DIPARTIMENTO DI SCIENZE CHIMICHE

UNIVERSITÀ DEGLI STUDI DI PADOVA

Exploring the Therapeutic Potential of Catalytic Antioxidants

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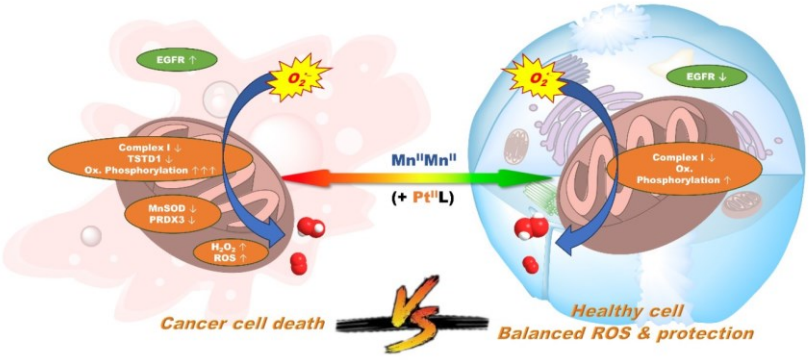
O_2 redox chemistry powers aerobic life through the fundamental processes of natural photosynthesis and cellular respiration. However, failure in the O_2 reduction mechanism leads to the release of toxic reactive oxygen species (ROS). The accumulation of ROS results in rapid, barrierless, short-range, and non-selective oxidation processes, causing "oxidative stress," which is linked to various pathologies such as inflammation, neurodegenerative diseases, and certain types of cancer.

The body's natural defense against ROS involves the coordinated action of superoxide dismutases (SOD), catalases (CAT), and glutathione peroxidase, which together convert the superoxide radical anion ($O_2^{\bullet -}$) and H_2O_2 into O_2 and H_2O through a cascade mechanism.

A recently reported dinuclear Mn_2L_2 core has shown strong dual SOD/CAT functional mimicry, enabling effective cascade detoxification of $O_2^{\bullet -}$ to O_2 [1-3]. Here, we investigate the SOD-like mechanism by: (i) directly measuring catalytic activity, (ii) identifying key intermediates in the dismutation pathway, and (iii) determining whether catalysis occurs via a mono- or dinuclear Mn center, based on the Mn_2-core conformation.

Furthermore, we evaluated the in vitro activity of the Mn_2-core, both alone and in combination with Pt complexes, revealing remarkable selectivity between cancerous and healthy cells. In vitro assays on cell viability, ROS levels, cellular Mn uptake, and proteomics analyses provided insights into the mechanisms underlying these biological effects, highlighting the Mn_2-core's potential for anticancer therapy [4,5].



References

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