Infrared alert

Infrared radiation is indirectly involved in skin photoageing as it induces the formation of ROS in the mitochondria of cells in the dermis and subcutaneous adipose tissues. **Daniel Schmid**, **Franziska Wandrey**, **Esther Belser** and **Fred Zülli** present a new active ingredient to target the effects of IR on skin ageing

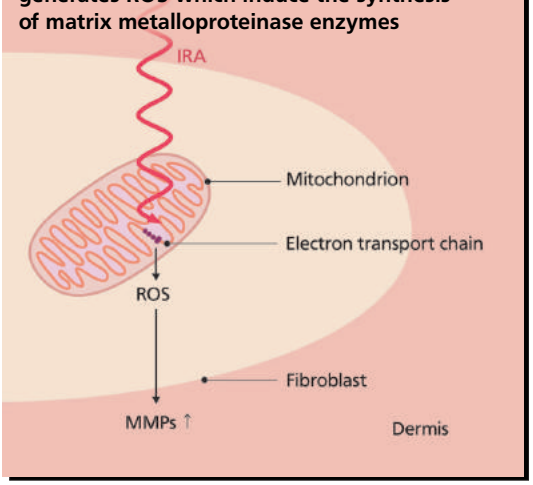
Recent studies have showed that infrared (IR) radiation is involved in photoageing of the skin. IR is the long wavelength part of the solar radiation that reaches the earth's surface. It is subdivided into near IR (760-1,400nm) and far IR. Only near infrared, also called IRA, penetrates deep into the skin reaching the subcutis, whereas longer wavelength IR is absorbed in the epidermis, producing heat. UV radiation, which is of higher energy than IR radiation induces photochemical effects, such as DNA damage. Furthermore, it is known that exposure of skin to UV induces the expression of matrix metalloproteinases (MMPs), enzymes responsible for collagen degradation and thus skin ageing. In 2008, Krutmann *et al* showed that IR radiation also induced an upregulation of the matrix metalloproteinase-1 (MMP-1) in human skin[1]. They found that IR radiation leads to the formation of reactive oxygen species (ROS) in the mitochondria of fibroblast cells[2]. It seems that IR is absorbed by components of the electron transport chain in the inner membrane of the mitochondrion. Thereby ROS are formed, which ultimately leak into the cytoplasm where they induce upregulation of MMP expression (figure 1). Mitochondria are cellular organelles and represent the powerhouses in our cells. Their respiratory activity, based on the electron transport chain, generates chemical energy in form of adenosine triphosphate (ATP). Absorption of IR radiation in the electron transport chain directly affects ATP production. Both increased expression of MMP enzymes and compromised energy production in mitochondria are responsible for the skin-ageing effect of IR radiation.

NATURAL PROTECTION VS IR RADIATION

InfraGuard (INCI: Caesalpinia spinosa fruit pod extract, propylene glycol, Helianthus annuus sprout extract, sodium benzoate, phenoxyethanol and aqua/water) combines an

Figure 1

Absorption of IRA in the mitochondrion generates ROS which induce the synthesis of matrix metalloproteinase enzymes



extract of sunflower shoots with *Caesalpinia spinosa* tannins. InfraGuard is designed to protect the skin specifically against the harmful effects of IRA; the sunflower shoot extract was found to support the overall health of mitochondria and the *Caesalpinia spinosa* tannins are highly efficient, stable antioxidants.

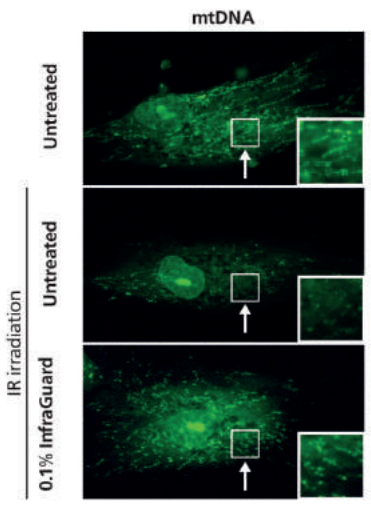
Sunflowers produce an array of secondary plant metabolites for defense against fungal pathogens and insect herbivores. The shoots of a plant are known to be the richest in secondary metabolites. *Caesalpinia spinosa* is a small tree native to the Andes area in South America. The fruits are 10cm long pods containing four to seven black seeds. The pods are very rich in hydrolysable tannins with gallic acid as the main constituent. Tannins have antimicrobial and astringent effects[3]. The mechanism is based on the tendency of tannins to bind to proteins on the cell walls of fungi or bacteria, or by coagulation of tissue proteins. Tara tannins are also known as efficient antioxidants.

GENERAL SUPPORT OF MITOCHONDRIA

As outlined in the introduction, absorption of IR radiation compromises mitochondrial efficiency and thus cellular energy production. The sunflower shoot extract was tested for stimulatory effects on energy production. Reconstructed epidermis tissue models were cultured in a medium with 2% of the sunflower shoot extract. After four weeks' culture, the cellular energy level (ATP) of the epidermis tissue in a control medium was reduced compared with freshly reconstructed epidermis. But the epidermis cultured in the sunflower shoot extract medium contained significantly more ATP. This is a strong indication for improving the efficiency of mitochondria and thus for protection of the skin against IRA.

Figure 2

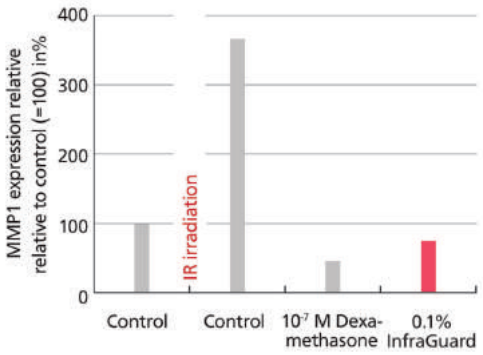
InfraGuard maintains mitochondrial DNA content during IR irradiation. Each picture shows a single cell with the cell nucleus and hundreds of mitochondria as intensely green fluorescent dots around the nucleus



THE SUNFLOWER SHOOT EXTRACT WAS FOUND TO SUPPORT THE OVERALL HEALTH OF MITOCHONDRIA AND THE *CAESALPINIA SPINOSA* TANNINS ARE HIGHLY EFFICIENT, STABLE ANTIOXIDANTS

Figure 3

InfraGuard completely prevents IR radiation-induced upregulation of MMP-1 expression



EXCEPTIONAL ANTIOXIDATIVE POWER

The technique of electron spin resonance (ESR) spectroscopy was used to analyse the antioxidant activity of InfraGuard. Electron spin resonance is a tool typically used for the study of radicals formed in solid materials. Molecules from which an electron is removed, produce an unpaired spin. ESR spectroscopy is also applicable to opaque, viscous and coloured samples, and therefore suitable for the analysis of antioxidants in cosmetic products or ingredients. The method measures the reducing activity against the stable test radical diphenyl-picryl-hydrazyl. The method allows for the analysis of the reduction potential, as well as the reaction time: the kinetic component. The result is called 'antioxidative power' (AP). Unit 1 corresponds to the activity of pure vitamin C. InfraGuard was found to be almost as active as vitamin C. But the latter is known to be very unstable once in solution. InfraGuard outperforms other natural antioxidants, such as resveratrol or green tea, by a factor of ten or more.

FULL PROTECTION OF MITOCHONDRIA

Primary human fibroblast cells were used as a cell model to demonstrate that InfraGuard can block mitochondrial and total cellular ROS production after IR radiation. A fluorescent dye served as a probe to detect ROS. The cells were exposed to IR radiation for one hour at 33°C in presence or not (control) of InfraGuard. Immediately, fluorescence was recorded for 60 minutes in a microplate reader. In control cells, IR radiation induced an increase in mitochondrial ROS of 82%. Treatment with InfraGuard not only completely protected the mitochondria against IR radiation exposure, but even decreased the ROS concentration far below

the level of non-exposed cells. Epifluorescence microscopy was used to analyse individual cells for mitochondrial DNA content. A fluorescent dye was used to label mitochondrial DNA after exposure to IR radiation. Compared with non-irradiated cells, one hour of IR exposure reduced the mitochondrial DNA content by 21% (figure 2). In the presence of InfraGuard, the DNA content was reduced only by 8%. Regarding total cellular ROS, an increase of 89% was detected in control cells, whereas in treated cells the increase was only 19%. As mentioned in the first paragraph, IR radiation-induced formation of mitochondrial ROS was found to cause upregulation of MMP expression. Experiments done with primary human fibroblast cells showed that InfraGuard could completely prevent the formation of MMP-1 after exposure to IR radiation (figure 3). Dexamethasone was used as positive control.

COMPLETE SUN PROTECTION

For a clinical trial, 32 volunteers were selected who spent summer holidays in a warm, sunny climate for two to six weeks. The 26 women and six men, 35-61 years old, applied twice daily during the entire vacation time an SPF30 sun cream with 2% InfraGuard onto the inner side of the forearm. The same cream without InfraGuard (placebo) was applied onto the other forearm. Before and after the holidays, skin firmness, elasticity, TEWL (skin barrier) and density (DermaScan C) were measured. After vacation, skin barrier, firmness and density were deteriorated on the skin area where only the sun cream was applied (figure 4). Use of 2% InfraGuard not only protected the skin, it actually improved it in all the mentioned parameters. The ultrasound pictures clearly showed a reduction in regions of low dermal density in the skin area treated with InfraGuard (figure 5). Where only the sun cream was applied, the number of low dermal density regions increased during the summer holidays.

Figure 4

InfraGuard improves skin firmness and density

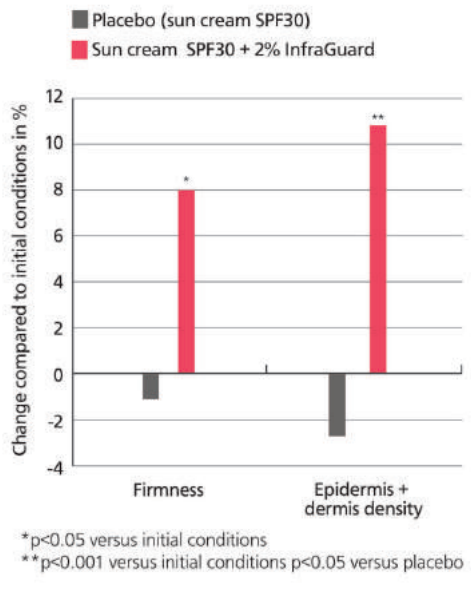
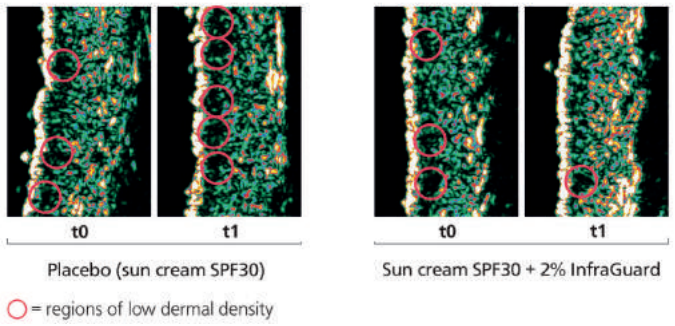


Figure 5

Before/after ultrasound pictures show that only the sun cream with InfraGuard protects the skin against loss of density



IRA PENETRATES INTO THE SKIN, DOWN INTO THE DERMIS AND THE SUBCUTANEOUS ADIPOSE TISSUE WHERE IT INDUCES FORMATION OF ROS IN THE MITOCHONDRIA

CONCLUSION

Not only UV but also IR radiation is responsible for skin photoageing. Whereas UV rays can directly damage molecules, the effect of IRA is indirect. IRA penetrates much deeper into the skin, down into the dermis and the subcutaneous adipose tissue where it induces formation of ROS in the mitochondria. The consequences are 1. mitochondrial impairment and 2. synthesis of MMP enzymes, which degrade collagen and elastin fibers. Using cell culture assays, we could demonstrate that InfraGuard targets both consequences: *Caesalpinia spinosa* tannins as strong, stable antioxidants block formation of ROS and the extract of sunflower sprouts helps to support mitochondrial efficiency. The results of the clinical study definitely demonstrate the *in vivo* relevance of IR exposure in skin ageing ●

Authors

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