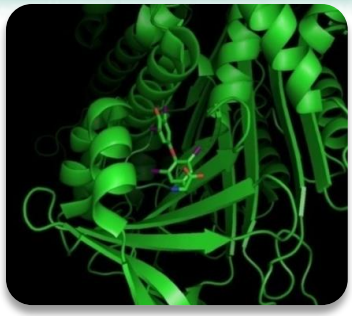
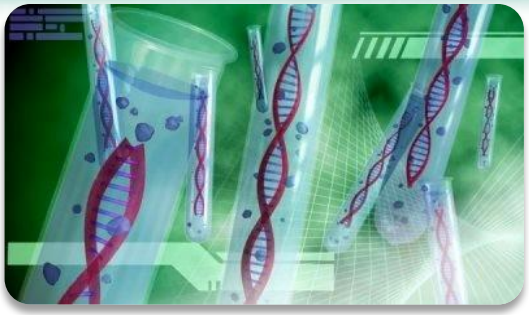




Clinical development of a novel polyherbal product for treatment of Atopic dermatitis & other chronic dermal inflammatory diseases

16th European Dermatology Congress
June 07-08, 2017 Milan, Italy

DABUR RESEARCH FOUNDATION

Dr Manu Jaggi

Chief Scientific Officer
Dabur Research Foundation, INDIA

SIRB 001 - The Product

SIRB-001 is a novel aqueous mixture of 3 Traditional Chinese Medicine (TCM) based herbs

Da-Huang
Radix et Rhizoma Rhei

Sheng Di Huang
Radix Rehmanniae

Jin Yin Hua
Flos Lonicerae

Product Properties

- Fully characterized
- Potent anti- inflammatory
- Clinically validated targets
- Found to be safe for human use
- Tested on over 150 patients
- IP: Over 50 patents filed
- Received provisional clearance for EU commercialization

The journey so far…

DEVELOPMENT OF SIRB-001

2010 2011 2012 2013

Preclinical R&D

Sirbal partners with DRF as a Research Partner

First patent filed

Identify biological target

SIRB-001 Characterization

Conducted Pre-clinical trials for Psoriasis

SIRB-001 Stability and safety research

SIRB-001 efficacy in generic inflammatory dermatological indications

The journey so far…

DEVELOPMENT OF SIRB-001

Ready for commercialization as an OTC product

	2014	2015	2016
Corporate/IP	Initiate IND enabling research	5 US patents granted	Receipt of clearance to sell OTC in Germany 50+ patent applications pending
Preclinical R&D	Pre-clinical trials on AD	Pre-clinical trials on Seborrhoea	1st INTL patent granted Pre-clinical trials on Acne
Clinical Trials	Completed 1st clinical trial for Psoriasis (Germany)	clinical trials for Eczema (India) Clinical trial for Scalp Psoriasis (India)	Clinical Trial Acne (India) Clinical Trial Seborrhoea (India)

R&D and Preclinical status

PRODUCT DEVELOPMENT & CHARACTERIZATION	Fingerprinting analysis performed by HPLC with nine marker compounds.
STABILITY	Studies of raw material and finished product show a shelf life of over 2 years
SAFETY	Extensive studies carried out in preclinical and clinical studies have demonstrated Sirbal's products are safe for topical administration
MECHANISM	Sirbal's products has been demonstrated to work as anti inflammatory & anti proliferative immuno-potentiating product. It down regulated key pro-inflammatory cytokines as TNF-α, IL17/IL23
EFFICACY	Sibal's products are found to be highly effective in several clinical trials for the treatment of Psoriasis, scalp psoriasis, eczema, Atopic Dermatitis, seborrhea and Acne.
REGULATORY	Sirbal's products were developed in accordance with U.S; EU and Indian guidelines and standards

Product development and characterization

- Fully characterized using HPLC, LC-MS & DNA Fingerprinting
- Marker Compounds identified & characterized in each of the constituent herbs of SIRB-001
- Specification developed to include description, marker compound, physicochemical, microbiological & biological analysis to meet global regulatory standards
- Stability performed at different temperature & humidity conditions as per ICH guidelines. Compatibility assessed with packaging material

SIRB-001- Safety

Extensive studies carried out in animals have demonstrated SIRB-001 safe for topical and oral administration

- Found to be safe for use in humans
- Does not cause any skin irritation, sensitization or toxicity
- Non mutagenic
- Does not cause irritation to the eyes
- Free from toxic substances such as parabens

SIRB-001- Clinical experience

Clinical Trials

SIRB-001 has been tested clinically in India and Germany with more than 150 patients.

SIRB 001 has shown excellent tolerability and efficacy in psoriasis, scalp psoriasis, seborrhea & eczema.

Product has completed clinical trials for atopic dermatitis & acne.

Highlights of clinical trial results

Indication	Site	number of subjects	Evidence of clinical efficacy	Key findings
Psoriasis	derma test	21		• Clinical efficacy reported in eight weeks • About 71% of subjects responded • More than 33% of subjects showed 50- 100% improvement in symptoms
Scalp psoriasis	CIDP	30		• Clinical efficacy reported in eight weeks • About 96% of subjects responded • More than 70% of subjects showed 50%–95% improvement in symptoms
Eczema	CIDP	30		• Clinical efficacy reported in four weeks • 83% of subjects responded • More than 46% of subjects showed 50%–85% improvement in symptoms
Seborrhoea	CIDP	30		• Clinical efficacy reported in four weeks • 100% of subjects responded • About 93% of subjects showed 50%–100% improvement in symptoms
Atopic dermatitis	derma test	25		• Clinical efficacy reported in six weeks • More than 76% of subjects in trial responded • About 33% of subjects showed 50%–100% improvement in symptoms
Acne	CIDP	30		• Clinical efficacy reported in eight weeks

Development of SIRB-001 cream

Preparation of different bases of cream using combination of oil/emulsifiers/water .

↓

Selection of preliminary bases based on its physical appearance and viscosity

↓

Trial Batches

↕

Characterization; Phase Separation; Spread ability; Microbial Analysis etc.

↓

In vitro Drug Release
(using dialysis membrane)

↓

Skin permeation studies
(Diffusion through rat skin)

↓

Stability studies (as per ICH guidelines)

SIRB-001 cream

Product formats for different indications

S.No.	Indication	Formulation		Details
1	**Psoriasis**		Cream	Non irritating to the skin
2	**Scalp Psoriasis**		Hair Lotion & Anti Psoriatic Shampoo	Free from SLS ; gentle on the damaged skin
3	**Seborrhoea**		Hair Vitalizer & Anti Dandruff Shampoo	Free from SLS ; easy spreadability of the Vitalizer
4	**Atopic Dermatitis**		Cream	Non irritating to the skin; fit for use by children
5	**Eczema**		Cream	Non irritating to the skin; fit for use by children
6	**Acne**		Acne gel	Non irritating to the skin;

Clinical Development of SIRB 001 as a new treatment modality for Atopic Dermatitis (AD)

STUDY DESIGN

PURPOSE
The purpose of this study was to examine the tolerability of Sirbal cream (SIRB-001) according to clinical-dermatological test criteria. Before the commencement of the trial, all participants were dermatologically examined and evaluated (EASI).

TEST PANEL
25 adult, female and male panellists.
Subjects suffering from atopic dermatitis in an interval not in need of medical treatment aged 18-73 years.

TEST PERIOD
42 days (6 weeks)

TEST AREA
Affected body area

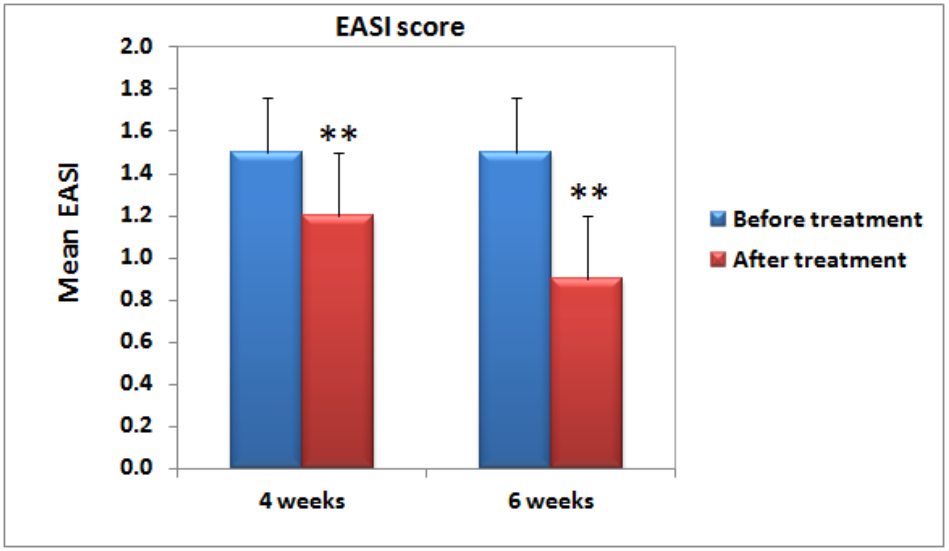
APPLICATION FREQUENCY
twice daily (morning and evening)

DERMATOLOGICAL ASSESSMENT CRITERIA

1. Erythema
2. Induration
3. Excoriation
4. Lichenification

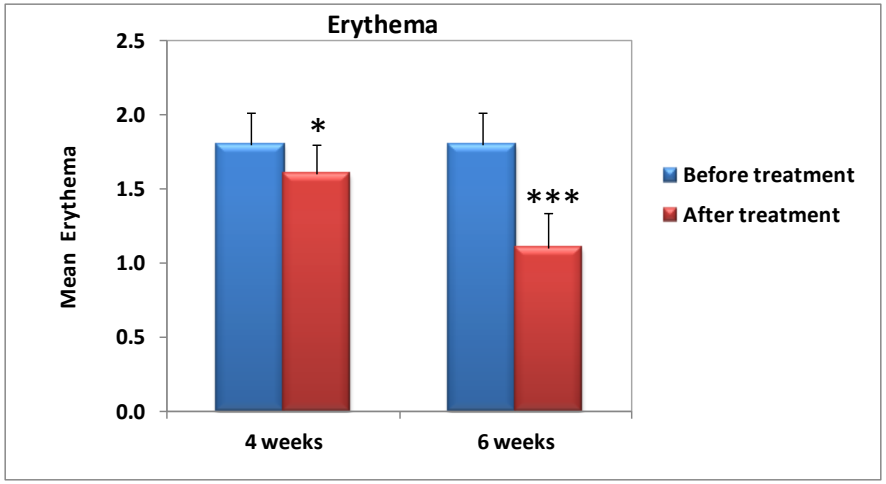
Effect of SIRB-001 on EASI score after 4 and 6 weeks of application

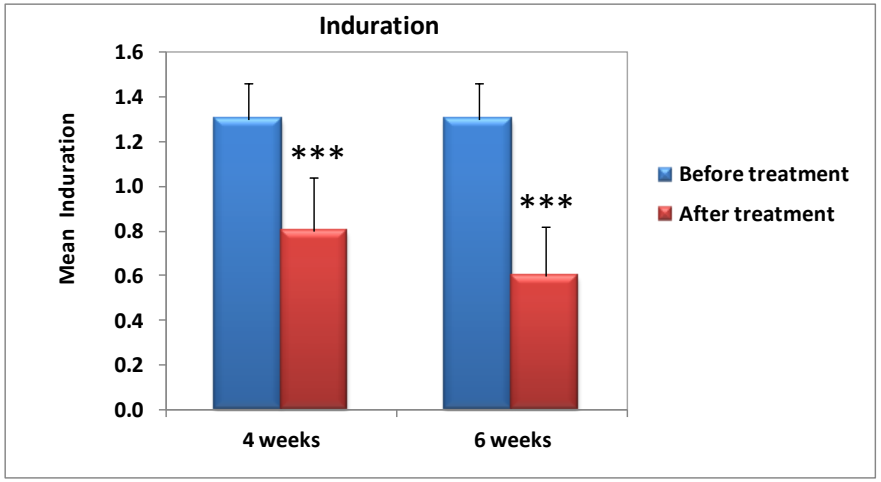
Weeks	Before treatment			After treatment			% Decrease in EASI scores (wrt Day-0)
	Mean EASI	SD	SEM	Mean PASI	SD	SEM	
4 weeks	1.50	1.300	0.260	1.20	1.500	0.300	20.0
6 weeks	1.50	1.300	0.260	0.90	1.500	0.300	40.0

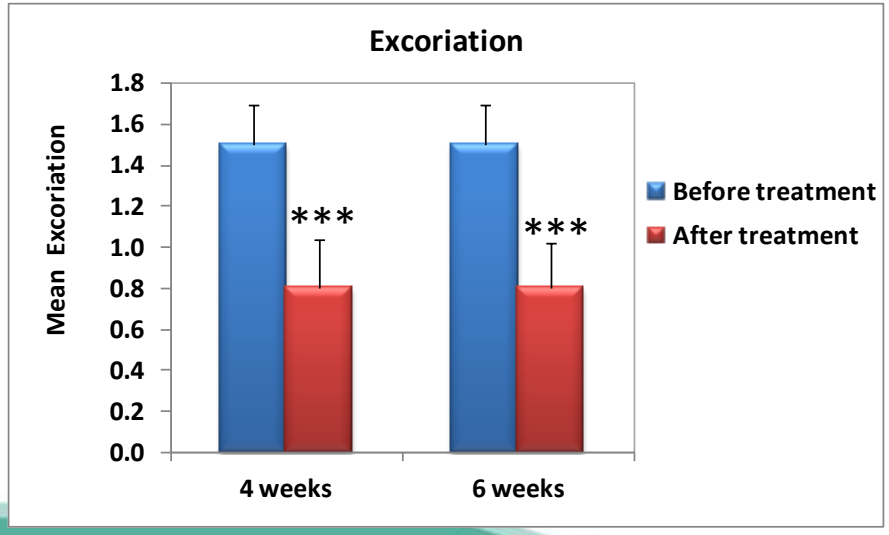


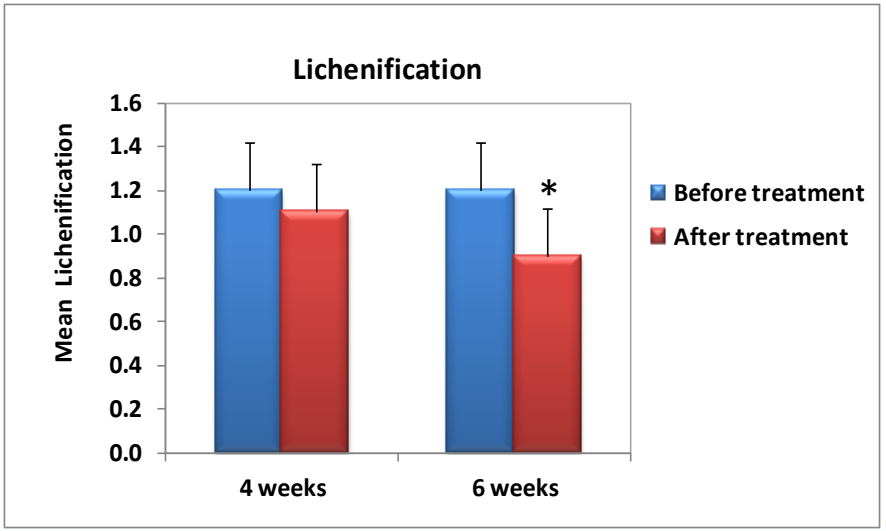
- SIRB-001 demonstrated significant decrease ($p<0.01$) in mean EASI score after 4 weeks and 6 weeks by 20% and 40% respectively as compared to untreated day-0 score.

Effect of SIRB-001 on erythema, Induration, Excoriation and Lichenification after 4 and 6 weeks of application

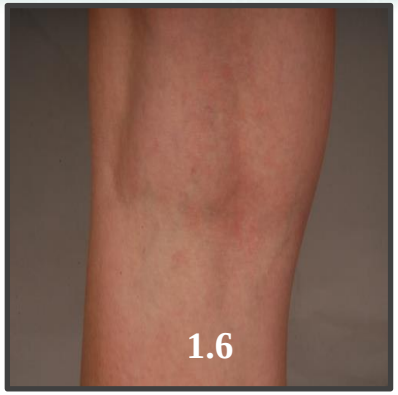
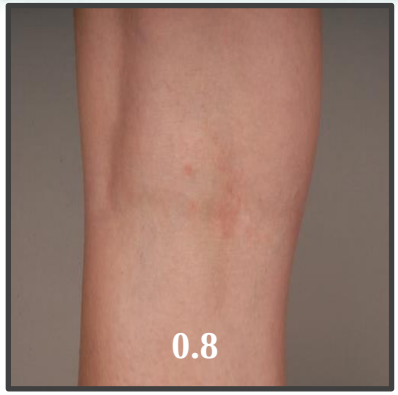
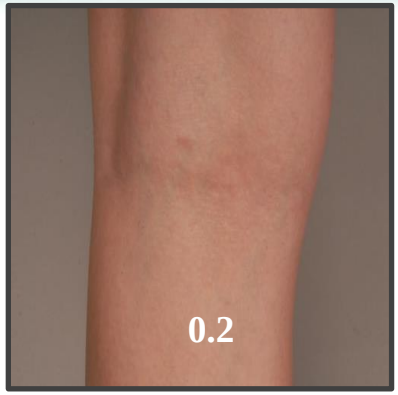
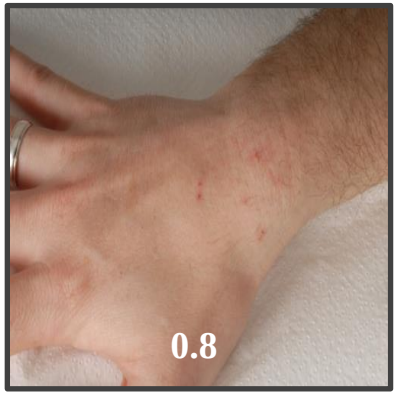
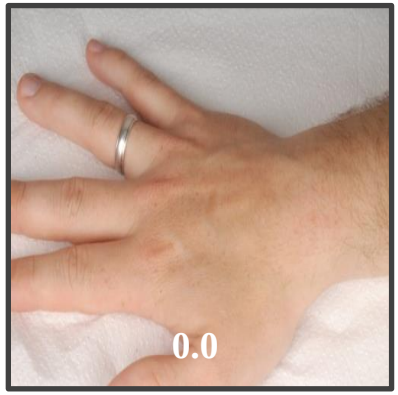
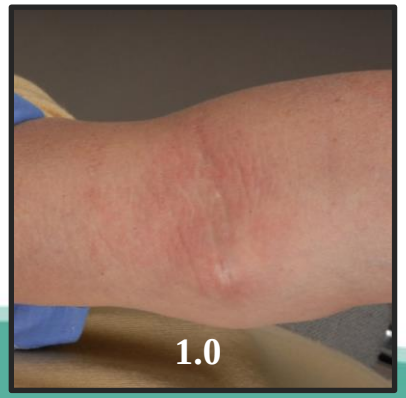
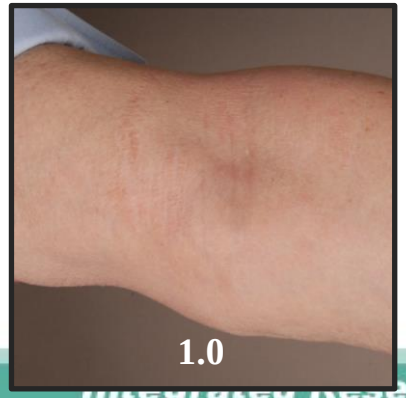
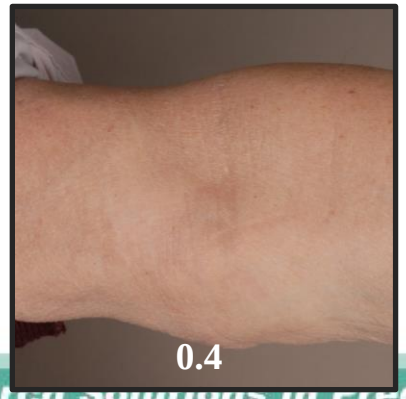








Efficacy- Atopic dermatitis

	Before application	4 weeks	6 weeks	% inhibition in EASI at 6 weeks
Subject-1				87.5%
Subject-2				100%
Subject-3				60%

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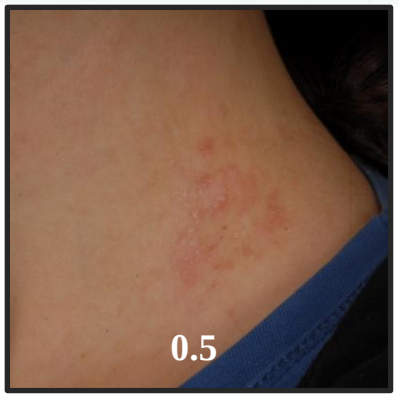
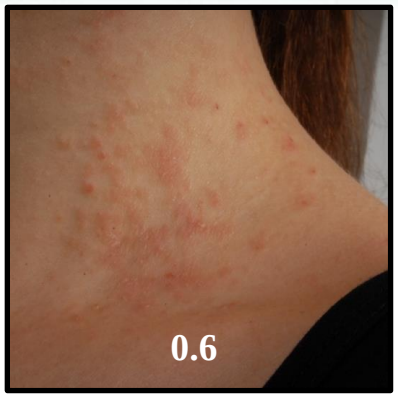
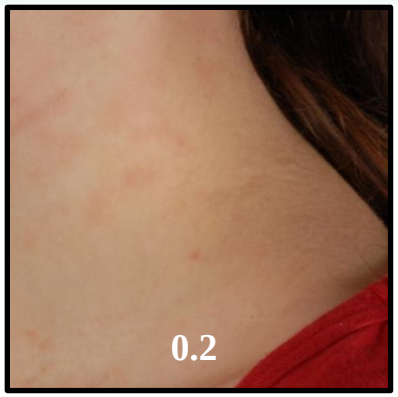
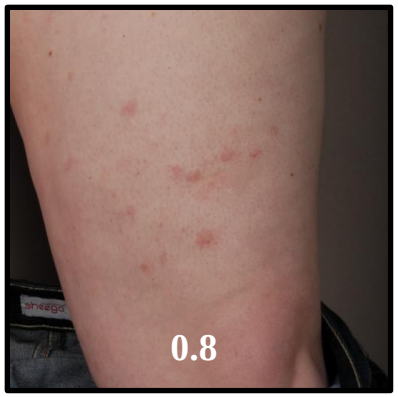
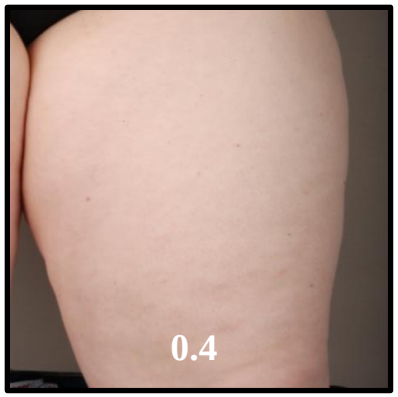
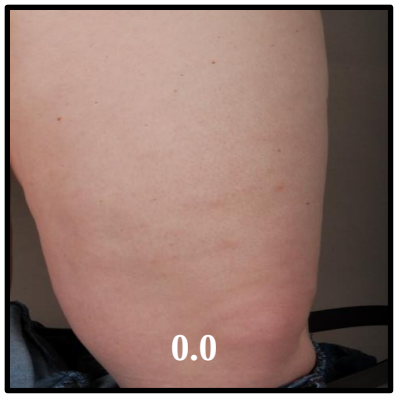
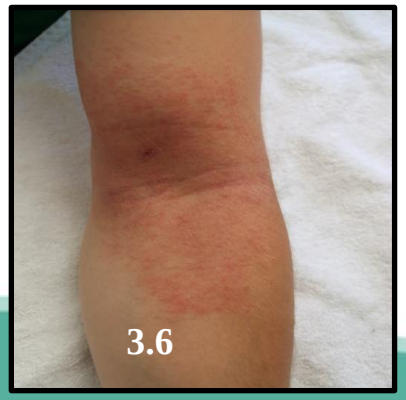
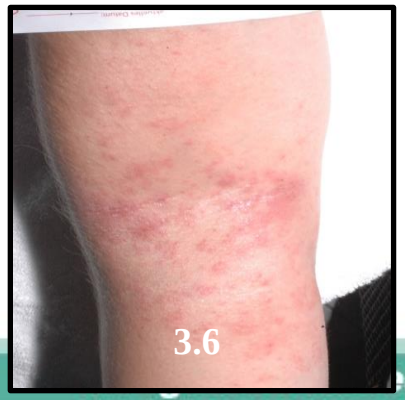
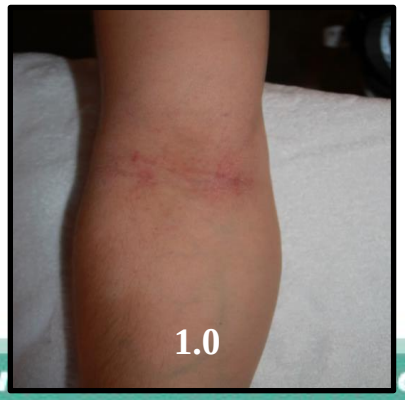
Efficacy- Atopic dermatitis

	Before application	4 weeks	6 weeks	% inhibition in EASI at 6 weeks
Subject-4				60%
Subject-5				100%
Subject-6				72.2%

CONCLUSION

- 25 study participants with mild to moderate atopic dermatitis tolerated the product Herbal cream (SIRB-001) very well in a 6-week application test under clinical-dermatological conditions and lead to an improvement of the atopic dermatitis evaluated with the EASI score.

- Herbal cream (SIRB-001) in practice does not lead to any undesired skin reactions due to any skin irritant or sensitizing characteristics of the product.

Clinical Development of SIRB 001 as a new treatment modality for Eczema

FIM Experience with Patients of Eczema

Basic information on Trial

Disease/Target Area	Eczema	Age group	18-65 Years
Product/Route	Polyherbal, Topical	Male/Female Ratio	Adequate
Type of Trial	Monocentric; Observational	Race	Asian, India
Subjects	30 (25 Completers)	Eczematous Lesion	≤10% (BSA)
Study Duration	4 Weeks	Severity (as per IGAS)	Mild to severe
Region	India		

Evaluation Criteria of the Study

Primary Criteria	Secondary Criteria
▪ Clinical Evaluation using ESI Score ▪ Clinical Evaluation using IGAS score ▪ Reduction of size and area of target lesions	▪ To assess the local skin tolerability and safety of the investigational product in subjects with eczematous lesions ▪ Biomarker analysis from serum sample ▪ To compare clinical improvement with serum IgE values ▪ Self-assessment questionnaire by subjects for assessment of efficacy and product acceptability

Regulatory Activities

EC Submission	30th Oct. 2015
EC Approval	16th Nov. 2015

IGAS : Investigator Global Assessment Severity Scale

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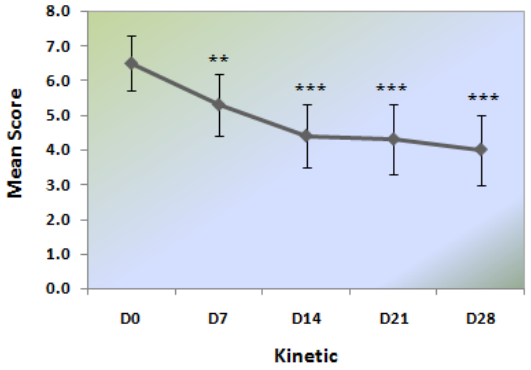
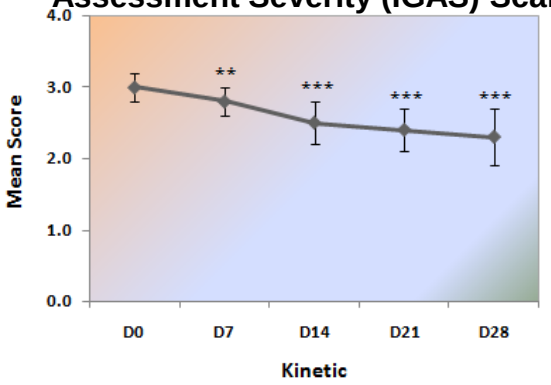
Safety & Efficacy…

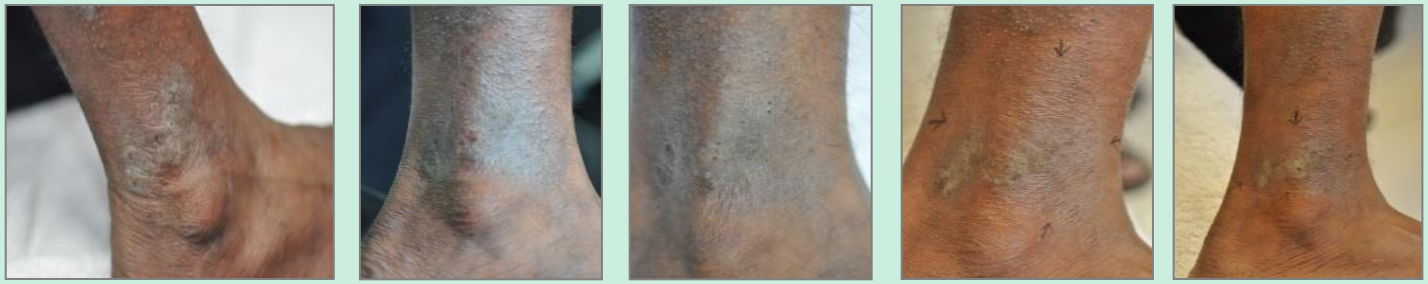
Effect of SIRB-001 on Eczema Severity Index (ESI)

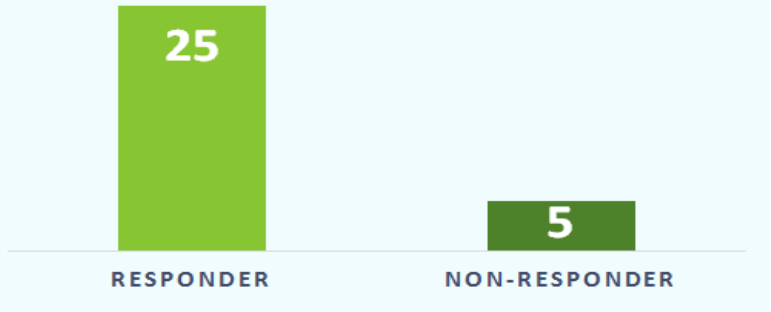


Effect of SIRB-001 on Investigator's Global Assessment Severity (IGAS) Scale



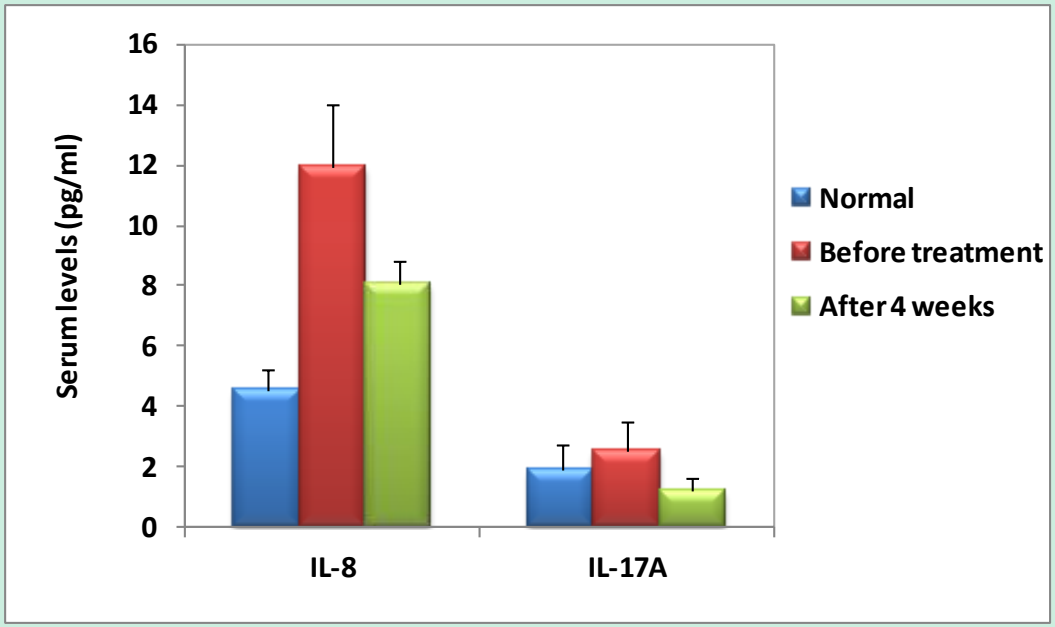
Baseline Visit (D0) **Day 7** **Day 14** **Day 21** **Day 28**





- Based on the observations during the study, the product, SIRB-001 Cream was found to be safe for topical application on human patients with eczematous lesions.
- More than 83% subjects responded to the treatment
- 46% of subjects shows improvement of more than 50% in ESI
- Maximum reduction in ESI observed was more than 85%

Cytokines in serum



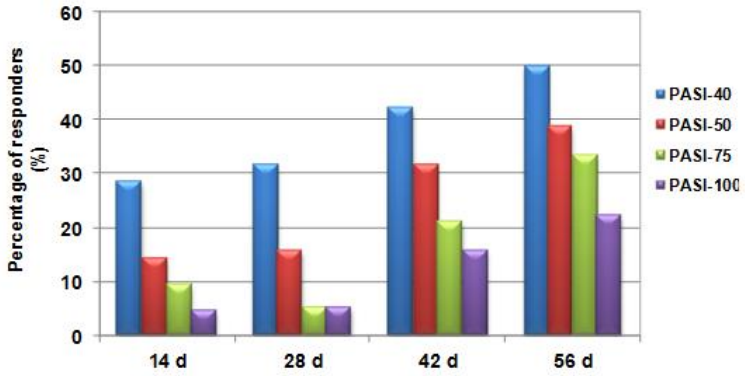
SIRB-001 demonstrated inhibition of IL-8 and IL-17A in serum of subjects by 32.5% and 50.8% respectively after 4 weeks of treatment.

Therapeutic potential of SIRB 001 in other chronic skin inflammatory diseases

Clinical Efficacy - Psoriasis

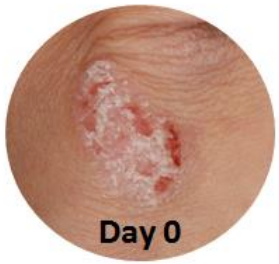
dermatest®
RESEARCH INSTITUTE FOR RELIABLE RESULTS
Taking your success personally

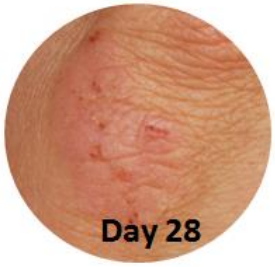
Clinical Trial done at Dermatest, Munster, Germany (21 patients)

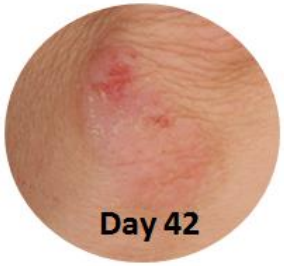


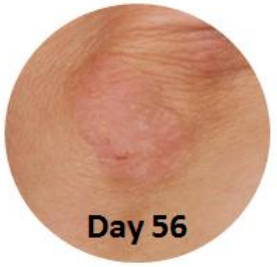
Clinical response of SIRB-001 measured by the percentage of patients achieving PASI-40 to PASI-100

- SIRB-001 demonstrated an increase in percentage of patients achieving PASI-40, PASI-50, PASI-75 and PASI-100 after 14d, 28d, 42d and 56d of treatment.
- SIRB-001 demonstrated an increase in the no of responders in both male and female patients after 14d, 28d, 42d and 56d of treatment
- SIRB-001 demonstrated an overall time dependent decrease in mean PASI scores by 2.7%, 16.6%, 28.7% and 31.5% on 14d, 28d, 42d and 56d respectively







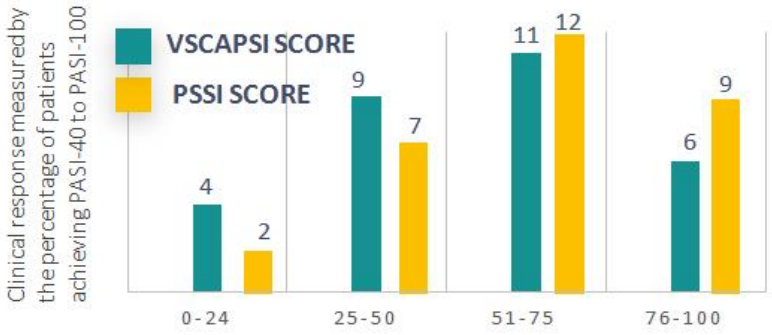


Clinical Efficacy - Scalp psoriasis

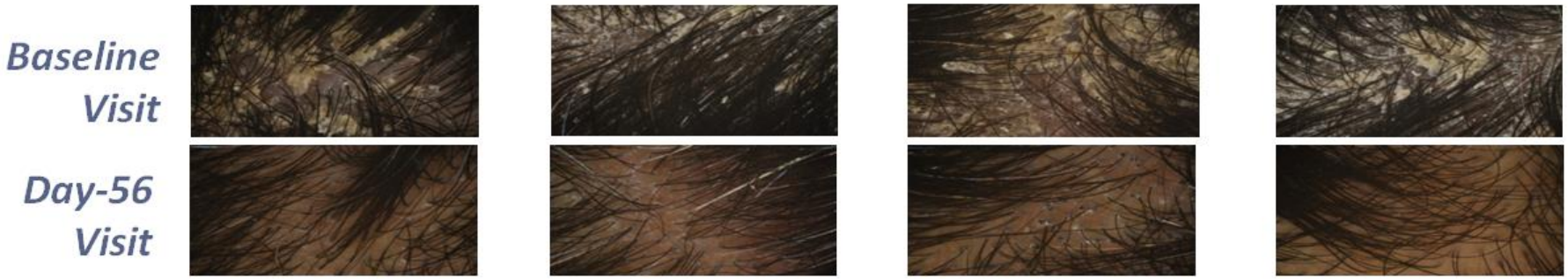
CIDP CENTRE INTERNATIONAL DE DEVELOPPEMENT PHARMACEUTIQUE

Clinical Trial done at CIDP New-Delhi, India (30 Patients)

Reduction of P SSI & VSCAPSI Scores using SIRB-001



- An Open-Label Study to Evaluate the Safety and Efficacy of SIRB-001 (S&L) a topical Polyherbal hair Shampoo & Lotion in patients with Scalp Psoriasis treated for 8 Weeks
- 70% of subjects shows improvement of more than 50% in PSSI
- > 56% of subjects shows improvement of more than 51% or more in terms of VSCAPSI
- No serious adverse event was reported in the study

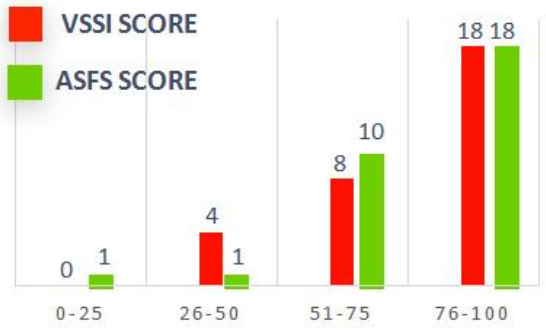


Clinical Efficacy - Seborrhoea

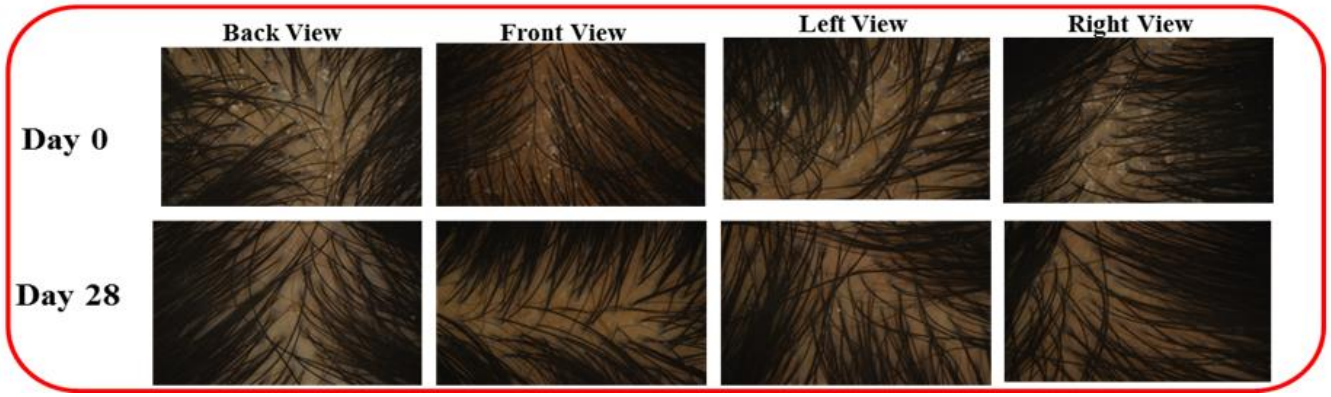
CIDP CENTRE INTERNATIONAL DE DEVELOPPEMENT PHARMACEUTIQUE

Clinical Trial done at CIDP New-Delhi, India (30 Patients)

Reduction of VSSI &ASFS Scores using SIRB-001



- **An open-label study to evaluate the safety and efficacy of hair vitalizer & shampoo (SIRB-001 HV & SIRB-001 SS) in patients with scalp seborrhoea, treated for 4 weeks**
- 93% subjects shows improvement in ASFS of more than 51%
- 60% of subjects shows improvement in ASFS of more than 76%
- >86% subjects shows improvement in VSSI of more than 51%
- >60% subjects shows improvement in VSSI of more than 76%

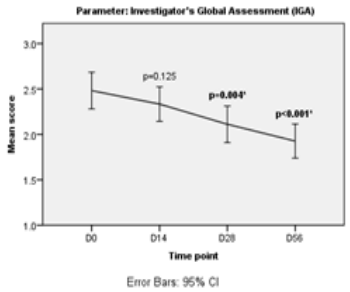


Clinical Efficacy - Acne

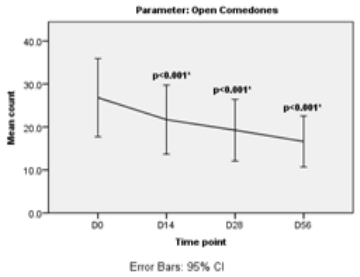
Clinical trial performed at CIDP, India (30 subjects)

Effect of SIRB-001 Gel on acne parameters after 8 weeks of application

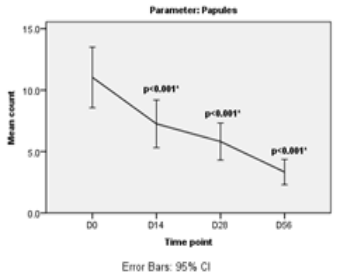
IGA score



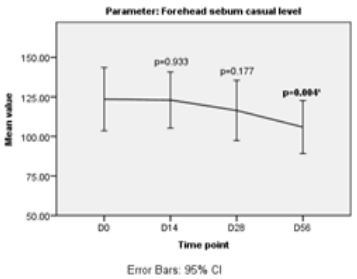
Non inflammatory lesions



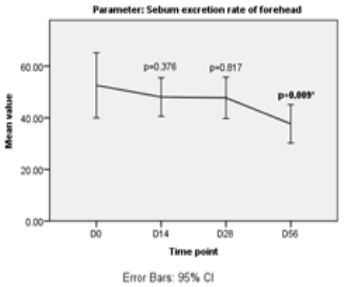
Inflammatory lesions



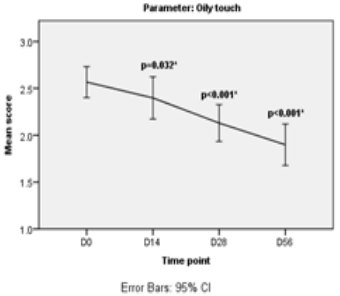
Casual sebum level



Sebum excretion rate



Oily touch



- An open label, mono-centric, before and after use comparative study was performed to evaluate the safety and efficacy of a topical polyherbal gel formulation (SIRB-001 Gel) in 30 subjects with acne, treated for 8 weeks, twice daily application.
- SIRB-001 Gel was found to be safe for topical application in acne prone subjects and was well tolerated.
- Significant reduction ($p<0.001$) in Investigator's Global Assessment (IGA) was observed at 8 weeks as compared to Day-0.
- Significant reduction in following parameters was also observed after 8 weeks as compared to Day-0 :
  - Non-Inflammatory lesion counts(open & closed comedones)
  - Inflammatory lesion counts (papules & pustules)
  - New Inflammatory lesion counts
  - Sebum casual level – Forehead, Cheek
  - Sebum excretion rate
  - Oily touch & shiny skin feel
- Good Product acceptability through Self-assessment questionnaire
- SIRB-001 is concluded to be safe and effective in acne patients.

Recent publications

Evaluation of anti-psoriatic potential of a novel polyherbal formulation by multiparametric analysis

Anti-psoriatic potential and safety of a novel polyherbal formulation

Development of a novel polyherbal topical product for the management of eczema & other chronic dermal inflammatory conditions

Development of a novel polyherbal topical formulation for the management of psoriasis

THANKS