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PREPARATION AND ANALYSIS OF COMPOUND LIPOSOME OF IRINOTECAN AND DIHYDROMYRICETIN

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Objective: To prepare compound liposome loading of irinotecan and Dihydromyricetin, and evaluate its pharmaceutical properties. Methods: The encapsulated rate of compound liposomes was determined by dextran gel method. The particle size distribution and Zeta potential were measured by nano-particle size and Zeta potential analyzer. Results: The EE of compound liposome loading of irinotecan and Dihydromyricetin was 82.58% and 71.45% respectively. The mean diameters of compound liposome were (123.1±1.8) nm and its PdI was below 0.20 and its Zeta potential was (-24.3±0.51) mV. Conclusion: The established method is fit for the preparation of compound liposome of irinotecan and curcumin. The analysis method is simple and accurate, which can be used to evaluate the property of compound liposome.

Keywords: irinotecan; dihydromyricetin; liposome; preparation

Dihydromyricetin（DMY）is a kind of dihydrogenated flavonols isolated from leaves and leaves of Vinegar, with anti-inflammatory, liver protection, regulating immunity and other pharmacological effects [1]. Irinotecan (CPT-11), as a Topo Ⅰ inhibitor [2], differs from traditional enzyme inhibitors in converting this ribozyme into a substance that is detrimental to DNA, the Topo- drug-DNA complex and is stable body. Liposomes as an effective drug delivery carrier, effectively control the drug release, prolong the plasma half-life of drugs, improve the bioavailability of drugs, reduce the toxic effects of drugs, etc., in the field of medicine has been rapid development.

Objective： In this study, dihydromyricetin was encapsulated in phospholipid bilayer, and irinotecan was encapsulated in the aqueous phase of phospholipid bilayers by active drug loading technology, and a synergistic anti-cancer model was designed.

1. Materials and methods

1.1 Instruments and reagents

Zetasizer Nano-ZS90 nano-particle size and Zeta potential analyzer; 756PC visible UV spectrophotometer;Hydrochloric acid irinotecan; dihydromyricetin ; Dihydromyricetin standard.

1.2 Methods

1.2.1 Preparation of Dihydromyricetin-irinotecan Compound Liposomes

Phospholipids and cholesterol in proportion, DMY dissolved in ethanol, take ammonium sulfate solution placed in ampoules, heating and insulation, the lipid solution into the phosphate buffer, continue to stir, so that ethanol volatile completely. The suspension was placed in a water bath ultrasonic system for ultrasound. Then, into the treated dialysis bag, placed in saline dialysis. Upon completion, add CPT-11 aqueous solution and incubate. Followed by a 0.22 μm microfilm.

1.2.2 Determination of enthalpy of irinotecan-dihydromyricetin complex liposome

The amount of compound liposomes was 0.5 mL. Sephadex G-50 was used as the eluent, and the flow rate was 1ml / min. A total of 25 copies were collected every 2mL. The contents of DMY and CPT-11 in the eluent were determined. The content of DMT and CPT-11 in the liposomes were recorded as W p, Of the drug content recorded as W t, according to the following formula to calculate the entrapment efficiency:

Enclosure rate (%) = W p / (W p + W t) × 100%

1.2.3 Determination of particle size, particle size distribution and zeta potential

Accurately measure the product 0.1 ml, diluted with ultrapure water 10 times, gently shake mix, remove the bubbles, into the instrument to detect the room, with Zetasizer Nano-ZS90 nano-particle size analyzer measured particle size distribution, the average particle size and Zeta Potential.

2.Results and discussion

The EE of compound liposome loading of irinotecan and Dihydromyricetin was 82.58% and 71.45% respectively. The

mean diameters of compound liposome were (123.1±1.8) nm and its PdI was below 0.20 and its Zeta potential was (-24.3±0.51) mV.

The entrapment efficiency is the most important indicator to evaluate the quality of liposomal preparations, and whether it can play the most efficient and low toxicity characteristics of common preparations. In this study, the dextran gel method was used to determine the entrapment efficiency, which could effectively separate the compound liposomes and free drugs. This method is convenient, fast, easy to operate, reproducible, and more suitable for quality control in the production process.

Particle size and its distribution are important indicators that affect the targeting, physical stability and clinical safety of liposomes. Therefore, it is one of the key factors in the quality control of liposomes. In this study, the particle size and distribution of the composite liposomes were measured by the particle size analyzer. The results showed that the particle size was uniform and normal distribution.

In this study, two kinds of anti-tumor drugs DMY and CPT-11 were encapsulated in liposome delivery system to prepare compound liposomes. The preparation process was simple and feasible, reproducible and high encapsulation efficiency.

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RESEARCH PROGRESS OF JAUNDICE AND RELATED ANIMAL MODELS

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Abstract: Jaundice can be seen in the development of a variety of diseases, due to the lack of ideal animal model, limiting the treatment of jaundice. In this paper, we reviewed the literature of jaundice and related diseases model in recent years, it includes hepatocellular jaundice, cholestatic jaundice and jaundice syndrome in traditional Chinese medicine(TCM). To analyze the mechanism and effect of the model, which can provide some basis for the study, prevention and cure of traditional Chinese medicine.

Key words: liver injury, cholestasis, jaundice syndrome, animal model

1. Introduction Jaundice (hyperbilirubinemia) is a common clinical disease, hemolysis and liver damage weakened liver cell uptake and bilirubin exclusion, leading to increased levels of bilirubin in the blood, manifested as skin, sclera and mucous membranes yellowish discoloration. Jaundice is a challenging disease that requires a reasonable and highly recognized jaundice animal model in-depth study to make further progress in diagnosis and treatment. So, establish a jaundice animal model similar with the human disease can improve the evaluation system of treatment of jaundice syndrome to achieve a better therapeutic effect.

2.Hepatocellular jaundice model Lipopolysaccharide (PLS) is a major component of the outer membrane of Gram-negative bacteria. Lipid A is a toxic and bioactive centre that produces a more durable and extensive immune injury to the liver[1]. The application of LPS has been recognized by the world as a highly repeatable model. Xinyan Peng intraperitoneal injection of LPS(4mg/kg) in mice, blood and liver tissue were collected after 8 hours. The level of serum ALT and AST was significantly increased. Pathology revealed the liver injury, liver cell necrosis, bleeding and inflammatory cell infiltration. The pathological basis of acute liver injury induced by CCl4 is free radical production and lipid peroxidation. Sumaira Sahreen established liver fibrosis model by intraperitoneal injection of CCl4 (0.5 ml/kg) olive oil solution twice a week for 8 weeks. D-galactosamine (D-GalN) can induce toxic liver injury model, and liver histopathological changes similar to human viral hepatitis. This is a classic animal model for the pathogenesis of viral hepatitis. Hui sun established the rat model of acute hepatitis by interaperitoneal injection of D-GalN (400mg/kg) , to find out the metabolic mechanism and special biomarkers of hepatitis rats[2]. In addition to the above drugs, aflatoxin, acetaminophen (APAP) and cyclosporine A were also used to establish animal models of chemical or drug-induced liver injury.

3.Cholestatic jaundice model α-Naphthalene isothiocyanate (ANIT) is a non-hereditary toxic drug that can induced the release of high concentrations of bile acids into the liver leading to liver injury[3], ANIT has the advantage of low carcinogenicity compared with other genotoxic drugs and can be widely used in rodent simulations of human intrahepatic cholestasis. Chlorpromazine is the main drug for the treatment of mental illness, its liver toxicity can not be ignored, it can inhibit the flow of bile in the body[4]. Qiaoling Yang was injected intraperitoneally with chlorpromazine (75mg/kg) to make rat cholestasis model. Serum biochemical markers and pathology showed that the model was successfully replicated. Obstructive jaundice is easy to form cholestasis, endotoxemia, lipid peroxidation, inflam-