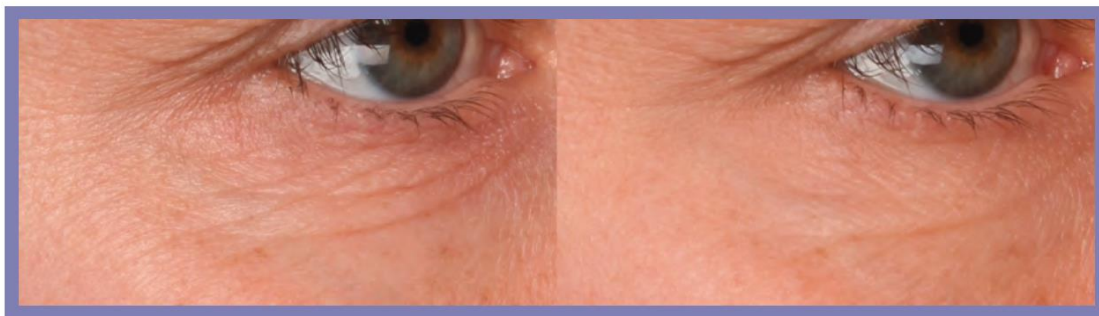


## CLINICAL DATA – HYDROXYPINACOLONE RETINOATE – NEXT GENERATION RETINOID

Hydroxypinacolone Retinoate is a cosmetic grade ester of all-trans retinoic acid. This skin care active ingredient belongs to a class of chemical compounds termed retinoids, which are derivatives of Vitamin A capable of binding to retinoid receptors in cells. The binding of retinoid receptors can epigenetically enhance gene expression, which effectively turns key cellular functions on and off. When skin cell retinoid receptors are bound with retinoids, a cascade of mechanisms that benefit skin structures and functions are 'switched on'. This can result in enhanced cell proliferation, biosynthesis of extracellular proteins and glycans, and improved cellular turnover. Stimulating these age defying processes in the skin is critical for fighting and reversing signs of ageing and overall skin balance.

### **Biological Pathways to youthful skin with Hydroxypinacolone Retinoate**

Stimulating cell proliferation and cell turnover are important for normalizing cell renewal and repair processes. Furthermore, as we age our skin becomes thinner and less elastic, leading to sagging, loss of thickness and wrinkles. Hydroxypinacolone Retinoate helps regulate cell processes to renew plumpness, elasticity and hydration to provide a radiant appearance. Moreover, Hydroxypinacolone Retinoate stimulates skin cell proliferation, restoring thickness to skin that has become thinner over time. These processes help reduce lines and wrinkles to promote a youthful appearance, while safeguarding skin from further wrinkle development. The effectiveness of Hydroxypinacolone Retinoate at reducing lines and wrinkles can be seen in Figure 1. Hydroxypinacolone Retinoate is also highly recommended for addressing acne due to its ability to regulate oil production. This cosmetic ingredient regulated cell turnover and numerous skin functions, which results in improved skin health, youthfulness and clarity.



**Figure 1** - Dramatic reduction of lines and wrinkles were observed after 14 days Hydroxypinacolone Retinoate application.

### **Challenges with older generation Vitamin A chemistries**

Although the benefits of retinoids have been known for decades, skin irritation, photochemical instability, and toxicity concerns have hindered their use. Retinoic acid is a prescription only topically applied ingredient recognized for its anti-ageing benefits, however it can be irritating to skin. In recent years, milder over the counter derivatives have become popular alternatives to Retinoic acid. These derivatives are metabolized to the active form by skin cells. Retinol (Vitamin A) is the most popular topical retinoid used to date, but unless stabilised in liposomes, its skin irritancy and instability to

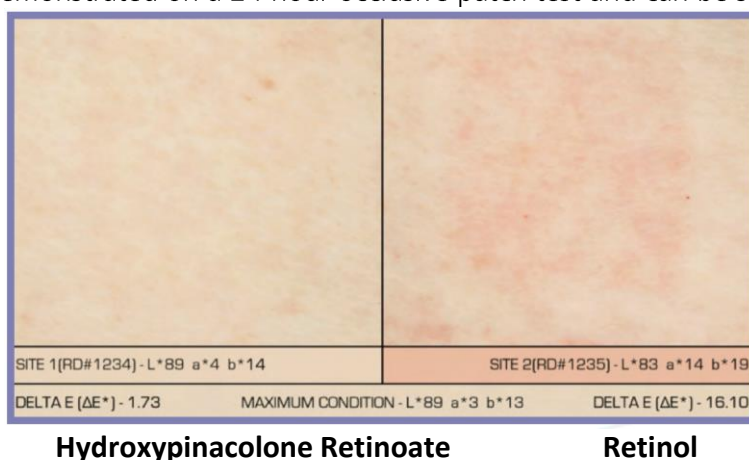
sunlight has limited its scope and appeal. Retinol esters are often used to lower the irritation potential and increase stability, but the trade-off is decreased retinoid activity and reduced potency.

### Hydroxypinacolone Retinoate advances opportunities in Vitamin A skin care

Hydroxypinacolone Retinoate is a next-generation anti-ageing product, delivering the performance of retinoic acid, retinol and retinoid derivatives with significantly lower irritation potential. The mechanism of action of Hydroxypinacolone Retinoate is advanced compared to standard retinol derivatives. To interact with retinoid receptors, retinol must first be metabolized to more active forms, such as retinaldehyde and retinoic acid using several enzymatic steps. Hydroxypinacolone Retinoate is unique in that it possesses innate retinoic acid activity, binding directly with retinoid receptors without the need for metabolic breakdown to more biologically active forms. Hydroxypinacolone Retinoate is dermatologically tested to offer less irritation potential than retinoic acid and most retinol derivatives, providing a gentle, safe and effective anti-ageing retinoid.

Clinical Results		
Assay	Subject	Result
Cumulative irritation patch	Human clinical panel	No irritation
Local irritation and sensitization potential assay	Human clinical panel	No adverse experiences
Skin roughness	Human clinical panel	50% improvement
Skin surface scaling	Human clinical panel	40% improvement
Skin irritation potential vs. standard retinol	Human skin cells	Lower irritation potential
Toleration under environmental stresses vs. unstabilised retinol	Human skin cells	Better toleration
Retinoid gene expression modulation	Human skin cells	Typical retinoid expression
In vitro percutaneous penetration	Human skin	Better toleration
In vivo percutaneous absorption	Human skin	Passed – proven safe

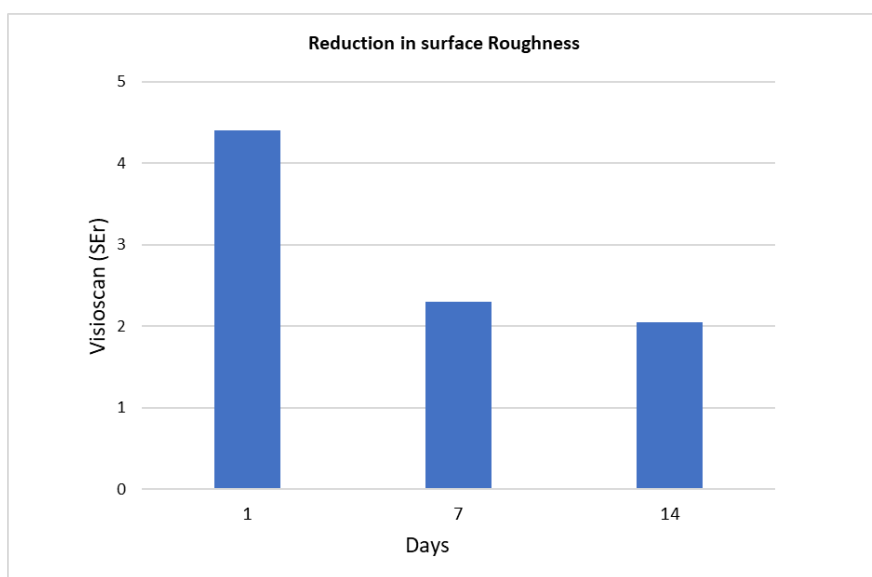
These results add credence to the beneficial safety and irritation profile of Hydroxypinacolone Retinoate as a topical cosmetic. The low irritation profile of Hydroxypinacolone Retinoate versus raw retinol was demonstrated on a 24-hour occlusive patch test and can be seen in Figure 2.



**Figure 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 dimethyl isosorbide.

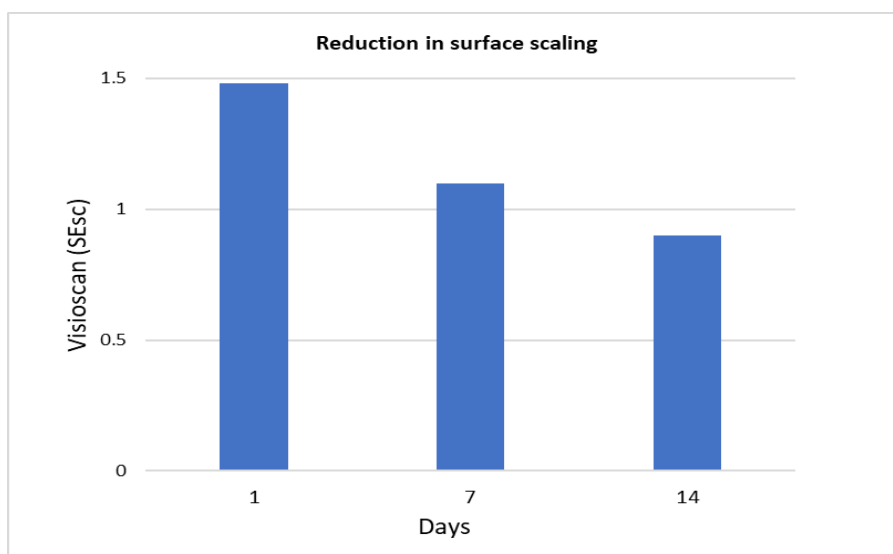
### Reduction in surface roughness

- A pilot-scale study to evaluate efficacy of Hydroxypinacolone Retinoate to reduce appearance of fine lines, facial wrinkles, age spots, surface roughness and scaling was performed
- Formulation # G101-235.02 (Skin Lightening Cream) containing 1% Hydroxypinacolone Retinoate
- Measurements performed by a Visioscan instrument
- Results at day 7 and day 14 are statistically significant (p-value < 0.05)
- 50% improvement in skin texture.



### Reduction in skin scaling

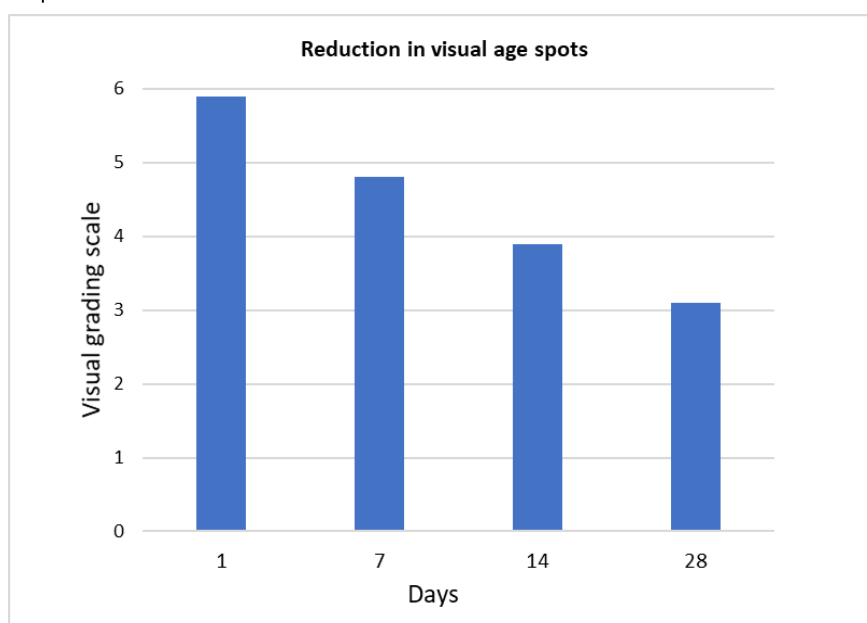
- Visioscan evaluation of the skin surface exhibited decreases in surface scaling
- Indicating reduced dryness and improved overall appearance.
- Results at day 7 and day 14 are statistically significant (p-value < 0.05)
- 40% improvement in overall appearance.



### Reduction in age spots



- Contributes to skin lightening and brightening
- Visual grading performed by a trained clinical evaluator using a 0-10 scale (best-to-worst)
- Results at day 7, day 14 and day 28 were statistically significant (p-value < 0.05)
- 50% improvement after 4 weeks

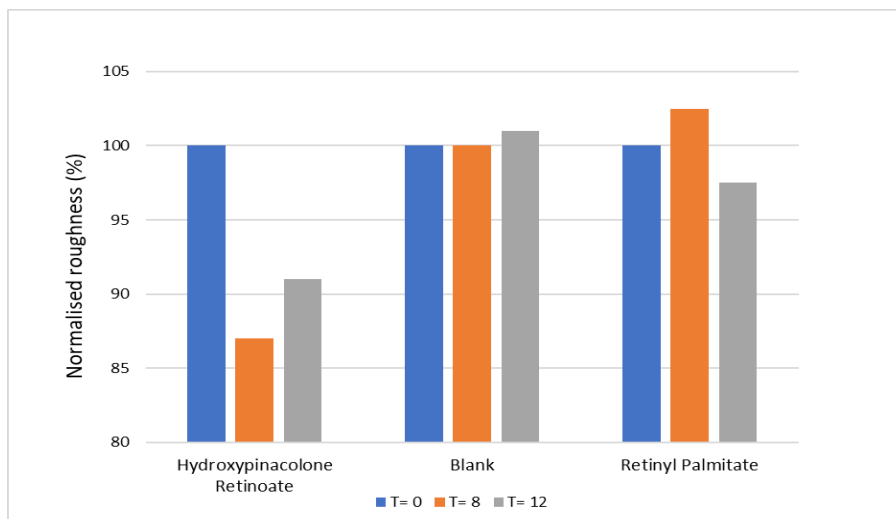


### Results: Statistical improvement in texture and UV spots

- Significant differences and improvement in texture (smoothness) and UV spots
  - **Texture** is primarily an analysis of skin smoothness. Texture measures skin colour and smoothness by identifying gradation in colour from the surrounding skin tone, as well as peaks (yellow) and valleys (blue) on the skin surface that indicate variations in the surface texture.
  - **UV spots** (age spots) occur when melanin coagulates below the skin surface as a result of sun damage. UV spots are generally invisible under normal lighting conditions and in their appearance are enhanced by the absorption of UV light by the melanin.
- Overall improvement in facial and hand photographs for subjects applying Hydroxypinacolone Retinoate.

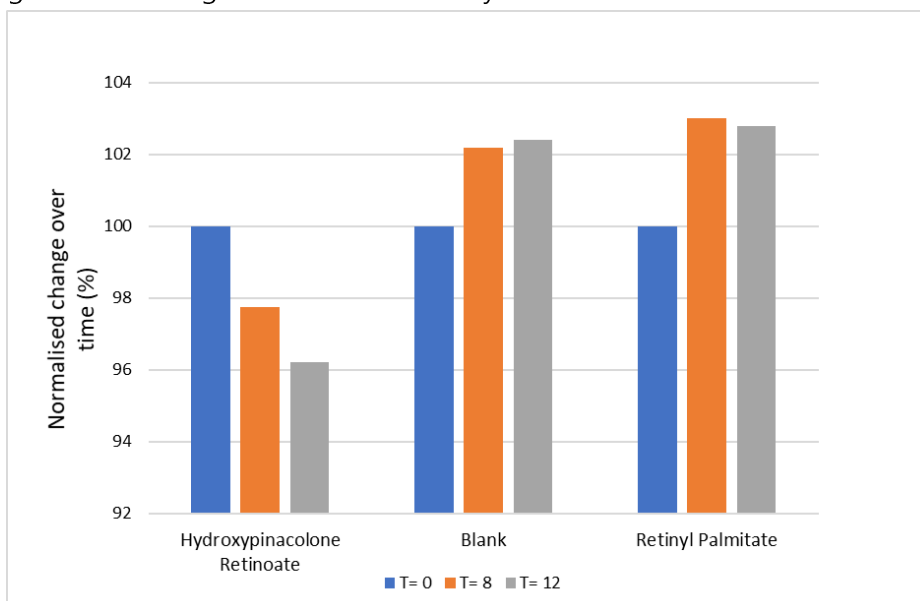
## Improved texture using Hydroxypinacolone Retinoate over time Canfield Texture

- Texture relates to skin smoothness
- Texture measures skin colour and smoothness by identifying gradations in colour from the surrounding skin tone, as well as peaks and valleys on the skin surface that indicate variation in the surface texture
- Significant decrease at T=12 for Hydroxypinacolone Retinoate (p-value <0.05)
- No significant change for blank or Retinyl Palmitate.

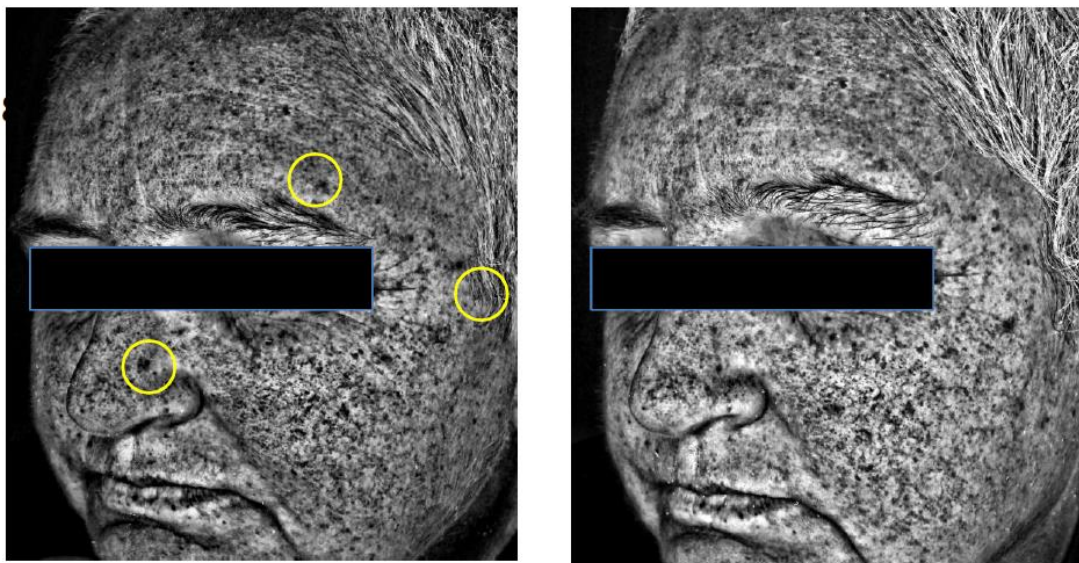


## Canfield UV Spots

- UV Spots (age spots) occur when melanin coagulates below the skin surface as a result of sun damage. UV spots are generally invisible under normal lighting conditions. The selective absorption of the UV light by the epidermal melanin enhances its display and detection by VISIA.
- Significant decrease at T=12 for Hydroxypinacolone Retinoate (p-value <0.05) and significantly different from blank and Retinyl Palmitate.
- No significant change for blank or Retinyl Palmitate.

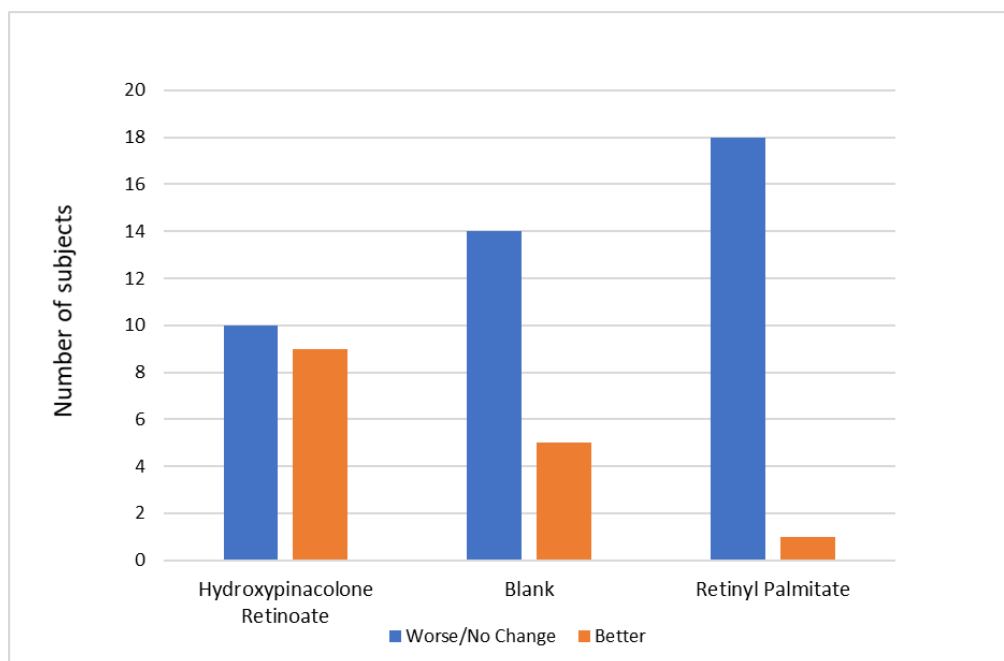


### Reduction of UV spots using Hydroxypinacolone Retinoate over time



### Facial photographic assessment

- Blinded grading of the face indicated the Hydroxypinacolone Retinoate serum resulted in more volunteers having noticeable improvement than the other two treatments.
- This supports the positive benefits of Hydroxypinacolone Retinoate.
- Results on this data were found to be significant (p-value < 0.05).

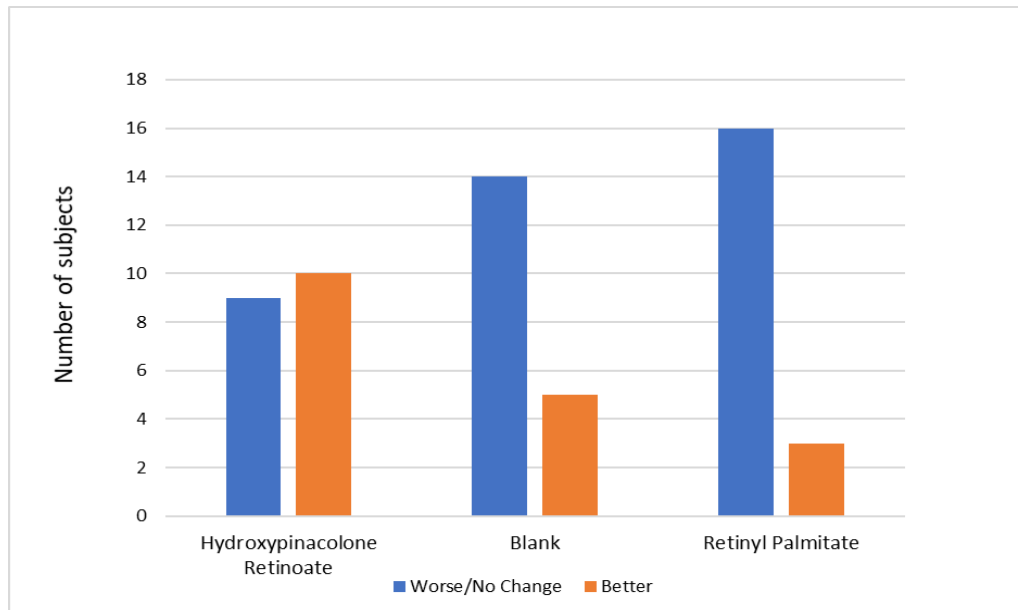


### Hand photographic assessment

- Blinded grading of the hand indicated the Hydroxypinacolone Retinoate serum resulted in more volunteers having noticeable improvement than the other two treatments.
- This supports the positive benefits of Hydroxypinacolone Retinoate.

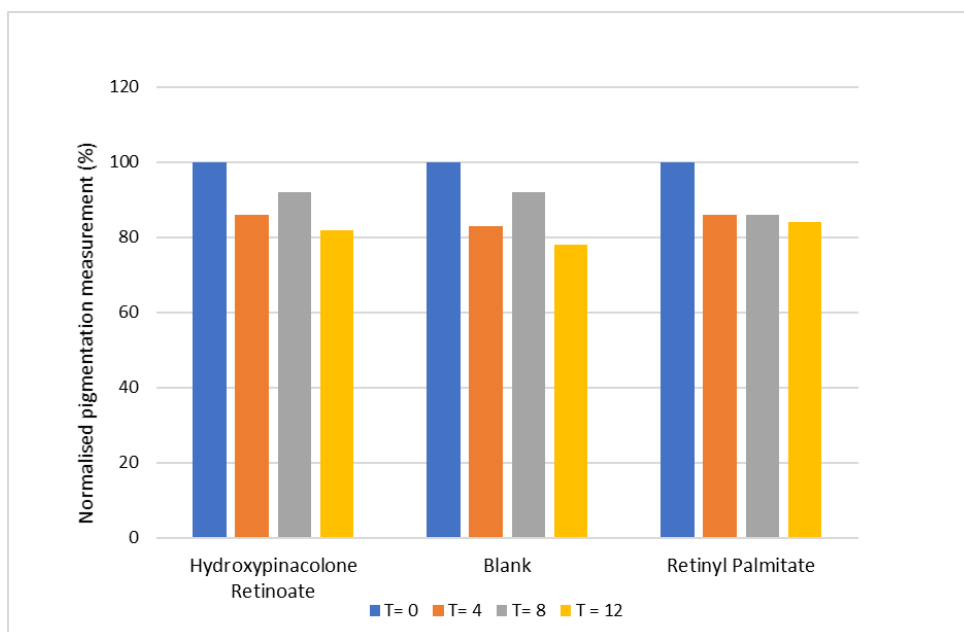


- Results on this data was found to be significant (p-value < 0.05).



### Hand pigmentation measurements

- Measurements of skin colour on 5 sites on the back of each hand using CIE colour space values (CIELAB) at T = 0; 4; 8; 12 weeks
- "No change" using Chromameter for the subjects
- Blank had a significant change (p-value < 0.05)
- Hydroxypinacolone Retinoate and Retinyl Palmitate had no significant change
- No irritation is observed and both retinoids prevented darkening of the skin.



**Performance**

Hydroxypinacolone Retinoate combats the appearance of fine lines and wrinkles for a more youthful appearance and improved texture. It also reduces uneven pigmentation improving brightness and luminosity and regulates cell renewal to increase skin firmness and elasticity. Reduction in pore size and excess oil is also observed leading to overall skin clarity. Hydroxypinacolone Retinoate delivers higher performance compared to most retinol derivatives, but with a significantly lower irritation potential.