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Effects of ozone on the biophysical properties and biological responses of human skin

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Ground-level ozone (O_3) stands among the most toxic environmental pollutants. It is a potent oxidant gas whose concentrations recently increased in many urban areas in numerous countries. Beside the well-known noxious effects of O_3 to the respiratory system, a growing literature has shown its harmful effects also on the cutaneous tissue. Being the largest organ and the first interface between the external environment and the human body, skin acts as a natural shield against several exogenous agents.

The first objective of this thesis was to provide a state of the art on the different approaches currently available to study O_3 exposure and the reported effects induced by O_3 on skin. Moreover, beside studying the biological effects of O_3 on skin, the thesis work aimed at increasing the knowledge related to the biophysical effects of O_3 on the cutaneous tissue, which was so far scarcely investigated. An optimized method allowing highly controlled O_3 exposures *in vitro* has been established using an in-house O_3 system. To learn more about the effects of O_3 on skin, three different skin models were used: a three-dimensional (3D) in-house reconstructed human epidermis (RhE), a stratum corneum (SC) biomembrane and a two-dimensional (2D) skin model. The experiments using RhE showed that O_3 concentrations up to an acute dose of 3.6 ppm for 3 hours did not induce a strong oxidative stress and pro-inflammatory response. However, it was demonstrated that O_3 impacted the chemical composition and organization of the superficial layers of the RhE. Moreover the studies using SC biomembranes, have also showed changes in physico-chemical properties of SC upon O_3 exposure. These results set the basis to identify possible correlations between the changes induced by O_3 exposure and the development or aggravation of skin diseases characterized by an abnormal lipid composition and organization. Furthermore these data might be useful to explain the long-term effects of O_3 on skin, measured in epidemiological studies. Finally, mimicking an impaired skin model (2D), it was demonstrated the importance of SC as barrier against the effect of O_3.

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