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Microfluidics for advanced drug delivery systems

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Considerable efforts have been devoted toward developing effective drug delivery methods. Microfluidic systems, with their capability for precise handling and transport of small liquid quantities, have emerged as a promising platform for designing advanced drug delivery systems. Thus, microfluidic systems have been increasingly used for fabrication of drug carriers or direct drug delivery to a targeted tissue. In this review, the recent advances in these areas are critically reviewed and the shortcomings and opportunities are discussed. In addition, we highlight the efforts toward developing smart drug delivery platforms with integrated sensing and drug delivery components.

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Introduction

In recent years, researchers have focused on developing novel drugs as well as strategies for their effective delivery to the target sites to improve the outcome of the treatment process. These strategies aim to enhance the drug bioavailability and specificity, reduce their cytotoxicity, and improve patients' comfort. A considerable portion of the pertinent literature has been devoted to the development of drug or gene carriers [1–3]. These activities range from developing biomaterials that enable controlled release of drugs to discovering antibodies or proteins that ascertain specificity of the site of action. For example, pH-responsive or temperature-responsive carriers have been synthesized via bulk methods for the release of the loaded drug in tissues with lower pH or higher temperature [4,5]. However, these conventional methods for synthesizing drug carriers may sometimes require large amounts of expensive drugs for fabrication and encapsulation to ensure the desired therapeutic response.

Generating a reproducible release profile requires the fabrication of monodisperse drug carriers, which may not be feasible with conventional methods such as emulsification [6]. Another challenging task using these bulk methods is to fabricate carriers for delivery of several drugs or growth factors with different release profiles, where a precise control over the composition of the employed carriers is required. Localized drug delivery is another active research area in which regular approaches such as hypodermic injection of drug or oral drug delivery are either not capable of controlling the drug release locally or maintaining the drug level over a long period of time [7]. Thus, devising strategies capable of addressing these challenges are important and will have significant clinical implications.

Recent advancements in microtechnologies and microfluidics have impacted various fields including drug discovery, biology, diagnostics, and tissue engineering [8•,9–12]. Microfluidic systems allow precise handling and manipulation of nano-liter and pico-liter volumes of liquid in a reproducible and tunable fashion. Thus, such systems have been employed for fabrication of complex drug carriers with precise size and composition leading to a predictable and tunable release profile [13•,14].

Microfluidic systems can be utilized for active and localized delivery of drugs in preprogrammed and minute quantities. This characteristic facilitates the administration of drugs with short half life or those that carry the risk of cytotoxicity upon systemic administration. Furthermore, some traditional delivery methods such as painful and hazardous injections can benefit from these microtechnologies by fabricating microneedles or needle-free injection systems [15]. Microfluidic systems have been recently designed for transdermal administration of drugs to improve patients' comfort and quality of life [16]. As a result of the recent advancement of biosensing platforms