Small Molecules for Lightening Skin

Tech ID: 18741 / UC Case 2007-640-0

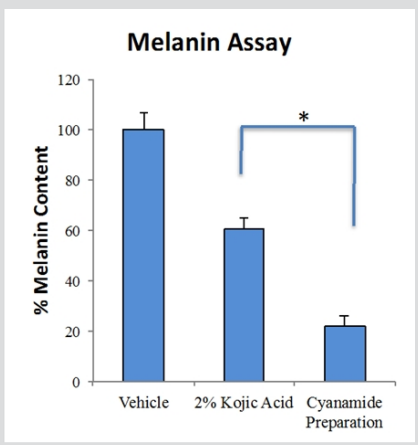
BACKGROUND

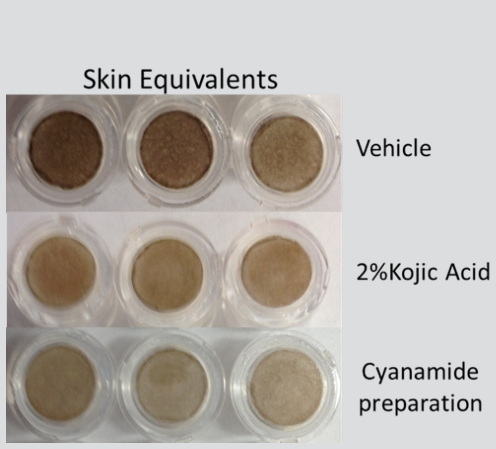
Skin hyperpigmentation is a common condition that can be the result of a clinical disorder (melasma), trauma, inflammation, or sun exposure. Currently available topical lightening agents for treatment of these conditions have safety concerns and have been pulled from over-the-counter products. Therefore, safe, novel depigmenting agents would have a potentially large consumer market. The present invention relates to methods and compositions for treating hyperpigmentary skin disorders based on the inhibition of a novel regulator of melanogenesis.

TECHNOLOGY DESCRIPTION

Using a genome-wide functional genomics approach designed to identify novel regulators of pigment production in human cells, researchers at UC Irvine determined that the enzyme aldehyde dehydrogenase (ALDH1A1) is novel regulator of pigment production.

Small molecule ALDH inhibitors were found to inhibit melanin accumulation by inhibiting the expression of key genes that are exclusively expressed in pigment cells. This mechanism is distinct from the mechanisms used by currently available pigment inhibitors. The most potent inhibitor found to date is the molecule cyanamide, a generic compound approved in Europe for alcohol aversion therapy. In vitro, cyanamide inhibits pigmentation in human skin cells. Cyanamide can inhibit melanin accumulation both histologically and quantitatively in skin equivalent models which closely mimic human skin.





The above figures demonstrate cyanamide can inhibit pigment accumulation in skin equivalents of darkly pigmented human skin (cyanamide, vehicle control, and kojic acid, a known skin lightener with side effects including skin irritation).

UCI researchers developed and tested 5 formulations, identifying one formulation that performed markedly better than the others. The preferred formulation was tested on healthy human subjects and did not produce any significant irritation.

Future Development Plans

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OTHER INFORMATION

KEYWORDS

Skin Lightening, Hyperpigmentation

CATEGORIZED AS

» **Medical**

» Disease: Dermatology

RELATED CASES

2007-640-0

Completion of stability testing is underway. We are currently looking for a commercial partner to further develop this product for skin lightening.

FEATURES/BENEFITS

- Our cyanamide formulation is effective in lightening human skin equivalents, is not sensitizing to mouse tails, and is non-irritating in a human RIPT study with human volunteers (>50 human subjects).
- Aldh1 (the target of cyanamide) depletion was shown to inhibit melanogenesis in both lightly pigmented and darkly pigmented melanocytes
- Cyanamide has been used in humans systemically for the treatment of alcoholism (oral formulation), therefore safety profile in humans is known.
- Known mechanism of action.
- Cyanamide inhibits melanin accumulation via a novel mechanism – it blocks the expression of melanogenic genes that are expressed in pigment cells.

PUBLICATIONS

- *"Genome-Wide siRNA-Based Functional Genomics of Pigmentation Identifies Novel Genes and Pathways That Impact Melanogenesis in Human Cells."* PLOS December 2008, Vol 4 (12): e1000298
- *"9-cis Retinoic Acid is the ALDH1A1 Substrate that Stimulates Melanogenesis in Human Skin."* http://onlinelibrary.wiley.com/doi/10.1111/exd.12099/abstract

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,889,081	02/13/2018	2007-640
United States Of America	Issued Patent	8,802,733	08/12/2014	2007-640

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