INTRODUCTION / ABSTRACT

Psoriasis is a chronic, inflammatory skin disorder, characterized by uncontrolled hyper-proliferation of keratinocytes in the epidermis, disturbed apoptosis, over-secretion of cytokines and angiogenic factors. Anti-psoriatic drugs function by targeting hyperproliferation of keratinocytes, enhancing apoptosis, suppressing inflammation and angiogenesis.

There is an unmet need for the development of herbal therapies for psoriasis on account of high cost and side effects associated with conventional treatments.

Traditional herbal medicines have been widely used for the treatment and management of dermatological inflammatory disorders.

We have developed a novel aqueous mixture (SIRB-001) of 3 Traditional Chinese Medicine (TCM) based herbs namely, Rheum palmatum L. (Da Huang), Rehmanna glutinosa Libosch (Sheng di huang) and Loniceria japonica (jin yin hua) (in the ratio 1:1:3).

SIRB-001 was found to exert highly efficacious effects in psoriasis patients.

Hence, we investigated the anti-psoriatic mechanism of SIRB-001 by using in vitro cell-based systems.

METHODS

Da huang (roots), Sheng di huang (roots) and Jin yin hua (flowers) were conventionally procured and mixed in the ratio of 1:1:3. Herbs were finely powdered, diluted with water, boiled and cooked at 70°C for 1 h. After centrifugation at 5000 rpm for 15 min, the supernatant was used as main stock for experiments. The yield of SIRB-001 extract was 30 mg/ml.

The anti-proliferative effect of SIRB-001 (1.100 – 1.5 v/v) was assessed using immortalized human keratinocyte cell line; HaCaT as the test model by MTT assay.

Pro-apoptotic effect of SIRB-001 was examined by flow cytometry and colorimetric methods.

Inhibitory effect of SIRB-001 (1:10:1:5 v/v) on inflammatory markers; TNF-α, IFN-γ, IL-6, NO and sPLA2 was determined in HaCaT cells against TNF-α stimulated levels by ELISA. Inhibition of IL-17/IL-23 axis was assessed in immune cells; murine splenocytes and human monocytic cell line (THP-1).

VEGF down-regulation in HaCaT cells was studied for anti-angiogenic potential.

Pathway mapping was done by kinase profiling using 2Lyte assays and Topoisomerase-II activity by Kinetoplast DNA Cleavage assay.

The synergistic anti-proliferative potential was also evaluated with standard anti-psoriatic agents such as Methotrexate (MTX).

HPLC fingerprinting

HPLC fingerprinting of SIRB-001 revealed the presence of chlorogenic acid (Rt=13.98 min), Acteoside (Rt=24.22 min) and Rhein (Rt=53.76 min) as identified by comparisons to the retention times and UV spectra of authentic standards under identical analytical conditions.

RESULTS

Anti-proliferative effect

SIRB-001 demonstrated significant (p<0.01) anti-proliferative effect in HaCaT cells. Encouraging results were also observed in combination with MTX.

SIRB-001 exhibited significant (p<0.01) pro-apoptotic effect mediated via early, mid and late markers.

Anti-inflammatory activity

SIRB-001 resulted in significant (p<0.01) downregulation of pro-inflammatory markers (TNF-α, IFN-γ, IL-6, NO, sPLA2) in HaCaT cells and IL-17/IL-23 secretion in immune cells.

Conclusions

SIRB-001 has exhibited in vitro anti-psoriatic properties in keratinocytes, immune cells and cell-free enzymatic assays.

The multifaceted anti-psoriatic action of SIRB-001 is executed by targeting all the hallmark features of psoriasis; hyper-proliferation, apoptosis, inflammation and angiogenesis in keratinocyte arm; IL-17/IL-23 inhibition in immune arm and key signaling markers.

These findings correlate with the anti-psoriatic effect of SIRB-001 in psoriasis patients and provides the scientific proof-of-concept for its anti-psoriatic claim.

Based on the diverse array of in vitro anti-psoriatic properties, SIRB-001 presents a promising and clinically useful polyherbal therapeutic agent for psoriasis.

Further, formulations of SIRB-001 have shown promising in vivo anti-psoriatic activity in TPA and IMQ induced animal models.

2 clinical studies with SIRB-001 based formulations have been successfully completed, demonstrating excellent anti-psoriatic efficacy.

Owing to its strong anti-inflammatory potential, SIRB-001 is also being clinically tested for efficacy in other dermatological skin indications, such as eczema and is showing encouraging results.

REFERENCES


