# Efficacy Of Leflunomide In Treatment Of Psoriasis Vulgaris

***Thesis***

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| AA | Arachidonic Acid |
| ACR | American College of Rheumatology |
| ALT | Alanin aminotransferase |
| AMPs | Antimicrobial Peptides |
| APC | Antigen-Presenting Cell |
| AST | Aspartate aminotransferase |
| BB | Broadband |
| BC | Before Christ |
| BMI | Body Mass Index |
| CCHCR | Coiled-Coil α-Helical Rod Protein |
| CD | Cluster of Differentiation |
| CDSN | Corneodesmosin |
| CLA | Cutaneous Lymphocyte-associated Antigen |
| COX | Cyclooxygenase |
| cPcASI | Computer aided psoriasis continuous area and severity score |
| CRABP | Cytosolic Retinoic Acid-Binding Protein |
| DC | Dendritic Cells |
| DHA | Docosahexaenoic Acid |
| DLQI | Dermatologic Life Quality Index |
| DMARD | Disease Modifying Antirheumatic Drugs |
| EGF | Epidermal Growth Factor |
| EGF-R | Epidermal Growth Factor Receptor |
| EPA | Eicosapentaenoic Acid |

# LIST OF ABBREVIATIONS

| | |
|---|---|
| FDA | Food and drug Admnistration |
| FS | Felty's syndrome |
| HEV | High Endothelial Venule |
| HLA | Human Leukocyte Antigen |
| ICAM | Intercellular Adhesion Molecule |
| IFN | Interferon |
| IL | Interleukin |
| INR | International Normalized Ratio |
| LCD | Liquor Carbonis Detergens |
| LEF | Leflumoide |
| LFA | Lymphocyte Functional Antigen |
| LS-PGA | Lattice-System Physician's Global Assessment |
| LT | Leukotriene |
| LCE | Late Cornified Envelope |
| MDA | Malondialdehyde |
| MHC | Major Histocompatipility Complex |
| MMP | Matrix Metalloproteinase |
| MOP | Methoxy Psoralen |
| MTX | Methotrexate |
| NB | Narrowband |
| NF | Nuclear Factor |
| NSAIDs | Non Steroidal Anti-inflammatory Drugs |
| P III –NP | Aminoterminal peptide of type III procollagen |
| PASI | Psoriasis Area and Severity Index |
| PDI | Psoriasis Disability Index |
| PGA | Psoriasis Global Assessment |

# LIST OF ABBREVIATIONS

| | |
|---|---|
| PGE2 | Prostaglandine E2 |
| PLSI | Psoriasis Life Stress Inventory |
| PMNL | Polymorph Nuclear Leucocyte |
| PsA | Psoriatic arthritis |
| PsARC | Psoriatic Arthritis Response Criteria |
| PSORIQoL | Psoriasis Index of Quality of Life |
| PUVA | Psoralen with Ultraviolet A |
| RA | Rheumatoid Arthritis |
| RAR | Retinoic Acid Receptors |
| rUMP | Ribonucleotide Uridine Monophosphate |
| SD | Standard Deviation |
| SLE | Systemic lupus erythematosus |
| SPSS | Statistical package for social science |
| TCR | T Cell Receptor |
| TGF | Tumor Growth Factor |
| TH | T Helper |
| TLRs | Toll Like Receptors |
| TNF | Tumor Necrosis Factor |
| UVA | Ultraviolet A |
| UVB | Ultraviolet B |
| VDR | Vitamin D receptor |
| VEGF | Vascular Endothelial Growth Factor |
| VPF | Vascular Permeability Factor |
| WG | Wegener's granulomatosis |

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# Introduction

Psoriasis is a multisystem disease with predominately skin and joint manifestations affecting approximately 2-3% of the population. Psoriasis may be associated with autoimmune diseases such as inflammatory bowel disease, diabetes, cardiovascular diseases and lymphoma[(1)].

Evidence suggesting that psoriasis involves immunologic mechanisms includes the efficacy of immunosuppressive drugs in controlling the disease such as: methotrexate, cyclosporine (cya), immune-targeting biologic agents, immunotoxins (denileukin, diftitox) and tumor necrosis factor (TNF) blocking biologics. Also exacerbation of psoriasis by certain cytokine therapies such as: Interferons (α, β, γ) and interleukin (IL2) supports this suggestion[(2)].

Psoriasis treatment options consist of topical therapies, phototherapy and systemic therapies including biologics[(3)].

Patients with moderate to severe psoriasis are candidates for systemic therapy including biologic agents and phototherapy[(4)].

Leflunomide is a type of drug known as a disease – modifying anti-rheumatic drug (DMARD). Leflunomide is used to treat rheumatoid arthritis (RA) and other types of arthritis where the immune system attacks its own tissues. The efficacy of Leflunomide in RA and anti-lymphocytic mode of action suggested that Leflunomide might be a promising candidate for the treatment of psoriatic arthritis and psoriasis[(5)].

Leflunamide has many advantages to offer in the treatment of (PsA) and psoriasis : it is well tolerated in the majority of patients, convenient and effective in moderating joint and skin symptoms and improving quality of life. In addition, orally administrated Leflunomide may have benefits in cost and ease of use compared with biologic agents[5].

# Aim of the work

The aim of this study is to evaluate the efficacy and safety of Leflunomide in treatment of patients with moderate to severe plaque type of psoriasis.

**Psoriasis** is a common cutaneous inflammatory hyperproliferative disorder. It is a life long disease with spontaneous remissions and exacerbations and characterized clinically by chronic, sharply demarcated dull red scaly plaques affecting mainly the extensor prominences, scalp, and the sites of trauma[6].

## History :

Hippocrates and his school (460-377 BC) provided objective and meticulous descriptions of many skin disorders. In their classification, dry scaly eruptions were grouped together under the heading 'lopoi'. This group probably included psoriasis and leprosy[7].

During 129-99 BC, the word 'psora' was first used to describe a skin disorder characterized by a scaliness of the eyelids, corners of the eyes, and scrotum. The condition was pruritic and excoriations were present. Although called psoriasis, this affliction was probably a type of eczema. In fact, the meaning of 'psora' is a desquamative condition[7].

Perhaps the oldest treatment for psoriasis has been exposure to sunlight. Even in pre biblical times, it was noted that 'leprosy' improved with exposure to the sun. At least some of these patients certainly had psoriasis. Until quite recently, new treatments for psoriasis were based on empiric observations[7].

## Epidemiology :

Psoriasis is a common disease that affects 2-3 % of world's population. There is significant geographical variability with the lowest incidence of the disease seen at the equator and increasing frequency towards the poles. Psoriasis is more common among northern European

Caucasians, less common among Asian or African populations and least common among natives of north and south America[8].

Although some studies find minor deviations, psoriasis is equally common in males and females[9]. Several studies have reported an earlier age of onset in females, but this is not universally observed. There is no evidence for morphological differences in psoriasis between males and females[10].

Psoriasis may first appear at any age. It is most likely to appear between the ages of 15 and 30 years but ranges from birth to the eighth or ninth decade. There was one case report documenting onset at 108 years of age[11].

Different age of onset peaks in patients with psoriasis were reported by Henseler and Christophers,[12] who showed that the possession of certain Human Leukocyte Antigen (HLA) class I antigens, particularly HLA-CW6, is associated with an earlier age of onset and with a positive family history. These findings led Henseler and Christophers to propose that two different forms of psoriasis exist: type I psoriasis with age of onset before 40 years and HLA-associated, and type II, with age of onset after 40 years and lacking HLA associations[12].

## Triggering factors :

1. **Trauma :**

The Koebner phenomenon i.e. the elicitation of psoriatic lesions by injury to the skin, is observed in approximately 25% of patients with psoriasis.[13] The lag time between the trauma and the appearance of skin lesions is usually 2-6 weeks. Studies show that HLA-CW6 positive patients show high incidence of the Koebner phenomenon[14].