Cellular and Molecular Biology

Journal homepage: www.cellmolbiol.org

Nano-lipid Contrast Agent Combined with Ultrasound-Guided SGB in Nursing Treatment of Lymphedema after Breast Cancer Surgery

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ARTICLE INFO

Original paper

Article history:
Received: November 12, 2021
Accepted: March 11, 2022
Published: March 31, 2022

Keywords:
Breast cancer postoperative care, nano-lipid contrast agent, ultrasound-guided SGB, nano-material nursing treatment application

ABSTRACT

At present, the application of nano-material technology in nursing treatment is more and more extensive, so the characteristics of a variety of chips tend to the medical field. Lymphedema after breast cancer surgery is common in the recovery period of patients, so the nursing work in this period is very important. In order to explore the effect of nano-lipid contrast agent combined with ultrasound-guided SGB in the nursing treatment of breast cancer postoperative lymphedema, the application scope of nano-lipid contrast agent combined with ultrasound-guided SGB and the promotion of nano-materials on cell growth were studied. 11 cases of breast cancer patients in our hospital in 2020 were selected to study the status of lymphedema in the infection stage and recovery stage. The branching effects of nano-lipid contrast agent and ultrasound-guided SGB were evaluated. The results showed that at the same density, the recovery time of lymph tissue in the nano-lipid contrast agent combined with the ultrasound-guided SGB group was significantly shorter than that in the control group. Due to the self-healing state, the recovery time was the most significant 3-7 days after surgery. At this time, the survival rate of self-healing cells was 34.75%, and that of the nano-lipid contrast agent group was 82.37%, which indicated that the nano-lipid contrast agent combined with ultrasound-guided SGB could effectively play the role of photodynamic therapy and synergistic therapy, and inhibit the growth of tumor cells. At present, many kinds of phototherapeutic agents can inhibit the growth of cancer cells and induce apoptosis of cancer cells. Safe and efficient nano photosensitizers have broad application prospects in the field of cancer treatment.

DOI: http://dx.doi.org/10.14715/cmb/2022.68.3.22

Introduction

Nanotechnology has been widely used in the world, although there are some problems in the field of the chip, in the process of more than 28 nm, the technology is still very mature. In medical care, the traditional application materials in the recovery period mostly appear in the form of chemistry. At present, more and more medical researchers try to apply nano-material technology to medical care (1-3).

Great progress has been made in the use of nanomaterials in the rehabilitation care of cancer patients. For example, the ADP research group reported a new drug nanomaterial delivery system loaded with paclitaxel glutamate cationic liposome, which can carry neutrophils and cross the blood-brain barrier to target the brain inflammatory site (1). Thian e s reported a kind of nanocrystalline coated with the drug by erythrocyte membrane. After surface modification with the targeted peptide, it can improve drug loading and has a long circulation effect. The bionic nano-lipid contrast agent has a significant targeted therapeutic effect on brain tumors and a variety of subcutaneous transplanted tumors (2). AAR reported a kind of nano vaccine based on PLGA. By loading adjuvant r837 into PLGA nanoparticles in advance, and then wrapping it with mannose modified cancer cell membrane, the obtained nano vaccine significantly stimulated the immune activity of antigen-presenting cells, thus effectively playing the role of killing tumor cells (3). Azhar reported a microneedle delivery system made of hyaluronic acid with high biocompatibility. The design of the microneedle is to first load anti-PD-1 and glucose oxidase into pH-sensitive dextran nanoparticles, and then load the nanoparticles into the microneedle (4). Using the local inflammatory response after tumor resection, Marella s constructed an inflammatory response DNA nano cocoon with CpG DNA rolling

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loop amplification technology for postoperative immunotherapy of tumor. DNA nano cocoons can release drugs under the inflammatory stimulation of tumor incision (5).

Grodzinski P reported a protein nanoscale gel binding to the T-cell membrane. When T cells recognize antigens, the cell membrane potential changes, leading to the sustained release of (6) from the nanoscale interleukin -15 in a specific tumor microenvironment. Soni N K used expanded T cells from iron oxide beads to treat immunodeficient SCID mice inoculated with melanoma. The results showed that the polystyrene particles coated with melanoma-specific MHCI or II antigen and costimulatory molecules could specifically activate CD8 + and CD4 + T cells, and nano-lipid contrast agent s significantly delayed tumor growth (7). Magorzata constructed magnetic nano ultrasonic SGBS by using surface-modified MHC Ig dimer and anti-CD28 iron dextran nanoparticles. Magnetic clustering nano ultrasonic SGB induced specific activation and expansion of CD8 + T cells, significantly prolonged the survival time of B16 tumor mice, and about 50% of the mice had complete tumor regression (8). Bogdan J proposed a variety of nanoparticles that can capture tumor antigen, which can specifically deliver tumor antigen to antigen-presenting cells, improve anti-tumor immune response, and enhance the remote effect of radiotherapy (9). In recent studies, Aziz s has prepared a new "nanobell" with the light-specific response, which uses silica-loaded perfluorobutane and gold nanorods to make it have the ability of light response and integration of diagnosis and treatment (10). The above research on the application of nano-materials at the cell level has greatly improved the inhibition rate of cancer cells, but this kind of protocell antibody still has a lot of shortcomings in drug transportation, compared with the nursing treatment of lipid contrast agent technology, there are still immune defects.

This article is to explore the effect of a nano-level lipid contrast agent combined with ultrasound-guided SGB in the care and treatment of lymphedema after breast cancer. The application range of nano-level lipid contrast agents combined with ultrasound-guided SGB and the effect of nanomaterials on cell growth promotion are studied successively. A sample of 11 cases of breast cancer patients in our hospital in 2020 was selected, and the lymphedema status during the infection and recovery period was studied. And the size of the branching effect of nano-level lipid contrast agent and ultrasound-guided SGB was evaluated.

Nano-lipid contrast agent and ultrasound-guided SGB

Nanotechnology Ultrasound-Guided SGB

Ultrasound-guided SGB (nano ultrasound SGB) is a new technology for cancer immunotherapy, mainly through the use of micro or nano-materials to present important signal proteins to T cells to activate the body's immune function to resist cancer, thus mimicking antigen-presenting cells (11). The design of ultrasound-guided SGB mainly includes three parts: (i) it has signal molecules related to the specific recognition of T cells (MHCI and MHCII); (ii) it has costimulatory signals needed to activate T cells, such as anti-CD28 monoclonal antibody; (iii) it has signal molecules that affect the release of cytokines from T cells, such as IL-2, IL-7 and IL-15. Compared with living cells, nano-lipid contrast agents are easier to produce and preserve and can be applied to a variety of tumors, eliminating the toxic side effects of engineered cells, and are not affected by the immunosuppressive tumor microenvironment (12).

In the beginning, the research on nano-lipid contrast agents mainly used micron-sized particles to amplify related immune cells in vitro. Polystyrene microparticles are one of the earliest materials used to activate T cells in vitro. The particle size of the microparticles is about 4 ~ 5 μ m (13). However, polystyrene is difficult to degrade and easy to form embolism, leading to biological toxicity. The magnetic beads coated with polystyrene on an iron oxide core can effectively expand T cells in vitro, and remove nano ultrasonic SGB from the expanded T cell population by magnetism before injection into the body (14). However, it is difficult to guarantee the survival rate and stability of the cells after reinfusion by means of expanding a large number of cells in vitro and reinfusion in vivo. In addition, T cell culture in vitro is a time-consuming and laborious process (15). Therefore, some scholars directly injected nano ultrasonic SGB to stimulate T cell proliferation in vivo to stimulate antigen-presenting cell function (16).

However, nano-lipid contrast agents can not completely prevent tumor growth. In addition, when micron-sized particles are applied in vivo, they are easy to accumulate in the lung, leading to serious side effects such as microvascular occlusion (17). In view of the potentially toxic and side effects of micron-scale nano ultrasonic SGB, nano-scale nano ultrasonic SGB has gained a higher favor, and its size is 100 ~ 200 nm, which can be enriched in lymph nodes (18). In vivo antigen-presenting systems constructed by nanomaterials can be divided into lipid-based antigen-presenting cells, polymer-based antigen-presenting cells and inorganic material-based antigen-presenting cells (19). Liposomes have good biocompatibility and biodegradability and have been widely used to construct nano ultrasonic SGB (20).

Barriers to Oral Drug Delivery

At present, nanomaterial angiography and SGB are widely used in various fields such as food, medicine and so on because of their multiple functions. However, due to the low stability of nanomaterial angiography and SGB, oral administration is the most direct, effective and convenient in a variety of drug delivery routes. However, due to the poor gastrointestinal environment, the role of nanomaterial angiography and SGB after entering has not been clear. It is often small, which greatly reduces the effectiveness of nano-materials contrast and SGB, so the study of taking after carrier ultrasound contrast is particularly important (21). A large number of studies have shown that the choice of the delivery system is very important in the potential application of nano-material contrast and SGB ultrasound contrast, protection and delivery (22). Different nanomaterials and SGB have different obstacles in the route of administration, but they have a significant impact on the effect, so it is particularly important to solve the way of administration (23). In order to overcome the adverse environment of nanomaterial imaging and oral administration of SGB, and improve the oral bioavailability of nanomaterial imaging and SGB, more and more multifunctional drug delivery systems have been designed and studied to ensure the effectiveness of nanomaterial imaging and SGB functions (24).

Delivery Compatibility

Nanomaterials and SGB can be encapsulated in functional foods, supplements, medicinal foods or pharmaceutical preparations with different physical and chemical properties and storage conditions (25). For example, the carrier can be liquid, gel, powder, capsule or tablet. In addition, these products can experience a series of temperature, light, oxygen and humidity in their whole life cycle. Therefore, the delivery carrier must be carefully designed to ensure that nano-materials and SGB are effectively packaged without negative impact on the required quality attributes (appearance, texture and taste) of the product, and remain stable in the process of production, transportation, storage and use.

Stability of Gastrointestinal Tract

After ingestion, the three-dimensional structure and function of nanomaterials and SGB may change with their movement in the human intestine. For example, when they are exposed to fluids in the gastrointestinal tract, they may undergo hydrolysis, structural rearrangement, or aggregation. The pH value of gastrointestinal fluid varies greatly in the whole gastrointestinal tract, from high acidity of the stomach to neutral or slightly alkaline of the duodenum. Various digestive enzymes (proteases) can hydrolyze nanomaterials and SGB and change their functions. Finally, the gastrointestinal fluid contains biosurfactants (bile salts and phospholipids), which may combine with nanomaterials and SGB and change their biological activity. The stability of nanomaterials and SGB in the gastrointestinal tract can be improved by trapping them in the carrier, thus isolating them from the stressors in the gastrointestinal fluid. This requires that the carrier does not decompose until it reaches the target area (e.g., mouth, stomach, small intestine or colon, depending on the application). In addition, these carriers must be impervious or low permeable to stressors (such as bile salts or digestive enzymes) in gastrointestinal fluids. Otherwise, the encapsulated nanomaterials and SGB will be degraded.

Gastrointestinal Absorption

The bioactivity of nanomaterials and SGB is limited because they can not be effectively absorbed by the human body. Nanomaterials and SGB must be

released from any matrix in which they are trapped and then pass through the gastrointestinal fluid and mucus layer before being absorbed by epithelial cells. Their transport rate and residence time will depend on the viscosity of the gastrointestinal fluid around them, which can be adjusted by adding thickeners and other components. Nanomaterials and SGB or the carrier material wrapping them must be small enough to penetrate the mucus layer. The particles in some delivery systems are relatively large (> 500 nm), so they cannot penetrate the mucus layer completely. However, they may dissociate or degrade in the gastrointestinal tract, thus releasing nanomaterials and SGB, and diffusing into the mucus layer. Once they reach the surface of epithelial cells, nanomaterials and SGB may be absorbed through a variety of mechanisms, such as active or passive transcellular pathway, cell bypass (tight junction) pathway or endocytosis. In addition, nanomaterials and SGB can be absorbed by different kinds of epithelial cells (such as intestinal epithelial cells or M cells), depending on their size and surface chemistry. M cells are usually more effective than intestinal cells in absorbing carrier particles (d < 500 nm). Due to the low absorptivity of many nano-materials and SGB, it is necessary to develop special materials to improve their absorptivity. Some penetrants can effectively deliver nano-materials and SGB to the effective part. Some delivery systems naturally contain components (such as surfactants or medium-chain fatty acids) that can increase the permeability of cell membrane, which may also help to increase the absorption of nano-materials and SGB.

Stability

The physical and chemical stability of nano-materials and SGB is very important and will affect its functionality. The three-dimensional structure and function of nanomaterials and SGB may be irreversibly changed by environmental factors, such as pH, ionic composition, solvent mass, temperature, pressure or surface adsorption. Therefore, it is particularly important to identify and specify the main factors that affect the imaging and SGB of encapsulated nanomaterials, such as the temperature or pH value of their denaturation. In many cases, delivery systems are specially designed to enhance the stability of nanomaterials and SGB by encapsulating nanomaterials and SGB under strong and effective protection.

Combination Therapy Model Based on Nanomaterials

The multi-functional delivery system based on nano-materials can combine immunotherapy with conventional treatment strategies such as surgery, chemotherapy, radiotherapy and phototherapy, which can further improve the effect of cancer immunotherapy. The combination of chemotherapy and immunotherapy has become a common clinical treatment, which can maximize the therapeutic effect of a malignant tumor. With the drug loading function of nanomaterials, chemical drugs and immunomodulators can be delivered at the same time to further improve the synergistic effect

$$P_{\text{immunity}}(d_i, w_j) = P(d_i)P(w_j|d_i), P(w_j|d_i) = \mu\sum_{k=1}^{K} P(w_j|z_k)P(z_k|d_i) \quad [1]$$

The expansion of variables is as follows

$$\mu(Ai, Aj) = \left[\log(\frac{|x_{A_i} - a_{A_j}|}{w_{A_j}}), \log(\frac{|y_{A_i} - y_{A_j}|}{h_{A_j}}), \log(\frac{w_{A_i}}{w_{A_j}}), \log(\frac{h_{A_i}}{h_{A_j}})\right] \quad [2]$$

$$W(T) = K(y(T-1),....,y(t-n),u(T-d-1),...,u(k-d-n)) \quad [3]$$

IDO (dioxygenase) can reverse the function of immunosuppressive T cells and promote the activation and proliferation of immune cells. In addition to traditional nanoscale lipid contrast agents, a tumor microenvironment responsive hydrogel scaffold containing gemcitabine, an immunotherapeutic checkpoint inhibitor anti-PD-L1, was also reported. aPD-L1-GEM@Gel after injection, the reactive oxygen species (ROS) in the tumor degrade the hydrogel scaffold and release the drug. In this system, hydrogel scaffolds are not the only repository of drugs, but also ROS scavengers in the tumor microenvironment. The tumor antigen released by radiotherapy can produce the immunostimulatory effect

$$f_R^{A_i} = w_G^{\text{ROS}} \cdot V \quad [4]$$

$$w_G^{\text{ROS}} = \max\left\{0, W_G \cdot \varepsilon(f_G^{A_i}, f_G^{A_j})\right\} \quad [5]$$

Similar to the immune mapping in IDO, ROS promotes the genetic transformation of cell antibody (WG)

$$W(T)=K(y(T-1),u(T-d-1)) \quad [6]$$

$$\mathrm{R837}(b)=2n\ln(\sigma)+n\ln(2\pi)+n\left\{\frac{n+tr(S)}{n-2-tr(S)}\right\} \quad [7]$$

PLGA nanoparticles loaded with immune adjuvant r837 and catalase, catalase can decompose hydrogen peroxide in tumors and improve tumor hypoxia for tumor radiotherapy sensitization. Radiotherapy can trigger the immunogenic death of cancer cells. Tumor fragments are used as tumor-associated antigens, which can stimulate anti-tumor immune response under the action of nanoparticles containing an immune adjuvant, and then combine with immune checkpoint inhibitors to effectively inhibit the growth of distal tumor

$$\mathrm{U}=\sum_{\mathrm{i}=1}^{\mathrm{g}}\left\{\mathrm{P_i}\left|\sum_{\mathrm{j}=1}^{\mathrm{k}}\mathrm{p_j}^{(\mathrm{i})}\right.\right\} \quad [8]$$

$$\mathrm{g}=\left\{P_1\middle|D,L,f_2,Q,d,l \quad P_2\middle|f_1,\mu \quad P_3\middle|N,M,I\right\} \quad [9]$$

$$\mathrm{P}=\sum_{S-1}^{U}\sum_{d-1}^{K}f_s,DV_s,d \quad [10]$$

In the above formula, u represents the immune coefficient, P is the evaluation coefficient of the state, and G represents the immune state in different periods. Photothermal therapy (PTT) can kill the tumor by generating heat energy from the materials with high photothermal conversion efficiency gathered at the tumor site under the irradiation of an external specific light source. Photothermal therapy is similar to radiotherapy. Tumor residues produced by thermal ablation can also produce immune stimulation. However, due to the immune escape mechanism of the tumor, the anti-tumor immune response induced by light and heat is difficult to maintain for a long time. After laser irradiation, ICG can induce the dynamic response of luminescence and tumor immunogenicity, and increase the proportion of T lymphocytes immersed in the tumor. This nanotechnology-based immunotherapy significantly improves tumor tolerance and provides a new strategy to solve the problem of low tumor immune response.

$$y_i=\beta(u_i,v_i)+\sum_{j=1}^{p}\beta_j(u_i,v_i)x_{ij}+\varepsilon_j\beta_j \quad [11]$$

$$\sigma_{\mathrm{ikjl}}=\begin{cases}\dfrac{\mathrm{n}}{\Delta_{\mathrm{ikjl}}}\sqrt{\sum_{\mathrm{s}=1}^{\mathrm{n}}(\mathrm{x_{ik}}(\varepsilon)-\mathrm{x_{jl}}(\varepsilon))^2\Delta_{\mathrm{ikjl}}(\varepsilon)} & \Delta_{\mathrm{ikjl}}>0;\\ 0 & \Delta_{\mathrm{ikjl}}<0\end{cases} \quad [12]$$

In the above formula, Y represents the precision of SGB, which can improve the ability of nanoparticles to accumulate in tumors, promote tumor vascular penetration, reshape the tumor microenvironment of immunosuppression, and stimulate systemic anti-tumor immune response. To improve the ability of drug-controlled release and design a more sophisticated responsive delivery system. More individualized immunotherapy was designed for different patients. Secondly, different from traditional tumor-targeted therapy, targeted immune cells are another way to improve the effect of immunotherapy. By selectively delivering immunostimulants to antigen-presenting cells or resident immune cells in peripheral tissues, it can effectively trigger an anti-tumor immune effect and avoid damage to normal tissues.

In addition, we can also design nano preparations for in situ drug delivery to reduce the dosage, prevent the occurrence of off-target effects and prolong the drug retention time. In terms of the safety of nanomaterials, it is necessary to study the biocompatibility and in vivo transport behavior of nanomaterials, and to evaluate the immunogenicity coefficient (δ) of nanomaterials

$$\delta_{\mathrm{ikjl}}=\sum_{\delta=1}^{n}\delta_{\mathrm{ikjl}}(\varepsilon) \quad [13]$$

$$x_i=\sum_{j=1}^{n}\omega_{ij}y_j-\theta_i \quad [14]$$

When the x value is positive, it means that the system has an obvious tumor regression effect on the 4T1 model with low immunogenicity. This therapy can improve the sensitivity of the tumor microenvironment. Combined local immunotherapy can effectively inhibit the development of a tumor and avoid the side effects of systemic administration. Radiotherapy is mainly the use of high-energy radiation for the local treatment of malignant tumors.

Materials and methods

Research Content

In order to explore the effect of nano-lipid contrast agent combined with ultrasound-guided SGB in the nursing treatment of breast cancer postoperative lymphedema, the application scope of nano-lipid contrast agent combined with ultrasound-guided SGB

and the promotion of nano-materials on cell growth were studied. 11 cases of breast cancer patients in our hospital in 2020 were selected to study the status of lymphedema in the infection stage and recovery stage. The branching effects of nano-lipid contrast agent and ultrasound-guided SGB were evaluated.

Experimental Design

Preparation of nano-scale lipid contrast agent solution: zirconium oxychloride (Zr ocl28h2o), SGB (h2tcpp) and benzoic acid were dissolved in N, N-dimethylformamide (DMF). Nano-scale lipid contrast agent was prepared by hydrothermal synthesis with heating and stirring. Nano-scale lipid contrast agent was ultrasonically dispersed in water (240 W, 5 min) to obtain different concentrations of Nano-scale lipid contrast agent solution.

Nano-scale lipid contrast agent combined with ultrasound-guided preparation of SGB: SGB powder was dissolved in dimethyl sulfoxide (DMSO) to prepare a solution, mixed with Nano-scale lipid contrast agent dispersion, stirred for 12 h in dark at room temperature, centrifuged for 30 min (14000 R, 20 ℃), and then centrifuged and washed twice to obtain the composite drug carrier material Nano-lipid contrast agent combined with ultrasound-guided SGB, SGB powder was purchased from Suzhou Yibaiao Biotechnology Co., Ltd. Instruments used in the experiment: BioTek microplate analyzer, probe ultrasonic dispersing instrument, carbon dioxide incubator, 655nm laser, Agilent liquid chromatography-mass spectrometry.

In order to evaluate the therapeutic effect of nano-lipid contrast agent combined with ultrasound-guided SGB, we prepared nano-lipid contrast agent combined with ultrasound-guided SGB with the mass ratio of nano-lipid contrast agent and SGB of 1:2, and the concentrations were 0,5 μ g / ml, 10 μ g / ml and 50 μ g / ml (measured by nano-lipid contrast agent). In order to investigate the chemotherapy effect of single drug SGB in the composite material, we compared the killing effect of nano-lipid contrast agent combined with ultrasound-guided SGB and nano-lipid contrast agent under the same light conditions. Human breast cancer cell T47D was seeded in 96 well plates and incubated with a nano-lipid contrast agent combined with ultrasound-guided SGB solution for 6 h. The light condition was set at 30MW / cm2 for 5min. The experiment was repeated according to the above steps as the contrast, while the dark treatment group was set as the control, and the cell survival rate was calculated.

Results and discussion

Nursing Effect of Nano-lipid Contrast Agent Combined with UltrasoundGuided SGB

A large number of studies have shown that nanoparticles are widely used in nano-materials contrast and SGB ultrasound contrast, protection and delivery. It has been reported that liposome nanoparticles have been used to encapsulate insulin, anticancer peptide and viral antigen in the clinic. In addition, digestive enzymes, some nanomaterials and SGB have also been widely concerned, but not all of these applications are oral. In order to explore the synergistic effect of nano-lipid contrast agent combined with ultrasound-guided SGB composite, nano-lipid contrast agent combined with ultrasound-guided SGB composite with a concentration of 5 μ g / ml, 10 μ g / ml and 50 μ g / ml was prepared. Similarly, the 96 well plates was seeded with 10000 cells per well in advance, and the light condition was 60MW / cm2 for 10min. The same concentration of nano-lipid contrast agent group was set as the control. The results are shown in Table 1.

The material structure of the nano-chip is shown in Figure 1. This kind of material is not only used in the medical field but is also involved in various electronic technology fields. The characteristics of colloidal particles used to encapsulate nanomaterials and SGB will depend on their characteristics and the properties of the final product used for drug delivery. The important characteristics that affect the ability of colloidal particles to encapsulate, protect and transport nano-materials and SGB are important indicators for carrier selection. Colloidal particles used to encapsulate nanomaterials and SGB can be produced using a range of different edible ingredients, such as proteins, polysaccharides, lipids, phospholipids and surfactants. These components affect the functional properties of colloidal particles (such as their ability to encapsulate, protect, retain and release nanomaterials and SGB). Therefore, it is very important to select the most suitable component to make the carrier.

As shown in Table 2, the shape and size of selected colloidal particles must also be controlled for specific

applications. Colloidal particles with diameters ranging from about 10 nm to 1 mm can be produced, depending on the composition used to assemble them and the nature of the manufacturing process. In most cases, colloidal particles are spherical, but they can also be in other forms, including oval, cube, fibrous or irregular.

Table 1. Synergistic efficacy of nano-level lipid contrast agent composite materials

Training set ratio	Carrageenan	Pectin	Oily water	Microemulsion	Nanoemulsion	Lotion
CD44	1.73	1.21	0.87	1	1.93	1.85
HARE	2.19	3.62	2.08	3.81	2.07	1.21
LYVE-1	2.27	2.24	5.91	3.42	2.83	2.59
RHAMM	3.48	3.74	5.86	3.06	3.48	4.36
SGB	4.28	1.5	4.73	2.26	4.98	2.18
Alginate	4.41	3.59	2.32	4.91	1.54	5.5

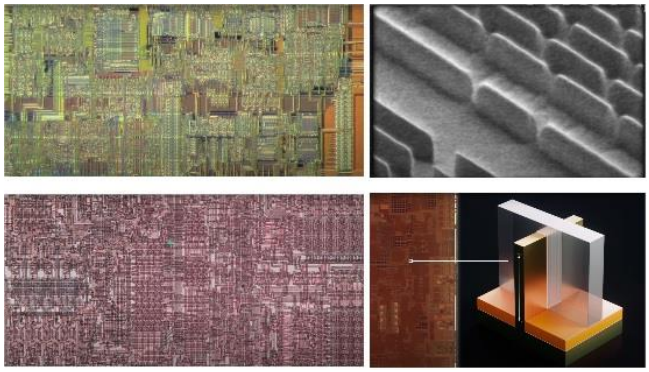

Figure 1. Detailed display of electronic nanomaterials. (Part of the detailed picture from Internet: Parksystems.cn)

Table 2. The shape and size control ratio of colloidal particles

Percent	CD44	HARE	LYVE-1	RHAMM	SGB	Alginate
20%	0.97	1.21	0.56	0.48	1.87	0.93
30%	1.09	2.26	3.95	2.89	3.6	3.92
40%	5.18	2.21	4.6	3.07	4.23	4.23
50%	3.42	3.33	1.57	2.53	5.8	4.01
60%	4.61	4.17	3.82	2.99	4.29	1.26
80%	2.28	1.39	2.15	4.04	4.09	2.04
100%	3.47	6.02	2.75	4.54	1.41	6.25

The operation of the lipid contrast agent is shown in Figure 2. The drugs carried by nano-materials have a strong correlation with cell regulation, such as cell migration and proliferation. In addition, drugs carried by nanomaterials play a key role in wound healing, angiogenesis and the construction of intercellular matrix. The drug carried by nano-materials has a wide molecular weight distribution (1 × 106 ~ 1 × 109 kDa). The drug carried by high molecular weight nano-materials will be degraded into small molecules and enter into lymphatic vessels, lymph nodes, blood, liver, kidney and other tissues. The functions of drugs carried by different molecular weight nanomaterials in the human body are different. Drugs carried by high molecular weight nanomaterials are closely related to maintaining the integrity and water content of intercellular matrix, while drugs carried by low molecular weight nanomaterials are closely related to receptor-mediated intracellular signal transduction.

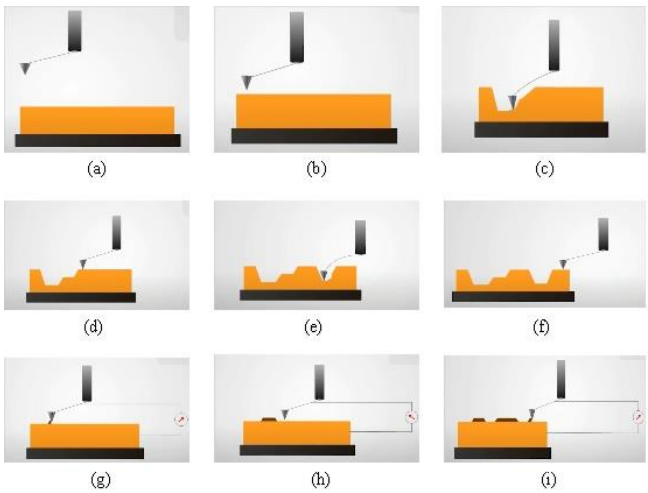

Figure 2. Schematic diagram of the operation process of lipid contrast agent. (Part of the detailed picture from Internet: Parksystems.cn)

As shown in Figure 3, under the condition of light and the same density, the recovery time of lymph tissue in the nano-lipid contrast agent combined with the ultrasound-guided SGB group is obvious. Due to the self-healing state, it is the most significant 3-7 days after surgery. At this time, the survival rate of self-healing cells was 34.75%, and that of the nano-lipid contrast agent group was 82.37%, which indicated that the nano-lipid contrast agent combined with ultrasound-guided SGB could effectively play the role of photodynamic therapy and synergistic therapy, and inhibit the growth of tumor cells. At present, many kinds of phototherapeutic agents can inhibit the growth of cancer cells and induce apoptosis of cancer cells. Safe and efficient nano photosensitizers have broad application prospects in the field of cancer treatment.

The processing process from 23nm to 6nm is shown in Figure 4. Due to the existence of such technology, the decomposition of HYAL1 can be

compensated to a large extent by β - exoglycosidase, while the defect of hyal2 can cause the death or serious defect of mouse embryos. In addition to enzymatic degradation, drugs carried by nanomaterials can also be decomposed by reactive oxygen species produced by a variety of cells under stress conditions. With the help of various damage models, the degradation mechanism of superoxide and peroxynitrite on drugs carried by nanomaterials has been preliminarily clarified. Of course, this technology is not mature yet.

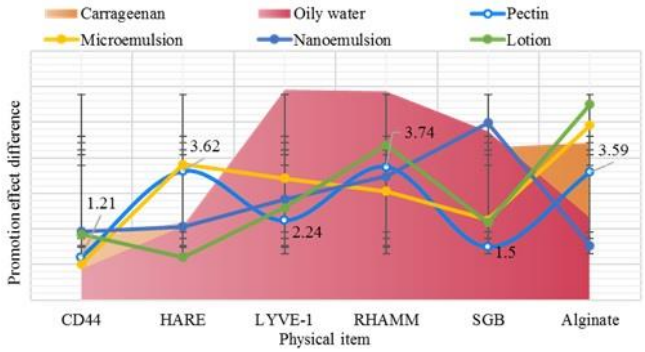

Figure 3. The survival rate of self-healing cells and SGB contrast-enhanced ultrasound

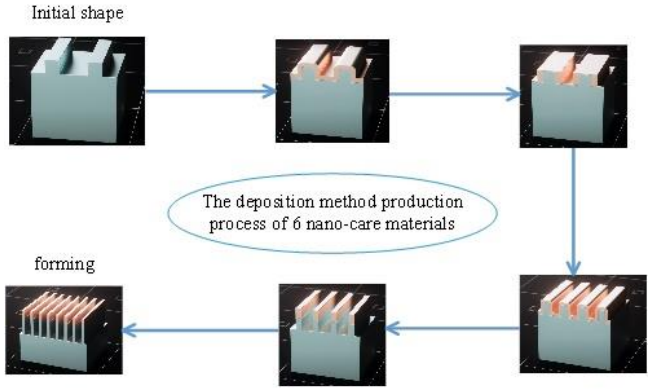

Figure 4. The deposition method production process of 6 nano-care materials. (Part of the detailed picture from Internet: Parksystems.cn)

Characteristic Analysis of Nano-materials and SGB

As shown in Figure 5, the size and structure of nanomaterials and SGB affect their retention and release in the delivery system. The molecular weight of nanomaterials and SGB is generally less than 10 kDa, but the three-dimensional structures of different kinds of small molecular peptides are different, and their shapes, sizes and structures are also different. After different degrees of purification, the purity of peptides is different. There are small peptides with a single component, peptides mixed with multiple components, and even crude peptides with low purity and some other non-specific functional substances, which depend on their biological functions, extraction methods and processing operations. Therefore, the molecular sizes of nanomaterials and SGB may vary from several aspects of Nanometers to hundreds of nanometers or more. When the delivery system is separated, such as oil-water emulsion, nano-emulsion or emulsion, the molecular size of nanomaterial radiography and SGB should be smaller than the size of the water if it wants to be successfully wrapped. On the other hand, when using biopolymer microencapsulated, the molecular size of nanomaterial radiography and SGB should be larger than the pore size of the biopolymer network formed within the colloidal particles, so as to achieve physical ultrasound contrast and restricted release through diffusion.

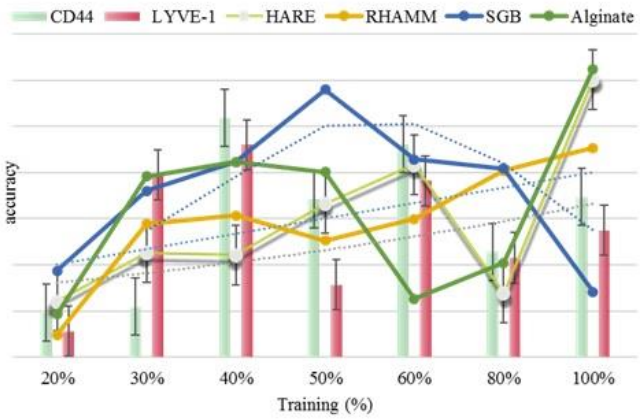

Figure 5. Dimension of mixing of multiple components

The electrostatic properties of nanomaterials and SGB also affect their functional properties in the delivery system, because the retention and release of nanomaterials and SGB depend on the nature of any electrostatic interaction between polypeptides and carrier materials. Therefore, information about the electrical properties of nanomaterials and SGB is usually essential for the design of effective delivery systems. As shown in Figure 6, the retention/release of nanomaterial imaging and SGB in biopolymer microgels is strongly influenced by the electrical interaction between molecules and microbiopolymers.

When pH is lower than its isoelectric point, nanomaterials and SGB are electrostatically attracted by anionic biopolymers such as alginate, carrageenan or pectin, but when pH is higher than their isoelectric point, they are electrostatic repulsed. Therefore, due to the change of electrostatic interaction, they may be retained at low pH and released at high pH. However, the opposite phenomenon occurs on cationic biopolymers, such as chitosan or polylysine. Therefore, if we want to develop a suitable delivery system, we must consider the electrical properties of the loaded materials. In addition to considering the net charge, the complex chemical and physical properties of nanomaterials and SGB are also very important to determine their interaction with the delivery system.

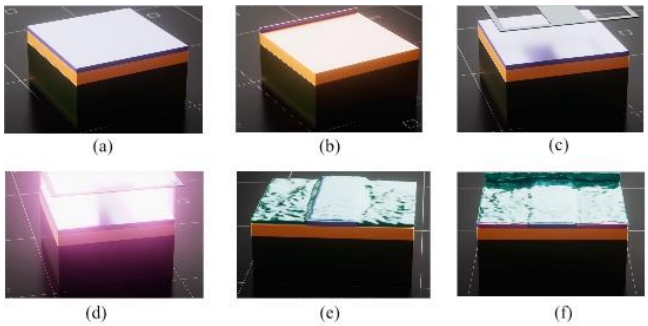

Figure 6. Nanomaterials imaging and SGB in biopolymers. (Part of the detailed picture from Internet: Parksystems.cn)

The polarity of the nanomaterial contrast agent and SGB is another key factor affecting the contrast-enhanced ability of the nanomaterial contrast agent. It affects the three-dimensional structure, solubility, surface activity and molecular interaction of the nanomaterial contrast agent and SGB. Nanomaterials and SGB may be mainly polar, nonpolar or amphiphilic, which depends on the number and distribution of hydrophilic and hydrophobic amino acids in polypeptide chains, which in turn affects their structural arrangement in aqueous solution. The polar group can form dipole-dipole interaction with water, but the non-polar group can't. One of the main driving forces of molecular folding is the decrease in the number of hydrophobic nonpolar groups exposed to water. As shown in Figure 7, nanomaterials and SGB may be soluble or insoluble in an aqueous solution, depending on their surface polarity. The surface activity of nanomaterial radiography and SGB depends on the distribution of its polar and nonpolar groups. Many peptides are two affinity molecules that can be adsorbed on the air-water, oil-water or solid water interface, which makes them useful as functional components to stabilize foam, latex or suspension.

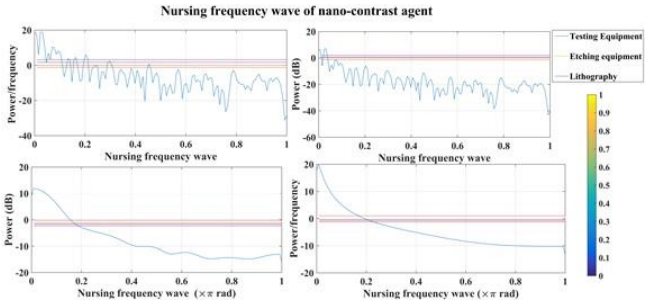

Figure 7. Compatibility of Nanomaterials Contrast and SGB Water Solution

It has become a trend to establish delivery systems for nanomaterials imaging and SGB delivery, and a wide range of carriers can be selected. Polymers and nanoparticles are the most commonly used materials so far because they can control the release of nanomaterials imaging and SGB, or functionalize them to target specific organs. As shown in Figure 8, the targeting of nanoparticles can be achieved by surface functionalization. In addition to the biocompatible lipid prepared by melting at physiological body temperature (37 ℃), the nanoparticles will not melt at body temperature but will be digested by intestinal fluid. At the same time, it can also protect the unstable and sensitive nano-materials and SGB from thermal, chemical, photochemical or oxidative degradation. Therefore, nanoparticles are considered as a colloidal drug delivery system, which can be used in different drug delivery routes. In this paper, the therapeutic peptide oral drug delivery systems, such as lipid particles, polysaccharide particles, inorganic particles and synthetic functional particles, published in recent years, are systematically described.

As shown in Table 3, the penetration of the mucous layer and the absorption of epithelial cells also depends on the size of the granules, and the smaller granules usually have higher permeability. In addition, the interfacial properties of colloidal particles, such as chemistry, polarity, charge, rheology and thickness, play an important role in many of their functional properties, such as physicochemical stability and

interaction with the surface. These properties can be controlled by assembling colloidal particles from different components. Surface charges can be manipulated by adsorbing charged emulsifiers or biopolymers onto their surfaces, which can be used to tailor their functions for specific applications. Colloidal particles can exist as a single individual uniformly distributed in the whole system, or as clusters of different sizes and shapes.

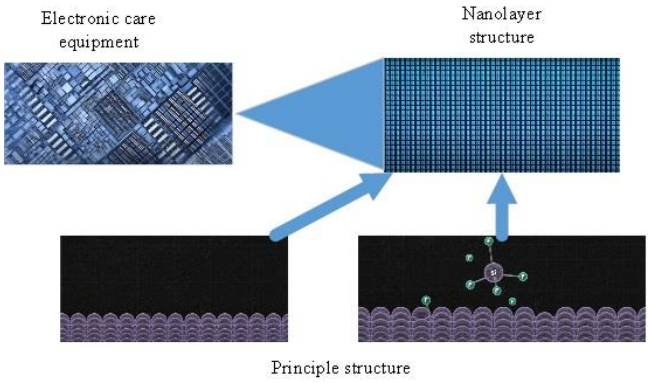

Figure 8. Nanomaterials imaging and SGB delivery system. (Part of the detailed picture from Internet: Parksystems.cn)

Table 3. Penetration of the mucus layer and absorption of epithelial cells

Item	CD44	HARE	LYVE-1	RHAMM	SGB	Alginate
Carrageenan	1.9	0.35	1.06	0.69	0.45	1.35
Pectin	2.04	3.89	3.77	1.63	3.9	3.87
Oily water	4.24	4.05	5.36	2.49	2.08	2.29
Microemulsion	3.41	2.19	4.2	2.51	2.59	3.51
Nanoemulsion	2.15	4.43	2.32	3.68	4.87	1.16
Lotion	1.22	1.29	5.51	3.82	3.11	6.59

As shown in Figure 9, the cellular signal transduction response generated by HA protein receptor interaction strongly depends on the drug molecular weight and cell phenotype carried by nanomaterials. Drug receptors carried by nanomaterials are distributed in the human liver, joints, eyes, skin and other organs. These receptors are involved in the endocytosis and degradation of drugs carried by nanomaterials. Among them, CD44 is the most concerned receptor because it is widely distributed in various cells. The binding of drugs carried by nanomaterials to CD44 is closely related to cell adhesion, cell migration, induction of hematopoietic differentiation and activation of cell signal transduction. It has been reported that in addition to the cellular response of fibroblasts and smooth cells to growth factors, the combination of drugs delivered by nanomaterials with RHAMM can also regulate angiogenesis related to endothelial cell proliferation. Hare and LYVE-1 play important roles in receptor-mediated endocytosis and degradation of drugs carried by nanomaterials in the lymphatic system. Due to the wide distribution of drug receptors carried by nanomaterials in vivo and their unique interaction with biological tissues, drugs carried by nanomaterials have been successfully used as targeted ligands for drug delivery and tissue engineering.

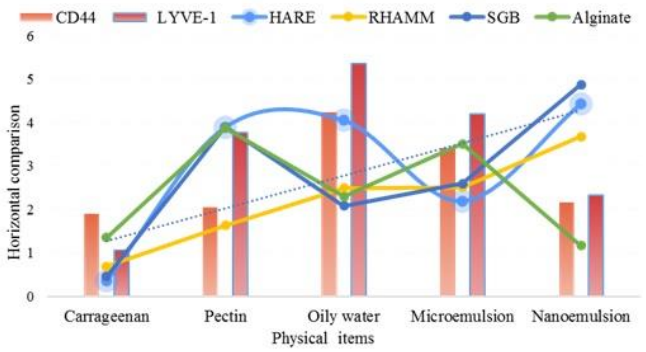

Figure 9. The cellular signal generated by HA-protein receptor interaction

Compared with the traditional small molecule SGB, its structure is stable and not easy to agglomerate. Monomethyl auristatin e (MMAE) can effectively inhibit mitosis by inhibiting tubulin polymerization, leading to cell cycle arrest and apoptosis. Compared with traditional chemotherapy drugs, it has a stronger killing effect on cancer cells. Similar to other small molecule anticancer drugs, SGB has poor water solubility, poor selectivity and high systemic toxicity. Using nanomaterials as drug carriers to make anticancer drug nano-preparations can overcome the above shortcomings. Nano drug preparation is easy to be administered and the residence time in the blood circulation system is greatly prolonged (25-27).

Many studies have reported that drug receptors carried by nanomaterials are closely related to endocytosis, degradation and signal transduction. The drug receptors carried by nanomaterials mainly include CD44, RHAMM, hare and LYVE-1. The drugs carried by nanomaterials not only have a strong correlation with human physiological activities but also have the advantages of biodegradability, non-

immunity, viscoelasticity, targeting and biocompatibility. In the early stage of nursing care, most of the drugs carried by nanomaterials are isolated from the human umbilical cord and cock crowns. HA is mainly used as a vitreous supplement in ophthalmic surgery and a viscoelastic supplement in the treatment of osteoarthritis. The intelligent nano-lipid contrast agent constructed by biomaterials has shown excellent advantages in tumor immunotherapy and has broad development prospects (27-28). However, most of the studies are still limited to the animal level, and there are still many challenges in future clinical conversion. In the design of nano-lipid contrast agents, first of all, we need to further improve the targeting ability of nanoparticles and optimize the size, morphology and surface properties of nano-carriers. In the design of new nano drugs, priority should be given to the clinical approved medical materials to prepare nano-drug carriers, and the potential effects of the prepared nano drugs on normal tissues should be systematically investigated to avoid the toxic effects caused by long-term accumulation. In conclusion, nanomaterials have a great effect on cancer immunotherapy, and the combination therapy based on nanomaterials can effectively inhibit and prevent tumor growth and recurrence. However, nano-lipid contrast agents for immunotherapy are still in the initial stage of research, and more work is needed to promote clinical transformation in the future. Nanomaterials and SGB have a series of biological activities and functional properties, which make them suitable for use as therapeutic or adjuvant agents, such as antihypertensive, antibacterial, antioxidant, enzyme, hormone and immune activity. Therefore, it can be used as a supplement or specially designed for functional food to intervene in some chronic diseases, which will produce considerable benefits to the human body. For practical and consumer compliance reasons, oral administration is usually the most beneficial. However, nanomaterials and SGB need to go through many difficulties in oral administration. The severe chemical environment in the human gastrointestinal tract (such as strong acid and enzyme-active gastric juice) is the biggest obstacle. Therefore, nanomaterials imaging and SGB may need to use delivery systems to deliver drugs to protect them from degradation during storage and transit through the gastrointestinal tract and release them in the desired position in the human body (28-29).

The main advantages of the nano platform are as follows: (i) the porous structure of the nano-lipid contrast agent is easy to load chemotherapy drug MMAE with a high loading rate; (ii) the nano-lipid contrast agent has no obvious cytotoxicity in a certain concentration (100 μ g / ml) and can induce apoptosis of human breast cancer cells MDA-MB-231 and T47D under certain light conditions; (iii) The nano-lipid contrast agent combined with ultrasound-guided SGB composite is easy to prepare. It can effectively play the role of chemotherapy when stimulated by 30MW / cm2 and 5min light, and has no obvious cytotoxicity when there is no light; (iv)60mW/cm2, 10 min Under the condition of light, nano-lipid contrast agent combined with ultrasound-guided SGB composite can effectively play the synergistic effect of chemotherapy and photodynamic therapy, and a small amount of composite can achieve good tumor cell killing effect. Compared with related research work, the drug concentration required for nano-lipid contrast agent combined with ultrasound-guided SGB composite to produce an effective killing effect is lower. In this paper, we hope that the composite nano drugs can inhibit more types of tumor cells, discuss the possibility of broad-spectrum anti-tumor, or use nano-lipid contrast materials to carry other anti-tumor drugs to induce apoptosis of specific types of tumor cells. The above results show that the nano-lipid contrast agent platform designed in this paper can effectively combine the advantages of the nano-lipid contrast agent and SGB, and provide a new direction for the development of photodynamic therapy in the field of cancer (25-29).

Conclusions

Based on the photosensitive effect and drug loading characteristics of the SGB nano-lipid contrast agent, we designed a nano-lipid contrast agent drug loading platform, a nano-lipid contrast agent combined with ultrasound-guided SGB, and investigated the killing effect of nano-lipid contrast agent on human breast cancer cell MDA-MB-231. Nano-lipid contrast agent combined with ultrasound-guided SGB combined with nano-drug was applied to human breast cancer cell T47D The ablation of the tumor cells achieved a good inhibitory effect. In this paper, we found that

SGB-based nano-lipid contrast agent nano-lipid contrast agent as nano photosensitizer can ablate breast cancer cells, and use nano-lipid contrast agent loading drug MMAE to build a nano-lipid contrast agent loading platform to achieve the synergistic effect of chemotherapy and photodynamic therapy. By changing the light intensity and time, the cytotoxicity of the nano-lipid contrast agent alone and the nano-lipid contrast agent combined with ultrasound-guided SGB were compared under the same light conditions. The results showed that nano-lipid contrast agent combined with ultrasound-guided SGB group was better than single lipid contrast agent group Nano-lipid contrast agent combined with ultrasound-guided SGB nano-drug delivery platform can effectively combine chemotherapy and photodynamic therapy, play a synergistic anti-tumor effect and overcome the limitations of single treatment mode.

Acknowledgments

Not applicable.

Interest conflict

The authors declare that they have no conflict of interest.

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