



Technology Summary: Long-Circulation Liposome for Drug Delivery

Opportunity Statement

The drug-delivery market is changing drastically due to the introduction of new techniques and routes of delivery. The widely preferred drug carriers include soluble polymers, microparticles made of insoluble or biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes, micelles, drug-loaded biodegradable microspheres and drug polymer conjugates. In recent years, liposomes have seen phenomenal progress in drug-delivery systems and have received increased attention from the pharmaceutical community.

Liposomes are artificially prepared vesicles made of a lipid bilayer that can encapsulate drugs and used as a drug carrier system for the treatment of cancer and other diseases. Encapsulation of a drug in liposomes prevents its early degradation and alters the biodistribution profile in the body. This enables higher concentrations of the drug in the desired tumor site, leading to improved effectiveness, while a lower concentration reaches into the vital organs, such as the heart and kidney, thus reducing the toxicity of the drug.

Problem

Conventional liposomes are eliminated rapidly from the biological fluids (e.g., blood), and therefore lack the stability to establish long circulation times required to realize the full efficacy of the drug.

Therefore, there is a need for the development of a long-circulating liposome that is not immediately recognized in the body. Such a liposome would create a mode of delivery that is long-lasting, reduces toxicity and stabilizes the encapsulated drug, thereby improving the efficacy of the drug.

360ip Partner's Solution

The 360ip Partner's invention relates to the preparation method and application of a hydrophobic-modified dextran-modified long-circulating liposome. The novel liposome consists of a phospholipid, cholesterol and hydrophobic-modified dextran.

The technology involves the following process steps:

Preparation of Hydrophobic-Modified Dextran

1. Synthesis of Carboxymethyl Dextran
 - 1.1. Reaction of dextran and NaOH solution containing bromoacetic acid is carried out to obtain white flocculent carboxymethyl dextran.

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2. Synthesis of Hydrophobic-Modified Dextran

- 2.1. Carboxymethyl dextran is dissolved in a water solution containing 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide and N-hydroxysuccinimide to activate carboxyl, which is then combined with the amino terminal of oleylamine to obtain the hydrophobic modified dextran.

Method of Preparation of Hydrophobic-modified Dextran-modified Liposome

1. Preparation of Hydrophobic-modified Dextran-modified liposome

- 1.1. Phospholipid, cholesterol and hydrophobic-modified dextran are dissolved in organic-mixed solvent.
- 1.2. Rotary evaporation is performed in a constant-temperature water bath.
- 1.3. Hydration sonication is performed to obtain pan-blue opalescent liposome suspension.

2. Homogenization of the Liposome

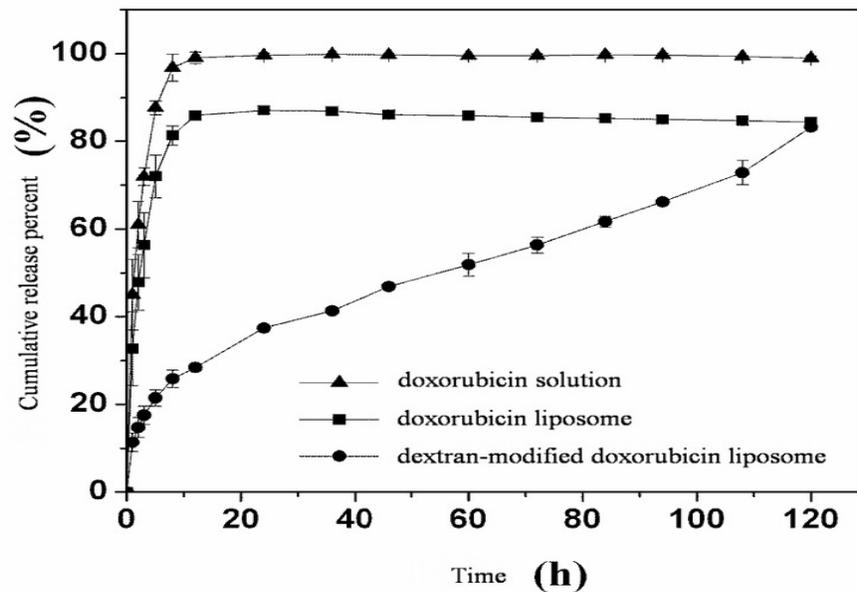
- 2.1. Liposome suspension is filtered by a microporous membrane with a corresponding pore diameter for achieving the homogenization. The molar ratio of the cholesterol to the phospholipid is 0.28-1; and the weight ratio of the hydrophobic-modified dextran to the phospholipid is 0.075-0.375. The organic mixed solvent is selected from chloroform and methanol, and the volume ratio of the two is 1-3.

Compared to existing methods, this long-circulating liposome has the following advantages:

- Long-time circulation: Reduction in the phagocytosis of the liposome by the reticuloendothelial system slows down the clearing speed of the liposome, thus prolonging the residence time in the blood.
- Targeting functionality: As free carboxyl exists on the modified dextran of the invention, the modified dextran can be reacted with targeting groups very conveniently, thereby further improving the active targeting function of the liposome.
- High encapsulation rate: The encapsulation rate to a variety of drugs can be more than 95%.
- Uniformity of liposome: This is achieved by filtering blank liposome suspension by the microporous membrane with the corresponding pore diameter.
- Particle size: The average particle size of novel liposome is 50-200nm.
- Enhanced stability: A part of a hydrophobic chain segment of the hydrophobic-modified dextran enters into a hydrophobic layer of the liposome due to entropy driving, which enhances the stability of the internal structure of the liposome.
- Good re-dispersion capacity: The liposome has uniform dispersion, shape and appearance.
- Low cost: The synthesis method of the modified dextran is simple, feasible and low cost.

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- Preservation: The liposome can also be freeze-dried for preservation.



Patents

360ip's Partner has filed one patent application on this technology and plans to seek protection in multiple jurisdictions.

360ip is seeking interested parties for the licensing, further development and commercialization of this technology-based product.

For additional information, contact:

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