

Nevertheless, it was withdrawn from the market in early 2014 due to a decline in its use and the existence of similar drugs. Tositumomab itself is a murine IgG2a mAb directed against the CD20 antigen, which is found on the surface of normal and malignant B lymphocytes.

Several mAbs labeled with different radioactive nuclides, including the α -emitter ^{211}At ,⁷⁸ are currently under study in cancer models.

5 POLYMER-DIRECTED ENZYME PRODRUG THERAPY APPROACHES

PDEPT is a two-step antitumor approach that uses a combination of a polymeric prodrug and a polymer–enzyme conjugate to generate selective cytotoxicity. In a preliminary study of this approach, administration of the previously mentioned doxorubicin conjugate PK-1 was followed by administration of a conjugate of the proteolytic enzyme cathepsin B (Figure 13.37). This conjugate also used the copolymer of HPMA and the Gly-Phe-Leu-Gly tetrapeptide linker, and its antitumor activity showed advantages compared to PK-1 alone.⁷⁹

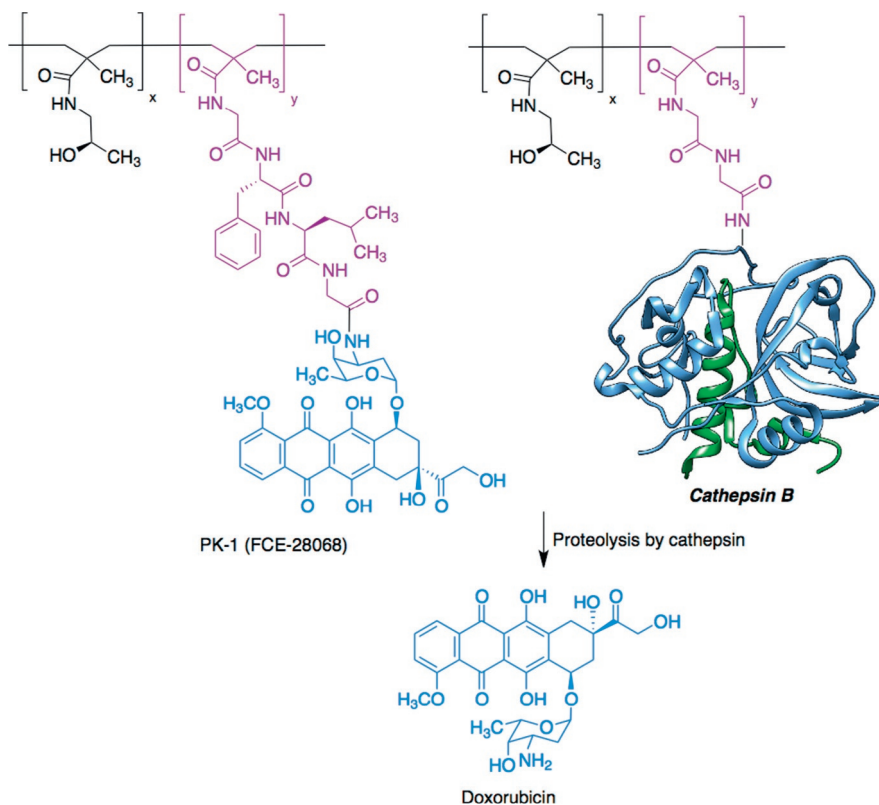


FIGURE 13.37

Targeting and liberation of doxorubicin by the PDEPT approach. The structure of cathepsin B was generated from Protein Data Bank reference 1K3B using Chimera 1.81.