Skin protection against global pollution:

Three possibilities of actives using secondary metabolites derived from extracts of **Schisandra chinensis, Buddleja officinalis and Rhodomyrtus tomentosa**

By: Ranouille Edwige, Bridon Emilie, Boutot Carine, Berthon Jean-Yves, Filaire Edith

Greentech. Biopôle Clermont-Limagne 63360 Saint Beauzire, France
Université Clermont Auvergne, UMR 1019 INRA-UcA, UNH (Human Nutrition Unity), ECREIN Team, 63000 Clermont-Ferrand, France
Contact mail: edithfilaire@greentech.fr (0033)0473339900

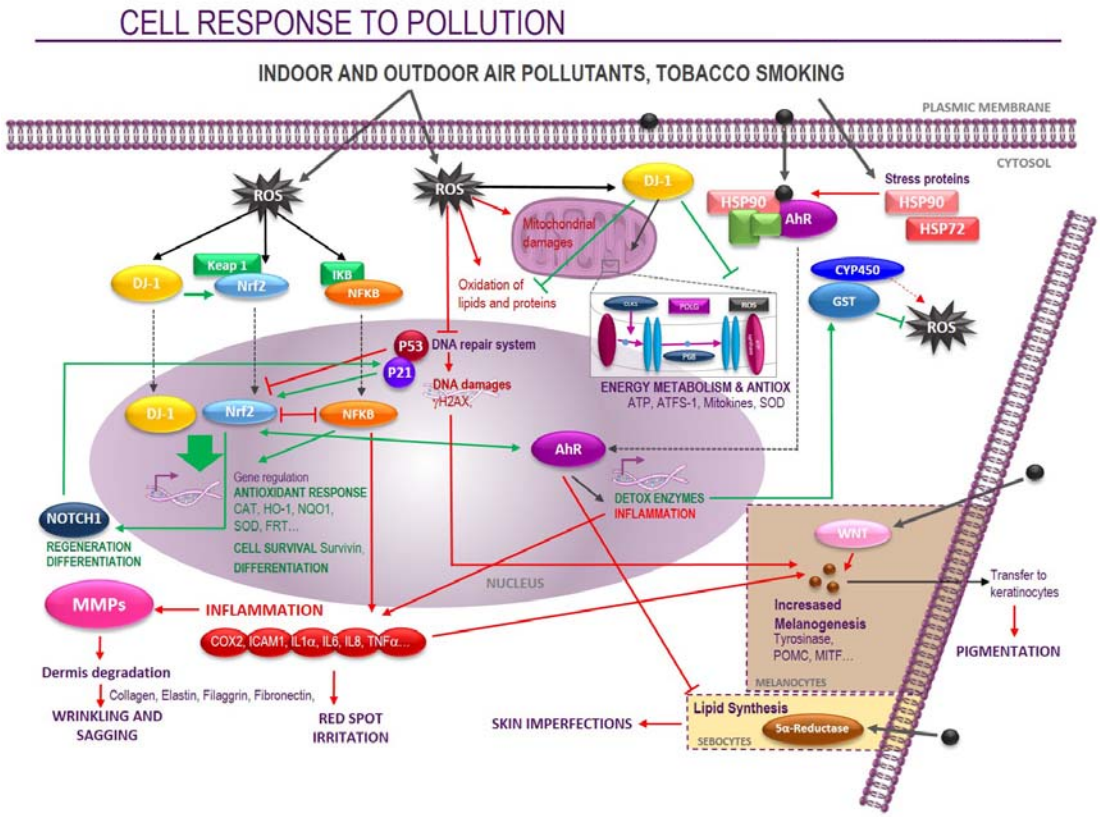

Figure 1. ROS induced by global pollution activate several signalling pathways

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The human skin, and mainly the upper layer of the epidermis, plays the role of a barrier, but is also one of the first and major targets of air pollutants. Air pollutants include those of environmental origin, as well as those of anthropic origin (Valacchi et al., 2012). Major air pollutants with effects on the skin include the solar ultraviolet radiation (UVR), polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds (VOCs), nitrogen oxides (NOx), particulate matter (PM), and cigarette smoke. The actions of various air pollutants may be amplified in the presence of other air pollutants and with the interaction of UVR, and form major active components of the pro-oxidant smog (Kampa and Castanas, 2008). Depending on the nature of these pollutants and the integrity of the skin, the modes of the penetration of pollutants differ. Alterations that disturb the skin barrier function, in either stratum corneum lipid metabolism or protein components of the corneocytes, are involved in the development of various skin diseases. The protective ability of the skin is not unlimited, and problems arise when an abnormal exposure to environmental stressors exceeds the skin's normal defensive potential (Valacchi et al., 2012). Air pollutants may induce severe interference of normal functions of lipids, DNA and/or proteins of the human skin via oxidative damage, leading to skin aging, inflammatory or allergic conditions such as atopic dermatitis, psoriasis and acne, and skin cancer (Krutmann et al., 2017). This article focuses on the effect of different forms of pollution and the role of secondary metabolites of plants to preserve skin healthy.

Pollution and cell response

The role of the solar spectrum, comprised of ultraviolet light, specifically UVB (290-320 nm) and UVA (320-400) in causing skin damage, including skin cancers, has been well documented. In recent years, the contribution of visible light

(400-700 nm) and infrared radiation (above 800 nm) in causing skin damage, similar to the photodamage caused by UV light, is also being elucidated. In addition, other atmospheric factors such as air pollution have been implicated in premature skin aging (Mc Daniel et al., 2018).

The common denominator that links skin damage to the different solar wavelengths and airborne pollutants is the enhanced production of reactive molecule species within the skin cells followed by increased oxidative stress, inducing damage to cellular components such as proteins, lipids, and nucleic acids.

Figure 1 summarizes all these mechanisms.

Besides signaling pathways illustrated in Figure 1, polycyclic aromatic pollutants and tryptophan photoproduct generated by UV irradiation bind to and activate Ahr. The activated Ahr translocates from the cytoplasm into the nucleus, binding to its specific DNA recognition site, and upregulates the transcription of responsive genes, such as cytochrome P450 1A1 (CYP1A1). Besides its physiological role in the detoxification of dioxins, the activity of CYP1A1 can be deleterious because it generates mutagenic metabolites and ROS. Moreover, AhR activation (MMP, COX2) potentiates inflammation, which could increase acne.

As human skin is repeatedly exposed to all form of pollution (including light), protection of its cells depends on an elaborated antioxidant defense system of enzymes and antioxidants for neutralization of ROS, biotransformation and elimination of electrophilic species, and maintenance of redox homeostasis. Besides known transcription factors such as Nrf2, DJ-1, which is stabilized by Nrf2, is a multifunctional protein expressed in almost all tissues involved in various physiological processes such as transcriptional regulation, anti-oxidative stress reaction, mitochondrial regulation, and signal transduction. More precisely, DJ-1 promotes Nrf2 binding to antioxidant response elements by which Nrf2 can regulate the expression of several endogenous antioxidative enzymes and reduce ROS production to protect mitochondria and can also respond to oxidative stress. Additionally, it protects mitochondria by directly maintaining mitochondrial complex I activity and translocating into mitochondria as an endogenous antioxidant.

Molecules in Plants and usefulness in cosmetic to limit pollution alterations

Schisandra lignans

A possible approach to attack ROS-mediated disorders for both preventive and treatment means is based on the use of substances, which can be found in plants as secondary metabolites. *Schisandra chinensis* is a traditional Chinese herbal medicine that has been used for the treatment in Asia for thousands of years. Schisandra lignans such as schisandrin, schisandrin A, deoxyschisandrin and γ- schisandrin, are the major constituents of S. chinensis, and more than 40 of them have been isolated by now (Chun et al., 2014). The biologically active compounds in the *Schisandra* species are lignans with a dibenzo[a,c]cyclooctadiene skeleton, which were found to possess several beneficial pharmacological effects, including a hepatoprotective effect, and exhibiting potent anti-oxidative and anti-inflammatory properties, detoxification, and anti-carcinogenic activity. Based on these data, Greentech Research proposed URBALYS®, which is a powerful global anti-pollution skin protector with 4 global actions to protect skin from pollutants :

1) it protects at molecular level by activating genes implicated in redox balance, detoxification and skin barrier integrity

2) it protects at cellular level by limiting the induction of the inflammation and detoxification pathway and by modulating the cellular defences and maintaining the redox balance

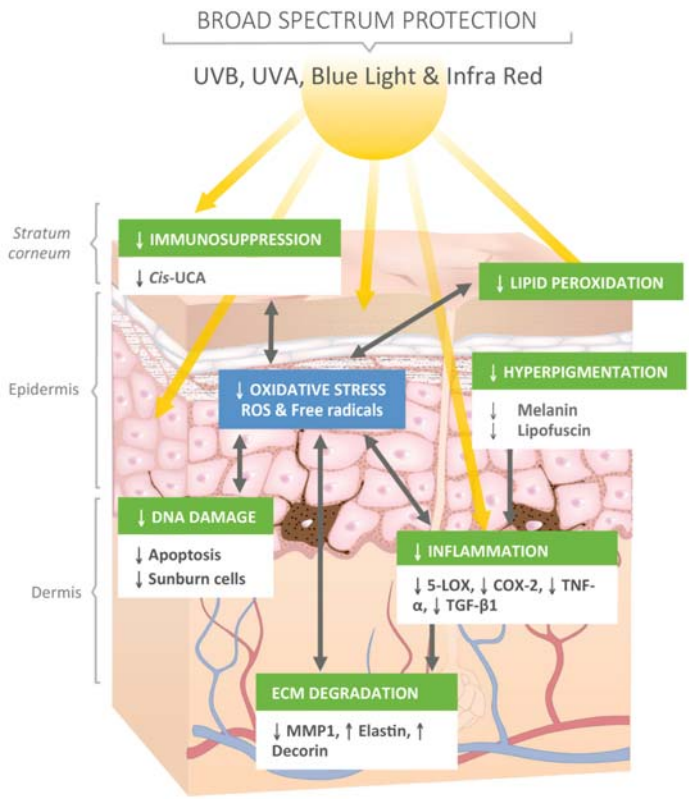

Figure 2: 360° action of SOLIBERINE® to protect from broad spectrum

3) it protects at tissular level by strengthening the cutaneous barrier and maintaining the dermis integrity, thus limiting the penetration of pollutants.

4) it protects at organ level from pollution aggression after only 7 days of treatment since it reequilibrates skin barrier homeostasis, increases microcirculation, allows skin to breathe and preserves the glowing complexion of the skin.

URBALYS® also protects from prolonged pollution aggression since it improves hydration, protects skin homogeneity, increases skin radiance and luminosity and attenuates skin spot intensity after 21 days of pollution exposition (Ranouille et al., 2018).

Phenylpropanoids

Plant-derived phenylpropanoids (PPPs) compose the largest group of secondary metabolites produced by higher plants, mainly, for the protection against biotic or abiotic stresses such as wounding, UV irradiation, and numerous studies have been focusing on the molecular mechanisms of biological activity of natural PPPs . These mechanisms include the suppression of both the production of IL-1B and the activation of NF-kB, the activation of caspase 3, the inhibition of the transcriptional activity of the COX-2 gene. Based on these data and using a translational approach, Greentech Research evaluated the photoprotective effect of active PPPs extracts (such as verbascoside) from *Buddleja officinalis* (BO), a shrub in the Buddlejaceae family known for their wound healing, anti-inflammatory, diuretic, anti-allergic, antiviral and antibacterial properties. Strong of its experience with vegetal extraction and purification, SOLIBERINE® was obtained from BO through a high-tech process, leading to a powerful cellular protector ultra-concentrated in verbascoside and echinacoside.

SOLIBERINE® has a 360° action to protect from broad spectrum (Figure 2).

In fact:

1) Under UV-B exposure, it stimulates elastin production preserving extra cellular matrix, and reduces melanin production preventing hyperpigmentation.

2) Under IR radiation, SOLIBERINE®, by inhibiting MMP-1 release, preserves extracellular matrix and prevents its premature degradation induced. It reduces pro-inflammatory mediators and this inhibition is persistent during time.

3) Under blue light exposure, SOLIBERINE® protects from oxidative stress and inflammation and significantly increases decorin expression. It also protects from blue light-induced senescence. An in vivo study was also realized: SOLIBERINE® maintains skin's colour and radiance by preventing erythema UV-induced and post-inflammatory hyperpigmentation.

Piceatannol and Rhodomyrtone

An increasing number of studies indicate a link between skin problems and exposure to airborne pollutants (Krutmann et al., 2018). A skin care product dedicated to acne may provide a protective barrier from pollution, restore microbiome balance to prevent over abundant bacteria (including Propionibacterium. acnes) colonization and control disease severity and post-inflammatory pigmentation.

Moreover, the product need to have sufficient UVA and UVB protection. Pathophysiology of acne involves three factors, hyperseborrhoea and dysseborrhea, abnormal follicular keratinization and P. acnes proliferation in the pilosebaceous unit. Thus, acne requires complete action on all identified targets to achieve the balance of healthy and clear skin. Based on its ethnopharmacology and pharmacognosy knowledges, Greentech Research has focused on Rhodomyrtus tomentosa (RT), all parts of this plant (leaves, roots, buds and fruits) being used in traditional Vietnamese, Chinese and Malaysian medicine for long time.

Ellagitannins, stilbenes, anthocyanins, flavonols and phenolic acids are the phenolic compounds identified in the fruit. Among them, piceatannol, a stilbene, has biological activities, including antioxidant, anti-inflammatory, antimicrobial properties, and is photoprotective candidate for UV-induced skin damage (Shiratake et al., 2017).

RT also contains acylphloroglucinols with rhodomyrtone as the main compound. Rhodomyrtone showed strong antibacterial activity against a wide range of Gram-positive pathogenic bacteria, as well as anti-biofilm property against staphylococci causing severe infections. More specifically rhodomyrtone inhibits *Propionibacterium* acnes proliferation (Wunnoo et al., 2017).

In order to highlight multifunctional properties of ACNILYS® as anti-acne active ingredient, we developed different cellular models and in vivo study and prove ACNILYS® efficacy on prevention of hyperseborrhea, limitation of *P. acnes* proliferation and its deleterious effects, and on reduction of inflammation induced by dysseborrhea.

Conclusion

Human skin exposed to solar UV radiation and pollution dramatically increases ROS production and oxidative stress, inducing a cascade of events that involved a variety of cell/molecular signalling pathways. The oxidative stress effects on skin aging induce damage to DNA, reduce production of antioxidants and activation/inhibition of various signalling factors that ultimately lead to the production of MMPs that degrade collagen and elastin in the dermal skin layer.

By adapting themselves to environments, plants produce a wide variety of secondary metabolites with biological activities. They have the potential to decrease oxidative stress and increase skin cellular longevity in human skin. It is the case for phenylpropanoids, lignans, piceatannol and rhodomyrtone. Based on its ethnopharmacological and pharmacognostic knowledges, Greentech Research proposed three active ingredients named URBALYS®, SOLIBERINE®, and ACNILYS® to preserve the skin and maintain its health in a global way.

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