CHAPTER

47

Effects of Air Pollution on Skin: Dermatologic Options

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47.1 INTRODUCTION

Air pollution is a serious problem worldwide, especially in well-developed and industrialized countries. Much evidence exists on the relationship between air pollution and the development or exacerbation of cardiovascular and respiratory diseases; however, fewer studies concern the impact of air pollution and particulate matter on skin integrity. This overview highlights key evidence on the disruption of the skin barrier in association with the size and content of particulate matter and proposes potential options for skin care to minimize skin damage.

47.2 MATERIALS AND METHODS

A literature review was performed using ClinicalKey, Google Scholar, OvidMedline, and PubMed using combinations of the following words: air pollution, skin, stratum corneum, indoor pollution, outdoor pollution, particulate matter, sensitive skin, nitrogen dioxide, ozone, eczema, psoriasis, atopic dermatitis, acne, skin cancer, and tobacco smoke. Key findings were collected from the most recently published original articles.

47.3 RESULTS

47.3.1 Disturbed Skin Barrier

Pan et al. demonstrated that urban dusts with an average diameter of 11 μm composed of polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyl congeners, pesticides, and dioxins significantly disturbed stratum corneum (SC) and tight junctions (TJs) by diminishing proteins essential to barrier function leading to a subsequent increase in transepidermal water loss (TEWL). Particulate matter (PM) with soluble heavy metal content had negligible effects on SC and TJs. Although other studies have associated ultrafine particles (UFPs) with being more dangerous to human health than larger particles,[6] Pan et al. attribute the more significant damage of larger particles in their study to particle content rather than size. Another significant finding was that in PM-treated skin, ascorbic acid and tretinoin absorption were significantly increased, presumably related to disrupted skin barrier. The potential danger in this is the possibility of overabsorption of substances applied via topical administration; therefore, caution should be taken in the long-term use of products containing these acids.

47.3.2 Development or Exacerbation of Atopic Dermatitis

Two studies found atopic dermatitis (AD) symptoms were present when concentrations of small-particle air pollutants such as $PM_{2.5}$, PM_{10}, NO_2, heavy metals, and total volatile organic compounds (TVOCs) were higher in ambient air.[24,22] Additionally, indoor air pollution was associated with AD symptom aggravation.[23] Song et al.

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observed a cohort of children with AD and found AD symptoms positively associated with ambient UFP levels and itch symptoms positively associated with the previous days UFP levels but not with larger particles or other gaseous pollutants.[49] This suggests the ability of UFPs to penetrate skin. A study limitation was that the symptoms were documented by parents instead of by a physician. Huss-Marp et al. observed the effect of exposure to airborne volatile compounds and house dust mite (HDM) on barrier function and dermal blood flow in AD patients compared to controls. TEWL was significantly increased post exposure to volatile organic compounds (VOCs), indicating disruption to barrier function. Note that there was a 48 h delay, which can be attributed to the time it takes for significant amounts of VOCs to penetrate skin and exert an effect. In patients with AD, dermal blood flow was increased after combined exposure to VOCs and HDM. Also, AD patients showed a significant increase in skin reaction to an atopy patch test with HDM after exposure to VOCs, compared to controls.[20] This suggests that exposure to air pollution impairs barrier function and may allow aeroallergens to penetrate the skin more readily, making the skin more vulnerable to the observed AD skin reactions. NO_2 and formaldehyde, common indoor air pollutants, were used to evaluate the effects of polluted air on barrier function by analyzing TEWL and skin roughness. Eberlein-Konig et al. found that all subjects had increased TEWL after exposure to NO_2 but only AD patients had significantly increased TEWL after formaldehyde exposure. Control subjects had significantly increased roughness after NO_2 exposure.[12] Additionally, traffic-related air pollution and environmental tobacco smoke have been significantly associated with AD prevalence.[30,47]

47.3.3 Development of Psoriasis

Ozden et al. evaluated risk factors associated with development of pediatric psoriasis and observed more frequent reports of tobacco smoke exposure in the year preceding diagnosis when compared to controls.[41]

47.3.4 Oxidative Stress

Skin is a major target organ of environmental oxidative stress because it is constantly in contact with substances that interact with the barrier to form reactive oxygen species (ROS). Lefebvre et al. evaluated the quality of skin in people in two cities of Mexico, Mexico City, considered highly polluted, and Cuernavaca, considered free of pollution. Mexico City subjects had dryer skin, significantly lower Vitamin E and squalene concentrations, and higher lactic acid and oxidized protein levels, while Cuernavaca subjects had higher chymotrypsin-like activity and interleukin-1α levels. Additionally, Mexico City subjects had higher levels of dermatographism and urticarial antecedents.[31] The higher levels of interleukin-1α in the Cuernavaca population deserves further investigation because other studies suggest exposure to air pollutants increases these levels.[7,34,53] Thiele et al. observed impact of ozone exposure on Vitamin E and lipid peroxidation levels. In a dose-dependent matter, ozone reduced α- and γ-tocopherol levels (parameters of Vitamin E concentration) and increased malondialdehyde (MDA, parameter of lipid peroxidation). Interestingly, repeated exposure to the lowest level of ozone exerted cumulative stress effects as shown by α- and γ-tocopherol depletion and MDA increase.[50] Although this experiment was performed in murine SC, the latter findings are important because they more accurately reflect human exposure to pollutants in day-to-day life. Vitamin E depletion and MDA increase are evidence of oxidative stress. Another study also demonstrated oxidative damage in skin tissue models by exposing it to concentrated air particles (CAPs). Increased levels of F_2-α isoprostanes (marker of oxidative damage), increased phospholipid oxidation, and increased intracellular ROS production were observed.[35]

47.3.5 Inflammation

Choi et al. observed the relationship between Asian dust storm particles (ADSPs), including pollutants from urban and industrial emissions, and inflammation. There was a significant increase in gene transcription of cytokines IL-6, IL-8, and GM-CSF, which are involved in the proinflammatory response.[7] Diesel exhaust particles (DEPs) also increased in IL-8 levels. Related to this, increased activation of transcription factor NF-κB, a moderator of a variety of proinflammatory cytokines including IL-8, was observed after exposure to nontoxic concentrations of DEP, representing effects of day-to-day exposure.[34] Additionally, tobacco smoke increased expression of inflammatory cytokines IL-1α, IL-8, as well as Egr-1, a regulator of the inflammatory response.[21,52,56]

47.3.6 Skin Aging

Huls et al. found in two cohorts, Chinese women and German women, that they had facial lentigines partially associated with exposure to NO_2, a toxic gas found in traffic-related air pollution. This is significant because these

populations are largely ethnically diverse but presented similarly.[19] In addition, Vierkotter et al. observed that higher levels of soot, traffic-related air pollution, as well as PM were associated with more pigment spots on the face and more pronounced nasolabial folds.[54] Note that air pollution does not solely originate from outdoor sources but can also manifest indoors from particulates associated with cooking. In two Chinese populations, Li et al. observed that cooking with solid fuels was highly associated with a more-wrinkled appearance on the face and dorsal hands, particularly.[33] A study limitation, as reported by the authors, was the use of questionnaire-based data to assess indoor air pollution exposure. A more reliable method of indoor air pollution measurement and air composition analysis would be preferred. Composition of solid fuels for cooking or heating include PM, PAH, CO, nitrogen oxides, e.g. NO_2, and sulfur dioxide.[15] Additionally, in vitro and in vivo studies have observed a decrease in new collagen synthesis, increase in tropoelastin, and matrix metalloproteinases (MMPs) after exposure to tobacco smoke, suggesting its role in premature skin aging.[57,29]

47.4 DISCUSSION

Air pollution comes from many sources, including traffic emissions, factories, and human activities, and contains compounds including PM, ozone, NO_2, and volatile organic compounds, and each component has its own proposed mechanism of interaction with the skin barrier.

PM, ranging in size from $PM_{2.5}$ to PM_{10}, is composed of metals, minerals, and organic and biological compounds surrounding a carbon core. PMs come from crustal material, motor vehicle exhaust, as well as factory emissions.[28] They generate ROS in the lungs,[11] however, it is not known if they have the same effect upon interacting with skin. PMs, however, contain PAH, a potent ligand for the aryl hydrocarbon receptor (AhR). Activation of AhR is involved in gene expression in keratinocytes and melanocytes that contribute to wrinkle formation and pigment spot formation, known markers of skin aging. It has been suggested that activation of AhR can lead to the production of ROS.[27a] Some PMs carry heavy metals such as Cu, Mn, Ni, Pb, and Ti,[55] which can also cause the production of ROS.[35] UFPs are more concerning, however, because of their potential to penetrate skin and directly incorporate into the vascular system. Gulson et al. applied sunscreen to human volunteers twice daily for five days and found small amounts of Zn tracer in the subjects' blood, suggesting that long-term retention of UFPs on the skin can be absorbed and enter blood circulation.[18a] These substances presumably penetrate SC by the transepidermal route or via pore transport. The transepidermal route includes the transcellular or intercellular route and via pore transport includes the transglandular or transfollicular route.[5,51a]

Ozone can normally be found in the troposphere, but it is also produced at ground level from the combustion of fossil fuels, vehicle emissions, and when ozone precursors react with sunlight (UVR), NO_x, and VOCs. Ozone is a strong oxidant so it reacts quickly with biological targets, depleting antioxidants and damaging biomolecules.[42,51] When ozone interacts with murine skin, Vitamin E levels are depleted and MDA levels are increased, as shown by Thiele et al.[50] Possible mechanisms of Vitamin E's action against ozone include reacting with it directly to destroy it or scavenging for PUFA-derived radicals (polyunsaturated fatty acids that form free radicals with ozone).[50] Depletion in Vitamin E levels indicates an effort by the body to buffer the creation of ROS.

NO_2, an air pollutant that mainly comes from vehicle emissions and combustion of fossil fuels, causes generation of free radicals that can oxidize amino acids in tissue proteins or initiate lipid peroxidation of polyunsaturated fatty acids in pulmonary cell membranes.[12] This mechanism of action may also take place when NO_2 interacts with SC.

Volatile organic compounds come from motor vehicles, gasoline evaporation, industrial plants, but also household items such as wood-based products, paints, and floor finishes.[9,40] Ushio et al. showed keratinocytes exposed to VOCs increased cytokine levels, which could lead to an inflammatory response and exacerbate inflammatory conditions such as atopic dermatitis, psoriasis, and acne.[53]

Tobacco and secondary tobacco smoke are associated with cardiovascular and respiratory disease and cancer. Tobacco smoke is composed of thousands of different compounds including carcinogens such as benzo[a]pyrene and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone as well as oxygen radical-forming substances such as catechol and hydroquinone.[16] Upon interaction with skin, chemicals in tobacco smoke collectively induce an inflammatory response, oxidative stress, TEWL, and tumor cell generation. This suggests their role in the development of inflammatory diseases such as atopic dermatitis, psoriasis, and acne, as well as basal and squamous cell carcinomas.[32]

47.4.1 Relationship to Sensitive Skin

Sensitive skin is a condition that involves hyperreactivity of the skin to stimuli such as environmental factors and cosmetic products that are otherwise well tolerated.[1] Sensitive skin can present with visible irritation such as

erythema and scaling or subjective responses such as itching, stinging, and burning.[26] The prevalence of sensitive skin has been an important concern, particularly in industrialized countries. It has been reported that 44.6% of a representative sample of the American population consider themselves to have sensitive skin.[37] In Europe, 38.4% of subjects reported sensitive skin, as well as 39.46% of students in Beijing colleges and universities.[36,39] Because certain air pollutants disrupt SC, deregulate barrier function, increase TEWL, and are associated with skin pigmentation, it is plausible that air pollution is an indirect cause of sensitive skin.[13]

47.4.2 Relationship to Inflammatory Diseases: Atopic Dermatitis, Psoriasis, and Acne

47.4.2.1 Atopic Dermatitis

Atopic dermatitis is a chronic inflammatory skin condition caused by environmental as well as genetic factors and involves a disruption of the skin barrier and the immune system.[38,2] According to the international study of asthma and allergies in childhood, AD prevalence continues to increase in children in developed and developing countries, and air pollutants are significantly associated with AD development as well as exacerbation of symptoms.[54a] More specifically, VOC, airborne nitrogen, formaldehyde, particulate matter, and UFPs significantly worsen AD symptoms in AD patients. These findings suggest that while healthy skin can also be affected by air pollution, diseased skin is generally more vulnerable to further damage.

47.4.2.2 Psoriasis

Psoriasis is a chronic inflammatory skin disease affecting 2% of people in Europe and North America.[8] The most common form is chronic plaque psoriasis, accounting for 90% of cases and presenting with monomorphic lesions that are erythematous and scaly.[3] In psoriatic skin, Th17 cells and IL-17 play a predominant role in pathogenesis.[25] PM increases Th17 differentiation and, as mentioned previously, an inflammatory response. Therefore, air pollutants that enhance the differentiation of Th17 cells and production of proinflammatory cytokines such as particulate matter, tobacco smoke, diesel exhaust particles, and urban and industrial emissions may play a role in the exacerbation of psoriasis.

47.4.2.3 Acne

Acne vulgaris, another chronic inflammatory disorder involving sebaceous glands, ducts, and hair follicles, is caused by a combination of genetic, environmental, and hormonal factors. Acne affects mostly children and adolescents, and these patients will typically present with comedones, papules, pustules, and cysts.[17] In accordance with this inflammatory disorder, cytokines play a role in lesion formation and patients have increased interleukin levels.[17] Because air pollutants and tobacco smoke induce an inflammatory response upon skin interaction, this suggests the role of air pollutants in acne vulgaris exacerbation.

47.4.3 Relationship to Skin Cancer

Melanoma and nonmelanoma (basal and squamous cell carcinoma) skin cancers are the most common types of cancer in white populations, and the incidence is increasing rapidly.[10] Recent studies have shown a relationship between air pollutants and incidence. Environmental exposure to tobacco smoke and high-PAH levels are associated with increased incidence and production of basal and squamous cell carcinomas.[45,4,48,46] Tobacco smoke causes the generation of ROS and proinflammatory cytokines, which may lead to DNA damage, DNA repair system damage, as well as an upregulation of cell proliferation. Additionally, PAH is a potent ligand for AhR, a transcription factor. Excessive PAH binding to AhR can promote skin cancer development.

47.4.4 Proposals for Skin Care

Among the many air pollutants, PAHs, heavy metals, CAPS, ozone, and tobacco smoke produce ROS upon interaction with skin. Topical application of antioxidants can help buffer the generation of ROS. The antioxidant network maintains an equilibrium between pro- and antioxidants by intervening at different stages of the oxidation process via free radical and lipid peroxyl radical binding, metal ion binding, and removing damaged biomolecules.[50] Ozone specifically depletes Vitamin E levels and increases MDA levels. Therefore, topical tocopherol application can slow or prevent this process via its antiinflammatory action.[14] Topical application of tocopherol has also been shown to reduce incidence of skin tumors caused by UV radiation,[14] suggesting it could also be used to combat the

carcinogenic effects of tobacco smoke and PAH. Topical application of a single antioxidant such as Vitamin E or C as well as combinations of antioxidants show photoprotective effects, suggesting that they may play a similar role is protection against air pollutants.[51] Interestingly, melatonin has strong antioxidant properties and strongly suppresses ROS as well as UV-induced erythema.[51] Again, this suggests melatonin can be used in the prevention of oxidative damage caused by air pollution. The two main routes of tocopherol uptake are via direct percutaneous uptake and hair follicles to reach the dermis.[14]

PM can carry PAH, a potent ligand for the AhR receptor involved in pigment spot formation, wrinkle formation, and the generation of ROS. Therefore, topical application of an AhR antagonist can inhibit these processes. Multiple air pollutants have also be shown to weaken the skin barrier, therefore the application of topical agents to enhance the skin barrier could protect the skin from this kind of damage. Industrial air pollutants, traffic-related air pollutants, and tobacco smoke are associated with an inflammatory response, so antiinflammatories may protect against these substances. Finally, topical application for retinoids was proven to present and repair clinical features of photoaging, suggesting it may produce a similar effect on skin exposed to air pollution.[18]

47.5 CONCLUSIONS AND FUTURE CONSIDERATIONS

In conclusion, air pollutants such as tobacco smoke, CAPS, VOCs, ozone, and NO_2 are significantly associated with an inflammatory response, weakened barrier function, and oxidative stress, which can lead to the development or exacerbation of inflammatory skin diseases, skin aging, as well as skin cancer. Our challenge rests in decreasing the effects of air pollution on skin and identifying evidence-based interventions that will decrease damage when removal is not practical or delayed. Further studies should be conducted on the mechanism of action of these pollutants as well as the possible preventive effects of topical antiinflammatories, receptor antagonists, and barrier enhancers.

Original Articles and Key Findings

Title	Reference Number	Key Findings	Notes
Impact of urban particulate pollution on skin barrier function and subsequent drug absorption.[43]	PMID: 25680853	1649b tx: • Diminished cytokeratin, filaggrin, E-cadherin • Increased TEWL • More skin furrows • Upregulation of TIM, annexin A2, MDH • Increased skin absorption of ascorbic acid and tretinoin 1649a tx: • Negligible role in damaging SC and TJ • Composition but not size was primary factor governing PM-induced skin toxicity	• Performed on pig • PM concentration may not reflect day-to-day exposure
Influence of short-term exposure to airborne Der p 1 and volatile organics on barrier function and dermal blood flow in AD and healthy individuals.[20]	PMID: 16499645	• Short-term exposure to mixture of VOCs lead to significantly increased TEWL • AD and healthy individuals reacted similarly with impairment of skin barrier toward exposure with VOCs • Increased skin blood flow after combined exposure to VOCs and Der p 1 in AD • TEWL (all subjects) and skin blood flow (AE patients) significantly increased 48 h after exposure • After VOC exposure, applied APT with HDM significantly enhanced in AE patients compared with control (filtered air alone)	• Performed on human

Original Articles and Key Findings

Title	Reference Number	Key Findings	Notes
Ozone exposure depletes vitamin E and induces lipid peroxidation in murine stratum corneum.[50]	PMID: 9129228	• O_3 depletes vitamin E (significantly decreased levels of alpha and gamma tocopherol) in dose-dependent fashion and induced lipid peroxidation (significantly increased MDA concentrations) in SC • Repeated exposures to lowest tested O_3 level (1 ppm) exerts cumulative oxidative stress effects (significant vitamin E depletion and MDA increase) • α-Tocopherol more readily depleted than γ-tocopherol	• Performed on hairless mice
Epidemiological evidence that indoor air pollution from cooking with solid fuels accelerates skin aging in Chinese women.[33]	PMID: 26055797	• Cooking with solid fuels significantly associated with a 5–8% more severe wrinkle appearance on face and a 74% increased risk of fine wrinkles on dorsal hands in both studies combined	• Cross-sectional study • Composition of indoor air pollution may vary geographically • Used questionnaire-based data
Influence of airborne NO_2 or FA on skin function and cellular activation in AD and control subjects.[12]	PMID: 9449520	• AD and control subjects showed significantly increased TEWL after NO_2 exposure • AD patients showed significantly increased TEWL after FA exposure • Control subjects showed significantly increased roughness after NO_2 exposure	• Performed on human
Evaluation of impact of urban pollution skin quality: multicenter study in Mexico.[31]	PMID: 25655908	• Skin moisture significantly higher in Cuernavaca and indicating a dryer skin in Mexico City • Significantly lower Vitamin E and squalene concentrations and significantly higher lactic acid concentrations in Mexico City • Significantly higher chymotrypsin-like activity in Cuernavaca • Higher oxidized protein levels in Mexico City • Significantly higher IL-1α levels in Cuernavaca • More dermographism and urticarial antecedents in Mexico City	• Clinical evaluation by dermatologist • Multicenter clinical study
Acute health effects of urban fine and ultrafine particles (UFP) on AD children.[49]	PMID: 21367405	• Positive association between ambient UFPs and symptom exacerbation in AD children • Itch symptoms positively affected by previous day's UFPs • Significant effect of temperature on AD symptoms	• Don't show any temperature data • Subjective measurements • Exposure data from fixed sites rather than personal monitoring
TRAP contributes to facial lentigines development: epidemiological evidence from Caucasians and Asians.[19]	PMID: 26868871	• Exposure to NO_2 significantly associated with more lentigines on the cheeks in both cohorts	• Lentigines evaluated by skilled personnel • Analysis of SALIA population and Chinese Taizhou cohort
Skin damage mechanisms related to airborne particulate matter exposure.[35]	PMID: 26507108	• CAPS exposure significantly increased LDH release, increased F_2-α isoprostane levels (oxidative damage), increased phospholipid oxidation, increased intracellular ROS production, increased IL-1α levels, presented TUNEL positive nuclei (DNA fragmentation), PM present in upper and deeper cell layers	• Performed on RHE tissue and immortalized human keratinocyte HaCaT cell line

Original Articles and Key Findings

Title	Reference Number	Key Findings	Notes
AD symptoms influenced by outdoor air pollution.[24]	PMID: 23763977	• Spring: AD symptoms presented when temperature was lower and styrene was higher • Summer: AD symptoms presented when NO_2 and toluene were higher • Autumn: AD symptoms presented when temperature and TVOC were higher • Winter: AD symptoms presented when $PM_{2.5}$ and TVOC were higher • Throughout study: AD symptoms presented when outdoor PM_{10}, $PM_{2.5}$, toluene and TVOC were higher	• Subjective measurements • Exposure data from fixed sites rather than personal monitoring • Small cohort
Airborne particle exposure and extrinsic skin aging.[54]	PMID: 20664556	• Significant association between TRAP and pigment spots, nasolabial fold • Increase in soot, TRAP, and PM_{10} associated with more pronounced nasolabial folds	• SALIA study cohort
Environmental tobacco smoke and AD symptom risk among school children in South Africa: a cross-sectional study.[47]	PMID: 26310401	• Environmental exposure to tobacco smoke at school and home significantly associated with ever having AD and AD symptoms	• Questionnaire-based data could be subjective
Traffic-related air pollution, climate, and prevalence of eczema in Taiwanese school children.[30]	PMID: 18449213	• TRAP's NO_x and CO associated with AD	• Exposure data from fixed sites rather than personal monitoring • Parental reports of children
AD, respiratory allergies, and TRAP in birth cohorts from small-town areas.[27]	PMID: 19713084	• AD prevalence at age 6 significantly higher in children residing in areas with higher TRAP	• Questionnaire based data • Parental reports of children
Association between small particle air pollution, climate, and childhood AD prevalence and severity: a US population-based study.[22]	PMID: 26842875	• AD associated with higher mean annual NO_2, SO_2, SO_3, As, Ni, Pb, V, Zn • Moderate-severe AD associated with higher mean annual NO_3, OC, $PM_{2.5}$, Cu, Pb, Zn	
Environmental risk factors in pediatric psoriasis: a multicenter case control study.[41]	PMID: 21615473	• Exposure to tobacco smoke associated with development of pediatric psoriasis	• Etrospective data collection • Questionnaire based data
Indoor air pollution aggravates AD symptoms in children.[23]	PMID: 25781186	• Indoor air pollution increased risk of aggravated AD symptoms in children • Itch symptoms correlated with toluene levels	• Exposure data from fixed sites rather than personal monitoring
Effect of environmental pollutants on production of proinflammatory cytokines by normal human dermal keratinocytes (hKC).[53]	PMID: 10092052	• DEP and FA associated with stimulation of IL-1β production by hKCs	• Performed on normal hKCs
Activation of NF-κB by DEP in mouse epidermal cells through phosphatidylinositol 3-kinase/Akt signaling pathway.[34]	PMID: 15130773	• DEP significantly stimulated NF-κB activity	• Performed on JB6 P^+ mouse epidermal cell line (CI 41)
Asian dust storm particles (ADSP) induce broad toxicological transcriptional program in HEK.[7]	PMID: 21056094	• ADSPs significantly increase mRNA levels of cytochrome P450 enzymes CYP1A1, CYP1A2, CYP1B1 • ADSPs increased transcription of IL-1β, IL-6, IL-8, GM-CSF, CASP14	• Performed on HEK

Original Articles and Key Findings

Title	Reference Number	Key Findings	Notes
Cigarette smoke-induced IL-1α involved in pathogenesis of adult acne.[56]	PMID: 24648681	• Smokers significantly associated with higher IL-1α and LPO in comedones	• Sampled comedone content in acne patients
Benzo(a)pyrene, induces oxidative stress-mediated IL-8 production in human keratinocytes via AhR signaling pathway.[52]	PMID: 21316925	• BaP induced nuclear translocation of AhR from cytoplasm • AhR activation subsequently induced CYP1A1 mRNA and protein expression • BaP induced IL-8 production in dose-dependent manner • BaP induced ROS production	• Performed on NHEKs
Upregulation of TNF-α secretion by cigarette smoke is mediated by Egr-1 in HaCaT human keratinocytes.[21]	PMID: 20653771	• Over 20% CSE concentration significantly reduced HaCaT keratinocyte viability • CSE increased Egr-1 protein expression in dose-dependent manner • CSE increased ERK1/2, JNK1/2, and p38kinase phosphorylation in time-dependent manner • CSE increased TNF-α secretion in dose-dependent manner	• Performed on HaCaT human keratinocyte cell line
Alterations of ECM induced by tobacco smoke extract (TSE).[57]	PMID: 10836612	• TSE induces MMP-1/3 mRNA expression • TSE induces MMP-1 protein • TSE inhibits type I/III procollagen production • TSE decreases collagen biosynthesis	• Performed on cultured skin fibroblasts from nonsmokers
MMP-1 and skin aging in smokers.[29]	PMID: 11289356	• Significantly more MMP-1 mRNA in skin of smokers compared to controls	• Skin biopsy samples from human subjects

AD, Atopic dermatitis; *AE*, atopic eczema; *APT*, atopy patch test; *CAPS*, concentrated ambient particles; *CSE*, cigarette smoke extract; *DEP*, diesel exhaust particles; *ECM*, extracellular matrix; *FA*, formaldehyde; *HDM*, house dust mites; *HEK*, human epidermal keratinocytes; *LDH*, lactate dehydrogenase; *LPO*, lipid peroxide; *MDA*, malondialdehyde; *MDH*, malate dehydrogenase; *NHEK*, normal human epidermal keratinocytes; *PM*, particulate matter; *RHE*, reconstructed human epidermis; *ROS*, reactive oxygen species; *SC*, stratum corneum; *TEWL*, transepidermal water loss; *TIM*, triosephosphate isomerase; *TJ*, tight junctions; *TRAP*, traffic related air pollution; *TUNEL*, terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick end labeling; *TVOC*, total volatile organic compound; *tx*, treatment; *UFP*, ultrafine particles; *VOC*, volatile organic compounds.

Proposals for Skin Care

Air Pollutant	Potential Treatment
PM, UFP, PAH	Topical application of skin barrier enhancer
PM, NO_2, VOC, UFP, FA, TRAP, tobacco smoke	Topical application of antiinflammatory
Ozone, CAPS, PAH, tobacco smoke, heavy metals	Topical application of antioxidants (Vitamins E, C and melatonin)
NO_2, soot, TRAP, solid fuels	Topical application of retinoids

CAPS, Concentrated ambient particles; *FA*, formaldehyde; *PAH*, polycyclic aromatic hydrocarbons; *PM*, particulate matter; *TRAP*, traffic related air pollution; *UFP*, ultrafine particle; *VOC*, volatile organic compounds.

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