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Mechanisms and biomaterials in pH-responsive tumor targeted drug delivery: a review

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ABSTRACT

As the mainstay in the treatment of various cancers, chemotherapy plays a vital role, but still faces many challenges, such as poor tumor selectivity and multidrug resistance (MDR). Targeted drug delivery using nanotechnology has provided a new strategy for addressing the limitations of the conventional chemotherapy. In the last decade, the volume of research published in this area has increased tremendously, especially with functional nano drug delivery systems (nanocarriers). Coupling a specific stimuli-triggered drug release mechanism with these delivery systems is one of the most prevalent approaches for improving therapeutic outcomes. Among the various stimuli, pH triggered delivery is regarded as the most general strategy, targeting the acidic extracellular microenvironment and intracellular organelles of solid tumors.

In this review, we discuss recent advances in the development of pH-sensitive nanocarriers for tumor-targeted drug delivery. The review focuses on the chemical design of pH-sensitive biomaterials, which are used to fabricate nanocarriers for extracellular and/or intracellular tumor site-specific drug release. The pH-responsive biomaterials bring forth conformational changes in these nanocarriers through various mechanisms such as protonation, charge reversal or cleavage of a chemical bond, facilitating tumor specific cell uptake or drug release. A greater understanding of these mechanisms will help to design more efficient drug delivery systems to address the challenges encountered in conventional chemotherapy

Key words: pH-sensitive nanocarriers, tumor targeted drug delivery, pH-sensitive bond, protonation, intracellular delivery, PEG detachment