Protection against protein oxidation by lipophilic and hydrophilic antioxidants in model systems using bovine serum albumin (BSA) in solution alone, or in an emulsion with linolenic acid methyl ester (LnMe) was found to be strongly dependent on the oxidation initiator. Tocopherol, Trolox, or the carotenoids astaxanthin and canthaxanthin were incubated with BSA or BSA/LnMe and oxidation was initiated either with the water-soluble azo-initiator 2,2′-azo-bis-(2-amidinopropane) hydrochloride (AAPH), or FeCl₃ and ascorbate, or the Fenton system using FeCl₂/EDTA/H₂O₂, or with the singlet oxygen generating species anthracene-9,10-dipropionic acid disodium 1,4 endoperoxide (NDPO₂). The results show that all the antioxidants tested were inefficient in the system with FeCl₃/ascorbate. However, with the other initiating agents, the hydrophilic antioxidant, Trolox, was the most effective in preventing both protein and lipid oxidation. In contrast the lipophilic antioxidants were ineffective in preventing oxidation of BSA in aqueous solution, but did show some moderate antioxidative activity on protein and lipid in the BSA/LnMe system. Using the singlet oxygen generating system it was also demonstrated that Trolox always provided better protection of the protein than tocopherol and the carotenoids in both the BSA and the BSA/LnMe systems. In conclusion, prevention of protein oxidation using a water-soluble antioxidant has a protective effect on the lipid fraction and this approach deserves further attention in complex biological systems.