



Psoriasis: What is New and What is News

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Abstract

Psoriasis is a proliferative autoimmune skin disease which is affecting 2% of worldwide population. It is characterized by itching, skin rashes and red scalps with white scales on the skin. Though, different types are reported, common existing form of psoriasis is plaque psoriasis. The epidemiology of disease seems to be remained unknown, but the incidence varies, surrounded by the different countries. The patho physiology of the disease appears as drastic cellular changes occur both in epidermis and dermis which narrates to keratino cytehyper proliferation. Earlier available medications like emollients and some keratolytic agents has not proven promising role in controlling the disease burden. But, in advance regimen, with wide range of therapeutic mediators like coal tar, anthranil in, calcineurin inhibitors, methotrexate, retinoids, cyclosporine are proven to be effective in treating mild psoriasis to severe psoriasis. In recent years, phototherapy has once again emerged as most recommended due to ease of treatment and its intoxications. Hence, this review emphasizes the therapeutic agents available in market and its effectiveness in controlling the psoriasis.

Keywords

Psoriasis; Psoriasis vulgaris; Topical agents; Biological agents; Traditional medicine; Systemic therapy.

INTRODUCTION

Psoriasis is a lifelong autoimmune ailment which is characterized by white to red colour patches of abnormal skin with patches of itchy and scaly. The term psoriasis derived from Greek word "psora" which means "itch". It is a chronic skin disease, touching about 2% of worldwide population³. It is non-epidemic infection and horrible skin disorder, which can include a whole system of person. It is mostly inherited and mainly categorized by sharply marinated crusty, erythematous plaques that expand in a relatively equal distribution. The majority areas are the scalp, fingers and toes, palms, soles, umbilicus, gluteus, underneath the breasts and genitals, elbows, knees, shins and sacrum⁵. It can

also cause inflammation in joints, which can be acknowledged as psoriatic arthritis. Most scientific studies states that *psoriasis vulgaris*, which affects around 85 to 90% of all patients with the disease. The probable factors triggering psoriasis include mental strain, skin damage, systemic infections and intestinal upsets. Different types of psoriasis have been reported such as plaque psoriasis, psoriatic arthritis, scalp psoriasis, flexural (inverse) psoriasis, guttate psoriasis, pustular psoriasis, nail psoriasis, erythroderma which can be diagnosed by solid conclusion such as skin biopsies etc. The etiology of this particular disease was leftover indistinct, although there is a sign for heritable predisposition. It is outmost maltreated

diseases from olden days, which continues now to search of a good remedy. This review has comprehensively provided the detailed report on psoriasis and its associated therapy.

CLINICAL TYPES OF PSORIASIS

Plaque Psoriasis

This type is widely spread, affecting 80–90% of those with psoriasis. Plaques are definite, red, elevated lesions crowned with silvery-white scales and are habitually seen over the extensor surfaces of the limbs, particularly the elbows and knees, over the scalp and at the hairline. Plaques can be huge or little and may itchy, while itching is not an important aspect of plaque psoriasis. Nail concern can occur, manifesting as pitting and departure from the nail bed (onycholysis).

Flexural Psoriasis

The lesions in flexural psoriasis are visibly demarcated, pink lesions that lack scales. The sites usually affected are the skin folds, particularly the groynes, perianal regions and genital skin. Less commonly the skin folds and the umbilicus may be affected in the case. Flexural psoriasis is exasperated by sweat and roughness and there is a risk of minor infection.

Pustular Psoriasis

This can arise in localized (palmo plantar) or generalised forms. Generalised pustular psoriasis, a cruellest form of erythrodermic psoriasis with severe systemic departure in which sterile pustules and scaling expand over the trunk and limbs. It causes extensive inflammation with malaise, pyrexia and circulatory interruption. It can be toxic, as the skin loses its capacity to maintain well-organized thermoregulation and liquid balance. It can develop instinctively or sometimes as an obstacle of potent corticosteroid therapy (particularly when high-dose systemic steroids are quickly withdrawn). Management is like to that of blisters in burn patients, as the interference to the skin's functions must be minimised and controlled. Palmom plantar psoriasis is restricted to sterile pustule formation on the palms and soles without systemic indications. It is familiar in cigarette smokers, usually in middle-aged women and few of classic plaque psoriasis patients.

Generalized Pustular Psoriasis (GPP)

Widespread pustular psoriasis is a very rare type of psoriasis, but it is lifelong aggressive disease characterized by inflammation of skin. This condition also called as vonzumi psoriasis. These types of psoriasis is related to the plaque psoriasis and palmo plantar psoriasis. The patient is with pyrexia containing red, painful skin scattered with mono-

morphic, sterile pustules, which may combine to form sheets. During pregnancy, in presence of a GPP it can be triggered by infection and revelation from drugs.

Palmoplantar Pustulosis

Palmoplantar pustulosis presents as sanitary, yellow surroundings of erythema and scaling affecting the palms and/or soles. The pustules are gentle and weaken to form dark brown coloration with adherent scale/crust. Palmoplantar pustulosis is often linked with psoriatic nail involvement. Approximately 25% of cases are allied with common psoriasis vulgaris, but it is now assumed that palmoplantar pustulosis may not be a form of psoriasis. This termination is derived from genetic studies showing no group with Human Leukocyte Antigen (HLA) Cw6 on chromosome 6p which are correlated to chronic plaque and guttate psoriasis.

Guttate Psoriasis

Guttate psoriasis, the word derived from the Greek word *gutta* meaning a droplet, defines the sensitive inception of account less of tiny, 2–10 mm diameter lesions of psoriasis. These are generally distributed in a centripetal approach while guttate lesions can also involve head and limbs. Naturally, guttate psoriasis occurs an acute haemolytic streptococcal illness of the pharynx or tonsils. This is most in children and rarely in adults. The number of lesions is up to 100 and commonly 5 or 10 will be seen. Guttate psoriasis accounts for 2% of the whole cases of psoriasis. In children, a delicate period of guttate psoriasis is usually self; in adults, guttate flares may confuse chronic plaque disease. Although a trivial number of studies have been done on long-term prediction of children with acute guttate psoriasis, one study shown that 33% of patients with acute guttate psoriasis ultimately developed chronic plaque disease.

Erythroderma

The contribution of the skin by vigorous psoriasis is recognized as erythroderma and is attained in two forms. Firstly, chronic plaque psoriasis might slowly develop as plaques and becomes confluent and extensive. Furthermore, erythroderma may be an expression of unhinged psoriasis caused by infection, drugs, or withdrawal of corticosteroids. Erythroderma may harm the thermal functions of the skin and leads to hypothermia, high cardiac output leads to malfunctioning and metabolic changes including hypoalbuminaemia, and anaemia due to loss of iron, vitamin B12 and folic acid.

Psoriatic Nail Disease

Fingernails are more commonly affected than toenails. The common consequence is small pits in the nail plate, resulting from imperfect nail formation in the proximal part of the nail matrix. The nail may likewise remove from the bed at its distal or lateral attachments, which is acknowledged as onycholysis. Orange yellow zones may be existing below the nail plate and are labeled "oilspots". Further, the nail plate may become, thickened, dystrophic, and finally discoloured. Yellow, keratinous may accumulate under the nail plate which is called as

subungula hyperkeratosis.

SYMPTOMS AND IMPACT OF PSORIASIS ON PATIENT LIFE

The common symptoms of psoriasis were dry skin, itching and burning sensation, signs of pustular psoriasis, depression, painful swollen joints and genital lesions etc. Psoriasis causes excessive corporal, intellectual, and communal burden¹³. The quality of life, in general, is often significantly impaired. There is also mental non well-being, like depression, leads to the negative impact on patients or people. The people, who are suffering from psoriasis are facing social discrimination and psychologically devastation. Also in psoriasis, factors in the immune systems and other biochemical substances that normally control organized explosion and mellowing of epidermal cells are impaired. The reason is inflammation and amplified propagation of skin cells leading to the distinctive clinical kind of scaling and redness. It may produce infections such as strep throat of skin infections etc., Psoriasis is also formed by insects bite, severe sunburns, stress, cold weather, smoking, heavy alcohol consumption, vaccinations, dry skin and diet.

EPIDEMIOLOGY

World Health Organization (WHO) says that, Psoriasis is the utmost dominant autoimmune disease in the United States. According to present studies¹⁸, as many as 7.5 million Americans, approximately 2.2% of the population have psoriasis. 125 million people worldwide. 2% to 3% of the total population have psoriasis, according to the World Psoriasis Day consortium. Studies show that between 10% and 30% of people with psoriasis also develop psoriatic arthritis. Psoriasis prevalence in African Americans is 1.3% compared to 2.5% of Caucasians. It is to estimates of the prevalence of psoriasis have varied across studies. The prevalence of psoriasis in adults ranged from 0.91 to 8.5 percent, and same in the case of children are in between 0 to 2.1 percent. The study stated that 25% of people with psoriasis

could be classified as having sensible to severe psoriasis. Around the world, the one- third of people's affecting psoriasis report a family history of the disease.

PREVALENCE OF PSORIASIS IN INDIA

The prevalence data of psoriasis occurrence in India was obtained from hospital-based studies and only few studies derived from large population areas. In India, most of the studies are done by hospital-based studies. These studies conducted on medical colleges in north India such as Dibrugarh, Calcutta, Patna, Darbhanga, Lucknow, New Delhi and Amritsar. The incidence of the psoriasis along with the total dermatological patients ranged between 0.44 and 2.2%, in generally the overall prevalence of psoriasis is 1.02%. Higher incidence of psoriasis is Amritsar 2.2% compared to eastern India because that it may be associated with different environmental conditions like temperature, food habits, life style, and genetic differences etc. Highest prevalence on male and female patients was noted in the age of 29 to 30 years and the proportion of male to female (2.46:1). The study conducted on north India described the prevalence of psoriasis to be 0.8% among the psoriatic patients but the sample size of the study was very small. The ratio of male to female was 2.5:121. It was noted that females has low incidence compared to males. Later the study was conducted on large number of patients, the incidence of psoriasis among dermatology outpatients was found to be 2.8%, although the ratio of male and female continued to be the same.

IMMUNOPATHOGENIC MECHANISM IN PSORIASIS

Psoriasis is characterized by an abnormal, disproportionate and rapid progress of epidermal layer of the skin. The skin cells are damaged during wound repair and an excess of skin cells result from the pathological events in psoriasis. These changes occur in the evolution progress of keratinocytes induced by inflammatory messengers affect three subtypes of white blood cells. The seveiled inflammatory messengers stimulate keratinocytes. Which cause mutations of genes involved in the skin functions for development of psoriasis. Dying cells are released DNA which acts as inflammatory messengers in psoriasis and stimulates the receptors to releases the interferon³⁰. Keratinocytes besides exude cytokines such as interleukin 1, interleukin 6, and tumour necrosis factor (TNF) α , which produce inflammation. Now a days phototherapy is one of the most common treatments for psoriasis by using nb uvb and psoralen ultraviolet A (PUVA) are used for the therapy. There is also strong scientific evidence

which describes that phototherapy is best and therapy to treat acute psoriasis.

PATHOPHYSIOLOGY AND COMPLICATIONS OF PSORIASIS

Psoriasis is a kind of skin disorder described by the excessive growth of skin epithelial cells and it is a T lymphocyte-mediated autoimmune disease. The pathophysiology of psoriasis

considers the cellular pathological changes that occur in both epidermis and dermis. There are two main processes that occur in development of psoriasis. The first process in psoriasis is characterized by excessive growth and reproduction of skin cells. The second process of the disease is characterized by immune-mediated disorder in which the excessive reproduction of

skin cells occur. However, the effective use of therapies designed to inhibit T-cell activation, such as cyclosporine in the late 1970s, and interleukin (IL)-2 toxin and alefacept, (lymphocyte function-associated antigen-3-Ig) and IL-17A more latterly, has led to a paradigm shift in psoriasis pathogenesis to an immune cell mediated inflammatory etiology. It is also diminished CD4-T-cell roots an over-activation of CD8-T-cells, which are accountable for the development of psoriasis in HIV patients. The complications of psoriasis include psoriatic arthritis, eye conditions, folate deficiency cancers, heart problems, obesity and diabetes, bad

body temperature regulation, zumbusch psoriasis metabolic syndrome. Other autoimmune diseases like celiac disease, sclerosis and the inflammatory bowel disease called crohn's disease, parkinson's disease, kidney disease etc. Peoples having psoriasis is a great risk for heart attack too. Drinking alcohol is considered as a complication of psoriasis. Chaffing and irritation from heat and sweat, Secondary fungal infections particularly candida (thrush), from rubbing and scratching of skin, sexual difficulties are few complications on over usage of strong topical steroid creams. Other complications include secondary bacterial infections, disturbed protein and electrolyte balance, renal and liver impairment, malabsorption of nutrients and therapeutic drugs

DIAGNOSIS

A Diagnosis of psoriasis is based on the nature of the skin and its characteristics. Diagnosis is generally done by clinical examination. At hand, there is no precise tests are available to diagnose psoriasis, sometimes biopsy may be carried out to differentiate it from fungal infection. Diagnosing the joints by pain and using X-ray and bone scanning methods.

Psoriasis diagnosis includes the study of dermatological conditions such as discoideczema, seborrheic eczema, pityriasisrosea nail fungus orcutaneous T-cell lymphoma also dermatologic manifestations of systemic illnesses with psoriasis.

TREATMENT AND MANAGEMENT OF PSORIASIS

Various treatments are available for the management and control the symptoms of psoriasis. Nowadays different therapies are obtainable to cure the disease such as topical, phototherapy and systemic therapy. The symptoms of psoriasis can be managed somehow by regular diet and water intake.

Diet

Take minimum 2 litres of water per day to control the symptoms of psoriasis. Eat a lot of vegetables and green leafy vegetables to control the symptoms. This does not cure the disease, but it may reduce the symptoms. Peoples having the poor diet it may affect the skin. Some vitamin tablets like zinc tablets are taken daily can help reduce psoriasis. Drinking alcohol is the risk factor for psoriasis because the white blood cells, including the T cells will release on dilation of blood vessels due to alcohol intake. Some cool drinks, dairy products, condiments and fried dishes affect the skin. On the other hand, Omega-3 fatty acids containing fish oils are thought to reduce inflammation and help to boost the immune system.

Topical Therapies

Treatment associated with application of semisolid preparations on the skin is known as topical treatments. These are the utmost used as mode of treatment for patients with psoriasis.

Emollients

Emollients provide soothing feeling to the scales hence it become less itchy. It also keeps the skin moist by that the emollients reduce the dryness and helps to prevent scaling and promote the penetration of the medicament through the skin. Patients should avoid the usage of soaps while bathing and washing. It is common to permit about 30 minutes following applying an emollient before taking other psoriasis treatments.

Keratolytic

Topical preparations that contain salicylic acid can help decrease excessive scaling but may occasionally irritate the adjacent skin. Salicylic acid (2-10%) combined with steroids, coal tar and dithranol which produce effective results.

Steroids

The steroids are the choice to treat the flakes on milder areas like on face and under arms. But potent steroids are preferably used to remove thickened plaques on soles on palms. The potent topical steroids are corticosteroids, clobetasol propionate or betamethasone propionate applied once or twice

daily. In prolonged use of topical steroids which cause skin atrophy, hair growth, hypopigmentation⁵³. Different newer formulations are available to enhance the delivery of topical corticosteroids. Examples, the foam form of betamethasone valerate had superior efficacy for scalp psoriasis compared with lotion⁵⁴. A clobetasol propionate spray is also available are easy to apply to large areas.

Tar Preparations

Tar preparations are helpful to remove loose scales of the patches of psoriasis. Tar preparations are available in the form of creams or ointments or shampoos. This aid most patients, but many find the muntidy and they can stain clothing. Coal tar relieve the itchiness, swelling and flaking of skin. Tar shampoo should be placed in hair for 5 to 10 minutes before rinsing it out. Triamcinolone is a compound of crude coal tar which is applied individual plaques twice daily to produce better results. An alternative is 4 to 10% liquor carbon detergent in triamcinolone cream or ointment is used.

Dithranol (Anthralin)

Dithranol is good for chronic scaly psoriasis in selected areas and can be prescribed for use at home. It is an effective drug for plaque psoriasis. Skin irritation and brownish discoloration of the skin are some of the side effects of dithranol. Short contact therapy is used to avoid these side effects. Dithranol (0.1-1% concentration) is applied once a day and washed off thoroughly after 10 minutes to one hour. It may produce stain clothing.

Topical Vitamins

These analogues are effective for the treatment of psoriasis including following agents like calcipotriene and calcitriol. Calcipotriene is synthetic Vitamin D3 analogues effective for the treatment of psoriasis. The mechanism of action is epidermal proliferation leads to enhance the growth of normal cells and has anti-inflammatory effects. The combination with topical steroids it's more effective compare than the other agents. It is also combined with phototherapy is used. Some common side effects are irritation and skin atrophy. Vit-D3 helps to control calcium and phosphorus in the body and can also be produced by the skin when exposed to UVB light^{58, 59}. Calcitriol is the vitamin D3 analogue. It acts similarly with the calcipotriene and involves the drug's capacity to inhibit keratinocyte proliferation and stimulate keratinocyte differentiation. It also impedes T cell proliferation and other inflammatory messengers.

Tazarotene (Calcineurin Inhibitors)

Tazarotene is a third-generation topical retinoid available as a cream, gel, and foam. Tazarotene properties are similar to that of Vita-A. In the treatment of psoriasis, it may be used in a combination with a corticosteroid cream or ointment, calcipotriol or phototherapy. It is official for treatment of psoriasis, acne, and photo damage. It is available in two strengths that are 0.05% and 0.1%. Common adverse effects include dry skin, itchiness, redness, flaking the skin. Tazarotene is under the category X that contraindicated for pregnant women.

Tacrolimus

It is immunosuppressive drugs that are useful in the controlling of atopic dermatitis, can also use for psoriasis. It may be topical steroid application may have trouble some side effects. 0.1% concentration of tacrolimus is active against psoriasis. There were few reports on that, the topical tacrolimus produces lymphoma and skin cancer in children and adults. The mode of action is inhibiting the production of interleukin-2 and promotes the development and proliferation of T cells. It is also used in the treatment of eczema, ulcerative colitis etc.

Systemic Therapies

A number of systemic medications are used for the treatment of psoriasis. Many guidelines are published about the treatment of psoriasis with systemic therapies such as the American Academy of Dermatology and European S3-Guidelines on the systemic treatment of psoriasis⁶³. The choice of systemic drugs include such as methotrexate, cyclosporine, apremilast, systemic retinoids and biologic agents which improve psoriasis through immune modulation, are also used for the treatment of this psoriasis⁶⁴.

Folic Acid Antagonists

Methotrexate is the folic acid antagonist has been used successfully in the treatment of psoriasis. Along with anti-cancer activity, the MTX is also having anti-psoriatic activity. It acts by inhibiting dihydrofolate reductase then activation of folic acid leads to inhibit the synthesis of DNA⁶⁶. It is usually administered low-dose regimen such as once weekly. Similar doses are used in patients with rheumatoid arthritis.

Systemic Retinoids (Acitretin)

Retinoids are derivatives of vitamin A are used for the treatment of severe psoriasis, including pustular and erythrodermic psoriasis. The choice of retinoid in psoriasis is acitretin. In a retinoid study with acitretin therapy conducted in 6 of 11 patients with psoriasis and HIV infection achieved to get excellent results of skin diseases⁶⁷. The dose range is 25 mg every day to

maintaining dose is 50mg daily. Acitretin can be used in combination with UVB or PUVA therapy. This combination therapy, peoples having a higher response to better tolerance and less UV exposure. Common adverse effects include cheilitis and alopecia. Acitretin is teratogenic agent designated in men and in women of reproductive potential.

Systemic Calcineurin Inhibitors

Cyclosporine is the T-cell suppressor which is effective in patients with severe psoriasis. The dose range between 3 to 5 mg/kg per day orally. Development is generally observed within four weeks. The use of cyclosporine in psoriasis is based upon multiple studies improve the effective management of psoriasis⁷¹. It acts on T-cells and produces inhibitory effects. The usual dose is 3-5mg/kg give orally in two divided doses. Major adverse effects are nephrotoxicity and hypertension. It may enhance the risk of cancer. It is contraindicated in renal dysfunction, hypertension, pregnancy lactation. Immunosuppressive or nephrotoxic drugs, oral retinoids should be administered by using experience dermatologists.

Biological Agents in Psoriasis Treatment

Biologic therapy is a significant therapy to treat psoriasis. The agents which are available for the treatment of psoriasis in the USA, which include Alefacept, etanercept, infliximab, adalimumab, ustekinumab, secukinumab, and pexelizumab. Itolizumab is a biologic agent marketed in India.

Etanercept (Enbrel)

The etanercept is the TNF-alpha inhibitor is used for the treatment of psoriasis⁷³. It is approved by the US Food and Drug Administration (FDA) for adults with psoriatic arthritis and severe plaque psoriasis. Standard dosing for etanercept for adults is 50 mg sub cutaneous twice weekly for the initial three months of therapy, followed by a 50 mg injection once weekly for maintenance therapy. The standard pediatric dose is 0.8 mg/kg weekly. The anti-etanercept antibodies have been providing in 10-20% of patients treated with the drug for psoriasis. Etanercept is a recombinant human TNF-receptor that antagonizes the action of TNF receptor by competitively inhibiting its interaction with cell-surface receptors. Etanercept is effective for patients with rheumatoid arthritis and in patients with psoriatic arthritis.

Infliximab (Remicade)

The TNF-alpha inhibitor infliximab is useful for patients with moderate to severe plaque psoriasis and appears to generally be welltolerated⁷⁵. It is also used for the treatment of adult rheumatoid arthritis, ulcerative colitis, and Crohn's disease. The effective

dose is 5 mg/kg. It binds to trans membrane TNF- α . Molecules, there by neutralizing the effects of TNF- α which is administered by intravenous route. A common risk factor is chest pain, hypertension, and shortness of breath and only rarely will severe reactions with hypotension and anaphylaxis occur. It has been the efficient treatment of inflammatory bowel diseases (IBD).

Adalimumab (Humira)

Adalimumab is a new anti-TNF agent. Adalimumab is a human monoclonal antibody that is accepted by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of rheumatoid arthritis and psoriatic arthritis. It is a human Immunoglobulin G1 monoclonal antibody that binds with TNF- α the dose range of adalimumab is 80mg for adults in subcutaneous injection followed by 40 mg given every other week. This medication used to treat rheumatoid arthritis, psoriatic arthritis, Crohn's disease, ulcerative colitis, chronic psoriasis. Side effects are lymphoma solid tissue cancers, liver injury, demyelinating central nervous system disorders and cardiac failure.

Ustekinumab (Stelara)

Stelara is a human monoclonal antibody that targets interleukin (IL)-12 and IL-23. It is used to treat moderate to severe psoriasis. Dose calculated based on the weight of the patient. Standard dosing for adults weigh 100 kg is 45 mg given at weeks 0, 4, and every 12weeks thereafter. The mode of action is blocked interleukin IL-12 and IL-23 which activate certain T-cells. It binds to the p-40subunit of both IL-12 and IL-23⁷⁷. The common adverse effects reporting a serious allergic reaction, upper respiratory infection, headache, and tiredness.

Alefacept (AMEVIVE®)

Alefacept is an immunosuppressant drug. It is a recombinant protein which effective for the treatment of psoriasis. It is used to control inflammation in moderate to severe psoriasis, where it interferes with lymphocyte activation. Alefacept interferes with lymphocyte establishment by exclusively binding to the lymphocyte antigen and inhibiting LFA-3/CD2 (Cluster of differentiation 2) interaction. The majority of T lymphocytes in psoriatic lesions is the memory effect or phenotype characterized by the incidence of the CD45RO marker¹, that circumstances activation markers (e.g., CD25, CD69) and discharge inflammatory cytokines, such as interferon. Alefacept also causes a decreasing subset of CD2+ T lymphocytes mainly CD45RO+, most probably by bridging between CD2

on target lymphocytes and immunoglobulin Fc receptors on cytotoxic cells, such as natural killer cells. Some risk factors are lymphopenia, malignancies such as melanoma skin cancers, other solid tumours, and lymphomas, hepatic toxicity like cirrhosis, liver failure, pharyngitis, cough, dizziness, nausea, pruritus.

Natural Remedies for the Treatment of Psoriasis

Traditional medicines hold a great promise as a source of easily available effective therapy for skin diseases to the people, particularly in tropical developing countries, including India. Herbal remedies for psoriasis are increasingly popular and mainstream.

***Aloe barbadensis* (Family: Liliaceae, Common name: Aloe vera)**

Aloe vera is a stem less, drought resisting, succulent plant belongs to the family Liliaceae and has been used since ancient times for medicinal purposes. Recent research has shown that the pharmacologically active agent is used for the psoriasis treatment. The active agents have shown considerable palliative, antipruritic, wound healing and anti-inflammatory properties, thus mitigating consideration of aloe vera as an effective remedy for the management of psoriasis.

***Origanum vulgare* (Family: Lamiaceae, Common name: Oregano oil)**

Another herbal remedy for psoriasis is oregano. It is having antibacterial and anti-fungal properties which can be helpful with infections that are induced by psoriasis. It is a commonly used spice for baking and cooking. Oregano oil can be purchased at most health food stores. A lot of people have contacted the Psoriasis Foundation to request them recognize that use of oregano oil, either orally or topically, has helped their psoriasis.

***Curcuma longa* (Family: Zingiberaceae, Common name: Turmeric)**

Turmeric is a most important constituent of curry powders used in catering. The spice has an extended narration of being used in habitual Indian and Chinese medicine. Turmeric is a dietary supplement; on the other hand, many people who call the food action use the powdered form of the spice and mix it in with their food. Turmeric has also been reported to aid reduce the puffiness, soreness and inflammation associated with arthritis.

***Allium cepa* (Family: Liliaceae, Common name: Onion)**

Allium cepa is preferred by patients with seborrheic keratoses to estimate the ability of onion extract gel to improve the appearance of scars following excision has shown that this extract gel improved

disfigure smoothness, redness, feel and global manifestation at the excision site at study weeks 4, 6 and 10 as assessed by the blinded investigator.

***Allium sativum* (Family: Liliaceae, Common name: Garlic)**

The study conducted on Swiss albino mice in whom skin cancer was induced by 7,12-di methyl benzo(a)anthracene (DMBA) exposure and best chemo preventive action of garlic was observed in mice in which garlic treatment. Garlic intake delayed the development of skin papilloma in animals and concurrently decreased the size and number of papillomas, which was also reflected in the skin histology of the treated mice. Hence, it was strongly believed that garlic can be a potent medicine in the prevention of psoriasis.

***Berberis vulgaris* (Family: Berberidaceae, Common name: Barberry)**

Barberry is available in capsules, teas, or tinctures. It is used as an antioxidant, anti-inflammatory, and apparently, prevents toxin formation in the bowel. Berberine is an active compound in this herb, which is used for psoriasis which is more potent than chloramphenicol. It is also used as antibiotics to kill or prevent the growth of the microorganism. It causes diarrhea, dysentery, urinary tract infections and cholera. It can also be reduced high blood pressure.

***Capsicum annum* (Family: Solanaceae, Common name: Cayenne, Capsicum)**

Cayenne [Figure 3G] contains capsaicin which has been demonstrated to reduce itching and pain in psoriasis. It appears to work by depleting neurotransmitters in the sensory nerves. The American Academy of Dermatology was studied by the skin infections by using cayenne, externally applied, was an effective herb for pruritic psoriasis.

***Silybum marianum* (Family: Daisy family, Common name: Milk thistle)**

Milk thistle is supposed to facilitate to stop psoriasis outbreaks by cheering proper liver function. The liver neutralises certain toxins associated with psoriasis. Antibiotics are not directed for the routine treatment of psoriasis. Milk thistle helps to inhibit human T-cell activation. This herb is having anti-inflammatory properties as well as decreases the unbalanced proliferation of skin cells. Few adverse effects have been seen i.e gastrointestinal disturbances and mild allergic reactions. Milk thistle products are available in the form of tablets or liquid extract and it's purchased in health food store.

Homeopathic Approaches in Psoriasis

The most ecstasy for psoriasis patients is the desertion of the rashes. The disappearances of the itchy/scaly skin itself do not mean the disease is

waning that is, Skin itchiness can be easily made to vanish with steroidal topical applications which usually mask the complaint. Likewise, suppressive immune therapy with steroidal drugs will also mask the complaint, but very temporarily. The allopathic way of approach is usually against causative factor or disease. But Homeopathy treats the indications of patient's leads excellent results for one patient to compare to another patient. Also, in other systems, the medicines are selected to stop the proliferation

of epidermis or infection. Homoeopathy is safe and offers betterment by enhancing the energy to psoriasis without any side effects. Homoeopathic medicines usually helpful in belongings of psoriasis are Ars alb, Arg Nit, Baryta Mur, Corralium, Crabapple, Hudrocytole, Kali ars, Kali Brom, Lycopodium, Natpulp, Phosphorus, Psoralea, Psorinum, Pulsatilla, Urtica urens, etc. These medicines should be taken by taking the instruction of qualified Homoeopath.

Table 1: Topical therapies of psoriasis treatment

S.No.	Drug name	Brand name	Dose	Manufacturer
1	Clobetasol propionate,	Clobex, Diprolene	Lotion/Spray/Shampoo, 0.05%, Ointment, 0.05% applied on affected area	Galderma Laboratories Inc.
2.	Coal tar	Psoriasin	Use one or two times a day,	Merck Sharp & Dohme Alva-Amco Pharmacal Companies, Inc
3.	Anthralin	Dianthrol	0.1-1% concentration is applied once a day and washed off thoroughly after 10 minutes to one hour	Agon Pharma Private Limited Pune
4.	Calcipotriene	Daivonex®	Cream, 0.005%. Apply a thin layer of Daivonex Cream to the affected skin twice daily and rub in gently and completely	Croslands (Ranbaxy laboratories)
5.	Tazarotene	Tazorate forte	Topical cream 0.1%: For the topical treatment of patients with acne vulgaris: Cleanse the face gently. Use enough to cover the entire affected area	Glenmark (gracewell SPL)
6.	Tacrolimus	Acroli forte	0.03% ointment: Apply a thin layer to the affected areas 2 times a day and rub in gently and completely	Zydus Cadila Healthcare Ltd. Mumbai

Table 2: Systemic therapies of psoriasis treatment

S.No.	Drug name	Brand name	Dose	Manufacturer
1	Methotrexate	Alltrex	Single Dose: 7.5 mg/week orally, IM, or IV Divided Dose: 2.5 mg orally, IM, or IV every 12 hours for 3 doses once a week, Maximum weekly dose: 20 mg	Miracalus Pharma Pvt Ltd
2.	Acitretin (Systemic retinoids)	Aceret	The dose range is 25 mg every day to maintaining dose is 50mg daily.	Glenmark pharmaceuticals Ltd
3.	Cyclosporine (Systemic Calcineurin inhibitors)	Graftin (25mg)	The usual dose is 3-5mg/kg given orally in two divided doses	Ranbaxy Laboratories Ltd.

Table 3: Biological agents used for treatment of psoriasis

S.No.	Drugname	Brand name	Dose	Manufacturer
1	Etanercept	Enbrel	Standard dosing for etanercept for adults is 50 mg s.c twice weekly for the initial three months of therapy, followed by a	Takeda Pharmaceuticals, Japan Wyeth [now part of Pfizer]
2.	Infliximab	Remicade	The dose range is 5 mg/kg.	Janssen Biotech, Inc. (formerly Centocor Biotech, Inc.)
3.	Adalimumab	Humira	The dose range of adalimumab is 80mg for adults in subcutaneous injection followed by 40 mg given every other	Abbott Laboratories
4.	Ustekinumab	Stelara	Standard dosing for adults ≤ 100 kg is 45 mg given at weeks 0, 4, and every 12 weeks	Janssen Biotech, Inc. (formerly Centocor Biotech, Inc.)
5.	Alefacept	AMEVIVE®	severe plaque psoriasis, following a 7.5 mg intravenous (IV) weekly	Astellas pharma US

Figure 1 (A, B, C, D, E, F): Clinical types of psoriasis

Figure 2 (A, B, C, D, E, F): Symptoms of psoriasis


Figure 3(A, B, C, D, E, F, G, H, I): Natural Therapeutic agents in the management of psoriasis.



CONCLUSION

Psoriasis is considered as a chronic, immune modulated inflammatory disease. A new understanding of this complex disease has catalyzed the development of targeted biological treatments. This review provides an understanding of pathophysiology and clinical complications of psoriasis along with treatments. Herbal therapies provides a few options for increasing safety and efficiency in the management of psoriasis. This review will surely prove to be an exposure to patients suffering from psoriasis as well as the medical practitioners, pharmacists, nurses and other persons involved in giving and taking the treatment and the management of psoriasis and help them to recognize the infection in a much better way to take safe and valuable treatment

REFERENCES

- Jain S. Dermatology: Illustrated Study Guide and Comprehensive Board Review. 2nd ed. Chicago. Springer: 2017.
- Menter A, Gottlieb A, Feldman SR, Van Voorhees AS, Leonardi CL, Gordon KB, *et al.*, Guidelines of Care for the Management of Psoriasis and Psoriatic Arthritis: Section Overview of Psoriasis and Guidelines of Care for the Treatment of Psoriasis with Biologics. Journal of the American Academy of Dermatology. 2008; 58:826-50.
- Christophers E. Psoriasis- Epidemiology and Clinical Spectrum. Clinical and Experimental Dermatology. 2001; 26:314-20.
- Shrivastav S, Sindhu R, Kumar S, Kumar P. Anti-Psoriatic and Phytochemical Evaluation of Thespesia Populnea Bark Extracts. International Journal of Pharmacy and Pharmaceutical Science. 2009; 1:176-85.
- Lo K, Ho L. In Psoriasis: Handbook of Dermatology and Venereology. Hong Kong: Social Hygiene Service, Department of Health. 1997.
- Griffiths CE, Barker JN. Pathogenesis and Clinical Features of Psoriasis. The Lancet. 2007; 370:263-71.
- Kuchekar AB, Pujari RR, Kuchekar SB, Dhole SN, Mule PM. Psoriasis: A Comprehensive Review. International Journal of Pharmacy & Life Sciences. 2011; 2:857-887.
- Zhou Y, Wu H, Zhao M, Chang C, Lu Q. The Bach Family of Transcription Factors: A Comprehensive Review. Clinical Reviews in Allergy & Immunology. 2016; 50:345-56.
- Walter LF GS. Histopathology of the skin. 3rd Ed. Massachusetts (NY): Lippincott Williams & Wilkins; 1981.
- Martin BA, Chalmers RJ, Telfer NR. How Great is the Risk of Further Psoriasis following a Single Episode of Acute Guttate Psoriasis. Archives of Dermatology. 1996;132(6):717-8.
- Asumalahti K, Ameen M, Suomela S, Hagforsen E, Michaelsson G, Evans J, *et al.*, Genetic Analysis of PSORS1 Distinguishes Guttate Psoriasis and Palmoplantar Pustulosis. Journal of Investigative Dermatology. 2003; 120:627-32.
- O'Doherty CJ, Macintyre C. Palmoplantar Pustulosis and Smoking. British Medical Journal (Clinical Research Ed). 1985; 291:861-4.
- Fujii R, Mould J, Tang B, Brandt H, Pomerantz D, Chapnick J, *et al.*, PSY46 Burden of Disease in Patients With Diagnosed Psoriasis in Brazil: Results From 2011 National Health and

14. Wellness Survey (NHWS). Value in Health. 2012;15:A107.
15. Tang MM, Chang CC, Chan LC, Heng A. Quality of Life and Cost of Illness in Patients with Psoriasis in Malaysia: A Multicenter Study. *International Journal of Dermatology*. 2013;52:314-22.
16. Augustin M, Kruger K, Radtke M, Schwappl I, Reich K. Disease Severity, Quality of Life and Health Care in Plaque type Psoriasis: A Multicenter Cross Sectional Study in Germany. *Dermatology*. 2008; 216:366-72.
17. Russo PA, Ilchef R, Cooper AJ. Psychiatric Morbidity in Psoriasis: A Review. *Australasian Journal of Dermatology*. 2004; 45:155-61.
18. Sampogna F, Tabolli S, Abeni D. Living with Psoriasis: Prevalence of Shame, Anger, Worry, and Problems in Daily Activities and Social Life. *Acta Dermato Venereologica*. 2012;92:299-303.
19. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM. Global Epidemiology of Psoriasis: A Systematic Review of Incidence and Prevalence. *Journal of Investigative Dermatology*. 2013;133:377-85.
20. Nickoloff BJ. Skin Innate Immune System in Psoriasis: Friend or Foe. *Journal of Clinical Investigation*. 1999; 104:1161.
21. Okhandiar R, Banerjee B. Psoriasis in The Tropics: An Epidemiological Survey. *Journal of the Indian Medical Association*. 1963; 41:550.
22. Bedi T. Clinical Profile of Psoriasis in North India. *Indian Journal of Dermatology, Venereology, and Leprology*. 1995;61:202.
23. Kaur I, Handa S, Kumar B. Natural History of Psoriasis: A Study from the Indian Subcontinent. *The Journal of Dermatology*. 1997; 24:230-4.
24. Sachappert S. Ambulatory Care Visits to Physician Offices, Hospital Outpatient Departments and Emergency Departments: United States 1996. National Center for Health Statistics. *Vital Health Statistics*. 1998; 13:1-37.
25. Ouyang W. Distinct Roles of IL-22 in Human Psoriasis and Inflammatory Bowel Disease. *Cytokine & Growth Factor Reviews*. 2010; 21:435-41.
26. Palfreeman AC, McNamee KE, McCann FE. New Developments in the Management of Psoriasis and Psoriatic Arthritis: A Focus on Apremilast. *Drug Design, Development and Therapy*. 2013; 7:201.
27. Cedeno-Laurent F, Gomez-Flores M, Mendez N, Ancer-Rodríguez J, Bryant JL, Gaspari AA, *et al.*, New Insights into HIV-1-Primary Skin Disorders. *Journal of the International AIDS Society*. 2011; 14:5.
28. Baliwag J, Barnes DH, Johnston A. Cytokines in Psoriasis. *Cytokine*. 2015;73(2):342-50.
29. Roberson ED, Bowcock AM. Psoriasis Genetics: Breaking the Barrier. *Trends in Genetics*. 2010; 26:415-23.
30. Ramos-e-Silva M, Jacques C. Epidermal Barrier Function and Systemic Diseases. *Clinics in Dermatology*. 2012; 30:277-9.
31. Dombrowski Y, Schaubert J. Cathelicidin LL-37: A Defense Molecule with a Potential Role in Psoriasis Pathogenesis. *Experimental Dermatology*. 2012; 21:327-30.
32. Duarte I, Cunha JAJd, Bedrikow RB, Lazzarini R. What is the most Common Phototherapy Prescription for Psoriasis: NB-UVB or PUVA. *Prescription behavior. Anais Brasileiros De Dermatologia*. 2009; 84:244-8.
33. Koo JY. Current Consensus and Update on Psoriasis Therapy: A Perspective from the US. *The Journal of Dermatology*. 1999; 26:723-33.
34. Lapolla W, Yentzer BA, Bagel J, Halvorson CR, Feldman SR. A Review of Phototherapy Protocols for Psoriasis Treatment. *Journal of the American Academy of Dermatology*. 2011; 64:936-49.
35. Krueger J, Bowcock A. Psoriasis Pathophysiology: Current Concepts of Pathogenesis. *Annals of the Rheumatic Diseases*. 2005; 64:30-6.
36. Rahman P, Elder J. Genetic Epidemiology of Psoriasis and Psoriatic Arthritis. *Annals of the Rheumatic Diseases*. 2005; 64:37-9.
37. Yaqoob P. Fatty Acids as Gatekeepers of Immune Cell Regulation. *Trends in Immunology*. 2003; 24:639-45. Ortonne JP. Aetiology and Pathogenesis of Psoriasis. *British Journal of Dermatology*. 1996; 135:1-5.
38. Ellis CN, Gorsulowsky DC, Hamilton TA, Billings JK, Brown MD, Headington JT, *et al.*, Cyclosporine Improves Psoriasis in a Double Blind Study. *The Journal of the American Medical Association* 1986; 256:3110-6.
39. Gottlieb SL, Gilleaudeau P, Johnson R, Estes L, Woodworth TG, Gottlieb AB, *et al.*, Response of Psoriasis to a Lymphocyte-Selective Toxin (DAB389IL-2) Suggests a Primary Immune, but not Keratinocyte, Pathogenic Basis. *Nature Medicine*. 1995;1(5):442-7.
40. Abrams JR, Kelley SL, Hayes E, Kikuchi T, Brown MJ, Kang S, *et al.*, Blockade of T Lymphocyte Costimulation with Cytotoxic T Lymphocyte-Associated Antigen 4-Immunoglobulin (CTLA4Ig) Reverses the Cellular Pathology of Psoriatic Plaques, including the Activation of Keratinocytes, Dendritic Cells and Endothelial Cells. *Journal of Experimental Medicine*. 2000; 192:681-94.
41. Abrams JR, Lebwohl MG, Guzzo CA, Jegasothy BV, Goldfarb MT, Goffe BS, *et al.*, CTLA4Ig-Mediated Blockade of T-cell Costimulation in Patients with Psoriasis Vulgaris. *Journal of Clinical Investigation*. 1999; 103:1243.
42. McInnes IB, Mease PJ, Kirkham B, Kavanaugh A, Ritchlin CT, Rahman P, *et al.*, Secukinumab, A Human Anti-Interleukin-17A Monoclonal Antibody, in Patients with Psoriatic Arthritis (Future 2): A Randomized, Double-Blind, Placebo Controlled Phase 3 trial. *Lancet*. 2015; 386:1137-46.
43. Nancy Weigle M, Duke. Psoriasis. *American Family Physician*. 2013; 87:626-33.
44. Johnson MAN, Armstrong AW. Clinical and Histologic Diagnostic Guidelines for Psoriasis: A Critical Review. *Clinical Reviews in Allergy & Immunology*. 2013; 44:166-72.
45. Mease PJ, Armstrong AW. Managing Patients with Psoriatic Disease: The Diagnosis and Pharmacologic

- Treatment of Psoriatic Arthritis in Patients with Psoriasis. *Drugs*. 2014; 74:423-41.
46. Soyland E, Funk J, Rajka G, Sandberg M, Thune P, Rustad L, *et al.*, Effect of Dietary Supplementation with Very-Long-Chain n-3 Fatty acids in Patients with Psoriasis. *New England Journal of Medicine*. 1993; 328:1812-6.
 47. Bjorneboe A, Smith AK, Bjorneboe GEA, Thune P, Drevon C. Effect of Dietary Supplementation with n-3 Fatty acids on Clinical Manifestations of Psoriasis. *British Journal of Dermatology*. 1988; 118:77-83.
 48. Calder PC. n-3 Polyunsaturated Fatty acids, Inflammation, and Inflammatory Diseases. *The American Journal of Clinical Nutrition*. 2006; 83:1505-19.
 49. Bayliffe AI, Brigandi RA, Wilkins HJ, Levick MP. Emerging Therapeutic Targets in Psoriasis. *Current Opinion in Pharmacology*. 2004; 4:306-10.
 50. Lebwohl M. Future Psoriasis Therapy. *Dermatologic Clinics*. 1995; 13:915-23.
 51. Brown AC, Hairfield M, Richards DG, McMillin DL, Mein EA, Nelson CD. Medical Nutrition Therapy as a Potential Complementary Treatment for Psoriasis- Five Case Reports. *Alternative Medicine Review*. 2004; 9:297-307.
 52. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, *et al.*, Guidelines of Care for the Management of Psoriasis and Psoriatic Arthritis: section 6. Case-based Presentations and Evidence-based Conclusions. *Journal of the American Academy of Dermatology*. 2011; 65:137-74.
 53. Franz TJ, Parsell DA, Halualani RM, Hannigan JF, Kalbach JP, Harkonen WS. Betamethasone Valerate foam 0.12%: A Novel Vehicle with Enhanced Delivery and Efficacy. *International Journal of Dermatology*. 1999; 38:628-32.
 54. Lebwohl M, Ali S. Treatment of Psoriasis. Part 1. Topical Therapy and Phototherapy. *Journal of the American Academy of Dermatology*. 2001; 45:487-502.
 55. Goodfield M, Kownacki S, Berth-Jones J. Double-Blind, Randomized, Multi centre, Parallel Group Study Comparing a 1% Coal tar Preparation (Exorex) with a 5% Coal tar Preparation (Alphosyl) in Chronic Plaque Psoriasis. *Journal of Dermatological Treatment*. 2004; 15:14-22.
 56. Tzaneva S, Honigsmann H, Tanew A. Observer-Blind, Randomized, Inpatient Comparison of a Novel 1% Coal tar Preparation (Exorex) and Calcipotriol Cream in the Treatment of Plaque type Psoriasis. *British Journal of Dermatology*. 2003; 149:350-3.
 57. Walter JF, Stoughton RB, Dequoy PR. Suppression of Epidermal Proliferation by Ultraviolet Light, Coal tar and Anthralin. *British Journal of Dermatology*. 1978; 99:89-96.
 58. Kragballe K. Treatment of Psoriasis with Calcipotriol and other Vitamin D Analogues. *Journal of American Academy of Dermatology*. 1992; 27:1001-8.
 59. Grant WB, Holick MF. Benefits and Requirements of Vitamin D for Optimal Health: A Review. *Alternative Medicine Review*. 2005; 10:94-111.
 60. Rizova E, Corroller M. Topical Calcitriol—Studies on Local Tolerance and Systemic Safety. *British Journal of Dermatology*. 2001; 144:3-10.
 61. Weinstein GD, Krueger GG, Lowe NJ, Duvic M, Friedman DJ, Jegasothy BV, *et al.*, Tazarotene Gel, A New Retinoid, for Topical Therapy of Psoriasis: Vehicle-Controlled Study of
 62. Safety, Efficacy and Duration of Therapeutic Effect. *Journal of the American Academy of Dermatology*. 1997; 37:85-92.
 63. Brown BD. Management of Psoriasis: An Update. *Bulletin on Drug & Health Information Foundation for Health Action*. 2006; 13:1.
 64. Nast A, Gisondi P, Ormerod A, Saiag P, Smith C, Spuls P, *et al.*, European S3-Guidelines on the Systemic Treatment of Psoriasis Vulgaris—Update 2015—Short Version—EDF in Cooperation with EADV and IPC. *Journal of the European Academy of Dermatology and Venereology*. 2015; 29:2277-94.
 65. Schmitt J, Rosumeck S, Thomaschewski G, Sporbeck B, Haufe E, Nast A. Efficacy and Safety of Systemic Treatments for Moderate-to-Severe Psoriasis: Meta-analysis of Randomized Controlled Trials. *British Journal of Dermatology*. 2014; 170:274-303.
 66. Nast A, Jacobs A, Rosumeck S, Werner RN. Efficacy and Safety of Systemic long-term Treatments for Moderate-to-Severe Psoriasis: A Systematic Review and Meta-analysis. *Journal of Investigative Dermatology*. 2015; 135:2641-8.
 67. Shalom G, Zisman D, Bitterman H, Harman-Boehm I, Greenberg-Dotan S, Dreier J, *et al.*, Systemic Therapy for Psoriasis and the Risk of Herpes Zoster: a 500 000 Person Year Study. *The Journal of the American Medical Association dermatology*. 2015; 151:533-8.
 68. Buccheri L, Katchen BR, Karter AJ, Cohen SR. Acitretin Therapy is Effective for Psoriasis Associated with Human Immunodeficiency Virus Infection. *Archives of Dermatology*. 1997; 133:711-5.
 69. Tanew A, Guggenbichler A, Honigsmann H, Geiger J, Fritsch P. Photochemotherapy for Severe Psoriasis without or in Combination with Acitretin: A Randomized, Double-Blind Comparison Study. *Journal of the American Academy of Dermatology*. 1991; 25:682-4.
 70. Lam J, Polifka JE, Dohil MA. Safety of Dermatologic Drugs used in Pregnant Patients with Psoriasis and other Inflammatory Skin Diseases. *Journal of the American Academy of Dermatology*. 2008; 59:295-315.
 71. Strober BE, Siu K, Menon K. Conventional Systemic Agents for Psoriasis. A Systematic Review. *The Journal of Rheumatology*. 2006; 33:1442-6.
 72. Faerber L, Braeutigam M, Weidinger G, Mrowietz U, Christophers E, Schulze H, *et al.*, Cyclosporine in Severe Psoriasis. *American journal of clinical dermatology*. 2001; 2:41-7.
 73. Ho V, Griffiths C, Albrecht G, Vanaclocha F, León-Dorantes G, Atakan N, *et al.*, Intermittent Short Courses of Cyclosporin (Neoral (R)) for Psoriasis Unresponsive to Topical Therapy: A 1-year

- Multicentre, Randomized Study. British Journal of Dermatology. 1999; 141:283-91.
74. Iyer S, Yamauchi P, Lowe N. Etanercept for Severe Psoriasis and Psoriatic Arthritis: Observations on Combination Therapy. British Journal of Dermatology. 2002; 146:118-21.
 75. Hsu L, Snodgrass B, Armstrong A. Antidrug Antibodies in Psoriasis: A Systematic Review. British Journal of Dermatology. 2014; 170:261-73.
 76. Gottlieb AB, Masuda S, Ramamurthi R, Abdulghani A, Romano P, Chaudhari U, *et al.*, Pharmacodynamic and Pharmacokinetic Response to Anti-Tumor Necrosis factor- α Monoclonal antibody (infliximab) Treatment of Moderate to Severe Psoriasis Vulgaris. Journal of the American Academy of Dermatology. 2003; 48:68-75.
 77. Takeuchi T, Yamanaka H, Ishiguro N, Miyasaka N, Mukai M, Matsubara T, *et al.*, Adalimumab, A Human Anti-TNF Monoclonal Antibody, Outcome Study for the Prevention of Joint Damage in Japanese Patients with Early Rheumatoid Arthritis: The Hopeful 1 Study. Annals of the Rheumatic Diseases. 2014; 73:536-43.
 78. Koutruba N, Emer J, Lebwohl M. Review of Ustekinumab, An Interleukin-12 and Interleukin-23 Inhibitor used for the Treatment of Plaque Psoriasis. Therapeutics and Clinical Risk Management. 2010; 6:123.
 79. Roberts JL, Ortonne J-P, Tan JK, Jaracz E, Frankel E, Group ACS. The Safety Profile and Sustained Remission Associated with Response to Multiple Courses of Intramuscular Alefacept for Treatment of Chronic Plaque Psoriasis. Journal of the American Academy of Dermatology. 2010; 62:968-78.
 80. Krueger GG, Papp KA, Stough DB, Loven KH, Gulliver WP, Ellis CN, *et al.*, A Randomized, Double-Blind, Placebo-Controlled Phase III Study Evaluating Efficacy and Tolerability of 2 Courses of Alefacept in Patients with Chronic Plaque Psoriasis. Journal of the American Academy of Dermatology. 2002; 47:821-33.
 81. Bos J, Hagenars C, Das P, Krieg S, Voorn W, Kapsenberg M. Predominance of "Memory" T Cells (CD4+, CDw29+) over "Naive" T cells (CD4+, CD45R+) in both Normal and Diseased Human skin. Archives of Dermatological Research. 1989; 281:24-30.
 82. Ekor M. The Growing use of Herbal Medicines: Issues Relating to Adverse Reactions and Challenges in Monitoring Safety. Frontiers in Pharmacology. 2013; 4:177.
 83. Syed TA, Ahmad SA, Holt AH, Ahmad SA, Ahmad SH, Afzal M. Management of Psoriasis with Aloe vera extract in a Hydrophilic Cream: A Placebo-Controlled, Double-Blind Study. Tropical Medicine & International Health. 1996; 1:505-9.
 84. Davis R, Parker W, Samson R, Murdoch D. Isolation of a Stimulatory System in an Aloe Extract. Journal of the American Pediatric Medical Association. 1991; 81:473-8.
 85. Tabassum N, Hamdani M. Plants used to Treat Skin Diseases. Pharmacognosy Reviews. 2014; 8:52-60.
 86. Shams-Ghahfarokhi M, Shokoohamiri M-R, Amirrajab N, Moghadasi B, Ghajari A, Zeini F, *et al.*, *In vitro* Antifungal Activities of Allium cepa, Allium sativum and Ketoconazole Against some Pathogenic Yeasts and Dermatophytes. Fitoterapia. 2006; 77:321-3.
 87. Das I, Saha T. Effect of Garlic on Lipid Peroxidation and Antioxidation Enzymes in DMBA-Induced Skin Carcinoma. Nutrition. 2009; 25:459-71.
 88. Rao SG UA, Udupa SL, Rao PGM, Rao G, Kulkarni Calendula and Hypericum: Two Homeopathic Drugs Promoting Wound Healing in Rats. Fitoterapia. 1991; 62:508-10.