A HOLISTIC APPROACH FOR SENSITIVE SKIN

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Veronique Maurin
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AGENDA

SENSITIVE SKIN
What Is It?

CONSUMERS MARKET INSIGHTS
Market Opportunities
Consumers Needs & Expectations

HOLISTIC APPROACH
for Sensitive Skin
with Symrise Solutions
SENSITIVE SKIN

WHAT IS IT?
SENSITIVE SKIN
WHAT IS IT?

Sensitive skin:

- Is a complaint, originally defined as a minority and now claimed by a majority of women in industrialized countries and nearly half of men.
- Is one of the most common disturbing skin conditions with high impact on life quality.
- Is a term used by individuals who perceived themselves to have more reactive facial skin to applied products and/or environmental factors than the general population.
- Represents a syndrome of physiological reactions NOT a disease entity.

Sources:
Sensitive skin:
- Describes a condition of the skin **defined by**:
  - **Sensory sensations**: tightness, stinging, pricking, burning, tingling, pain and less frequently itching mainly on the face
  - **Symptoms**: erythema and flush/redness
- Is a **hyper-reactive skin**, characterized by exaggerated sensorial reaction to environmental or topical factors, including hard water and cosmetics
- The degree of skin sensitivity depends on the individual

Sources:
- S. Ständer, S.W. Schneider, C. Weisshaupt, T.A. Luger, L. Misery.; "Putative Neuronal Mechanisms of Sensitive Skin"; Experimental Dermatology
SENSITIVE SKIN
MARKET OPPORTUNITIES
CONSUMER MARKET INSIGHTS
Epidemiologic Studies

Markets Opportunities

☑ Rates of skin sensitivity have increased steadily over time, particularly among men

☑ Higher prevalence of Self-Declared Sensitive Skin:
  - EU, the US and Japan
    - Approx. 50% of women
    - Approx. 30% of men
  - China
    - Approx. 36% of the population

A big concern
A global growing potential

Sources:
- S. Ständer, S.W. Schneider, C. Weisshaupt, T.A. Luger, L. Misery., “Putative Neuronal Mechanisms of Sensitive Skin”; Experimental Dermatology 2009
3 TYPES OF CONCERNS

- **Anger:** - 52% of consumers say that their skin is a “sensitive skin” (worldwide*).

  - 43% of Chinese consumers describe their skin as “a sensitive skin”: they want to do something about it

- **Visible signs:** Redness (flushes, red cheeks...), Dull Complexion, Rashes, Dehydration, Thinness of skin

- **Sensorial Signs:** Tightness, Tingling/Stinging, Scratching

*Sources: Symrise LE Consumer Database 2012 (12 500 interviews in Brazil, China, France, Germany, USA) Global Sensitive Skin Exploration 2012 (including Chinese female focus groups 20-30 & 35-45 y.o.) Global Aging Exploration 2012 (including Chinese female focus groups 18-25, 25-35, 35-50 and 50-65 y.o.)
SENSITIVE SKIN
CONSUMER EXPECTATIONS

Innovative products vs. visible and sensorial signs

Soothing remedies for peace, energy and beauty

Inside out action: moisture and nurture

Reinforced skin barrier & repair

Purity and minimized risks of allergy

*Sources: Symrise LE Consumer Database 2012 (12,500 interviews in Brazil, China, France, Germany, USA)
Global Sensitive Skin Exploration 2012 (including Chinese female focus groups 20-30 & 35-45 y.o.)
Global Aging Exploration 2012 (including Chinese female focus groups 18-25, 25-35, 35-50 and 50-65 y.o.)
HOLISTIC APPROACH
FOR SENSITIVE SKIN
WITH SYMRISE SOLUTIONS
SENSITIVE SKIN
WHAT’S HAPPENING INSIDE?

1. DAMAGES IN SKIN BARRIER
   - Loss of NMF, lipids, proteins etc.

2. RELEASE OF PRO-INFLAMMATORY FACTORS
   - Keratinocytes
   - Mast cells
   - Sensory nerves
   - 1st level of pro-inflammatory mediators
   - 2nd level of pro-inflammatory mediators
   - Excessive activation of heat receptors
   - Release of itching mediators
   - Change in nerve sensitivity

3. ITCHING
   - BURNING / STINGING / TIGHTNESS

4. REDNESS

5. Change in keratinocyte proliferation & differentiation

6. WEAKENED SKIN BARRIER
   - Increased susceptibility to external factors

7. DRY, SENSITIVE SKIN

FACTOR 1
- MECHANICAL FACTORS
  - Shaving, waxing, hair dryer etc.

FACTOR 2
- PHYSICAL FACTORS
  - Sunlight, Temperature, Humidity etc.
- CHEMICAL FACTORS
  - Depilatories, Retinol, preservatives etc.
SKIN BARRIER IMPAIRMENT
Ceramide BIO / SymRepair® 100

SKIN MECHANISMS OF ACTION

- Deficiency in key SC lipids & structural integrity
- Hyper proliferation & shedding of keratinocytes
- Decrease of hydration level

SKIN REACTIONS

BARRIER IMPAIRMENT WATER LOSS & DRY SKIN

SYMRISE SOLUTION

Barrier repair & topical applications of lipids with
SymRepair® 100 CeramideBio
SKIN BARRIER REPAIR COMPLEX
SymRepair® 100

THE BENEFITS

- Highly effective skin barrier repair complex containing a patented ceramide combined with bisabolol and phytosterols
- Based on the 3 key components of the lamellar bi-layers of the stratum corneum
- Quickly reconstitutes lamellar bi-layers resembling those of the skin
- Restores health into skin barrier for less irritated skin, prevents from water loss, reduces redness (clinical data)
- Protects and repairs dry skin

THE PRODUCT

- Clear, colorless to pale yellow, oil soluble
- Use level: 1 – 4%
- INCI: Hexyldecanol, Bisabolol, Cetylhydroxyproline Palmitamide, Stearic Acid, Brassica Campestris (Rapeseed) Sterols
- Product number: 445662
- Cetylhydroxyproline Palmitamide: **QD registered**
- China compliant
SKIN BARRIER IMPAIRMENT
Ceramide Bio / SymRepair® 100

✓ Ceramides: important constituent of the lipid bilayer
✓ Permeability barrier: corneocytes enveloped by lipid bilayers

„Brick and Mortar“ - Model (P.M. Elias)

Corneocytes are the bricks, the lipid bilayers are the mortar
CeramideBIO is a new, synthetic ceramide. Its structure is similar to natural Ceramide 2.

Major advantages of CeramideBIO:
- Very low melting range
- Easy to formulate
- Non-apoptotic (unlike other ceramides)

Compound Melting range:
- Ceramide 2: 90 - 105 °C
- Ceramide 3: 120 - 130 °C
- CeramideBIO: 53 - 59 °C
BARRIER REPAIR – SDS MODEL
CeramideBIO - DOSE RESPONSE RESULTS

- Clinical study 20 human subjects with winter-dry skin
- Test parameters: TEWL: major indicator of barrier integrity & Redness: erythema, indicator of irritation
- Skin barrier disruption by treatment with 2% SDS for 24h (occlusive)
- Application of test products (2 mg/cm²) twice daily for 5 days on volar forearm
- Measurements on 1 day before SDS treatment (D-1) & days 3 & 5

Barrier integrity (%) on day 5 after SDS damage (based on TEWL)

- Optimum barrier repair efficacy with 1% Ceramide BIO
- Optimum barrier repair efficacy – up to 80% @ 0.1% which corresponds to 4% SymRepair® 100
BIOCHEMICAL CONSEQUENCES OF A WEAKENED BARRIER

- Cutaneous barrier perturbation stimulates cytokine production in the epidermis of mice
  
  "Moreover, the mRNA levels for epidermal IL-1α, IL-1β and GM-SCF also were elevated 7-fold over controls, after either acetone treatment or tape stripping."

- Stress induced changes in skin barrier function in healthy women

  The interview stress caused a delay in the recovery of skin barrier function as well as increases in plasma cortisol, norepinephrine, IL-1β and IL-10, TNFα, ...

- Epidermal interleukin-1 alpha generation is amplified at low humidity: implications for the pathogenesis of inflammatory dermatoses

  "...the amount of IL-1α in the epidermis was higher in animals kept in a low-humidity environment than in a high-humidity one."

→ Anti-irritants support epidermal barrier repair
Dragosantol® 100
A POTENT CYTOKINE INHIBITOR

- INCI: Bisabolol
- Synthetic, nature identical d,l alpha bisabolol
- Purest synthetic bisabolol available (> 95%, Farnesol << 0.1%)
- IL-1α, TNFα & LTB4 inhibition
- Hyaluronic Acid stimulator
- Monocyclic, unsaturated sesquiterpene alcohol
- Clear, colorless, oil-soluble liquid
- Easy to handle
- Very low odor
- Stable (pH 3 to 12)
- Recommended concentration: 0.05% to 0.2%
- Dermatologically and toxicologically safe
- Approved for use in oral care applications
- China and Japan QD compliant
CeramideBIO SYNERGISM WITH BISABOLOL - TEWL

Barrier integrity (%) on day 5 after SDS damage (based on TEWL)

Synergistic effect of 0.1% CeramideBIO and 0.1% Bisabolol

→ 73% Barrier repair!
CeramideBIO SYNERGISM WITH BISABOLOL - REDNESS

Erythema reduction (%) on day 3 after SDS damage

Synergistic effect of 0.1% CeramideBIO and 0.1% Bisabolol
REDNESS / ERYTHEMA
SymRelief® 100

SKIN MECHANISMS OF ACTION

Release of key inflammatory cytokine IL-1α from keratinocytes, macrophages ...
→ biosynthesis of other proinflammatory mediators
→ increase in blood flow vascular permeability

Formation of lipid mediators (Prostaglandins, Leukotriens, Platelet Activating Factor) from keratinocytes

SKIN REACTIONS

REDNESS & ERYTHEMA

SYMRISE SOLUTION

Anti IL-1α & TNFα & PGE-2, LTB4 with SymRelief® 100

• IL-1α: Interleukin 1 α
• TNFα: Tumor necrosis factor α
• PGE-2: Prostaglandin E2
• LTB4: Leukotrien B4
**ANTI-IRRITANT SECOND GENERATION**

**SymRelief® 100**

**THE BENEFITS**
- Synergistic blend of anti-irritants
  - Dragosantol® 100, the purest synthetic nature identical Bisabolol
  - Natural ginger extract
- Triple anti-irritant efficacy, effective inhibitor of:
  - IL-1α, TNF α, COX-2 & PGE2 (*in vitro*) & hyaluronan stimulator
- Proven synergistic effect of bisabolol and ginger
- Visibly reduces redness and rashes in 2 days!

**THE PRODUCT**
- Pale yellow to light brown clear liquid
- Soluble in alcohol, glycols and oils
- Stable in a wide range of pH and up to 80°C
- Use level: 0.05 to 0.2%
- INCI: Bisabolol, Zingiber Officinale (Ginger) Root Extract
- Product number: 367692
- China compliant (MOH 2003)
Clinical study: 20 human subjects with winter-dry skin

Test Products:
- vehicle (Placebo)
- vehicle + ginger extract (10 ppm)
- vehicle + bisabolol (1000 ppm)
- vehicle + 0.05% SymRelief® 100

Subjects: Number of individuals: 20

Test Area: Inner sides of forearms

Application: 4-6 h after SDS treatment, then for 7 days, twice daily

Evaluation:
- Before treatment with SDS
- 4-6 h after SDS treatment
- 4-6 h after the last daily application on day 1, 2, 3, 5 and 7

Skin Parameter: Skin Redness
SDS ERYTHEMA TEST RESULTS

Erythema Reduction after SDS Treatment
Synergistic Effect of Bisabolol + Ginger Extract

\(^{(SDS - \text{baseline}) = 100 \% \text{ erythema}}
\text{baseline = 0 \% \text{ erythema}}\)

* p < 0.05 vs Placebo
* p < 0.05 vs Placebo & synergistic
BURNING & STINGING – TRPV1
SymSitive® 1609

SKIN MECHANISMS OF ACTION
Excessive activation of skin's sensory fibres

SKIN REACTIONS
BURNING STINGING

SYMRISE SOLUTION
Anti-nerve Hyper-activation with SymSitive® 1609
FAST SKIN RELIEF
SymSitive® 1609

THE BENEFITS
- Helps to increase the skin's tolerance threshold by its regulating action & by reducing symptoms associated with sensitive skin
- Mechanism of action: TRPV1 antagonist
- Shows an immediate soothing effect by reducing burning, stinging and tingling
- Calms over reaction of the skin & scalp
- Applications:
  - Sensitive skin overreacting to cosmetics like retinol, alpha hydroxy acids, phenoxyethanol, hair coloration and hair relaxers
  - Hair / Scalp

THE PRODUCT
- Nature identical 4-t-butylcyclohexanol found in berries of pistacia lentiscus
- Clear colorless solution, soluble in alcohol, glycols, oils
- Stable at pH 3-12 and up to 50°C
- Use level: 1 – 3%
- INCI: Pentylene Glycol, 4-t-Butylcyclohexanol
- Product number: 399944
TRPV1 EXPRESSION
A KEY PLAYER

TRPV1: the best characterized receptor in the epidermis highly expressed in sensitive skin,

High levels of TRPV1 in over sensitive skin

Undetectable levels in non sensitive skin

Low levels of TRPV1 in normal skin

Tissues collected from a subject at limb amputation
Facer et al. BMC Neurology 2007, 7:11
COSMETIC INTOLERANCE SYNDROME
IN VIVO STUDY

PROTOCOL

20 subjects
1.2 % SymSitive 1609 in o/w emulsion

Selection of subjects

Assessment 1 & 3 min after treatment
Noxious sensory stimulation at D1 & D5
[Sauna exposure + lactic acid sting test]

Sting test

Treatment (5 days – 8 applications)

Day 1                         2                          3                          4                         5

Application of the O/W emulsion - Active versus placebo

RESULTS - Reduction of overall Irritation vs placebo

SymSitive® 1609:
- Statistically significant reduction in overall facial irritation (p=0.03)
- Immediate effect -65% versus placebo !!
SKIN MECHANISMS OF ACTION

Release of itch mediators (Histamine, tryptase & TNF-alpha) from mast cells.

SKIN REACTIONS

ITCHING

SYMRISE SOLUTION

Anti histamine release with SymCalmin®
FAST SKIN ITCH RELIEF
SymCalmin®

THE BENEFITS

- Soothing product based on a nature inspired ingredient from oat
- 4 different levels of action:
  - Anti-histamine, anti-NK1 receptor antagonist, anti-irritant & anti-oxidant
  - Reduces itch, inflammation & the clinical symptoms associated with dry, itchy mature skin
  - Protects the skin from daily aggressions & effects of premature aging
  - Inhibits the first steps of the inflammatory cascade by its radical scavenging activity

THE PRODUCT

- Nature inspired, synthetic Dihydroavenanthramide D
- Clear, odorless liquid with very light color, soluble in ethanol, glycols and common cosmetics oils
- Stable in a wide range of pH and up to 80°C
- Use level: 0,1 – 2%
- INCI: Butylene Glycol, Pentylene Glycol, Hydroxyphenyl Propamidobenzoic Acid
- Product number: 143535
ANTI-HISTAMINE ASSAY IN VITRO

RESULTS

- Dihydroavenanthramide D inhibits Histamine net release from peritoneal mast cells, stimulated by substance P.

![Graph showing the inhibition of Histamine net release by Dihydroavenanthramide D at different concentrations.](image)
IN VIVO STUDY
DRY SKIN CONDITIONS

Protocol:
- 40 subjects (35-80 years) with visible dry skin and itching
- 4 weeks double blind study - subjects use one product for 2 weeks and cross over to use the other product for the next 2 weeks
- Test products (double-blinded): Emulsion A (vehicle) & Emulsion B with 2% SymCalmin
- Measurement time points: Baseline - week 2 (study cross over point) & week 4
- Parameters: scaling (10 point ordinal scale; 0 - none & 9 - severe); erythema & Itch

Results after 2 weeks - Investigator analysis*

SymCalmin®: significantly reduces the clinical symptoms associated with dry itchy skin such as scaling, erythema and itch!!

*(based on the subjects’ impression after interviewing them by the investigator)
A HOLISTIC SOLUTION FOR SENSITIVE SKIN
SUPPORTED BY TEXTURES COLLECTION

- SymRepair® 100
- SymRelief® 100
- SymSitive® 1609
- SymCalmin®
A holistic approach across the Symrise portfolio to improve skin tolerance by optimizing the formulation

- High safety profile ingredients
- Moving to gentler / milder emulsifiers
- Minimizing number of ingredients
- Reducing usage level of preservatives / UV filters
SENSITIVE SKIN TEXTURE COLLECTION
AROUND THE WORLD...

GLOBAL
A UNIVERSAL SOLUTION

5 TEXTURES
DEDICATED TO SPECIFIC REGIONAL SENSITIVE NEEDS

IN THE US
Specific focus on: DAMAGED ITCHY SKIN

GLOBAL
UNIVERSAL SOLUTION
A chassis formulation containing a core of mild emulsifier, emollient, product protection system

IN LATAM
Specific focus on: FRESHNESS due to hot climate

IN ASIA
Specific focus on: SKIN LUMINOSITY

IN EUROPE
Specific focus on: LONG-TERM DAMAGES
SYMRRISE
INGREDIENTS DEDICATED TO SENSITIVE SKIN

SOOTHING
- 367692 SymRelief® 100
- 399944 SymSitive® 1609
- 445662 SymRepair® 100
- 143535 SymCalmin®

COOLING
- 399952 Frescolat® ML Cryst

PRODUCT PROTECTION
- 979940 SymSave® H
- 841129 Hydrolite® 6
- 108580 SymDiol® 68

ANTI-AGING
- 844033 Dragosine®
- 510494 SymWhite® Plus

MOISTURIZING
- 510027 Hydroviton® Plus

FUNCTIONALS
- 677660 Emulsiphos®
- 109854 Dragoxat® 89
- 683541 Dracorin® GOC
- 181598 SymMollient® S
- 660061 Isodragol®

SUN PROTECTION
- 106796 Neo Heliopan® AP
- 622501 Neo Heliopan® 357
- 600154 Neo Heliopan® 303
- 103275 SymTiO® S
- 386557 SymHelios® 1031

BOTANICALS
- 103565 Shea Butter Fair Trade (refined)
- 351601 Actipone® Honeysuckle Flower
- 139445 Actipone® Nut Grass
- 628612 Cotton Seed Oil
SYMRISE,
ALWAYS INSPIRING MORE...

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