Sunlight, Diet and Pollution – Effects on Oxidative Stress and Skin Ageing

KEYWORDS: Ageing; Skin; Reactive Oxygen Species; Sunlight; Diet; Pollution

ABSTRACT
Skin is subject to stress from external factors, which have the potential to cause premature ageing. Oxidative stress from the generation of reactive oxygen species has been increasingly implicated as a driving force in skin ageing, leading to loss of skin structure and function. While intrinsic skin ageing driven by genetics is inevitable, our exposure to some of the extrinsic factors that affect the process are under our influence. Sunlight, diet and pollution can all affect the oxidative environment of the skin. This review details the current research into the effects of these factors on oxidative stress in the skin.

INTRODUCTION
Ageing is a process in which losses of structure and function accumulate over time. This leads to a reduction in the capability of an organism to cope with stress from the environment and function in a normal capacity. This process is observed in all animals, and while humans have extended average lifespan in recent years with modern healthcare knowledge, we are still susceptible to the effects of aging over our lifetime. However, the exact underlying biological causes of the ageing process remain unclear.

The largest organ in the body, the skin is the barrier that protects us from external insults. Ageing in the skin is influenced by both intrinsic and extrinsic factors. Intrinsic ageing refers to changes in physiology which are mainly influenced by genetics. In the skin this manifests as an increase in roughness, redness due to visible vasculature, a reduction of elasticity seen as an appearance of fine lines and atrophy causing a reduction in apparent plumpness (1). Extrinsic ageing is caused by insults to the skin including sunlight exposure, smoking and pollution. These damage the skin by causing secretion of pro-inflammatory signals, direct DNA damage and oxidative stress that results in loss of structure and function (2). The accumulation of these losses over time result in premature skin ageing (3). This manifests as the formation of pronounced wrinkles and pigmentation. Extrinsic factors have been found to be responsible for as much as 80% of visible aging in facial skin (4).

Oxidative stress occurs when a cell’s antioxidant capacity cannot cope with an excess of reactive oxygen species (ROS). The widely accepted mitochondrial free radical theory of ageing posits that this imbalance in oxidation and antioxidant capacity leads to cell damage, ageing and death (3). The mitochondria are the cellular organelles which are responsible for converting glucose into a form of energy that can be used by the cell (3). This is done by a process of oxidative phosphorylation and the electron transport chain (ETC) in the mitochondrial membrane. A low concentration of ROS, as is produced by the ETC in healthy cells, is necessary for signalling and the normal function of cells. Mitochondrial ROS production has the capacity to cause oxidative stress, and the mitochondria themselves are sensitive to oxidative damage. The mitochondrial DNA (mtDNA) is located close to the ETC, so both the ETC components and the mtDNA which codes for them are susceptible to oxidative damage. The mtDNA have minimal repair mechanisms compared to nuclear DNA, so when damaged can cause mis-production of ETC components which cause increased ROS leak from the ETC (5). This can feed back, further damaging mtDNA, leading to a “vicious cycle” (Fig. 1) (2).
Solar light and pollution cause increases in ROS and mtDNA damage, contributing to the vicious cycle of mitochondrial damage and ROS generation. Oxidative stress caused by raised ROS levels results in nuclear DNA damage, oxidation of lipids and proteins and downstream signals which eventually result in a premature ageing phenotype.

With ageing there is an increase in senescent cells (6). These are cells which have irreversibly arrested the cell cycle and can no longer proliferate, induced as a protection mechanism against cancer. This occurs when cells receive unbalanced proliferation signals or high levels of damage and mutation (6). Oxidative stress can cause cellular damage and DNA mutation, and high levels of this stress has been linked to an increase in senescent cells (7). Mitochondrial ETC component activity has been shown to decrease with age, potentially contributing to decline in bioenergy, and this has been shown to correlate with an increase in senescence (8). This may be to be due to the reduced efficiency of the aged ETC increasing ROS in the cell contributing to the balance tipping towards senescence and an ageing phenotype in the skin.

SUNLIGHT
Sunlight is one of the most well studied insults to skin. Sunlight that reaches skin is comprised of 6% ultraviolet radiation (UVR), 40% visible light and 54% infrared radiation (IR) (5). UVB is known to cause sunburn and has been linked to cancer since the 1920s (9). Since then there has been a great amount of research into the effects of UVR. It is now known that UVR is responsible for causing DNA damage and oxidative stress leading not only to sunburn, but also the long-term structural and functional changes to the skin that are seen with photoageing. The rate of photoageing in an individual will depend on their exposure and skin pigmentation, as melanin provides protection from UVR. UVB is the causal factor of sunburn, and is absorbed mainly in the epidermis. It has the ability to directly break DNA strands, leading to tumourigenic mutations. UVA has a longer wavelength than UVB, and does not deliver the energy required to break DNA strands. However it penetrates more deeply, absorbed mainly in the dermis. Amongst other targets it causes dysfunction in the mitochondrial ETC, generating ROS which can damage DNA and cause mutations (5). One study found UVA-generated mutations were more frequent in human skin carcinomas than UVB-generated mutations (10). mtDNA mutations are linked to premature ageing, and mtDNA deletions can be 10 times higher in sun-exposed skin (11). mtDNA damage has been developed as a biomarker of UVR exposure and oxidative stress in skin, but until recently the effects of individual UVR wavelengths was unknown (12). It has now been shown that mitochondria from the human epidermis and dermis are both highly damaged by the higher-energy UVB, but mitochondria from the cells derived from the dermal layer are more sensitive to UVA (13). The ROS also causes signalling cascades which upregulate matrix metalloprotease proteins (MMPs) which are responsible for breaking down the extracellular collagen which provides structure in the dermis. Loss of this collagen is one cause of the deep wrinkles associated with photoageing.

Longer wavelengths found in the visible and IR regions of the solar spectrum may also have an impact on skin ageing. Visible and IR light together were shown to increase MMP expression in humans, and visible light alone
was shown to be able to increase ROS and MMP expression at doses that could be received in sunlight (14). The effects of IR alone is a more disputed area. There is evidence it has the capacity cause damage but it has also been argued to have no effect at all, or even to be beneficial to the skin (15).

**POLLUTION**
A more recent development in the field of extrinsic skin ageing is the influence of pollution. We are exposed to pollutants during day to day life from sources including factories, traffic and cigarette smoking. Pollutants come in gaseous and particulate forms, which can cause damage through different mechanisms, including direct and indirect ROS generation (16). Ultratine particles produced by traffic have been shown to localise to mitochondria and to induce oxidative stress (17). A study in Germany on Caucasian women showed that particulate air pollution from traffic emissions and soot was be associated with an increase in facial pigment spots and prominence of nasolabial folds (18). This could be due to the particulate matter itself and/or to polycyclic aromatic hydrocarbons (PAHs), a group of chemicals that are often found bound to soot particles (19). These act by directly forming oxidative radicals and by being catalysed to carcinogenic epoxides and ROS generating quinones (20). Ozone is a gas produced by traffic and industrial activity which is found at high concentrations in smog and has been implicated in skin health. A higher rate of skin-related emergency room visits was found in populations exposed to high concentrations of ozone (21). It is thought to cause oxidative stress though the generation of ROS and generation of cytotoxic aldehydes (22). Animal studies have shown that ozone depletes endogenous antioxidants vitamin C and E in the skin and increased markers of oxidative stress (22). UV light is known to deplete vitamin E through oxidative stress in the skin, and it has been proposed that there is a synergistically damaging effect when skin is exposed to both UV and ozone(22). However it may be possible to prevent against ozone damage to the skin. An exogenously applied vitamin E solution attenuated the effects of ozone, demonstrating that it may be possible to prevent pollution-derived oxidative stress (23).

**DIET**
Diet has become an increasingly researched area in relation to human health, ageing and oxidative stress. Diets high in sources of antioxidants such as the Mediterranean diet have been shown to increase longevity and reduce age related illness such as neurodegeneration (24). This may be due to an ability to reduce oxidative stress and senescence (25). There are indications that the Mediterranean diet is associated with reduced risk of melanoma, suggesting an impact of this diet on the skin (26). Dietary antioxidant intake has been linked to higher levels of antioxidants in the skin, and as extrinsic stressors such as sunlight are known to reduce the antioxidant capacity of the skin, dietary antioxidants may allow protection against this ageing stimulus (27, 28). A diet enriched with lycopene, an antioxidant found in vegetables, has been shown to provide protection from UVR induced mtDNA damage and MMP increase (29). However antioxidants have not always been shown to have any beneficial effects on lifespan or skin ageing. A systematic review has shown that the when delivered as a supplement, some antioxidants are associated with increased mortality (30). Further research is necessary to determine the effects of individual antioxidants and their intake through the diet and supplementation.

**IMPORTANCE OF MITOCHONDRIA-MEDIATED DAMAGE**
Mitochondria are considered to be responsible for the majority of oxidative stress within the cell, generating up to 90% of the total ROS (31). As mitochondrial dysfunction is both a cause and a result of oxidative stress, mitochondria are potentially a therapeutic target for preventing the "vicious cycle" that leads to cellular damage. Mitochondrial targeted antioxidants have shown to reduce aging phenotypes in animal studies where non-targeted antioxidant therapies have shown no benefit, but this has yet to be trialled in human skin (32).

**MARKET RELEVANCE OF POLLUTION, SUN AND DIET**
Consumers have long understood the damaging effects of UVR and in more recent years have linked solar exposure to premature skin aging, conscious of the need to wear sunscreens not only to protect from sunburn but also to minimise the appearance of fine lines and wrinkles. Today’s consumers are better informed than ever, demanding solar protection in their daily use products and colour cosmetics. In fact 16% of all facial skin care and colour cosmetics launched on the market in 2017 included a sun protection claim (33).
For pollution, widespread news coverage in recent years, coupled with increasing urbanisation, has led to growth in consumer awareness of the damaging effects of pollution. As individuals realise that exposure to daily pollutants may be inescapable they are seeking defensive strategies to incorporate into their everyday skincare regimes. As a result, the Personal Care market has witnessed a global surge in the demand for pollution protection products. In skincare and colour cosmetics the number of new products launched globally that made reference to pollution increased by 209% from 2007 to 2017 (33).

Beauty benefits of foods are now also a hot topic within the health and wellbeing sector, with a Mediterranean-style diet receiving a lot of media attention and individuals seeking to consume a diet rich in anti-oxidants, as well as topically applying anti-oxidants in their skincare creams.

For beauty conscious individuals the ability to minimise damage from extrinsic factors of ageing is essential, and taking a holistic approach to anti-ageing is becoming ever more customary in their daily lives. Thus research in to this field is vital for the Beauty Industry in order to respond with innovations that meet consumer needs.

CONCLUSIONS
Extrinsic skin ageing is highly influenced by oxidative stress. Mitochondria are implicated in this ageing phenotype through ROS production leading to oxidative stress and senescence. Environmental factors such as sunlight and pollution both have the ability to induce the generation of ROS in the skin, which can overwhelm the skin’s antioxidant/ROS balance to cause oxidative stress (2). Diet can affect this process, although the effect of individual components such as anti-oxidants is not yet well defined. The further development of interventions to reduce oxidative stress from environmental factors will be beneficial to skin health and is an area of commercial interest.
REFERENCES

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