Cysteamine: Clinical efficacy, safety and tolerability versus best-in-class treatments for melasma

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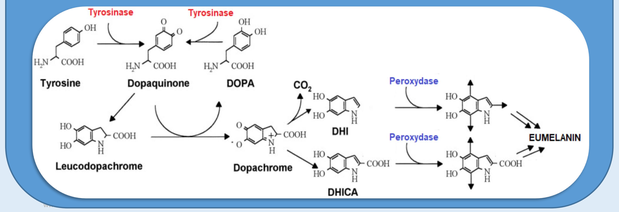
Introduction

- Cysteamine is an aminothiol naturally present in human body cells as an antioxidant resulting from the degradation of Coenzyme A.[1]
- Cysteamine hydrochloride is known for its potent depigmenting effect since 1960's when Chavin tested it through injecting cysteamine into the black goldfish skin.[2] Other *in vitro* and animal *in vivo* studies showed the higher depigmenting efficacy of this cysteamine compared to hydroquinone.[3-5]
- However, rapid oxidation and very offensive odor made it difficult for topical use.[6]
- An innovative technology has now been released to stabilize and deodorize cysteamine. Cysteamine thus became utilizable for the first time in a topical product.[7]
- Stabilized cysteamine has demonstrated significant effectiveness for the treatment of melasma by two double-blind randomized and vehicle control clinical studies, showing both greater reduction in mMASI score and melanin index compared to placebo.[7- 8]

Mechanism of Action

Cysteamine has a broad action in the regulation of melanogenesis:

- **Enzymatic effect:** inhibition of tyrosinase and peroxidase, essential enzymes in the melanogenesis pathway leading to the conversion of tyrosine into dopaquinone, and to the polymerization of indoles into melanin.[9]
- **Chemical effect:** chelation of mineral ions, preventing Fenton-type reactions.[10]
- **Antioxidant & Quencher of free radicals:** suppression of all the oxidation steps in the melanogenesis process & prevention of photo-oxidation (ie darkening of melanin precursors in the epidermis). [11]
- **Cascade reaction:** increase of intracellular glutathione, amplifying natural depigmenting effects.[12]
- **Keratolytic effect:** by breaking keratin disulfide bonds, it enhances the removal of melanin contained in the superficial epidermis layers and accelerates the epidermal turnover for generation of new non-pigmented skin layers.[13]



5% Stabilized Cysteamine (ST-CYS-5%) versus modified Kligman's formula (mKF)[14]

Material and methods

Double-blinded, Investigator-driven, randomized

50 female with melasma, 20-50 years old, assigned in 2 groups:

•ST-CYS-5% 15min application + moisturizer + sunscreen (daily, 16weeks)

•mKF overnight application (4% hydroquinone, 0.05% retinoic acid and 0.1% betamethasone) + moisturizer + sunscreen (daily, 16 weeks)

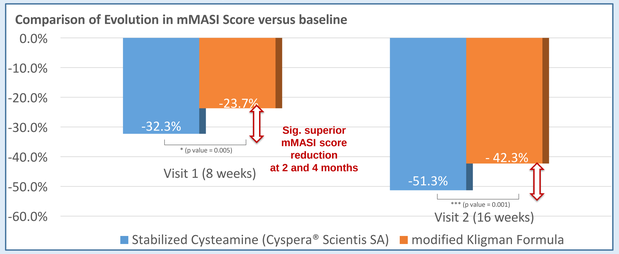
Evaluation of mMASI score; Investigator Global Assesment & Patient questionnaires

Evaluation at baseline, 8 weeks and 16 weeks

Efficacy Results

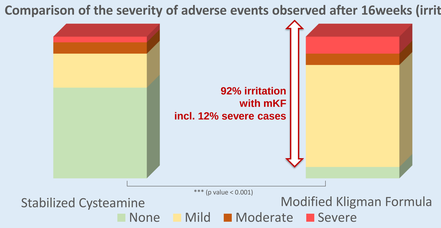
At both week 8 and week 16, ST-CYS-5% produced significantly greater reductions from baseline in modified Melasma Area Severity Index (mMASI) (32.3%, 51.3%), compared to mKF (23.7%, 42.3%; P = .005 and .001, respectively).

Investigator global assessment and patient self-assessment scores were similar for both treatments at each time-point.



Safety & Tolerability results

In all and at 16 weeks, 64% of patients treated with ST-CYS-5% reported no skin irritation, whereas only 8% of patients treated with mKF reported no skin irritation.



5% Stabilized Cysteamine (ST-CYS-5%) versus Tranexamic Acid mesotherapy (TXA)[15]

Material and methods

Single-blinded, Investigator-driven, Randomized

54 female with melasma, 18-50 years old, assigned in 2 groups:

•ST-CYS-5% 30min application (daily, 16weeks)

•TXA 0.05ml (4mg/mL) administered mesotherapy (every 4 weeks for 8 weeks)

Evaluation of mMASI score and Melanin Index

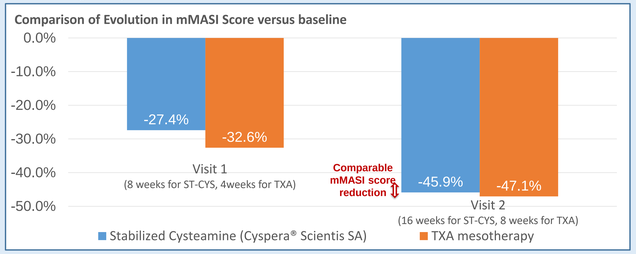
Evaluation at baseline, 8 weeks and 16 weeks for group ST-CYS-5%

Evaluation at baseline, 4 weeks and 8 weeks for group TXA

Efficacy Results

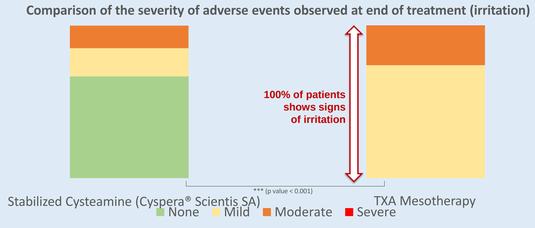
The degree of improvement of mMASI reduction was 45.9% for ST-CYS-5% after 16 weeks and 47.1% for multiple sessions of TXA mesotherapy. No patient in either group had recurrence of melasma in the follow-up period.

In both group and at both visits, Melanin index measured by Dermacatch was equally reduced (p>0.1).



Safety & Tolerability results

Complications were significantly more frequent in the TXA group.



5% Stabilized Cysteamine (ST-CYS-5%) versus Hydroquinone 5% (HQ)[16]

Material and methods

Double-blinded, Investigator-driven, Randomized

20 female with melasma, >18 years old, assigned in 2 groups :

•ST-CYS-5% 15min application + moisturizer + sunscreen (daily, 16weeks)

•Moisturizer + HQ4% + sunscreens (daily 16weeks)

Evaluation of mMASI score & Quality of Life (QoL) questionnaire

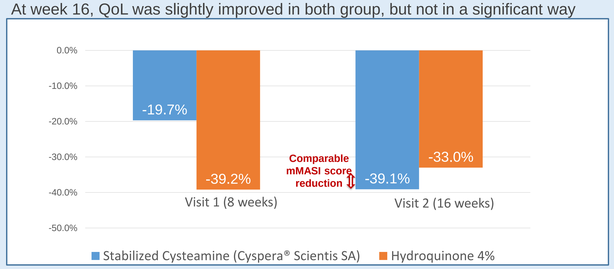
Evaluation at baseline, 8 weeks and 16 weeks

Efficacy Results

Various limitations for this study due to large number of drop out in both groups and small number of volunteer initially recruited (*n= 9* in HQ group, *n=5* in ST-CYS group)

At week 16, ST-CYS-5% was shown to be slightly superior in MASI score reduction compared to HQ4% when analyzed as per protocol (-39.1% versus -33%, p=0.96)

At week 16, QoL was slightly improved in both group, but not in a significant way



Conclusion : Stabilized topical cysteamine was proven to be significatively more effective for the treatment of melasma and better tolerated than the modified Kligman's formula. When compared to Hydroquinone and physician administered mesotherapy tranexamic acid (TXA), stabilized cysteamine was shown to be as effective and better tolerated.

According to these results, **cysteamine can be considered the first line non-hydroquinone treatment for melasma**.

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