

Supplementary materials

BOX1. Systems affecting RedOx homeostasis

ROS sources: ROS can be produced endogenously as a consequence of different physiological processes. ROS are generated during normal cellular metabolism, during inflammation or as a consequence of the innate immune response to infections. The main enzymes involved in ROS production are **mitochondrial enzymes** of the respiratory chain, xanthine oxidase (**XO**), NADP(H) oxidase (**NOX**), endothelial nitric oxide synthetase (**eNOS**), and myeloperoxidase (**MPO**). ROS production can also increase as a consequence of the exposure to chemical and physical factors (such as pollution and ultraviolet light) or unhealthy lifestyle habits (e.g. smoking and unhealthy diet).

<u>Endogenous Sources</u>	<u>Exogenous Sources</u>	<u>Lifestyle Habits</u>
Mitochondria Respiratory Chain	Pollution	Smoking
XO	Ultraviolet Light	Unhealthy Diet
NOX	Ionizing Radiation	Sedentary
eNOS	Drugs	Alcohol Abuse
MPO	Environmental Toxins	Physical activity Overtraining
	Pesticides	Psychological Stress

Antioxidant defences:

Enzymatic antioxidant defences are represented by proteins endowed with catalytic activities. They are characterized by high specificity toward a defined species of ROS. In this class are grouped superoxide dismutase (**SOD**), glutathione peroxidase (**GPx**) and catalase (**CAT**).

Non-enzymatic antioxidant defences are represented by chemical substances, amino acids or peptides that directly or indirectly quench or inhibit the oxidation of endogenous macro-biomolecules (proteins, lipid and nucleic acids). In this class are grouped ascorbic acid (**Vitamin C**), α -tocopherol (**Vitamin E**), glutathione (**GSH**), carotenoids and flavonoids.

Direct antioxidant defences are represented by both enzymatic or non-enzymatic antioxidants able to donate one or more electrons both *in vivo* and *in vitro*. In this class are grouped enzymes (**SOD**, **GPx**, **CAT**) and non-enzymatically active molecules (**Vitamin A**, **Vitamin E**, **Vitamin C**, **GSH**, **carnosine**).

Indirect antioxidant defences are represented by non-enzymatic antioxidants which increase the production of NADH antioxidant equivalents. Therefore, they do not directly quench or inhibit oxidation. They mainly act as co-factors in different metabolic pathways (e.g. Pentose Phosphate Pathway, PPP) or are involved in relevant transformation processes, such as the conversion of homocysteine (pro-oxidant) to cysteine (antioxidant). **Vitamins of the B group** and **polyglucosamine** are good examples of natural indirect antioxidants.^{13,16}