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RESEARCH ARTICLE

PLANT STEROIDS AS A PROSPECTIVE REMISSION INDUCER IN PSORIASIS- A REVIEW

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Abstract

About 1-3% of world's population is affected by autoimmune skin disorder, Psoriasis. Psoriasis is characterized by red and inflamed skin, silvery scales; itchy and painful sometimes lead to bleeding. Steroids like corticosteroids both systemically and topically are the mainstay of the treatment. However efficacy of steroids is beyond comparison, but they equally hold the foremost position in producing devastating side effects. Moreover, withdrawal or reduction of steroids carries huge risk in the deterioration of psoriasis. The objective of this review is to enlist few Plants with steroids as their chemical constituents which may be used as prospective treatment for remission inducer in psoriasis. An exhaustive literature review has been performed to study the plants structurally which resemble glucocorticoids in order to have minimal side effects and better potent lead compounds.

Introduction:-

Psoriasis is a chronic inflammatory disease which is characterized by clearly delimited erythaematousplaques with large silvery scales and/or mild itching. Psoriasis is marked by 'Auspitz sign' (expanded blood vessels underneath the plaque), 'tache de bougie' (waxy appearance Induced as a result of scratching the skin) or Koebner phenomenon (psoriasis at the site of at scars and minor skin injuries). It has been observed that 5–10% of psoriasis patients have Psoriatic Arthritis (PsA), which mainly affects the distal interphalangeal joints and metacarpophalangeal joints. [Buxton, P.K., Morris-Jones, R.. 2009]. Psoriasis is proved to be an immune mediated disorder, where a normal skin cell gets faulty interpretation for a pathogen, and thereby sends a signal that causes over production of new skin cell (Fig 1). This is a lifelong condition, which does not have a permanent cure, but provides symptomatic treatments for controlling the severity of symptoms produced by it. Treatment of mild to moderate psoriasis is done by multiple drug therapy; topical therapies like corticosteroids, vitamin D_3 analogues, and combination products are used in the primary level of treatment. Steroids like corticosteroids both systemically and topically are the mainstay of the treatment. The others used for the same include vitamin D analogues, tazarotene and calcineurin inhibitors.(Menter, A.et al 2008;Gottlieb, A.2009;Hsu, S. et.al.; Menter, A.,et al.2008).These drugs are also used systemically. Glucocorticoids (steroidal anti-inflammatory drugs) are widely used to suppress the inflammation by binding to the glucocorticoid receptor on multiple signaling pathways. Glucocorticoids show potential adverse effects like immunosuppression, hypertension, osteoporosis and metabolic disturbances which contradict their long term

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use.(Menter et al.2009; Sultan, A, RaufRaza 2015; Menter,A et al 2010; Patel, S 2015; Berger.A et al 2004). This article focuses on the prospective use of products of herbal origin with steroid like activity. These medicinal plants contain chemical constituents that resemble to the steroids in structure and their literature review supports their use as anti-inflammatory drugs.(Straus D.S, Glass C.K 2007; Schacke H et al,2004)

Molecular Pathogenesis of psoriasis

The pathogenesis of psoriasis starts with changes in keratinocytes and immune cells which are the major cell types related to psoriasis. (fig 2) These two lead in formation of vicious psoriasis-producing cycle. The LL37 cathelecidin /nucleic acid complex and the newly generated lipid antigen are derived from keratinocyte and identified as launching the initial T cell activation, especially the subset of T lymphocyte-expressing IL-17A (Th17 cells). On stimulation, the Th17 cells various mediators are released such as IL-17A, IL-17F, and IL-22, to elicit keratinocyte proliferation and inflammatory-marker production. The activated keratinocytes further are responsible for generation of antimicrobial peptides, cytokines, and chemokines as chemoattractants for infiltrating the immune cells; this infiltration results in amplification of the immune responses (Milani, M.; Sparavigna, A.,2018). The chemo attractants that were derived from keratinocytes can activate the recruitment of plasma cytoid DCs, T cells, macrophages, and neutrophils to cause skin inflammation and leads to silvery patch.

Herbal alternative as remission of Psoriasis

Plant Steroids

Phytoconstituents like alkaloids, flavonoids, glycosides, saponins, steroids, resins, tannins flavonoids, sesqiterpene lactones etc. present in the plants have shown to exert physiological and therapeutic effects. Secondary metabolites from these constituents are responsible for the medicinal properties. These metabolites share a common feature that is steroid moiety with four carbon rings.

Parent compound of all steroids is **cholesterol moeity.** Many plants contain this steroid with basic perhydro-1, 2-cyclopenteno-phenanthrene. Different classes of steroids are formed with slight variation in this framework with the introduction of functional groups at several points. The steroidal nucleus can be numbered and rings may be lettered. Steroids are biosynthetically formed from isopentenylpyrophospate moiety. With the exception of vitamin D, all steroids possess the skeleton of cyclopentophenanthrene or a skeleton derived by one or more bond scissions, ring expansions or contractions. Methyl group is normally present at C-10 & C-13 and mostly an alkyl side chain is present at C-17.(AbdEi Bahaman A.A, et al.,1991)

Active steroid components isolated from these plants have been reported to act through various methods like inhibition of epidermal cell proliferation, promoting formation of granular cells, decreasing serum IL-2 levels, inhibition of T- cell activity by induction of apoptosis. (Fig.2)

Classification of Steroids

Steroid can be grouped according to a number of criteria as described below:

1. On their chemical structure (side chain attached to the ring D),
2. Site of production (ovarian or adrenal steroids),
3. Biological functions (a **glucocorticoid** or sex steroids) and molecular actions (an estrogen receptor agonist)
4. On the basis of biochemical effects.

This review presents classification which is based on its pharmacological actions. It is described in the Table 1. The major plant steroids found in nature with their active constituents are listed in Table 2.

Psoriasis is concurrently observed with epidermal changes so herbal treatment focuses on keratinocyte-proliferation inhibition, modulation of keratinocyte differentiation, and apoptosis as main therapeutic targets.

Physalis angulata:

Physalis angulata belongs to Solanaceae family. World tropical and subtropical regions use their fruits as medicine. It has been discovered by the researchers traditional uses, phytochemical constituents of this species. Antimalarial, anti-inflammatory and post-partum effects are the prominent properties shown by Physalisangulata traditionally. According to them, the plant has been used locally for its antinociceptive properties, antiparasitic, antimicrobial, antihelmenthic, immunosuppressive properties. Sudhakaret. al. in 2009 studied leaves of this plant for its wound healing activity. (SudhakarC.Reddy,2009)The plant contains steroids namely Physalins which are available in the

form of D, I, G, K, B, F, E and Physagulins namely E, F, G. The structures and dominance in the plant is shown below. Aqueous extracts produce sturdy changes in inflammation and may act as immunomodulators, interfering with the cyclooxygenase pathway, aggregation of lymphocytes, Nitric Oxide, and TGF-β production. [Pinto et al, 2010]

Ichnocarpus fructescens:
It is an evergreen shrub known as "Black Creeper" which belongs to the family Apocynacae. Traditionally, this plant has shown to have pharmacological activities like anti-inflammatory, analgesic, antipyretic, membrane stabilizing, anticancer, hepatoprotective etc. The studies on various parts of the plant like roots, leaves and flowers have proved for their ethno medical uses like roots for anemia and kidney stone. Leaves for headache, wounds in the middle of fingers, skin eruptions, wound healing. The presence of beta sitosterolglucoside and beta sitosterol predominantly demonstrated anti-inflammatory activities. [Chaudhary K et al 2012]

Hemidesmus indicus:
It is commonly known as Anantamool. The family to which it belongs is Apocynaceae, widely distributed throughout India especially in different areas of West Bengal. It is a slender, laticifereous, semi-errect endangered shrub; shows immense medicinal values. Sitosterol, is considered to be an ubiquitous component of several plants. [Banerji A. et al, 2017]The well knownphytosteroidβ-sitosterol, Sitosterolglucoronate has been separated from the roots of H. indicus. [Swathi S et al. 2019].Desinine, Indicine, Hemidine, Indicusin, Hemidesceine, Emidine, Medidesmine, Hemisine, Demicine, Denicusine, Cholesterol, Campesterol, 16-dehydropregnenolone, Heminine is various forms of steroids present in the H. indicus. Various pharmacological significance of H. indicus like anticancer, antiarthritic, anti microbial, antidiahorreal, anti-inflammatoy effect, antileprotic actions etc have been endorsed by researchers.

Phyllanthus reticulatus:
Commonly known as Black Honey, shrub belonging to the family phyllanthaceae is known for many medicinal properties like antiplasmodial, hepatoprotective, antidiabetic, hypocholesterolemic, anti-inflammatory, anti-nociceptive, anti-bacterial and antioxidant activity. This shrub is large, branched with angled smooth or tuberculate branches. The leaves look to be simple, variable in size with alternate lancceolate arrangement. The chemical constituents of the plant consist of tannic acid, terpenoids, flavonoids, phenolic compounds and steroids as main. Jamal A.K et. al. conducted a phytochemical study on the leaves leading to isolation and identification of three compounds like lupeol, lupeol acetate, and stigmasterol. [Jamal A. K, 2008] Saha A. et. al. studied the pharmacological activity of different extracts ofPhyllanthus reticulatus in mice model an evaluating their effects as analgesic and anti-inflammatory. [Saha .A 2007]

Solanum pubescens:
It is a shrub at ground level and is a wild plant. It is a weed of forest and mostly found in the hills of South-Eastern Ghats in Andhra Pradesh and southern India. [Sumanlatha P, 2013] It belongs to the family solanacae. The investigation showed that Solanumpubescens is a rich source of essential oils, alkaloids, flavonoids, saponins, steroids, tannins and coumarins, which are pharmacological active too. [Haseeb Ur. R 2014] Traditionally, it is used in the treatment of headache, menstrual pain, rheumatoid arthritis, tuberculosis, ulcers etc. [Hemamaline K, Vijeesha M, 2012] Literature review described its pharmacological properties like antidiabetic, [Hemamalini K, 2012] hepatoprotective, [Hemamalini K, Ashok P 2011] gastroprotective, [Nijjyoti P, 2012] anti-inflammatory, [Deepika R, 2013] anti-anxiety, anti-depressants, [Bharghav A, et al 2012] myorelaxant and antidiarrheal. [KhareC.P,2004]

Citrullus colocynthis:
A perennial herb which belongs to the family Cucurbitaceae. Its is wild in nature and most commonly found in the sandy lands of North West, the Punjab, Sind, and Central and southern India, and coromandal coast. Apart from India also found in Arabia, West Asia, and Tropical Africa and in the Mediterranean region. In Sanskrit it is popular as - Indravaruni, Chitrapala or Bitter apple. Root, bark and leaves are also used medicinally. Due to the presence of colocynthinit shows mild stomachache, bitter tonic, diuretic and antilithic property. Chemical constituents include Cucurbitane type triterpene glycoside vizcolocynthoside A & B; fatty acids like Fatty acid like Stearic, Myristic, Palmitic, oleic, Linoleic, Linolenic acid; protein, vitamin B1 and B2, Flavonoid glycoside quercetin. [Borhade, 2013] Disparate pharmacological effects of Citrullu scolocynthis are studied by researchers like antioxidant, anti-diabetic, antimicrobial, anticancer, anti-inflammatory, analgesic, gastrointestinal, reproductive, protective. (Saba, A.B., Oridupa, A.O.,2010) Saba AB et. al. performed isolation of Cucurbitacins, a triterpenoid steroids. The findings

endorsed that it is efficient antioxidant and this property lies in their ability to scavenge free-radicals such as hydroxyl radical, superoxide anions and singlet oxygen. It also showed that cucurbitacins adequately inhibit lipid peroxidation and oxidation. (Rajamanickam, E,et al. 2010) The study performed by Rajamanickam, E. et.al. showed the anti-inflammatory activity of C. colocynthis leaf extract. Carrageenan air pouch model were used in rats to induce paw edema and sub acute inflammation. Anti-inflammatory activity of the extract is due to the presence of flavonoids like apigenin, quercetin, naringein and luteolin. Additionally these prevent the synthesis of prostaglandins and have therapeutic application on inflammation. [52]

Moringa oleifera:

It is a native of Indian subcontinent and is commonly known as 'drumstick tree' or 'horseradish tree'. It belongs to the family moringeacae. Famous for folk medicinal uses which are attributed to the presence of functional bioactive compounds, such as phenolic acids, flavonoids, alkaloids, phytosterols, natural sugars, vitamins, minerals, and organic acids.(Anwar, F et al.2007). Diversified parts of this plant such as the leaves, roots, seed, bark, fruit, flowers, and immature pods have shown their pharmacological potential in treating various ailments like heart and plasma stimulants, pyrexia, tumor, epilepsy, inflammation, ulcer, spasm, diuretic, used to treat hypertension, cholesterol lowering, antioxidant, diabetes, liver tonic, antibacterial, and antifungal activities, and are being employed for the treatment of different ailments in the indigenous system of medicine.(Hosseinzadeh H, et al. S. 2005a.;2005b)

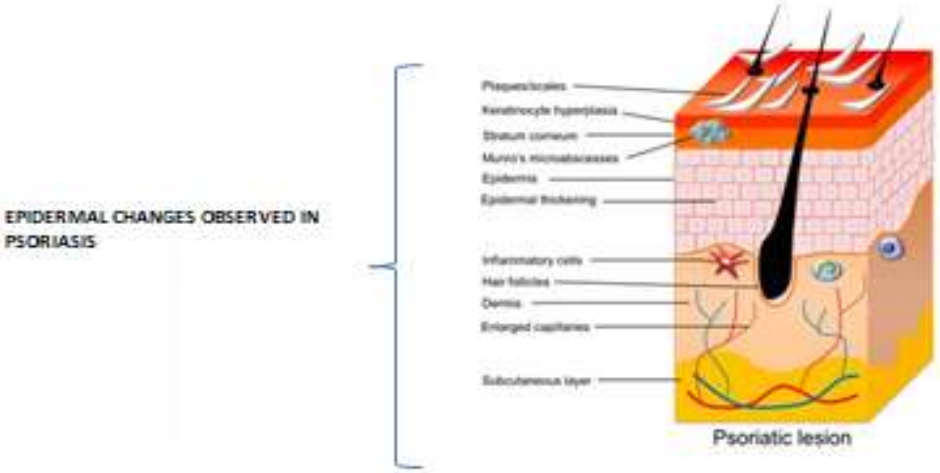


Figure 1:- Epidermal changes in psoriasis.

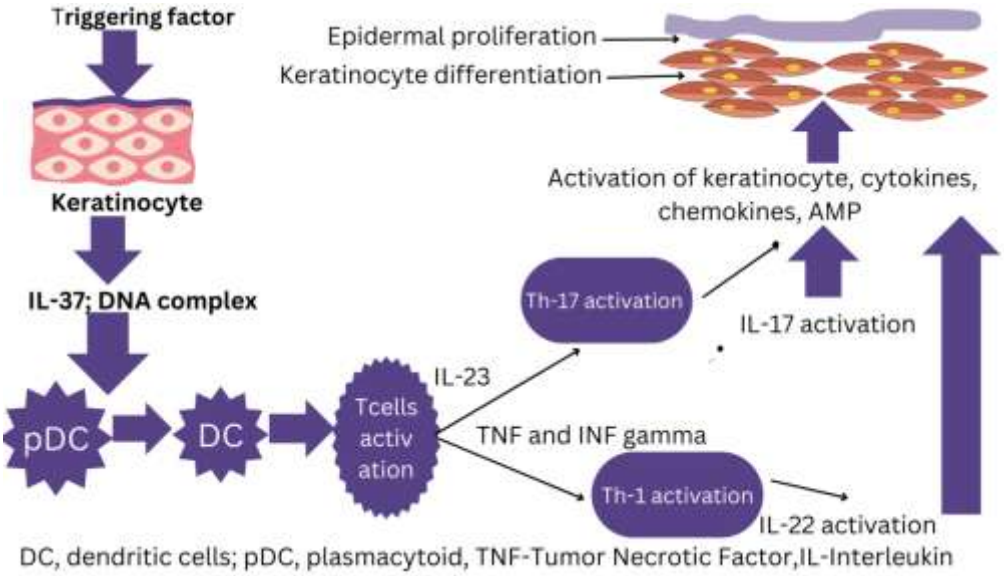


Figure 2:- Involvement of mediators in the pathogenesis of psoriasis.

Table 1:- Chemical Structures of VariousPlant Steroids.

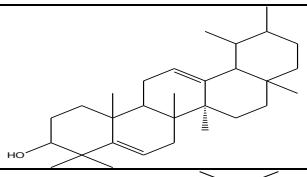
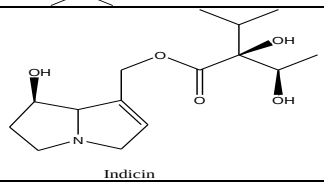
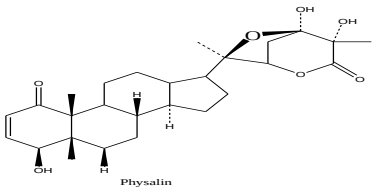
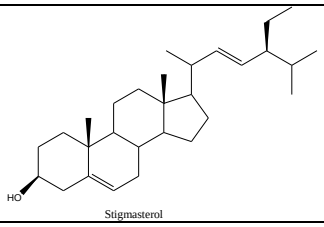
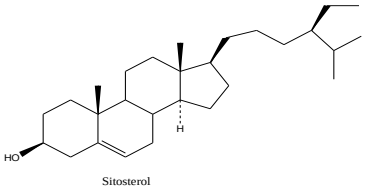
S. No.	Name of Compound	Structure
1	Alpha Amyrin	
2	Indicin	 Indicin
3	Physalin	 Physalin
4	Stigmasterol	 Stigmasterol
5	Sitosterol	 Sitosterol

Table 2:- PharmacologicalClassification of Plant Steroids.

Pharmacological actions	Name of plant steroids	Chemical structure	Examples	References
Growth promoting phytochromes	Brassinosteroids	Cholestane with two vicinal diols and varoioussubstitutents in position C-24.	Catasterone, Brassinolides	(Mandava N.B,1988)
Cardiotonic. Ionotropic agents	Bufadienolides	Steroid with C-24 polyhydroxy with six membered pyronering at C-17.	Helleborin, Scillaridine, Physodine	(Yokota T,1997)
Cardiotonic, Antibactirial	Cardenolides	C-24 steroids with five membered lactone ring located at C-17.	Digoxin, Digitoxin, Digitoxigenin	(Krnn L Kopp B.1998; Manuel M et al2001)
Antitumor, anti-bacterial, anti-inflammatory,	Cucurbictacins	C-30 oxygenated triterpenoids with methyl group at C-4.	Cucurbitacin D, CucurbitacinC	[Conception, 2005,Denan L et al 1997;Dinan et al 2001;Sarkar et al.1999

hepatoprotective				
Molting hormones for plants	Ecdysteroids	C-27 steroids with 7-en-6–one chromotphore and methyl gp at C-3.	Ecdysoneoogonoial	[Sun J et al 2005; Dinan L et al.,1999
Antifungal, Sex hormone, Antitussive	Sapogenenins, steroid saponinns	C-27 Oxygenated steroids with a hydroxyl group at C-3.	Spirostanol (diosgenin, sarsepogenin)	(Dinan L 1995;Braille E et al 2007)
Antiinflammatory, Sex Hormone	Steroidal alkaloids	Steroidal skeleton with nirogen integrated into a ring or asa substituent	Solasodine, Solasonine	[QuanH.J 2005; Roddick J.G 1985)
Immunosuppressive, hepatoprotective, Diarrhoea, Rheumatic fever	Withasteroids/ Withanolides	Steroids with C-28 with δ-lactone, the side chain linked to steroid nucleus at 17α or 17β.	Withaferin A, Ipchromolide, With anolide.	[Nazruillarv2001;KirSonJ 1981; Mohammad K et al 1992;Dian L et al 1996.]

Conclusion:-

Conventional therapies for the treatment of Psoriasis like glucocorticoids, vitamin D analogues, tazarotene, and phototherapy have been used for years. This review briefed about the possibilities of use of plant steroids for the remission of psoriasis, which can be used adjuvant to the traditional treatments without producing undesirable side effects. Further, validation of use of steroidal moieties found in plants like amyrin, physalin, stigmasterol, and sitosterol for the treatment of many inflammatory diseases like psoriasis has been done in this review.

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