Strategies of antioxidant drug discovery

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Oxidative stress, a state of imbalance between oxidants and antioxidants in favor of the oxidants, is known to be implicated in a wide range of diseases including cancer and many inflammatory, cardiovascular and neurodegenerative diseases. The high reactivity of the oxidants (known as reactive oxygen species or ROS) allows them to attack biological structures; membrane lipids, nucleic acids, proteins and enzymes, resulting in irreversible cellular damage. To counter this harmful wave, chemical antioxidants have been widely used as food complements despite their side effects. Recently, more attention has been offered to natural antioxidants, found mostly in plants, because of their extraordinary diversity and above all their inoffensive nature.

Normally, living organisms are equipped with an arsenal of enzymatic and non-enzymatic endogenous antioxidants. In oxidative stress condition, this natural wall of defense is overwhelmed by oxidants (coming from the outside, or produced by the cellular enzymes) causing the balance to succumb. That's the reason behind the importance of providing the organism with exogenous antioxidants.

An antioxidant is defined as "a molecule capable of slowing or preventing the oxidation of other molecules". To do so, it can act as a free radical scavenger, a chelating agent (catching bivalent ions involved in primary ROS to much more toxic species), a reducing agent or an inhibitor of one the most important producers of ROS in living cells (xanthine oxidase and NADPH oxidase).

This work offers an enlarged overview of the recent and most effective strategies used in discovering antioxidants in natural sources, from *in vitro* tests to clinical trials.

Key words: Oxidative stress, antioxidants, scavenger, animal models, NADPH oxidase.