The broad field of antioxidants has now expanded into wide areas affecting foods and health. This review will cover general chemical aspects of antioxidants, their evaluation in complex foods and biological systems. Mechanistic and analytical problem areas will be identified in an attempt to sort out facts from fiction in the field. Although there is a vast body of literature on structural effects on the activity of antioxidants in solutions, our understanding is limited on how these structural effects apply in multiphase foods and biological systems. In foods, metal-complex interactions greatly influence the activities of antioxidants. In biology, antioxidants depend on interfacial interactions between cellular sites, enzyme cofactors, inhibitors and immune systems. The common use of artificial azo initiators to evaluate antioxidants is greatly discouraged because it has led to confusion and misleading interpretation in different complex foods and biological systems. Interfacial antioxidation depends on partition between different emulsion phases that affect stability and activity of natural antioxidants of different polarity. A careful choice of different antioxidant protocols for foods and biological systems is required to determine the effects of different products of lipid oxidation. The activity of antioxidants in foods depends on different interactions with lipids, proteins and sugars, synergistic effects of phospholipids, plants and beverage sources of phenolic compounds. Plant polyphenols constitute the most important dietary antioxidants evaluated by a multitude of in vitro tests. The extensive worldwide research on biological antioxidants is generally based on the hypothesis that the health of an individual is influenced by the efficiency of various protection systems against oxidant damage. The nutritional approach to antioxidant therapy is however poorly understood due to multiple interacting factors that relate degenerative diseases to diet and to oxidation. Because of lack of reliable biomarkers of oxidative stress, animal and human feeding studies have produced controversial and mixed results. The true impact of oxidation processes in biological tissues is controversial. The results of most in vitro and in vivo studies to assess the effects of phenolic antioxidants in biological systems is extremely difficult to interpret because questionable methodology has been used to measure oxidation and the oxidative susceptibility of polyunsaturated lipids and other biological targets.