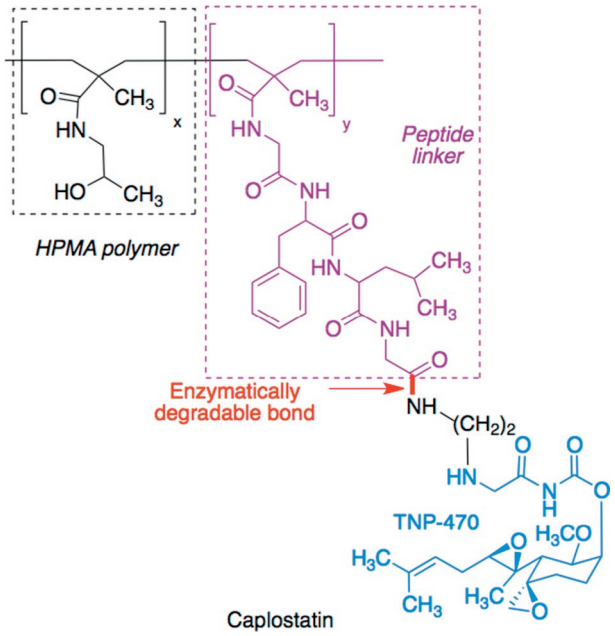

4.3 POLY-(L-GLUTAMIC) CONJUGATES

Another group of polymers designed for passive targeting through the EPR effect that are under clinical trials are the conjugates of poly-(L-glutamic) acid (PGA). They have the advantage over HPMA and PEG polymers of being biodegradable and therefore not subject to the previously mentioned 40-kDa limit in molecular mass. The main PGA conjugates under study are prodrugs of paclitaxel (CT-2103) and camptothecin (CT-2106).[59] Paclitaxel polyglumex (CT-2103, Xyotax®)[60] is the most advanced anticancer drug conjugate in clinical trials. Phase III studies have shown promising activity against NSCLC,[61] and it is also active against several cancers. In 2006, it received fast track designation from the FDA for the treatment of advanced NSCLC in patients with a poor performance status. It was proposed to minimize normal tissue exposure to free drug and evade bacterial multidrug resistance efflux pumps via pinocytotic tumoral uptake. The poor solubility of taxanes requires the inclusion of surfactant vehicles such as Cremophor EL® in their commercial formulations, but paclitaxel polyglumex does not contain this toxic vehicle due to the ability of polyglutamic acid to render highly hydrophobic molecules soluble.