Chapter 14
Nanoparticle-Based Drug Delivery Systems for Cardiovascular Applications

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ABSTRACT

Nanomedicine has vastly improved the treatment and diagnosis of many cardiovascular conditions such as atherosclerosis, myocardial ischemia, myocardial infarction, restenosis, and thrombosis. A few nanoparticle drug delivery systems that are currently being tested and used in clinical trials include lipid-based drug delivery, controlled drug release, and specific targeting. The chapter describes the various drug delivery methods, the various nanoparticles, and their application on specific cardiovascular conditions. This chapter compiles examples of specific clinical trials that are being conducted, using nanoparticles for therapy of cardiovascular conditions.

INTRODUCTION

The application of nanotechnology in medicine has greatly increased over the past couple decades. Nanotechnology uses and manipulates materials of nano-scale to assist with drug delivery in the body, as well as detecting and diagnosing diseases. Nanoparticles possess unique physical properties such as large surface area to mass ratio, high reactivity, and nano-size, which allow them to overcome many limitations presented by traditional drug delivery methods (Zhang et al., n.d.). Nanoparticles are a practical method of drug delivery because they can be modified to target specific areas, therefore increasing affectivity.

Current drug delivery methods that are used for cardiovascular applications include lipid-based oral delivery, drug delivery via the coronary venous system, microbubbles, and nanoparticles for controlled-release delivery. Nanoparticles are currently being used for diagnosis and therapy of various cardiovas-

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cular conditions such as atherosclerosis, thrombosis, myocardial infarction, myocardial ischemia, and restenosis. Clinical studies show that polyglycolic acid-polymer (PLGA) and liposome nanoparticles are an effective drug delivery system to help treat these cardiovascular conditions. Surface-level modification of nanoparticles is being tested to help with drug targeting to specific regions of inflammation and injury. These advancements with nanotechnology allow for more specific and controlled drug treatment options, therefore improving therapeutics in cardiovascular applications.

TYPES OF CARDIOVASCULAR DRUG DELIVERY SYSTEMS

Cardiovascular drug delivery is unique because the vascular system provides drugs for systemic effects, as well as to specific organs. Local administration of drugs include methods such as drug delivery into the myocardium, drug delivery via the coronary venous system, injection into coronary arteries using a cardiac catheter, intrapericardial drug delivery, and the release of drugs into arterial lumen using stents (Jain, 2008). Drug delivery to the cardiovascular system is administered and mediated through various means. The main types of cardiovascular drug delivery include the use of microbubbles, ultrasound, lipid-based oral delivery, controlled-release drug delivery, and nanoparticle delivery.

Microbubble Drug Delivery Systems

Microbubbles are 1μm-1mm in size and are used as contrast agents for ultrasound imaging and targeted drug delivery. An example of a therapeutic application of microbubbles includes microbubble-enhanced sonothrombolysis. Clinical trials of microbubble-enhanced sonothrombolysis treatment are being conducted in acute ischemic stroke and acute myocardial infarction. Microbubbles can be used to target antigenic determinants expressed on endothelial cells by incorporating targeting ligands onto the surface of the microbubbles (Unger, Porter, Lindner, & Grayburn, 2014). Microbubbles can be loaded with therapeutic agents and can be delivered to specific areas of the cardiovascular system. Delivery of therapeutics can be achieved by; microbubbles being manufactured to incorporate bioactive substances in the microbubble shell, microbubbles being incubated with bioactive substances so the substance attaches to the microbubble shell, and microbubbles and bioactive substances being co-administered (Mayer & Bekeredjian, 2008).

Lipid-Based Drug Delivery Systems

Lipid-based drug delivery systems are used for improving oral bioavailability, sustaining and controlling drug release, improving drug stability, reducing food intake effect, targeting injured sites, and for combination therapy. Lipid based drug delivery systems optimize oral delivery of cardiovascular drugs (Rao, Tan, Thomas, & Prestidge, 2014). A specific type of lipid-based drug delivery system is self-emulsifying drug delivery systems (SEDDS), which are commonly used for cardiovascular drugs. Self-emulsifying drug delivery systems incorporate more hydrophilic surfactants and co-solvents in order to reduce oil and water tension of emulsion droplets. SEDDSs can reduce the re-dispersed emulsion droplet size and therefore create a small, localized, dispersion (Rao, Tan, Thomas, & Prestidge, 2014).