as simple way as *in vitro*, *i.e.*, as free-radical inhibitors. The oxygen radical anion $O_2^{\bullet-}$ seems to be the main source of ROS in aerobic organisms. However, there are specific enzymes, superoxide dismutases (SOD), in cells and tissues and the enzyme reacts with the $O_2^{\bullet-}$ with a rate constant of about 2×10^9 L mol^{-1} s^{-1}. Meanwhile, the rate constants for the reactions of ascorbic acid and 5,7,8-trimethyltocol (water-soluble α-tocopherol derivative) with the $O_2^{\bullet-}$ radical do not exceed 10^5 L mol^{-1} s^{-1} while those for hydroxypyridine antioxidants are no more than 10^2 L mol^{-1} s^{-1} (see ref. 38–40). For Mito-Q (ubiquinone-based antioxidant), the rate constant for the reaction with $O_2^{\bullet-}$ in water can be as high as 10^8 L mol^{-1} s^{-1} according to pulse radiolysis data.[41] However, in this case, too, it remains an order of magnitude lower than for SOD. In principle, mitochondria-targeted antioxidants can be accumulated in mitochondria.[41,42] However, they can hardly be accumulated up to a concentration comparable with the amount of SOD (about 10^{-5} mol L^{-1}) without considerable disturbance of the operation of mitochondrial bionanoreactors.

Yet, as was mentioned above, the reliability of the SOD protection is limited so that there exists a finite probability that the $O_2^{\bullet-}$ would penetrate the SOD defense, about 2 radicals from every hundred thousand.[10–12] The radicals that penetrate the defense system can react with H_2O_2 to give the hydroxyl $OH^{\bullet}$ radical. However, it is also known that the enzymes catalase and glutathione peroxidase, which catalyze hydrogen peroxide decomposition to water and oxygen, always occur near SOD. The rate constant for the reaction of the antioxidant α-tocopherol with the $OH^{\bullet}$ radical can be as high as 8×10^{10} L mol^{-1} s^{-1} (see ref. 38–40). The $OH^{\bullet}$ radical is known to react, however, with any organic molecules as a strong oxidant with rate constants close to the diffusion limit ($>10^{10}$–10^{11} L mol^{-1} s^{-1}).[38–40] Therefore, none of antioxidants can compete for hydroxyl radicals *in vivo* with other organic molecules that are obviously always present around this radical in considerably greater numbers than the molecules of any antioxidant. Of course, the peroxyl radicals $RO_2^{\bullet}$ can appear in reactions of $OH^{\bullet}$ radicals with lipids. In addition, $OH^{\bullet}$ radicals initiate oxidation of proteins, oxidative degradation of DNA and so on (see, for example, ref. 50–52). *In vivo*, however, $RO_2^{\bullet}$ and other products of peroxidation arise mainly as secondary products in the reactions that accompany cell death on apoptosis and autophagocytosis during utilization of the cellular waste by lyzosomes and peroxysomes (see, for example, a review in ref. 53). The rate constants for the reactions of synthetic and natural antioxidants with $RO_2^{\bullet}$ in model reactions may range up to about 10^6 L mol^{-1} s^{-1}. However, the antioxidants are unlikely to be highly necessary for scavenging the active radicals in the catabolism. Besides, the reports on *in vivo* yields of the DNA oxidation products for both mitochondrial and nuclear DNA are overestimated due to various artifacts.[50] Thus, manifold effects of antioxidants *in vivo* can hardly be interpreted on the basis of simple chemical analogy with the action of the same antioxidants as radical scavengers *in vitro*.