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Pollution & epigenetics: A toxic relationship

The oxidative stress resulting from exposure to pollution results in epigenetic changes in skin cells that can persist long after the harmful exposure has ended. **Franziska Wandrey**, **Daniel Schmid** and **Fred Zülli** present an active ingredient that addresses both the short and long term effects of pollution on skin

The contribution of environmental pollution is one of the major areas of concern when it comes to skin ageing. In particular, air pollution is directly in contact with our skin and it contributes to skin ageing on a daily basis.

The main sources of air pollution are industrial combustion (diesel exhaust fumes and coal), traffic and construction works. Air pollution consists of gases such as ozone and very fine particles that are known as particulate matter. These particles, which are between 0.1µm and 10µm in size, can remain in the atmosphere for weeks and contain toxic compounds such as heavy metals and allergens.

Industrial combustion, traffic and construction works contribute to air pollution, which comprises gases like ozone and fine particulate matter

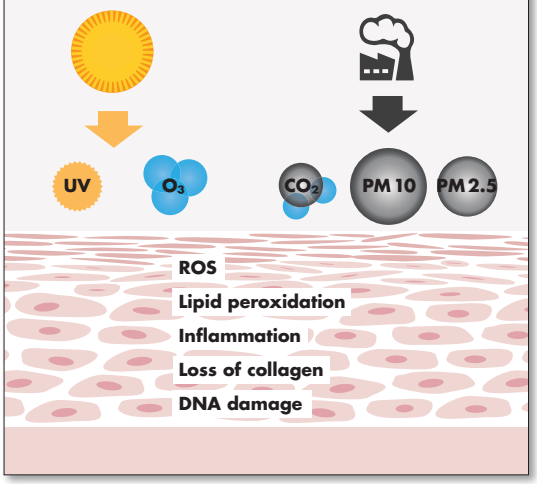
THE EFFECTS OF POLLUTION ON SKIN

Our skin is often the first organ to come into contact with air pollution. Particulate matter is especially dangerous for the skin as it not only sits on the surface but can also penetrate into pores and therefore transport toxic substances into deeper skin layers.

In combination with exposure to UV light, these particles cause oxidisation reactions within the skin, which lead to the formation of reactive oxygen species (ROS), inflammation and the loss of collagen (figure 1).

Furthermore, lipid peroxidation caused by ROS leads to skin barrier dysfunction, which creates a vicious cycle as more PM can enter the skin. The result is irritated, uneven skin that will age more rapidly.

Figure 1
Different pollutants attack our skin on a daily basis. Exposure to UV exacerbates the harmful effects of pollution on our skin, leading to skin damage, inflammation reactions and skin ageing



POLLUTION & EPIGENETIC CHANGES

Recent research has shown that the short term effects of oxidative stress are not the only danger: continuous exposure to air pollution causes epigenetic changes in our cells that can persist in the long term, even after the harmful exposure is no longer there.

Epigenetics can be explained as being a structure above the genome (epigenetics = 'on top of genetics') that regulates gene expression without changing the DNA code. DNA, which makes each individual unique, holds the instructions for building all of the parts of the body and it is wrapped around proteins that are called histones. Epigenetic regulation works by covering DNA and histones with chemical tags (figure 2). These marks, which, for example, include histone methylation, acetylation and phosphorylation, make some genes either readable or not readable without changing the DNA sequence.

In the past few years, an effort has been made in order to elucidate the effect of pollution on epigenetics. For example, steel workers who inhale higher amounts of particulate matter and

heavy metals showed a distinct increase in histone H3 lysine 4 dimethylation (H3K4me2) in their blood. This shows that long term pollution exposure changes the epigenetic code of our cells. Therefore, a multi-level protection is needed, not only to shield the skin from unwanted exposure to pollutants and detoxify the skin by neutralising dangerous chemicals that manage to enter the skin, but also to prevent long term epigenetic changes that are caused by pollution.

For the first time, we have been able to demonstrate a distinct histone modification pattern for histone H3 in skin cells that are exposed to pollution and identify an artichoke extract that is able to counteract these pollution-induced epigenetic changes.

Depolluphane EpiPlus (INCI: Lepidium sativum sprout extract, Cynara scolymus (artichoke) leaf extract, pullulan, sodium carboxymethyl betaglucan, Caesalpinia spinosa gum, maltodextrin, aqua/water) consists of this artichoke extract combined with an organic cress sprout extract and a smart polysaccharide complex in order to protect the skin against pollution in a threefold manner over the course of three distinct timelines.

Continuous exposure to air pollution causes epigenetic changes in our cells that can persist in the long term, even after the harmful exposure is no longer there

IMMEDIATE ANTI-POLLUTION SHIELD

The plant extracts are sprayed onto a carrier that is based on a mixture of different polysaccharides. This smart polysaccharide complex performs various functions on the skin: its film forming capability shields the skin from unwanted exposure to pollutants, whereas its biochemical activity enhances the skin's immune function and helps to strengthen the skin barrier.

The pollution-protection abilities of the polysaccharide complex were assessed in a placebo-controlled clinical study. A group of 21 women, aged between 20 and 44 years (average age: 31 years), received a standardised single application of a cream that contained 2% cress sprout extract encapsulated on a smart polysaccharide complex (Depolluphane) and the corresponding placebo cream in distinct zones on their forearms; 20 minutes after product application, microparticles that modelled atmospheric pollution (1µm on average) were applied to the forearm. On average, significantly fewer microparticles (-18.6%) adhered to the area that was pretreated with 2% Depolluphane compared with a non-treated zone. The forearm was then rinsed in a standardised manner.

Cynara scolymus (artichoke) leaf extract is a key component of Depolluphane EpiPlus; cells treated with artichoke leaf extract before exposure to urban dust exhibit a histone modification profile similar to cells that have not come into contact with urban dust at all

Figure 2
Our DNA is wrapped around proteins called histones. These histones can be chemically modified to epigenetically control gene expression: the genes are switched on or off

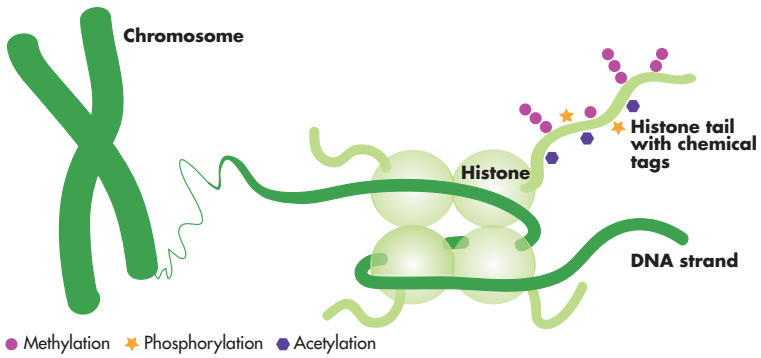
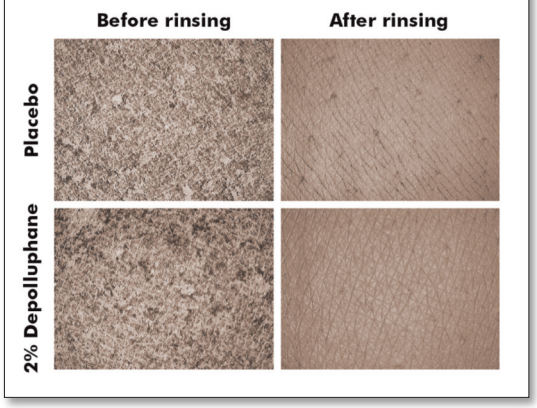


Figure 3
The smart polysaccharide complex prevents microparticle adhesion and facilitates their removal from the skin



Pictures of the defined zones were taken before and after the rinsing of the microparticles. Representative images of the average effect showed that the microparticles were more efficiently rinsed off in the zones that were pretreated with 2% Depolluphane (figure 3). Quantification by image analysis demonstrated that a single treatment with 2% Depolluphane resulted in a significantly lower quantity of microparticle adhesion and a more efficient removal of microparticles compared with the non-treated zone, as well as the placebo treated zone. Therefore, Depolluphane EpiPlus shields the skin from environmental pollutants and facilitates their removal during cleansing.

SHORT TERM SKIN DETOXIFICATION

The ability of the organic cress sprout extract to activate enzymes that help in the skin detoxification process was investigated. Keratinocytes were treated or not (control) with 0.05% or 0.2% cress sprout extract. Three antioxidant enzymes were chosen as representatives of 'detox' enzymes and analysed for their gene expression: NADPH:quinone reductase 1 (NQO1) is a major anti-carcinogenic enzyme that transforms quinones into stable hydroquinones. Heme oxygenase 1 (HO-1) is induced following exposure to oxidative stress such as UV, which indicates its role in cellular defense. Thioredoxin reductase 1 (TrxR1) works together with NADPH in order to control the redox balance of the cell. Treatment with the cress sprout extract induced expression of all

Table 1: Treatment of keratinocytes with the organic cress sprout extract increases the production of detoxification enzymes

	Enzyme expression relative to control (%)	
Concentration of cress sprout extract	0.05 %	0.2 %
Detox enzymes		
NADPH:quinone reductase 1	75	214
Heme oxygenase 1	212	4,182
Thioredoxin reductase 1	184	2,316

three detox enzymes in a concentration-dependent manner (table 1).

In addition, the organic cress sprout extract significantly reduced protein carbonylation in keratinocytes treated with particulate matter. This shows that Depolluphane EpiPlus protects cells from free radicals and helps skin cells to defend themselves against pollution.

LONG TERM EPIGENETIC PROTECTION

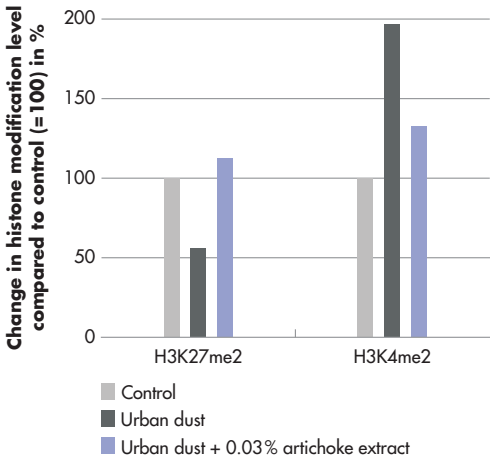
A novel assay was designed in order to test whether air pollution influences the epigenome of skin cells. This assay combined the long term treatment of keratinocytes with pollution with the subsequent analysis of histone modifications. Keratinocytes were either treated or not treated (control) with urban dust for a period of five weeks in either the presence or absence of 0.03% artichoke extract.

At the end of the incubation period, histones were isolated from the cells and the histone H3 modifications were detected and quantified. Cells that were treated with urban dust showed a distinct change in the histone modification pattern and some of the reported changes from other cell types in the literature could be reproduced. This demonstrates that long term exposure to air pollution does have a negative effect on the epigenome of skin cells.

Keratinocytes that were treated with 0.03% artichoke extract exhibited a histone modification profile that was similar to control cells that had not come into contact with urban dust. In figure 4 there are two modification examples displayed: histone 3 lysine 27 dimethylation (H3K27me2) and histone 3 lysine 4 dimethylation (H3K4me2). However, there were more than ten other such histone modification changes that were caused by urban dust. These cumulatively led to an average change in histone modification levels of 50%. When cells were treated with 0.03% artichoke extract, the histone modification levels were also closer to those of control cells, with an average modification level change of just 19%. This demonstrates a protective effect of Depolluphane EpiPlus on skin cells against the long term epigenetic changes that are caused by air pollution.

Depolluphane EpiPlus protects the skin against pollution in a threefold manner over the course of three distinct timelines

Figure 4
Long term exposure to urban dust changes the epigenetic histone modification signature of keratinocytes. Treatment with 0.03% artichoke extract prevented these epigenetic changes



TRIPLE ACTION VS URBAN POLLUTION

To summarise, Depolluphane EpiPlus ensures a complete protection against urban pollution through its triple action (figure 5):

- It immediately shields the skin against particulate matter;
- It fortifies the skin's own defense mechanism in the short term by activating detoxification enzymes;
- It protects the skin in the long term by preventing epigenetic changes that are caused by pollution ●

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Figure 5
The three anti-pollution mechanisms of Depolluphane EpiPlus