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Retinyl palmitate for high level efficacy when combined with 10-hydroxy stearic acid

Poster 586

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Introduction:

Retinol and its derivatives are generally accepted as the gold standard active ingredient for anti-aging treatments however, retinol also has known drawbacks such as instability in formulation and can cause skin irritation for a subgroup of sensitive people. In certain applications the use of retinyl palmitate (Vitamin A palmitate) could be a preferred alternative because it is generally more stable than retinol and less irritation issues have been reported. Retinyl palmitate (RP) is the palmitic ester form of retinol and as such an inactive precursor. It is abundant in skin as storage form of the vitamin A. Once retinyl palmitate is applied topically on skin, an additional conversion step to retinol is required before it can be further processed to retinoic acid, the active form (figure 1). The efficiency and the mechanisms of conversion via microbial or skin derived enzymes is not yet clearly known and for this reason we wanted to test it on human skin to directly quantify the positive effects. Previously we discovered the PPAR agonist 10-HSA and showed various anti-aging benefits on skin [1]. Furthermore, we demonstrated the boosting effect on the efficacy of retinol when combined with 10-HSA as (PPAR)-alpha agonist [2] (figure2). A strong synergistic response on collagen III synthesis was observed. However, we haven't shown so far that this concept could also be applied to other retinol derivatives such as retinyl-esters.

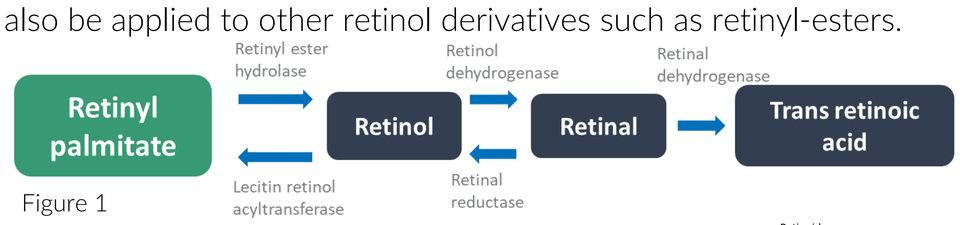


Figure 1

1) The first objective of the study was to measure ex vivo on human skin the efficacy of retinyl palmitate on boosting collagen I and III and fibrillin-1 level in the dermis.
2) The second objective was based on our retinol boosting concept to measure ex vivo on human skin the efficacy on collagen III synthesis by the combined treatment of retinyl-palmitate with 10-HSA and compare to the effect of the single ingredients.

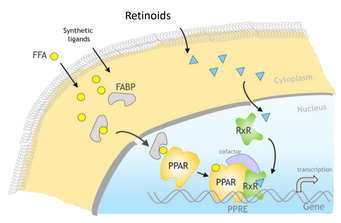


Figure2: PPARs heterodimerize with retinoic X receptor PPAR-RXR to induce amplified gene expression response in the cell nucleus. FFA = free fatty acid as typical PPAR agonist, FABP = fatty acid binding protein, RXR= retinoic receptor

Materials & Methods:

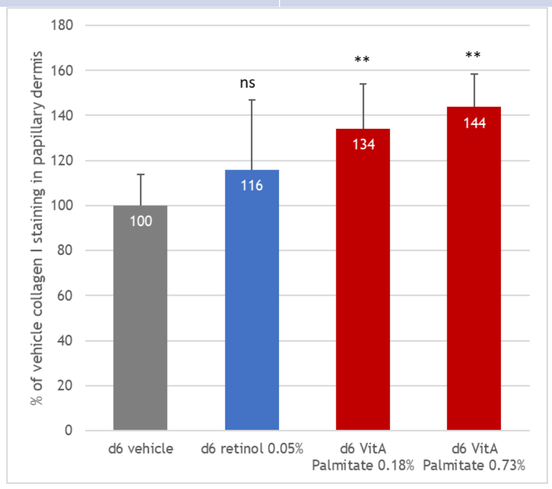
Ex vivo assay. We used ex vivo abdominal human skin of female donors for the application of the test compounds (retinyl palmitate at 0.18% and 0.73%, retinol at 0.05% and 0.1%) to the skin surface. Two different skin donors were used, aged 45years for collagen I staining and another for collagen III at age of 49years. The biological activity of the compounds was then assessed after 6 days of treatment by quantification of collagen I or III in the dermis via histologic immunostaining. The vehicle V of all tested products was a mix of 30% propylene glycol / 70% ethanol.

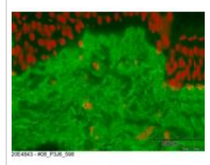
	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Skin Analysis	x						x
Product application	x	x	(x for collagenIII)		x		

Results & Discussion:

1. Collagen I Stimulation

Collagen1 staining in % at day6	Vehicle	0.05% Retinol	0.18% RP	0.73% RP
Mean ± SD	55.6 ± 7.6	64.4 ± 17.3	74.6 ± 11.1	79.9 ± 8.1




0.73% retinyl palmitate

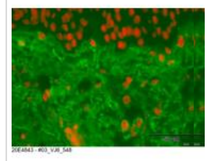
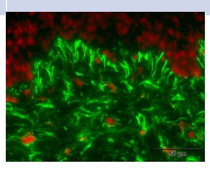

Vehicle treated

Figure 3: Results of collagen I immunostaining on *ex vivo* human skin from a 45years old female donor. Values represent % stained area in the papillary dermis normalized to the control (100%). d6 = stained after 6 days of treatment, n=9 replicates analysed per condition and error bars represent standard deviations. P-value by t test. Images on right side represent examples of histologic preparations showing green fluorescence in dermal part from collagen I immunostaining with lower image from vehicle and upper image at 0.73% retinyl palmitate. Cell nuclei are visible in red.

2. Fibrillin I Stimulation

Fibrillin1 staining in % at day6	Vehicle	0.05% Retinol	0.18% RP	0.73% RP
Mean ± SD	26.3 ± 2.6	24.7 ± 5.5 (n.s.)	31.4 ± 5.8 (p<0.05)	30.4 ± 4.9 (p<0.05)



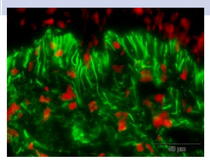


Figure 4: Representative images with green fluorescence of fibrillin-1 immunostaining on ex vivo human skin from a 49years old female donor. Image on the left side is the vehicle treated skin after 6 days (vehicle solvent was 30% propylenglycol/70% ethanol) and image on right side is treated with 0.73% retinyl palmitate in same solvent.

3. Collagen III Stimulation

Collagen III staining in % at day6	Mean ± SD (% vs vehicle) p value
Vehicle	27 ± 6.8 (100% ± 25.2)
0.1% Retinol	57.4 ± 4.7 (212.6% ± 17.4) <0.01
0.5% RP	67.1 ± 8.3 (248.5% ± 30.7) <0.01

4. Boosting Effect with 10-HSA

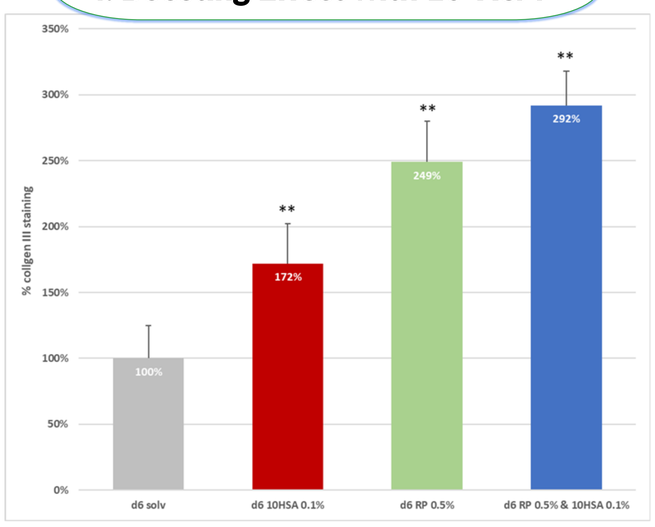


Figure 5: Results of collagen III immunostaining on ex vivo human skin from a 49years old female donor quantified as % stained area compared to the control (solvent only) normalized to 100%. RP = retinyl-palmitate, d6 = stained after 6 days of treatment, solvent was 30% propylenglycol/70% ethanol, n=9 replicates per condition and error bars represent standard deviations. ** Statistical significance versus control at p<0.01

Conclusions:

- In these studies, we now showed that retinyl palmitate is a direct booster of collagen I and III in human skin and the combination of retinyl palmitate (RP, 0.5%) with 10-HSA (0.1%) also worked out very well as collagen III synthesis was further increased with synergy observed.
- In contrast to data reported by others [3], we showed retinyl palmitate to be a very valid candidate for antiaging treatments and higher level of performance could be achieved when combined with 10-HSA.

References:

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