



# DESIGN AND SELECTION OF PHYTOCHEMICALS FROM SCIENTIFICALLY KNOWN ANTIPSORIATIC PLANTS BY MOLECULAR DOCKING METHOD AND ANTIPSORIATIC EVALUATION

Mrs Ghousia begum<sup>1</sup>, Mohammed Ibrahim<sup>2</sup>

1. Associate Professor, Hospital and Clinical Pharmacy, Prathap Narender Reddy College of Pharmacy, Shamshabad, Hyderabad, Telangana, India.
2. Professor, Dept. of Biotechnology, Prathap Narender Reddy College of Pharmacy, Shamshabad, Hyderabad, Telangana, India.

## Abstract:

This study has been undertaken to design the selected phytochemicals from the anti-psoriatic plants by molecular docking method and also to evaluate the anti-psoriatic effects of these phyto-chemical extractions. Psoriasis causes great physical, emotional and social burdens in general, and is often significantly impaired. Disfiguration, disability, and marked loss of productivity are common challenges for people with psoriasis.

To determine the application of prepared formulation on the psoriatic patients for obtaining Psoriasis Area Severity Index (PASI). There is no proper cause and treatment is based on external factor

Docking is a method which predicts the direction of molecules and is used to design the drug. And also used to bind the molecules to the suitable binding site. Molecular docking is a method used to structure the drug design. Herbs that are used for the management of psoriasis are Turmeric, Neem, Guggal, Jasmine flower, Garlic and etc. One can use Anti-psoriatic drugs under the observation of trained practitioner. One should forecast the drug efficacy on basis of patients genetics. Co-morbidities can occur in patients with psoriasis, so it is significant to carefully monitoring of the psoriatic patients by primary care providers.

## INTRODUCTION

Psoriasis is a persistent immune-mediate disorder, which occur when the immune cells such as T-lymphocytes attacks it own skin cells. The skin condition are characterized by scaly, flaky, itchy, red papules and plaques. Lesions on nails, elbows, knees and hands. Both male and female are effected by Psoriasis. However, there is no therapy for the treatment of psoriasis as it is a autoimmune disorder. It is not easily spreadable. psoriasis is a condition that generally affects the skin layer. Psoriasis looks like infection, but it is nothing but inflammation of skin.

## IMMUNOPATHOGENESIS:

In psoriasis the resistant organism is more active than the normal characterized by skin inflammation and the creation of skin cells are faster than normal. Newly produce skin cells goes to the surface, usually it takes nearly 3-4 weeks in normal skin. Generally in psoriasis the dead cells stick to one another within 3 to 4 days, which forms the thick flaky patches called as plaques. The immune cells protect our body from foreign particles like pathogens and viruses etc by producing antibodies, it differentiate healthy tissues from the foreign tissues. It is separated into two types. Innate response is a quick and non specific attack on any foreign micro-organism or particles that enters into human body.

Adaptive response is a slow response that resists more stress damage caused by foreign micro-organism and provides specific antibody and is very effective when similar microbes attack next time.

### **ROLE OF IL-23 TARGET SPECIFICITY:**

IL23 is a protein. IL-12 subunit IL-12p40 combined with IL-23p19 to forms IL-23 which is usually a cytokine. IL-23 was discovered by Oppmann. IL23 bind to a receptor which is collected from IL-23R and IL-12Rb1. The IL-23 cause more severe skin lesions than the one cause by IL-12. Biological agents have been allied to the clinical assistance in psoriatic patients. Inflection of IL-23 is done by cyclosporin A, UV therapy. For genetic studies IL-23 and IL-23R gene signals pass through the receptors, (Kanda and Watanabe, 2008; Zaba et al. (2007). IL-23 injection induces IL-22 which depends on the inflammation activity (dermal). T-cells use in mouse models are specifically CD4 dependant psoriasis. IL-23/Th17 which is a type-1 seditious path representation, in which Th1, Tc1 are present (cytotoxic T cell type-1). Therefore, both the IL23 and IL12 are produce in DCs that interacts with neutrophils and endothelial cells which are the chief cause of type-1/Th17. Both interleukins have a subunit called p40 which shows clinical effects on autoimmune-type diseases specifically in psoriasis and chronic diseases. A selective transcription inhibitor known as STA-5326 are very effective in preclinical studies on rat models of CD along with anti-IL-3 and IL-12, which is done by clinical phase I, II, and III trials in chronic plaque-type psoriasis by both IL-23 and IL-12. (Burakoff et al., (2006)

### **ROLE OF IL-12 TARGET SPECIFICITY:**

The IL-12 is a protein and IL-12p40 is subunit of IL-12 which gives high-quality natural activity when combined with IL-23p19 (Parham et al., 2002). Receptors composed of subunits IL-12Rb1 and IL-23R signals which are bind by IL-23. Jak1 family binds by IL-12Rb1 and is related to Tyk2, whereas the IL-12Rb1 is a receptor and the IL-23R is allied with Jak2 (Capon et al., 2007). IL-12p40 and IL-12p35 are used in animal models specially in investigational autoimmune myelitis and collagen-induced arthritis. IL-12B code of IL-12p40 is a subunit of Interleukin-12. Th1 cells produce IFN-g as well as lymphotoxin and IL-12R $\beta$ 1 signaling pathway (Capon et al., 2007). IL-12 composed of IL-12Rb1 subunits, which is linked with the Jak relations. The T-cells development is based on IL-12 protein and on the activated transcription factor. From these convincing collected genetic data, we found a combination between the IL-12B and psoriasis. IL-12 is effective against the plaque-type psoriasis. Anti-IL-12p40 shows good profile safety during the treatment.

### **ROLE OF STAT3 TARGET SPECIFICITY:**

The activated stat3 are characterized in psoriatic lesions by epidermal keratinocytes, which is induce by increased in the levels of cytokines and growth factors. A stat3 inhibitor STA-21 (ochromycinone) is a antibiotic which is examined to know whether STA-21 is functional in the prevention of skin lesions in both animals and human psoriasis. Through the c-Myc and cyclinD1, and proliferation is done by STAT-21. Treatment with STA-21 was done by transcription of nuclear in human keratinocytes which is a cytokine-dependent inhibitor. K5.Stat3C transgenic mice, forms lesions and Stat3 is active in keratinocytes which can be treated with the growth supporter (TPA). A gene-targeted human epidermis revealed that IL-22 mediates a effector cytokine by Th17 that forms a cross link between immunocytes and keratinocytes by stat3. (Zheng et al., 2007) Transgenic Stat3 distraction oligonucleotides inhibits the lesion and can cause epidermal hyperplasia. And increased in stat3 stimulates the ligand with an antibody in psoriatic lesions which shows a powerful Stat3 indication in nuclei (Song et al. (2005). Stimulation of normal human keratinocytes, cause a rapid translocation with Interleukin-22 and Interleukin-6 of Stat3 and STAT-21 in human carcinoma cells. It indicates that stat-3 inhibits signals in cancer cell lines. However, inclusion of stat3 with STAT-21 inverted the effect of Interleukin-22 in signals. Epidermis showed Stat3 activation over and above up-regulation of Raf/MAPK pathway. These results together provoked us to carry a clinical study with the STAT-21 for psoriasis patients specially in ointments preparation..

### **ROLE OF TNF-ALPHA TARGET SPECIFICITY:**

TNF-alpha is a cytokine in psoriasis, these inflammatory cytokines occurs in two forms TNF-a and TNF-b which usually known as lymphotoxin-alpha (LT $\alpha$ ). The inflammatory cytokines forms in two biological forms that are soluble TNF and trans-membrane TNF. Both biological forms can bind to receptors, TNFR1 or TNFR2, on the surfaces of many cells in the immune cascade. A nuclear factor kappa B1 (Nf- $\kappa$ B1) regulates a variety of inflammatory genes. A genetic tendency of psoriasis shows attention on HLA-Cw6 which is a antigen and is not susceptible gene for psoriasis. Increased secretion of cytokines can cause inflammation of cells and tissue damage.

Tumor necrosis factor- $\alpha$  is a protein found in lesions of psoriasis, passionate and scatter appearance is by dermal DC's and focally by keratinocytes and Langerhans cells. TNF- $\alpha$  levels in psoriatic skin is higher in blister then the normal healthy cells. TNF- $\alpha$  linked with (PASI) scores particularly in erythema. After synthesis it binds to the receptor which induces keratinocytes and endothelial cell which devotes molecule and results in the production of chemokines, such as IL-8. Which may further lead to the inflammation of cells causing plaque. TNF-alpha activates the nuclear factor- $\kappa$ B signal pathway which usually effect the cell endurance and anti-apoptotic effects. TNF and nitric oxide synthase increased in lesions. TNF-alpha induces the th-17 which produces cytokines through the pathway(NF- $\kappa$ B), but by blockade of NF- $\kappa$ B and can cause the loss of IL-17A production from CD4+ T cells in psoriatic lesions.

### STATISTICAL DATA OF PSORIASIS:

On 24 May the world health assembly (WHO) has approved a declaration on psoriasis. This report has been written to make the people about the awareness of psoriasis. The psoriasis ranges from 0.09 to 11.4% all over the countries. And in the urban countries it ranges from 1.5 to 5% and the prevalence is day by day increasing. Usually 75% of the psoriasis cases has been seen in those patients who are below 45 years. A review of published literature has shown that there are total 68 articles of prevalence ranges of psoriasis of 20 countries. Psoriasis is mostly occurs in the Northern Europe which ranges from 3-37 and least in the Eastern Asia which ranges from 37-45. However it is hard to evaluate the data of prevalence rate of psoriasis due to the different methodologies. The Global burden of psoriasis is measure by disability-adjusted life year (DALY) which is equal to the years lived with disability (YLDs) and years of life lost (LLDs). In India prevalence rate ranges from 0.44 to 2.8% and in Hyderabad it is around 8%. In India the plaque type psoriasis is very common which is around 50%.

### TYPES OF PSORIASIS:

There are various types of psoriasis, they are:

**PLAQUE PSORIASIS:** It is a common type observed in most of the population. It is also known as psoriasis vulgaris. It is characterized by silver and scaly layer, these appears on the various part of the body such as on the knees and elbow. It effects around 70-80 percentage of the population.

#### Causes:

Its actual cause was not yet known, but it can cause due to immune disorder. It cause due to infections also.

#### Symptoms:

It shows symptoms such as:

Rashes, Biopsied.

Skin becomes thicker and inflamed, Eczema.

**GUTTATE PSORIASIS:** It appears in the shape of red spots (small) on the skin coat. It effects about 10-15% of the population. It appears on the limbs, scalp and sometimes on face. The spots are in drop shape.

It is cause due to the inflammatory disorder and also due to the environmental factors. It causes the skin flaky and red. It also causes due to some drugs.

**Symptoms:** It includes

Red spots

Lesions, Red papules

#### Triggers:

Stress

Infections such as upper respiratory infections

Tonsilitis.

**INVERSE PSORIASIS:** Other name of inverse psoriasis is Flexural psoriasis is appears in the shape of red and shiny form. It is specially appears in skin-folds such as armpits and groin area. It also appears under the breasts.

**Causes:** It is caused due to the genes and also one can effect due to sunburns, infections, severe stress and also due to some drugs.

#### Triggers:

Diet, Allergies, Environment

**Symptoms:** It includes

Red scaly skin, Inflamed skin

Friction in skin, Lesions change.

#### Complications:

On the sensitive and thin skin lesions appear.

Injured skin is most likely to be effected.

Skin folds become warm and moist which lead to be effected by bacteria.

**PUSTULAR PSORIASIS:** Pustular psoriasis forms in the shape of pustules bounded by red skin.

**Causes:** It is caused due to changes in immune response and genetics.

**Symptoms:** It includes:

Fever, loss of appetite.

Muscle weakness, pulse problem.

**PALMOPLANATAR PUSTOLOSI:** It is a blisters that occurs on palms and soles of the body.

**Causes:** It can cause by several factors like smoking, environment and also due to the stress etc. The actual cause is unclear.

**Symptoms:** It includes: Tiny blisters with yellow pus, Scaly plaques, Painful cracks and sores.

**Triggers:**

Injury or wounds and skin infections.

Stress and sun burns.

Allergens and bug bites.

**ERYTHRODERMIC PSORIASIS:** It is a atypical type of psoriasis and it looks like burns. In this type our body is not able to control the temperature. It appears on huge segment of the body, it looks like large pieces.

**Causes:** It cause due to poorly controlled plaque psoriasis and bad sunburn and also due to excess intake of alcohol. Sometimes due to major stress one can cause psoriasis.

**Symptoms:** It include Strong pain, Papules or blisters, Severe itching Heart problem, Swelling, joint pains and fever.

**Complications:** They are pneumonia and sepsis. protein loss and congestive failure. Fluid retention.

**SCALP PSORIASIS:** It occurs in the shape of scaly patches, sometimes extend to the neck and forehead. It is a non-spreadable disorder

**Causes:** The causes of scalp psoriasis is unclear, but it is generally occur due to genetic disorder.

**Symptoms:** Hair loss, Red bumps, Itching and flaking, Seborrheic dermatitis.

**PSORIATIC ARTHRITIS:**

It is a disorder that effects those who are suffering from psoriasis. It can involve in any segment of the body including joints, fingertips and the spine.

**Causes:** It occurs when the immune system attack its own healthy cells. It also occur due to the environmental and genetic factor.

**Symptoms:** It includes: Foot pain: Tendons and ligaments. Swollen fingers and toes. Lower back pain: Spondylitis.

**NAIL PSORIASIS:** It occur generally due to the fungal infection.

**Causes:** It can cause due to the genetic and environmental factors.

**Symptoms:**

Discolored nails and pitting.

Changes in the shape of nail or thickness, Grooves and crumbling of the nail.

**Topical treatment:** Retinoids, Babchi, Dithranol, Corticosteroids and Vitamin D analog etc, are used in topical treatment and it is the first line generation to treat psoriasis. (Kragballe and Kang et al.). Vitamin D inhibits the proliferation by declining the invention of IL-8 and Keratinocyte differentiation. Excess use of Vitamin D can cause skin irritation. And to overcome this problem increased the amount of **Calcipotriol** on the hazy skin by applying liposome gel reduce the skin irritation. Whereas Calcipotriol is a Vitamin D analog. **Coal tar** is mainly normally used to treat psoriasis as it reduces itching and inflammation of the skin, excess use can cause irritation due to its strong odor. Coal tar is available in creams and oils and it is not supposed to be used by pregnant women.

**Ultraviolet rays:** Exposure to the sunlight reduces the skin inflammation, but intense sun exposure can cause skin damage.

**UVB phototherapy:** UVB light is very effective against mild to moderate symptoms of psoriasis. UVB phototherapy is used to manage the widespread psoriasis, to avoid if any side effects like redness, itching etc. To overcome this moisturizer is use.

**HERBS AND PSORIASIS:**

Herbal formulations like Aloe vera, oats, turmeric and tree tea oil are used to treat psoriasis. Aloe vera act as a lubricating agent hence it reduces the inflammation, relief pain, increases the collagen and reduce irritation. Aloe vera shows good safety and efficacy, as Aloe vera gel is more effective for skin including erythema due to dilation of blood

vessels. Sometimes aloe vera gives allergic reaction at that time discontinue the treatment. Aloe vera consist of Vitamin B1, B2, B6, E, C and folic acid etc. Other herbal formulation like apple cider vinegar is used for scalp psoriasis to reduce itching sensation. Turmeric consist of active ingredient, curcumin which act as a anti-inflammatory agent and hence used for psoriasis patients. MahoniaAquifolium is a antibacterial herb which is generally used for good immune response. Other alternative treatments include coal tar ointments, dead sea salts, capsicum, steroid based creams etc. are used to treat psoriasis.

### SELECTION OF PHYTOCONSTITUENTS:

Based on the effective reaction of the plants on the psoriasis patient the plants are selected. Then we find the chemical name of each selected plants. Chemical constituents selected are Kaempferol, Glycitein, Cinnamic acid and Punicic acid to treat psoriasis against IL-12, IL-23, STAT-3 and TNF- ALPHA inhibitors. We have selected 100 plants by the literature after selection, we find chemical constituents of each plants. Then we find their binding activity, we choose the one with best binding site. After selection we did their safety and toxicity test. We did Docking of selected plants targets like IL-12, IL-23, STAT-3 and TNF- ALPHA inhibitors. Then we proceed with safety and toxicity test to know the toxicity value. We had selected only those targets with good class (toxicity class 5) along with the LD50 value of each targets. We choose only those targets inhibitors with good LD50 value. After this we did analysis and extraction followed by formulation of the chemical constituents.

### ANIMAL TOXICITY STUDIES:

Animals for experiment should be procured by the CPCSEA. Test is carried on Rabbits of age 6-8 weeks and the animals should be acclimatized. Animals should be handle carefully so as to protect from stress, the newly arrived animals should be observed the signs of rabbits like illness, injury or if any abnormal situation. The animals should be feed with good food and water and the animals must be store in separate rooms to avoid the disease if any. The animals should be place in a elevated average of personnel cleanliness. The animals should be place in a shady room for 12 hours, between the temperature 20-24 and humidity should be 30-70%. The animal should be protected from the substances like pesticides and heavy metals.

Formulation	Rabbit	24h		48h		72h		Mean Value
		Erythematic Score	Edema Score	Erythematic Score	Edema Score	Erythematic Score	Edema Score	
Kaempferol, Glycitein, Punicicacid, Cinnamic acid	1	0.1	1	0.2	0.	0	0.1	0.23
	2	0.2	0.1	1	0.1	0.2	0.3	0.31
	3	1	0.2	0.1	0.1	0	1	0.38

### ACUTE SKIN IRRITATION TEST:

The principles of ADME are applied to these studies in order to know the safety and toxicity of the same drug in human subjects.

**Draize skin test:** 3 Rabbits are used for the experiment and the time of study is 3 days or 72 hours under the observation. The sample is applied on the dorsal part of the rabbit, which is applied by shave and abraded. After shaving apply the sample on the 1\4 square of the dorsal part of the rabbit ,three squares are made on the rabbit. On one square part the sample is apply and covered with plastic sheet, then the rabbit is kept under the observation in order to know the toxic effect if any, in a room temperature. The studies are carried in order to know the erythema and edema score. The animal should be handle carefully so that the rabbit should not supposed to cause any harm to himself. After 3 days observation the Erythema and Edema score of all three rabbits is 0.23, 0.31, 0.38.

**RATIONAL SELECTION OF PHYTOCONSTITUENTS IN PSORIAIS:**

Rational Selection of Kaempferol, Glycitein, Cinnamic acid and Punicic acid against the four targets. Kaempferol inhibits STAT3, Glycitein inhibits IL12, Punicic acid inhibits IL23 and Cinnamic acid inhibits TNF alpha. We used 800 chemicals then we did Energy minimization of each chemical constituents by using MOE software. Molecular docking of the selected plants is done by using software know as ChemDraw. Through the aid of IUPAC names of the phytoconstituents in the ChemDraw we found the structures of the chemical constituents. And through the aid of protox software we found the high class toxicity value. After this extraction is done which is followed by Gel Formulation for the Evaluation of Safety & AntiPsoriatic activity in Human Subjects. Evaluation and safety test were done on animals before doing on humans subjects.

**RATIONAL DRUG DESIGN:**

Rational drug designing is a method which shows the trials and errors in Drug Discovery of a new drug. Which is mostly used in primitive days, because of its huge time consuming, manpower and money. Rational drug designing is used drug development and identification of suitable drug and target, rational drug designing is a world's most scientific method of identifying the potential drug candidate with appropriate molecular targets with the predicted binding to the active site of molecular target, such as molecular Docking quantitative structural of activity, pharmacokinetic, toxicological relationships, COMFA, COMSIA and PASS. Drug Discovery involves crude extract of targets for drug testing without rationality. The normal drug plan involves the selection of phytochemicals by extracting crude drugs for docking by molecular docking to find good interaction with active binding active site to the amino acids in clinical health practice for psoriasis is a good method for rational drug testing.

**DOCKING:-**Docking is a method which predicts the direction of molecules and is used to design the drug. And also used to bind the molecules to the suitable binding site. Molecular docking is a method used to structure the drug design.

**INTERACTION OF GLYCITEIN WITH IL-12**

Interaction Data of glycitein with IL12

Ligand: :

Receptor: 4GRW: IMMUNE SYSTEM

Heavy atoms: ligand = 32, receptor = 2418

ligand	receptor	residue	chain	type	score	distance
H 4909	OE 2611	GLU	173	4GRW 1	H-don 48.5%	1.39
H 4892	O 4389	TYR	292	4GRW 1	H-don 62.0%	1.71
O 4908	O 4769	HOH	597	4GRW 2	H-don 90.7%	0.67
O 4908	O 4769	HOH	597	4GRW 2	H-acc 90.7%	0.67
C 4856	CE 1795	TYR	114	4GRW 1	weak 0.0%	3.91

**INTERACTION OF PUNINIC ACID WITH IL-23**

Interaction Data

Ligand: :

Receptor: 4GRW: IMMUNE SYSTEM

Heavy atoms: ligand = 20, receptor = 1013

ligand	receptor	residue	chain	type	score	distance
H 2089	O 456	ILE 52	4GRW 1	H-don	42.1%	1.45
O 2087	N 451	ILE 52	4GRW 1	H-acc	44.9%	2.63
C 2064	O 382	ASN 47	4GRW 1	weak	0.0%	4.22
C 2066	O 382	ASN 47	4GRW 1	weak	0.0%	3.55
C 2068	O 382	ASN 47	4GRW 1	weak	0.0%	2.63

**INTERACTION OF KAEMFPEROL WITH STAT-3**

Interaction Data of kaempferol with human stat3 target

Ligand: :

Receptor: 5U5S: TRANSCRIPTION

Heavy atoms: ligand = 33, receptor = 1033

ligand	receptor	residue	chain	type	score	distance
H 2064	O 815	MET 51	5U5S 1	H-don	36.0%	1.78
O 2063	ND 1316	ASN 81	5U5S 1	H-acc	35.3%	3.04
C 2124	O 447	PRO 28	5U5S 1	weak	0.0%	2.89
C 2114	O 502	LYS 31	5U5S 1	weak	0.0%	3.06
C 2114	C 501	LYS 31	5U5S 1	weak	0.0%	3.52

**INTERACTION OF CINNAMIC ACID TNF-ALPHA**

Interaction Data of cinnamic acid with tnf alpha

Ligand: :

Receptor: 5U5S: TRANSCRIPTION

Heavy atoms: ligand = 13, receptor = 1033

ligand	receptor	residue	chain	type	score	distance
H 2085	O 447	PRO 28	5U5S	1 H-don	73.2%	1.54
H 2085	O 502	LYS 31	5U5S	1 H-don	10.7%	2.82
H 2081	O 815	MET 51	5U5S	1 H-don	34.9%	1.75
H 2083	O 815	MET 51	5U5S	1 H-don	18.6%	3.12
H 2079	OD 1315	ASN 81	5U5S	1 H-don	69.4%	1.48
O 2063	OH 680	TYR 43	5U5S	1 H-acc	67.8%	2.49
O 2080	ND 1316	ASN 81	5U5S	1 H-acc	93.8%	2.57
O 2063	O 447	PRO 28	5U5S	1 weak	0.0%	4.37

**REVIEW OF LITERATURE:**

1. **Tundis R et al.**, states that psoriasis is a auto-immune disorder. It is not a infection and is non spreadable disease. It occurs at any stage and it is effected by both the environmental and genetic factors. Natural compounds, molecular targets and mechanisms may help in designing a new Anti-psoriatic drugs. The herbal formulas and phytochemicals may help in finding the efficacy of treatments. Natural products are used in the management of psoriasis and also for many skin diseases. Mechanisms of these molecules may help to develop an effective and preventive treatment for psoriasis.

2. **B.V.Vakil et al.**, states, Anti-psoriatic agents substitutes are used in analogues of flavonoids like kaempferol and quercetin in order to recognize the biological activity and the molcular weight of the newly designed drugs. The current study is helpful in designing new drug and also to know chemical synthesis with more effective Anti-psoriatic agents.

3. **Chandrasekar R et al.**, states that skin diseases are divided into two types that is acute and chronic conditions. Chronic diseases can't be cure but can be managed by using drugs, many herbal remedies are used to treat skin disease like psoriasis. The medicinal drugs used gives so many side effects to overcome this problems the researchers are finding for new, safer and effective drugs from the natural products. This review has been prepared in order to collect objective and to collect pharmacological reports on anti-psoriatic plants along with their formulation. Plants selected have significant value and also active chemicals (phytoconstituents).

4. **Andrea Nicole et al.**, states that psoriasis is inflammatory skin disorder, the cases of psoriasis is increasing day by day, with a impact on patients quality of life. Due to the unstable diet and daily life most of the humans are effected by both genetic and environmental factors. Alternatives medicines are chosen by the patients due to the unsatisfactory therapeutic options in terms of safety and efficacy. The review is about the use of pharmacological herbal remedies with anti-psoriatic activity. Numbers of plants act as a anti-psoriatic agents, it also deals with the interaction of phytochemicals molecules and immuno-pathogenesis mechanisms. The formulations are tested in vitro and vivo especially for patients with Psoriasis vulgaris.

5. **Massimo Biondi\* et al.**, states that Boswellic acid is used for number of diseases. A topical administration is used to carry active compounds in eczematous and psoriatic patients. Vacciniummyrtillus is very effective in the treatment of psoriatic lesions, which is generally a seed oil. Boswellic acids is very effective against psoriasis including inflammatory diseases and asthma.

6. **Mahovic D et al.**, states that psoriasis is a auto- immune disorder which is spread all over the world. The two response help to manage the psoriasis disease. Acupuncture shows a positive effect on psoriasis and the data is collected from the literature. The acupuncture method is used to prevent number of diseases. This review reveals that psoriasis and chronic migraines is treated with acupuncture course. Phototherapy is used instead of other therapies to treat psoriasis. When the acupuncture treatment is going on the patient should not used other therapies excluding bland emollients.

#### **AIM :**

To perform the extraction of chemical constituents and evaluation of chemical constituents.

To study the safety and psoriatic activity of poly-phyto formulation of anti-psoriatic drugs

#### **OBJECTIVES:**

- To perform the selection of chemical constituents.
- To perform molecular docking of phyto-constituents.
- To perform prediction toxicity of phyto-constituents.
- To Assess the changes in the skin before and after application of formulation.

#### **NEED FOR THE STUDY:**

Psoriasis causes great physical, emotional and social burden in general, is often significantly impaired Disfiguration, disability and marked loss of productivity are common challenges for people with psoriasis.

To determine the application of prepared formulation on the psoriatic patients for obtaining Psoriasis Area Severity Index (PASI).

There is no proper cause and treatment is based on external factor

#### **PLAN OF WORK**

- SELECTION OF PLANTS WITH IL12, IL23STAT3, TNF ALPHA TARGETACTIVITY.
- SELECTION OF PHYTOCONSTITUENTS.
- DOCKING OF PHYTOCONSTITUENTS.
- SAFETY AND TOXICITY STUDIES.
- EXTRACTION AND ANALYSIS.

- FORMULATION PREPARATION.
- PRECLINICAL TESTING ON ANIMALS.
- APPLICATION OF FORMULATION TESTING ON HEALTHY HUMAN VOLUNTEERS

#### **EXTRACTION OF CHEMICAL CONSTITUENTS:**

##### **KAEMPFEROL:**

kaempferolis purchased from Herbal health limited: C-2, Himayatnagar, Indra Park Road.

Hyderabad - 500025 Telangana, India.

##### **PUNINIC ACID:**

**APPARATUS:** Blender, beaker, separating funnel and magnetic stirrer.

**CHEMICALS:** Hexane, 10% NaoH.

**PROCEDURE:** Pomegranate seeds were dried in aseptic conditions shade dried with little or absence of sunlight. The dried up seeds were detached and further crushed into fined powder with the aid of mixer. The crushed seeds were transfer into the a beaker and boiled and refluxed with hexane. To the hexane layer 10% NaoH solution is added and subjected to heating for 10-20 minutes. The extract is taken into separating funnel and removed the hexane layer. To the water layer add fresh hexane and remove the hexane layer that consist of puninic acid. Evaporate the residue and the puninic acid percentage 65-85% (purification).

##### **IDENTIFICATION TEST:**

Test for carboxyl group:  $Kmno_4$  + extract on the TLC plate and development tank prepare  $Kmno_4$  solution. Immerse the TLC plate in the  $KMNO_4$  solution.

**IDENTIFICATION:** White spot appears carboxyl group presence.

##### **GLYCITEIN:**

**APPARATUS:** Beakers, separating funnels, glass rod, tripod stand, and spatula.

**CHEMICALS:** Soya bean powder, Hcl, ethyl alcohol, NaoH, Sodium sulfite, and ethyl acetate.

**PROCEDURE:** Soya bean powder is collected from Big Bazar. The powder is blended in the blender and is pass through the sieve-no=60 and fined powder is collected. Then prepare the 0.1ml Hcl and boiled for 20 minutes, then to it add ethyl alcohol. Perform vacuum filtration by using buchner funnel to evaporate ethyl alcohol. And to the obtain solution add 10% NaoH and heat in a separating funnel, then adjust PH from 5-10. Add ethyl acetate to solution and shake the separating funnel and remove the ethyl acetate layer. After this once again add ethyl acetate to the solution and discard the water layer and collect ethyl acetate layer. Add Sodium Sulfate to ethyl acetate layer and heat. After heating the collect the final product.

**CINNAMIC ACID:** Cinnamic acid is purchased from India Mart.

##### **GEL FORMULATION:**

Take 0.2grams of carbopol and dissolved it in water and mixed it well. After dissolving a thick paste forms keep the sample to the corner. Then check the solubility of four samples, Kaempferol is dissolve in water, Hexane is dissolve in water, Glycitein is dissolve in alcohol and Cinnamic acid is dissolve in water. Then dissolve all the four solutions in

polyethylene glycol. Now mix this solution to the above thick paste solution and mixed it continuously. By continuously stirring a thick gel is form, now add triethylamine to the thick gel and adjust the PH 5-7. Then to the gel add preservatives that ismethylparaben and propylparaben in order to preserved the gel.

## RESULTS AND DISCUSSION:-

### RESULT:

The phytochemicals selected based on rational approach is found to be less toxic and has pharmacological activity. Animal studies are This method convenient and time-saving when compared to the Trial and Error method.

**CONCLUSION:**Rational selection of phyto-chemicals were docked by molecular docking is already present in Ayurvedic practice and the formulation prepared was tested on the preclinically. Rational selection is method of reducing animal killing and sacrifice

### ABBREVIATIONS:-

ADME:- Absorption, Distribution, Metabolism, Excretion.

CD4+:- Cluster of differentiation

COMFA :- Comparative Molecular Field Analysis.

COMSIA :- Comparative Molecular Similarity Index Analysis.

CPCSEA:- The Committe for the purpose of Control and Supervision of Experiments on Animals.

DC'S:- Dendritic Cells.

HLA :- Human Leukocyte Antigen.

IFN g:- Interferon Gamma.

IL-12:- Interleukin - 12.

IL-23:- Interleukin - 23.

IL-12RB1:-Interleukin - 12 receptor b1.

IL-23P19:- Interleukin - 23p19.

IL-23R:- Interleukin -23 receptor.

IL-12p35 - Interleukin - 12p35.

JAK1:- Janus Kinase 1.

JAK2:- Janus Kinase 2.

LD-50:- Lethal Dose - 50.

LT-ALPHA:-Limphotoxin - Alpha.

NF-KB1:- Nuclear Factor Kappa B1.



PASI :- Psoriasis Area Severity Index.

STAT-3:- Signal Transducer and Activator of Transcription- 3.

STAT-21:- Signal Transducer and Activator of Transcription - 21.

Th1:- T helper cells 1.

Th17:- T helper cells 17.

TNF-ALPHA:- Tumor Necrosis Factor- Alpha

TNF-R1:- Tumor Necrosis Factor - Receptor 1.

TNF-R2:- Tumor Necrosis Factor - Receptor 2.

TPA :- Tissue Plasminogen activator.

TYK1:- Tyrosine Kinase 1.

TYK2:- Tyrosine Kinase 2.

PASS :- Pull-Aim-Squeeze-Sweep.

#### REFERENCE:

1. Antonella Di Cesare<sup>1,2,3</sup>, Paola Di Meglio<sup>1,3</sup> and Frank O. Nestle<sup>1</sup>: The IL-23/Th17 Axis in the Immunopathogenesis of Psoriasis, *Journal of Investigative Dermatology*, (2009) 129, 1339–1350; doi:10.1038/jid.2009.59; published online 26 March 2009.
2. Ken Miyoshi<sup>1,5</sup>, Mikiro Takaishi<sup>1,5</sup>, Kimiko Nakajima<sup>1</sup>, Mitsunori Ikeda<sup>1</sup>, Takashi Kanda<sup>1</sup>, Masahito Tarutani<sup>1</sup>, Tatsuo Iiyama<sup>2</sup>, Naoki Asao<sup>3</sup>, John DiGiovanni<sup>4</sup> and Shigetoshi Sano<sup>1</sup>: Stat3 as a Therapeutic Target for the Treatment of Psoriasis: A Clinical Feasibility Study with STA-21, a Stat3 Inhibitor, *Journal of Investigative Dermatology*, (2011) 131, 108–117; doi:10.1038/jid.2010.255, published online 2 September 2010.
3. P J Mease: Tumor necrosis factor (TNF) in psoriatic arthritis: pathophysiology and treatment with TNF inhibitors, Correspondence to: Professor P J Mease, Seattle Rheumatology Associates, 1101 Madison St, Seattle, WA 98104, USA; [pmease@u.washington.edu](mailto:pmease@u.washington.edu), April 2002.
4. Bonesi M, Loizzo MR, Provenzano E, Menichini F, Tundis R: Anti-Psoriasis Agents from Natural Plant Sources, 2016;23(12):1250-67.
5. P. K. Sharma and B. V. Vakil: Predictive QSAR analysis of Flavonoid analogues as Anti-psoriatic agents, Guru Nanak Institute for Research and Development, G. N. Khalsa College, Nathalal Parekh Marg, Matunga, Mumbai - 400019, Maharashtra India. 2017.
6. Chandrasekar R.\* Sivagami B: Alternative treatment for psoriasis - MNR College of Pharmacy, Published on May 15, (2016).
7. Stefano Togni,<sup>1</sup> Giada Maramaldi,<sup>1</sup> Francesco Di Pierro,<sup>2</sup> Massimo Biondi<sup>3</sup>  
<sup>1</sup>Indena S.p.A., Milan, Italy; <sup>2</sup>Velleja Research, Milan, Italy; <sup>3</sup>Dermatology Unit, ASL Piacenza, Piacenza, Italy: A cosmeceutical formulation based on boswellic acids for the treatment of erythematous eczema and psoriasis, 11 November volume 2014: 7 Pages 321-327.
8. Mahović D<sup>1</sup>, Mrić F: Acupuncture as a Complementary Method of Traditional Psoriasis Treatment: Myth or Reality: 2016 Aug;24(3):221-2.