

Original Research Article

Effect of *Caesalpinia Pulcherrima* Leaf Extract against Imiquimod Induced Psoriasis in Mice Model

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Abstract: Psoriasis, a non-communicable and immune-mediated inflammatory skin disorder, which is characterized by sharply demarcated, red, scaly plaques most often on the elbows, knees, scalp, and lumbar area. Available modern therapy for psoriasis has adverse events that lead to further complications in patients. Therefore, searching for effective and safe anti-psoriatic drugs in relative low price from traditional medicine or natural products has enormous social and economic benefits. *Caesalpinia pulcherrima* has wide traditional usage for various disorder including skin diseases. Current study was undertaken to evaluate the anti-psoriatic effect of ethanolic leaf extract of *Caesalpinia pulcherrima* against Imiquimod induced psoriasis in Swiss mice. Ethanolic extract of *Caesalpinia pulcherrima* leaves were prepared by exhaustive extraction method. The animals were divided in to four groups of six animals each, and the groups were served as normal control, psoriasis control, reference control and 1% *Caesalpinia pulcherrima* treated group. Retino-A 0.025% was used as reference drug. After induction of psoriasis with Imiquimod 5% cream, all the test drugs were applied topically for 16 days. At the end of the study, erythema (Intensity Score), skin thickness and epidermal thickness were measured as an index of psoriasis. 1% of ethanolic leaf extract of *Caesalpinia pulcherrima* showed anti-psoriatic activity by significantly reducing the erythema, skin thickness and epidermal thickness compared to Imiquimod induced psoriasis in Swiss mice. From the result it was concluded that, ethanolic extract of *Caesalpinia pulcherrima* leaves exhibited anti-psoriatic activity.

Keywords: *Caesalpinia pulcherrima*, Psoriasis, Erythema, Imiquimod, Retino-A and Skin disease.

INTRODUCTION

Psoriasis is a chronic, immune-mediated inflammatory skin disease that is often associated with systemic manifestations. It is a lifelong disease that can have negative impact on patients' quality of life. Psoriasis has a strong genetic component but environmental factors play an important role in the presentation of this disease (Lonnberg AS *et al.*, 2016). Psoriasis affects approximately 2.0% to 3.0% of the world's population (Springate DA *et al.*, 2017). To date, epidemiological studies have demonstrated variable prevalence among different population and ethnic groups worldwide. Higher prevalence rates were found in western countries while lower rates were observed in Latin Americans, Indians, Africans (Egypt and Tanzania) (Parisi R *et al.*, 2013), and in Asia at less than 0.5% (Rachakonda TD *et al.*, 2014). The wide variation in estimates of prevalence between regions

may be attributed to the differences in ethnic or racial composition, genetics, and environmental and climate conditions (Alexis AF and Blackcloud P, 2014). Conventional therapies such as corticosteroids, vitamin D3 analogues, and calcineurin inhibitors are currently used as topical therapies in mild psoriasis. Severe psoriasis often necessitates treatment with phototherapy or systemic agents including methotrexate, cyclosporine, and acitretin (Menter A *et al.*, 2009). However, most of these regimens have well documented arrays of adverse effects that seem to be the main factor hampering patients' adherence to long-term psoriasis treatment (Manter A *et al.*, 2008), suggesting a need for development of a drug that would provide improved effectiveness but with fewer side effects. Traditional medicine, which provides front-line pharmacotherapy for billions of people worldwide, represents a possible source of a solution.

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The wood is bitter, dry, sour, cooling; cure "vata" biliousness, fever, delirium, ulcers, strangury, urinary concentration and blood complaints. It is considered astringent and sedative. It is useful in vitiated condition of pitta. An infusion of the wood is a powerful astringent and emmenagogue. It is used in atonic diarrhea and dysentery, and its paste in rheumatism, hemorrhages and to treat wounds. Hot aqueous extract and chloroform extract of wood exhibited inhibitory action on cyclic AMP phosphodiesterase. The methanolic extract of the *Caesalpinia pulcherrima* lignum showed sleep time-elongation effect in mice and significant anti-hypercholesteramine activity. Brazilin dye is reported to have anti-inflammatory activity (Pawar *et al.*, 2008). The trunk wood possesses antibacterial, demulcent and haemostatic properties. It is used in contusion, wounds, dysmenorrhoea, impetigo, leucorrhoea and anaemia (Kirtikar and Basu, 1987). El-Nashar HAS *et al.*, 2015, reviewed several pharmacological activities by using extracts of different plants of *Caesalpinieae* tribe were reported to possess a wide range of pharmacological activities, including anti-oxidant, anti-bacterial, anti-inflammatory, cytotoxic, anti-diabetic, antifungal, hepatoprotective, gastroprotective, analgesic, anti-arthritis, anti-filarial, antimalarial, anthelmintic, amoebicidal, diuretic, anti-psoriatic, anti-estrogenic, anti-fertility, wound-healing, anxiolytic, cardioprotective, immunomodulatory and anti-HIV activities. The study was designed to evaluate the anti-psoriatic efficacy of ethanolic leaf of extract *Caesalpinia pulcherrima* against Imiquimod induced psoriasis in mice.

MATERIALS AND METHODS

Plant Collection and Authentication

The leaves of *Caesalpinia pulcherrima* were collected from the outskirts of Erode district. The plant was identified as *Caesalpinia pulcherrima* and authenticated by the botanist, Botanical Survey of India, Agricultural University, Coimbatore. The voucher specimen (BSI/SRC/11/72/2017-18/Sci/01297) has been deposited in the herbarium for future reference.

Preparation of Extract

The collected leaves were washed in running tap water to remove soil debris, shade dried and ground to coarse powder. The powder was then subjected to exhaustive extraction using 90% ethanol, at room temperature for 7 days by maceration. The ethanolic extract is concentrated by vacuum distillation to dry. The collected extract was stored in desiccators and used for further pharmacological study.

Animals

Swiss albino mice of either sex, weighing between 18- 22 gm were used for this study. The animals were obtained from animal house, of Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry. The animals were placed at random and allocated to treatment groups stainless steel cages. Animals were housed at a temperature of $24 \pm 2^\circ\text{C}$ and relative humidity of 30 – 70 %. A 12:12 light: day cycle was followed. All animals were allowed to free access to water and fed with standard commercial pelleted rat chaw (M/s. Hindustan Lever Ltd, Mumbai). All the experimental procedures and protocols used in this study were reviewed and approved by the Institutional Animal Ethics Committee (932/a/06/CPCSEA).

Imiquimod Induced Psoriasis

The animals were divided into four groups. Each group consists of six mice. All the animals were shaved on the back using commercially available hair removal cream. After 24 h of hair removal, 62.5 mg of Imiquimod (translating 3.125 mg of active compound) was applied on the shaved back using the applicator brush for 7 consecutive days for all the animals except for normal group (Van der Fits L, *et al.*, 2009).

Group-I mice served as normal control received normal saline. Group-II mice served as disease control which was induced psoriasis with Imiquimod 5% cream at a dose of 62.5 mg (translating 3.125 mg of active compound) on the shaved back topically for 7 consecutive days. Mice were given acetate in drinking water for 7 days to enhance Imiquimod-induced skin inflammation (Muruganatham N *et al.*, 2011). Group-III mice served as standard control which was induced psoriasis same as Group-II animals. On the 8th day, Retino-A 0.025% was applied topically for the other 16 days. Group-IV mice were induced with psoriasis same as Group-II animals. On the 8th day, *Caesalpinia pulcherrima* leaf extract was applied topically as a 1% concentration for 16 days. On every alternate day, the thickness of skin was measured using a digital micrometer. The increase in skin thickness was taken as a measure of skin inflammation. The severity of inflammation on the back skin- an objective scoring system was developed based on the clinical Psoriasis Area and Severity Index (PASI). Erythema and epidermal thickness were scored independently on a scale from 0 to 4: 0, none; 1, slight; 2, moderate; 3, marked; 4, very marked (Nadeem A *et al.*, 2017).

Statistical Analysis

Results were expressed as mean \pm SEM. The data were analyzed by using one way analysis of variance (ANOVA) followed by Dunnet's 't' test using Graph Pad version 3. P values < 0.05 were considered as significant.

RESULT

Table 1. Effect of ethanolic leaf extract of *Caesalpinia pulcherrima* against Imiquimod induced psoriasis in mice

Drug Treatment	Erythema (Intensity Score)	Skin Thickness (mm)	Epidermal Thickness (mm)
Group I Normal Control	-	0.83±0.02	0.22±0.02
Group II Psoriasis Induced Control Imiquimod 5%	9.53±0.65	3.07±0.22	1.43±0.09
Group III Reference Control Retino-A 0.025%	2.77±0.09***	0.97±0.02**	0.25±0.01**
Group IV <i>Caesalpinia pulcherrima</i> 1%	2.97±0.13***	0.98±0.04**	0.26±0.01**

Values are in mean ± SEM (n=6), *P<0.05, **P<0.01, ***P<0.001 Vs Induced Control

Anti-psoriatic activity of ethanolic leaf extract of *Caesalpinia pulcherrima* was studied against Imiquimod induced psoriasis in mice and the results were shown on table 1. Erythma, skin thickness and epidermal thickness of Psoriasis control was 9.53±0.65, 3.07±0.22 and 1.43±0.09 respectively. There was significant (P<0.001) decrease in the Erythma to 2.77±0.09 compared to induced control and the skin thickness & epidermal thickness was also significantly (P<0.01) decreased in the animals treated with Retino – A. The test drug ethanolic leaf extract of 1% *Caesalpinia pulcherrima* has also produced similar effect as that of the reference control. It was also significantly (P<0.001) decreased in the Erythma to 2.97±0.13 compared to induced control and the skin thickness & epidermal thickness was also significantly (P<0.01) decreased to 0.98±0.04 and 0.26±0.01. The effect produced by *Caesalpinia pulcherrima* was equipotent as that of the reference control Retino – A.

CONCLUSION

Ethanolic leaf extract of *Caesalpinia pulcherrima* exhibited anti-psoriatic activity against Imiquimod induced psoriasis in mice. The study authenticates the folk claim of *Caesalpinia pulcherrima* which could be used as natural therapeutic drugs to prevent complications of psoriasis. Further investigation on *Caesalpinia pulcherrima* is needed to evaluate the efficacy as well as exact mechanism of its antipsoriatic property.

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