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ROS scavenging by small-molecule antioxidants: key to a neglected treasury of bioactive compounds

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Small molecule antioxidants are well-known for their broad range of bioactivities. Most, if not all these bioactivities are connected to the ability of such compounds to interfere with redox biochemical processes. It is now well known that antioxidants modulate oxidative stress mostly through enzymatic processes, and their direct effect on the levels of reactive oxygen and nitrogen species (RONS) through free radical scavenging is rather negligible *in vivo*. Nevertheless, the oxidizable nature of such compounds assures that RONS scavenging does take place when they face a chemical environment provided by oxidative stress. Therefore, locally emerging metabolites of antioxidants oxidized through ROS scavenging must also be considered when evaluating their complex bioactivity [1].

In the lecture, several examples are presented that support the above notion. Biomimetic oxidation of various small-molecule antioxidants can lead to the formation of chemically stable oxidized species with dramatically altered bioactivity profiles as compared to their parent compounds. In our most recent proof-of-concept study we found that the potent antitumor agent graviquinone can be formed *in situ* upon ROS scavenging by methyl-*p*-coumarate, an abundant dietary antioxidant [2].

The above perspective suggests that chemically oxidized metabolites of antioxidants represent a rich segment of chemical space with a particularly high drug discovery potential.

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