

Z-Care™

Natural effective support for acne, oily and inflamed skin care

At the heart of Frutarom's TopicRange for oily and acne skin problems, we focus Z-Care™ - a botanical blend based on traditions of Chinese medicine (TCM), brought by modern science to the 21st century.

The blend was developed to support the care of oily skin, inflammatory conditions and acne.

Acne Pathophysiology

Acne is a multi-factorial condition involving the hair-sebum units (pilo-sebaceous follicles), which pathophysiology is complex and not completely understood.

The result is a usually a bothersome condition that sometimes causes deep lesions and scars.

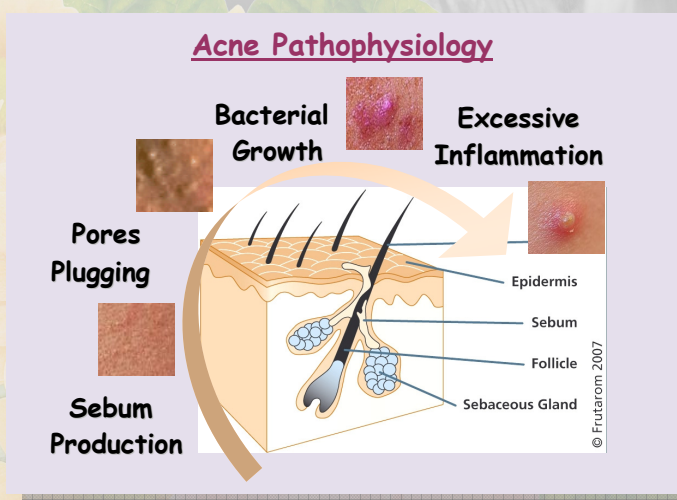
1. **Excess sebum production** triggered by androgen stimulation, correlating with formation of **open "black" comedos**.
2. **Obstruction of the follicles** by immature keratinocytes, leading to formation of **closed "white" comedos**.

3. **Proliferation of bacteria** (*propionibacterium acnes*) triggering release of **inflammatory mediators** and development of **inflammatory ("red") pimples**.
4. **Excessive inflammation** and rupture of the plugged follicle to the dermis, causing formation of **papules, pustules and eventually scarring**.

Acne treatment

Acne treatment is aimed at:

1. Facial cleansing to open the pores
2. Reduction of sebum secretion
3. Maturation of keratinocytes to prevent exfoliation
4. Anti-bacterial and anti-inflammatory treatments



Z-Care™ concept

1. **Focusing on excessive inflammation** - addressing the causes of inflammation as well as the inflammatory process that leads to severe lesions and scarring.
2. **Natural holistic solution** by its own - covering multiple aspects of treatment.
3. **Adjunct to existing medical treatment** - improving efficacy and reducing the need to use multiple preparations.
4. **Supporting healthy skin** - reducing irritation that often accompanies medical treatment, and promoting healing.

Anti-inflammatory focus

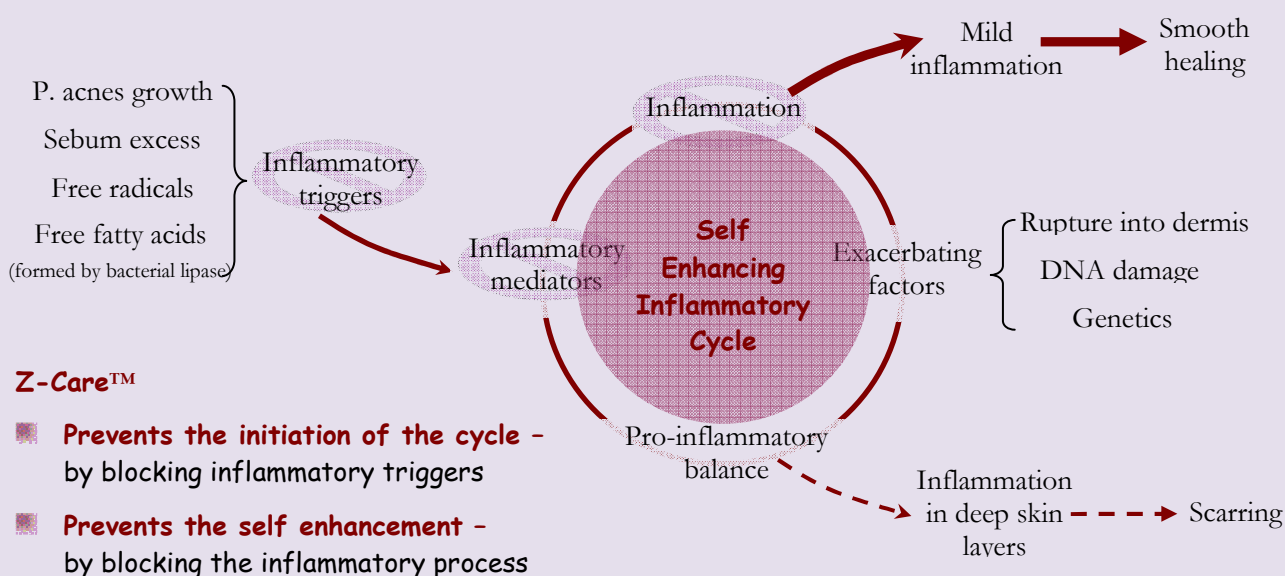
Inflammation in acne is triggered by many factors that increase the release of pro-inflammatory mediators: growth of *P. Acnes*, bacterial lipase activity leading to formation of free fatty acids, generation of reactive oxygen species and more.

Regretfully, reducing these pro-inflammatory factors is just not enough, since recent studies reveal that once initiated, the **inflammatory process can get out of control and a vicious cycle of self enhancement begins.**

Z-Care™ is active **against the inflammatory triggers**, while **strongly inhibiting the inflammatory process** itself, **preventing the vicious cycle** that leads to deep inflammation and scarring.

Z-Care™

Action - focusing on excessive inflammation



Ancient traditions & Modern technology

The tale of TCM formulations describes 4 roles of the herbal extract:

1. **Emperor** – is the principal and most potent herb in the formula.
2. **Minister** – is the right hand of the emperor, supporting its effects.
3. **Assistant** – is preventing undesirable effects that might limit the emperor's activity.
4. **Servant** – is usually serving the formula constituents, prolonging and enhancing their effects.

Z-Care™ formulation is based on 4 active herbs assigned to the tale roles. Each active extract is purified by affinity based chromatographic methods enriching it with active markers.



Rhubarb *heum Palmatum Root Extract*



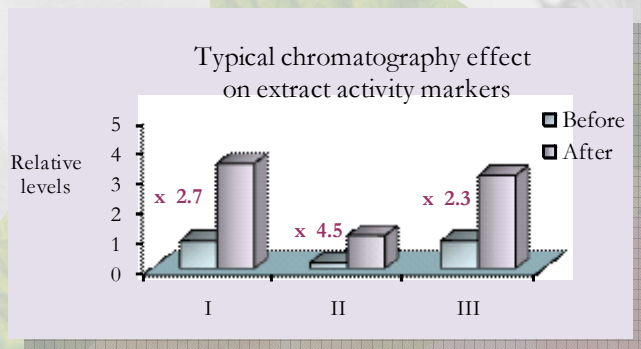
Scutellaria *Scutellaria Baicalensis Root Powder*



Portulaca *Portulaca Oleracea Extract*



Chrysanthemi *Chrysanthemum Indicum Flower Extract*



Rhubarb (*Rheum palamtum*)

The Emperor- determining the main effect

- 1) **Main activity: strong anti inflammatory action-** anti-inflammatory properties of rhubarb and its active anthraquinones by regulating the Nitric Oxide and NF Kappa β pathways.
- 2) **Sebum regulation-** down regulation of androgen receptor, which is an important determinant of sebocyte activity.
- 3) **Wound healing support** – positive effect on fibroblasts growth in healing.

Scutellaria (*Scutellaria baicalensis*)

The Minister - Supporting the emperor's effects

- 1) **Anti-inflammatory activity** – binding of different chemokines and acting on the COX pathway complementing emperor's activity.
- 2) **DNA protection** – protects DNA against radical damage to prevent the self enhancement of the inflammatory cycle.
- 3) **Sebum regulation** – further action on Androgen receptor regulation.

Potulaca (*Portulaca oleracea*)

The Assistant – preventing undesirable effects

- 1) **Anti irritant activity** – prevents irritation in detergent and other formulations that disrupt the skin barrier.
- 2) **Wound healing support** – improves wound healing thereby aiding to prevent the undesirable scarring after inflammation is stopped.
- 3) **Anti bacterial activity** – Quercetin, is active against *P. Acnes* and increases its sensitivity to antibiotics. It also inhibits microbial lipase activity.

Chrysanthemi (*Chrysanthemum indicum*)

The Servant – strengthening the formulation

- 1) **Anti-oxidant activity & UV protection** – protecting the active ingredients of the formula on the skin and thus increasing its activity.



In vitro anti inflammatory activity

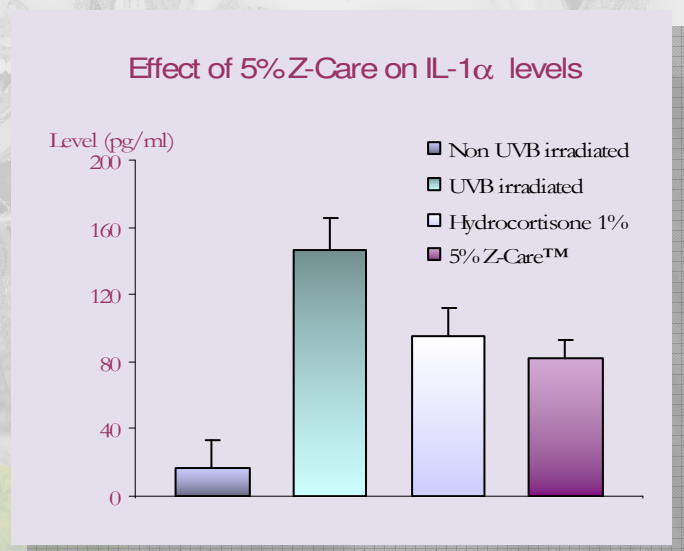
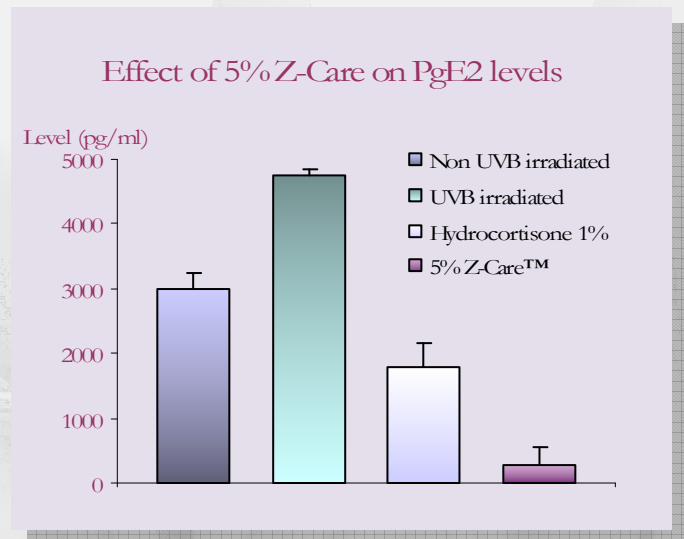
Anti-inflammatory activity of Z-Care™ was tested on an epidermis model (EpiDerm by MatTek). EpiDerm tissues were irradiated with 300 mJ/cm² to initiate an inflammatory response. One hour after the insult, when the inflammatory cascade has been activated, 50 µl of 5% Z-Care™ were applied.

24 hours after the application of 5% Z-Care™ levels of IL-1α and PgE2, two major mediators of inflammation, were determined. The results of the anti-inflammatory EpiDerm study are presented in the right charts.

Z-Care™ in 5% formulation significantly inhibits major inflammatory markers in epidermal cells.

- 95% reduction in PgE2 after inflammatory insult.
- 91% reduction in PgE2 compared to normal non-insulted tissue.
- 44% reduction in IL-1α after inflammatory insult.
- Stronger activity compared to control of Hydrocortisone 1%.

Cell viability was measured during the same test by an MTT assay, to demonstrate that Z-Care doesn't reduce cell viability. This reflects well on the low skin irritation potential of Z-Care™.



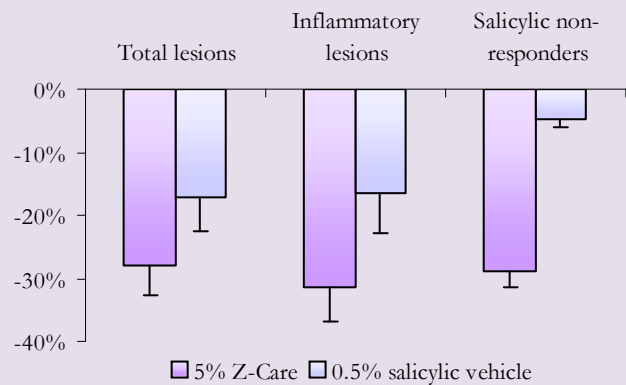
Clinical trial - Acne spot treatment

Z-Care™ was tested for spot treatment of acne lesions on 28 women. 5% Z-Care™ with 0.5% salicylic acid was compared to a vehicle containing 0.5% salicylic acid. Clinical evaluation was performed by a dermatologist on days 0, 2, 4, 6, 9 and 12 of product use.

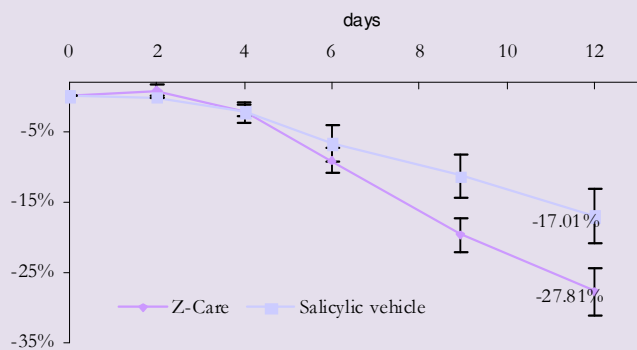
Z-Care™ 5% formulation caused fast clearance of acne lesions in study subjects:

- A clear and significant reduction begins after **6 days** of treatment.
- **28%** reduction in total lesions after 12 days, compared to 17% in the control group.
- **30%** reduction in inflammatory lesions after 12 days, compared to 16% in the control group (**0.5% salysilic**).
- **29%** reduction in total lesions in subjects not responding to 0.5% salicylic – a **clear benefit as an adjunct to salicylic**.

% change in acne lesions after 12 days of spot treatment



Acne clearance rate during 12 days of spot treatment



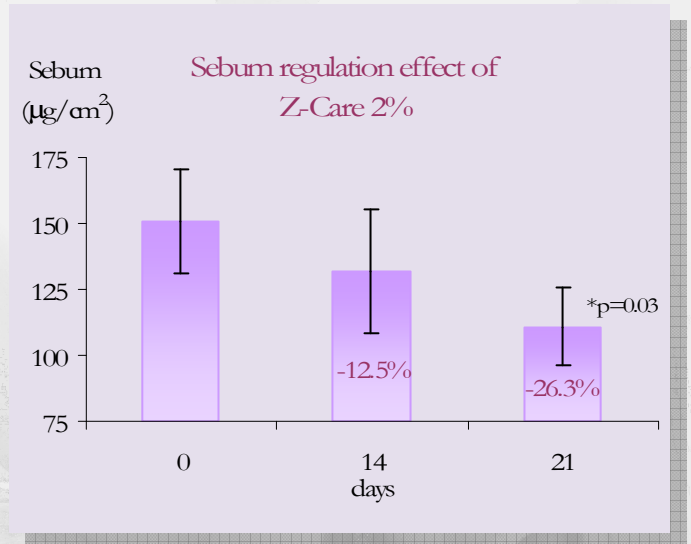
Clinical trial - maintenance sebum regulation

Z-Care™ maintenance effect on sebum secretion was tested on 10 young males with oily skin ($> 100 \mu\text{g}/\text{cm}^2$) and mild or occasional acne lesions.

A neutral formulation containing 2% Z-Care™ as a single active ingredient was used by the panelists for 3 weeks twice daily.

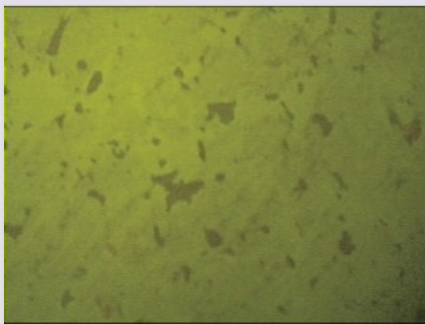
Sebum secretion was evaluated by a SebuMeter® after 14 and 21 days.

- Sebum secretion was reduced by **26.3%** after 21 days.

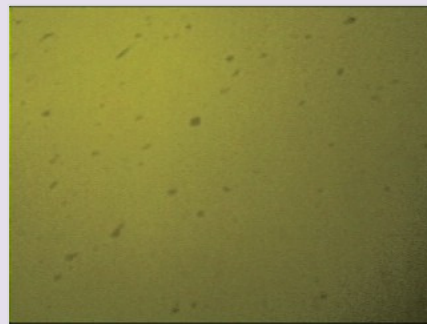


Z-Care™ 2% Sebum reduction

Before



After 3 weeks



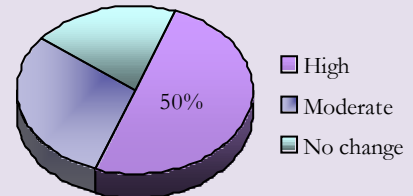
Reduction of spot number and size after 21 days by Visipor® UV camera

Panelist's evaluation- maintenance care

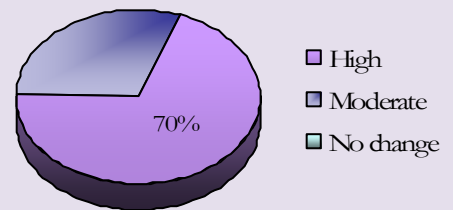
Z-Care™ 1% addition to an existing acne formulation of 11 panelists was evaluated based on subject's own evaluation.

- 80% of the subjects noted an improvement of acne condition compared to their old treatment.
- 70% of the subjects noted a significant improvement in inflammation levels.
- The average satisfaction score of the panelists was 8.6 on a 1-10 scale.

Panelists satisfaction evaluation



Improvement of inflammatory lesions



Z-Care™ 1% maintenance effect

Before



After 4 weeks



TopicRange™

Our Solutions for oily and acne prone skin



Z-Care™

Supports acne treatment

Supports acne treatment, Boosts salicylic acid effect, maintenance of sebum level



TopicLife™ Linum

Sebum control – woman

Regulation of sebum secretion, reduction of pore size – efficacy in woman



TopicPure™ Pumpkin Seed

Sebum control – male

Inhibition of 5 alpha reductase, 30% decrease in sebum secretion after 21 days – efficacy in man



TopicPure™ Willow Mix

Anti-inflammatory activity

Natural salicylic acid for inflammation and irritation control