Granactive Retinoid

THE POWER OF RETINOL WITHOUT THE IRRITATION

Presented by John Gormley
Director of Regulatory Affairs
**Granactive Retinoid:**

“A next generation anti-aging active for cosmetics”

- **High performing nonprescription retinoid ester**
- **Anti-aging**
  - Improved fine lines and wrinkles
- **Non-irritating**
  - (as compared to retinol)
- **Improved skin clarity**
- **Easy to formulate**
- **Brighter, more youthful appearance**
  - for healthier complexion

*Partner over Supplier*
Balancing the Activity Profile of Retinoids

Growth
Vision
Reproduction
Immunity
Cancer prevention
Normal - Healthy skin

Skin irritation
Instabilities
- O$_2$
- Photochemical
- Heat
Toxicity – high oral IU’s
Regulatory

Retinol: A highly recognized active for cosmetics and dermatology

Use to smooth wrinkles, unclog pores, lighten superficial brown spots, improve the texture of the skin...

...BUT with a well documented irritation profile

Partner over Supplier
The “all trans” retinoid family

- **Retinoic Ester** - Dermatology/cosmetics
  - *Granactive Retinoid*
  - Hydroxypinacolone Retinoate (HPR)

- Retinol – Dermatology/cosmetics
- Retinol Esters – Cosmetics
- Retinal – Vision / cosmetics

- Retinoic acid (RA)
  - Rx – drug (standard for receptor activity)

*Partner over Supplier*
# Retinoids: What's the difference?

<table>
<thead>
<tr>
<th>Retinoid</th>
<th>Benefits</th>
<th>Drawbacks</th>
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</table>
| Granactive Retinoid (Hydroxypinacolone Retinoate) | Low irritation index  
Enhanced activity  
Correct oxidation state  
Improved stability | UV / oxygen |
| Retinol                        | Well characterized activity  
Well known in market | UV / oxygen  
Skin irritation  
Lowest stability  
Lowest oxidation state |
| Retinol Ester                  | Low irritation index  
Well known in market  
Improved Stability | UV / oxygen  
Lowest activity  
Lowest oxidation state |
| Retinal                        | Potentially more effective than retinol if enzymatic metabolism to retinoic acid is the target | UV / oxygen  
Poor shelf stability  
Not in final RA oxidation state |
| Retinoic Acid                  | Anti aging recognized by FDA                  | Prescription medication  
Irritation  
UV / oxygen |
HPR  10x stability over retinol 50°C

0.1% by wt. retinoid in DMI, low Actinic glass, N2 atm, 50°C water bath, shaken samples HPLC results.

NO ANTIOXIDANTS INCLUDED
Granactive Retinoid

- INCI: Dimethyl Isosorbide (and) Hydroxypinacolone Retinoate
  - 10% retinoid active (in Gransolve DMI)
    - BHT/BHA free

- Gransolve DMI:
  - Solvent for actives, including retinoids
    - Both water and oil compatibility
  - Safe/mild to use on skin and around the eyes
  - Enhances penetration of retinoid and actives to the epidermis
Granactive Retinoid: Applications and Formulation

- Emulsions, serums and anhydrous systems
  - Add to the oil phase of all emulsions, 1-3% use level
  - Recommended in night time and treatment applications

- Co-formulated other active ingredients, photo-stabilizers, and even sunscreens for daily wear.
  - Formulas may be more stable than individual raw materials

- Use Conditions that favor stabilized retinoid compositions:
  - antioxidants, chelating agents, neutral pH, dark and air-tight containers
Granactive Retinoid: Skin renewal

**Image 1.** Dramatic reduction of lines and wrinkles was observed after 14 days Granactive Retinoid (2%) application. Demo formula – Retinoid Serum. Applied twice daily.

**Image 2.** After application on a 24 hour occlusive patch test, hydroxypinacolone retinoate demonstrated a significantly lower irritation profile versus retinol. Test samples were 0.5% retinoid in Gransolve DMI.
Granactive Retinoid: Skin renewal

**Image 1.** Dramatic reduction of lines and wrinkles was observed after 14 days Granactive Retinoid (2%) application. Demo formula – Retinoid Serum. Applied twice daily.

**Image 2.** After application on a 24 hour occlusive patch test, hydroxypinacolone retinoate demonstrated a significantly lower irritation profile versus retinol. Test samples were 0.5% retinoid in Gransolve DMI.
Granactive Retinoid: No irritation

Image 1. Dramatic reduction of lines and wrinkles was observed after 14 day Granactive Retinoid application.

Image 2. After application on a 24 hour occlusive patch test, hydroxypinacolone retinoate demonstrated a significantly lower irritation profile versus retinol. Test samples were 0.5% retinoid in Gransolve DMI.
Granactive Retinoid: No irritation or sensitization found

- 24hr Patch Test 0.5% HPR in DMI (vs 0.5% Retinol)
  - See Image on prior slide
- Human Repeat Insult Patch Test (HRIPT)
  - 50 subjects, 9 Inductions
    - 1) Demo formula incl. 0.2% HPR
    - 2) 0.5% HPR in Silicone elastomer + petrolatum vehicle
      - Both tests - No irritation after 21 days
- Sponsored clinical - 21 day cumulative irritation test
  - 0.1% HPR test emulsion – zero irritation
Granactive Retinoid:
Reduction in surface roughness

Test formula:
Skin Lightening Cream
Granactive Retinoid: Reduction in skin scaling

Reduction in Surface Scaling

40% Improvement in overall appearance

Days

Visioscan (SEsc)

1.5
1.0
0.5
0.0

1 7 14

~60% Improvement after 4 weeks
Granactive Retinoid: Reduction in age spot

Contributes to Skin Lightening / Brightening

Reduction in Visual Age Spots

~50% Improvement after 4 weeks

Visual Grading Scale
Granactive Retinoid: 14 Day Questionnaire Summary

100% panelist agreed significantly with:

- Reducing roughness and dryness
- Improving:
  - the skin’s softness and smoothness
  - skin’s radiance, tone and clarity
  - the skin’s firmness, tightness and elasticity
  - the skin’s overall appearance
Granactive Retinoid:
14 Day Questionnaire Summary

- 80% of panelist agreed significantly with:
  - Reducing appearance of fine lines and wrinkles
  - Diminishing appearance of age spots and skin discolorations
  - Improving the texture of sun-damaged skin
Granactive Retinoid:

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<tr>
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<th>Subject</th>
<th>Result</th>
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<tbody>
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<td>In-vitro Cells lines</td>
<td>Better toleration</td>
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<td>Typical retinoid expression</td>
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<td>In-vitro Cells line</td>
<td>Good Activity on two RAR receptors</td>
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Key Contributions by: Dr. Ron Lerum  
Partner over Supplier