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Journal of Dermatology and Clinical Research

Research Article

Topical Therapies Based on Gene-Expression of Novel Retinaldehyde Cyclodextrin Complexes

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Submitted: 30 October 2014

Accepted: 19 January 2015

Published: 04 February 2015

Keywords

- Retinaldehyde
- Cyclodextrin
- Skin Antiaging
- Topical Therapy
- Acne
- Cellular Oxidation
- Topical Delivery System

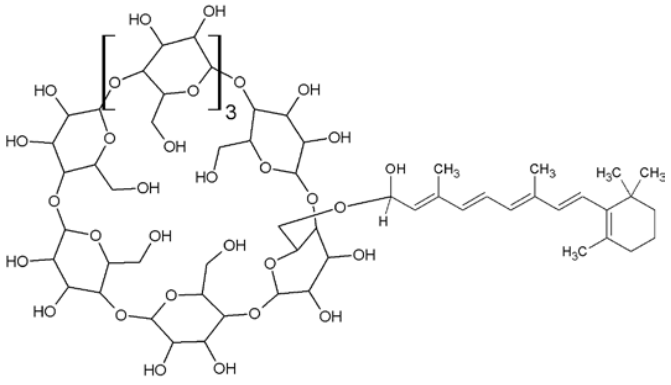
Abstract

Gene expression data of a novel compound, retinaldehyde γ-cyclodextrin hemiacetal (RCHA), are reported here in that show certain exclusive dermatologic attributes of RCHA offering opportunities for topical therapies not provided by retinaldehyde itself.

INTRODUCTION

Retinaldehyde (retinal) has gained worldwide popularity in dermatologic and cosmetic products for a variety of skin treatment applications, including ever-popular skin antiaging and acne [1-3].

A novel complex of retinaldehyde with cyclodextrin, retinaldehyde γ-cyclodextrin hemiacetal, has now been prepared. The gene-expression data of RCHA reveal potential for new topical therapies for skin care that, quite surprisingly, go beyond those of retinaldehyde itself. (Formula I).



RCHA and related compounds are prepared by the reaction of a polyene aldehyde, such as retinal, with a cyclodextrin, such as γ-cyclodextrin. There is a covalent chemical bond formation between said reacting molecules that results in the formation of the corresponding hemiacetal [4].

Gene-expression profiling is increasingly gaining momentum in the discovery of more efficacious and safer agents for topical treatments. Recent examples of gene-expression studies for topical applications are wide-ranging, of which antiaging [5], skin lighteners [6], hormonal skin aging [7], wound healing [8], and dermatitis [9] are worthy of note.

Concordantly, a gene-expression testing of RCHA was performed vis-a-vis retinaldehyde [10].

MATERIALS AND METHODS

Solutions of 0.1% retinaldehyde were prepared fresh on the day of application. RCHA Powder was provided with an initial retinaldehyde concentration of 4%. A 0.1% retinaldehyde solution was prepared by adding 25mg RCHA to 1.0mL of 100% DMSO. Crystalline retinaldehyde was provided with an initial retinaldehyde concentration of 99%. This was diluted to 1% (10.1 mg in 1mL of 100% DMSO) to create a stock solution. 100 µL of stock solution was added to 900 µL 100% DMSO to create a 0.1% retinaldehyde working solution.

GENE-EXPRESSION DATA ANALYSIS

Raw data generated with the Quant Studio 12K Flex software was imported into Real Time Stat Miner software v4.2 for statistical analysis using the relative quantitation (RQ) method. In the first step of an RQ analysis, the CT value of the target gene is normalized to the CT value of an endogenous control gene for each sample to generate the delta CT (dCT). dCT values are calculated in order to normalize/control for variability between the samples that may occur during the experimental procedures. Raw data analysis is typically expressed in log scale and then converted to linear Fold Change. A log10RQ value of 1.0 is equivalent to a 10-fold change in gene expression. A log10RQ value of 0.3 is equivalent to a linear fold change of 2.0. The Log10RQ values have been converted to linear fold change values to simplify data interpretation. Fold change values of 2.0 or greater are typically considered biologically relevant, but in the personal care industry, fold-change values of 1.5 are often seen in marketing materials.

Table 1: Gene Expression of Retinal γ-Cyclodextrin Hemiacetal (Rcha) for Topical Therapies.

Gene Identity	Gene Name	Fold Change Values		Gene Function	RCHA Skin Benefit
		RCHA	Retinaldehyde		
BMP2	Bone morphogenetic protein 2	-1.69	ns	Melanogenesis down-regulated	Skin whitening
GSTT1	Gutathione S transferase theta 1	2.44	ns	Oxidative Protection up-regulated.	Anti-oxidant
IL1A	Interleukin 1 alpha	-2.02	ns	Inflammatory response down-regulated.	Anti-inflammatory
IL1B	Interleukin 1 beta	*n/a*	2.39	Inflammatory response up-regulated.	Retinaldehyde is inflammatory
IL6	Interleukin 6	-2.04	ns	Inflammatory response down-regulated.	Anti-inflammatory
IL8	Interleukin 8	-1.92	ns	Inflammatory response down-regulated.	Anti-inflammatory
PTGS2	Cyclooxygenase 2 (COX-2)	-2.6	ns	Inflammatory response down-regulated.	Anti-inflammatory
ITGB4	B4 integrin	1.89	ns	Cell adhesion up-regulated	Skin barrier & firming
KLK5	Kallikrein 5	1.96	ns	Desquamation up-regulated.	Faster skin cell turnover
MMP1	Matrix metallopeptidase 1/collagenase	-1.82	ns	Extracellular matrix breakdown down-regulated.	Collagen protection
TGM1	Transglutaminase	-1.7	ns	Keratinization up-regulated.	Skin barrier function
MITF	Micropthalmia-associated transcription factor	-1,46	ns	Melanogenesis is down-regulated	Skin whitening
TP63	Transformation protein 63	2.22	ns	Senescence down-regulation	Retardation of skin aging

RESULTS AND DISCUSSION

A tabulation of RCHA properties that are unique to this molecule over retinaldehyde is provided in (Table 1). These data clearly indicate RCHA provides a topical method of treating, reducing the occurrence of, or improving the symptoms associated with melanogenesis, oxidative damage, inflammation, skin irritation from inflammation, loss of cell adhesion, loss of desquamation, extra-cellular including connective tissue matrix breakdown and skin tone loss thereof, loss of keratinization, cellular senescence, skin aging from cellular senescence, loss of skin whiteness, loss of skin barrier function, loss of skin firmness, inflammation from rosacea, skin disfigurements and skin discoloration from rosacea, inflammation from acne, skin rinkles and fine lines from cellular senescence, cellular oxidation, loss of skin collagen, and topical wounds.

CONCLUSION

Retinaldehyde γ-cyclodextrin hemiacetal provides opportunities for formulating topical treatments for unprecedented consumer desirable skin care attributes.

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Cite this article

Peter D, Stanek J, (Late) Orozco C, Gupta S (2015) Topical Therapies Based on Gene-Expression of Novel Retinaldehyde Cyclodextrin Complexes. J Dermatolog Clin Res 3(2): 1047.