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Review

Role of polyanhydrides as localized drug carriers

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Abstract

Many drugs that are administered in an unmodified form by conventional systemic routes fail to reach target organs in an effective concentration, or are not effective over a length of time due to a facile metabolism. Various types of targeting delivery systems and devices have been tried over a long period of time to overcome these problems. Targeted delivery or localized drug delivery offers an advantage of reduced body burden and systemic toxicity of the drugs, especially useful for highly toxic drugs like anticancer agents. Local drug delivery via polymer is a simple approach and hypothesized to avoid the above stated problems. Polyanhydrides are a unique class of polymer for drug delivery because some of them demonstrate a near zero order drug release and relatively rapid biodegradation in vivo. Further, the release rate of polyanhydride fabricated device can be altered over a thousand fold by simple changes in the polymer backbone. Hence, these are one of the best-suited polymers for drug delivery, with biodegradability and biocompatibility. The review focuses

Abbreviations: 5-ASA, 5-aminosalicylic acid; AWGC, Apatite-wollastonite glass ceramic; BTC, 1,3,5-benzenetricarboxylic acid; CHAC, Calcium hydroxyapatite ceramic; 4-HC, 4-hydroperoxycyclophosphamide; IL-2, Interleukin-2; MCPH, Methacrylated carboxyphenoxy hexane; MCPP, Methacrylated carboxyphenoxy propane; MSA, Methacrylated sebacic acid; P(BA-PA), Poly(brassylic acid-pentadecandioic acid); P[(CBF)-ASA], poly(5-carboxybutylformamide)-2-acetyl salicylic anhydride; P(CPP-SA), Poly[1,3-bis(p-carboxyphenoxy) propane-co-sebacic anhydride]; P(CPH-SA), Poly[1,3-bis(p-carboxyphenoxy) hexane-co-sebacic anhydride]; P(CPM-SA), Poly[1,3-bis(p-carboxyphenoxy) methane-co-sebacic anhydride]; P(CPOEG-5), Poly(1,14-bis(p-caboxyphenoxy)-3,6,9,12-tetraoxatetradecane oligo(penta)ethylene glycol); P(CPP-IPA), Poly[1,3-bis(p-carboxyphenoxy) propane-co-isophthalic acid]; P(CPV), Poly[5-(p-caboxyphenoxy)-valeric acid]; P(DDDA-TA), Poly(dodecane dioic acid-tetradecanedioic acid); P(EAD-SA), Poly(erucic acid dimer-sebacic acid); PFA, Poly(fumaric anhydride); P(FAD-SA), Poly(fatty acid dimer-sebacic acid); PGA, Poly(glycolic acid); PLA, Poly(lactic acid); PLGA, Poly(lactide-co-glycolide); PLA-PSA-PLA, Poly(lactic acid)-poly(sebacic acid)-poly(lactic acid); PMMA, Poly(methyl methacrylate); P(OA/LAD-SA), Poly(Oleic acid/linoleic acid dimer-sebacic acid); P(RA-SA), Poly(ricinoleic acid-sebacic acid); PSA, Poly(sebacic anhydride); PSA-b-PEG, poly[(sebacic acid)-b-polyethylene glycol]; P(TA-IPA), Poly(terephthalic acid-isophthalic acid); P(TA-SA), Poly(terephthalic acid-sebacic acid); (P(TMA-Glycine-co-SA)-b-PEG), poly(trimellitylimidoglycine-co-sebacic anhydride)-b-polyethylene glycol; SA, Sebacic acid; TMA-ala, N-trimellitylimido-β-alanine; TMA-gly, N-trimellitylimido-glycine; TRH, Thyrotropine releasing hormone.

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on the advantages of polyanhydride carriers in localized drug delivery along with their degradability behavior, toxicological profile and role in various disease conditions.

Keywords: Biodegradable polymers; Polyanhydrides; Localized delivery; Cancer; Implants

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1. Introduction

The constant efforts of drug delivery scientists have been to maximize the therapeutic effect of the drug and minimize the adverse effects. Drugs given by conventional routes like oral, IV, IM injections are distributed to all body parts which include both, target and non-target sites. This creates a burden on the whole body system, while the requirement is only at a particular site in the body. There are many drugs, both old and new pharmaceuticals and new molecular entities, that can be administered in a way that it not only improves safety and efficacy but also in some cases, results in new therapies [1]. Many disease conditions like cancer (especially solid tumors) [2], thrombosis, restenosis [3], osteomyelitis [4], local infection [5], glaucoma and retinal disorders [6] are difficult to treat by systemic therapy. The complexity of these diseases and the serious consequences limit the systemic therapy. For example, diseases of the retina are difficult to treat with systemically administered drugs because of the blood-retinal barrier and potential systemic toxicity; hemorrhagic complications arise when antithrombotic agents are administered systemically; and cancer treatments such as systemic therapy for a localized tumor often results in serious side effects [7]. The last decade witnessed a huge amount of research aimed at creating new drug delivery systems, because of the disadvantages associated with systemic drug delivery. Several strategies have been explored to deliver the drug to a specific site or body compartment but delivery via polymer is one of the simplest approaches. Polymers find a widespread application in therapeutics and localized use of polymers has its own importance. Polymers for localized application can play structural,