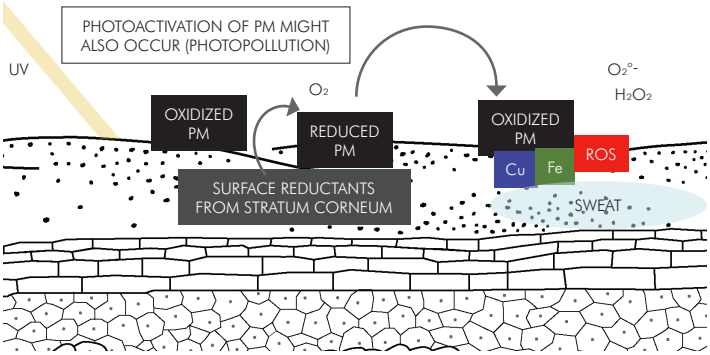
SkinCeuticals

ANTI-POLLUTION BENEFITS OF C E FERULIC BASED ON THE FIRST IN-VIVO CLINICAL TRIAL

INTRODUCTION

We have shown the accumulative harmful effects caused by frequent environmental insults such as ozone (O3), diesel engine exhaust (DEE) as a source of particulate matter (PM), and ultraviolet (UV) light have all been shown to play a role on atmospheric aggressors by inducing skin damage through disruption of redox homeostasis and induction of pro-inflammatory status. Here, we begin with the impact of an additional environmental stressor that has become very prevalent in particulate matter (PM). Metals like iron (Fe) and/or copper (Cu) are abundant in PM and are known to contribute to the formation of reactive oxygen species (ROS), which eventually lead to skin damage. A visual of this is shown in **Figure 1** the Fenton reaction may be catalyzed by iron or copper provided by the particle, the very reactive hydroxyl radical is generated from hydrogen peroxide and strongly reacts with lipids from sebum or stratum corneum proteins.

Figure 1: Possible mechanism allowing ROS production by particulate matter (PM) matter containing transition metals.



Atmospheric pollution and sunlight are one of the main environmental stressors in urban life. Interestingly melasma for example is more frequent in animals living in polluted areas on urban-industrial sites. Although topical antioxidants have been shown to help reduce the impact of sunlight on skin damage, our new science shows that within an in-vivo clinical study two strong messages are clinically proven: 1) Impact of accumulative exposure of environmental stressors like particulate matter (PM) and ultraviolet radiation induces oxidative stress and inflammation in skin and 2) Topical C E Ferulic serum mitigates the impact of the accumulative exposure of environmental stressors with a clear reduction in these stressors.

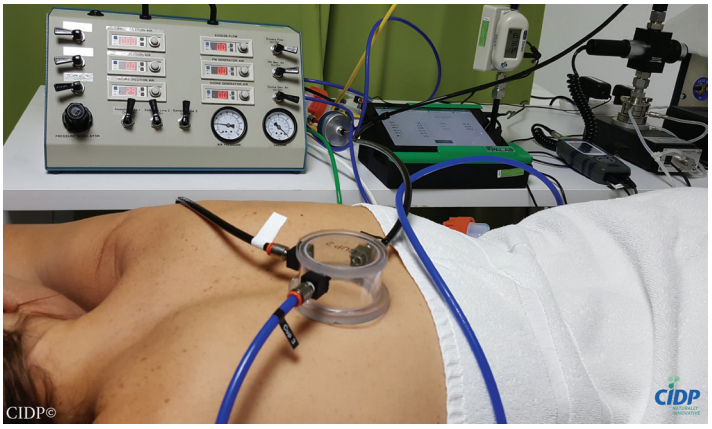
OBJECTIVE

Our goal was to evaluate the ability of a topical C E Ferulic serum containing 15% L-ascorbic acid, 1% α-tocopherol, and 0.5% ferulic acid; to prevent oxinflammatory skin damage induced by PM with and without UV in an in-vivo model.

EXPERIMENTAL METHODOLOGY

A 4-day double-blinded clinical study was conducted on the back of 15 female subjects aged 18-40 years. During the 4 consecutive days, the back test zones were treated daily with/without C E Ferulic pre-treatment. The test zone without any treatment served as control.

Figure 2: New indoor controlled in-vivo exposure methodology supplying UV and pollution, measuring damage and protection.



The Controlled Pollution Exposure system has been developed by CIDP. The Innovative pollution exposure system to in-vivo and ex-vivo controlled exposure to pollutants (O3, Ambient Particles), allows monitoring and control of the concentration and flux of different pollutants. Photo courtesy of CIDP- www.cidp-cro.com

Exposure Conditions

- Control (no exposure)
- Particulate matter (PM)
- Particulate matter (PM) + UV

Exposure time each day

- PM for 2 hours
- 2J/cm2 for 5 minutes

D-squame and biopsy samples were collected for biomarker analysis at the end of study. The expression of four key biomarkers were selected, two indicating oxinflammatory damage and two indicating skin barrier damage; respectively. Nuclei were stained with DAPI (4, 6-diamidino-2-phenylindole) to assess gross cell morphology. The control was also utilized to validate the effects of the atmospheric aggressors on the skin tissue. All were measured using immunofluorescence to assess whether the atmospheric aggressors acted synergistically in promoting aggressor-induced skin damage.

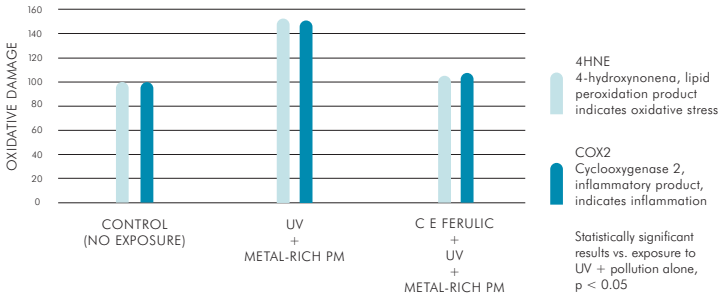
RESULTS

After 4 days of daily exposure to PM with and without UV, analysis of D-squame showed significantly greater total iron and copper content, respectively, in the top 3 cutaneous layers compared to unexposed control.

Figure 3 and Figure 4: C E Ferulic Prevents Oxinflammation Skin Damage Induced by PM + UV

C E Ferulic topical application demonstrated the following:

- 48.91% decrease in 4HNE vs. PM + UV exposed skin
- 44.54% decrease in COX2 vs. PM + UV exposed skin



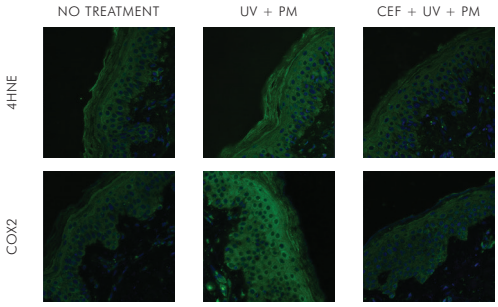
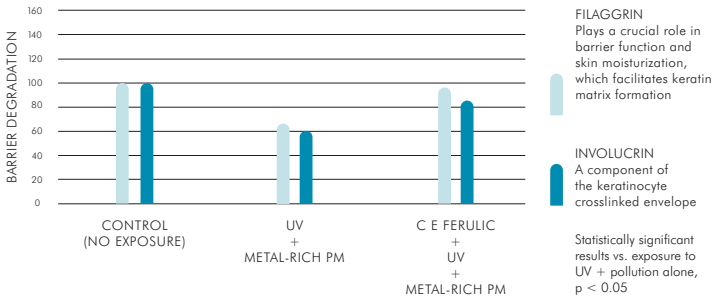
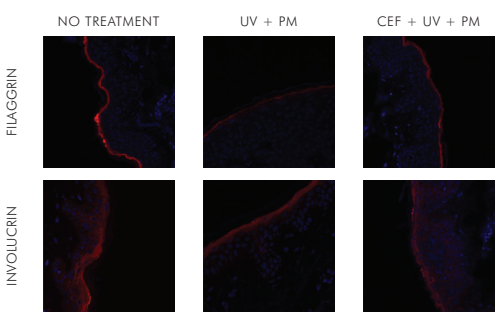


Figure 5 and Figure 6: C E Ferulic Prevents Loss of Skin Barrier Proteins Induced by PM + UV

Application of topical serum rescued PM + UV induced loss of filaggrin and involucrin:

- 27.53% increase in filaggrin vs. PM + UV exposed skin
- 22.58% increase in involucrin vs. PM + UV exposed skin





CONCLUSION

This new science in-vivo methodology demonstrates topical C E Ferulic can counteract oxinflammatory damage induced by the combinations of air pollutants PM and UV and maintain the structural integrity of the skin barrier. This was demonstrated when serum treated explants maintained involucrin and filaggrin levels, suggesting that C E Ferulic's effect is protective after the combined UV and PM exposures. This is likely due to the antioxidant properties quenching the ROS generated from the presence of the Fenton reaction.

Besides the structural damage, skin explants exposed to accumulative environmental aggressors PM + UV displayed an altered oxidative and inflammatory status, depicted by increased levels of 4HNE and COX2.

In summary, the new methodology has captured the impact of UV and PM in an in-vivo model and demonstrated the preventative effect of applying topical C E Ferulic serum to minimize cutaneous damage which can accelerate skin aging as well-established in literature.

1. Pambianchi, E.; Ferrara, F.; Pecorelli, A.; Benedusi, M.; Choudhary, H.; Therrien, J.; Valacchi G. Deferoxamine treatments improves antioxidant cosmeceutical formulation projection against cutaneous diesel engine exhaust exposure. Antioxidants 2021, 1-14.
2. Krutmann, J.; Bouloc, A.; Sore, G; Bernard, B; Passeron, T. The skin aging exposome. J Dermatol. Sci. 2017, 85, 152-161.
3. Puri, P. Effects of air pollution on the skin: A review. Indian J Dermatol Venereol Leprol. 2017, 83, 415-423.
4. Fuks, K.; Woodby, B.; Valacchi, G. Skin damage by tropospheric ozone. Hautarzt 2019, 70, 163-168.
5. Marrot, L.; Nouveau, S. Pollution-induced oxidative stress in skin and related potential antioxidant Protection. Pollution Induced Oxidative Stress, Handbook of Cosmetic Science and Technology. 29, 288-300.
6. Passeron, T.; Krutmann, J.; Andersen, M.; Katta R.; Zouboulis, C. Clinical and biological impact of the exposome on the skin. J. Euro. Acad. Dermatol. Venereol. 2020, 34, 4-25.
7. Marrot, L., Pollution and sun exposure: a deleterious synergy, mechanisms and opportunities for skin protection. Curr. Med. Chem. 2018, 25, 5469-5486.
8. Kim, Y.; Lim, M. Skin barrier dysfunction and filaggrin. Archives of Pharm. Res, 2021, 44, 36-48.
9. Zobiri, O.; Zucchi, H.; Dimitrov, A; Marrot, L. Repeated exposures to UVA1 and particulate matter-associated pollutants trigger epidermal barrier dysfunction in skin epithelialization model. J. Investi. Dermatol. 2022, 202, 1-12.
10. Tarnowski, B.; Spinale, F.; Nicholoson, J. DAPI as a useful stain for nuclear quantitation. Biotech Histochem. 1991, 66, 297-302.
11. Grether-Beck, S.; Felsner, I.; Brenden, H., Marini, A.; Jaenicke, T.; Aue, N.; Weiss, T.; Uthe, I.; Krutmann, J. Air pollution-induced tanning of human skin. Br. J. Dermatol. 2021, 185, 1026-1034.