A BETTER INSIGHT INTO PSORIASIS AND *SOLANUM XANTHOCARPUM* AS AN ANTI-PSORIATIC AGENT

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Abstract:
Psoriasis is an autoimmune disorder that manifests itself through keratinocyte proliferation. On average, it affects 2-5% of the world's population. The treatments available for psoriasis are not effective much and are very much task taking and challenging, while some treatment leaves with unwanted adverse effects. So herbal treatments getting a preferable choice of therapy nowadays. The plant kingdom is a potential source of chemical components with a wide range of pharmacological actions because of plants' tremendous propensities to synthesize a variety of bioactive chemicals with different structural properties. For this reason, a large number of phytopharmaceutical medicines are undergoing psoriasis testing. This review shows an update on the information on psoriasis and the treatment of psoriasis using *Solanum xanthocarpum*. Finally, we provide a thorough analysis of widely used, well-established medicines and information on their limitations and new developments in innovative, targeted medications for psoriasis. Additionally, this allows researchers to study the effectiveness of *Solanum xanthocarpum* in treating psoriasis in the future.

Keywords: Psoriasis, *Solanum xanthocarpum*, pathophysiology, recent developments.

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1. Introduction:

Psoriasis is an ongoing provocative cutaneous infection described by the development of layered, indurated, erythematous plaques. Psoriasis has three important histologic features: epidermal hyperplasia; expanded, noticeable veins in the dermis; and a provocative penetration of leucocytes, overwhelmingly into the dermis. Not just restricted to the skin, psoriasis likewise influences joints and nails. Psoriasis is for the most part separated into five clinical classifications: plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, and psoriatic joint inflammation(1).

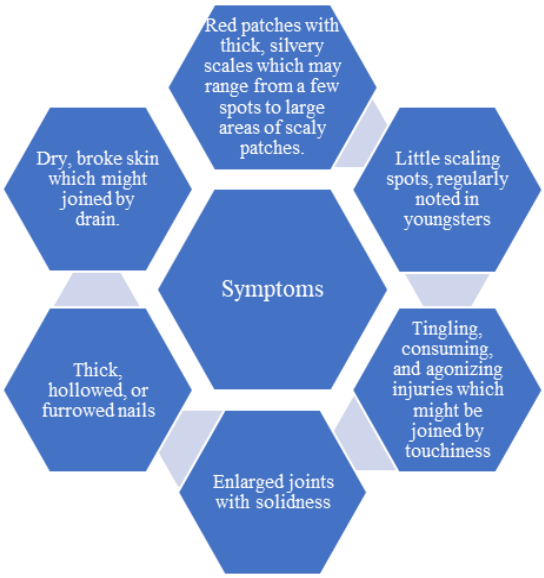

Figure.1 (Symptoms of Psoriasis which varies from person to person)

1.1. Clinical Classification:

Psoriasis is divided into six major types based on the body part affected by the disease with the internal and external appearance of affected regions. Those are explained below as Psoriasis Vulgaris, Inverse psoriasis, Guttate psoriasis, Pustular psoriasis, psoriatic joint inflammation, and Erythrodermic psoriasis (2–7).

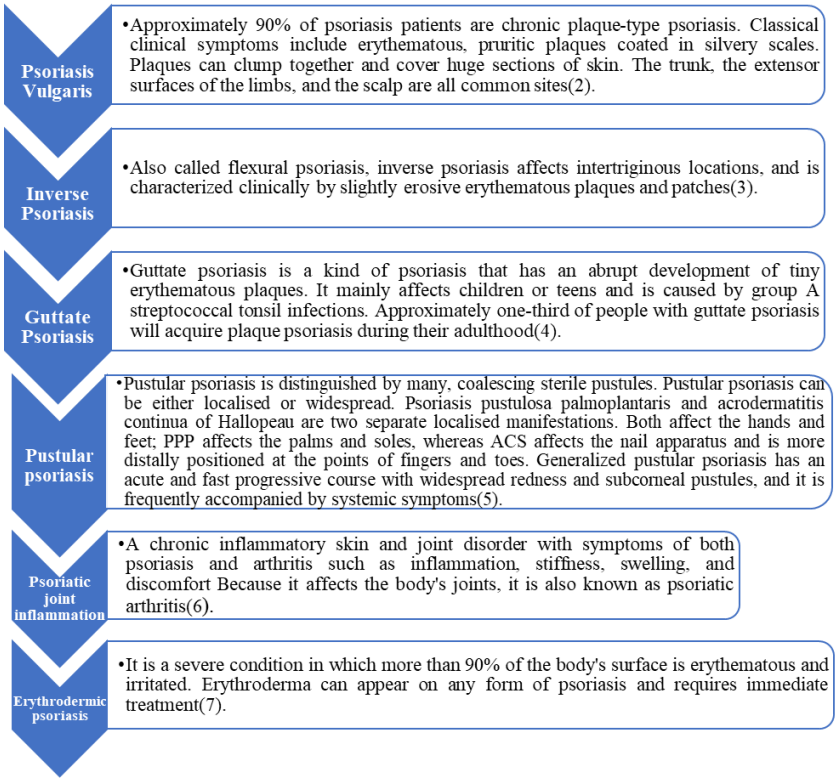

Figure.2 (clinical classification of Psoriasis which explains about psoriasis vulgaris, inverse psoriasis,

guttate psoriasis, pustular psoriasis, psoriatic joint inflammation, erythrodermic psoriasis.)

1.2. Pathophysiology of psoriasis and its mechanism of action:

Psoriasis is a cell-mediated inflammatory skin illness that is treatment resistant. Toll-like receptors and cytokines such as interferon INF-α, TNFα, IFN7, and IL12,22,23,17 are related to the pathogenesis of psoriasis. IL23/IL17 have a critical role in the progression of psoriasis. In the pathogenesis of psoriasis, antimicrobial peptides, dendritic cells, growth factor (TNF-α), IL23, Th17, IL17, IL22, and signal transducer and activator of transcription (STAT)3 all play a part(1,8–12).

a. Role of Antimicrobial peptides (AMPs): AMPs contain a positive charge and an amphipathic design and are composed of 12-50 amino acids. They contribute to security by killing dangerous germs such as bacteria, protozoa, parasites, and illnesses. AMPs alter vertebrate responses by serving as chemotactic specialists, angiogenic components, and cell proliferation regulators. In psoriasis, keratinocytes, neutrophils, and macrophages interact and eject certain AMPs, such as -defensins, S100 proteins, and cathelicidin, in response to injury and cytokine stimulation. Defensins are cationic microbicidal peptides that come in three varieties: defensins, and. Human neutrophil peptides (HNPs) 1-6 are subtypes of the -defensins, with HNPs 1-3 accessible in psoriatic sore sizes. Human -defensins (hBDs) 1-4 are four different types of -defensins that have been discovered(13–15). In contrast to IL17A and IL22, which promote hBDs 2 in keratinocytes, TNF and IFN7 boosts hBDs 2 and 3, which are present in psoriatic scales, respectively. It is unclear what function defensins play in the pathophysiology of psoriasis(16,17). A low molecular weight protein subclass called S100 proteins (9-13 kDa). Psoriasis mostly expresses S100A7 (psoriasin), S100A8 (calgranulin A), S100A9 (calgranul B), S100A12 (calgranul C), and S100A15. The synthesis of β-defensin 2, S100A9, S100A7, and S100A8 was induced by the interactions of IL22, IL17A, IL17F, and keratinocytes. S100A7 (psoriasin), a potent and specialised chemotactic fiery protein for T cells and neutrophils, is present in psoriasis. The C-terminal peptide of hCAP18 is used to make cathelicidin LL37 (18,19). Plasmacytoid DCs (pDCs), which TLR9 uses to identify self-DNA, are primarily responsible for pDC activation in psoriasis. In addition, keratinocytes release type I IFN when exposed to LL37 and self-DNA, which has been linked to the progression of psoriasis. TLR7 is activated by LL37-RNA structures, but TLR8 is activated by LL37-RNA structures in pDCs. When started mDCs move toward deficient lymph hubs, and they produce TNF, IL23, and IL12. TNF, IL23, and IL12 are also produced by Slan+ monocytes in response to LL37-RNA activation. Individually, IL23 and IL12 induce the differentiation of normal T cells into Th17 and Th1 cell subsets(20,21). (Figure.3)

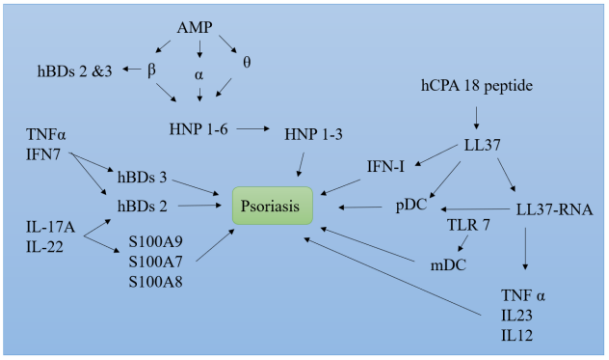

Figure.3 (the pathogenesis of psoriasis followed by AMPs mechanism of action)

b. Role of A Disintegrin and Metalloprotease Domain Containing Thrombospondin Type 1 Motif-Like 5 (ADAMTSL5): An autoantigen has been identified as ADAMTSL5, a protein present in melanocytes. In the presence of HLA-C*06:02, intraepidermal CD8 T cells identify ADAMTSL5 on melanocytes. Keratinocytes generate ADAMTSL5 in association with IL17 activation, and CXCL1, a neutrophil chemotactic and melanocyte transcription factor, promotes ADAMTSL5 production (22). Melanocytes become more prevalent in psoriasis, and T lymphocytes—in particular, cytotoxic T cells—co-regulate them. Since melanocytes in psoriasis do not exhibit signs of cell death, it is hypothesised that they are rational targeting of such non-cytotoxic CD8+ T cell-intervened innate immunity. The ADAMTSL5 articulation design is comparable to LL37 in that it mimics T-cell penetration and DC accumulation in the superficial dermis in psoriasis. In psoriasis, IL17 or TNF blocker medication greatly reduces the outflow of ADAMTSL5 and LL37 with DCs, neutrophils, macrophages, and T cells(23). This suggests that HLA-class II particles communicate on the upper shell of allergen cells inside dermis lymphoid tissue constructs to deliver ADAMTSL5 and LL37 towards autoreactive CD4+ T cells plus HLA-Cw6*02 to CD8+ T cells(24)(25). (Figure.4)

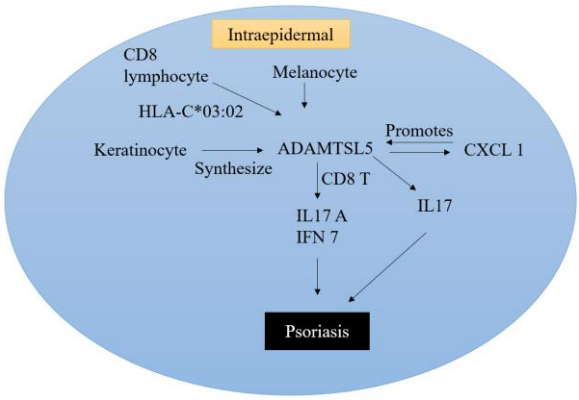

Figure.4 (psoriasis pathogenesis by ADAMTSL5 mechanical pathway)

c. Role of Dendritic cells (DCs): The skin has a mind-boggling variety of DCs, the majority of which are epidermal Langerhans cells (LCs), bone-marrow-derived cutaneous regular DCs (cDCs), pDCs, incendiary DCs (iDCs). DCs have a crucial role in psoriasis since they are a clear source of IFN, TNF, IL12, and IL23. Under pathologic settings, pDCs begin in the bone marrow and move to the skin. Because of intracellularly Toll-like receptors (TLRs) including TLR7 and 9, pDCs recognise viral nucleic acids and therefore generate a significant number of class I IFNs(24). Incorrect self-nucleic acid recognition by pDCs results in IFN delivery and the initiation of psoriatic aggravation. AMPs such as LL37, hBD 2, hBD3, and lysozyme can aggregate self-DNA or RNA into particles that are endocytosed by pDCs, activating TLR7, 8, and 9. IFN was indeed thought to act like an intermediate cytokine all along pivoting between IL23 and IL17 during psoriatic aggravation. IFN stimulates the production of IL12, IL15, IL18, and IL23 by young cDCs. IFN also attaches CD4+ T cells either to Th1 as well as Th17 cells and quickens the transformation of human monocytes becoming iDCs. In addition, IFN increases IL22 responsiveness in epidermal keratinocytes by enhancing IL22 receptor articulation. Under normal conditions, cDCs are also related to immune system T cell consumption, communication of calming cytokines and inhibitory receptors such as IL10, transforming growth factor (TGF), and IL27, and establishing administrative T cell homeostasis (Tregs)(26,27). The deregulation of this resistance component has been linked to several immune system disorders, including psoriasis. -melanocyte-stimulating chemical alleviates psoriasis by boosting tolerogenic DCs and decreasing human and murine Th17 cell proliferation and cytokine generation. Cytokines such as IL6, TNF, IFN, and LL37-RNA structures activate cDCs. When activated, cDCs release a plethora of pro-inflammatory cytokines, including IL12 and IL23, both of which are critical in the development of psoriasis(28,29). iDCs are assumed to be produced from monocytes and can attract T cells to Th1, Th2, and Th17 cells as well as release cytokines including IL1, IL6, TNF, IL12, IL22, and IL23. In psoriasis, TNF and iNOS-delivering DCs (Tip-DCs) and 6-sulfo LacNAc DCs (slanDCs) are accounted for as iDCs, and they activate T cells to release IL17, IL22, TNF, and IFN7. Additionally, upon TLR7/8 activation in vitro, LCs had a higher limit for releasing IL23 in comparison to sonic labourers, and they are intimately connected to T cells in patients that experienced a virtually full decrease after TNF antagonist therapy. This suggests that LCs may be linked to the recurrence of psoriasis, albeit to a lesser extent than moderate-stage psoriasis(30,31). (Figure.5)

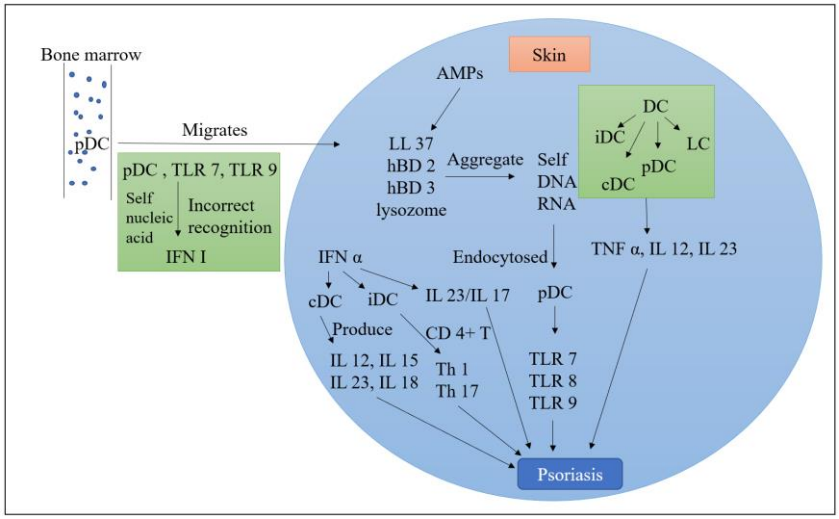

Figure.5 (crucial mechanism of DCs in the pathogenesis of psoriasis)

d. Role of IL23/IL17 Axis: Th17, Tc17, natural lymphoid cells, and 7T cells in the skin produce IL17. IL17 is produced in response to IL23 communication via dermal DCs. IL17, as well as TNF, IL26, and IL29 (IFN1), are released under clear conditions, such as psoriasis autoantigens and also specific natural upgrades (e.g., injury or disease). These cytokine signals activate CCAAT enhancer-restricting protein (C/EBP) or, STAT1, and atomic element kB, causing a feed-forward fiery reaction in keratinocytes. This feed-forward effect hastens the progression of psoriasis(32). TNF and IL17 collaborate to enhance the IL17-initiated record of a few proinflammatory characteristics (e.g., TNF, IL1, IL6, and IL8). These enhance the segregation of Th17 in skin cells, the stimulation of mDCs, and the exhaustion of lymphatics. Epidermal hyperplasia is modulated by IL17 by stimulating STAT3, therefore, increasing keratinocytes that generate IL19 and IL36. Moreover, STAT3 is also triggered by IL22, which is primarily generated by Th17 and possibly IL20, and it increases epidermal hyperplasia(33,34). The top dorsal and gritty sections of the epidermal of psoriatic wounds are enlarged, as are keratinocyte-determined responsible for binding, such as S100A7/8/9, hBD2, lipocalin-2, and CCL20, as well as transcription markers that are induced by IL17 (for example, C/EBP or C/EBP). When keratinocytes are activated in psoriasis, CXCL1, CXCL2, CXCL3, CXCL5, and CXCL8 are discharged (i.e., IL8). Keratinocytes are stimulated to produce CCL20 by IL17A, IL22, and TNF. CCL20 draws CCR6+ cells like mDCs and Th17 cells and activates the inflammatory process by creating a favourable chemotactic feedback loop. Angiopoietin-2, platelet-derived growth factors, and vascular endothelial growth factors are produced by psoriasis keratinocytes, leading to erythematous skin lesions (35,36). (Figure.6)

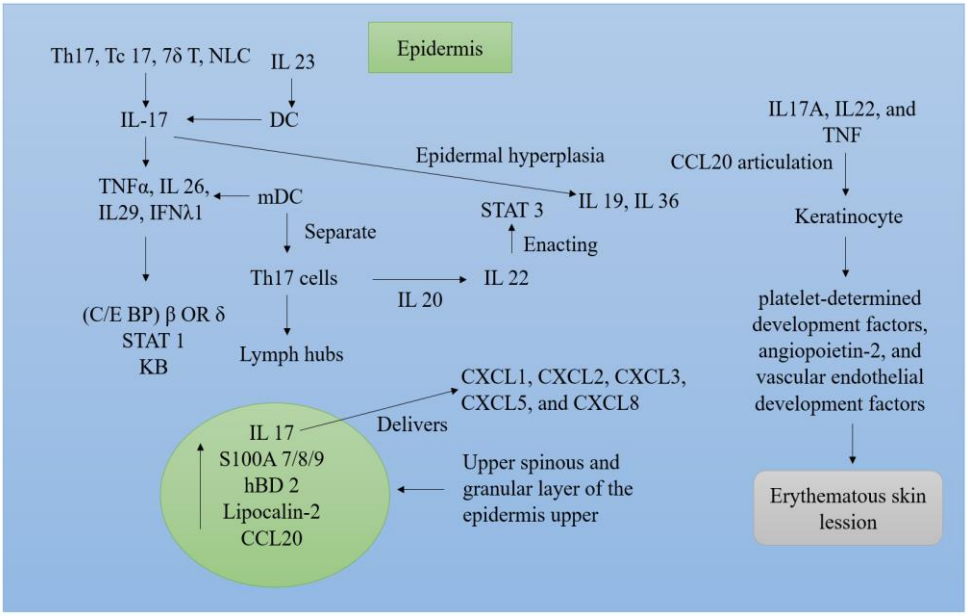

Figure.6 (the pathogenesis mechanism of IL23/IL17 axis involved in psoriasis)

e. Role of Aryl Hydrocarbon Receptor (AhR): Skin cells have high levels of the AhR, a cytoplasmic substituents regulator and record mediator. AhR ligands include both internal and foreign particles as well as dioxins (37,38). The atomic variable erythroid 2-related factor-2 (NRF2) record factor originates oxidative pressure via CYP1A1 and kills oxidative pressure via AhR enactment. Furthermore, AhR regulates the balance of the Th17/22 framework, which is important in the development of psoriasis(39,40). The amount of Th17 cells, the IL-23 receptor, as well as the Th17 ace record factor retinoic corrosive associated vagrant receptor C (RORC) were all decreased by AhR agonists. Similarly to this, AhR in skin vascular endothelial cells (VECs) is crucial for the development of psoriasis(41–43). (Figure.7)

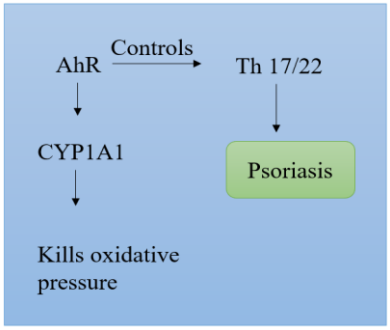

Figure.7 (pathogenesis mechanism of AhR in psoriasis)

Dendritic cells present in the subcutaneous region of the skin produce cytokines like Interleukin-12 (IL-12), Interleukin-23 (IL-23). IL-23 has two subunits i.e, p19 and p40. IL-23 induces the T helper 17 cells (T_H 17 cell), and the DNA protein RORγt present inside the T_H 17 cell makes Interleukin-17 (IL-17). IL-17 gets converted into IL-17A and IL-17F which binds to the receptors IL-17RA and IL-17RF respectively. Also, the IL-17 triggers tumour necrosis factor α (TNF-α), which is produced from T_H1 cells by IL-12, and then this TNF-α binds the TNF receptor (TNFR). These TNFR, IL-17RA, and IL-17RF receptors are present in the cell membrane of a normal cell. After the binding of TNF-α, IL-17A, and IL-17F to TNFR, IL-17RA, and IL-17RF receptors respectively, this causes psoriatic inflammation in the dermis region of the skin(1,44). (Figure.8)

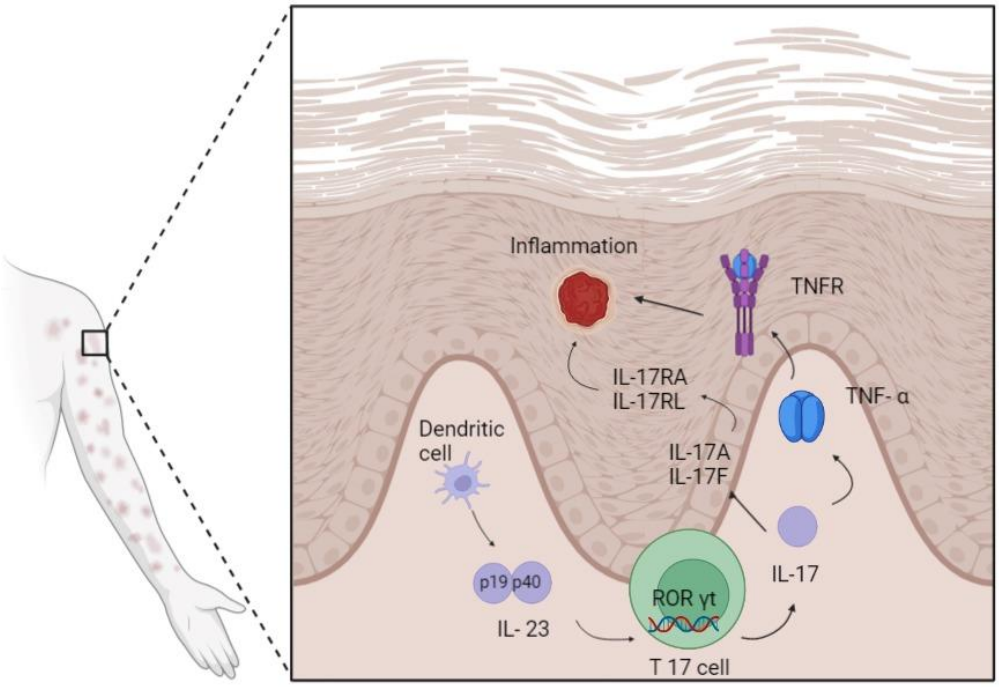

Figure.8 [IL-23: Interleukin 23, T 17: Helper T cell, IL-17: interleukin 17, TNF-α: Tumour necrosis factor α, IL-(17F, 17A, 17RL,17RA): interleukin (17F, 17A, 17RL, 17RA), TNFR: tumour necrosis factor receptor.]

2. Current treatment options for psoriasis:

Currently available oral systemic therapy includes Retinoid, Cyclosporine A, Methotrexate, Apremilast, etc. Currently Available Biological Therapies include: TNFα Inhibitors, IL23 Inhibitors, IL17 Inhibitors, RORγt Inhibitors, IL36 Receptor Antagonist, Janus Kinase (JAK) Inhibitors, Sphingosine-1-Phosphate (S1P) Agonist, Rho-Associated Kinase (ROCK2) Inhibitor, etc.(45–47)

a. Topical treatments have become the most preferred for treating psoriasis. In the present era, it is primarily on calcineurin inhibitors, topical retinoids, topical vitamin D analogues, and topical corticosteroids. Some examples are calcitriol and calcipotriol (or calcipotriene) as vitamin D analogues, tazarotene as a topical retinoid and tacrolimus as a calcineurin inhibitor.

b. When topical therapy is no longer reliable, the size and seriousness of the lesions have developed worse, or the patient is in pain, systemic treatment is required(48). In these cases, methotrexate is the most commonly used systemic agent. Methotrexate has been used in the treatment of psoriasis for over 50 years. It's an analogue of folic acid and its mechanism of action it's based on the competitive inhibition of the dihydrofolate reductase enzyme. Therefore, it's going to inhibit the synthesis of cofactors that are necessary to produce nucleic acids, and consequently, the synthesis of T lymphocytes and keratinocytes is compromised. Initially used as an immunosuppressant to avoid the rejection of transplanted organs, ciclosporin proved to be quite effective as an anti-psoriatic drug. Its effect is due to the inhibition of calcineurin blocking the production of inflammatory cytokines and inhibiting the activation of T lymphocytes. (49,50)

c. It is best to avoid using this medicine concurrently with other medications that are processed by cytochrome P450. Acitretin is the only systemic retinoid approved for the treatment of psoriasis. It's very effective, especially in the erythrodermic and pustular types of psoriasis. Exerts its psoriatic effect by modulation of the differentiation and proliferation of the epidermis. The treatment begins with a lower dosage, and then slowly increases the dose.

d. Acitretin serves as the most widely used treatment for the majority of intense varieties of psoriasis, even though the fact that it should not be for use during pregnancy or in women who are nursing, as it has adverse effects such as xerosis, nail and hair breakage, and that its effectiveness is dose-dependent.

e. Using phototherapy for treating dermatosis is an extremely old procedure(15,51). This consists of controlled and repetitive solar expositions to ultraviolet radiation (UV) through artificial sources, which are absorbed by endogenous chromophores localized in the skin. The radiation used can be UVA or UVB. UVA radiation (320–400 nm), when used in monotherapy, is ineffective but associated with photosensitizing agents, systemic or topic (psoralen) is quite effective, and the treatment is called PUVA (psoralen + UVA radiation). This treatment inhibits cytokine release and minimizes epidermic proliferation. UVB light (290–320 nm) alters cellular processes and has a greater biological impact. Broadly or narrowband beams can be produced, and narrowband beams are thought to be more efficient than UVB broad emitters, producing longer remission times and fewer epidermal responses (fewer treatments result in burns and erythema). To achieve better treatment outcomes and optimum efficacy, these therapies—PUVA and UVB—can be combined with additional topically applied or systemically administered medications.

f. Unfortunately, despite their widespread usage, these treatments have a lot of negative side effects, making it necessary to develop alternative treatments with fewer side effects and better outcomes, such as nanotechnology-based therapies(52,53). Nanotechnology-based appro-aches for treating psoriasis on the skin Nanocarriers, a family of cutting-edge techniques with dimensions under 100 nm, have been taken into consideration for the management of dermatological conditions. The incorporation of nanotechnology has garnered a lot of attention and provides several benefits over traditional formulations. Researchers have cautiously explored many nanocarriers for dermatological uses. The primary benefit of these nano-based formulations is the decrease in side effects brought on by conventional therapies, but they also have improved drug penetration and increased drug release patterns to help patients reach their therapeutic goals(54).

3. Problems with current therapies used for psoriasis:

a. Topical therapy:

Corticosteroids: They are potent medications that reduce inflammation, but their prolonged use is not recommended. They thin the skin and may result in stomach ulcers, weakened bones, and early cataract development. After some time, these drugs could no longer be effective(55).

Vitamin D: Epidermis proliferation is slowed by synthetic vitamin D compounds like calcipotriene and calcitriol. Topical corticosteroids or other medications of this sort may be employed together. In sensitive locations, calcitriol could induce less irritability. The cost of calcitriol and calcitriene is often higher than that of topical corticosteroids(56).
Retinoids: Skin inflammation and heightened photosensitivity are the most frequent adverse effects. For women who are pregnant, nursing mothers, or planning a pregnancy, tazarotene is not recommended(57).

Calcineurin inhibitors: Tacrolimus and pimecrolimus are examples of calcineurin inhibitors that minimise rough development and soothe rashes. These may prove especially beneficial in places with thin skin, such as the area around the eyes, where retinoids or steroid lotions might irritate or injure the skin. The potentially elevated risk of lymphoma and skin cancer makes this medication unsuitable for prolonged usage. Also forbidden for women who are pregnant, nursing, or planning a pregnancy(46).

b. Oral therapy:

Methotrexate: It suppresses inflammation, which might lessen the psoriasis sufferer's puffiness and itching. Prevent psoriatic arthritis-related joint discomfort as well. 20% to 30% of persons usually report an improvement in their psoriasis symptoms. Methotrexate’s potential negative effects include nausea, hair loss, and liver illness. If a person routinely consumes large amounts of alcohol, has liver or renal illness, a stomach ulcer, or any of these conditions, they should not take

methotrexate. Also, it is unsafe for pregnant or nursing mothers. It could make you feel tired, lose your appetite, and have an unsettled stomach. Long-term methotrexate users require regular testing to check their blood levels and liver function(58).

Cyclosporine:
Cyclosporine suppresses the immune system to operate. In addition to headaches, joint discomfort, muscle twitching, excessive hair growth, and elevated blood pressure, persons using cyclosporine may also suffer tingling, paralysis, pins & needles, headaches, and numbness in their skin. Avoid using cyclosporine in case of renal failure, cancer, high blood pressure, attempting to get pregnant, or have ever had kidney failure. Cyclosporine raises the risk of infection and other illnesses, including cancer, just as other immunosuppressive medications. Long-term cyclosporine users require regular testing to check their blood pressure and renal health(46).

Apremilast: It is a focused therapy that diminishes the functioning of an immune cell enzyme that triggers inflammation. Diarrhoea, nausea, headaches, chest infections, anxiety, and losing weight are typical adverse effects of apremilast(46).

c. Light therapy:
The skin regularly gets better with this more intensive therapy, which is frequently recommended for more severe psoriasis. Patients might experience short-term adverse effects such as nausea, headaches, burning, and itching. Dry, wrinkling skin, spots, exposure To ultraviolet hypersensitivity, and an elevated chance of malignancy, including melanoma, are a few potential long-term adverse effects(52).

4. Role of herbal drug treatment and its benefits:
Herbal treatments are being used since ancient days and show appropriate results to date in comparison with conventional therapies in many diseases. Also, these are more affordable than conventional treatment, effective for chronic diseases, and show a synergistic effect in combination with other herbal drugs whereas only fewer have the antagonistic effect, have fewer side effects can stabilize hormones and metabolism process in the body, these are easier to obtain from the nature and also easier to make formulation out of these for use, some of them strengthen the immune system. Herbal treatments showed many positive effects in approaching several kinds of diseases without causing any unwanted effects. Plenty of such responses are shown by herbal treatment, which drags the attention of the research society to research these herbal materials against related diseases and betterment of the medication to enhance the potency of the drug with better treatment of the disease(59).

5. *Solanum xanthocarpum*:
S. xanthocarpum is a herbaceous annual plant with 90 genera and 2000-3000 species. It is indigenous to NE Tropical Africa, the Arabian Peninsula, S. Iran, S. Central China, and Indo-China. The crop is primarily grown in the northern Indian states of Uttar Pradesh, Bihar, Uttaranchal, Punjab, West Bengal, Assam, and others. It grows wild in Manipur and is found across the hills and valleys. It is typically cultivated from March to April and yields fruit from May to June. It grows in many types of soil but thrives in dry and hot temperate climates. Fruits of *S. xanthocarpum* contain solanocarpidine and carpesterol, a sterol. Dasamulasava root is one of its ingredients. Diuretics are made from seeds. Berry juice is said to be beneficial for sore throats. A decoction of the plant is used to treat gonorrhoea, and it is also supposed to help females conceive. *S. xanthocarpum* has been promoted as helpful for Tamakwasa and Kasa Roga (cough) (bronchial asthma). In Chhattisgarh, where it is used alone or in combination with other local and foreign plants to treat over 100 common diseases, it is regarded as a very beneficial plant for healing practices. According to Ayurveda, it is unpleasant, palatable, laxative, anthelmintic, purgative, and helpful for bronchitis, asthmatic, temperature, constipation, pains, piles (particularly bleeding piles), thirst, renal, and cardiac disorders(60)(61).

5.1. Botanical description: Botanical names for this plant include Solanum Xanthocarpum, Solanum surattense, and Solanum virginianum; it is a member of the Solanaceae family and the Magnoliophyta division of the Plantae kingdom; the Magnoliopsida class; and the Solanales order. Common names for it in India include Yellow-Berried Nightshade, Choti Katheri, Kantkari, and Kateli. The fruits, leaves, stems, and entire plant are the parts of this herb that are utilised.

Root	10-45 cm long, just several mm to two centimetres in diameter, nearly cylindrical, with so many perfect beams and so few axial wrinkles, with the incidental scar or a few nodules and small sticky sap. The circumferentially helped smooth surface reveals a slim wood and broad convenient fuel tank of wood, breakage, narrow, and astringency.
Stem	Provides a wide, bristly, with predominant stems and hubs, coloured when completely new, fresh-faced parts encased in many hair strands, fully grown ones coriaceous, squints more pronounced in young stems emerging almost spherical forward towards the distal part, stem parts 8–10 mm thick of different length, outer surface light coloured, when dry, the surface pale yellow colours and soft, circumferentially helped smooth texture reveals a very narrow the bark and prevalent wood, centre demonstrates a massive and distinguishable, pith and cortex.
Leaves	Shape and design, exstipulate, petiolate or elliptical, fragment or comment thread, prolonged hairy, greener, 4-12.5 cm long and 2-7.5 cm broad, full of sharp2 tufts of hair, shallow pith, breakage medium to somewhat fibrous.
Flower	0.5-1.3 cm long, tightly prickle, pedicellate, bisexual, ability to empower, uniform, perfect, vivid blue or bluish violet, fruiting bodies, gamosepalous, tubular small, lobed, regression, acute, The calyx is gamopetalous, with tendon, acute, bristly lobes that are 1-2 cm long and magenta. The inflorescence is five and is epipetalous, basifixed, with fibrils that are short and 1-1.5 cm in length. Perhaps the other is odd shaped and measures 0.7-0.8 cm in length. The ovary is supreme, ovate, orbicular, and bilocular.
Fruit	Underripe fruits are diversified with green and white bands, while ripened fruit displays various yellow and white colours. Berries are circular, 0.8–1 centimetre in diameter, and are encircled by compliance in the process at the base.
Seeds	A succulent, 0.2 cm in diameter, circle, plain, and abundant endosperm contains sterile, unpleasant, and pungent fruit.

Table.1 (Botanical description of *S. xanthocarpum*¸ describes about different plant parts)

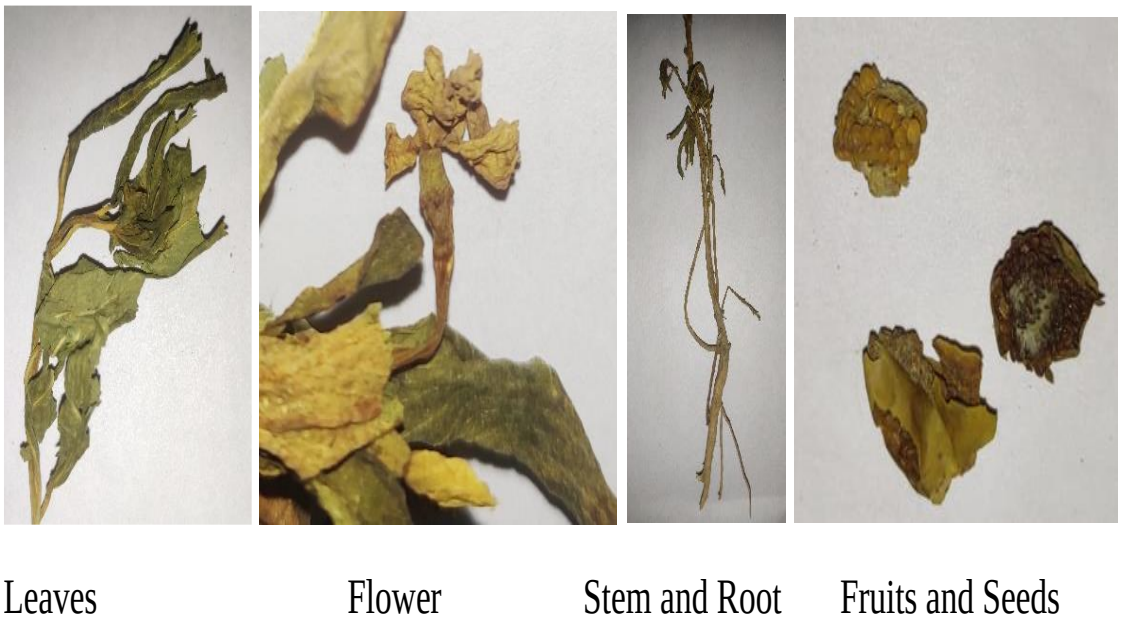

Figure.9 (different plant parts of *S. xanthocarpum*)

5.2. Chemical constituents: Alkaloids, sterols, saponins, flavonoids, and their glycosides are all present in the plant, along with carbohydrates, fatty acids, amino acids, etc. Campesterol, Campesterol, β- sitosterol, cycloartenol, stigmasterol, lupeol, solasodine, diosgenin, tomatidenol, α-solamargine, apigenin, scopoletin, esculatin, coumarin, methyl caffeate, caffeic acid(62). See Figure 8.

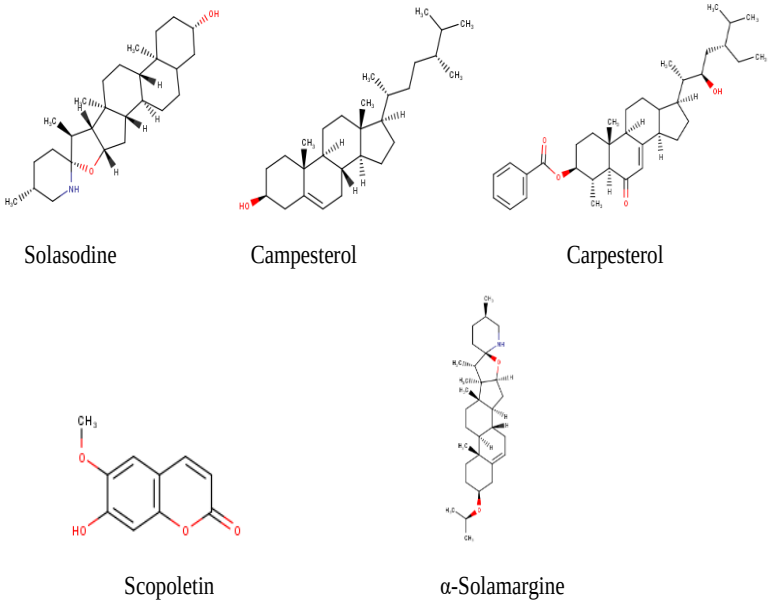

Figure.10 (phytochemical constituents contained by *S. xanthocarpum*

5.3. Clinical uses of *S. xanthocarpum*:

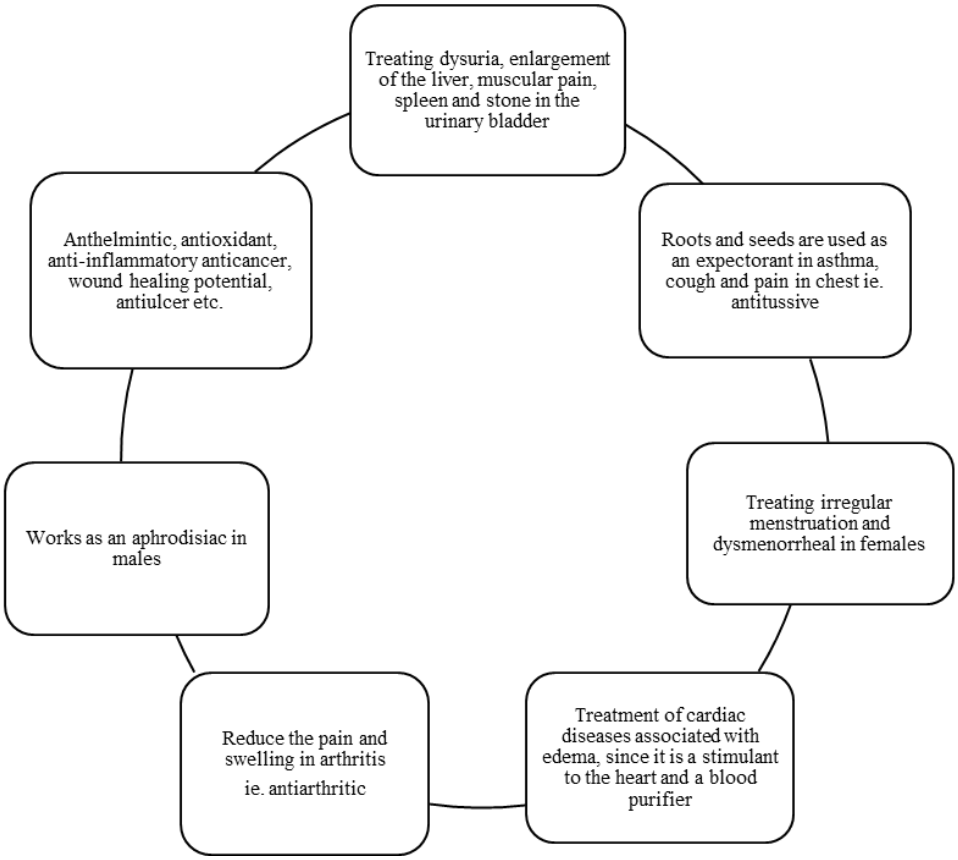

Figure.11 (clinical uses of *S. xanthocarpum*)

5.4. *S. xanthocarpum* in psoriasis:

In addition to curing diseases, synthetic medications have serious adverse implications for human health. On the different side, synthetic therapeutics, which are medicines that do not exist naturally occurring, are created in a laboratory using a variety of approaches. Herbal remedies are thought to be less hazardous as well as having fewer negative effects than synthetic medication, even if they are sometimes less strong than those substances. The most important standards for any medication, whether it is manufactured naturally or artificially, are its potency, safety, selectivity, and lack of toxicity. The use of herbal medicines in

planned comprehensive therapy is beneficial for the treatment of practically all diseases. The majority of those who live in rural and underprivileged areas have unwavering confidence in herbs, medicinal plants, and traditional treatments since they are much inexpensive than manufactured medicines. They are correct since they have no fatal adverse effects and may be used to treat any ailment(59). The investigation was carried out to determine the effectiveness of the stem from S. xanthocarpum in treating skin disorders like psoriasis since the plant's stem has historically utilized to treat a variety of skin chronic conditions and because the plant's fruits already had been shown to have anti-inflammatory characteristics(62–64). Scientific evidence has been provided to substantiate the tribes' ancient assertions that S. xanthocarpum stems may treat inflammatory skin conditions like psoriasis. There is evidence that S. xanthocarpum can cure psoriasis by reducing pro-inflammatory cytokines including IL-17 and IL-6(65)

5.5. Mechanism of action

A reduction in the generation of cytokines including TNF-, IL-1, IL-6, and IL-17, all of which participate to the inflammatory disease, has been associated with the phytoconstituents present in S. xanthocarpum. Chlorogenic acid, one of the phytoconstituents, is a natural antioxidant with the ability to heal wounds and lowers proinflammatory cytokines including IL-1, TNF-, and IL-6 inflammation-related signal, which are crucial in the development of psoriasis(65). (Figure.12)

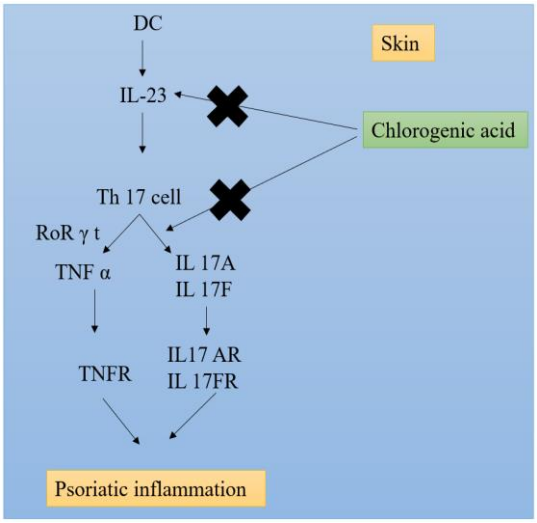

Figure.12 (mechanism of action targeted by *S. xanthocarpum* for the treatment of psoriasis)

5.6. Marketed formulations available for *S. xanthocarpum*:

Name of formulation	Uses
Kantakari capsule	Used for dietary supplement
Kantakari tablet	Used for fever, osteoarthritis, etc.
Kantakari powder	Used as an expectorant (relief from cough and cold), for asthma, and indigestion, boost immunity
Kantakari shampoo	Used for hair loss and scalp treatment
Kantakari cough and cold syrup	Used for cough and cold
Kantakari Ghrita	Used for severe respiratory diseases like asthma and bronchitis
Kantakari Avaleha / kantakaryavaleha	Used for dry productive cough, cold, and breathlessness

Table.2 (Preveously available formulations of *S. xamthocarpum*)

5.7. Recent developments on *Solanum xanthocarpum*:

N. Shivnath et al., in a recent study checked the potency of fruit extract of *Solanum xanthocarpum* in promoting chondrocyte proliferation by in vitro test and the protection of cartilage damage in disease osteoarthritis through collagenase-induced osteoarthritic rats' model. The MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) test and flow cytometry were used to investigate the proliferative effectiveness of *Solanum xanthocarpum* fruit extract on chondrocytes put in a serum-free medium. In cell cycle analysis, we hypothesised that the active components in *Solanum xanthocarpum* fruit extract were lowering the proportion of cells in the G0/G1 phase and raising the percentage of cells in the S phase of the cell cycle. The results of the *in vivo* osteoarthritis model also indicate that the fruit extract of *Solanum xanthocarpum* has statistically significant chondroprotective action on rat articular cartilage. Based on the results of the acute oral toxicity test, two dosages of extract were administered for thirty days: 250 and 500 mg/kg bw. The body weight of rats in arthritic control was significantly lower than in normal control in this study. When compared to their arthritic control, oral treatment of *Solanum xanthocarpum* fruit extract showed remarkable recovery at both high and moderate dosages. Because of the presence of antioxidants and flavonoids, this study indicates the chondroprotective effect of the powerful medicinal

herb *Solanum xanthocarpum*. The diseased state raised matrix metalloproteinase-3 and cyclooxygenase-2 expression while decreasing COL-2 expression in cartilage, as seen in the disease control group against the normal control. *Solanum xanthocarpum* fruit extract reduced collagenase-induced matrix degradation and inflammatory gene expression while maintaining cartilage integrity. (66)

P. Velu et al. evaluated the antioxidant and lipid peroxidation potency obtained by *Solanum xanthocarpum* leaves in the disease hepatocellular carcinogenesis which was induced by diethylnitrosamine in the male Wistar Albino rats. Evaluated histopathologically and measured the total body weight, liver weight, serum liver enzymes, hepatocarcinogenesis indicators, antioxidant enzymes, lipid peroxidation, and oxidative stress markers. There was a decrease in body weight and liver weight in the disease-induced animals in comparison with normal control animals, but the *Solanum xanthocarpum* aqueous leaves extract-treated animals brought the body and liver weights up to near normal levels. Serum liver marker enzymes such as aminotransferase, alanine aminotransferase, Alkaline phosphatase, Lactate dehydrogenase, and gamma glutamyltranspe-ptidase were remarkably increased in activity in the diseased rats in comparison with the normal control rats, whereas the *Solanum xanthocarpum* aqueous leaves extract-treated animals (150 and 300 mg/kg bw) neutralized these markers to near normal levels. Due to the antioxidant efficiency of the plant, this managed the antioxidant enzyme levels to restore to near normal levels in the *Solanum xanthocarpum* aqueous leaves extract-treated animals than compared disease induced animals. This showed the antioxidant potency possessed by *Solanum xanthocarpum*. The oral administration of *Solanum xanthocarpum* aqueous leaf extract in higher dose i.e., 300 mg/kg of bw potentially able to bring the lipid peroxidation and oxidative stress markers like Thiobarbituric acid reactive substances, lipid hydroperoxides and conjugated dienes decreased to near normal levels. The increase in the dosage showed an increase in treating neoplastically transformed cells which were examined by a hepatic histomorphology study and the higher dose brought a normal morphological appearance similar to the histopathology of normal animals compared with the disease control animals. All these data indicate the potency of *Solanum xanthocarpum* having anticancer pharmacological activity and treating potentially the disease hepatocellular carcinoma. (67)

P.K. Patel et al. investigated antiurolithiatic activity by the saponin-rich fraction prepared from fruits of *Solanum xanthocarpum. In-vitro* data showed the percentage of inhibition of aggregated calcium oxalate dihydrate crystals due to the highest dose of the prepared extract (100µg/ml) was found to be more than 98% which was brought up by a change in the morphology of crystals. Ethylene glycol 0.75% in drinking water was used in the animal model to cause urolithiasis in male Wistar rats. The urinary parameters and serum parameters i.e., urinary output, pH, calcium, oxalate, uric acid, phosphate, magnesium, citrate, creatinine, urea etc. were evaluated and observed in the comparison between model control and treatment showed these values maintained up to normal levels. *Solanum xanthocarpum* was brought up to the near level as the results obtained by the Cystone (750 mg/kg BW) which was used as the positive control. This predicted a possible pharmacological activity of antiurolithiasis through the inhibition of calcium oxalate crystal formation with a better outcome towards inhibiting nephrolithiasis and the urinary concentration of stone-forming constituents. (68)

Talib Hussain et al. investigated the ability of a fruit extract from Solanum xanthocarpum to prevent renal failure and nephrotoxicity brought on by gentamicin. This was confirmed by observing a decrease in levels of urea and creatinine in plasma and urine, as well as a significant decrease in urine volume as compared to normal control animals. It is characterised by severe proximal tubular necrosis, renal failure, and a significant increase in kidney weight in Wistar rats and Swiss albino mice treated with only gentamicin. However, when compared to the gentamicin-treated group, urine volume rose considerably after treatment with *Solanum xanthocarpum* fruit extract. 400 mg/kg bw *Solanum xanthocarpum* fruit extract raised urine volume to control levels. Following gentamicin therapy, decreases in renal Superoxide dismutase, Catalase, and glutathione activity showed inhibition of endogenous enzymatic antioxidant machinery. Treatment with *Solanum xanthocarpum* fruit extract effectively reduced gentamicin-induced decreases in Superoxide dismutase, Catalase, and glutathione activity levels. Glomerular and tubular epithelial changes were considered mild in the groups treated with gentamicin + *Solanum xanthocarpum* fruit extract 200 & 400 mg/kg bw i.e., animals treated with Solanum xanthocarpum fruit extract 200 mg/kg bw showed karyokinesis and mild tubular epithelial changes while in the case of animals treated with *Solanum xanthocarpum* fruit extract 400 mg/kg showed regeneration in tubular epithelial cells. Co-

administration of *Solanum xanthocarpum* fruit extract lessened the negative effects of gentamicin-induced nephrotoxicity possibly by inhibiting the free radical-mediated process. Research shown that Solanum xanthocarpum fruit extract inhibits the harmful effects of gentamicin in the biochemical and histopathological parameters by acting in the kidney as a strong scavenger of free radicals(60).

K Poongothai et al. studied *Solanum xanthocarpum* leaves showing antihyperglycemic and antioxidant activity in adult male Wistar rats by following the alloxan-induced diabetic rat model in which diabetes was induced by alloxan. The hypoglycaemic action may be accomplished by boosting either the pancreatic production of insulin from the preexisting beta cells or by its liberation from the bound state, which is one potential method for facilitating the impact that insulin has on plasma. The antihyperglycemic activity including body weight, blood glucose, and serum insulin was brought up to a normal level in comparison with the normal rats. The enzymatic antioxidant activity was evaluated by superoxide dismutase, catalase, and glutathione peroxidase level in the kidney and 50% inhibition of epinephrine auto-oxidation/min was observed. (69)

6. Role of nanomaterials in psoriasis

Nanotechnology combined with phytoconstituents is a green strategy with favourable therapeutic benefits and minimal therapeutic side effects. Nanomedicines are extremely effective in medication delivery, illness detection, and therapy outcome monitoring. Theranostic nanomedicine is a fast-expanding discipline that may be used to provide the optimum therapeutic effect. Theranostic nanomedicines can contain phytoconstituents as pharmaceuticals, which are very useful for both therapeutic and imaging purposes(70).

Recently, a number of technologies have been created to increase the effectiveness of topical drug therapy for the treatment of psoriasis. The possibility to add novel compounds into topical psoriasis therapy is provided by a number of innovative drug carriers. Transferosomes, liposomes, niosomes, and proniosomes are vesicular drug delivery systems. Small, multi-, or unilamellar vesicles called liposomes are made of phospholipids, cholesterol, and long-chain fatty acids. The hydration of non-ionic surfactants, cholesterol, and other lipids results in the formation of niosomes. They can increase skin penetration and medication release. Because they are also biodegradable, biocompatible, and osmotically active, they don't need particular storage conditions. Transferosomes are relatively readily deformable nanocarriers having an aqueous compartment surrounded by surfactants and lipids. Their most striking benefit is their flexibility, which allows them to pass through tiny pores. Non-vesicular drug delivery systems, such as foams, gels, and nanoparticles, have been created to provide improved and enhanced topical therapy(71).

Because of the low side effects, liposomal drug delivery therapy may be the first choice. Liposome-based nanomedicines boost medication therapeutic effects and are beneficial against psoriasis. Solid lipid nanoparticles, liposomes, polymeric nanoparticles, and other nanocarriers have been discovered to be beneficial in treating psoriasis(72). Several nanocarriers, including liposomes, silver nanomaterials, nano-emulsions, and microspheres, have recently been identified in conjunction with herbal medicines. The nano delivery technology used to administer herbal treatments as potent plant compounds soluble in different solvents like chloroform and methanol is not appropriate for distribution as such. For the treatment of numerous chronic illnesses, including psoriasis, the nano delivery method has proven to be an effective strategy(54). Topical therapy is the mainstay of psoriasis treatment. Pharmacological therapy is now more effective, and patients are happier as a result of recent advancements and discoveries. Topical psoriasis therapy's effectiveness, safety, and comfort are being improved by recent developments such nanoparticles, ethosomes, and niosomes(73).

7. Regulatory aspects in herbal drug technology:

The literature of a recognised traditional system of medicine should disclose the herbal remedies and plants that are currently in use, and they should be processed in the same way as described in the literature for good manufacturing practises to ensure that the procedure is standard.

Included phase 1 clinical trial studies are not crucial. Regardless of whether the correct requirement to assess the toxicity in animals has been decreased or not, it is essential that the compounds that are to be examined be available in the Indian System of Medicine and are described in their texts.

Up until a report shows toxicity or when to take the herbal medicines—likely 3 months or so—a toxicity research is not crucial for the phase 2 clinical trial.

In each of these cases, it is crucial to do a 4- to 6-week toxicity assessment on the two kinds of animals.

Clinical studies for herbal medicines should only be conducted following standardisation of the same and to guarantee that the indicators discovered for products under evaluation are constant.

Clinical trials for plant-based medications must also follow the same rules on informed consent, subjects, inducements for participation, information to be provided to the subject, withdrawal from the study, and research, including children or people with limited autonomy.

The competent scientific and ethical committees of the involved Institutions must authorise these experiments. Therefore, when an Ayurveda, Siddha, or Unani physician is a co-investigator in the study, it is imperative that plant drug clinical trials be conducted.

Any allopathic doctor conducting clinical trials of the plant without having knowledge of or training in all three medical systems would not be morally acceptable or reasonable. Thus, an expert should be involved in these systems, and the clinical assessment should be conducted collaboratively(74–78).

8. Summary and Conclusion

Psoriasis is an autoimmune chronic cutaneous inflammatory disease in which conventional treatment options are not that effective against the complete cure of the disease with lethal side effects and systemic toxicity. Herbal treatments may be a beneficial comparison to conventional therapies. So many herbal drugs showed beneficial results against psoriasis and out of these, *S. xanthocarpum* has evidence of novel treatment against the disease psoriasis by the stem extract of the plant. In ancient times also this plant has been used for dermatological disorders which may provide basic evidence about its effectiveness against the skin diseases like psoriasis. The guidelines regulated by the Pharmacy Council of India and AYUSH have to be followed for further research or clinical trials on the plant *S. xanthocarpum.* Nowadays many options are available for the treatment of psoriasis and as it is a very complicated problem, it drags the attention of the researcher to research this disease. Because none of the available treatments is completely secure and effective for the disease without causing any patient compliance. Therefore, the challenge is to develop a suitable medication for psoriasis which is may possible with the help of a herbal approach, as these have comparatively lesser or no side effects. *S. xanthocarpum* has anti-psoriatic activity and requires a better biological activity which may be done by enhancing the formulation properties and many others that obstacle the anti-psoriatic potential. Additionally, the clinical trials may require following the required guidelines because some patents have been permitted on nanocarrier formulation of anti-psoriatic agents. Thus, the nanocarrier formulation for drug delivery systems provides a predictable platform in clinical dermatology to bring huge beneficial treatment options for psoriatic patients.

9. Future Prospects

Worldwide, psoriasis requires emerging medical attention and has serious clinical problems with a progressive increase in the number in the human population. Present conventional therapy is lacking for the cure of the disease or may have serious adverse effects like skin cancer or any systemic toxicity.

In change with the approach of treatment from conventional to herbal with the help of novel drug delivery protocols, the problems may be resolved. *S. xanthocarpum* is a herbal choice for the treatment of psoriasis and has already signified evidence of activity against the disease.

By the application of a nanotechnology drug delivery system, the formulations of the *S. xanthocarpum* in the form of solid metallic nanocarrier, lipid-based nanocarrier, and polymer-based nanocarrier may enhance the permeability rate in the topical therapy and vastly increase in the potency of the herbal drug may be observed in both topical and systemic route for drug delivery.

Thus, a better result shown by *S. xanthocarpum* in the treatment of psoriasis may be achieved. Another approach may be the only separated phytoconstituents which are specifically responsible for the treatment of psoriasis present in the plant *S. xanthocarpum* need to be formulated in the form of nanoformulations and test against the disease psoriasis or against any target site-specific like enzyme or receptor which plays the pathophysiological key feature in psoriasis. However, huge attention and effort are required for the exploitation of these approached methods.

Nowadays in the advanced society of artificial intelligence, there are some Apps developed by different organisations to check, regulate, treat and guide the patient suffering from psoriasis. ‘Imagine’ is an app developed by LEO’s innovative lab to track the severity and symptoms of the disease by capturing pictures of the patients. ‘MyTherapy’ is an app that shows suitable medication for patients suffering from psoriasis and also works as a medication reminder and health tracker. The ‘Flaym’ app connects patients

suffering from psoriasis and helps the patients to try the best effective medication by taking feeding themselves. So, in this field, a possible future outcome could be developing an app which can track the progress and recovery of psoriasis in different patients and accordingly advise them to take suitable medication from time to time with the facility of complete medical guidance through mobile or other devices. This should upgrade from time to time and collect information from the worldwide network the research works are ongoing with psoriasis and their results, accordingly it replaces the medication with a better one and this includes the herbal treatment options also.

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