CHAPTER 3

Smart Drug Delivery Systems

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1. INTRODUCTION

Living systems can react to environmental stresses to fit their functionality and structure to mutations in nature through the actions of complex sensing mechanisms, regulating and actuating functions, and feedback command operations. Creating biomaterials by dynamic and adjustable features could reply to the microenvironment variations by internal or external stimuli is an important challenge. Responding to circumstance is a key feature of a smart drug delivery system (DDS) [1,2]. They are able to respond to single/multiple or internal/external stimuli such as pH, temperature, enzymes, hypoxia, oxidation, reduction, light, ultrasound, inflammation-responsive, and magnetic or electric fields. Their responses depend on the chemical or physical state of the surrounding circumstances that include swelling, destruction, or solution-to-gel transitions [3].

Since the 1960s, stimuli-responsive polymers have been used as practical biomaterials for biomedical uses including the triggered-release delivery of biological cargos. Also, liposomes have been investigated as alternative DDSs with the capability to reduce the toxic side effects [4]. Stimuli-responsive block copolymers are determined as copolymers whose blocks could undergo comparatively great and sudden, chemical or physical variations in response to minor environment stimuli [5]. Smart macromolecules such as liposomes, micelles, and dendrimers produced by stimuli-responsive polymers which network can pass from a collapsed to an expanded state at transition conditions. Also, their smart surface hydrophilicity and possessing stimuli-responsive groups as a function of a stimulus can provide a responsive interfaces [6].

In the recent years, many efforts have been made to design smart stimuli-responsive DDSs for multiple applications. They are very favorable candidates for producing "smart" platforms which could be applied in numerous biomedical uses from targeted-DDSs to tissue-specific imaging. Recognition of biological systems can help scientists to design future "SMART MATERIALS" that perform a significant role in effective DDSs and diagnostics devices. Smart-embedded theranostics devices could control by either the patient or doctor and report treatment progress. Structural modifications of drug carriers can develop an infinite number of smart materials [7].

During the response to pathogens, inflammation is a primary natural defense mechanism. Particular features of inflammation microenvironment are overexpression inflammatory and matrix-remodeling enzymes, upregulation of special cell surface receptors, increasing permeability blood vessels, acidic pH, and high oxidative stress have been exploited in the inflammation-responsive DDSs development. Smart macromolecular DDSs could be selectively accumulated in the inflammatory region through passive targeting owing to the improved EPR (permeability and retention effect) and cell-mediated targeting of inflammation-recruited phagocytic cells such as macrophages or direct targeting to particular overexpressed cell surface receptors in the inflammatory sections [8].

This chapter focuses on some of the most common stimuli-responsive nanocarriers that were developed for smart medical technologies. Using stimuli nanocarriers for toxic drugs such as chemotherapy drugs or contrast agents to special organs or tissues of the body with a special condition, that nanocarriers can respond to its condition, could have been one of the most promising fields in the future of nanomedicine.

2. pH-RESPONSIVE DRUG DELIVERY SYSTEMS

Various cellular parts have their especial pH points; for example, lysosomal and late endosome pH is approximately 4.5 [9], peroxisome pH between 6.9 and 7.1 [10], mitochondria pH is approximately 8 [11], and cancerous tissues pH is around 6.5 whereas physiological pH is approximately 7.4 [12,13]. Therefore cancerous tissues

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