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Effect of Curcumin in Psoriasis

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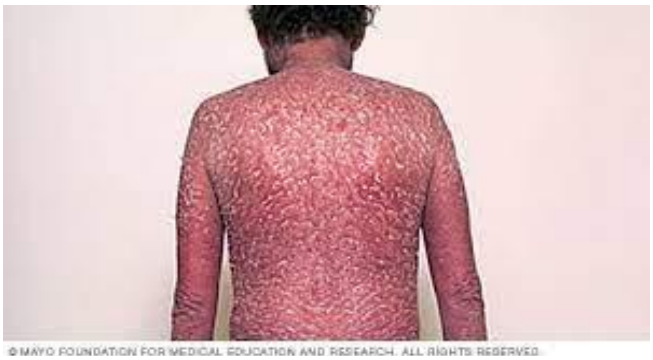
Abstract: ***Psoriasis it is a chronic autoimmune & inflammatory non communicable disease. it is usually highly expressed as inflamed red erythematous plaques which is supported by silvery scales. The presence of these scaly patches is an outcome of the unusual proliferation of excessive epidermis, incomplete cornification and preservation of nuclei in cells of statum corneum. The mechanism of action by which curcumin shows as anti-inflammatory response of TNF-stimulated human endothelial cells by interfering with NF-kB. Furthermore, the curcumin is also capable of preventing the platelet-derived growth factor. Curcumin is also to suppress the excessive production of TNF-α by activated macrophages the curcumin has been shown to directly bind to the receptor-binding sites of TNF-α by covalent and non-covalent interactions, blocking the subsequent TNF-dependent activation of NF-k.***

Keywords: Psoriasis, Curcumin, Pathogenesis, Plague, Guttate, Inverse, Pustular, Erythrodermic, Koebner

Psoriasis it is a chronic autoimmune & inflammatory non communicable disease comes from a Greek word “Psora”- means being itchy & “Iasis” means a condition. The disease has a prevalence of world-wide 2%, with a higher prevalence of about 4-6% in developed countries.

The disease is usually highly expressed as inflamed red erythematous plaques which is supported by silvery scales. The presence of these scaly patches is an outcome of the unusual proliferation of excessive epidermis, incomplete cornification and preservation of nuclei in cells of stratum corneum, unlike normal skin. Some Histopathological features are observed in the psoriatic skin includes hyperplasia of epidermis with a significant differentiation of keratinocyte, presence of prominent inflammatory infiltrate, increased angiogenesis. Psoriasis etiology is multi-factorial with an amalgamation of hereditary factor (family background) and environmental factor (alcohol, contagion, drugs, stress) triggering the immuno-histological changes observed in the skin. These areas are red, purple, or pink, itchy, dry and scaly. It varies in severity from small, localized patches to complete body coverage. Injury to the skin can also trigger the psoriatic skin changes at that spot, which is called as the Koebner.



Types:

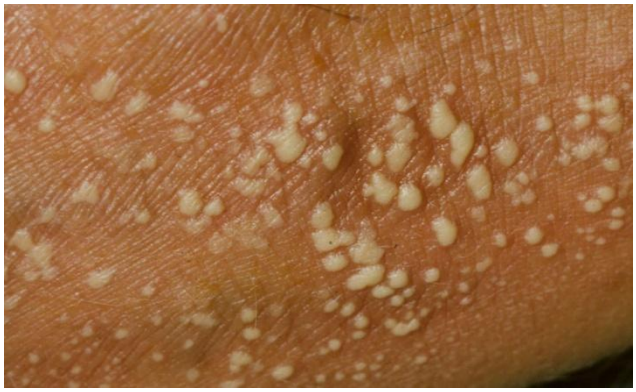
The five main types of psoriasis are
1) Plauge psoriasis (Psoriasis vulgaris)
2) Guttate psoriasis
3) Inverse psoriasis
4) Pustular psoriasis
5) Erythrodermic psoriasis

1) Plauge psoriasis or Psoriasis vulgaris:

The most frequently seen clinical form of psoriasis, is Psoriasis vulgaris, it constitutes nearly about 90% of cases. Clinically it is observed as a erythematous plaques with a sharp boundaries, covered with pearlescent squamae. Lesion demonstrate it is symmetric distribution, and they are most frequently localized on Knees, scalp, elbows and sacral region. Predilection for these lesions may be a result of traumatic incident. (1, 2) If the surface of psoriatic plaque is scraped with a blunt scalpel, squamae fall off as layers of white lamellae that exhibit coherence after removal, much like candle wax. This desquamation is called as “wax sport phenomenon.” It is a sign of the parakeratotic hyperkeratosis. If further psoriatic plaque is scrapped, a wet layer adhered to the lesion it can be revealed. This is the last layer of the dermal papillae of the epidermis, and it is a pathognomonic sign of psoriasis, known as “last membrane phenomenon.” Further scrapping of the plaque, it reveals erythematous background and bleeding foci which is appearance of small red pinpoints known as “Auspitz sign, ” signifying papillomatosis on tips of dermal papillae. Around healed psoriatic plaques, a hypopigmented macular ring can be observed, it is called as “Woronof ring”. (1, 2, 3) The pathogenesis of this ring has not been fully understand, that’s why it is thought to be related to decreasing levels of prostaglandin in healing lesions. (4)

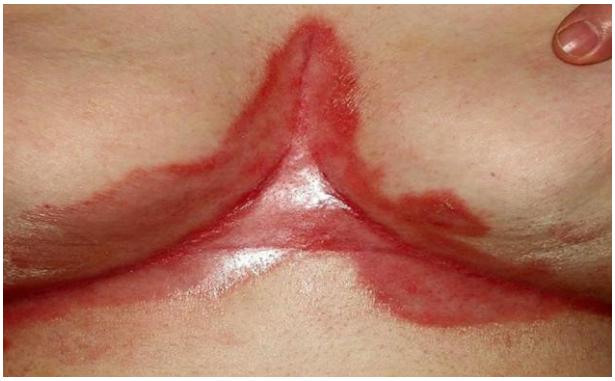
2) Guttate psoriasis

This type of psoriasis that is frequently seen in children and young adults. Lesions onset suddenly with an appearance like small droplet, and less frequently as squamous psoriatic papules, itmanifesting after streptococcal infections. This form of psoriasis is most frequently associated with HLA-Cw6 gene. Often elevated the titers of antistreptolys, With regression of the infection, lesions generally disappear spontaneously. Lesionsare mostly seen on the regions of trunk, proximal part of extremitiese, scalp, and face. They regress within 3-4 months. Sometimes these lesions are enlarge and take the shape of Psoriatic plaque. (5)



3) Inverse psoriasis

Psoriasis that is located generally in skinfolds is termed as inverse psoriasis or flexural psoriasis. Squamous lesions do not form due to friction and moisture in the skin folds. Lesions manifest as a bright red, infiltrative, symmetric, fissured plaques with distinct controus. Fissured plaques with sharp contours these are diagnostic for this form of psoriasis. It is more frequently observed in obese individuals, and there is tendency to develop seborrheic lesion. This form of psoriasis is generally more resistant to classical treatments. (6)

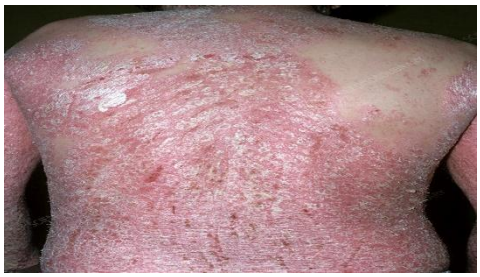


4) Generalized pustular psoriasis

This form of psoriasis is a rarely seen, that progress with pustules. it is most frequently seen in young individuals. It can also develop independently or as a complication of psoriasis vulgaris, such as secondary to abrupt withdrawal of systemic steroid treatment, intervening triggering factors, hypocalcaemia, or irritant treatment. It onsets or occur suddenly on an erythematous background in association with general symptoms, such as high fever, Iassitude, and polyarthralgia. Increase in sedimentation rate, lymphopenia leukocytosis, and negative nitrogen balance can been seen. These Pustules are dry within a few days and followed by eruption of new pustules. Peripustular erythema has tendency to disseminate, and thus it can result in condition of erythrodermia. It should be promptly treated. If disseminated form is not treated, the acute phase may lead to a fatal course. (6, 7, 8)

5) Erythrodermic psoriasis

Psoriatic lesions affect nearly about 80% of the body surface in this generalized form of psoriasis. Predominantly erythematous lesions are seen, typical papules and plaques lose their characteristics features. Desqumation is not so as distinct. In patients with erythrodermic psoriasis, hypothermia due to wide spread vasodilation can been seen. Desquamation may also lead to protein loss and related systemic problems, such as edema of the lower extremities, and hepatic cardiac and renal failure can occur. In addition, to protective barrier of the skin is impaired, leading to potential development of systemic reactions. Most frequently, it can develop as a complication of psoriasis vulgaris, or it can onset independently as a erythrodermic psoriasis. Nail disorders mat also be very dramatic. Dermatopathic lymphadenopathy and sever pruritus may be observed. In case of erythroderma, presence of small areas of intact skin should be evaluated for psoriatic erythroderma or ptyriasis rubra pilaris (PRP) erythroderma. There is no specific clinical laboratory finding. There is substantial risk of cardiovascular shock or septic shock; therefore, these psoriatic findings should be followed closely. It can also besever, potentially fatal, and treatment-resistant clinical picture. (1, 2, 6)



Pathogenesis

Psoriasis it is a hyperproliferative skin disease with increased rate of epidermal turnover the pathogenesis of psoriasis is inter inked to various celluar mechanisms & the role of T cells, antigen presenting cells (APCS) keratinocytes, langerhanscells, macrophages, natural killer cells; an array of Th-1 type cytokines, as well as certain growth factors like vascular endothelial growth factor (VEGEF); keratinocytes growth factors (KGF), etc; these factors can be suggested to play a key in the pathogenesis of psoriasis. (1) it is an immunologically mediated disese, the activation of T lymphocytes leads to the inflammation in the dermal component & secondary to the inflammatory events there is also the condition of epidermal hyperproliferation (2)

Various mechanisms are hypothesized to be involved in the pathogenesis of psoriasis:

a) T cell function
b) Role of dendritic cell
c) Hyperproiferation of keratinocytes
d) Angiogenesis
e) Cytokine mediators
f) Genetic factors
g) Reduced aptosis
h) Role of oxidants & antioxidants in psoriasis

1) T cell function:-T lymphocytes are consists of a functionally distincit population of helper T cells and cytohytic Tcells. The main function of t cells is to recognize the processed peptide antigen that are attached to protien encodedc by the MHC class-11 genes. Therefore, the activation of T cells needs Apsc to process present peptide fragments on the Apc cell surface. The T cells secondary function is to secrate various lymphokinetics that's why T cells also inhibit immune responces in this role, these are known as suppress T cells. Distintic cell membrane, these protiens are expressed by different populations of T cells. CD4 positivity is shown by most of the helper T cells while cytolytic and supressor cells are called as CD8 positive. Activation of T cells requries three steps. (9)

- Binding
- Antigen-specific activation (signal 1)
- Non-antigenic-specific cell-cell-interaction (signal 2)

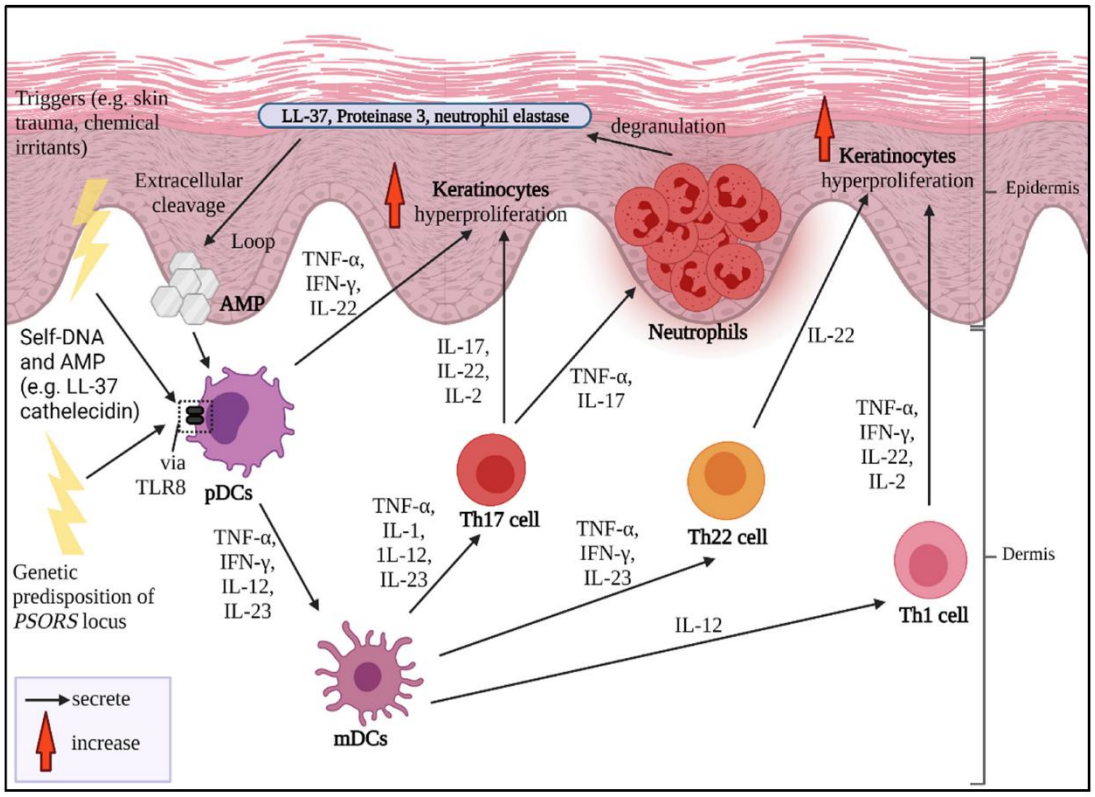
2) **Role of dendritic cells**:-It serve as a major class of antigen presenting cells found in increased abumdance in psoriatic skin lesions. (10) Langerhans cells are a type of immature dendric cell (iDC) found in normal epidermis and can also be found in psoriatic lesion. (11) iDCs are derived from blood monocytes or other myeloid precursors and these cellsv have a immunostimulatory role. These iDCs are further stimulated to become a mature DCs (mDCs). Psoriatic lesions show a marked increase in dermal DCs. XIIIa and CD11c are expressed by myeloid DCs or iDCs, and CD83 and DC-LAMP protiens are positive for Mdc.

3) **Hyperproliferation of keratinocytes**:-The skin provides a protective mechanism through its a multilayerd structure. The epidermis consists of five layers, which is stratum basale, statum spinosum, stratum granulosum, stratum lucidum, and statum corneum. Mainly the cells of keratinocytes are formed in the stratum basale and further they migrate towards the statum corneum. These cells moves towards the surface, their organells disapper and are filled with keratin. The topmost layer of keratin provides a protective feature. in normal condition the epidermal cell cycle is completed in about four weeks. But in psoriatic skin, the epidermal cell cycle is accelerated. Cell division in the baasal layer occurs every 1.5 days, and the migration of keratinocytes to the stratum corneum occurs within approximately 4 days. This results in hyperproliferation of keratinocytes.

4) **Angiogenesis**:-Keratinocytes that are produce proangiogenic cytokines (VEGF, IL-8), but the precise mechanism for angiogenesis in psoriasis is still unknown. In psoriasis condition the endothelial cells swell and become activated these activated endothelial cells migrates, sprout, and lay down a basment membrane with pericytes for structural support to form novel vessel networks. (12) This results in widening of the intercellular spaces, and hence, dermal blood vessels dilate thus making it easier for leukocytes to migrate into the skin. (13)

5) **Cytokine mediators**: In psoriais, the production of cytokines result in epidermal hyperproliferation, vascular dilation, and dermal inflammation. The cytokines involved in the developed of psoriasis include the granulocyte-macrophage colony stimulating factor (GMCSF), epidermal growth factor (EGF), IL-8, IL-12, IL-1, IL-6, IL-γ, and TNF-α. These cytokines result in keratinocyte proliferation, neutrophil migration of Th 1 type of response, angiogenesis, upregulation of adhesion molecules, and epidermal hyperplasia

6) **Reduced aptosis:-**In order to maintain a constant thickness of the epidermis layer the proliferation of keratinocytes in normal epidermis is regulated by the apoptptic cell death. The epidermal hyperplasia characterstic of psoriasis is suggested to be due to P53 overexpression and these proliferating cells typically express Bcl-2 that protects them against apoptic stimuli, while differentiated cells lose the Bcl-2 expression. (14)



Signs and symptoms: The signs and symptoms of psoriasis can vary depending on the type of psoriasis you have. The 5 most common symptoms of psoriasis include:

- Rashes or patches of red, inflammed skin, often coverd with loose, silver-colored scales; in sever cases, the plaques will grown and merge into one another, covering large areas.
- Itchy, painfull skin that can crack or bleed
- Small areas of bleeding where the involved skin is scratched
- Problems with your fingernails and toenalis, including discoloration and pitting; the nails may also beign to crumble or detach from the nail bed.
- Scaly plaques on the scalp

Psoriasis is an immune system problem. Certain triggers may make your symptoms worse, including/ risk factors:-

a) **Stress**:-Keep calm and try to stay relaed. Outbreaks are more likely to pop up when you are anxious
b) **Cold, dry weather**:-Any climate that relives dry skin will help. Try to spend sometime in wa. rm sunny weather and high humidity.
c) **Some medicines**:-Tese include some " beta-b; locker" drugs used to treat high blood pressure and heart disease; lithium, a treatment for bipolar disorder; and pills taken to treat malaria.
d) **Infection**:-There is a short list of infections including step throat and tonsillits that can triggers a special kind of psoriasis outbreak. It looks like small drops that shown up mainly on your torso and limbs. HIV infection can also make it worse.
e) **Skin injury**:-In some people, the tiniest cuts, bruises, and burns can cause an outbreak. Even tattoos and bug bites might trigger a new lesion.
f) **Alcohol**:-Drinkig, especially heavy drinking in young men, many trigger or worsen symptoms and interfere with treatments. Combing certain psoriasis medications with alcohol can have dangerous side effects, especially for women in their child bearing years.
g) **Smoking**:-Uing tobacco or bearing around second hand smoke raises your risk of getting psoriasis and makes existing conditions worse. (15)

Turmeric History

The exact origin of turmeric is not known. Ayurveda is an ancient Indian system of natural healing that is still practiced today. Ayurveda translates to "science of life"- ayur meaning "life" and Veda meaning "science or knowledge".

Since ancient times, inhaling fumes from burning of turmeric is used to reduce congestion. Turmeric juice was used to heal wounds. Also turmeric paste was applied to all sorts of skin conditions like smallpox and chicken pox, blemishes and shingles. Ayurvedic literature contains over 100 different terms for turmeric, including jayanti, meaning "one who is victorious over diseases, " and matrimanika, meaning "as beautiful as moonlight." It has always been considered an auspicious material in the subcontinent, both amongst the Aryan cultures and the Dravidian cultures and its value may extend far in history to the beliefs of ancient indigenous peoples. Turmeric's common name in the north is haldi which derives its name from the Sanskrit word haridra, and in the south it is called manjal, a word that is frequently used in ancient Tamil literature.

Turmeric has a long history of medicinal use in South Asia and is cited in Sanskrit medical treatises and widely used in Ayurvedic and Unani systems. Susruta's Ayurvedic compendium, dating to 250 B. C., recommends an ointment containing turmeric to relieve the effects of poisoned food.

Turmeric has a special place in Indian tradition and worship too. It is used to worship Sun God. It was used to worship the Sun during the solar period of India. It was mentioned in the Artharveda of India. It is also worn by people as a part of purification process. The usage of turmeric in India is documented in various forms. Turmeric was also used by Buddhists. Buddhists monks travelled to various parts of the world to dye their robes. There are also evidences that turmeric was used as a part of Chinese medicine around 1, 000 years ago. In China it was mentioned in the Pent-Sao of the 7th century. Turmeric was not part of western world till recently. There have been only a few evidences stating its usage and importance in Europe. While turmeric has always been an important part of Ayurvedic system, western herbalist did not recognize its benefits till late 20th century.

Turmeric has been used for 4000y to treat a variety of conditions. Studies show that turmeric may help fight infections & some cancers, reduced inflammation and treat digestive problems. Turmeric has been used in both ayurvedic and Chinese medicine as an anti-inflammatory, to treat digestive & liver problems, skin disease and wounds.

Curcumin is a powerful anti oxidant. Antioxidant scavenge molecules in the body known as free radicals, which damage cell membranes, tamper with DNA and even cause cell death. Antioxidants can fight free radicals and may reduce (or) even help prevent some of the damage they cause.

Curcumin lowers the levels of two enzymes in the body that cause inflammation it also stops platelets from clumping together to form blood clots. (16, 17, 18)

Plant Profile

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Monocots
Clade	Commelinids
Order	Zingiberals
Family	Zingiberaceace
Genus	Curcuma
Species	C. longa

Distribution: Andhra Pradesh, Tamil nadu, Orissa, Karnataka, West Bengal, Gujarat. (19)

Description: An upright herb with large, oblong leaves that are dark green on the upper surface and pale green underneath its pink -white flowers grow on a spike-like stalk and have small, brown seeds. Turmeric only produces via its underground stem (rhizomes) which is thick and ringed with the bases of old leaves

Uses

Anti-inflammatory
Anti-carcinogenic
Anti-oxidant
Antimutagenic
Antidiabetic
Antimicrobial

Composition of Turmeric

More than 100 components have been isolated from turmeric. The main component of turmeric the root is a volatile oil, containing turmerone, and other coloring agents called curcuminoids in turmeric. Curcuminoids consist of curcumin demethoxycurcumin, 5'-methoxycurcumin, and dihydrocurcumin, which are found to be natural antioxidants (20). In a standard form, turmeric contains moisturecontent (>9%), curcumin (5-6.6%), extraneous matter is (<0.5% by weight), mould (<3%), and volatile oils (<3.5%). Volatile oils include d-α-phellandrene, d-sabinene, cinol, borneol, zingiberene, and sesquiterpenes (21). There are a variety of sesquiterpenes, like germacrone; termerone; ar-(+)-, α-, and β-termerones; β-bisabolene; α-curcumene; zingiberene; β-sesquiphellanderene; bisacurone; curcumenone; dehydrocurdione; procurcumadiol; bis-acumol; curcumenol; isoprocurcumenol; epiprocurcumenol; procurcumenol; zedoaronediol; and curlone, many of which are specific for a species. The components responsible for the aroma of turmeric are turmerone, arturmerone, and zingiberene. The rhizomes are also reported to contain four new polysaccharides-ukonans along with stigmasterole, β-sitosterole, and cholesterol, and 2-hydroxymethyl anthraquinone (22). Nutritional analysisare also showed that 100 g of turmeric contains 390 kcal, 10 g total fat, 3 g saturated fat, 0 mg cholesterol, 0.2 g calcium, 0.26 g phosphorous, 10 mg sodium, 2500 mg potassium, 47.5 mg iron, 0.9 mg thiamine, 0.19 mg riboflavin, 4.8 mg niacin, 50 mg ascorbic acid, 69.9 g total carbohydrates, 21 g dietary fibre, 3 g sugars, and 8 g protein (23). Turmeric is also a good source of ω-3 fatty acid and α-linolenic acid (2.5%; 24.)

Mechanism of action of curcumin in psoriasis:-

1) The mechanism of action by which curcumin showsas anti-inflammatory response of TNF-stimulated human endothelial cells by interfering with NF-kB. Furthermore, the curcumin is also capable of preventingthe platelet-derived growth factor.
2) Curcumin is also to suppress the excessive production of TNF-α by activated macrophagesthe curcumin has been shown to directly bind to the receptor-binding sites of TNF-α by covalent and non-covalent interactions, blocking the subsequent TNF-dependent activation of NF-k.

3) As a phosphorylase kinase inhibitor, the curcumin exhibitsas anti-oxidant, anti-inflammatory, anti-microbial and anti-carcinogenic activities (25). Molecular and cellular pharmacological research on curcumin has shown that it has inhibitory effects on NF-κB, MAPK, and cytokines (26, 27). For example, it down-regulated the expression of various proinflammatory cytokines (TNF-a, IL-2, IL-1, IL-6, IL-8, and IL-12) by inactivatingthe NF-κB (28, 29). Curcumin also suppresses the phosphorylation and nuclear translocation of signal transducers and activators of various transcription (STATs), including STAT3, STAT1, and STAT4 [12]-14. It is thus possible that curcumin inhibits cytokines, NF-κB and the activation STAT3, which contribute to inflammation and keratinocyte proliferation in psoriasis. All of the above information suggests that curcumin is very potential value for the treatment of psoriasis.

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