International Invention of Scientific Journal

Available Online at http://www.iisj.in

eISSN: 2457-0958

Volume 05 | Issue 09 | September, 2021 |

Original Article- MICROBIOLOGY AND BIOTECHNOLOGY

Botanical warriors to combat pro-inflammation mediators – A way forward for Psoriasis management

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Article Received 26-07-2021 /Article Accepted 26-08-2021 / Article Published 10-09-2021

Abstract

Psoriasis is an auto immune condition with clinical symptoms such as scaling and inflammation and often the inflammatory mediators play a major role in psoriasis condition. Management of pro-inflammatory mediators does not require steroidal preparations instead certain botanicals can be effectively used. A tectonic shift in the treatment strategy of psoriasis is required from direct drug intervention to management of pro-inflammatory mediators. We, in the present study have established the role of certain herbs in neutralizing the pro-inflammatory molecules such as IL alpha 1, TNF and IL8 using HaCaT cell line. Our findings prove the usefulness of certain botanicals to prolong the remission phase of Psoriasis. Details are presented in the article.

Key words: Psoriasis treatment, Pro-inflammatory mediators, inflammation, Psorolin B

How to Cite:

Amruthavalli, G., V, A., & R, G. (2021). Botanical warriors to combat pro-inflammation mediators – A way forward for Psoriasis management. *International Invention of Scientific Journal*, *5*(09), Page: 21-24. Retrieved from https://iisj.in/index.php/iisj/article/view/341

Introduction

Botanicals and the allied preparations have been used extensively for the management of various diseases by man since time immemorial (1).Undoubtedly the herbal actives have shown promising therapeutic value for various alignments. The botanicals (herbal actives) are always used either as a conglomeration of several plants or single herb preparation which contains several phyto-actives of the same plant. The non-communicable disease burden has increased significantly in the recent times at global level alongside increased incidences of various infectious diseases including the COVID-19 that shocked the world (2,3).

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For the management of non-communicable diseases like psoriasis, people have started to rely on herbal remedy as the herbal remedies are relatively cost effective, known to produce less side-effects and are often prepared with known species of plants having edible value (safe).Several herbal preparations have shown effect in the management of Psoriasis with remarkable reduction in inflammatory reactions as well resulting in prolonged remission phase (4). We were agog to know how the herbal preparations may be offering relief from the inflammatory reactions in psoriasis which always manifests in cyclic manner.

In order to understand the above science we have used a formulation that contains the herbal extracts of *Wrightia tinctoria*, *Cynadon dactylon, Boswellia serrata* and *Hydnocorpus igdhiyana* besides ochre of iron to study.

We have studied the effect of the above herbal-metal conglomerate in an immortalized Keratinocyte cell culture insulted with non-ionizing UV rays to release inflammatory mediators and then studied the release of the key pro-inflammatory molecules such as IL 6, IL 8 and TNF alpha 1 by enzyme linked absorbent assay (ELISA).

Findings of the study gave us a new dimension to postulate the importance of pro-inflammatory mediation by herbal actives and the use of botanical preparations to manage Psoriasis and avoid inflammatory manifestation.Details are presented in the paper.

Materials and Methods

Preparation of extracts of the *Wrightiatinctoria, Cynodondactylon, Boswelliaserrata, Hydnocorpusigdhiyana*

The above plant materials (leaf or total plant or seed whichever is applicable) were taken and boiled in coconut oil by keeping the solute: solvent ratio at 1:33.3. Then the mixture was filtered and the filtrate was used.

Preparation of herbal formulation (extract conglomerate):

Oil extracts of *Wrightiatinctoria and Cynodondactylon* were mixed at 3.33% and the other two oil extracts were mixed at 1% and then adjusted to 100ml with the help of base (coconut oil or cream). To the above conglomerate, the ochre of iron at 0.2% was added.

Cell culture and UVB irradiation

Immortalized keratinocytes HaCaT cells were used for the present study and the cells were cultured in Dulbecco's modified Eagle medium (DMEM) containing 10% fetal bovine serum (FBS) and 1% antibiotics (100 U/mL penicillin and 100 µg/mL streptomycin) and incubated in a humidified incubator at 37°C and 5% CO2 (5).

HaCaT cells were irradiated by UVB (25 mJ/cm2) using a UV lamp with a peak emission of 312 nm.

Cell Viability Assay

Cell viability after treatment with extract conglomerate at 10, 20, 30 and 50 µg/ml was determined using the colorimetric 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl- 2H-tetrazolium bromide (MTT) assay (6).

HaCaT cells were seeded at 5×10^4 cells per well in 24-well plates and were then treated with various concentrations of test products; incubated for 24 h. Then, the media in all wells was replaced with MTT solution (5 mg/mL) and the plates were again incubated for 4 h at 37°C. Finally, the MTT-containing medium was removed by aspiration and 1 mL of dimethyl sulfoxide (DMSO) was added to each well. The absorbance was measured at 540 nm.

Determination of IL-6, IL-8 and TNF-α (7)

HaCaT cells were seeded in 24-well plates at a density of 5×10^4 cells per well for the determination of TNF-α, IL-8, and IL-6 levels. After 24 h, the cells were irradiated with 25 ml/cm^2 UVB (as described in the cell culture and UVB irradiation section above) and treated with various concentrations of extract conglomerate as described previously, the cells in DMEM medium were incubated for further 24 h. The culture supernatant was harvested and the levels of cytokines released were measured using ELISA kit.

3. RESULTS

The extract conglomerate(herbal formulation) did not exhibit cytotoxic activity up to a concentration of 50 µg/mlsuggesting the safety aspect of the extract conglomerate. Table 1

Table 1: Effect of Extract conglomerate on cell viability

Products	% viable cells versus concentration of the product (µg/ml)			
	10	20	30	50
Extract conglomerate	100	100	90	85

The extract conglomerate has induced the release of all three pro-inflammatory mediators such asIL-8, TNF-α and IL-6 in a concentration dependent manner. Table -2.

Table 2: Effect of extract conglomerate on release of pro-inflammatory mediators

Treatment details	Release of IL-8, TNF-α and IL-6 (%)		
	IL-8	TNF – α	IL-6
0	18	22	76
UV	100	100	100
UV+10	60	90	90
UV+20	50	80	70
UV+30	40	70	50
UV+50	20	50	40

Discussion:

The treatment strategy of Psoriasis needs a tectonic shift from direct drug intervention to modifying the dermal immune ecosystem from releasing the pro-inflammatory mediators which are the precursors to cyclic inflammatory flare up of Psoriasis. The above treatment strategy is needed largely because psoriasis is an incurable disease. Psoriasis is known to exhibit two distinct phases such as meek scaly phase and agonizing inflammatory phase. More often the management of inflammatory phase demands steroidal or immune suppressant therapy and mitosis inhibitors (8). The flare up repeat is controlled by several individual and exogenous factors such as age, food habits, occupation, co-morbid conditions, immune surveillance (Atopy and hypersensitivity) etc. The exogenous factors largely include the climatic factor. Therefore controlling either the intrinsic factors and or the exogenous factors is quite difficult to prevent the episode of inflammatory flare up. At the same time the use of steroidal intervention for prolonged period of time especially in case of frequent repeat of flare-up would produce severe side-effects than the inflammatory manifestation of Psoriasis. Time has come the treatment ground of psoriasis must shift from the treatment to prevention of flare-up because psoriasis is an incurable auto immune disorder.

Our present attempt is to bring a credible science out of herbal conglomerate if possible so that their usefulness for the management of psoriasis can be explored. In our effort we got success and relatively credible scientific evidence for the herbal conglomerate of *Wrightiatinctoria*, *Cynadondactylon,*

Boswelliaserrata and *Hydnocarpusidhiyana*besides ochre of iron for the management of Psoriasis. The modification of pro or pre inflammatory mediators such as IL 6, IL 8 and TNF αare essential to prevent the inflammatory flare up. The present study has clearly shown that the herbal conglomerate can effectively impair the pro-inflammatory molecules and thereby delay the inflammation episode and give high quality of life to psoriatic patients. Although our inferences were more from in vitro studies but the directions clearly indicate the therapeutic potential of herbal conglomerate if further intense research is applied. Further the herbal conglomerate should not be positioned or promoted as drug instead must be promoted for pretreatment intervention or post recovery management purposes only. More intense research may be required to establish unequivocally the therapeutic value and associated mechanism of action of the herbal conglomerate that we have tested. Considering the prior art of the herbs used in the conglomerate either individually or collectively having used for managing psoriasis, our study gives further validation to the scope of herbal preparations for the management of Psoriasis at global level. Further the use of all the above herbs in ancient healing practices in India such as Ayurveda and Siddha reinforce the scientific credence of ancient healing practice and how accurately the herbs have been understood by our ancient science for treating several diseases.

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