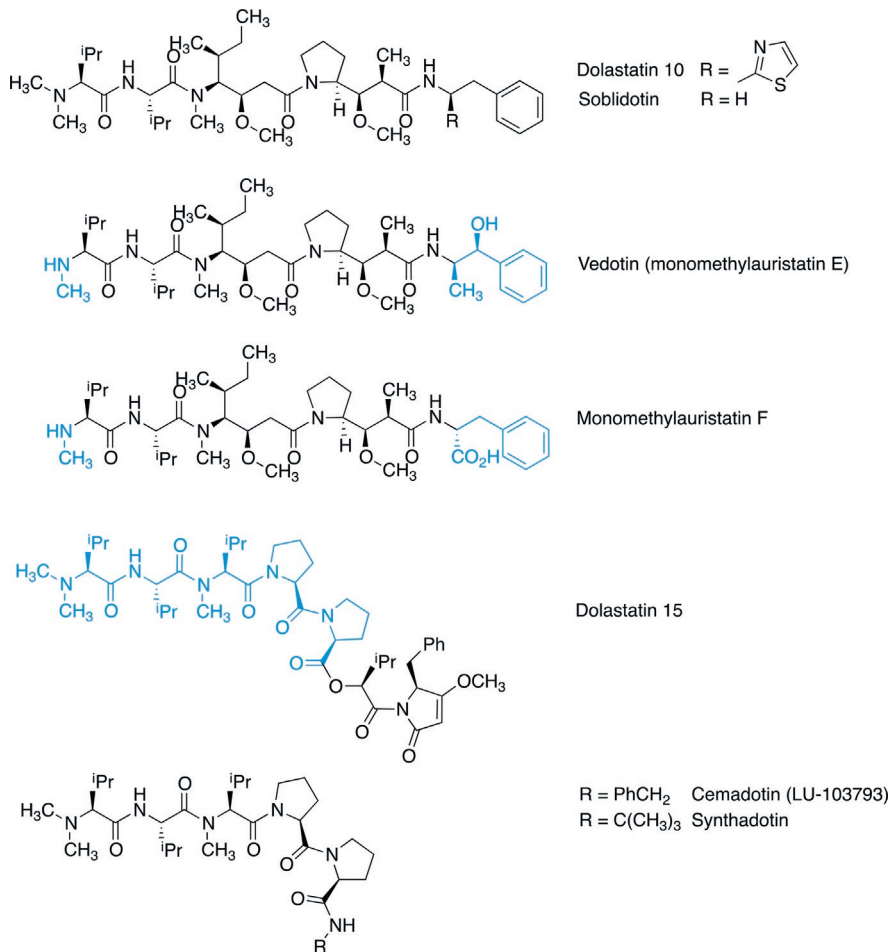


Dolastatin 10, a linear peptide,¹⁸ was isolated in 1987 from an Indian Ocean mollusk, the sea hare *Dolabella auricularia*. Although this compound progressed to phase II trials as a single agent, it did not demonstrate significant antitumor activity against prostate cancer¹⁹ nor metastatic melanoma.²⁰ Soblidotin (auristatin PE, TZT-1027) is another dolastatin 10 analog that has undergone clinical trials.²¹

Vedotin (monomethylauristatin E) is a secondary metabolite from a *Symploca* cyanophyte. Due to its high potency, it has been used as the cytotoxic payload of a large number of drug–antibody conjugates, which are discussed in Section 4.6 of Chapter 13.



Dolastatin 15 is a related seven-subunit depsipeptide, also obtained from *D. auricularia*. Many synthetic analogs of this natural product have been prepared, among which cemadotin (LU-103793)²² and synthadotin (ILX651) have entered clinical trials. The latter compound has the advantage of being orally active and seems to be promising for the treatment of non-small lung cell cancer and refractory prostate cancer.²³