33]. It was also found that 40% of patients

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have decreased desire to initiate sexual intimacy [35] Psoriasis-related body image issues, social network changes, and diminished sexual intimacy may be chronic stress triggers, endangering the well-being of patients and their partners as well as their interpersonal connections [45]. The life of a person may also be impacted according to the type of treatment he is receiving, the cost, and the pain involved in that [49]. A direct relationship has been observed between depressive order and the severity of the disease [50]. Psoriasis also affects the physical functioning of an individual due to poor sleep quality that results due to itching and pain [51]. The limitations in physical functioning increase the mental distress of the patients due to limitations in their social activity [52]. The elements that impact the quality of existence are summarized in Figure 6.

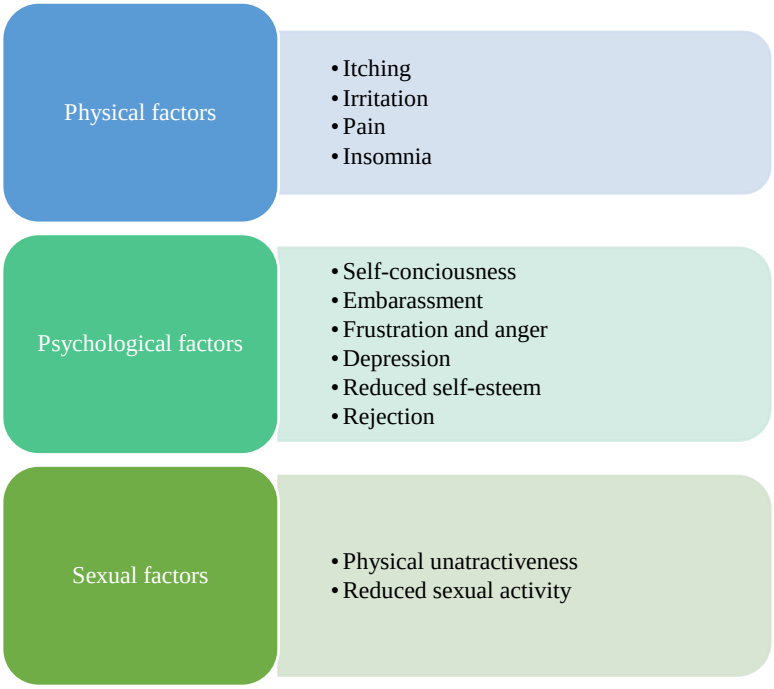

Figure 6. Factors affecting the quality of life.

Effect on Work and Profession

The capacity to work and income levels may be greatly affected by psoriasis. Mild-to-severe psoriasis may affect not only one's capacity to work but also their ability to find work. Psoriasis affects one's career and employment decisions, and thus, income [38]. There appears to be a negative relationship between income, work, and the severity of psoriasis [39]. According to a different study, 60% of those with psoriasis missed work, missing 26 days on average annually [40]. Psoriasis affects a person physically, psychologically, and socially. Physically, it affects daily activities, work and career, personal relationships, and mobility and causes physical symptoms. Psychologically it affects the mental health, emotional functioning, and self-image of the person. Socially it affects the sexual behavior, social contacts, and social life of the person [41].

Psoriasis And Depression

95% of patients with psoriasis face psychiatric problems. The problems included depression in 44% and anxiety in 35% of the patients. Psychological disorders also included alcohol abuse, OCD (obsessive-compulsive disorder), social anxiety, schizophrenia, and several other disorders [27]. Depression is directly linked to the severity of pruritis in patients. As pruritis improved, the depressive symptoms were found to be reduced. Psoriasis is also linked to suicide. Several studies showed that a significant number of patients had the thought of committing suicide [44]. As per recent studies, Psoriasis significantly increases psychosocial morbidity. Between flares and during them, some patients have reported experiencing moderate to severe anxiety levels, sadness, and rage. These

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emotional responses have a significant impact and dramatically disturb the functional state of our patient population. The current study also showed that a sizeable proportion of patients think stress and emotional factors are crucial in causing their psoriatic flares. Patients typically suffer higher levels of sleep impairment as anxiety, despair, and pruritus worsen, which can easily exacerbate the patients already changed emotional state [30]. The effect of psoriasis on psychology also depends on the age of the start of the illness. If the onset is before the age of 40, it causes more psychological stress [34].

Because psoriasis affects so many aspects of a person's life, it may have negative consequences on their social and emotional well-being. Routine tasks and social interactions may be frequently impaired as a result, raising partners' morbidity. As a result, the quality of life of a psoriatic patient's partners and members of the family may be greatly impacted [46].

Since there is no particular cure for this disease, both pharmacologic and non-pharmacologic therapies strive to reduce the negative effect of the disease to enhance well-being [47]. Earlier physicians believed that the severity and scope of the sickness have a direct impact on the patients' wellbeing. But later, studies showed that these both do not have a direct correlation [48]. Thus, different instruments were introduced to determine the quality of existence in individuals with psoriasis.

Because psoriatic lesions are visible, people with psoriasis frequently endure social stigma and rejection. [53] People assume that it is a communicable disease and hence may publically reject the patients like asking them to leave the pool or the gym. Such incidents can decrease the self -esteem and lead to embarrassment and shame. Thus, they start avoiding public places and reduce their social interactions which ultimately affects their quality of life [54].

QoL Evaluation

It's critical to assess how psoriasis affects a patient's quality of existence to determine appropriate therapies. To determine how psoriasis is playing role in affecting a patient's quality of existence, several helpful generics, QoL particular to dermatology and diseases are available. [58] The QoL instruments for psoriasis are listed in the Table 3.

Table 3. Techniques for assessing the quality of life in people with psoriasis.

QoL Instrument	Score	Comments
Short form 36 [59]	0-worst state of health 100-best state of health	It consists of 36 questions and measures 8 health dimensions- functioning on a physical and social level, role restrictions brought on by emotional and physical issues, common perceptions of physical and mental well-being, exhaustion, and pain in the body [60]
Sickness Impact Profile	0%- a state of good health without any physical or behavioral abnormalities brought on by sickness 100%- a significant negative effect of sickness on behavior [61]	It is a health status indicator based on how well someone performs in daily activities.
Psychological General Well-Being Index (PGWBI) Psychological General Well-Being Index (PGWBI) Psychological General Well-Being Index (PGWBI)	0-110 Higher the score, the greater the psychological well-being [62]	It is a measure of the subjective opinion of one's wellbeing
Psoriasis Disability Index	0-45 A high score implies a high impairment of QoL	It consists of a set of 15 questionnaires [63]

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Psoriasis Life Stress Inventory (PLSI)	0-45 A high score implies a high level of daily stress. [64]	It measures the psychosocial morbidity connected to psoriasis. It examines how psoriasis patients are affected by daily pressures. It seeks to assess how psoriasis affects society
Psoriasis Index of Quality of Life	0-25 A higher score indicates higher psychosocial impact [65]	It includes issues with socializing, intimate bodily contact, personal independence and reduced emotional stability, sleep quality, and relaxation, as well as factors associated with apprehension of unfavorable responses from others. Patients earn one point for each unfavorable comment they agree with for each item.
Psoriasis Area and Severity Index	0-72 5-10-moderate disease >10-severe disease [66]	It evaluates and scores the patient's reaction to treatment as well as the seriousness of the psoriatic lesions of the patient.

SF-36- The SF-36 is a well-known generic 36-item report on one's own health status questionnaire that evaluates eight health status domains, including physical performance-Having trouble doing physical tasks like showering or dressing (10 items), usual physical role activities-constraints caused by physical health in terms of job and other everyday activities (4 items), body pain-how terrible and constricting is pain (2 items), conceptions of general health -how the patient perceives their overall health (5 items), vitality-Having energy vs. being drained and worn out (4 items), social functioning-physical or emotional issues that impede on typical social interactions (2 items), typical emotional role activities-limits due to emotional issues with the job and other daily activities (3 items), and mental health-feeling anxious and depressed as opposed to content, joyful, and calm[67] (5 items) All SF-36 results were scaled from 0 to 100. An improved well-being with respect to health was indicated by a higher score. [68] The SF-36 was created as an indication of general health status for use in demographic surveys and policy evaluation analysis [69].

Psychological General Well-Being Index

The degree of a person's subjective psychological well-being is gauged by the Psychological General Well-Being Index (PGWBI). It assesses an in-depth representation of oneself of intrapersonal affective or emotional states that express a feeling of personal well-being or suffering, capturing what we may refer to as a subjective experience of well-being. The tool generates a psychological well-being index and consists of 22 standardized items (6 items for the short form). The whole measure offers subscales to evaluate the following areas: vitality, positivity, self-control, positive well-being, anxiety, and depression [70].

Psoriasis Disability Index

It is a questionnaire designed for a particular disease that has been verified in opposition of the UK Sickness Impact Profile, which is a general health assessment tool. Its overall score reflects the patient's experience on the disease of the skin over the previous month, a period chosen to allow the PDI to be used to reflect the change in disability following therapy [71].

Psoriasis Area and Severity Index

assess plaque discoloration, layering, scalability, and coverage. It can be used by a doctor to assess the seriousness and extent of psoriasis as well as the efficacy of psoriasis treatments [72]. The percentage of the body that is affected by psoriasis symptoms is calculated as part of the scoring and is graded on a scale from extremely mild to none at all [73]. Scaling, thickness, and discoloration are

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all measured in the intensity part of the score. The following scoring method can be used by a doctor to rate every single one of these symptoms:

0: no symptoms
1: minor symptoms
2: a few mild signs
3, serious signs
4: extremely serious symptoms [74]

Future Therapeutic Prospects

For the treatment of psoriasis, various methods are being used like topical and systemic therapies for mild and severe psoriasis respectively. But these methods have certain limitations such as toxicity and skin irritation. Biologic therapies came as a superior alternative. With the increase in innovations and technologies, drug-delivery systems based on nanotechnology can be used for treatment purposes. Its effect is long-term and has better efficacy. The problems of physicochemical stability, low solubility, toxicity, and bioavailability can be solved with the help of nanotechnology. Preclinical and clinical investigations have demonstrated the effectiveness of reducing pharmacological adverse effects at tightly controlled medication delivery at optimum therapeutic dosages using nanoparticles. Nanoparticles are produced by the application of nanomedicine to extend the half-life of a medicament, making it easier for the active pharmaceutical ingredients to be delivered via nanocarriers to their intended action site. Topical nanocarriers have received more interest recently because they offer improved skin penetration and regulated release at a lower dosage regimen. There has been a lot of research done on different types of nanoparticles for topical psoriasis treatments. There is significant interest in these applications for polymeric nanoparticles, such as dendrimers, nanospheres and nanocapsules.

Due to their ability to enhance anti-psoriatic activity following drug encapsulation, hydrogels have recently gained popularity in the treatment of psoriasis. It is anticipated that hydrogels would play a crucial role in future nano-based medication delivery methods to further enhance the therapeutic profiles due to the increased interest and study in them. Photothermal therapy (PTT), a new technology that uses use nanoparticles to destroy cancer cells through localized thermal treatment and is more advanced than traditional phototherapy treatments, can also be used to treat psoriasis. [75]

According to certain reports, nanostructures may alter the immune system. This would be extremely important when employing nanostructures to deliver medications to treat inflammatory disorders like psoriasis. Different types of nanostructures such as liposomes, dendrimers, tranferosomes, ethosomes, and nanosuspensions can be used for the treatment of psoriasis.

The imiquimod plaque psoriasis model's cyclosporine-loaded cationic liposomes exhibit acceptable shear thinning behavior and decreased levels of inflammatory markers when applied topically. Long-term maintenance of the therapeutic action is made possible by the cyclosporin's slow release from liposomes. One of the drugs that is most frequently recommended for the systemic treatment of psoriasis is methotrexate (MTX). Nonetheless, there are some hazards associated with using this medication systemically. As a result, numerous research was carried out to administer MTX topically utilizing different nanocarriers. In a recent study, liposomes contained MTX at four distinct doses, ranging from 0.05 to 0.5%. These formulations' entrapment efficacy was evaluated and found to be higher than 89%. The in vivo tests were conducted on a mouse model of psoriasis brought on by imiquimod. The toxicity analysis established that the formulation's 0.05% toxicity level is lower. Hence, a unique method of treating psoriasis might be thought of as the topical liposomal formulation of MTX.

Drugs can be effectively delivered into systemic circulation over the skin with the help of microneedles, which also improve patient compliance. The micron-sized construction prevents pain perception while applying the microneedles to the skin. Moreover, the skin heals quickly after the

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removal of microneedles. It produces a micron-sized transport route that has dimensions larger than molecules. The stratum corneum is broken up by the microneedles, boosting permeability and enabling efficient additional treatment for the treatment of psoriasis. Based on these important benefits, it is possible to anticipate more advancements in psoriasis treatment using microneedle-based drug delivery than with any other technology currently under study. Figure 7 compares the efficacy of microneedles and conventional drug delivery systems like creams and ointments. Microneedle causes the drug to penetrate the dermis while the creams and ointments have poor drug permeation.

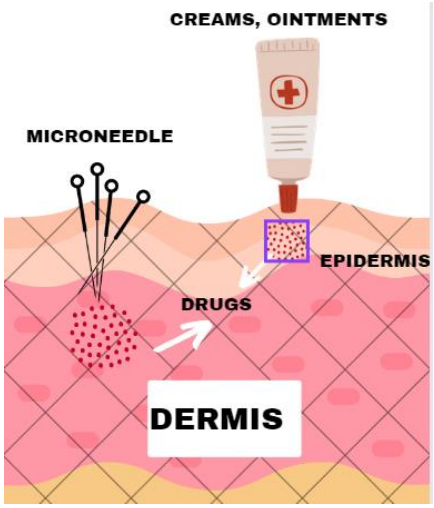

Figure 7. The figure compares the efficacy of microneedles and conventional drug delivery systems like creams and ointments. Microneedle causes the drug to penetrate the dermis while the creams and ointments have poor drug permeation.

Due to their negative side effects, current psoriasis therapies are ineffectual. There is no proof that topical therapy, radiation, phototherapy, systemic and biologic treatments are effective or lessen side effects. Posttranslational drug development and cutting-edge drug delivery technologies are two promising directions for an effective treatment approach against psoriasis. It's interesting to note that sophisticated biologic delivery systems combine these two tactics and are seen to be beneficial.

The available treatment plans based on traditional formulations are general and linked to systemic toxicity. The use of nano-formulations in novel drug delivery strategies may offer the only chance for the creation of highly effective, low-toxic treatment methods. It has a simple skin entry, penetrates the skin more deeply, and can deliver drugs to specific areas of the body with a better benefit-risk balance. Nanocarriers improve penetration through all skin-crossing pathways, including those in the trans-appendage pathway that travel intracellularly, across cells, and via the hair follicle shafts, by increasing the surface area to volume ratio. The future potential of various nano-formulations, including liposomes hydrogels, solid lipid nanoparticles, nanostructured lipid carriers, ethosomes, microspheres, micelles, transfersomes, microneedles, etc. in psoriasis treatment methods is currently being researched. The majority of them have been tested in animal models and have shown encouraging outcomes. So, after they pass clinical studies, these might be the future therapeutic platforms [76].

CONCLUSION

Psoriasis is a prevalent skin condition that requires long-term therapy due to both its high prevalence and the significant negative effects it may inflict on patients' quality of life. External factors, such as traumas, the environment, disease, food, mental tension, or medicines, may have an impact on the onset of psoriasis and its clinical manifestation. Psoriasis is a persistent, recurrent, and

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disfiguring illness that has a significant negative influence on social, vocational, and other aspects of functioning.

People may not live up to their "full life potential" due to the severe stress on the body, mind, society, and economy linked with psoriasis.

The current evaluation identifies a number of potential areas for further study. The inspection of the general well-being is one of the initial areas of focus.

A more thorough examination of the psychological and social functioning of psoriasis sufferers is a second topic of focus. First, it was found in four investigations that psoriasis mostly impairs psychological or psychosocial functioning. Second, there was a dearth of the information offered on pertinent topics like sexual behavior, body image, certain emotions, and concerns about psoriasis.

These scant data do, however, suggest that patients may experience humiliation, self-scrutiny, and poor bodily perception in particular. And lastly, this study's findings show that social connections with people are more likely to be impacted by psoriasis than social connections and links to friends and family.

To make sense of these challenges, more research will be required.

The investigation of the correlation between the seriousness of disease and quality of living is a third area of focus. Among studies that varied in disease severity, no alteration was observed in mind, body, social interaction, or in comprehensive life quality. This is most likely caused by the studies' heterogeneity.

Research has revealed that factors related to psychology and society may have a substantial impact on anticipating life quality. The quality of life of psoriasis patients may be impacted by their susceptibility to stress, their capacity to manage their impairments, and their access to social support. These factors may perhaps account for a significant portion of the variation across patients. This branch of study might help us comprehend this link better.

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