four isomers react *in vitro* with the $RO_2^{\bullet}$ radical with approximately the same rate constants of about 10^6 L mol^{-1} s^{-1}. In living nature, however, mainly α-tocopherol is encountered. As shown in experiments on cell cultures and isolated enzymes, this form of vitamin E inhibits a key regulator enzyme of biosynthesis, protein kinase C, inhibits 5-lipoxygenase and phospholipase A_2 and also activates protein phosphatase 2A and diacylglycerol kinase. It was proved that α-tocopherol modulates the expression of genes encoding the synthesis of a number of protective proteins, including α-TTP, α-tropomyosin, and collagenase. Moreover, α-tocophenyl phosphate, rather than the antioxidant phenolic form of vitamin E, serves as the bioregulator. It has been suggested that α-tocopherol acts as a ligand for yet unidentified specific proteins, membrane receptors or transcription factors, capable of regulating signal transduction and gene expression.[67]

Furthermore, there are more and more data indicating that the therapeutic effects of many pharmaceutical drugs are due to their beneficial action not only on the cells and tissues of the host organism but also on gastric and intestinal microbiota. The number of microbiota cells in the gastrointestinal tract, on the skin, and in some other organs and tissues nearly exceeds the number of cells of the host organism.[68–70] Of even greater importance is that the microbial cells produce physiologically active substances that markedly affect all organs and tissues, including the immune system.[71–74] Moreover, there are the data that show that the microbial metabolites promote metabolic benefits in the brain cells *via* gut–brain neural circuits.[69,74,75] As a matter of fact, a new synthetic biomedical concept has emerged that the human microbiota is a source of therapeutic drug targets.[76–78]

Meanwhile, most polyphenol compounds, including flavonoids, which are traditionally regarded as "natural antioxidants", refer to the extensive class of physiologically active compounds long known as phytoalexins. Moreover, phytoalexins are synthesized in plant tissues for fighting against bacterial and fungal infections and for acting like antibiotics as inhibitors of transcription and translation of particular proteins in the cells of the infecting organism.[79–81] In view of the advances of systems biology, one can suggest that the so-called antioxidants, both natural and synthetic ones, attack the organism's microbial population. In high doses, these substances are toxic, as implied, because of their deleterious effects on the microbiota. In low doses, however, the same compounds produce favorable effects on the organism's microbiota and, thereby, increase the system reliability and lifespan of the organism. One can further assume that the so-called "mitochondria-targeted" compounds like MitoVit-E and SkQ affect actually the microbiotic cells. Thus, in this century, which is the century of systems biology, the theory that was put forward in the early 20th century by Metchnikoff about the considerable effect of the microbial population on the body health and aging is actually revived.[82] One can say with reasonable confidence that "Metchnikoff arises".

It has rather long been questioned whether the synthetic and natural antioxidant molecules work *in vivo* in the same way as *in vitro*, *i.e.* as simple chemical scavengers of $OH^{\bullet}$ and other active radicals.[12,39,40,56–59] Indeed, over