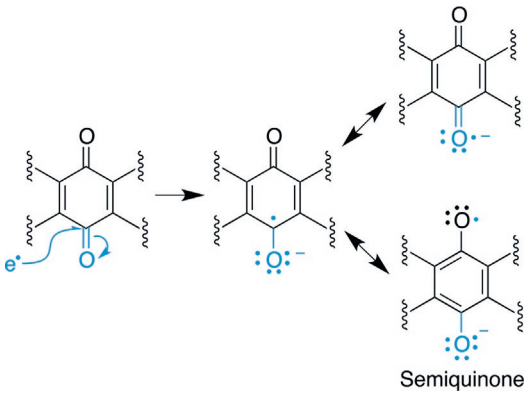

FIGURE 4.15

Captodative stabilization of semiquinone radicals.

(captodative effect). In the case of quinones, the ease of formation of the so-called semiquinone radicals by one-electron reduction is due to their stabilization through the captodative effect of the electron-releasing negatively charged oxygen atom and the electron-withdrawing carbonyl groups (Figure 4.15).

The reversibility of semiquinone formation allows these radicals to induce one-electron reduction of oxygen molecules to superoxide anions, leading to an overall increase in the electron flow to oxygen derived from the activity of enzymes such NADPH dehydrogenase, xanthine dehydrogenase, and the reductase domain of nitric oxide synthase (Figure 4.16).[30]

A competitive reaction of semiquinone **4.25** can take place, involving loss of daunosamine. Thus, two molecules of **4.25** can disproportionate to give the starting quinone and hydroquinone **4.26**, which is unstable and evolves by elimination of the sugar moiety to give the anthracycline aglycon (Figure 4.17).[31] Because of their relatively high lipophillicity with regard to the glycosides, these

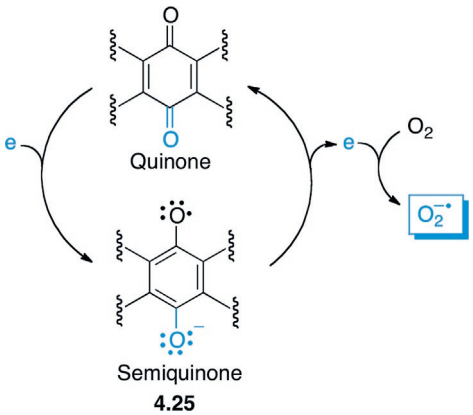

FIGURE 4.16

Electron flow from semiquinone radicals to oxygen molecules.