82. CN114983967 - HUMIC ACID-GD NANO-CARRIER, PREPARATION METHOD AND APPLICATION IN DRUG DELIVERY

[ZH]

Humic Acid-Gd Nanocarrier, Preparation Method and Application in Drug Delivery

TECHNICAL FIELD

The present invention belongs to the technical field of nano pharmaceutical preparations, and specifically relates to a humic acid-Gd nanocarrier, a preparation method therefor, and an application thereof in drug delivery.

BACKGROUND

In recent years, cancer severely threatens the life and health of humans due to its morbidity and lethality. Treatment against tumors also experiences long term exploration, development and research. Conventional methods of tumor treatment have surgery, radiotherapy and chemical drug therapy, and current therapeutic means have increased gene therapy, targeted therapy, photothermal therapy, photodynamic therapy, immunotherapy, etc.Chemotherapy is still a main means for clinically treating tumors, chemotherapy mainly plays a role in chemical drugs, chemical drugs can be circularly distributed to most organs and tissues of the whole body along with blood, and the proliferation of tumor cells can be inhibited or tumor cells can be directly killed by utilizing different action mechanisms (for example, inhibiting DNA replication and transcription) by utilizing chemical drugs, so that tumor cell apoptosis is promoted, and tumor recurrence is inhibited. Although the method of chemical treatment has an effect on inhibiting malignant tumors, especially for tumor patients with metastasis tendency or metastasis already occurring, chemotherapy is a preferred treatment regimen.However, the chemical treatment drug exerts a higher drug concentration, poor drug selectivity, and systemic administration, and cannot specifically target the tumor site, so that it is difficult to kill tumor cells without affecting the physiological function of normal cells, which can cause serious damage to normal tissues and organs, and the generation of drug resistance of chemotherapeutic drugs also greatly limits the application thereof. In order to improve the therapeutic effect of the anti-tumor drug, reduce a series of side effects brought about by the anti-tumor drug, reduce the pain of the patient, and urgent need to seek a new treatment method.

With the advancement of nanotechnology, nano-medicine may become a breakthrough to the inherent defects of existing cancer treatment strategies. Compared with the traditional chemotherapy method, the nano-drug delivery system constructed by taking the nano material as the core shows great advantages: (1) the solubility of the refractory drug is increased, absorption is promoted, and the curative effect is improved; (2) some nano materials have unique size and surface structure characteristics, so that the nano materials can be directly or indirectly loaded or packaged, and single or multiple responsiveness control release is realized, so that the treatment effect is improved, and the toxic and side effects on normal tissues or cells are reduced; and (3) after the nano particles and the medicine are combined to prepare the nano preparation, the nano preparation can generate an aggregation phenomenon at lesion positions such as tumors through the in-vivo EPR effect.so as to increase the targeted therapy ability of the drug and reduce the toxic and side effects of the drug; (4) the nano drug is mostly protected by the shell, so that the drug can be prevented from being degraded by nuclease and the like, the drug activity is prevented from being reduced, and the stability of the drug is improved; and (5) the cycle time of the drug in blood is prolonged, and the phagocytosis of the mesh endothelial system is reduced. According to these advantages of the nanoparticles, an anti-cancer drug with a strong anti-cancer effect but also a large side effect is combined with a nano material with superior performance, which is undoubtedly a good idea. Meanwhile, the multifunctional nano diagnosis and treatment agent integrating drug transportation and imaging shows huge potential in the aspects of visualization of drug transportation and real-time monitoring of lesion killing, and is increasingly concerned with people.

In recent years, photothermal therapy (PTT) has become an important cancer adjuvant therapy method. PTT requires a near-infrared light heat conversion nanoparticle to cause a local medium to generate a high temperature under near-infrared light irradiation, causing cancer cells to produce irreversible damage or death. Near-infrared light has deeper tissue penetrability and lower phototoxicity, and at the same time, due to low oxygen in tumor tissue, PTT has laser-controlled tumor ablation and non-oxygen dependence, and has special advantages in treating tumors. In addition, the PTT nanoparticles guided by tumor imaging not only can accurately identify the size and position of the tumor, but also can monitor the treatment effect of the tumor region in real time, which is crucial to improving the treatment effect.

Inorganic nanomaterials such as gold nanoparticles, black phosphorus nanomaterials, graphene and other carbon nanomaterials have excellent photothermal conversion capability, but the inorganic nanomaterials have low solubility and poor dispersibility in an aqueous solution, and have the disadvantages of poor biocompatibility and easy agglomeration when applied in the field of biology, and can easily cause blood vessel blockage in vivo; PEI, liposome, chitosan and the like, although the organic nano material has good biocompatibility, is relatively good in solution degree in water, is not easy to agglomerate into large particles, has a single function, and does not have imaging capability and treatment capability.In order to endow the inorganic nano material with better biocompatibility, most scientific research workers coat or combine the inorganic nano material with an organic nano material to

form a complex composite nano material, the organic and inorganic compound is complex in preparation process and troublesome to operate, large-scale production is not facilitated, and in the synthesis process, the medicine utilization rate is extremely low.

Therefore, the present invention prepares a nanocarrier which has good biocompatibility, good dispersibility in an aqueous solution and long-term stability, and also has magnetic resonance imaging capability and photothermal therapy capability, and is used for loading an anti-tumor chemotherapeutic drug to form a nanodrug delivery system to better solve the problem of tumor treatment.

SUMMARY OF THE INVENTION

In order to solve the above technical problem, the present invention provides a humic acid-Gd nano-carrier, a preparation method therefor, and an application thereof in drug delivery. Humic acid and metal gadolinium (Gd) are complexed to form a nanoparticle carrier and loaded with an anti-tumor chemotherapy drug, so that the nano-drug delivery system has the functions of chemotherapy, photothermal therapy and the like, constructs a drug delivery system for combined treatment of tumor microenvironment response and nuclear magnetic resonance imaging guidance, and will become an effective solution for tumor treatment.

The present invention is specifically implemented by the following technical solutions.

A first object of the present invention is to provide a method for preparing a humic acid-Gd nanocarrier, comprising the following steps:

S1. Purification and Activation of Humic Acid

dissolving sodium humate with an inorganic acid, performing ultrasonic treatment, centrifuging, and taking a supernatant; using an inorganic acid as a dialysate, dialyzing the supernatant, and then drying;

S2. Preparation of Humic Acid-Gd Nanocarriers

The preparation method comprises the following steps: dissolving soluble Gd salt in an acidic solvent to prepare a Gd salt solution; and mixing the Gd salt solution with an aqueous solution of humic acid treated in the step S1, stirring and reacting at room temperature, dialyzing and drying to obtain the humic acid-Gd nano carrier particles.

Preferably, in S 1, the inorganic acid is 0.01 M hydrochloric acid, nitric acid or sulfuric acid.

Preferably, in S 2, the soluble Gd salt is Gd (NO3) 3 or GDCL3.

Preferably, in S2, the mass ratio of the soluble Gd salt to the humic acid is 1: 5-20.

Preferably, in S 2, the acidic solvent is a hydrochloric acid solution having a pH of 3-5.

It is a second object of the present invention to provide a humic acid-Gd nanocarrier prepared by the above preparation method.

A third object of the present invention is to provide an application of the humic acid-Gd nanocarrier described above in drug delivery.

A fourth object of the present invention is to provide a preparation based on a humic acid-Gd nanocarrier, comprising the nanocarrier and a chemotherapeutic drug coated in the nanocarrier.

A fifth objective of the present invention is to provide a preparation method of a preparation based on a humic acid-Gd nanocarrier, comprising the following steps:

The preparation method comprises the following steps: dissolving soluble Gd salt in an acidic solvent to prepare a Gd salt solution; and then mixing the Gd salt solution with a humic acid aqueous solution subjected to purification and activation treatment, then adding a chemotherapeutic drug, stirring and reacting at room temperature, dialyzing, and drying to obtain the preparation.

Compared with the prior art, the present invention has the following beneficial effects:

Firstly, humic acid (HA) and metal gadolinium are complexed to form a nanoparticle carrier, the nanocarrier is well dispersed in an aqueous solution, is stable for a long time, has excellent biocompatibility, and then uses a nanocarrier to load an anti-tumor chemotherapy drug, so that the nanodrug delivery system has both chemotherapy and photothermal therapy functions, constructs a drug delivery system for combined treatment of tumor microenvironment response and nuclear magnetic resonance imaging guidance, and will become an effective solution for tumor treatment.

It should be emphasized that the inventive step involves selecting a traditional Chinese medicine component humic acid and metal gadolinium which have physiological activity and excellent biocompatibility to prepare a nano-carrier with imaging capability, drug loading capacity, photothermal therapy property and passive targeting capability through an extremely simple preparation method, the preparation method is extremely simple, excessive modification and modification are not needed, large-scale production can be achieved, and the treatment effect is good.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a scanning electron microscope (A) and DLS particle size distribution diagram (B) of a drug carrier prepared in Example 1;

FIG. 2 is an in vitro drug release study of the nano-drug preparation prepared in Example 1 under different pH conditions;

FIG. 3 is a photothermal effect analysis of the drug carrier prepared in Example 1 under different concentrations and different powers;

FIG. 4 is a magnetic resonance imaging of the drug carrier prepared in Example 1 at different concentrations;

FIG. 5 shows the biocompatibility of the drug carrier prepared in Example 1 by co-incubating with non-small cell lung cancer A549 cells at different concentrations;

FIG. 6 shows that the drug carrier prepared in Example 1 is co-incubated with non-small cell lung cancer A549 cells at different concentrations and is irradiated with 808 nm laser to explore the photothermal therapy effect of the drug carrier on A549 cells;

FIG. 7 is a chemotherapy therapeutic effect on A549 cells by co-incubating nano-drug formulations prepared in Example 1 with non-small cell lung cancer A549 cells at different concentrations;

FIG. 8 shows the chemotherapy treatment effect of the nano-drug preparation and the clinical nano-drug on A549 cells by co-incubating the nano-drug preparation prepared in Example 1 and the liposome doxorubicin and non-small cell lung cancer A549 cells used clinically at present;

FIG. 9 is a photothermal/chemotherapy effect of HA-Gd-DOX prepared in Example 1 in mice.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

In order to enable those skilled in the art to better understand the technical solutions of the present disclosure, the present disclosure will be further described below with reference to specific embodiments and drawings, but the embodiments are not limited to the present disclosure.

The experimental methods and detection methods in the embodiments described below are all conventional methods, such as no special description; the reagents and materials can be purchased on the market, for example, without special description.

The present invention provides a method for preparing a humic acid-Gd nanocarrier, comprising the following steps:

S1. Purification and Activation of Humic Acid

dissolving sodium humate with an inorganic acid, performing ultrasonic treatment, centrifuging, and taking a supernatant; performing dialysis on the supernatant by using an inorganic acid as a dialysate, and then performing drying; wherein the inorganic acid is 0.01 M hydrochloric acid, nitric acid or sulfuric acid;

S2. Preparation of Humic Acid-Gd Nanocarriers

The preparation method comprises the following steps: dissolving soluble Gd salt in an acidic solvent to prepare a Gd salt solution; mixing with the humic acid aqueous solution treated in S1, stirring and reacting at room temperature, dialyzing and drying to obtain humic acid-Gd nano carrier particles; wherein the soluble Gd salt is Gd (NO3) 3 or GDCL3; and the mass ratio of the soluble Gd salt to the humic acid is 1: 5-20, and the acidic solvent is a hydrochloric acid solution with the pH value of 3-5.

A humic acid-Gd nanocarrier-based preparation, comprising the nanocarrier and a chemotherapeutic drug coated in the nanocarrier.

The preparation method of the preparation based on the humic acid-Gd nanocarrier comprises the following steps:

The preparation method comprises the following steps: dissolving soluble Gd salt in an acidic solvent to prepare a Gd salt solution; and then mixing the Gd salt solution with the humic acid aqueous solution treated in the step S1, then adding a chemotherapeutic drug, stirring and reacting at room temperature, dialyzing, and drying to obtain the preparation.

DETAILED DESCRIPTION IS PROVIDED BELOW BY SPECIFIC EMBODIMENTS.

Example 1

[1] Purification and Preparation of HA

Prior to the synthesis of HA-GD-DOX, HA macromolecules need to be prepared and purified from sodium humate. The sodium humate was first dissolved with a 0.01 M hydrochloric acid solution and centrifuged at a high speed of 8000 r/min for 15 minutes to remove insoluble substances. The supernatant was put into a dialysis bag having a molecular interception of 14000 kDa, dialyzed with 0.01 M HCl for 24 h to remove excess Na +, and then freeze-dried in a freeze dryer, the resulting solid powder is HA prepared and purified from sodium humate particles containing impurities.

[2] Preparation of HA-Gd

200 mg of HA subjected to purification and acidification is dispersed into 300 mL of deionized water, ultrasonic treatment is performed for 5 min, 20 mg of Gd (NO3) 3 is dissolved in a hydrochloric acid solution with 5 mL of PGS = 4.0, ultrasonic is fully dissolved for 5 min and then added to a carboxyl-activated HA solution, after stirring at room temperature for 2 h, dialysis is performed for 24 h in a dialysis bag with a molecular interception amount of 14000 kDa, Gd < 3 + > which does not participate in the reaction is removed, and the product is freeze-dried in a freeze dryer and collected to obtain HA-Gd nanoparticles.

[3] Preparation of HA-DOX

200 mg of HA after purification and acidification was dispersed into 300 mL of deionized water, sonicated for 5 min, and then 20 mg DOX was added to the reaction system. After stirring for 2 h at room temperature for sufficient reaction, the mixture is transferred to a dialysis bag having a molecular interception amount of 14000 kDa for dialysis for 24 h, so as to remove DOX that does not participate in the reaction and is not loaded onto HA, and the product is lyophilized and collected in a freeze dryer to obtain HA-DOX nanoparticles.

[4] Preparation of HA-Gd-DOX

200 mg of HA subjected to purification and acidification is dispersed into 300 mL of deionized water, ultrasonic is performed for 5 min, 20 mg of Gd (NO3) 3 is dissolved in a 5 mL hydrochloric acid solution having a pH of 4.0, ultrasonic is fully dissolved for 5 min and then added to HA having activated carboxyl, stirring is performed for 2 h at room temperature for sufficient reaction, then 20 mg of DOX is added, and after stirring for 2 h at room temperature for full reaction, the mixture is transferred to a dialysis bag with a molecular interception amount of 14000 kDa for dialysis for 24 h.to remove Gd3 + that does not participate in the reaction and DOX not loaded onto the HA, freeze-drying the product in a freeze dryer and collecting to obtain the HA-Gd-DOX nanoformulation.

Example 2

[1] Purification and Preparation of HA

Prior to the synthesis of HA-GD-DOX, HA macromolecules need to be prepared and purified from sodium humate. The sodium humate was first dissolved with a 0.01 M nitric acid solution and centrifuged at a high speed of 8000 r/min for 15 minutes to remove insoluble substances. The supernatant was put into a dialysis bag having a molecular interception of 14000 kDa, dialyzed with 0.01 m nitric acid for 24 h to remove excess Na +, and then freeze-dried in a freeze dryer, the resulting solid powder is HA prepared and purified from sodium humate particles containing impurities.

[2] Preparation of HA-Gd

200 mg of HA subjected to purification and acidification is dispersed into 300 mL of deionized water, ultrasonic treatment is performed for 5 min, 20 mg of Gd (NO3) 3 is dissolved in a hydrochloric acid solution with 5 mL of PGS = 4.0, ultrasonic is fully dissolved for 5 min and then added to a carboxyl-activated HA solution, after stirring at room temperature for 2 h, dialysis is performed for 24 h in a dialysis bag with a molecular interception amount of 14000 kDa, Gd < 3 + > which does not participate in the reaction is removed, and the product is freeze-dried in a freeze dryer and collected to obtain HA-Gd nanoparticles.

[3] Preparation of HA-DOX

200 mg of HA after purification and acidification was dispersed into 300 mL of deionized water, sonicated for 5 min, and then 40 mg DOX was added to the reaction system. After stirring for 2 h at room temperature for sufficient reaction, the mixture is transferred to a dialysis bag having a molecular interception amount of 14000 kDa for dialysis for 24 h, so as to remove DOX that does not participate in the reaction and is not loaded onto HA, and the product is lyophilized and collected in a freeze dryer to obtain HA-DOX nanoparticles.

[4] Preparation of HA-Gd-DOX

200 mg of HA subjected to purification and acidification is dispersed into 300 mL of deionized water, ultrasonic treatment is performed for 5 min, 20 mg of Gd (NO3) 3 is dissolved in a 5 mL hydrochloric acid solution having a pH of 4.0, after ultrasound is fully dissolved for 5 min, reactants are added to HA which has activated carboxyl, stirred at room temperature for 2h and fully reacted, then 40 mg Dox is added, and after stirring for 2 h at room temperature for full reaction, the mixture is transferred to a dialysis bag with a molecular interception amount of 14000 kDa for dialysis for 24 h.to remove Gd3 + that does not participate in the reaction and DOX not loaded onto the HA, freeze-drying the product in a freeze dryer and collecting to obtain the HA-Gd-DOX nanoformulation.

The material prepared in Example 1 and the material prepared in Example 2 are similar in performance, and the following is characterized in that only Example 1 is taken as an example.

[1] Scanning Electron Microscope

The morphology of the drug carrier prepared in Example 1 was characterized by using a Zeiss Solution 300-type scanning electron microscope produced in the United States, before testing, the sample needs to be adhered to the sample stage with a conductive adhesive and subjected to 30 s gold spraying treatment, and the magnification is 0.5-50 K.

As shown in FIG. 1A, the particle size distribution is uniform, the morphology is controllable, and the method is suitable for large-scale production.

[2] Dynamic Laser Particle Scattering Analyzer (DLS)

The particle size distribution of HA-Gd nanoparticles after HA and metal Gd < 3 + > conjugated complexation and the HA-Gd-DOX nano preparation loaded with chemotherapy drug DOX are measured by adopting a NiCoMP nano-ZLS/Z3000 model laser nano-particle size distributor. HA-Gd and HA-Gd-DOX were formulated into a water dispersion with a concentration of 1 mg/mL, then diluted to 100 μg/mL, and then an appropriate amount of sample solution was added to the transparent cuvette and the U-shaped potential cup [before being washed three times with ultrapure water, and washed three times with ultrapure water before sample replacement determination]are placed in a dynamic laser nano-particle size distribution instrument [pre-started up and preheated for half an hour before being used and related instrument parameters are set] for determination and recording of respective particle size distribution values.

FIG. 1B shows a DLS particle size analysis result of the nanocarrier, indicating that the nanocarrier has a uniform particle size distribution and a size of 125 nm.

[3] Stimulation Responsiveness Release of DOX in HA-Gd-DOX

PBS with different pH values [5.0 and 7.4] was selected as a stimulation release medium to study the pH responsive release behavior of DOX in HA-GD-DOX. 10 mL of HA-Gd-DOX with a concentration of 1 mg/mL was added to a dialysis bag with a molecular interception amount of 14000 kDa and placed in a 100 mL release medium, and gently stirred at room temperature. The 2 ml release medium was collected at a given time interval and 2 ml of fresh medium was added to the solution. The collected solution was used to determine the concentration of DOX with an ultraviolet-visible spectrophotometer at a wavelength of 480 nm.In vitro drug release research is performed on the nano-drug preparation prepared in Example 1 under different pH conditions, as shown in FIG. 2, the pH-responsive release of the HA-Gd-DOX nano-drug delivery system prepared in FIG. 2 is significant, indicating that the nano-delivery system can be controlled and released in tumor cells.

[4] In Vitro Magnetic Resonance Imaging Effect of HA-Gd

In order to quantitatively determine the magnetic resonance imaging performance of HA-Gd nanoparticles, an HA-Gd aqueous solution of different concentrations [500,750,1000, 2000, 3000 μg/m] was placed in a 1.5 mL centrifuge tube, and a magnetic resonance imaging picture was acquired with a 3.0 T clinical MRI scanner.

The drug carrier prepared in Example 1 described above is subjected to magnetic resonance imaging at different concentrations, as shown in FIG. 4, the preparation nanocarrier has magnetic resonance imaging capability.

[5] In Vitro Photothermal Effect of HA-Gd

In order to quantitatively determine the photothermal performance of HA-Gd nanoparticles after laser irradiation, an HA-Gd aqueous solution with different concentrations [0,100,150, 200, 250, 300 and 400 μg/m] was placed in a quartz cuvette and irradiated with 808 nm laser with a power density of 1.0 W/cm2 for 5 min, and the temperature change of the solution was recorded in an HA-Gd aqueous solution at a position perpendicular to the optical path of the thermocouple probe with a precision of 0.1° C. At the same time, 0.5 W cm 2, 0.8 W cm 2, 1.0 W cm 2, 1.2 W cm 2, 1.5 W cm 2, and 1 are used 8 An HA-Gd solution with a concentration of 300 μg/mL was irradiated with a laser intensity of W/cm2 for 5 min, and a thermocouple probe with a precision of 0.1°C was inserted into an HA-Gd aqueous solution at a position perpendicular to the optical path to record the temperature change of the solution.

The drug carrier prepared in Example 1 described above is subjected to photothermal effect analysis at different concentrations and different powers, as shown in FIG. 3A, the prepared HA-Gd nanocarrier has a good photothermal effect and exhibits concentration dependence; and the photothermal effect of the HA-GD prepared as shown in FIG. 3B presents illumination intensity dependence.

[6] Explore the biocompatibility of HA and HA-Gd to A549 cells

In vitro cell biocompatibility test was performed on A549 cells by CCK -8 colorimetric method. Cells were inoculated into a 96-well cell culture plate with 5 × 103 cells per well, cultured at 37°C and 5% CO2. After the cells were co-incubated with HA and HA-Gd at different concentrations for 24 h and 48 h, a CCK -8 solution [10 μL, 2 mg/mM] was added per well, and after 2H, the OD value was determined at 450 nm wavelength with a microplate reader.

The drug carrier prepared in Example 1 was co-incubated with non-small cell lung cancer A549 cells at different concentrations to explore its biocompatibility, as shown in FIG. 5, both HA and HA-Gd nanocarriers have superior biocompatibility to A549 cells.

[7] Explore the photothermal therapy effect of HA-Gd on A549 cells.

Cells were inoculated into a 96-well cell culture plate with 5 × 103 cells per well, cultured at 37°C and 5% CO2. After the cells were co-incubated with HA-Gd with different concentrations for 2 h, one of the plates was irradiated with 808 nm laser, the power was 1.2 W/cm2, the irradiation time was 5 min, the other pore plate was used as a control group, the CCK -8 solution [10 μL, 2 mg/mM] was added to each hole after 22 h was continuously cultured at 37°C and 5% CO2, and the OD value thereof was measured at 450 nm wavelength with an ELISA instrument.

The drug carrier prepared in Example 1 is co-incubated with non-small cell lung cancer A549 cells at different concentrations and is irradiated with 808 nm laser to explore the photothermal therapy effect of the drug carrier on A549 cells. As shown in FIG. 6, the HA and HA-Gd nanocarriers prepared in FIG. 6 have a weak killing effect on cells at a low concentration, but the photothermal therapy effect thereof is gradually obvious at a high concentration.

[8] The chemotherapy effect of HA-GD-DOX on A549 cells is explored.

Cells were inoculated into a 96-well cell culture plate with 5 × 103 cells per well, cultured at 37°C and 5% CO2. Cells were co-incubated with HA-DOX and HA-Gd-DOX at different concentrations for 24 h, 48 h and 72 h, after 2 h, the OD value was determined at 450 nm wavelength with a microplate reader

The nano-drug preparation prepared in Example 1 is co-incubated with non-small cell lung cancer A549 cells at different concentrations to explore the chemotherapy treatment effect on A549 cells, and the nano-drug preparation prepared as shown in FIG. 7 has a good killing effect on A549 cells.

[9] The chemotherapy effect of HA-GD-DOX and clinical drug liposome doxorubicin on A549 cells is explored.

Cells were inoculated into a 96-well cell culture plate with 5 × 103 cells per well, cultured at 37°C and 5% CO2. Cells were incubated with HA-GD-DOX and LIPO-DOX at different concentrations for 24 h, 48 h and 72 h respectively, and then a CCK -8 solution [10 μL, 2 mg/mM] was added to each well, and after 2h, the OD value was determined at 450 nm wavelength with a microplate reader.

The nano-drug preparation prepared in Example 1 and liposome doxorubicin and non-small cell lung cancer A549 cells are co-incubated to explore the chemotherapy treatment effect of the nano-drug preparation and the clinical nano-drug on A549 cells, and the nano-drug preparation prepared as shown in FIG. 8 and the nano-drug used clinically have a better killing effect on A549 cells.

[10] Exploring the Anti-Tumor Effect of HA-Gd-DOX in Mice

In order to evaluate the photothermal/chemotherapy effect of HA-GD-DOX, the tumor-bearing mice are divided into seven groups [only 5]. Two mice were injected with 100 μl/HA-GD and HA-GD-DOX, respectively, 24 h and then irradiated with near-infrared light of 808 nm and 1.0 W/cm2 for 5 min. The remaining five mice were injected with 100 μL PBS, DOX, HA-GD, LIPO-DOX and HA-GD-DOX, respectively, without receiving near-infrared light irradiation. Tumor size was recorded every 2 days during treatment. After the treatment is finished, the tumor-bearing mice are euthanized and dissected, and tumors are collected.

In order to evaluate the photothermal/chemotherapy effect of HA-GD-DOX prepared in Example 1 in mice, and compared with the chemotherapeutic drugs used clinically, the A549 tumor-bearing mice were divided into 7 groups (only 5). Two mice were injected with 100 μL of HA-GD and HA-GD-DOX, respectively, 24 h and then irradiated with near-infrared light of 808 nm and 1.0 W/cm2 for 5 min. The remaining five groups of mice were injected with 100 μL PBS, DOX, HA-GD, LIPO-DOX and HA-GD-DOX, respectively, without receiving near-infrared light irradiation. Tumor size was recorded every 2 days during treatment. After the treatment is finished, the tumor-bearing mice are euthanized and dissected, and tumors are collected.As shown in FIG. 9, as shown in FIG. 9, a tumor volume change curve of mice in different groups within 14 days is treated, indicating that the HA-Gd-DOX nano-drug preparation prepared in Example 1 has a better effect of treating tumors within mice.

Obviously, those skilled in the art can make various modifications and variations to the present invention without departing from the spirit and scope of the present invention. Thus, if these modifications and variations of the present invention fall within the scope of the claims of the present invention and their equivalents, they are intended to encompass these modifications and variations.