

***In vitro* effects of bioactive extracts of local Italian cultivars: from molecular mechanisms to potential nutraceutical applications for consumers' well-being**

Phytochemicals are non-nutritional compounds, naturally present in food and beverages, which exert beneficial effects on human health. The present Doctorate Thesis evaluates the biological properties of bioactive extracts prepared from Italian cultivars/products on different *in vitro* models to test their ability to ameliorate conditions of cellular oxidative stress, often associated with the occurrence of degenerative pathologies, such as cancer and neurodegenerative processes. The two classes of biomolecules investigated, polyphenols and carotenoids, are largely present in the three different foods and beverage investigated, e.g. red wine, elderberries and pumpkin. The results obtained suggest the existence of novel mechanisms triggered by red wine polyphenols and resulting in the protection of erythrocytes from plasma oxidizing species. These compounds are able to increase antioxidant defences in erythrocytes by activating Plasma Membrane Redox System. Moreover, we hypothesized that red wine polyphenols (73 µg/ml gallic acid equivalents) trigger a slight, but significant increase of intracellular reactive oxygen species, which induces a cellular adaptive response, which, in turn, increases antioxidant defences in erythrocytes. This aspect highlights the preventive role of polyphenols, which, through this mechanism of cellular adaptation against oxidative stress, can prevent the onset of degenerative and age-depending diseases related to oxidative damage, including neurodegeneration. In fact, the present work also describes an *in vitro* neurodegenerative model aimed to investigate the protective role of a polyphenolic extract from *Sambucus nigra* berries against oxidative damage induced by neurotoxic agents. We demonstrated that the efficacy of *S. nigra* polyphenolic extract (500 µg/ml, w/v) to effectively protect neuronal cells from apoptosis is probably related to its ability to modulate the cellular antioxidant response. The data obtained provide an initial indication for future clinical trials addressed to prove the preventive role of these natural extracts against degenerative conditions. Finally, a different class of antioxidant compounds, carotenoids from *Cucurbita moschata*, showed a functional effects on the proliferation of malignant cell lines. The mechanism of action of a carotenoid-enriched extract (200-400 µg/ml)

has been investigated on two malignant cell lines, Caco-2 and SAOs, derived from a colon adenocarcinoma and an osteosarcoma, respectively. The results obtained indicated that pumpkin carotenoids do not directly kill cancer cells, but slow down their proliferation. This effect was associated with an alteration of the energetic metabolism which resulted in a decrease in intracellular concentration of ATP and the activation of autophagy. Probably, the “not-protective” autophagy detected directly or indirectly induces cellular differentiation in malignant cells, a possibility that deserves further investigations.