Superior Comb Branched Polymers for Drug Delivery

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BRIEF DESCRIPTION

Background:

Polymeric delivery of chemotherapeutics has successfully improved cancer treatments over the past two decades. Polymers well-suited for drug delivery applications confer high solubility, long circulation half-life, biocompatibility, low toxicity, and high accumulation at tumor sites. Research into polymer parameters affecting these criteria has guided drug developers toward optimally sized polymers and the exploration of polymer architectures. Recently, increased polymer branching has been shown to increase drug circulation times and decrease elimination by the kidney. A novel branched polymer system and its simple synthesis comprise this drug delivery advancement.

Summary:

UCSF researchers have discovered a PEGylated polymer system that is superior to known PEGylation technologies. This system consists of a polyester comb branched-PEG hybrid characterized by a highly branched polymer structure in which the branches detach hydrolytically. Biodistribution studies showed that, in comparison with linear polymers of the same molecular weight, comb branched polymers were able to escape kidney clearance, extending its blood circulation half life. High levels of tumor accumulation were found for comb branched polymers with molecular weights as low as 44kDa in mice bearing subcutaneous C26 colon carcinoma. The polymers degrade to lower molecular weights at both normal physiological pH and mildly acidic pH, enabling complete clearance by renal excretion and minimizing residual polymer buildup in kidneys and other organs.

Historically PEGylation has been associated with several manufacturing disadvantages, none of which handicap the comb branched polymer synthesis. PEGylated dendrimers are typically synthesized by coupling activated PEG chains to dendrimer cores, whose synthesis require multiple

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OTHER INFORMATION

KEYWORDS

dendrimer, PEG,

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CATEGORIZED AS

- **Biotechnology**
  - Health
- **Materials & Chemicals**
  - Biological
  - Polymers
- **Medical**
  - Delivery Systems
  - Disease: Cancer
  - Therapeutics

RELATED CASES

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steps. To reduce the number of synthetic steps to reach a high molecular weight, expensive functionalized PEGs are required. Alternatively, synthesis of PEG dendrimers is also possible through radical polymerization using core initiators. While this yields polymers with high molecular weight and low polydispersity, these core intiators are difficult to synthesize or not biodegradable. In contrast, UCSF's comb branched polymers are easily synthesized using inexpensive and commercially available starting materials. The resulting polymer has a polymer distribution index of less than 1.15, indicating the synthesis is well-controlled. Its narrow polydispersity, together with consistent drug loading, leads to reproducible pharmacokinetic behavior. The synthetic advantages and improved pharmacokinetic properties of the comb branched polymer system make them ideal for the next generation of chemotherapeutics.

ADVANTAGES

- Reduced elimination of the polymer by kidneys leads to improved tumor accumulation and improved therapeutic effectiveness
- Robust and simple chemistry yields high molecular weight low polydispersity polymers
- Low cost synthesis with simple attachment of drug
- Entire polymer, including the core initiator, is biodegradable into low molecular weight fragments via polyester linkages

PATENT STATUS

Patent Pending

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