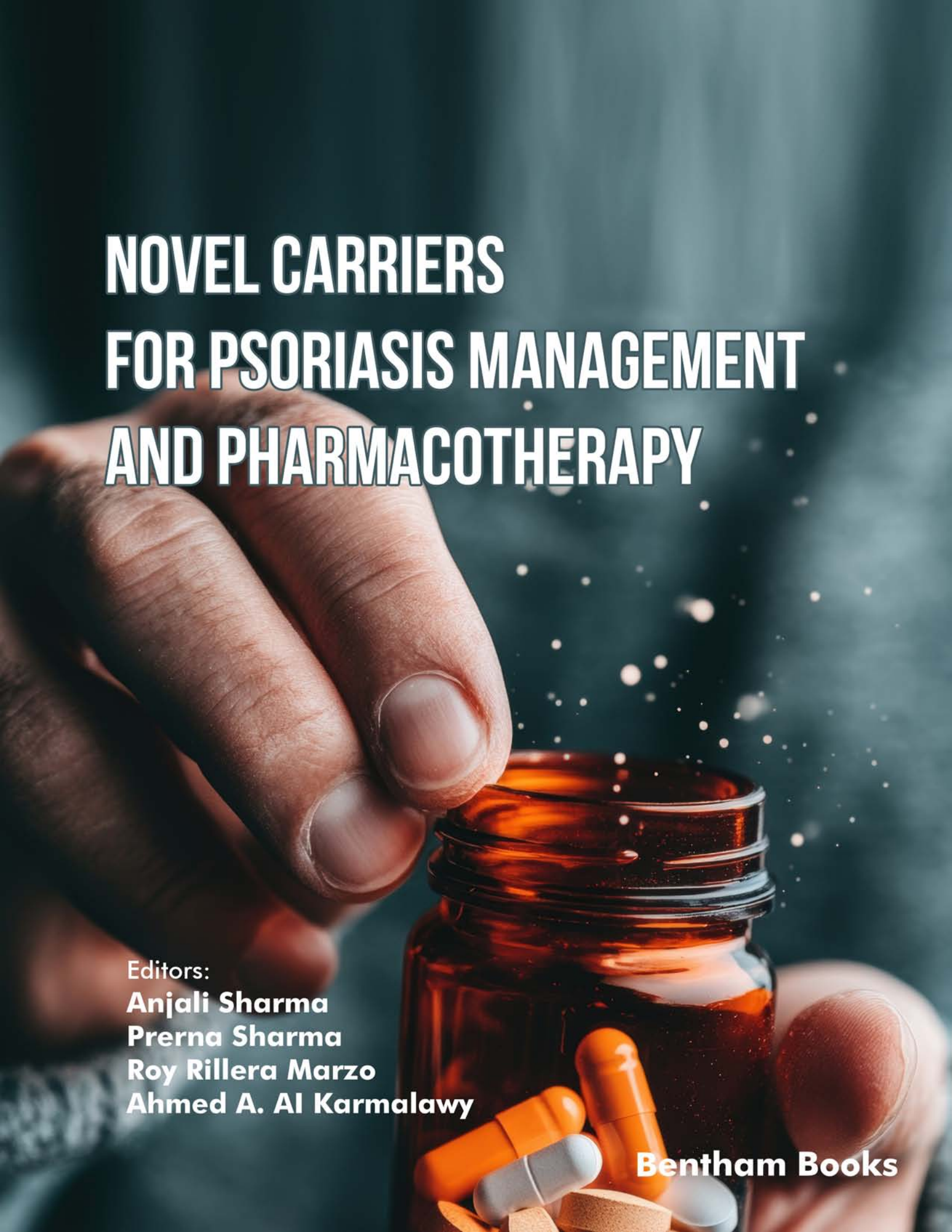
NOVEL CARRIERS FOR PSORIASIS MANAGEMENT AND PHARMACOTHERAPY



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Novel Carriers for Psoriasis Management and Pharmacotherapy

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FOREWORD

The treatment landscape for psoriasis has undergone significant evolution over the past few decades, yet the quest for more effective and targeted therapies remains ongoing. Traditional topical treatments, systemic medications, and biologics have provided relief to many patients, but challenges such as limited efficacy, side effects, and patient adherence persist. The advent of novel drug delivery systems offers a promising avenue to overcome these hurdles and enhance the therapeutic outcomes for psoriasis patients.

"Novel Carriers for Psoriasis Management and Pharmacotherapy" is a timely and essential contribution to the field of dermatological pharmacotherapy. This book meticulously explores the potential of innovative carriers in improving drug delivery, ensuring better penetration, controlled release, and reduced systemic exposure. It sheds light on the transformative impact that these advanced delivery systems can have on treating psoriasis.

The authors and contributors to this book are distinguished experts who bring a wealth of knowledge and experience in pharmaceutical sciences, dermatology, and drug delivery technologies. Their collective insights provide a thorough understanding of the current state and prospects of novel carriers in psoriasis management.

As we look forward to the next generation of psoriasis treatments, this book stands as a testament to the relentless pursuit of excellence in research and clinical practice. It is an invaluable resource for anyone dedicated to advancing the field of psoriasis therapy and improving patient care.

I commend the authors for their outstanding work and dedication in bringing this comprehensive and insightful book to fruition. It is a must-read for researchers, healthcare professionals, and students eager to stay abreast of the latest developments in psoriasis management and pharmacotherapy.

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PREFACE

Psoriasis is a chronic, inflammatory skin disease affecting millions of people worldwide. Despite numerous advancements in understanding its pathogenesis and the development of therapeutic strategies, psoriasis remains a challenging condition to manage effectively. The need for novel and efficient delivery systems to enhance the therapeutic efficacy of existing and new drugs is paramount.

"Novel Carriers for Psoriasis Management and Pharmacotherapy" aims to bridge the gap between current treatment limitations and emerging innovations in drug delivery systems. This book provides a comprehensive overview of the latest advancements in carrier technologies, including nanostructured lipid carriers, liposomes, ethosomes, and other cutting-edge formulations designed to optimize the delivery of therapeutic agents to psoriatic lesions.

Through detailed chapters contributed by leading researchers and experts in the field, readers will gain insights into the principles of carrier design, the mechanisms of action, and the therapeutic potential of various novel carriers. Additionally, the book discusses the challenges and future directions in the development and clinical application of these advanced delivery systems.

We hope this book serves as a valuable resource for researchers, clinicians, and students interested in dermatology, pharmaceutical sciences, and drug delivery technologies. By exploring the intersection of psoriasis management and innovative drug delivery systems, we aim to inspire further research and development, ultimately improving the quality of life for patients suffering from this debilitating condition.

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CHAPTER 1

Understanding Psoriasis: A Chronic Skin Condition

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Abstract: The ancestral form of immune-mediated ailments, psoriasis, can affect the joints, the skin, or both. An interdisciplinary team of professionals with diverse expertise is often necessary to effectively treat the disease. Several challenges are associated with psoriasis, including its high frequency, chronicity, disability, and the coexisting medical disorders that often accompany it. Understanding the importance of immune regulation in psoriasis, along with the interactions between the innate and adaptive branches of the immune system, has been instrumental in controlling the progression of this multifaceted disease, which affects individuals in ways that go beyond skin involvement. Psoriasis is a widespread skin condition that causes both emotional and physical suffering. Like other dermatoses, visible disfigurement may cause an increasingly undesirable response in others, which can account for a large portion of the disease's noticeable psychological stress. The present day disease demand has been exacerbated by several coexisting issues and including the syndrome of metabolism and cardiovascular conditions brought on by the syndrome. Certain environmental risk factors, including trauma (*e.g.*, the Koebner phenomenon), infection, and medication, have been linked to the development of this inflammatory skin disorder. Psoriasis of the plaque type is distinguished by itchy plaques covered with silvery scales. Both adaptive and innate immune responses can contribute to psoriatic inflammation; however, innate immune responses appear to be more prevalent in psoriasis, regardless of plaque type. Comorbid diseases comprise psoriatic arthritis, the metabolic syndrome or its components, cardiovascular issues, and a host of additional conditions, including depression and anxiety, nonalcoholic fatty liver, Crohn's disease, and cancer.

Keywords: Inflammatory skin disease, IL-17 inhibitors, IL-23 inhibitors, Koebner phenomenon, Psoriasis, Psoriatic arthritis, Skin lesions, TNF-inhibitors.

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INTRODUCTION

Background

Since the inception of human existence, psoriasis has been a prevalent condition. These days, it has become recognized as a distinct skin condition influenced by both immunological and environmental factors. Even considering its prevalence, chronicity, and outward manifestations, historical accounts of psoriasis in the manuscripts of ancient physicians are scarce. As dermatologists began to appear around the latter part of the century, the field of skin care developed into a distinct field. Psoriasis became acknowledged as a disease over time. Many intellectuals across different civilizations — both well-known and lesser-known — have documented the existence of psoriasis-like skin sores. Hippocrates (460–377 BCE) was an Ancient Greek physician who used the terms "psora" (itchiness) and "lopoi" (scaly skin) to refer to inflammatory skin diseases, such as psoriasis. A landed gentry by the name of Cornelius Celsus (25 BCE–50 CE) described a skin ailment that afflicted both the skin and the nails generations afterward during the Roman Empire. During antiquity and the medieval era, there was a limited written record of skin diseases, which sometimes led to misconceptions in discourse. This tendency endured for centuries, most notably in the Middle Ages, when psoriasis sufferers and leprosy sufferers were subject to similar social exclusion. This convergence underscores the persistent challenge of accurately understanding and treating cutaneous disorders, shedding light on the significant advances in contemporary dermatology that have enabled a deeper differentiation and classification of these conditions [1]. The shadowy past illuminates today's specialist knowledge, yet it took a while for various skin illnesses to be understood rather than mysterious. English physician Robert Willan, who greatly advanced the science of dermatology in the late nineteenth century, described psoriasis and other skin disorders in great detail, providing doctors with clear diagnostic standards. His groundbreaking study methodically classified distinct forms of psoriasis, including guttate, which involves tiny patches; scalp-centric; and palm, which affects the hands. When Dr. Willan referred to psoriasis as "lepra vulgaris," he was reflecting on the inadequate understanding of the condition at the time. His groundbreaking work laid down the foundation for contemporary dermatology and profoundly influenced our understanding of skin ailments. His thorough documentation remains a valuable source of knowledge for medical experts. Throughout the course of the century, medical professionals and scholars amassed a vast amount of knowledge about psoriasis, including detailed descriptions of its various forms. John M. Moll and Verna Wright made a significant discovery in 1973 when they published research demonstrating that psoriasis or psoriatic arthritis is a distinct condition, setting it apart from rheumatoid arthritis. Scientists now acknowledge that psoriasis is more than just a

skin ailment; it is an autoimmune disease that endures and causes inflammation throughout the whole organism. Modern therapeutic strategies have been significantly influenced by this evolving understanding, particularly through the application of biologics that target specific components of the immune system [2].

Epidemiology

Millions of individuals worldwide suffer from a persistent inflammatory skin condition each year. The red, itchy, scaly lesions of this autoimmune illness affect approximately 3.2% of adults and 0.13% of children in the United States alone. According to certain demographic estimates, there are approximately 80 new cases per 100,000 people each year. Location has a significant effect on prevalence, with estimates indicating rates as low as 0.5% in some parts of Asia and as high as 8% in Norway. The most intriguing aspect is that psoriasis affects men and women with nearly equal incidence across a wide range of populations. Although the illness may develop at any stage of life, there is a unique doubling chance of developing it initially in the years 18 to 39 and again in the years 50 to 69. Psoriasis presents enduring challenges regardless of when it manifests; nevertheless, new insights and innovative therapies offer renewed hope. The stage in life at which psoriasis first appears can vary depending on whether inherited or environmental factors cause it. For instance, having the human leukocyte antigen (HLA)-C*06 variants, a genetic element that influences one's propensity, has been linked to an earlier onset of psoriasis. Especially those who are prone, external cues such as stress or recent trauma may accelerate their symptoms. The complex interplay of biological and lifestyle elements introduces heterogeneity into the typical course of disease onset and progression across [3].

There were no restrictions on the area, ethnicity, or period that were taken into account. Seventy-six suitable empirical findings have been incorporated in the aforementioned systematic review after fulfilling all eligibility requirements. Estimates for the prevalence of psoriasis in individuals ranged from 0.5% to 11.4%, although estimates for children varied from 0% to 1.3%. A few prevalent conditions that are known to worsen with age are psoriasis. There is little information available concerning the epidemiology of psoriasis. The degree of data now obtainable is not accessible to everyone due to its origins in only twenty countries, most of which belong to wealthy portions of the world. There are geographical imperfections, especially about economically disadvantaged regions where there has not been much research into epidemiology [4].

CHAPTER 2

Pathophysiology and Molecular Basis of Psoriasis

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Abstract: Psoriasis, a papulosquamous skin disease, is estimated to affect 2% of the global population. Traditionally believed to be a problem largely affecting keratinocytes in the epidermis, psoriasis has recently been identified as one of the most common immune-related diseases. Though this condition may manifest at any life stage, a dual distribution of age was observed, having a peak occurring between the ages of 20 and 30 as well as 50 and 60. Psoriasis possesses a complicated etiology that includes immunologic, hereditary, and systemic/local factors. Psoriasis shows an immense negative impact on human life quality, probably equivalent in comparison to coronary artery disease, type 2 diabetes, depressive disorders, and carcinoma, regardless of the fact that it usually possesses a minor influence on survival. The unregulated development of keratinocytes is the main constraint behind psoriasis, and improper regulation of the immune system serves as a pathophysiological factor. The pathogenesis generally includes the cooperation among several populations for immunocytes along with corresponding transmitting molecules that are: (1) innate immunocytes, which are mediated by antigenic-displaying cells, such as neutrophils, the cells of Langerhans, and natural-killing T lymphoid cells (2) acquired or adaptable immunocytes, which are facilitated by developed CD^{4+} and CD^{8+} T lymphocyte residing in the epidermis. The result of such immunological dysfunction leads to inflammation, which causes clinical lesions as well as histopathological inflammation, diagnostic of psoriasis development and perpetuation. The standard of lifestyle in patients has increased with biologic treatments, which focus on the cytokine-mediated pathophysiology of psoriasis. This book chapter will cover the molecular basis and primary pathophysiology of psoriasis.

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Keywords: Molecular targets, Mechanism of action, Psoriasis, Pathophysiology, Skin disorder.

INTRODUCTION

The human body's largest organ, the skin, acts as armor to shield our bodies from the outside world. It is made up of the dermis, epidermis, and hypodermis as its three primary layers [1]. The topmost part of the skin, termed the epidermis, is mostly composed of keratinocytes, which provide waterproofing and protection against UV radiation [2]. Underneath the skin's outer layer, the dermis provides a home to numerous glands, including sebaceous glands and sweat glands, vessels for blood, and nerve fibers [3]. Through mechanisms like perspiration, the skin is essential in controlling the body's temperature [4]. The skin plays a significant role in the synthesis of vitamin D when exposed to sunlight [5]. The skin's appearance and health may be subjected to a number of variables, such as genetics, age, diet, and environmental exposures [6]. A persistent inflammatory skin condition caused by the immune system, psoriasis is characterized by distinctive, colored, scaly patches. It is among the most common autoimmune diseases, affecting approximately 2% of people worldwide [7]. This disease is known for its relapsing and remitting nature, causing a significant physical and psychological burden on affected individuals [8]. Many comorbidities, such as psoriatic arthritis, diabetes, heart disease, and a condition called metabolic syndrome, are linked to psoriasis and psychological disorders, further impacting the overall health and well-being of patients [9].

Environmental factors, impaired immune system responses, and genetic susceptibility interact intricately in the pathogenesis of psoriasis [10]. The development of psoriasis is significantly influenced by genetic factors, with strong familial aggregation observed in affected individuals [11]. Psoriasis has an important detrimental effect on people's quality of daily life, frequently equal to the effects associated with other persistent illnesses like depressive disorders, diabetes, and carcinoma [12]. Due to the obvious form of skin rashes and the discomfort and irritation they cause, stigmatization in society and emotional distress may result, which can negatively impact various aspects of daily life [13].

Epidemiology of Psoriasis

A common persistent inflammatory skin condition, psoriasis affects about 2% of people globally [14]. This psoriasis prevalence varies across different geographic regions and ethnic groups, with higher rates observed in certain populations [15]. Psoriasis may develop at any age; however, there are two distinct stages of its onset, typically occurring within the age ranges of 20-30 and 50-60 [16]. Studies

have shown that the prevalence of psoriasis is transformed by genetic, environmental issues, and lifestyle variables, contributing to variability in its occurrence [17]. Psoriasis is associated with a substantial financial burden on individuals and healthcare systems. It has been connected to several medical conditions, such as psychological problems, a condition called metabolic syndrome, coronary artery disease, and arthritis caused by psoriasis, further impacting the overall health and well-being of patients [18]. Furthermore, the economic burden of psoriasis is substantial, with the total cost of the illness being increased by both immediate healthcare expenses and additional expenses related to disability and reduced productivity [19].

Prevalence and Age Distribution of Psoriasis

Prevalence

The prevalence of psoriasis varies significantly across populations, with estimates ranging from 0.27% to 11.4% in adults, depending on factors such as:

Geography: Prevalence varies based on location, with higher rates observed in certain regions like northern Europe and lower rates in Southeast Asia.

Ethnicity: Genetic predisposition plays a role, with higher rates among certain ethnic groups like Caucasians.

Age: Any person of any age can develop psoriasis; however, it typically manifests in two stages: early development (20–30 years) and late onset (50–60 years).

Here are some specific prevalence estimates:

- Global: 2.7% (lifetime prevalence)
- Italy: 3.5% at age 60-64 years
- United States: 1.6%
- North India: 0.44% to 2.8%
- Taiwan: 0.30% [20 - 24].

Age Distribution

The age distribution of psoriasis demonstrates a bimodal trend that includes two age-related groups:

Initiation very early: between the ages of 20 and 30

Delayed initiation, aged 50 to 60

CHAPTER 3

Combination Approach for the Management of Psoriasis

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Abstract: Psoriasis is a prominent autoimmune condition characterized by an abnormal increase in the production of skin cells, leading to the formation of thick, red, and scaly patches on the skin. Comprehending the intricate pathophysiology of this condition, which involves the deregulation of the immune system and inflammatory processes, is essential for the development of efficacious treatments. Existing treatment modalities, such as monotherapy, have inherent constraints in effectively managing psoriasis of moderate to severe intensity, resulting in persistent symptoms and reduced responsiveness to treatment. Therefore, using a combination strategy that focuses on various disease-causing pathways provides improved effectiveness in treatment, decreases the development of resistance, and improves patient outcomes. Nevertheless, it is crucial to carefully evaluate issues such as personalized treatment regimens, adherence to therapy, economic factors, and the handling of medication interactions and toxicities. Customized treatment methods, novel combination medications, and integrated therapy platforms have the potential to maximize psoriasis control. Thorough and personalized combination approaches hold great promise for improving the quality of life for individuals with psoriasis.

Keywords: Adherence therapy, Monotherapy, Psoriasis, Personalized combination approaches.

INTRODUCTION TO PSORIASIS

Psoriasis is a persistent autoimmune disorder marked by the rapid regeneration of skin cells, leading to the development of thick, red, scaly regions called plaques. This polygenic illness impacts about 2-3% of the worldwide population, establishing it as one of the most widespread persistent skin conditions globally. Psoriasis mainly appears on the skin but may also affect the nails, joints, and other

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organs, resulting in various clinical presentations and problems. Psoriasis manifests in several forms, with plaque psoriasis being the predominant subtype, representing about 80-90% of cases [1, 2]. Additional variations of psoriasis include (i) guttate psoriasis, which is defined by tiny, droplet-shaped lesions, (ii) pustular psoriasis, which is characterized by blisters filled with pus, and (iii) erythrodermic psoriasis, which involves extensive inflammation and shedding of the skin. Psoriasis may vary significantly in its severity and extent across people, ranging from isolated, moderate lesions to severe, widespread involvement that affects huge regions of the body surface [1, 2].

Epidemiology and Clinical Presentation

Psoriasis can affect individuals of various age groups, races, and ethnic backgrounds; however, it is most often seen in adults aged 15 to 35 years. Psoriasis is influenced by both hereditary and environmental factors, and having a family history of the illness raises the likelihood of experiencing it. Psoriasis symptoms may worsen or cause disease flares due to environmental stressors such as stress, infections, trauma, and certain drugs [3].

From a clinical perspective, psoriasis often appears as distinct, red patches on the skin that are covered with white scales. These plaques often manifest on areas of the body with extended surfaces, such as the elbows, knees, scalp, and lower back, but they may emerge on any part of the body. Psoriasis not only affects the skin but may also cause problems with the nails, such as pitting, thickness, and discoloration. It can also impact the joints, resulting in psoriatic arthritis in about 30% of patients [2, 3].

Impact on Quality of Life

In addition to its visible symptoms, psoriasis significantly impacts the overall well-being of patients, including their emotional state, social relationships, and ability to carry out everyday activities. The observable characteristics of psoriatic lesions may cause individuals to experience emotions of shame, self-awareness, and social seclusion, resulting in psychological anguish and diminished self-worth. Furthermore, the persistent and recurring characteristics of psoriasis, along with the uncertain progression of the condition, may lead to emotions of frustration, worry, and sadness in those afflicted [4].

Psoriasis not only causes psychological and social difficulties, but also raises the likelihood of other health problems, such as cardiovascular disease, metabolic syndrome, and psoriatic arthritis. These additional conditions further harm the overall health and well-being of sufferers. It is crucial to consider and meet the comprehensive requirements of patients with psoriasis, including their physical,

mental, and social aspects, to enhance treatment results and improve their overall well-being [1, 4].

UNDERSTANDING THE PATHOPHYSIOLOGY

Psoriasis is a multifaceted inflammatory condition characterized by disrupted immune responses, aberrant growth of skin cells called keratinocytes, and the interplay of genetic and environmental factors. Comprehending the fundamental pathophysiology is crucial for formulating effective therapy approaches to control this persistent illness.

Immune Dysregulation and Inflammatory Cascade

The dysregulation of immunological responses, namely involving T lymphocytes and dendritic cells, is a key factor in the development of psoriasis. Psoriatic lesions are characterized by the infiltration of activated T cells, mostly belonging to the Th1 and Th17 subsets. These T cells produce pro-inflammatory cytokines, including Tumor Necrosis Factor-alpha [TNF-α], Interleukin-17 [IL-17], and Interleukin-23 [IL-23], into the skin, all steps are illustrated in Figures 1-4. These cytokines activate keratinocytes and other immune cells, triggering a continuous process of inflammation and tissue damage. In addition, the deregulation of the innate immune system, which involves aberrant activation of dendritic cells and alterations in cytokine signaling pathways, plays a role in the inflammatory process of psoriasis.

Abnormal Keratinocyte Proliferation

Psoriasis is defined by abnormal growth and maturation of keratinocytes, resulting in excessive epidermal lesions [2]. Keratinocytes often experience regulated proliferation and differentiation as a component of the skin's healing mechanism. In psoriasis, the signaling pathways involving Nuclear Factor kappa B [NF-κB], Mitogen-Activated Protein Kinases [MAPKs], and Janus Kinase/Signal Transducer and Activator of Transcription [JAK/STAT] are not functioning properly, as shown in Fig. (**1**). This leads to an excessive growth of keratinocytes and a disruption in their normal development. This leads to the development of distinctive psoriatic plaques, which are characterized by a thicker outer layer of skin, longitudinal folds in the lower layer of skin, and the presence of abnormal keratinization [5, 6].

CHAPTER 4

Gene Therapies in the Management of Psoriasis

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Abstract: Psoriasis is a long-lasting autoimmune dermatological disorder affecting millions of individuals globally, causing substantial physical and psychological distress. While various treatment options, including topical creams, phototherapy, and systemic medications, resulted in relief for several sufferers, a significant portion of those affected by psoriasis remains inadequately treated. In recent years, gene therapy has emerged as a promising frontier in the field of dermatology, offering the potential for more effective and targeted treatments. This chapter reviews the current landscape of gene therapies for the management of psoriasis. It explores the underlying genetic factors contributing to psoriasis susceptibility, emphasizing the role of the immune system and the dysregulation of keratinocyte proliferation. The chapter also explores the various gene therapy approaches being developed to target these specific mechanisms. Recent advancements in gene editing technologies, such as CRISPR-Cas9, have paved the way for precise and targeted modification of genes associated with psoriasis. Researchers are developing strategies to either suppress overactive immune responses or correct genetic mutations that contribute to the pathogenesis of psoriasis. Promising preclinical and clinical results suggest that gene therapies hold the potential to provide long-lasting relief and even a cure for some patients. While gene therapy for psoriasis is still in its experimental stages, early trials have shown encouraging results with minimal side effects. It is essential to acknowledge the challenges and ethical considerations associated with gene therapy, including the need for rigorous safety and efficacy assessments. In conclusion, gene therapies offer a promising avenue for treating psoriasis, with the potential to revolutionize the management of this chronic condition. Ongoing research and clinical trials will determine the safety and effectiveness of these innovative approaches, ultimately providing hope for those suffering from psoriasis and paving the way for personalized, precision medicine in dermatology.

Keywords: Autoimmune, CRISPR-Cas9, Gene Therapy, Keratinocyte Proliferation, Psoriasis Management.

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INTRODUCTION

Psoriasis is a prevalent, persistent papulosquamous dermatological disorder that can develop at any age and varies in prevalence depending on the nation, indicating that environmental variables, genetic background, and ethnicity all influence its emergence [1]. It is related to a multitude of significant medical dysfunctions, such as psoriatic arthritis, depression, and cardiometabolic syndrome. Psoriasis is an inflammatory dermatological condition that affects approximately 60 million people and children worldwide [2]. One of the WHO's primary research priorities is determining the worldwide burden of psoriasis. It is characterized by erythematous plaques that are well-defined and covered with silvery-white scales, usually affecting the elbows, knees, trunk, and scalp in a symmetrical pattern. This is at least three times more than the number of DALYs caused by inflammatory bowel disease [3]. When genetic and/or environmental factors activate plasmacytoid dendritic cells, proinflammatory cytokines such as tumor necrosis factor [TNF]-α, interferon [IFN]-γ, interleukin [IL]-17, IL-22, IL-23, and IL-1β are produced; this refers to the initial stage of psoriasis [4]. Among the acknowledged environmental causes and correlations are streptococcal infections, physical trauma, specific medications (including antidepressants, antihypertensive meds, and anti-cytokine therapy), smoking, and alcohol addiction. It wasn't until 1841 that von Hebra recognized psoriasis as a distinct medical condition, dispelling the earlier belief that it was a variant of leprosy [5]. Hereditary factors primarily influence the pathophysiology of psoriasis. Situated on chromosome 6p21, inside a roughly 220 kb length of the major histocompatibility complex, is a substantial susceptibility locus for psoriasis known as PSORS1. An early onset of severe and unstable sickness is associated with the susceptibility allele within PSORS1, HLA-Cw6 [6]. The three primary histologic features of psoriasis are epidermal hyperplasia, dilated and prominent blood vessels in the dermis, and an inflammatory leukocyte infiltrate, primarily in the dermis. In addition to the skin, psoriasis also affects the joints and nails. The three main clinical manifestations of psoriasis are Generalised Pustular Psoriasis [GPP], psoriasis vulgaris, and psoriatic arthritis. Obesity, diabetes, metabolic syndrome, hypertension, hyperlipidaemia, psoriatic march, inflammatory march, and chronic kidney disease are other systemic disorders that may occur with psoriasis. Psoriasis patients frequently experience psychological difficulties and psychiatric conditions, including depression [7]. Fig. (**1**) illustrates the key symptoms of psoriasis, providing an overview of its clinical presentation, and Fig. (**2**) highlights the risk factors associated with the onset and worsening of psoriasis.

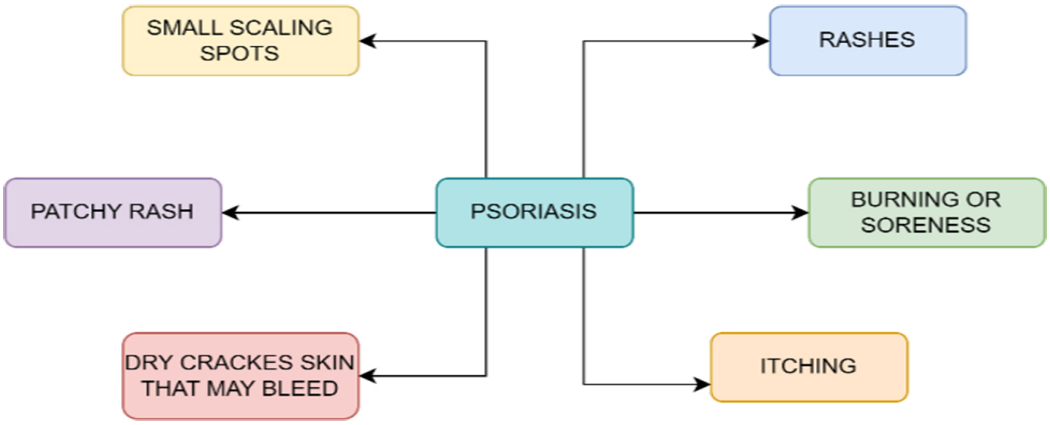

Fig. (1). Symptoms of psoriasis.

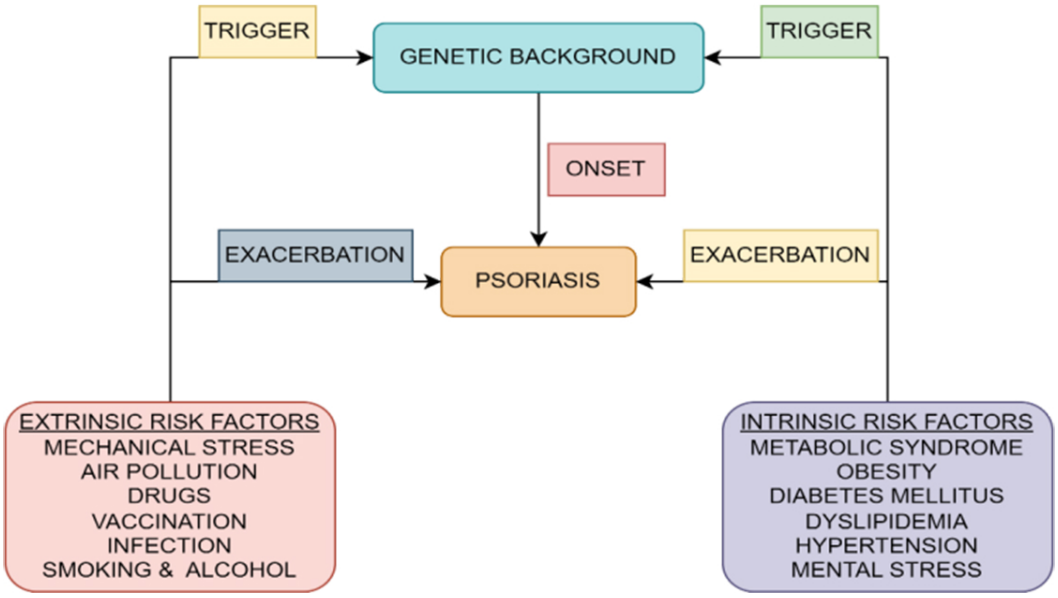

Fig. (2). Risk factors for onset and worsening of psoriasis [8].

PREVALENCE

Studies conducted recently indicate that around 8 million Americans suffer from psoriasis [9]. The World Psoriasis Day consortium estimates that approximately 125 million individuals worldwide, or 2-3% of the global population, suffer from psoriasis. Approximately thirty percent of individuals with psoriasis are likely to develop psoriatic arthritis [10]. 3.6 percent of Caucasians and 1.5 percent of African Americans suffer from psoriasis [11]. Due to variations in clinical presentation, psoriasis is probably underdiagnosed in African Americans and

CHAPTER 5

Conventional Therapies and Challenges in the Treatment of Psoriasis

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Abstract: Psoriasis is an autoimmune disease that re-emerges through the proliferation of keratinocytes. It occurs at any age, but is usually observed in temperate regions. It has a global population of 2 to 5 percent on average. The treatment of psoriasis remains a daunting task, with various challenges affecting treatment, including patient compliance and adherence, delicate patient profiles, psychological aspects, and skin as an obstacle to current delivery. Psoriasis is characterized by an excessive proliferation of cells, resulting in painful skin spots due to the absence of normal skin cell replacement, which occurs every 3 to 4 weeks. Treatment strategies for psoriasis depend on the severity and location of the injuries. The current chapter reviews the therapies and challenges associated with current treatments, including topical therapy, oral therapy, biological therapy, parenteral therapy, and phototherapy.

Keywords: Challenges, Psoriasis, Therapies, Treatment.

INTRODUCTION

Psoriasis is a frequently occurring, autoimmune, and inflammatory disease characterized by red, inflamed plaques and macules resulting from increased keratin-producing epidermal cell proliferation and poor differentiation. These plaques are often accompanied by silvery scales [1]. The highly inflamed lesions appear as a result of defective signals produced by the immune system to increase the mitosis rate of keratin-producing cells by tenfold [2]. This, in turn, leads to nuclear retention and incomplete cornification of stratum corneum cells. This disease develops at an early stage of life and progresses slowly throughout life. Psoriasis varies according to the affected tissues [3 - 6]. The prevalence of psoriasis has been reported to range between 0.09% and 11.43% [7]. Psoriasis, on

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average, affects 2% to 5% of the population worldwide [8]. Even if it spreadsglobally, its prevalence differs depending on the location and ethnicity. In general, the higher the latitude, the greater the prevalence [9].

As a result, compared to countries farther from the equator like Europe and Australia, Asia and Africa had lower rates of psoriasis [10].

Men and women are equally affected by psoriasis; however, women experience the disease's beginning substantially sooner [11]. The prevalence of the condition has multiplied during the past few years, according to recent studies [12]. A full cure remains elusive despite the plethora of therapeutic choices available today to lessen the disease's signs and symptoms. Some of the drawbacks of traditional medication delivery methods, such as topical treatments, include excessive dose frequency, poor drug penetration, and low patient compliance [13]. Conventional remedies are also limited by the toxicity of phototherapy and systemic therapy. Thus, it is crucial to investigate and create new safe and effective delivery methods for the treatment of psoriasis [14].

Current choices for Treatment

Conventional methods of treating psoriasis include topical, oral, biological, and parenteral treatments (Fig. **1**). Another treatment option for symptoms is phototherapy.

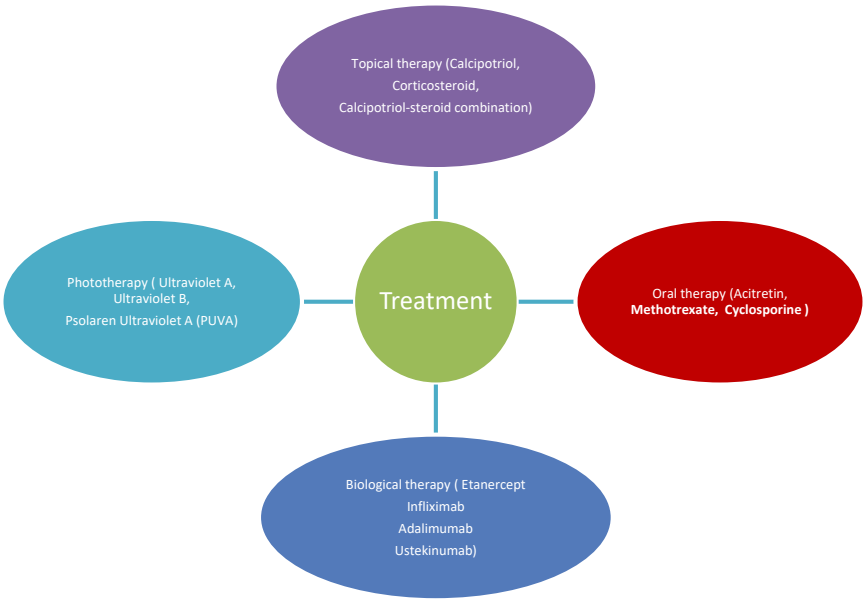

Fig. (1). Current Treatment choices for psoriasis.

Topical Therapy

Topical therapy for psoriasis typically yields moderately to unsatisfactory results and is often accompanied by irritation [15]. For mild to moderate psoriasis, topical therapy is considered the primary form of treatment. On the other hand, systemic administration combined with topical therapy may be helpful in extreme situations. Topical treatments may cause unwanted skin interactions, such as burning and irritation, which could lead to patient non-compliance [16].

Oral therapy

The majority of medications used in oral therapy for psoriasis are those that may be taken orally and administered successfully. When it comes to side effects, oral medications have more than topical treatments. As a result, it is not often acknowledged. To reduce adverse effects and increase efficacy, it is used as monotherapy, in combination with biologics, and phototherapy. When topical therapy is unable to alleviate symptoms, oral therapy is typically employed. Drugs frequently used in oral treatment include the following:

Acitretin

Since the 1970s, this acid metabolite of etretinate has been employed as a therapeutic agent. It is a retinoid that works by preventing keratinocytes from proliferating [17]. It is not immunosuppressive and is derived from vitamin A.

Methotrexate

It functions as an inhibitor of dihydrofolate reductase, an enzyme that is required for the synthesis of purines and pyrimidines during the synthesis of DNA. It is the most established and least expensive systemic medication for treating mild to moderate psoriasis. It reduces inflammation by breaking down into polyglutamate analogues, which raise the amount of the anti-inflammatory chemical adenosine [18]. It raises T-cell apoptosis and reduces epithelial layer hypertrophy [19]. It is also an immunosuppressive and anti-proliferative medication. Typically, folic acid supplements are advised in conjunction with it to lessen any potential negative effects. When used repeatedly, it might be harmful to the liver. There are many interactions between methotrexate and other medications, including salicylates and antibiotics. As a result, precautions should be taken while taking these medications.

Cyclosporine

For decades, this putative calcineurin inhibitor has been used to treat moderate to severe cases of psoriasis. It reduces the synthesis of IL2 as a result of this

CHAPTER 6

Phytopharmaceuticals in the Management of Psoriasis

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Abstract: Psoriasis is a globally prevalent chronic inflammatory condition. Traditional treatment methods often rely on immunosuppressive agents, which can have adverse effects on the human body. As a result, alternative therapies, particularly those utilizing phytoconstituents with immunomodulatory, antioxidant, and anti-inflammatory properties, have gained attention. This chapter explores the potential of medicinal plants and phytoconstituents in managing psoriasis symptoms and supporting long-term disease control. However, to fully harness the therapeutic benefits of these plant-derived compounds and integrate them into standard dermatological care for psoriasis patients, further research and rigorous clinical validation are essential.

Keywords: Bioactive components, Medicinal plants, Psoriasis, Pathology, *Psoralea corylifola*.

INTRODUCTION

Psoriasis, a longstanding autoimmune disease, has been recognized since ancient times [1]. It is one of the most common hereditary skin diseases, characterized by the abnormal proliferation and shedding of skin cells, leading to the formation of psoriatic plaques, pustules, and scaly patches [2]. The papillary dermis, the topmost layer of the dermis, is where the first lesions show up. At this point, blood vessels dilate and become more curved, allowing granulocytes and neutrophil-absorbing lymphocytes to migrate towards the epidermis, which remains visible as normal. This marks the beginning of abnormal keratinocyte proliferation and migration. As psoriasis progresses, the epidermis thickens and

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keratinocytes fail to fully differentiate. This leads to the loss of the granular layer and the development of parakeratosis, a condition in which keratinocytes retaintheir nuclei. In the later stages, certain skin cell populations proliferate excessively, resulting in the expansion of the spinous layer—a condition known as acanthosis. Removal of psoriatic plaques may lead to pinpoint bleeding due to the presence of dilated blood vessels extending into the upper dermis [3].

Psoriasis is categorized as an autoimmune disease, resulting from the dysfunction of key pathways and elements in the immune system [4]. Individuals who have severe psoriasis also have an elevated risk for metabolic syndrome, such as obesity, hypertension [5 - 7]. Although conventional therapies alleviate psoriasis symptoms, the literature suggests that a complete cure remains unattainable. This results in an urgent need to develop safe and effective, yet affordable, treatments for psoriasis. Recent research suggests targeting or regulating the activity of progressive cells involved in psoriasis using herbal drugs. Literature reviews have documented the effectiveness of herbal remedies in managing psoriasis, highlighting the supportive role of phytochemicals in treating psoriasis [8, 9]. Highlighting the impact of phytochemicals on oxidative stress and immune pathways, the review consolidates evidence on the anti-inflammatory and immunomodulatory effects of natural compounds, as well as their molecular interactions, which alleviate psoriatic inflammation and progression.

SUBSTANCES OF NATURAL ORIGIN—PLANTS AND PHYTOCHEMICALS WITH POTENTIAL THERAPEUTIC SIGNIFICANCE

In the ongoing exploration of innovative therapies, natural compounds have become a focal point, drawing attention due to their extensive diversity, favorable safety profile, and widespread availability [10]. Various clinical studies have demonstrated that specific natural substances of diverse origins exhibit the ability to alleviate psoriasis. These substances work by promoting apoptosis, inhibiting angiogenesis, suppressing inflammation triggered by reactive oxygen species, and overexpressing inducible nitric oxide synthase, among other molecular pathways [11, 12]. Some of the medicinal plants and their bioactive components are explained below:

Vegetal Medicinal Plants

Aloe vera

Aloe vera has earned global recognition as a traditional remedy for various ailments, including antiseptic, anti-inflammatory, wound-healing, and antidiabetic properties, particularly for skin disorders. Its gel, widely utilized in cosmetics and

pharmaceuticals, contains a plethora of potentially active components. Research suggests that these components play a role in mitigating the progression of psoriasis by alleviating skin itching and reducing inflammation. Research on a psoriatic model using TNF-α-stimulated HaCaT cells demonstrated promising outcomes, with various doses of Aloe vera extract administered over 24 hours supporting cell viability in these stimulated cells [13, 14]. Notably, an ethanolic extract derived from *Aloe vera* gel showed results comparable to tazarotene, indicating its potential as an effective treatment option for psoriasis. In essence, *Aloe Vera's* multifaceted therapeutic properties, supported by both traditional wisdom and scientific research, underscore its significance as a promising natural remedy for various health conditions, including psoriasis [15 - 17].

Artemisia capillaris

Artemisia capillaris has historically been employed in East Asia to address pyrexia and liver disorders as an herbal remedy [18]. Regarding psoriasis, the extract derived from *Artemisia capillaris* holds promise to inhibit excessive keratinocyte proliferation. Additionally, it reduces leukocyte influx by suppressing the expression of ICAM-1 and lowering nitric oxide levels through the inhibition of iNOS production [19, 20].

Hypericum perforatum

St. John's Wort (*Hypericum perforatum*) has a long history of traditional use [21]. In clinical trials, the topical application of St. John's Wort ointment demonstrated significant reductions in redness scores and the thickness of skin flakes compared to the placebo group [22]. Another study assessed the clinical effects of *Hypericum perforatum* as a topical treatment for plaque-type psoriasis. The results indicate a substantial reduction in erythema, scaling, and thickness [23].

Rehmannia glutinosa

Research indicates that *Rehmannia glutinosa* extract exhibits strong antioxidative effects, including scavenging free radicals, inhibiting iNOS, and reducing pro-inflammatory cytokines. It also lowers prostaglandin production by blocking the COX enzyme and thus suppresses chemotaxis through JAK-STAT inhibition, with efficacy demonstrated in both *in vivo* and *in vitro* studies [24 - 26].

Salvia miltiorrhiza

Salvia miltiorrhiza and its active compounds, known for anti-inflammatory, antioxidant, and antiproliferative effects, show potential antipsoriatic properties. *In vitro* studies on HaCaT cells and *in vivo* studies in IMQ-induced mice reveal

CHAPTER 7

Liposome-based Pharmacotherapy for the Management of Psoriasis

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Abstract: The chronic inflammatory skin disease, psoriasis, affects a large number of people globally. It is typified by immune system malfunction that results in a range of symptoms. The primary goal of conventional drug delivery methods for psoriasis treatment is to alleviate symptoms; however, these methods frequently fall short due to their poor safety and efficacy, low bioavailability, and limited effectiveness. Consequently, there has been an increase in interest in creating innovative drug delivery systems that might overcome these drawbacks. Liposomes, transferosomes, ethosomes, niosomes, emulsomes, dendrimers, hydrogels, nanoparticles, and others are examples of these novel drug delivery methods. Through modifications to pharmacokinetic and physiological factors, these formulations aim to enhance the therapeutic effects of medications. Liposomes are one of these systems that are the most promising for delivering medications to treat psoriasis. Liposomes are lipid bilayer-based tiny vesicles that can enhance the penetration of medications through the stratum corneum, the outermost layer of the skin. When applied topically, this increased penetration can improve the delivery of medications into or through the skin. Improved therapeutic results are a result of liposomes' many benefits, which include longer drug release and enhanced stability. The potential of liposomes as a drug delivery mechanism for treating psoriasis is the main topic of this chapter. By encapsulating anti-psoriatic medications inside liposomes, researchers aim to enhance treatment efficiency and target areas affected by psoriasis. Treating psoriasis with liposomes has the potential to enhance patient outcomes by overcoming the limitations of traditional drug delivery methods. In conclusion, the development of innovative medication delivery methods, such as liposomes, offers a viable strategy for managing

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psoriasis. Through the utilisation of liposomes' distinct characteristics, such as their enhanced drug penetration and extended release, scientists aim to augment the therapeutic outcomes of pharmaceuticals and improve the overall treatment of psoriasis.

Keywords: Drug delivery, Innovative formulations, Liposomes, Pharmacotherapy, Psoriasis, Skin Disease, Targeted therapy, Topical delivery.

INTRODUCTION

Psoriasis is a skin condition typified by the production of red, thicker plaques coated in silver-white scales, indicating autoimmune T-cell activity. The research shows that the precise cause of psoriasis is still uncertain. Psoriasis can now be treated with a variety of antipsoriatic medications, but these treatments are primarily aimed at relieving symptoms and can have serious side effects. Topical treatments, phototherapy, and systemic interventions are among the available treatments, but none of them offer a permanent cure. Researchers are actively investigating the potential of various colloidal carriers within drug delivery systems to overcome the limitations of current therapies, which include safety concerns, inefficiency, and unfavourable cosmetic outcomes. These limitations underscore the need for enhanced drug delivery systems in the treatment of psoriasis [1]. Different types of carriers, including ethosomes, liposomes, niosomes, transferosomes, solid lipid nanoparticles, microspheres, micelles, dendrimers, and other innovative platforms, are being investigated. Carriers offer opportunities to develop more effective therapeutic regimens for psoriasis by addressing the shortcomings of current treatments. By utilizing these advanced drug delivery systems, researchers aim to improve drug efficacy, minimize side effects, and ultimately enhance patient outcomes. Each carrier has its unique properties and benefits, which are being explored to optimize the delivery of the drug to the affected areas of the skin. The exploration of these novel drug delivery systems holds promise for revolutionizing the treatment of psoriasis. It offers the potential to deliver antipsoriatic drugs more efficiently, enhance drug stability and release, and improve patient adherence during prolonged use. Through these advancements, researchers aim to deliver improved outcomes for individuals with psoriasis and alleviate the challenges associated with conventional therapies [2]. Research on novel drug delivery methods for treating psoriasis is currently underway, with a focus on colloidal carriers. Using carriers, such as ethosomes, liposomes, niosomes, transferosomes, solid lipid nanoparticles, microspheres, micelles, dendrimers, and others, scientists aim to overcome the limitations of existing treatments and achieve better outcomes for patients with psoriasis. These developments could significantly alter the way this chronic skin condition is treated, offering safer and more efficient alternatives.

Alec D. Bangham made the initial discovery of liposomes at the University of Cambridge's Babraham Institute in the 1960s. These lipid-based structures consist of one or more concentric lipid bilayers enclosing an aqueous compartment. Liposomes were once made entirely of natural lipids; however, nowadays they can also include surfactants and a mixture of synthetic and natural lipids. They are remarkable in that they can contain lipophilic and hydrophilic substances in their lipid membrane and watery core. Liposomes are spherical in shape and can have a size range of several micrometers to a few nanometers. However, the diameter of liposomes employed in medicine is usually between 50 and 450 nm. Over the past 50 years, liposomes have been the subject of much investigation due to their similarities to cellular membranes and their ability to incorporate different molecules [3]. They are widely valued for their benefits in biology and technology as the best delivery vehicles for biologically active compounds in both *in vitro* [lab settings] and *in vivo* [living creatures] contexts. Indeed, liposomes are considered the most effective medication delivery technology available today.

Significant advancements have been made in the field of liposome research within the past 20 years. While some liposome-based biomedical applications are currently undergoing clinical studies or are about to enter the market, others have already received approval for general use. Hence, the emphasis is on critical elements that are essential for the creation of liposomal compositions intended for medicinal use. This chapter describes how the size, surface charge, and lipid organization of liposomes, as well as the physicochemical parameters of their membranes and component makeup, affect their efficacy. It also examines how these physicochemical characteristics impact liposome stability in the circulation, their ability to enter various types of tissues, their interaction with cells, and ultimately, their final destination in the body. The overview focuses on methods that have been developed to overcome the drawbacks of early-generation liposomes, which have been crucial in facilitating the transition from laboratory research to clinical trials or commercialization. Liposomes are versatile, lipid-based structures that have garnered significant attention in the scientific community [4]. They offer numerous advantages as drug delivery systems and have shown promising results in various biomedical applications. Understanding the physicochemical properties of liposomes and their impact on efficacy, stability, tissue targeting, and cellular interactions is vital for the development of improved therapeutic liposomal formulations.

TYPES OF PSORIASIS

The degree of inflammation, the location of the rash, the persistence of a patient's medical issues, and other clinical considerations are some of the variables that determine the classification of psoriasis into different categories. These categories

CHAPTER 8

Niosomes-Based Pharmacotherapy for the Management of Psoriasis

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Abstract: Background: Psoriasis is a long-term autoimmune disease that causes skin cells to develop quickly, resulting in thick, red, scaly areas on the skin's surface. The itchiness and pain associated with these patches can significantly impact the quality of life for those affected. The primary objectives of psoriasis therapy are to reduce inflammation, inhibit excessive skin cell growth, and alleviate symptoms.

Objective: Despite ongoing research efforts, patient satisfaction with existing topical therapies for psoriasis remains limited. There is a pressing need to enhance the safety, efficacy, and comfort of topical therapies by developing innovative drug delivery and carrier systems.

Method: Using niosomes, which are non-ionic surfactant-based vesicles that can encapsulate both hydrophilic and hydrophobic medications, is one intriguing strategy. The pharmaceutical industry has shown considerable interest in niosomes due to their potential to reduce toxicity and enhance therapeutic efficacy. With low toxicity and optimal targeting efficacy, these vesicles provide a unique method of delivering a variety of therapeutic agents, including chemical drugs, protein-based therapies, and genetic materials.

Results: Studies have reported that niosomes can increase drug bioavailability and stability, making them a viable option for drug delivery in the treatment of psoriasis. Compared to conventional topical treatments, niosomes offer improved stability during formulation and storage, which may lead to enhanced therapeutic outcomes and increased patient satisfaction.

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Conclusion: The use of niosomes represents a promising approach to enhancing topical therapy in the management of psoriasis. Their capacity to minimize toxicity and encapsulate a variety of medications, including hydrophilic and hydrophobic agents, makes them a desirable choice for improving the comfort, safety, and efficacy of psoriasis therapy. Continued research and development in this field could significantly advance the treatment of psoriasis and other dermatological conditions.

Keywords: Drug delivery system, Nanotechnology, Niosomes, Pharmacotherapy, Psoriasis.

INTRODUCTION

Psoriasis is an autoimmune disease that is influenced by both genetics and environmental factors. It causes inflammation and activates keratinocytes, leading to their proliferation and differentiation. Psoriasis affects approximately 2% of the global population, and significant progress has been made in its diagnosis and treatment. However, epidemiological data are available for only 19% of countries. Although psoriasis affects fewer than 1% of youth worldwide, regional differences exist in its incidence [1]. East Asia has the lowest frequency of psoriasis at 0.12%, whereas Western countries have an average incidence of around 2%. Norway has the greatest prevalence of psoriasis, accounting for 1.98% of its population. Although it may appear anywhere on the skin, psoriasis is categorized as an epithelial disorder characterized by red, scaly patches that are usually seen on the elbows, knees, scalp, and lower back. Other side effects include psychological diseases, cardiometabolic problems, and psoriatic arthritis [2].

To initiate and sustain the inflammatory state, including epigenetic modifications, targeting keratinocytes is crucial in psoriasis therapy regimens. Human keratinocytes, which proliferate up to 10 times faster than normal epithelial cells, are a hallmark of psoriasis. In response to injury, HaCaT generates distal antigens that stimulate dendritic cells at the primary level. Keratinocyte cells use pattern recognition receptors to identify tissue damage and external or pathogenic contaminants. Bacteriocins and inflammatory cytokines are among the secondary intermediates produced when HaCaT is activated. Due to their antibacterial, antispasmodic, antiproliferative, and antioxidant properties, Intrinsically Therapeutic Nanoparticles (ITNPs) are effective in treating a range of diseases. The field of psoriasis therapy has seen a revolutionary change since the FDA approved etanercept in 2004. Research has reported that different kinds of NPs may encapsulate different APIs. The best nano-based treatments for psoriasis, however, are liposomes and nanocapsules [3]. Lipid-based nanostructures, combined with anti-psoriatic drugs, improve skin permeability and reduce psoriasis symptoms. Furthermore, due to their large porous structure, which

promotes durability, extended dispersion, and percutaneous absorption, these treatments are more effective in treating psoriasis lesions. Colloidal carriers, such as lipoprotein nanostructures (NLCs) and solid lipid nanoparticles (SLNPs), facilitate the transport and dispersion of bioactive substances. NLCs and SLNPs are also efficient choices for targeted medication delivery.

The current method for treating superficial psoriasis is to ensure that the NPs remain on the afflicted region for an extended period by maintaining the nanomaterial composition during API release. Psoriasis, particularly in its advanced stages, is closely associated with inflammatory diseases, metabolic syndrome, and cardiovascular conditions [4]. Topical medications are used in short-term therapy for moderate to severe psoriasis and mild psoriasis. Innovative psoriasis treatments, such as siRNAs and targeted therapies for cutaneous (skin) and mucosal manifestations, are increasingly focused on genetic variations underlying the disease's etiology. Several studies have reported that although different APIs can be added to various lipid nanostructures, liposomes and nanoemulsions are the most effective carriers for psoriasis treatments. Anti-psoriatic agents delivered *via* SLNPs reduce the symptoms of psoriasis while increasing skin permeability. Nowadays, psoriasis may be successfully and safely treated using nanoformulations [5].

PATHOPHYSIOLOGY OF PSORIASIS

Pustular psoriasis, including localized forms, such as Palmoplantar Pustulosis (PPP), is a severe autoimmune condition characterized by abnormal epithelial stratification, inflammatory cell infiltrates, and a predominant Th1 and Th17 immune response. There is growing recognition that psoriasis is a systemic clinical issue rather than just a skin condition. This illness causes skin abnormalities and promotes the proliferation of HaCaT cells by activating pathogenic T lymphocytes and innate immune cells. While T cells play a central role in the development of Palmoplantar Pustulosis (PPP), an autoimmune disease, the role of B cells has only recently gained attention. Although T cell activation contributes significantly to PPP pathology, it does not fully explain all aspects of the disease [6]. Additionally, interactions between platelets and lymphocytes have been observed in psoriatic mouse models and other inflammatory conditions; however, their role within psoriatic lesions in human patients remains unclear [7].

An immune-competent skin model of inflammatory lesions has demonstrated a slow initiation of epithelial differentiation, hyperproliferation of basal keratinocytes, increased production of pro-inflammatory cytokines, and alterations in the expression of key transcriptional regulators. This highlights the

CHAPTER 9

Nanostructured Lipid-Based Pharmacotherapy for the Management of Psoriasis

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Abstract: Psoriasis, a chronic autoimmune skin disorder, poses a significant therapeutic challenge due to its complex Etiology and variable clinical manifestations. This abstract highlights recent advancements in novel carrier systems that revolutionize psoriasis management and pharmacotherapy. These innovative carriers aim to improve drug delivery, enhance therapeutic efficacy, and mitigate the adverse effects of conventional treatments. Psoriasis is characterised by hyperproliferation of keratinocytes, inflammation, and immune dysregulation. Conventional treatments often involve topical corticosteroids, phototherapy, or systemic immunosuppressants, each with its limitations, such as variable efficacy and side effects. The emergence of novel carrier systems, including liposomes, nanoparticles, and microneedle arrays, provides a promising avenue for addressing these challenges. Advanced drug delivery systems enable the precise delivery and management of the release of therapeutic agents, enhancing their penetration into the affected skin layers. Liposomal formulations, for instance, offer improved drug stability and sustained release, minimizing the need for frequent applications and reducing side effects. Nanoparticles provide a platform for encapsulating various drugs, offering enhanced solubility and bioavailability. Moreover, the integration of personalized medicine approaches into carrier design allows for tailored treatment regimens based on individual patient characteristics. This shift towards precision medicine holds the potential to optimize therapeutic outcomes and minimize adverse reactions.

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Keywords: Autoimmune skin disorders, Carriersystems, Drug delivery, Innovative formulations, Nanomedicine, Pharmacotherapy, Psoriasis, Personalized medicine, Targeted therapy, Topical treatments.

INTRODUCTION

Psoriasis, a skin disorder driven by autoimmune T-cell activity, manifests as red, thickened plaques covered by a silver-white scale, characterized by repeated episodes of inflammation and excessive skin thickening. Despite its prevalence, the exact origin of psoriasis remains unidentified. Contemporary treatments employ a diverse range of antipsoriatic drugs with varying mechanisms and administration routes [1]. However, many conventional therapies focus on symptom suppression and often yield notable side effects. Presently, treatment modalities include topical applications, phototherapy, and systemic interventions, yet none of these approaches guarantees a complete cure for the condition [2]. These methods are not only unsafe and inefficient but also contribute to unfavourable cosmetic outcomes and the associated side effects, resulting in less-than-ideal patient outcomes and poor adherence during prolonged use. A critical challenge in achieving effective therapy lies in the absence of a perfect carrier for antipsoriatic drug delivery. To address this limitation, researchers are actively exploring the potential of various types of colloidal carriers that are utilized within the drug delivery system. Some commonly used carriers are ethosomes, spherical lipid structures like liposomes, niosomes, transferosomes, solid lipid nanoparticles, microspheres, micelles, dendrimers, and other innovative platforms. The aim is to establish more effective therapeutic regimens by utilizing these distinct drug delivery systems, addressing the shortcomings of current treatments, and ultimately offering improved outcomes for individuals dealing with psoriasis [3].

Types of Psoriasis

Psoriasis is categorized into four types based on various factors, such as the extent of inflammation, rash localization, acute or persistent health conditions in patients, and various clinical factors. Various forms of psoriasis exist, such as plaque, guttate, pustular, and erythrodermic forms of the chronic skin condition. The prevalent form is chronic plaque psoriasis, also known as psoriasis vulgaris, characterized by the development of lesions from small papules that aggregate to form plaques [4]. Guttate psoriasis, on the other hand, results from an immune response that can be exacerbated by a *Streptococcal* infection. This begins with tiny pink raised bumps that periodically become flaky. Erythrodermic psoriasis is a type of psoriasis that can cause significant loss of protein and fluids, which can disrupt the body's normal balance (homeostasis). This severe form represents an

advancement of existing psoriasis and often necessitates hospitalization due to complications like increased sophisticated conditions, such as *staphylococcal* infections, pustulosis, arthropathy, and growth retardation can manifest [5]. Pustular psoriasis, a severe variant, refers to the appearance of pus-filled lesions on the surface of the skin, typically confined to the palms and soles, but potentially spreading to other areas. Although these lesions have minimal systemic effects, they can be challenging to manage. Frequently, generalized pustular psoriasis is accompanied by symptoms, such as fever and malaise, along with complications that include fluid retention, disturbances in electrolyte levels, and susceptibility to infection. This type of psoriasis is characterized by frequent recurrence, requiring vigilant and aggressive management [6].

Pathogenesis of Psoriasis

The physical expression of psoriasis at a biological level arises from a profound alteration in the process of keratinocyte transformation, resulting in the creation of scaly patches. The process initiates as fresh cells are produced within the basal layer of the epidermis and move towards the outer layer, collecting around keratin, known as the stratum corneum, while losing their organelles. These cells become filled with keratin upon reaching the stratum corneum, providing protective benefits to the skin. Under normal conditions, keratinocytes within cells in the basal layer undergo division approximately every two weeks, during the shedding and renewal cycle of the epidermis. New cells span approximately four weeks [7]. However, in the skin affected by psoriasis, there is an expedited cell cycle, leading to cell division every 1.5 days, and keratinocytes migrate to the stratum corneum within 4 days. This rapid pace results in inadequate development and maturation of cells, contributing to the characteristic scaly appearance of an epidermis that has a thickness, *i.e.*, 3 to 5 times greater than normal. Psoriasis is further characterized by histological markers, including neutrophil clusters present in the outer skin layer, and significant quantities of T-cells and dendritic cells are found within the subcutaneous layer [8]. Noteworthy features also include a significant presence of mononuclear leukocytes, which results in the alteration of blood vessels within the papillary dermal region into elongated or excessively proliferative forms, resulting in the redness of psoriatic lesions, attributable to considerable dilation of these blood vessels. Additionally, endothelial cells in psoriatic lesions exhibit characteristics resembling those of vessels with elevated endothelial characteristics typically found within lymph nodes, attributed to the attachment comprising lymphocytes, monocytes, and neutrophils. Activation of cells present in the endothelial layer is evident in psoriatic lesions, the existence of intracellular adhesion molecule-1 (ICAM-1 or CD54), vascular cell adhesion molecule-1 (VCAM-1 or CD106), and E-selectin (CD62E) during staining signifies the adherence of lymphocytes, monocytes, and neutrophils [9].

CHAPTER 10

Nanosponges as Drug Carriers for the Management of Psoriasis

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Abstract: Psoriasis is a chronic skin condition characterized by the hyperproliferation of keratinocytes in the epidermis, resulting in a high turnover rate of the epidermal cells. Apart from its physical manifestations, it also impacts an individual's psychological well-being. Its symptoms, such as pain, itching, and peeling, are more severe than those of other diseases, leading to a higher prevalence of depression and anxiety. Nanosponges are versatile nanoparticle platforms with porous, three-dimensional structures that can effectively encapsulate and deliver a wide range of drugs and bioactive molecules, owing to their distinct capabilities, including controlled release patterns and the ability to target delivery. In this review, the advantages of nanosponges as a drug delivery system for treating the disease will be discussed.

Keywords: Bioactive molecules, Epidermis, Nanosponges, Psoriasis, Targeted delivery.

INTRODUCTION

Delivery systems are continually improving day by day, enabling the controlled release of the drug at the proper place and precise intensity, providing a great mastermind that deserves all honor, simply trying to get the bull's eye goal while both hands and one leg are tied. [1] Nanofabrication, a new and complex development, can be considered akin to the invention of fire during the Stone Age [2].

Nanofabricationinvolve playing around with materials so tiny that you would need a microscope just to see them properly— materials whose properties can be enhanced by manipulating them at the nanoscale. Nanotechnology deals with

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dimensions at the level of nanometers, which is about as small as you can get without talking about individual atoms. Nanomaterials are real physical substances whose sizes fall within 1-100 nm; nanoparticles make up a special class owing to their size-specific features localized around interfaces — think oasis in a desert [3]. Various forms make up these nanoparticles, such as polymeric pearls, phospholipid pebbles, carbon clusters, spongy spheres (to store treasure troves of drugs), micellar marbles, dendrimer diamonds, *etc.* The impact of nanotechnology is profound, as it allows precise control at both spatial and temporal scales. Through a nanofabrication approach, certain designs of individual components can be manufactured and arranged in a way that the desired final substrate is obtained. This nano-synthesis and nanoassembly of engineered substrates make it possible to tailor chemical and physical features both on specific and macroscopic levels. A variety of substances, including antineoplastic agents, proteins, peptides, essential oils, DNA, and others, are organized into colloidal structures, commonly referred to as self-assembled nanostructures (NSs) [1].

Nanosponges are designated for medication delivery because of their distinctive features. Nanoscale drug carriers can do many beneficial things, like targeted medication delivery, controlled release patterns, and storing drugs of various classes in different sizes [1]. They can hold immiscible liquids, offer sustained release for up to 24 hours, reduce pain, improve flexibility, and stabilize the drugs. They can incorporate holes that are designed to serve the medications that are insoluble in water, in which case the nanosponges enhance the solubility and bioavailability of the drugs [2]. Furthermore, nanosponges are useful and flexible in pharmaceutical applications since they are low in toxicity, biodegradable, and may be designed for several delivery routes such as topical, oral, parenteral, and inhalational [2].

They can transport both hydrophilic and hydrophobic pharmaceuticals, which makes them ideal for drug delivery systems that ensure safe and controlled release of drugs over time [4].

Nanosponges represent a type of nanostructured material obtained by crosslinking polymers to build up a three-dimensional porous entity[2]. These nanosponges are able to encapsulate different types of hydrophilic and hydrophobic drug molecules and offer many benefits in comparison with other drug delivery systems (as shown in Fig. (**1**) below) [4].

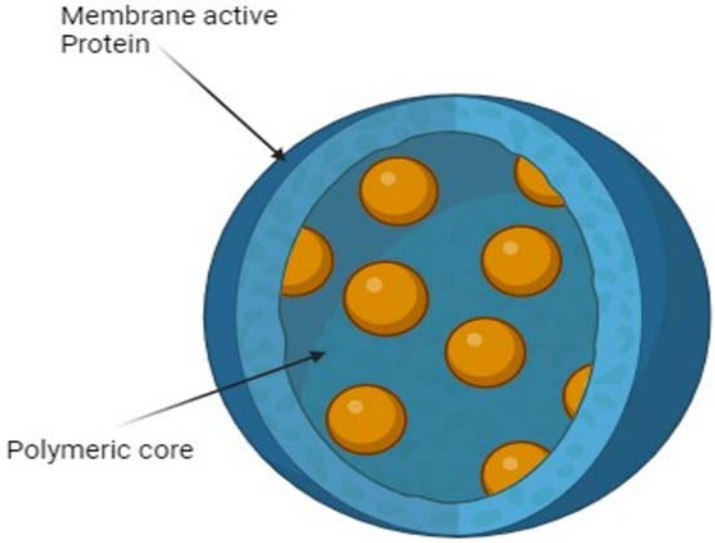

Fig. (1). Nanosponges.

The capacity of nanosponges to encompass the drugs, enhancing their solubility and bioavailability *via* the drug entrapment in their porous nature, results in an additional incredible application. The precise properties of nanosponges, like size, porosity, and surface functionality, can be finely regulated by using different, or tweaking the amount, of crosslinking polymers. It allows quicker disintegration and better control over drug release, which can have a great outcome if more complicated treatment is applied [4].

Not only do the nanosponges play a vital role in drug diffusion, but they also control the onset and duration of the drug's effect. This is because they are 3D-based and capable of holding drugs.

Nanosponges are composed of biodegradable and biocompatible materials, ensuring safety upon usage with a low toxicity level [4]. The efficacy of drug encapsulation relies on the size of the drug molecule and the available void space within the nanosponge structure [4].

Besides being platforms for drug delivery, nanosponges will be investigated for other purposes such as serving as biocatalyst/enzyme carriers and as oxygen delivery vehicles. They will also be used as solubility enhancers and poison sorbents.

Overall, nanosponges form the basis of universal nanoparticle systems that can trap and express a broad spectrum of drugs and biomolecules in a three-

CHAPTER 11

Polymeric Nanoparticles Based Pharmacotherapy for the Management of Psoriasis

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Abstract: Psoriasis is a chronic inflammatory skin disorder affecting millions worldwide, posing significant therapeutic challenges due to its complex pathophysiology and diverse clinical manifestations. Conventional treatment options often yield suboptimal results and are associated with adverse effects, highlighting the need for innovative therapeutic strategies. Polymeric nanoparticles [PNPs] have emerged as a promising approach, offering enhanced drug bioavailability, sustained release, and reduced systemic toxicity. This chapter provides a comprehensive overview of the application of PNPs in psoriasis management, emphasizing their advantages over conventional therapies. By addressing the limitations of existing treatments, PNPs offer a viable strategy for enhancing therapeutic outcomes and improving patient care in psoriasis management.

Keywords: Bioavailability enhancement, Drug delivery systems, Nanotechnology in dermatology, Psoriasis treatment, Polymeric nanoparticles, Sustained drug release, Targeted therapy.

INTRODUCTION

Psoriasis is an immune-mediated chronic skin condition. It is characterized by hyperproliferation and poor differentiation of keratinocytes, leading to patchy, scaly skin lesions. It can extend from a single location to the entire body, causing severe inflammation and the development of skin plaques. The prevalence of psoriasis varies across different regions, with higher reported incidence rates in Western countries compared to tropical and subtropical regions. Epidemiological studies indicate that genetic predisposition, environmental factors, and lifestyle differences contribute to this variation. An estimated 2-4% of people worldwide suffer from psoriasis; hence, anti-psoriatic drugs are predicted to command a

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nearly 18.8 billion USD market in 2021. Since psoriasis is a chronic illness, its effects extend beyond the patient's physical discomfort; they also impair their social and psychological well-being, which lowers their overall quality of life. In addition to affecting the skin, psoriasis exacerbates a number of comorbid conditions, including hyperlipidaemia, diabetes, peptic ulcers, psoriatic arthritis, cardiac problems, metabolic disorders, *etc.* Therefore, a major area of concentration in global public health and dermatology is conducting thorough studies on psoriasis to determine its risk factors, develop efficient therapies and preventive measures, and understand its pathophysiology. Although psoriasis can affect any part of the body, it typically begins in certain areas, such as the scalp, knees, or groin. Although there are other types of psoriasis based on appearance, plaque psoriasis, the most prevalent type, is distinguished by silvery skin scales caused by psoriasis vulgaris.

Plaque psoriasis, the most common variety of psoriasis, is characterized by psoriasis plaques of red, scaly lesions on the skin that are covered in silvery-white scales. Psoriasis has a pathophysiology that is linked to both the immune system and genetics [1]. Psoriasis is currently understood to be caused by the stimulation of dendritic cells in the skin, which activate the defense mechanism, including macrophages and T-cells, along with the facilitation of communication between the immune system and epidermal keratinocytes. These circumstances lead to an increase in cytokine production, which in turn triggers an overabundance of keratinocytes beginning in the basal layer of epidermis and the general inflammation of the skin linked to the development of psoriasis lesions. The pathophysiology of psoriasis is illustrated in Fig. (**1**).

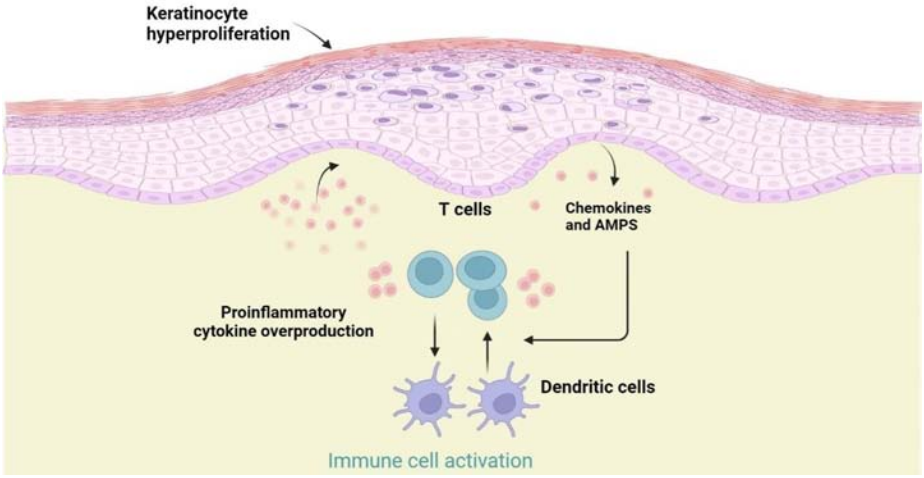

Fig. (1). Regulatory steps in psoriasis development.

This figure illustrates the key regulatory mechanisms involved in the pathophysiology of psoriasis, including immune system activation, inflammatory cytokine release, and keratinocyte proliferation. Understanding these steps is essential for identifying therapeutic targets and developing effective treatment strategies.

Conventional Treatment of Psoriasis

Many traditional psoriasis therapies are now available in the market and have been shown to be effective in alleviating discomfort and symptoms; however, the majority of them have several drawbacks.

Four primary methods are used in the management of conventional psoriasis: topical therapy, systemic therapy, biologic systemic therapy, and phototherapy [2]. Drugs administered systemically are typically needed for moderate-to-severe diseases. These consist of methotrexate [MTX], cyclosporine, fumaric acid esters, and acitretin. DNA synthesis is inhibited by MTX, a folic acid antagonist [3]. Nausea, loss of appetite, hepatotoxicity, and vomiting are the common adverse effects [4]. Cyclosporine is a potent immunosuppressant that can be used to produce remission and as a maintenance treatment for psoriasis [3]. Because of its retinoid side effects, which include teratogenicity, dry skin, conjunctivitis, and hair loss, acitretin is also used in very small dosages to treat psoriasis [5]. Fumaric acid esters are also used to treat psoriasis due to their anti-oxidative, anti-inflammatory, and immunomodulatory effects [6]. Along with a decrease in lymphocyte and leukocyte numbers, they frequently cause gastrointestinal symptoms [7]. Topical distribution is better than systemic dosage due to less immunosuppression and toxicity. The most common therapeutic agents used to treat psoriasis are retinoid analogues, corticosteroids, immunosuppressants, and dithranol; however, inadequate drug absorption *via* the skin continues to be a major barrier to traditional topical treatment [8]. Phototherapy is another fitting alternative to treat psoriasis. Various sources such as light-emitting diodes, strong pulsed light, pulsed dye laser, psoralen UVA, UVB, and photodynamic therapy have been studied [9]. Scholars have created a variety of lipid-based nanoparticles, including solid lipid nanoparticles, ethosomes, transethosomes, liposomes, niosomes, and nanostructured lipid carriers [10].

Psoriasis treatment is categorized into topical therapy, systemic therapy, and phototherapy, depending on the severity of the condition. Phototherapy and systemic treatments are primarily reserved for severe cases due to their potential carcinogenic and toxic effects. In contrast, topical therapies are considered safer as they directly target the basal layer of the epidermis, where psoriasis originates [2 - 4]. Commonly prescribed topical formulations include anti-inflammatory

CHAPTER 12

Metallic Nanoparticles-Based Pharmacotherapy for the Management of Psoriasis

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Abstract: Psoriasis, a chronic inflammatory skin disease, presents a significant therapeutic challenge. Conventional treatments often exhibit limited efficacy and adverse effects. This chapter examines the potential of metallic nanoparticles as a promising approach for managing psoriasis. By harnessing the unique properties of these nanoparticle-based pharmacotherapies, researchers have developed innovative drug delivery systems and therapeutic strategies. These nanoparticles offer advantages such as enhanced drug bioavailability, targeted delivery, and sustained release, leading to improved clinical outcomes. This chapter discusses the current state-of-the-art in metallic nanoparticle-based therapies for psoriasis, highlighting their mechanisms of action, potential benefits, and challenges. Furthermore, this chapter emphasizes the importance of addressing safety and toxicity concerns associated with metallic nanoparticles. While preclinical studies have demonstrated promising results, rigorous evaluation of their long-term effects and biocompatibility is crucial before widespread clinical application. Future research should focus on optimizing nanoparticle formulations, exploring combination therapies, and conducting well-designed clinical trials to establish the efficacy and safety of these nanomaterials in psoriasis management.

Keywords: Drug delivery, Metallic nanoparticles, Psoriasis, Psoriasis management, Skin disease.

INTRODUCTION

Psoriasis, a chronic autoimmune skin disease characterized by excessive inflammation and rapid skin cell turnover, presents significant challenges in long-term management. While current therapies offer relief, limitations exist, including

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side effects, lack of sustained efficacy, and difficulty in targeting specific cell types. Metallic nanoparticles (NPs) are emerging as a promising approach for treating psoriasis. This chapter explores the potential of AuNPs, AgNPs, and other metallic NPs for enhanced drug delivery, targeted therapy, and modulation of the inflammatory response in psoriatic lesions. We will discuss the mechanisms of action, recent clinical studies, remaining challenges, and future directions of metallic NP-based pharmacotherapy for improved psoriasis management.

Psoriasis: Overview and Burden

Psoriasis is a chronic, immune-mediated inflammatory skin condition that affects around 2% of the worldwide population [1]. It manifests as raised, red, scaly plaques typically on the elbows, knees, scalp, and lower back [2]. Psoriasis goes beyond a skin condition, significantly impacting patients' quality of life. Itching, burning, and pain associated with the lesions can cause significant discomfort and sleep disturbances [3]. The psychological burden is substantial, with increased rates of depression, anxiety, and social isolation due to the visible nature of the disease [4]. Furthermore, psoriasis is linked to an increased risk of developing comorbidities like cardiovascular disease, metabolic syndrome, and depression, highlighting its systemic impact [5]. Psoriasis represents a significant healthcare burden, with high costs associated with treatment and lost productivity. With no cure currently available, the focus lies on effective management strategies to improve patients' quality of life and well-being.

Current Psoriasis Treatments: Limitations and Challenges

Current treatment options for psoriasis offer varying degrees of success, but all have limitations. Topical corticosteroids are often the first line of defence, effective for mild to moderate cases but with potential for side effects like skin thinning with long-term use [6]. Systemic medications like methotrexate and cyclosporine can be highly effective but come with a risk of serious side effects requiring close monitoring [7]. Biologic therapies, a newer class of drugs targeting specific inflammatory pathways, have revolutionized treatment for moderate to severe psoriasis. However, these medications can be expensive, require injection or infusion, and may lose effectiveness over time, necessitating a switch to a different biologic [8]. Additionally, some patients with psoriasis do not respond well to any of the currently available treatments, highlighting the need for novel therapeutic approaches.

Promise of Nanomedicine in Psoriasis Management

Psoriasis, a chronic inflammatory skin disease, presents a significant challenge in achieving long-term control. Current therapies, while effective in some cases,

have limitations including side effects, lack of sustained efficacy, and difficulty targeting specific cell types. Nanomedicine, utilizing nanoparticles (NPs) in the 1-100 nanometre range, offers a promising avenue for overcoming these limitations [9]. NPs possess unique properties that make them ideal for psoriasis treatment. Their small size allows for deeper penetration into psoriatic lesions, enhancing drug delivery and potentially reducing systemic side effects [10]. Additionally, NPs can be functionalized to target specific cell types within the lesion, such as activated immune cells, for a more localized therapeutic effect [11].

Metallic nanoparticles, like gold and silver nanoparticles (AuNPs and AgNPs), are particularly promising due to their inherent anti-inflammatory and anti-proliferative properties, potentially offering therapeutic benefits beyond simple drug delivery [12]. Studies suggest these NPs can modulate the immune response, reduce inflammation, and inhibit the excessive growth of keratinocytes, key factors in psoriatic plaques [13]. Nanomedicine holds immense potential for revolutionizing the treatment of psoriasis. By combining targeted drug delivery, enhanced therapeutic efficacy, and potentially reduced side effects, metallic NPs offer a novel approach for improved patient outcomes and disease management.

METALLIC NANOPARTICLES FOR PSORIASIS TREATMENT

Metallic nanoparticles (NPs), like gold and silver nanoparticles (Fig. **1**), are emerging as a potential game-changer in psoriasis treatment. Their small size allows for deeper penetration into psoriatic lesions, potentially delivering drugs more effectively and reducing side effects. Beyond drug delivery, these NPs possess inherent anti-inflammatory and anti-proliferative properties. Studies suggest they can modulate the immune response, decrease inflammation, and inhibit excessive skin cell growth, all key contributors to psoriatic plaques. This unique combination of targeted delivery and therapeutic benefits makes metallic NPs a promising avenue for improved psoriasis management.

Types of Metallic Nanoparticles for Psoriasis

Gold Nanoparticles (AuNPs)

Gold nanoparticles (AuNPs) have become a star player in the field of nanomedicine due to their unique properties and potential applications in various diseases. These nanoparticles are essentially gold particles sized between 1-100 nanometres, offering a fascinating combination of physical, chemical, and biological characteristics [14]. One of the key advantages of AuNPs is their biocompatibility. Unlike some other nanoparticles, AuNPs exhibit minimal toxicity in human cells, making them a promising candidate for drug delivery systems [15]. Additionally, AuNPs possess a tunable surface chemistry, allowing

CHAPTER 13

Ethosomes – Based Pharmacotherapy for the Management of Psoriasis

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Abstract: Psoriasis is a chronic inflammatory skin disease in which over-activation of the immune system (T-cells, keratinocytes) leads to dilation of dermal capillaries of the epidermis and dermis due to excessive production of cytokines. It is primarily characterized by erythematous, itchy, and scaly patches on the exposed surfaces of the body, mainly the scalp, elbows, and knees. Environmental factors, genetics, bacterial infections, *etc*., also play a significant role in its occurrence. Numerous therapies like acupuncture, water therapy, phototherapy, meditation, herbal treatment, moisturizing treatment, use of nutritional supplements, and different drug formulations for topical (salicylic acid, dithranol, vitamin D, corticosteroids, tacrolimus) and systemic (methotrexate, cyclosporine, acitretin) use are beneficial in its management. Topical therapies, due to the skin's barrier effect, have poor penetration and absorption; therefore, to provide more controlled, targeted, nontoxic, secure drug delivery, nanoformulations are used nowadays. Local administration of drug-loaded nanocarriers, *viz*. liposomes, niosomes, ethosomes, nanoemulsions, transferosomes, *etc*. demonstrated improved penetrability and effectiveness at lesser doses while causing little systemic side effects. Ethosomes are emerging lipid vesicular nanocarriers containing phospholipids along with relatively high amounts of alcohol (mainly ethanol), which are responsible for the penetration of entrapped drugs (having diverse physicochemical parameters) deep into the skin. Because of their high safety, efficacy, stability, patient compliance, and simple manufacturing procedures, ethosomes act as one of the effective carriers for transdermal drug delivery. Various drug-containing ethosomes have been successfully designed and evaluated for the pharmacotherapy of psoriasis. Therefore, in this chapter, the main focus is to collate all the ethosomes-based drug formulations designed for the management of psoriasis.

Keywords: Ethosomes, Liposomes, Nanoemulsions, Niosomes, Pharmacotherapy, Transferosomes.

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INTRODUCTION

The skin is the human body's largest organ, with a complex structure comprising the epidermis and the underlying dermis, the two skin layers playing a substantial role in percutaneous absorption [1, 2].

Transdermal drug delivery is one of the frequently employed techniques for the administration of drugs having less stability in the gastrointestinal tract, high first-pass metabolism, or significant undesirable effects when taken orally. High patient compliance, non-invasive nature, ease of administration, controlled drug distribution, and less dose frequency are other major benefits [3]. Initially, the transdermal drug delivery approach (first generation) involves the usage of topical formulations in the form of gel or liquid spray to deliver the medication directly to the skin without using any complicated apparatus [4, 5]. Later, drug administration was made more effective with the use of vehicles and their analogs (second generation).

Nanovesicles, including liposomes, transfersomes, ethosomes, niosomes, and phytosomes, are some methods for transdermal drug delivery. These are nano-sized spherical bilayer vesicles composed of lipids or similar products like surfactants [6]. The ethosomes are among the innovative, novel lipid-based vesicular systems that provide superior drug delivery compared to other nanoparticles, particularly for transdermal applications. A phospholipid bilayer and an inner aqueous core containing the medication make up ethosomal vesicles [3]. The combination of lipid content and high ethanol concentration enhances their affinity towards lipophilic and hydrophilic (high molecular weight) compounds and significantly augments flexibility and deformability, enabling passing across the spaces between cells with negligible medication loss [6, 7].

The large ethanolic content also moves the vesicle’s surface charge toward strong negative values, causing electrostatic repulsions and thereby preventing vesicle aggregation. It alters the structure of the cell membrane and outer lipid layers of the skin, allowing vesicles to penetrate the skin layers. Thus, ethosomes can be regarded as soft, elastic vesicles with dimensions varying from 30 nm to several microns, which can transport the drug in both occlusive and non-occlusive conditions across the skin [3]. Considering all of these qualities, ethosomes can be regarded as an efficient method (lipid-based) for active drug distribution into or across the skin, and thus have numerous applications in various biological fields [7].

The Transdermal Drug Delivery System (TDDS) is preferred over conventional drug administration methods nowadays, as drugs can be administered accurately and safely using various delivery techniques across different types of skin, with

no first-pass metabolism [5], *i.e.*, they do not undergo any metabolic changes until they arrive at their target location. TDDS is non-invasive and non-allergenic if administered properly within the scheduled period and mechanism [8]. This enables the uniform delivery of medications at predetermined and regulated rates. Because of this, administering drugs *via* the transdermal route has gained wide popularity in the pharmaceutical sector. The incorporation of chemical enhancers, however, has shown no remarkable effect in improving the transdermal transport of small molecules [9].

Ethosomes are also preferred over liposomes because classic liposomes only reach the top layer of the stratum corneum and do not profoundly enter the skin. Transdermal delivery is established to be possible only with specialized vesicles like ethosomes containing good ethanolic content. Ethanol is a widely recognized effective permeability enhancer [10]. However, the ethanol content in liposome formulations is very low. Lipid vesicular systems *i.e.*, ethosomes, contain ethanol in quite high concentrations and thus are highly effective in increasing the penetration of various drugs through the skin.

Mechanism of Action of Ethosomes

Ethosomes work efficiently when vesicles, ethanol, and skin lipids work together. Due to better dispersion of active components, a more competent interaction is observed between ethosomes and skin lipids rather than with liposomes [3]. The ethanol-lipid interaction in the polar head group area lowers its transition temperature in the stratum corneum. This reduces the density of the lipid multilayer and increases fluidity, permitting the easy pervasion of the drug into deep skin layers [11]. Moreover, ethanol gives vesicles a smoother, more flexible texture, which allows them to penetrate the epidermal layer more deeply [12, 13].

Ethosomal Delivery Systems

The first ethosomes were discovered by Touitou and his students at the Hebrew University School of Pharmacy in 1995 [14] to transport active substances into deep layers of the skin and systemic circulation. The vesicular structure and the transition temperature of the lipids in ethosomes were studied using TEM and DSC, and it was concluded that, depending on the composition of the system, ethosomes may have one or many lamellar layers. Ethosomes were found to possess a higher degree of fluidity because of their low lipid levels [15].

Ethosomes are vesicular carriers composed of hydro/alcoholic/glycolic phospholipid, with a comparatively high amount of alcohol [11]. Ethosome-based drug delivery is gaining popularity in the present era [7]. Based on the components utilized in the formulations, there are three varieties of ethosomes [3]

CHAPTER 14

Transferosomes as a Drug Carrier for the Management of Psoriasis

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Abstract: The autoimmune condition psoriasis is typified by hyperproliferation of keratinocytes, lesions, and silver-white scales inside the epidermis. Environmental and genetic factors both contribute to its cause. For psoriasis, several medication targets and focused treatments have been discovered. To lessen the symptoms of this illness, numerous target-specific medicines have also been created. Psoriasis is being treated using a variety of techniques, such as herbal remedies, nano-carrier therapy, and conventional therapy. In this regard, delivery through the transdermal route is an intriguing choice because it is safe and convenient. Since transferosomes have a bilayered structure that makes it easier to encapsulate lipophilic, hydrophilic, and amphiphilic drugs with higher penetration efficiencies than regular liposomes, they are a popular option for transdermal medication delivery for psoriasis. Because of their flexibility, they can flex and sneak through small pores that are significantly smaller than their actual dimensions, while remaining intact as a whole vesicle. This chapter aims to explain the concept of transferosomes, their mode of action, various methods of preparation, and their current applications in psoriasis therapy.

Keywords: Autoimmune disease, Drug delivery, Psoriasis, Transferosomes, Transdermal.

INTRODUCTION

Psoriasis is an autoimmune skin disorder condition caused by environmental along with hereditary factors [1]. The skin ailment known as psoriasis is dry,

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inflammatory, persistent, and incurable. T cells and enhanced cytokine secretion— such as IFN-γ, IL-20, IL-23, IL-17, IL-22, and others—which promote keratinocyte proliferation—are the conditions' mediators [2]. It might have an impact on the entire body. Thickened crimson plaques with silver-white scales on top are visible on the skin. It is distinguished by a recurrent episode of inflammation and hyperkeratosis [3]. This illness is accompanied by severe medical conditions like psoriatic arthritis, seronegative arthritis form, and cardiovascular disease [4]. The area's most frequently impacted by psoriasis are the scalp, fingertips, foot, elbows, knees, buttocks, beneath the breasts, gluteus, umbilicus, and hands [5]. Males and females can both have psoriasis. It can happen at any age, although it usually occurs in the second and fourth decades of life, from 20 to 40 years old [6]. The frequency is higher in females in comparison to males. Rarely, kids are also impacted. The global incidence of psoriasis is approximately 2% in underdeveloped countries, with an average prevalence rate of 4.6%. Psoriasis affects approximately 1.02% of the population, with incidence rates ranging from 0.44% to 2.2%. Phototherapy is a treatment option for psoriasis that involves using ultraviolet [UV] light, and medications can be administered through several ways, including topical and systemic routes [7]. The body reacts to UV radiation by going into an autoimmune state. The treatment is limited by the negative effects of phototherapy, which include the need for frequent visits to specialty medical centers, sunburn risk, increased costs, and skin cancer risks in the long run for PUVA [Psoralen Ultraviolet-B] [8]. In the 1990s, Cevc *et al.* presented transferosomes, a novel kind of carrier system. They are composed of phospholipids and the membrane-softening agent edge activator [EA] that helps the transferosomes' ultra-deformable characteristic [For example, sodium cholate, Span 80, and Tween 80] [9]. When they get to the skin pores, they can spontaneously pass through them by altering the flexibility of their membrane [10]. These highly deformable, self-optimizing lipid aggregates were effectively applied for the transdermal delivery of proteins and peptides, as well as sustained release of targeted medicinal agents, in a variety of phase I and phase II clinical trials and comprehensive preclinical testing [10]. Thus far, transferosomes have emerged as the most remarkable and inventive transdermal drug delivery system. The researcher's term, the underlying concept, the techniques for preparation and characterization, and the elements influencing the entry into or conduct of a study on transdermal medication delivery using elastic vesicles will all benefit from an understanding of the particular characteristics of the initial generation of elastic vesicles, or transferosomes [11]. We provide an outline of mechanisms of action, several preparations, and engaging in or carrying out studies on the existing features of the initial generation of elastic vesicles [transferosomes], which might be beneficial for the researcher's review of elastic vesicle-based transdermal delivery of medications. We provide a summary of the mechanisms of action,

various preparations and characterization, with an emphasis on the most recent applications in the transdermal delivery of medications using current characterization techniques—elements influencing transferosome characteristics, along with a review including techniques and a focus on their latest uses in transdermal medication delivery.

MECHANISM OF ACTION OF TRANSFEROSOMES

Colloidal particles, or vesicles, are composed of amphiphilic molecules and consist of an aqueous compartment enclosed by a double layer that is concentric [12]. They are extremely valuable as vesicular drug delivery systems because of their capacity to transport hydrophilic medications, which are housed within the inner aqueous compartment, and hydrophobic medications, which are bound within the lipid bilayer [13]. Transferosomes are innovative drug carrier vesicles that are self-optimizing and entirely deformable [ultra-flexible]. Their ability to retain the integrity of the vesicle and their membrane flexibility are what primarily allows them to pass through the skin [14]. According to Cevc and Blume's research, transferosomes penetrate through the epidermis through a technique called hydrotaxis [xenophobia]. This is further clarified by the fact that, under a nonocclusive environment, moisture loss from the transferosomal formulation occurs after it is applied to the skin, explaining the moisture-seeking inclination in the direction of the deeper layers of the skin rather than a dry exterior landscape. Due to these channels, transferosomes that are ultra-deformable and slimy can cross the skin's moisture gradient [15]. Furthermore, the gradient evaporation leads to the development of the osmotic gradient. Furthermore, the body's heat-induced evaporation of skin surface water is what leads to the osmotic gradient to occur. This mechanism acts as a catalyst to enable the receptive transportation of medicinal substances across the skin from the application site toward the target region for local or systemic treatments at minimally harmful systemic concentrations (Fig. **1**) [16].

Transferosomes, then, are supramolecular structures made up of at least one kind of amphipathic agent and one type of bilayer-softening agent [edge activator], which significantly increases the flexibility and permeability of the lipid bilayer [17]. Some transferosomes contain small amounts of alcohol [propylene glycol or ethanol] in their formulations, which are utilized as cosolvents with strong solvating ability and to improve penetration. It has been suggested that ethanol can alter the polar head region of the lipid bilayer. Ethanol enhances the fluidity of the intercellular lipid matrix after penetration, which subsequently causes a decrease in the density of the lipid lamellae [18]. Transferosomes can penetrate the stratum corneum and get to their intended targets, which include blood circulation and the dermis. The vesicles' composition causes the transferosomal

CHAPTER 15

Emulsomes-Based Pharmacotherapy for the Management of Psoriasis

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Abstract:

Background: Psoriasis is an inflammatory, autoimmune skin condition that is driven by T cells & is characterized by abnormal keratinization, hyperkeratosis, angiogenesis, and inflammation of the skin's surface. There are now many different pharmacotherapies for it; nevertheless, standard formulation-based pharmacotherapy can only partially improve treatment outcomes. Recent developments in nanomedicine based on nanotechnology may make pharmacotherapeutic drugs for psoriasis more safe and effective.

Objective: The objective is to offer a comprehensive overview of the development & utilization of emulsomes for targeted delivery of anti-psoriatic agents. This addresses the various drugs, the pathophysiology of psoriasis in short, and the therapeutic issues that come with it. Below, we have discussed the collective reports of several medications operating on distinct psoriasis molecular targets as well as the function of nanomedicine in their efficient targeting.

Methods: The formulation techniques involved in preparing emulsomes loaded with anti-psoriatic drugs highlight the key parameters considered for their optimization. Various methods for characterizing emulsomes, such as particle size analysis, encapsulation efficiency determination, & surface morphology examination, are elaborated. The *in vitro* & *in vivo* experimental methods employed to assess drug release, skin permeation, and therapeutic efficacy are also detailed.

Results: Emulsomes-based formulations demonstrated superior encapsulation efficiency, sustained drug release, and enhanced skin penetration, leading to improved therapeutic outcomes in psoriasis management. Experimental findings and comparative analyses reveal the advantages of emulsomes over conventional drug delivery systems.

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Conclusion: Emulsomes-based pharmacotherapy presents a promising approach for targeted and efficient management of psoriasis. The chapter focuses on emphasizing emulsomes' potential to revolutionize psoriasis treatment paradigms and highlighting future research directions in this field.

Keywords: Drug delivery, Emulsomes, Lipid-based nanocarriers, Psoriasis, Targeted therapy.

INTRODUCTION

Psoriasis typically manifests as scaly and irritated patches on areas such as the knees, elbows, or scalp, although it can appear on other parts of body as well. Psoriasis symptoms may sometimes cycle, peaking for a few weeks or months and then fading or going into remission for extended periods of time [1]. Psoriasis may be treated in a variety of methods, and the kind and severity of your condition will determine the course of your care. While moderate and severe psoriasis may need medication, injections, or light therapies, mild psoriasis is often effectively treated using creams or ointments [2]. Controlling frequent triggers, such as skin injuries and stress, may also aid in the management of symptoms [3].

Psoriasis patients are at risk for developing additional severe illnesses, such as:

- Psoriatic arthritis is a persistent kind of arthritis characterized by joint pain, swelling, and stiffness.
- Cardiovascular events, such as strokes and heart attacks.
- Psychological challenges like depression, anxiety, and low self-esteem.
- A person's risk of developing certain malignancies, such as obesity, osteoporosis, uveitis (an inflammatory condition of the middle part of the eye), liver disease, and kidney disease may also increase if they have psoriasis [4].

Types of Psoriasis

Psoriasis is classified into many categories, which include:

Plaque Psoriasis

The most prevalent type manifests as elevated, red skin patches coated in silvery-white scales. The patches often form on the head, torso, and limbs, particularly the knees and elbows, and they normally grow symmetrically throughout the body [5].

Pustular Psoriasis

This kind is characterized by pustules, which are pus-filled lumps encircled by red skin. Although the hands and feet are often affected, there is a variant that affects the whole of the body. Stress, certain substances, diseases, and drugs may all cause symptoms.

Inverse Psoriasis

This variety manifests as red, smooth patches in skin folds, such as those under breasts, in crotch, or under armpits. Sweating and rubbing may exacerbate it [6].

Guttate Psoriasis

This kind of condition resembles little red spots and commonly affects the chest or limbs. It usually manifests in youngsters or young adults. Upper respiratory tract infections, such as strep throat, can cause outbreaks.

Erythrodermic Psoriasis

With red, scaly skin covering the majority of the body, this uncommon but severe type of psoriasis is characterized. It may be brought on by taking certain drugs, including corticosteroids, or by getting a terrible sunburn. People with poorly treated psoriasis often develop erythrodermic psoriasis, which may be quite dangerous [7].

Symptoms of Psoriasis

While each individual experiences psoriasis differently, some typical symptoms include:

- Typically found on elbows, knees, scalp, torso, palms, & soles of feet, areas of thickened, reddened skin covered in silver-white scales that may itch or cause a burning sensation.
- Dry, cracked skin that may bleed.
- Thickened nails with small dents and grooves.
- Poor sleep quality [8].

Achilles heel discomfort, back or neck pain, and stiff, swollen, or painful joints are some of the symptoms of psoriatic arthritis, a similar disorder that affects certain people. See your doctor right away if you have psoriatic arthritis symptoms because if you don't get treatment, the condition may cause irreparable harm. Psoriasis symptoms might appear and go [9]. There can be periods when

CHAPTER 16

Nanoemulsions-Based System for the Management of Psoriasis

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Abstract: The word "psoriasis" comes from the Ancient Greek word "*psora*," which means "itch." Severe itching is a common symptom of psoriasis, a chronic, non-contagious, inherited skin condition. It is an immune-mediated condition characterised by both hyperproliferation and inadequate keratinocyte differentiation in the epidermis of the skin. Although only affecting 2-3% of the population, this immune-mediated skin condition has a major harmful effect on the patient's quality of life. Although they have demonstrated poor efficacy and lack aesthetic value, topical psoriatic therapies such as emollients, coal tar, and dithranol are safer. Many strategies have been investigated by modern medicine to treat this condition (such as injectables, oral medication, and steroid-based lotions). However, none of these approaches have proven successful, as they lack an ideal and safe carrier that can deliver the anti-psoriatic medication to the patient safely and effectively, thereby achieving the greatest possible therapeutic impact. Researchers are working with nanotechnology to overcome the shortcomings of traditional treatments, aiming to improve the effectiveness of anti-psoriatic drug delivery and reduce its unfavourable side effects.

Utilising a colloidal model, nanoemulsion is a technique that applies high surface area active substances in the form of nanosized droplets to the skin's afflicted area. A number of advantages over traditional delivery methods are provided by nanoemulsions, which include decreased drug degradation and loss, avoided hazardous side effects, and higher drug bioavailability. Compared to coarse emulsions, nanoemulsions exhibit greater kinetic stability, prevent cream separation, significantly influence topical systems, and have a higher solubilization capacity.

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Significant research on nanoemulsion-loaded antipsoriatic medicines has previously been done. Many antipsoriatic drugs, including Capsaicin, Aceclofenac, Turmeric oil, Calcipotriol, Betamethasone Dipropionate, salicylic acid, Clobetasol propionate and others have been loaded into nanoemulsion using various preparation methods.

Keywords: Antipsoriatic medicine, Nanoemulsions, Psoriasis, Skin disease.

INTRODUCTION

Psoriasis is a skin condition characterized by relapsing and remitting. Although temporary remission is possible with treatment, there is no known cure for the condition. The illness is currently understood to be an inflammatory systemic immune-mediated condition that has multiple comorbidities. Heart disease, depression, and psoriatic arthritis are a few of them [1, 2]. The development of psoriasis is linked to the interleukin (IL)23/IL17 axis, which plays a significant role. The condition has three main histologic features: epidermal hyperplasia, dilated and prominent blood vessels in the dermis, and an inflammatory infiltrate of leucocytes, mainly into the dermis [3]. Biological therapies (tumour necrosis factor (TNF), IL-17, and IL-23 inhibitors), phototherapy (narrowband ultraviolet B radiation (NB-UVB) and psoralen and ultraviolet A radiation (PUVA)), standard systemic therapies (methotrexate, ciclosporin, and acitretin), and topical agents (vitamin D analogues and corticosteroids) are some of the options available for treating psoriasis [2, 3].

According to estimates from the Global Burden of Disease Study, 5.6 million Disability-Adjusted Life Years (DALYs) across all age groups were caused by psoriasis in 2016 [4]. Compared to inflammatory bowel disease, this is at least three times more. Additionally, metabolic syndrome, non-alcoholic fatty liver, cardiovascular disease, respiratory conditions, autoimmune diseases like Hashimoto's thyroiditis and autoimmune hepatitis, multiple sclerosis, and psychiatric disorders are all more common in people with psoriasis [5]. Compared to people without psoriasis, those with severe psoriasis had an increased overall mortality rate and a reduced life expectancy of 3.5 and 4.4 years, respectively, for men and women [5, 6].

Pathogenesis of Psoriasis

Psoriasis is a skin condition that results from various factors, including genetics. Studies have shown that genetics plays a significant role in individuals with early-onset plaque psoriasis, especially those under 40 years old. Heritability is estimated at 60-90%, and over 60 susceptibility loci have been identified through genome-wide association studies [4].

Psoriatic skin lesions overexpress antimicrobial peptides, such as LL-37, which activate dendritic cells, leading to inflammation. While it was initially thought that T-helper (Th)1 overactivation caused psoriasis, it has been discovered that Th17 cells play a more crucial role in the development of the condition. IL-23, mainly produced by dendritic cells, maintains their development [4, 7]. Th17 cells produce cytokines such as IL-17A, IL-17F, and IL-22, which lead to keratinocyte proliferation, TNF-α, chemokine (C-X-C motif) ligand (CXCL)1, and CXCL8 production. Psoriatic lesions are characterized by an increased number of dendritic cells and T cells [8].

Cytokines produced by the psoriasis condition create systemic inflammation, which can result in comorbidities such as metabolic syndrome, obesity, diabetes, and cardiovascular disease. Psoriasis is caused by a combination of abnormal antimicrobial activity, altered Toll-like receptor expression, and defective extracellular matrix deposition. Adipokines, proteins released by adipocytes, including leptin, adiponectin, and resistin, are vital components in regulating both innate and adaptive immunity, promoting healthy physiological function [9]. The pathogenesis of psoriasis is illustrated in Fig. (**1**).

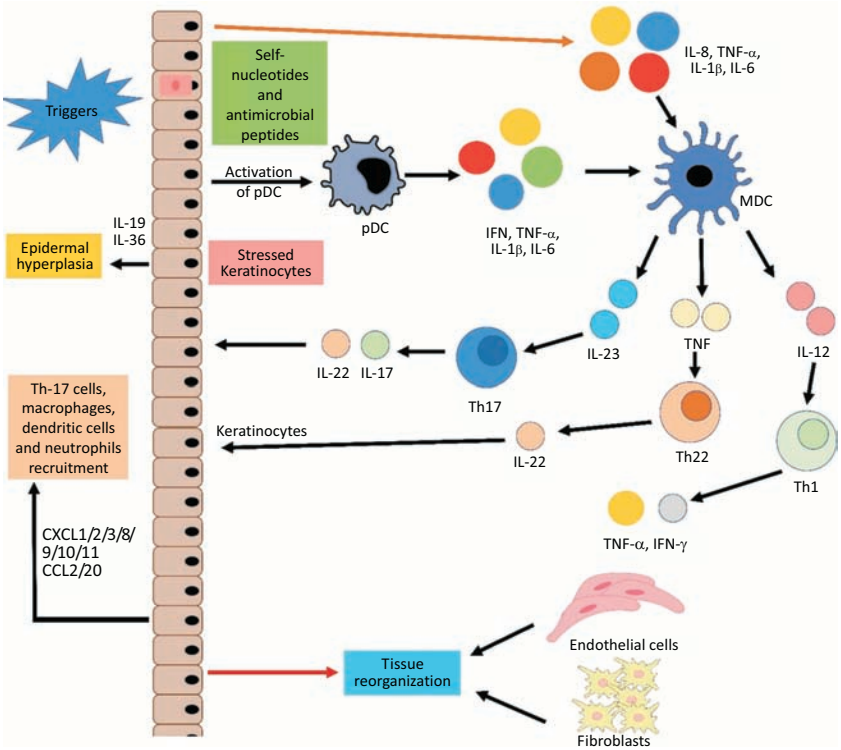

Fig. (1). Pathogenesis of psoriasis.

CHAPTER 17

Future Prospects of Novel Carrier-Based Pharmacotherapy

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Abstract: Psoriasis is a serious dermal plight characterised by inflammation and hyper-proliferation of the keratinized cells of the epidermis. Because of the complicated disposition of the disease, it has a severe pessimistic impact on the patient's overall well-being. Currently, a variety of medications are available for treating psoriasis, including conventional topical therapies, UVB therapy, intrinsic or systemic immune-modulators, and biologics, which aim to alleviate symptoms and thereby improve the quality of life for patients. Conventional topical therapies, though they constitute first-line therapy, have restricted efficacy because of the mediocre drug penetration properties, deposition, and dose-related toxicity. The latest progression in topical treatments, specifically with micro-scaled medical devices like micro-needles and nanoparticle-based carriers, lipid nanoparticles offer a promising future with significantly better therapeutic potency as it has a way better skin permeation, controlled release of the drug, targeting specific pathways, such as IL-23 inhibitors like mirikizumab and RORγt inhibitors, hence contributing to better drug delivery and efficacy for psoriatic plaques. These innovative and efficient therapies may cut down the side effects and may lead to improved and better patient adherence.

Keywords: Better adherence, Better skin permeation, Dose-related toxicity, Drug delivery, Drug penetration, Efficient therapies, Immune modulators, Inflammation, Leratinized cells, Lipid nano particles, Medical devices, Micro needles, Plaques, Proliferation, Psoriasis, Therapeutic efficacy, Topical therapies.

INTRODUCTION

Psoriasis is considered a multifactorial, chronic, and inflammatory disorder that is instigated by hereditary as well as environmental aspects [1]. It shows its impact

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on approximately 2–3% of the whole population. The dermal papillae telangiectasia, over-maturation of keratinized cells & conscription of provocative cells over the epidermis are the major features of psoriasis [2]. Whole areas of the skin of an individual's body can also be affected by this disease [3]. Patients suffering from this disease have higher risks of developing fatty liver, the occurrence of obesity, diseases related to the heart, hyperglycaemic conditions and several kinds of syndromes related to the general metabolism of the body in comparison to normal people. These possibilities are predominantly visible in patients who are suffering from severe psoriasis. The origin of this disease is still unidentified even after the conduction of a lot of research, but in recent studies it is quite known that this disease is basically prompted by the amalgamation of hereditary (*i.e.*, family history) as well as environmental factors (*i.e.*, alcohol, tobacco, infections, medications, stress) [4 - 7].

Patients suffering from psoriasis are concomitant to stigmatization physically, which complements the augmentation of the psychology-oriented complications in their very own emotional cum socio-professional lifestyle.

According to future considerations, the effective management of psoriasis can be achieved by employing various types of therapies, including topical therapy, phototherapy, and systemic therapy, which are among the primary effective alternatives for the efficient treatment of psoriasis. Contemporarily, diversified medications are available in the market for the treatment of psoriasis, for instance, conventional topical therapies, UVB (Ultraviolet B) therapy, and intrinsic or systemic modulators of the immune system, which generally target the palliation of the signs/symptoms & hence contribute to the improvement of the quality of the patient's life. Conventional topical therapies constitute the potential to act as first-line treatment as they hold constrained efficacy due to the unexceptional drug penetration characteristics, better adherence as well as dose-related toxicity. For mild stages of Psoriasis, topical treatment is the only treatment recommended as a first-line treatment. Conversely, systemic treatment or phototherapies are considered the type of treatments that efficiently work in severe conditions of psoriasis [8]. Various types of treatment regimens currently exist, which effectively diminish the signs and symptoms of psoriasis; however, among them, not a single method works as a comprehensive treatment method that can cure the disease entirely.

Psoriasis treatment with topical therapies is considered the conventional formulation, which is also bound to several kinds of complications such as restricted penetration of the drug, reduced patient adherence compliance, and elevated frequency of dosing, *etc.* [9].

Likewise, phototherapy and systemic therapy also exhibited several adverse effects, which involve toxicity of the liver and kidneys, cancer related to the skin and the basic problem of elevated blood pressure. These are the common disputes that limit the custom usage of presently existing conventional therapies for the treatment of psoriasis [9].

In the last few years, an NDDS (Novel Drug Delivery System) based nano-formulation has been widely reconnoitred by several scientists to succeed in the development of non-toxic and effective therapy for psoriasis, which will be considered among the future prospects for the successful treatment of Psoriasis as this technique holds the potential to enhance the therapeutic efficacy and provide long-standing effects [9]. Enhancement of therapeutic efficacy and reduction of toxicity through a dose reduction yields two outstanding effects that make nano-technology-based medicine a promising medication carrier for the future. This innovative method effectively works over the site-specific administration of medicines all over the areas of the skin for the treatment of psoriatic lesions and plaques [10 - 12].

In the last few years, most of the novel anti-psoriatic drugs also come into existence and got approval for markets are MAB (Monoclonal Antibodies), which target various patho-physiological procedures which are concerned for the development and advancement of this disease. Nevertheless, this antibody-based therapy is quite expensive for individuals who fall under the category of emerging economies [13 - 15].

In the latest progression in topical treatments, specifically with micro-scaled medical devices like micro-needles and nanoparticle-based carriers, lipid nanoparticles offer a promising future with significantly better therapeutic potency as it has a way better skin permeation, controlled release of drug, and targets definite pathways. For instance, Interleukin- 23 (IL-23) inhibitors (*e.g.,* Mirikizumab) and RORγt inhibitors. These will contribute to improved drug delivery and provide effectiveness against psoriatic plaques. These kinds of novel and efficient therapies might cut down the side effects and may lead to improved and better patient adherence in the future (16).

Classification of Disease on the Basis of Severity of Psoriasis

Psoriasis can be categorised into plaque, pustular, guttate, flexural and erythrodermic forms as per its clinical manifestations. The classification of psoriasis, along with its characteristic features, is presented in Table **1**.

CHAPTER 18

Psoriasis in the Modern World: Lifestyle, Diet and Holistic Approaches

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Abstract: Psoriasis, a chronic autoimmune skin condition that affects millions of people worldwide, is becoming more common because of modern lifestyle variables like stress, unhealthy eating habits, and pollution in the environment. This chapter explores the intricate relationship between illness and modern living, focusing on the management of psoriasis through dietary changes, lifestyle adjustments, and holistic approaches. It explores the effects of processed foods, inflammatory triggers, and gut health, emphasizing the value of nutritional methods and anti-inflammatory diets. The chapter also looks at alternative medicines like Ayurveda and Traditional Chinese Medicine and stress-reduction methods like yoga and mindfulness. This chapter offers a thorough manual for anyone looking for a natural, well-rounded approach to managing psoriasis in today's fast-paced world by fusing scientific knowledge with useful suggestions.

Keywords: Dietary changes, Lifestyle, Pollution, Psoriasis, Stress.

INTRODUCTION

Overview of Psoriasis

Psoriasis is an immune-mediated, persistent skin condition. Nearly 125 million people globally and about 3% of the US population suffer from psoriasis, a chronic skin condition [1]. The occurrence of psoriasis varies across nations and can manifest at any stage of life [2], suggesting that ethnicity, genetic makeup, and environmental factors influence the onset of the condition. The pathophysiology of psoriasis is largely influenced by genetic factors [3]. The

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World Health Organization [WHO] approved resolution WHA 67.9 in 2014, which urges international cooperation to combat stigma and promote awareness of psoriasis as a major non-communicable disease. In order to raise awareness of the disease's effects on public health, the resolution asked WHO to compile a global report on psoriasis [4]. For this study, a new, comprehensive systematic review of the global epidemiology of psoriasis was carried out. Through the use of a strict, methodical approach, the review sought to analyze all available data regarding the global epidemiology of psoriasis [5]. The immunological and genetic factors underlying the pathogenesis of psoriasis are well understood. This greater knowledge has led to the development of certain recently approved biological treatments for psoriasis, but it has also contributed to the development of others [6]. For example, the important role that tumor necrosis factor plays in the pathogenesis of the disease has been brought to light by the notable efficacy of medications that block the cytokine. Additionally, facts that psoriasis is not limited to skin conditions are mounting [7]. Studies on the epidemiology of psoriasis patients have revealed a higher standardized death rate, especially when it comes to heart disease and cancer. Comorbidities in psychology and psychiatry that are clinically significant are also frequent and may benefit from therapeutic intervention [8]. The immune system plays a role in psoriasis, as evidenced by the disease's therapeutic response to immunosuppressive drugs, the presence of clonal T-Cell Receptor [TCR] rearrangements in psoriatic skin, and the disease's transmission through bone marrow transplantation in humans and by purified T-cells in mice with prepsoriatic human skin [9]. The chemical mechanisms that trigger this immunological activation state remain unclear. According to recent comprehensive genomic sequencing of the MHC Class I region, HLA-Cw6 itself is most likely the functional mutation predisposing to psoriasis rather than a flag for some other nearby disease gene [10].

Types of Psoriasis

- Psoriasis Vulgaris

Chronic plaque psoriasis accounts for approximately 90% of psoriasis cases. The traditional clinical signs are erythematous, painful, well-defined plaques with silvery scales covering them. Large amounts of skin may be covered by the plaques when they combine. Common locations include the trunk, limb extensor surfaces, and scalp [10, 11].

- Reverse Psoriasis

Clinically characterized by somewhat erosive erythematous plaques and patches, inverse psoriasis, also known as flexural psoriasis, affects intertriginous sites [12].

- Guttate Psoriasis

One variety is guttate psoriasis, which presents as tiny erythematous plaques that appear suddenly. It typically affects kids or teenagers, and tonsil infections caused by group A streptococci are a common cause. Plaque psoriasis is a condition that approximately one-third of adults with guttate psoriasis may have during their lifetime [13, 14].

- Pustular psoriasis

Several sterile pustules that coalesce are the hallmark of pustular psoriasis. Both localized and widespread pustulosis are possible. It has been possible to identify two unique localized phenotypes: acrodermatitis continua of Hallopeau and psoriasis pustulosapalmoplantaris [PPP]. PPP only includes the palms and soles of the hands and feet, whereas ACS is more widely distributed at the tips of the fingers and toes and impacts the nail system [2].

Causes and Triggers

Mechanical Stress

This phenomenon, known as the Koebner phenomenon, occurs when skin lesions develop in non-affected areas of psoriasis patients following injury [15]. Recent reports have indicated that exposure to ultraviolet B radiation, radiotherapy, and even mild skin irritation might cause new psoriasis lesions [16 - 18]. However, psoriatic lesions are not always visible in the skin that is not affected following trauma [19, 20]. The manner in which the Koebner phenomenon develops can be influenced by the kind, location, intensity, and degree of trauma [21]. Moreover, the psoriatic keratinocytes' secreted NGF has functional activity. It is noteworthy that keratinocytes of psoriasis sufferers produce more NGF. This study indicates that NGF is involved in the pathophysiology of psoriasis and that the early stages of psoriasis lesions are responsive to NGF's regulatory role and receptor system. Psoriasis is one of the autoimmune inflammatory skin conditions that is mediated by TRM [22]. Resident memory T cells [TRM] are a non-circulating memory T cell subpopulation that endures over time in peripheral tissues.

Surprisingly, psoriasis patients' non-lesioned skin may develop and sustain psoriasis lesions due to skin-resident pathogenic T cells.

Air Pollutants and Exposure to the Sun

Air pollutants, including polycyclic aromatic hydrocarbons, volatile organic compounds, oxides, particulate matter, ozone, heavy metals, and UV radiation,

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