MultiEx BSASM™

Skin Soothing and Healing Formula

A proprietary ingredient

for eczema skin, sensitive skin and dry skin

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info@biospectrum.com
Atopic dermatitis (AD)

Typical area of AD

Main symptoms

- Skin dryness
- Acute itching
- Inflammation
- Scar
- Ooze from a sore
- Abnormal pigmentation
Characteristics of Atopic Dermatitis

- Increased loss of moisture in derma
- Decreased moisture content in keratinocyte
- Abnormal pH of the skin (increased basesity than normal skin)
- Decreased lipid content
- Enhanced transdermal delivery
- Induction of continuing itching
- Induction of inflammation and secondary infection
Characteristics of Atopic Dermatitis

- Hypersensitivity to external antigen such as allergic food – immunologically hypersensitiveness ↑
- IgE in blood – induce itching ↑
- CD4+ T-helper cell Th-2 phenotype IL-4, IL-5, IL-10 ↑
- CD4+ T-helper cell Th-1 phenotype IFN-γ ↓
- Activated Langerhans cell CD1a+, CD1b+, CD36+, IgE R+ ↑
- Monocyte, Mast cell Phosphodiesterase ↑, cAMP ↓
- Infected by virus and bacteria ↑
Developmental process of BSASM™

1. Database search for anti-inflammatory or Immuno-modulatory active compounds: 200 plants
2. NF-kB & IL-2 Promoter assay: selection of 7 plants
3. Combinatory analysis of selected plants: NF-kB, IL-2 assay

- **in vitro assay**
  - TNF-α production assay
  - IL-8 production assay

- IL-2 promoter assay

- Open clinical study for atopic dermatitis
BSASM™: Multi-herbal Preparation

BSASM is composed 7 kinds of plant extracts which show anti inflammatory effect and immunomodulatory effect simultaneously.

Camellia sinensis
Centella asiatica
Matricaria recubita
Rosemarinus officinalis
Scutellaria baicalensis
Glycyrrhiza glabra
Polygonum cuspidatum
### Composition of BSASM™

<table>
<thead>
<tr>
<th>Structure</th>
<th>Source and activity</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Camellia sinensis" /></td>
<td><strong>Camellia sinensis</strong> contains effective flavonoid, EGCG. EGCG was reported to be a potent anti-infective agent. In numerous experiments, EGCG has been demonstrated to exert its preventive activity against the development of caries and periodontal diseases.</td>
<td>Surh et al., 2001 Katiyar et al., 2001 Hong et al., 2001</td>
</tr>
<tr>
<td><img src="image2.png" alt="Centella asiatica" /></td>
<td><strong>Centella asiatica</strong>, The herb Centella asiatica is great in helping and treating the following problems and conditions; general tonic/anti-rheumatic/anti-arthritic/sedative vasodilator/energy/vitality/anti-ageing etc.</td>
<td>Shukla et al., 1999 (Phytother Res) Shukla et al., 1999 (J Ethnopharmacol)</td>
</tr>
<tr>
<td><img src="image3.png" alt="Glycyrrhiza glabra" /></td>
<td><strong>Glycyrrhiza glabra</strong>, The medicinal use of licorice in both Western and Eastern cultures dates back several thousand years. It was used primarily as a demulcent, expectorant, antitussive, and mild laxative. Licorice is known to exhibit many pharmacological actions, including estrogenic, aldosterone-like; anti-inflammatory (cortisol-like); antiallergic; antibacterial, antiviral; and anti-Trichomonas; antihepatotoxic; anticonvulsive; choleric; anticancer; expectorant; and antitussive activities.</td>
<td>Nishino et al., 1984 Akamatsu et al., 1991 Ohuchi et al., 1981</td>
</tr>
</tbody>
</table>
Table. Continued

<table>
<thead>
<tr>
<th>Structure</th>
<th>Source and activity</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Matricaria recubita" /></td>
<td><em>Matricaria recubita</em> has antioxidant and anti-inflammatory effects. In addition, it was reported to prevent carcinogenesis.</td>
<td>Lin et al., 2002 Liang et al 1999</td>
</tr>
<tr>
<td><img src="image" alt="Polygonum cuspidatum" /></td>
<td><em>Polygonum cuspidatum</em>, The extract of Polygonum cuspidatum was known to have anti-oxidant and anti-inflammatory effects.</td>
<td>Jang et al., 1997 Jang et al., 1998</td>
</tr>
<tr>
<td><img src="image" alt="Rosemarinus officinalis" /></td>
<td><em>Rosemarinus officinalis</em> is a source of highly active antioxidants belonging to the group of diterpene phenols. Antioxidants are important additives in cosmetic formulations for increasing their shelf life.</td>
<td>Masuda et al., 2001 Offord et al., 2002</td>
</tr>
<tr>
<td><img src="image" alt="Scutellaria baicalensis" /></td>
<td><em>Scutellaria baicalensis</em>, a mint family member, is grown in China and Russia. The root of this plant is used in traditional Chinese herbal medicines. It has antioxidant and anti-inflammatory effects.</td>
<td>Gabrielska et al., 1997 Nakajima et al., 2001</td>
</tr>
</tbody>
</table>
In vitro efficacy study of BSASM™

NF-κB promoter assay and IL-8 & TNF α production assay:

Anti-inflammatory effect
Cytokines regulated by NF-kB

- Tumor necrosis factor: TNF-α, TNF-β
- Interleukins: IL-1b, IL-2, IL-6, IL-12
- Chemokines: IL-8, Gro a/b/g, MIP-1, MCP-1, Rantes
- Colony stimulating factors: G-CSF, GM-CSF
- Interferons: IFN-β
Signaling pathway of NF-κB activation

Induction of Pro-inflammatory Cytokine genes
• LPS increased NF-κB reporter activity by 5-folds, whereas BSASM inhibited LPS-induced NF-κB reporter activity in a dose-dependent manner.

• LPS-induced NF-κB reporter activity was diminished by a half when BSASM was treated at 1% concentration.
BSASM significantly reduced the LPS-induced production of IL-8 dose-dependently in THP-1 cells.
Inhibition of LPS-induced TNF-α production

BSASM significantly reduced the production of TNF-α dose-dependently, suggesting the anti-inflammatory function of BSASM through inactivation of NF-kB promoter.
Atopic dermatitis is supposed to be caused by the immunological imbalance between Th1 and Th2 cells. Increased Th2 expressing IL-4 and IL-5 and decreased interferon-γ by Th1 cell.
T cell Receptor signaling pathway

Calcium-Activated Calmodulin + Calcineurin

Calcineurin-induced dephosphorylation

Calcineurin

NF-ATc

NF-ATc

Calcineurin

T cell Receptor (TCR)

Nucleus

Cytoplasm

Cyclosporin A

Tacrolimus

Pimecrolimus

FK-BP

Calcineurin

NF-ATc

NF-ATc

NF-ATc

IL-2 /T cell activation: Immune boosting
Immunomodulatory effect: Inhibition of PHA-stimulated IL-2 gene expression

PHA conspicuously activated IL-2 reporter activity by ten-folds. However, this increased reporter activity was inhibited by BSASM, indicating that BSASM has the potential to inhibit T cell activation and proliferation in Jurkat T cells.
Mode of action of BSASM™ in case of atopic dermatitis skin or irritable sensory skin.

The BSASM™ inhibits the TH2 cell activation induced by macrophage which can activate B cell activity. At the same time the BSASM™ release TH1 cell inhibition caused by the activity of IL-1 and TNF-α, and specifically inhibit the activity of COX-2 enzyme which is a major inflammatory signal-inducer in the mast cells.
Vicious circles of atopic dermatitis and BSASM™ target for its action.
Open clinical study for atopic dermatitis

- Performance: Dr. Kyu-Han KIM at the College of Medicine, Seoul National University, South Korea

- Volunteers: thirty children with mild atopic dermatitis (11 boys and 19 girls, 6-15 years)

- Treatment: twice a day

- Checking period: 2 weeks, 4 weeks
Statistically significant reduction (77%) of EASI score was observed 4 weeks after treatment with BSASM, compared with before treatment ($p=0.05$).
Decrease of pruritus was observed in a time of treatment dependent manner.

Pruritus, before treatment, also decreased significantly 4 weeks after treatment (p=0.05) by 38%.
Change of TEWL on the antecubital fossa: Moisturizing effect

TEWL on the antecubital fossa

*(TransEpidermal Water Loss)*

<table>
<thead>
<tr>
<th>Time</th>
<th>TEWL (g/m²/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 week</td>
<td>18</td>
</tr>
<tr>
<td>2 weeks</td>
<td>14</td>
</tr>
<tr>
<td>4 weeks</td>
<td>10</td>
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</tbody>
</table>

* *p<0.05*

TEWL on the antecubital fossa, decreased 4 weeks after treatment, by 41%.
Change of TEWL on the abdomen:
Moisturizing effect

TEWL on the abdomen

TEWL on the abdomen, decreased 4 weeks after treatment, by 44%.
Scientific Results: *In vitro* & Clinical study

Ameliorating effect of BSASM on atopic dermatitis

**Publication:**
- J. Ethnopharm. (Feb. 2005)
- Recent progress in Medicinal Plants (2006)

**Patent:**
- Korea & PCT application (Jul. 2004)
Other effects of BSASM™

• Anti-oxidant activity
• Soothing effect
In both DPPH and SOD assay, BSASM showed anti-oxidant activity in a concentration dependent manner.
### Soothing effect

<table>
<thead>
<tr>
<th>Test material</th>
<th>24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1+</td>
</tr>
<tr>
<td>1 Irritant (0.01% SDS)</td>
<td>3</td>
</tr>
<tr>
<td>2 Irritant + BSASM 1%</td>
<td>-</td>
</tr>
<tr>
<td>3 Irritant + BSASM 2%</td>
<td>-</td>
</tr>
<tr>
<td>4 Irritant + BSASM 3%</td>
<td>-</td>
</tr>
</tbody>
</table>

- BSASM completely reduced SDS-induced irritation at 1% concentration.
- BSASM is very effective soother (just use 1%) for any cosmetic formulations.
- BSASM can be used to prevent possibility of irritation problem in any finished cosmetics products, especially low quality-low priced products with low quality grade ingredients.
Human Skin Irritation Test of BSASM

Table. The results of human skin primary irritation test (n=30).

<table>
<thead>
<tr>
<th>No.</th>
<th>Test material</th>
<th>48hrs</th>
<th>72hrs</th>
<th>Reaction grade</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>1+</td>
<td>2+</td>
</tr>
<tr>
<td>1</td>
<td>Petrolatum</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>BSASM 0.5%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>BSASM 1.5%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>BSASM 5%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>BSASM 15%</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

BSASM has no troubles when applied to the skin

by Dermapro
Conclusion

BSASM: multi-herbal preparation

- AD-mitigating effect
- Anti-inflammatory effect
- Anti-oxidant effect
- Soothing effect
- No irritation
Temperature stability

BSASM™ is very stable after high temperature exposure by Autoclaving, 121°C.

We can measure color of BSASM which is defined as optical density at 420nm with an UV/BIS spectrophotometer. OD value was not altered by heating. Thus the color was not changed by heat exposure.
BSASM™ is very stable at any light condition with room temperature.

We can measure color of BSASM which is defined as optical density at 420nm with an UV/BIS spectrophotometer. OD value was not altered by light exposure. Thus the color was not changed by continuous light exposure.
Areas of Commercial Value

• A safe effective agent for skin diseases such as atopic dermatitis, psoriasis, or acne, and so on.

• A stable and effective agent over the pH range typically found in personal care products.

• Possess average thermal stability. It has value as an active ingredient in:

  • As an therapeutic agent for skin diseases:
  • As an inhibitor of sensory irritation:
    Skin products without any possible irritation problem; soaps, cleansers, lotion, gel, cream, and so on for persons with sensitive or normal skin.
Practical Hints

Recommended Use Level

• Usage levels may vary from 1% to 5%, depending on the formulation

• The typical usage level averages around 3% for dermatitis related products and 2% for general cosmetics for sensitive skin

How to Get the Most of BSASM™

• Do not add BSASM™ to the formulation at temperature above 55°C
• Avoid any strong oxidizers and UV or direct light.
• Avoid store at cool temperature, must be stored in room temperature.
Foreign Finished Products Containing BSASM

Some cosmeceuticals containing BSASM for AD in Korea

MultiEx BSASM Plus has been introduced in two products of Germaine de Capuccini. Germaine de Capuccini is a Spanish company.

**SO Delicate:** Facial serum included in their sensitive skin line S.O.S. D- Sensitizing

**Repair Night Progress:** Night serum very concentrate in actives, from their line Strategist
Green Cross

Skin care for Atopic dermatitis

• Manufacture: Green Cross Pharmaceuticals Co., Ltd.*, Korea

• Brand Name: TALS plus

• Product Name:
  - Ato Wash(300ml)
  - Ato Lotion(150ml)
  - Ato Serum(100ml)
  - Ato Cream(70g)

* The company is the third biggest pharmaceuticals company in Korea.
Clagen

Soothes irritating agents against synthetic ingredients in the Sun care products

- Manufacture: CLAGEN, Korea
- Company Name: MIEV
- Brand Name: Derma Guard Cream
- Product Name:
  - Derma Guard Cream SPF35/PA++
ICURE

Soothes wounded skin & irritated skin

- Manufacture: ICURE, Korea (Medical care in medical company)
- Company Name: ICURE
- Brand Name: Hydrogel Patch
- Product Name: Ato-P Hydrogel Patch
SSANGYOUNG

Wet tissue for skin soothing against irritated skin such as diaper rash

- Manufacture: SSANGYOUNG C&B*, Korea
- Brand Name: CUTIE
- Product Name:
  - Cutie Wet Tissue

* The company is the third biggest paper related house hold-health care products manufacturer in Korea.
BioSpectrum, Inc.

Specialty cosmetic actives from GREEN nature

World leading GREEN manufacturing and technology

Heartfelt GREEN satisfaction to customers