

# Novel Allyl PQQ Combination with Chlorogenic Acid and Methyl Gentsiate (HQ Analogs) for the Treatment of Hyperpigmentation

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## INTRODUCTION

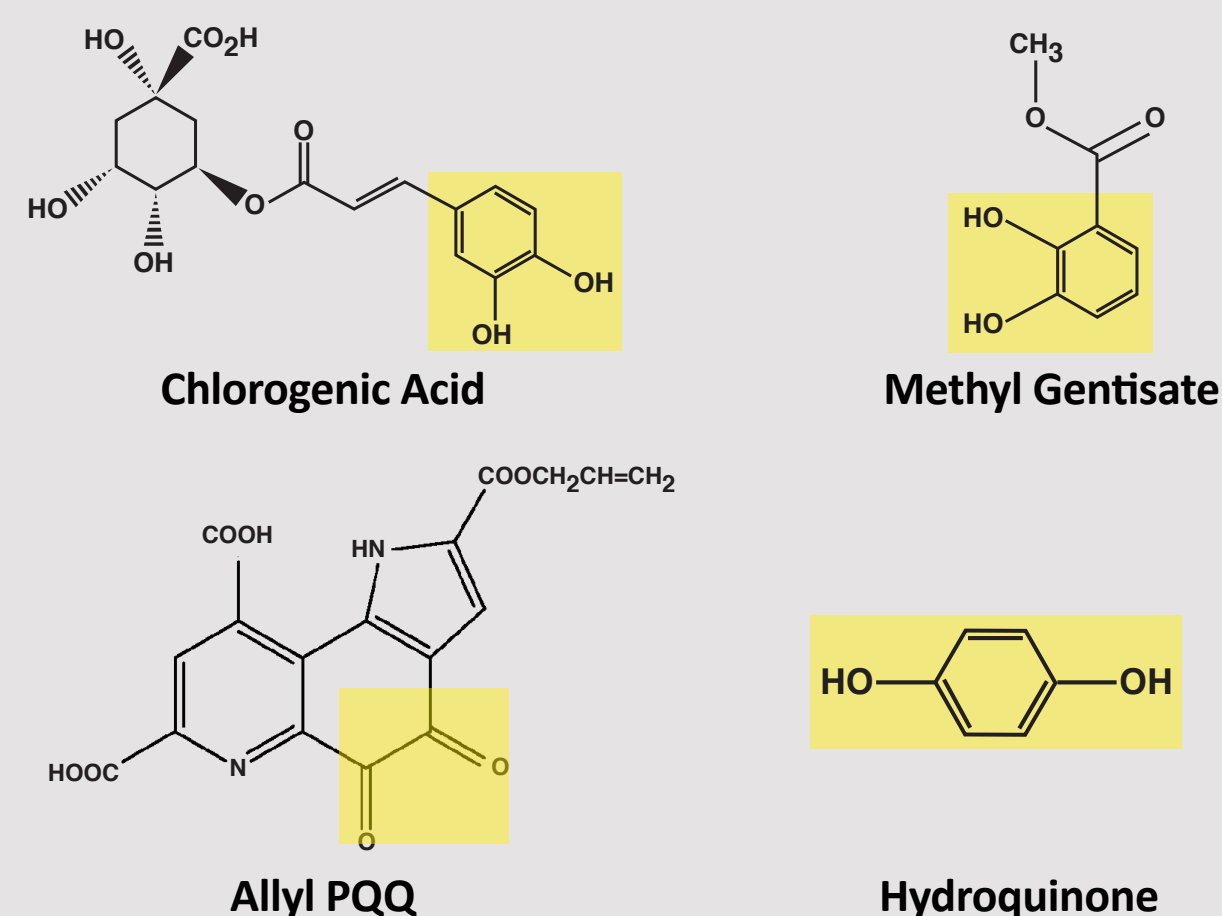
Hyperpigmentation may arise from any of a variety of sources including inflammation, acne vulgaris, photodamage, or as a symptom of numerous diseases. Hydroquinone (HQ) is an aggressive

and effective frontline therapy for hyperpigmentation, but despite pending final monograph status for OTC Skin Bleaching Drug Products by FDA in the US, HQ is a known cytotoxic compound.

## NOVEL COMBINATION HQ ANALOGS

The compound 2-allyl pyrroloquinoline quinone (allyl PQQ), a powerful recyclable electron transfer antioxidant, was demonstrated to be effective at reducing skin hyperpigmentation in prior studies. PQQ, an efficient free radical scavenger, is a coenzyme of methanol dehydrogenase within methanol-assimilating bacteria and has been detected from microorganisms as well as edible plants such as soy beans, green peppers, potatoes, spinach, and some processed food products.<sup>1</sup> Chlorogenic acid is a naturally occurring plant polyphenol antioxidant found in coffee (*Coffea arabica*) and eucommia (*Eucommia ulmoides*). Methyl gentsiate (methyl 2,5-dihydroxybenzoate), is the methyl ester of gentisic acid, a dihydroxybenzoic acid found in the African tree *Alchomea cordifolia*. Methyl gentsiate is a skin lightening agent originally demonstrated to deliver HQ type efficacy without cytotoxicity.<sup>2</sup> All of these compounds (see Figure 1 for molecular structure) effect pigmentation presumably by tyrosinase inhibition and function as HQ analogs. In this study, 0.05% Allyl PQQ, 1.0% chlorogenic acid and 2.0% methyl gentsiate were combined for the treatment of moderate to severe hyperpigmentation.

Figure 1. Antioxidant Hydroquinone (HQ) Analogs



## STUDY & METHODS

The purpose of this investigation was to evaluate the safety and efficacy of a topical treatment regimen using this HQ analog combination for moderate to severe hyperpigmentation. A three arm 30 subject 8-week clinical trial was conducted with one arm (n=10) dedicated to treating hyperpigmentation; subjects included women (mean age 52.8±8.65 years, range 41 to 65) with moderate to severe hyperpigmentation (grade 3 or higher on a 6-point scale). Standard inclusion and exclusion criteria were parameters affecting participation in the study.

Patients employed a three product treatment regimen consisting of a twice daily (morning and evening) application of Age Defying Cleanser (7.8 % lactic acid, 2% salicylic acid) followed by depigmentation

serum (0.05% Allyl PQQ, 1.0% chlorogenic acid & 2.0% methyl gentsiate), with a broad spectrum SPF 50 sunscreen in the morning and as needed. In addition the subjects received 50% AHA superficial chemical peel at day zero (baseline visit) and at 4 weeks, and used 30% AHA home peel pads 2-3 times per week depending on subject tolerability. Strict sun avoidance was essential. A light mineral powder foundation was provided for subjects to use in place of their ordinary foundation. The investigating physician evaluated hyperpigmentation (dyschromia) on a six-point scale (0 - None; 1 - Minimal; 2 - Mild; 3 - Moderate; 4 - Moderately Severe; 5 - Severe) at baseline, week 4 follow-up, and at study conclusion (week 8 follow-up).

## RESULTS & DISCUSSION

All 10 subjects completed study, with no adverse effects reported. The regimen was well tolerated.

Average dyschromia score at baseline was 3.1. At week 4 the average score was 2.6, a reduction of 16% from baseline (not statistically significant, p=0.0541), with a highly statistically significant (P<0.001) 42% reduction in dyschromia noted at week 8. This suggests a gradual, continuous improvement. See Table 1 for results and Figures 2 and 3 for Before/After pictures. The study was conducted in the eastern US during the summer months (Jun-Aug) which likely had a negative impact on skin pigmentation purely based on incidental climatic UV exposure during this period.

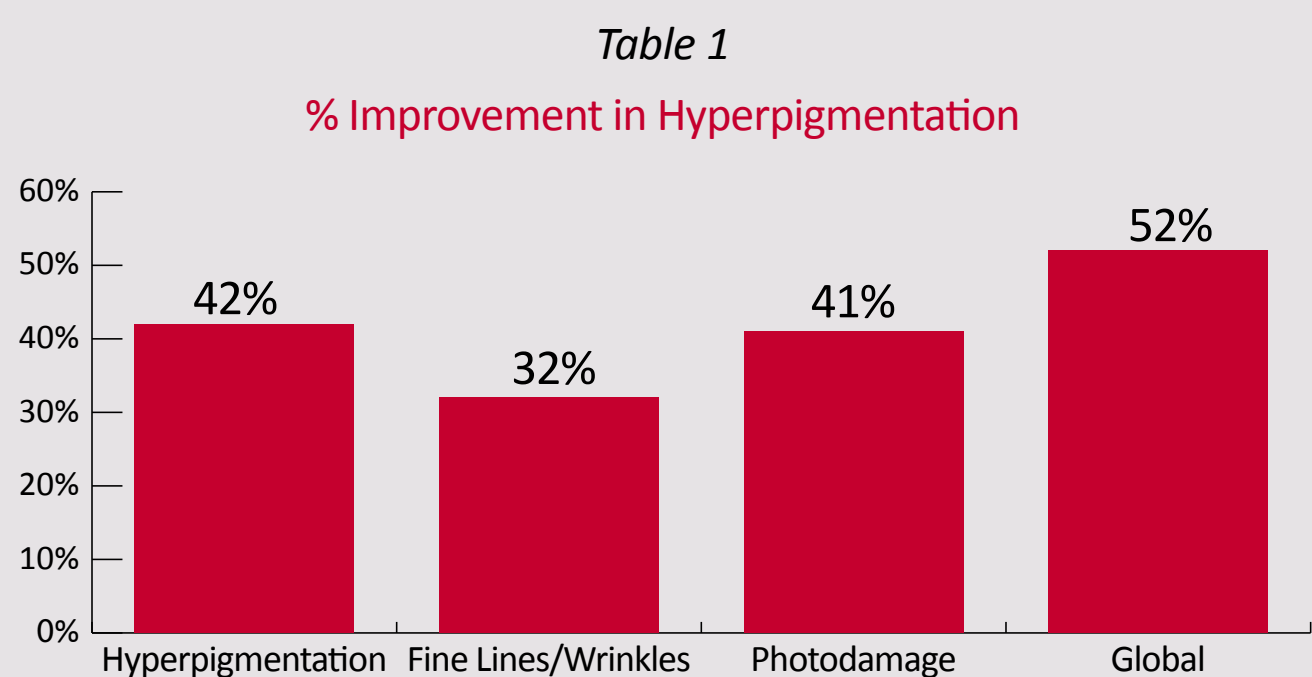


Figure 2 SUBJECT 18/LEFT SIDE - DAY 0 & 8 WEEKS



Figure 3 SUBJECT 6/LEFT SIDE - DAY 0 & 8 WEEKS



## CONCLUSIONS

The combination of 0.05% allyl PQQ, 1.0% chlorogenic acid, and 2.0% methyl gentsiate was successful at decreasing skin hyperpigmentation.

## DISCLOSURES

This study was sponsored by US Cosmeceutechs, LLC and conducted on their behalf by Dr. Gold. The primary author holds no interest or stock or direct affiliation with US Cosmeceutechs except in the capacity of a paid independent research consultant.

Joseph Lewis BS and Laura McHugh MS are employed by US Cosmeceutechs, LLC, owner of pending patents for technologies used in this study.

Arthur Pellegrino BS and Lavinia Popescu MS, MBA are employed by Elizabeth Arden, Inc., investor in US Cosmeceutechs, LLC.

## REFERENCES

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