

Because elsamicin A is an extremely potent inhibitor of topoisomerase II, these compounds are further discussed in Chapter 7.

7 BLEOMYCINS

The bleomycins are a family of natural glycopeptidic antibiotics produced by *Streptomyces verticillus* with clinical efficacy against several types of tumors, especially squamous cell carcinomas, testicular carcinoma, and malignant lymphomas.⁸³ The anticancer drug bleomoxane is a mixture of compounds, consisting primarily of the bleomycins A₂ (~60%) and B₂ (~30%). Bleomycins differ from other chemotherapeutic agents in that they produce very little bone marrow depression and are routinely used in cancer chemotherapy, mostly in combination with radiotherapy or other chemotherapeutic agents. Their most serious side effect is a dose-dependent induction of interstitial pneumonitis in approximately 45% of patients, with 3% developing fatal lung fibrosis;⁸⁴ this lung toxicity is probably unrelated to their toxicity to tumor cells. Bleomycin A₂ is the most thoroughly studied of the DNA-cleaving reagents.

The structure of the bleomycins is complex and is shown here. A large number of semisynthetic bleomycins, most notably BAPP and liblomycin, have been prepared by addition of alkylamines to the fermentation media.⁸⁵

