Advanced Drug Delivery Reviews 65 (2013) 104–120

Contents lists available at SciVerse ScienceDirect

Advanced Drug Delivery Reviews

journal homepage: www.elsevier.com/locate/addr

Advanced materials and processing for drug delivery: The past and the future ☆

Ying Zhang, Hon Fai Chan, Kam W. Leong *

Department of Biomedical Engineering, Duke University, 101 Science Drive, Durham, NC 27708, USA

ARTICLE INFO

Article history:
Accepted 16 October 2012
Available online 23 October 2012

Keywords:
Commercialized drug delivery system
Nanoparticle
Polyplex
Natural polymers
Polymer–drug conjugate
Combinatorial chemistry
Microfluidics
Particle replication in non-wetting template
Step-flash imprint lithography

ABSTRACT

Design and synthesis of efficient drug delivery systems are of vital importance for medicine and healthcare. Materials innovation and nanotechnology have synergistically fueled the advancement of drug delivery. Innovation in material chemistry allows the generation of biodegradable, biocompatible, environment-responsive, and targeted delivery systems. Nanotechnology enables control over size, shape and multi-functionality of particulate drug delivery systems. In this review, we focus on the materials innovation and processing of drug delivery systems and how these advances have shaped the past and may influence the future of drug delivery.

Contents

Abbreviations: CFL, continuous flow photolithography; DDS, drug delivery system; dex-HEMA, dextranhydroxyethyl methacrylate; EE, encapsulation efficiency; ELPs, elastomer-like proteins; EPR, enhanced permeability effect; GFP, green fluorescence protein; HFR, heparin–folic acid–retinoic acid; HPMA, N-(2-hydroxypropyl) methacrylamide; IPA, isopropyl alcohol; LBL, layer-by-layer; NPs, nanoparticles; O/W, oil-in-water; PAA, poly(acrylic acid); PDMS, polydimethylsiloxane; PEG, polyethylene glycol; PEG-DA, poly(ethylene glycol) diacrylate; PEG–PLA, poly(ethylene glycol)-b-polylactide; PEI, poly(ethyleneimine); PEO-PPO-PEO, poly(propylene oxide)- poly(ethylene oxide)- poly(propylene oxide); PFPE, perfluoropolyether; PGA, poly(glycol acid)/ poly (L-glutamic acid); PLA, poly(lactic acid)/polylactide; PLGA, poly (lactide-co-glycolide); PMMA, polymethyl methacrylate; pNIPAAM, poly(N-isopropylacrylamide); PRINT, particle replication in non-wetting template; PS, polystyrene; PTMC, poly(trimethylene carbonate); PVA, poly(vinyl alcohol); RAFT, reversible addition–fragmentation chain transfer; RES, reticuloendothelial system; S-FIL, step-flash imprint lithography; SDS, sodium dodecyl sulphate; SFL, stop flow lithography technique; SLP, silk-like proteins; W/O, water-in-oil; W/O/W, water-in-oil-in-water.

☆ This review is part of the *Advanced Drug Delivery Reviews* theme issue on "25th Anniversary issue — Advanced Drug Delivery: Perspectives and Prospects".

* Corresponding author. Tel.: +1 919 660 8466; fax: +1 919 660 0031.
E-mail address: kam.leong@duke.edu (K.W. Leong).

0169-409X/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.addr.2012.10.003

1. Introduction

Drug delivery is a field of vital importance to medicine and healthcare. Controlled drug delivery improves bioavailability by preventing premature degradation and enhancing uptake, maintains drug concentration within the therapeutic window by controlling the drug release rate, and reduces side effects by targeting to disease site and target cells. Since the first FDA approval of drug delivery system (DDS), Liposomal amphotericin B, in 1990, more than 10 DDS are now commercially available to treat diverse diseases ranging from cancer to fungal infection and to muscular degeneration (Fig. 1, Table 1) [1]. In improving therapeutic efficacy, DDS has benefited tens of millions of patients by relieving suffering and prolonging life. They have also changed the economics of drug development. Packaging an existing drug into controlled release formulations may not only improve its performance but also extend its patent life as a new product. The average cost and time required to develop a new DDS (approximately $20–50 million and 3–4 years) is significantly lower than that for a new drug (approximately $500 million and over 10 years) [2]. Not surprisingly the US market for advanced DDS has grown from $75 million in 2001 to $121 billion in 2010 [3]; the annual worldwide market for polymer-based controlled release system alone is estimated to be $60 billion in 2010 [4].

Exciting advances in genomics and systems biology have continued to identify new molecular targets. Future therapeutics will be increasingly nucleic acid (plasmid DNA, siRNA, mRNA, and aptamer) and peptidic (small peptide and protein) in nature. They have to act intracellularly, although the polar nature of nucleic acids and proteins hinders their cellular entry. They are also typically more fragile than small molecules. Drug delivery will hence play an increasingly important role in realizing the full potential of the next generation of therapeutics.

Innovations in materials chemistry have initially fueled the development of DDS, creating carriers that are biodegradable, biocompatible, targeting, and stimulus-responsive. Nanotechnology has joined forces in the past decade. The realization that size and shape of nanoparticles

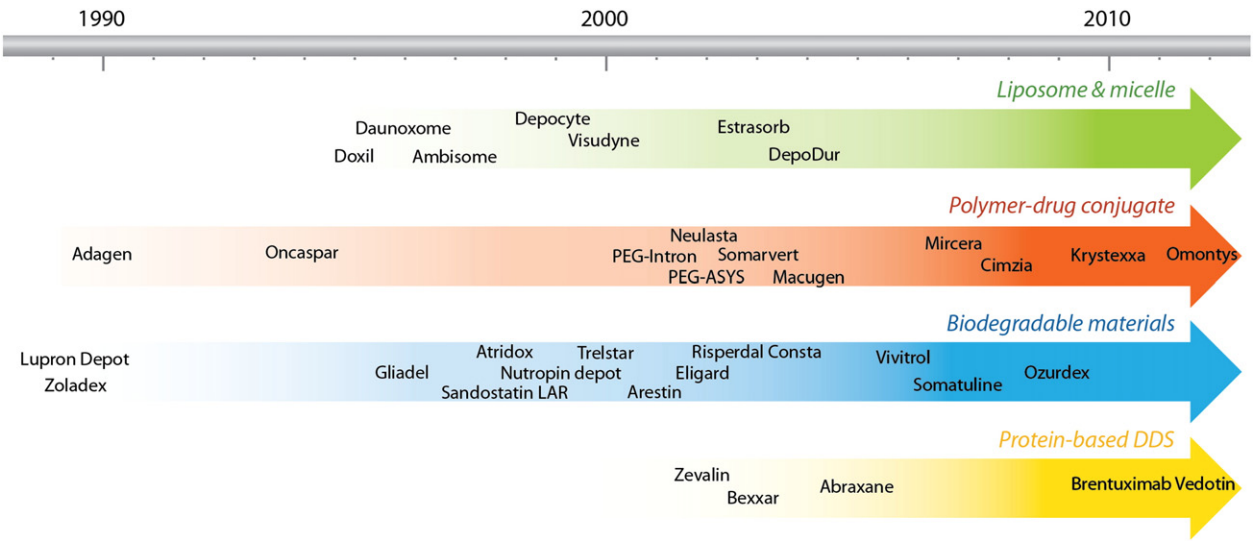

Fig. 1. Timeline showing FDA approved DDS in the market.