



FIGURE 4.51

Amifostine as a radioprotector.

pH and oxygen content due to the fact that their lower vascularization makes them hypoxic compared with normal tissue, and (2) many malignant tissues show a reduced expression of alkaline phosphatase. Amifostine has been FDA-approved to reduce xerostomia—a chronic dry mouth condition—in patients undergoing postoperative radiation treatment for head and neck cancer, in which the radiation port includes a substantial portion of the parotid glands. Xerostomia is a severe and often irreversible side effect of radiation therapy caused by damage to the salivary glands.

12 PHOTODYNAMIC THERAPY OF CANCER

Photodynamic therapy of cancer (PDT) is based on the use of compounds that are able to absorb harmless visible light energy and transfer it efficiently to other molecules in their vicinity or, alternatively, use it for photochemical reactions with biomolecules.¹³⁴ These compounds are normally known as photosensitizers (PS). After irradiation with light of the suitable wavelength, the PS molecules are excited from the ground state $\text{PS}(S_0)$ to a singlet excited state $\text{PS}^*(S_1)$ that can reverse to the ground state by nonradiative internal crossing (IC) or by fluorescent emission (F), the latter of which can be used for imaging and detection (photodynamic diagnosis, PDD). Alternatively, it may undergo an electronic rearrangement to the excited triplet state $\text{PS}^*(T_1)$ by intersystem crossing (ISC; Figure 4.52). Most reactions of relevance to photodynamic therapy take place in the triplet state, which must be sufficiently long-lived to give intermolecular reactions before its deactivation by emission of phosphorescence (P). In the Type 1 reactions, the PS triplet state reacts with an organic molecule (e.g., a component of the cell membrane) and transfers an electron to form a radical. These radicals may react further with oxygen, giving superoxide and other ROS. In Type 2 reactions, the PS triplet state transfers its energy directly to oxygen, leading to the formation of excited state singlet oxygen, a very potent oxidizer that is believed to be the main damaging agent acting by nonspecific oxidation of intracellular targets. The efficiency of these processes can be improved by increasing the stability of the triplet state, which can be achieved by spin-orbit coupling. In more familiar chemical terms, this involves the inclusion of heavy atoms in the structure of the photosensitizer—for example, by replacement of oxygen by sulfur, sulfur by selenium, or hydrogen by bromine or iodine.