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

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Introduction

• Cysteamine is an aminoethanol naturally present in human body cells as an antioxidant, resulting from the degradation of cysteine. 1,2
• Cysteamine hydrochloride is known for its potent depigmenting effect since 1960 when Chwastiik tested it through injecting cysteamine into the black goldfish strain.2 Other in vivo and animal in vitro studies showed the higher depigmenting efficacy of this cysteamine compared to hydroquinone.1,3
• However, rapid oxidation and very offensive odor made it difficult for topical use.4
• An innovative technology has now been released to stabilize and deodorize cysteamine. Cysteamine thus became usable for the first time in a topical product.5

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 dopaquinones, and to the pigmentation of cuticles into melanosomes.6
• Chemical effect: chelation of mineral ions, preventing Fenton-type reactions.7
• Antioxidant & Quencher of free radicals: suppression of all the oxidation steps in the melanogenesis process & prevention of photo-oxidation (darkening of melanin precursors in the epidermis).7
• Cascade reaction: increase of intracellular glutathione, amplifying natural protective effects.8
• Keratolytic effect: by breaking keratin disulfide bonds, it enhances the removal of melanin contained in the superficial epidermis layers and accelerates the epidemal turnover for generation of new non-pigmented skin layers.9
• Depigmenting effect 10 (Fig. 4). Cysteamine is effective in reducing pigmentation because it promotes a decrease in melanin synthesis and a reduction of the size and density of epidermal melanocytes.1,2,11

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

Material and methods
Double-blinded, investigator-driven, randomized 54 female with melasma, 16-50 yrs old, assigned in 2 groups:
- ST-CYS-5%: 15 min application + moisturizer + sunscreen (daily, 16weeks)
- mKF: overnight application (4% hydroquinone, 0.05% retinoic acid and 0.1% benzoyl peroxide) + moisturizer + sunscreen (daily, 16weeks)

Evaluation of mMASI score: Investigator Global Assessment & Patient questionnaires
Efficacy Results
At both week 6 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 (37.3%, 42.3%). P < 0.001 and 0.001, 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, 54% of patients treated with ST-CYS-5% reported no skin irritation, whereas only 8% of patients treated with mKF reported no skin irritation. Comparison of the severity of adverse events observed at 16 weeks (Table 1). Stabilized Cysteamine (Cyanpera® Scientific SA), modified Kligman’s Formula (mKF), N=50 per group.

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<tr>
<th>Time</th>
<th>Cysteamine</th>
<th>mKF</th>
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<tbody>
<tr>
<td>Visit 1 (1 week)</td>
<td>3.3%</td>
<td>13.3%</td>
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<tr>
<td>Visit 2 (8 weeks)</td>
<td>11.1%</td>
<td>11.1%</td>
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Comparison of Evanls of mMASI Score versus baseline

Visit 1 (1 week) | Visit 2 (8 weeks)
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<tr>
<td>100% Stabilized Cysteamine</td>
<td>65% mKF</td>
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Conclusion : Stabilized topical cysteamine was proven to be significantly more effective for the treatment of melasma and better tolerated than the modified Kligman’s formula. When compared to Hydroquinone and physician administered mesitherapy 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-phenoline treatment for melasma.

References