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# *Application of Nanotechnology in Biomedicine*

**Rizwan Jalali***

*Uni de Moncton, Canada*

**corresponding author*

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***Abstract:*** Nanotechnology is a hot spot of cutting-edge scientific and technological research in today's society. It is widely used in nano-drug carriers, functional nano-materials, nano-biosensors and micro-devices, and has promising applications. The purpose of this paper is to study the application of nanotechnology in biomedicine. A CT imaging-guided tumor photothermal therapy nanomedicine, Bi2S3 nanoflowers, is proposed. Based on the high X-ray attenuation and near-infrared absorption properties of Bi, and the high specific surface area of Bi2S3 nanoflowers, Bi2S3 nanoflowers have excellent CT imaging and photothermal treatment effects. On this basis, we first evaluated the characterization of Bi2S3 nanoflowers in the experiment, and confirmed that Bi2S3 nanoflowers are a kind of biosafety nanomedicine by evaluating the efficacy of bismuth sulfide nanoflowers at the cellular level. At the same time, it was confirmed by flow cytometry results and 4T1 live-dead staining data that Bi2S3 nanoflowers as a photothermal therapy drug induced significant tumor cell death.

## 1. Introduction

Bio-nanotechnology was born from the combination of nanotechnology and modern biotechnology, taking organisms as the research object, based on traditional biotechnology and modern biotechnology, and using the knowledge and methods of nanotechnology to conduct biomedical research and cultivation[1-2]. Research covers humans, individuals, organs and tissues at the cellular, subcellular, molecular and individual levels, providing new materials, technologies and methods for engineering research, disease diagnosis and drug therapy.

The field of nanotechnology has grown tremendously in the past and has many environmental applications. Nanomaterials are highly reactive due to their small size and large surface area, enabling them to be used as reducing agents and adsorbents. Schwarz-Plaschg C focuses on nitrate removal from aqueous systems using different nanomaterials, in particular nanoparticles, nanotubes, nanofibers, nanoshells, nanoclusters and nanocomposites. The limitations of nitrate removal using such nanomaterials and potential techniques to overcome these limitations are also discussed [3].

Some scholars have emphasized nanotechnology systems as an innovative herbal drug delivery system to improve the therapeutic effect and bioavailability of natural medicines. In addition, methods for preparing herbal nanoparticle formulations, their structures, and the need to use herbal medicines in combination with nanoparticles are discussed [4]. Therefore, it is of practical significance to study the application of nanotechnology in biomedicine [5].

In this paper, a green synthetic metabolizable three-dimensional bismuth sulfide nanoflower based on the biomacromolecule BSA (bovine serum albumin) was designed. The synthesis method is green and environmentally friendly, with mild conditions and good biocompatibility; bismuth sulfide (Bi2S3) nanoflowers have a special three-dimensional structure, high photothermal conversion efficiency and X-ray attenuation, and can be used in photothermal preparations and computers. Contrast agent for tomography; in addition, based on the isoelectric point of BSA, Bi2S3 nanoflowers will be degraded into small particles for excretion in the physiological environment, improving the biosafety during their application.

## 2. Research on the Application of Nanotechnology in Biomedicine

### 2.1 Nanotechnology

Nanotechnology is the preparation of functional nanomaterials with specific characteristics by manipulating atoms and blocks within nanoscale structures to precisely control the composition and size of desired materials. Physical and chemical properties are used in a targeted manner [6-7]. As one of the most active scientific and technological disciplines in modern society, nanotechnology presents unique opportunities in the intersection of biochemical analysis and basic medical research, and has broad application prospects. As a key component of nanotechnology, functional nanomaterials have attracted much attention due to their unique electrical, magnetic and mechanical properties. These properties mainly include surface effects, small-scale effects, dielectric confinement effects, and large-scale effects [8].

### 2.2 Classification of Nanomaterials

From the perspective of application fields, it includes nanoelectronic materials, nanobiomedical materials, nanometer optoelectronic materials, etc. [9]. From the perspective of nanostructures, including three-dimensional, two-dimensional, one-dimensional and zero-dimensional nanomaterials, it can be vividly understood as nano-blocks, planes, lines and dots. Three-dimensional nanomaterials refer to blocks containing nanostructures, such as nanoblocks containing small nanocrystals or nanomesoporous blocks containing nanoscale pores. Two-dimensional nanomaterials refer to nanomaterials with planar shapes such as nanofilms, nanoribbons, etc. One-dimensional nanomaterials refer to nanomaterials that are in the nanoscale range in two dimensions, and the dimensions in the other dimension are much larger than the above-mentioned two-dimensional dimensions, and even reach macroscopic dimensions. From the perspective of material shape, including nanowires, nanotubes, nanorods, etc. Nanotubes refer to a particle size between 1 and 100 nm, containing hollow and fine tubular structures, which can be single-walled or multi-walled nanotubes, such as carbon nanotubes. Zero-dimensional nanomaterials refer to tiny particles whose three dimensions are nanoscale, including clusters, quantum dots, nanoparticles, etc. [11-12]. The diameter of the clusters is usually no larger than 1 nm. Different from the specific structure and shape of molecules, atomic clusters have various spatial structures and shapes; unlike crystals, which have structural periodicity, they do not contain complete and regular crystals. Different clusters according to the number of atoms exhibit different physicochemical properties from single atoms, molecules, and macroscopic solids and liquids, such as quantum size effects, shell structures, and magic numbers [13]. Quantum dots refer to nanomaterials composed of thousands to millions of atoms. The restrictions in quantum dots from three aspects: electrostatic potential, material surface, and material interface give electrons, holes and excitons to the movement in three-dimensional space. bring constraints. Nanoparticles refer to granular substances with a diameter in the nanometer order (1~100nm), a volume larger than a cluster, and a nanomaterial with an atomic number between 103 and 107. Under normal circumstances, due to the small number of atoms and large specific surface area, nanoparticles have the characteristics of small channel material size effect, surface effect, quantum size effect and so on [14-15].

### 2.3 Oncology Diagnosis and Treatment

At present, the more common clinical imaging examinations are: CT, ultrasound, X-ray, MRI, etc.; pathological examination, including non-exfoliative cell puncture sampling diagnosis and exfoliative cytology examination, pathological examination is the most reliable tumor Diagnosis basis; endoscopy, which can directly observe the lesions of internal organs of the human body, and determine its specific location and scope, and then determine the nature of the lesions by examining the biopsy specimens, which greatly improves the diagnostic accuracy of tumors [16] -17]. The treatment of tumors is mainly divided into the following types: surgical resection, chemotherapy, targeted therapy. Targeted therapy is precise and gentle. For example, in the application of laser-induced tumor hyperthermia, the main function of nanoparticles is to absorb laser energy and convert it into heat energy, and the efficiency of absorption and thermal conversion is closely related to the size and shape of nanoparticles [18].

DDA theory can be used to calculate the optical properties of nanoparticles of arbitrary shape and composition. The main principle is to discretize the target particle into N cube dipoles, so that the surrounding scattered field can be approximately regarded as the superposition of the effect of each dipole. The dipole moment of the ith dipole can be expressed as Pj=ajEj, where aj represents the polarizability of the dipole and Ej represents the electric field strength at position rj [19-20]. The formula for calculating Ej is:

$$E_j = E_j^{inc} - \sum_{k \neq j} A_{jk} P_k \quad (1)$$

If Ajj is defined as Ajj=-aj-1, the dipole moment Pj can be obtained by solving the following system of equations:

$$\sum_{k=1}^{N} A_{jk} P_k = E_j^{inc} \quad (2)$$

Extinction, absorption and scattering factors can be obtained by calculating the ratio of the corresponding cross-sectional size to the effective particle radius Reff.

## 3. Approaches to the Application of Nanotechnology in Biomedicine

### 3.1 Experimental Materials and Instruments

4T1 mouse breast cancer cells were purchased from the Culture Collection (ATCC).

4-6 week old balb/c female nude mice (body weight 20 g) were purchased from Viton Lever Laboratory Animal Center.

The experimental equipment is shown in Table 1.

*Table 1. Experimental Apparatus*

| name | Instrument model |
|---|---|
| Infrared camera | FLIR E40 |
| Small Animal Computed Tomography | Triumph X -SPECT/X-O CT |
| Optical microscope | Nikon U-II Multipoint |
| Laser scanning confocal microscope | OlympusBX61W1 |
| Ultrapure Milli-Q water purifier | ELIX |
| Microplate reader | EL800 |

## 3.2 Preparation of Bismuth Sulfide Nanoflowers

(1) Bi(NO3)3•5H2O(48.5mg) was dissolved in 2mL HNO3(2M) to form A liquid.

(2) Add solution A to the BSA solution (0.5g 16mL DIwater) to form solution B. And avoid light stirring.

(3) After stirring for 30 min, NaOH was added quickly to adjust the pH to 12, and the reaction was carried out for 12 h.

(4) After the reaction, centrifuge at 9600rpm*20min to remove the supernatant, then wash the precipitate twice with three times of water at 9600rpm*20min, and finally use three times of water to disperse the precipitate for later use.

## 3.3 Observation of Cells by CLSM Imaging

The cells were divided into 5 groups, Ctr, Bi2S3(50μg/mL), laser(1w/cm2), Bi2S3(25μg/mL)+laser(0.5w/cm2), Bi2S3(50μg/mL)+laser(0.5w/ cm2) group, after adding the material, each group was incubated for 10 hours, and the three groups were irradiated with LWRL808 laser of corresponding power for 10 minutes, and incubated for 24 hours. The medium was discarded and washed 2 times with PBS. Then, a solution of 500 μL calcein (AM, 10 mM) and 500 μL propidium iodide (PI, 10 mM) in PBS was added to each well and incubated in the dark at 37 ℃, 5% CO2 10 minutes. Cells were then washed 2 times with PBS to remove residual nanoparticles and dead cells. Finally, cells were observed by confocal laser scanning microscopy. Green and red fluorescence indicate live and dead cells, respectively.

# 4.Analysis of the Application of Nanotechnology in Biomedicine

## 4.1 Characterization of Bismuth Sulfide Nanoflowers

To confirm the successful synthesis of the prepared nanomaterials, the samples were characterized using FT-IR spectroscopy.

*Table 2. Characterization of bismuth sulfide nanoflowers*

| Wavenumber (cm-1) | Bi2S 3 | BSA |
|---|---|---|
| 3000 | 2978 | 2773 |
| 2500 | 2408 | 2296 |
| 2000 | 1916 | 1794 |
| 1500 | 1400 | 1321 |
| 1000 | 936 | 803 |
| 500 | 412 | 375 |

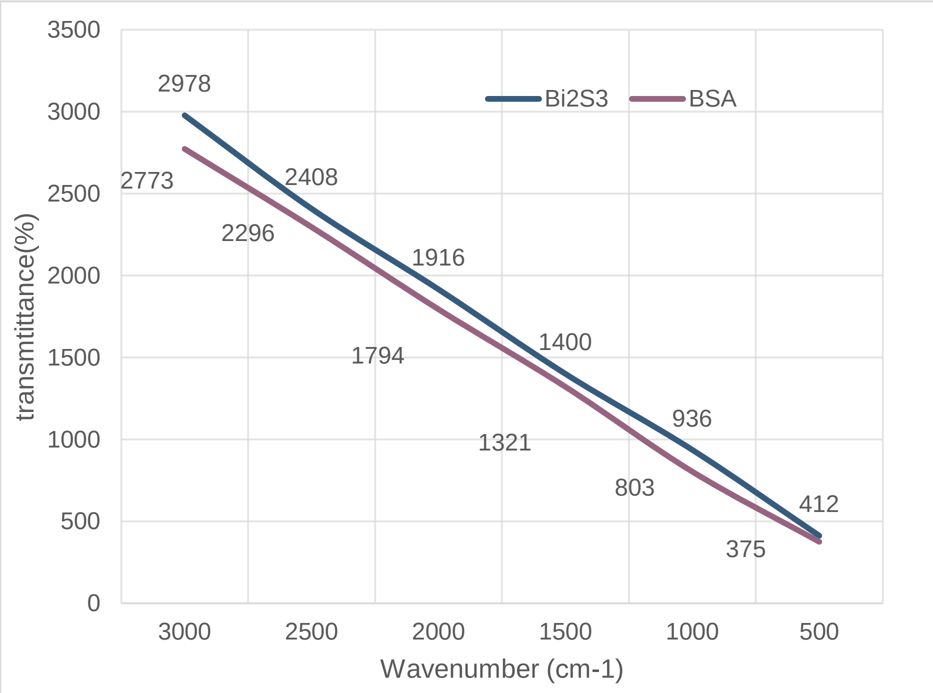


*Figure 1. Fourier transform infrared spectrum of Bi2S3 nanoflowers*

As shown in Figure 1, the bands of Bi2S3NPs are located in the same regions and have the same characteristics as those of pure BSA. The bands appearing at 1321cm-1, 803cm-1, and 375cm-1 are the amide and primary amine bands of BSA, and the bovine serum albumin-modified NPs showed a decrease in the -SH signal intensity at ≈2000cm-1, indicating that BSA Part of the S content in was converted into Bi2S3NPs. This proves the presence of BSA in the prepared Bi2S3NPs. At the same time, it also shows that the reaction of NP in the BSA molecule does not seem to affect the structure of BSA, as shown in Table 2.

## 4.2 Evaluation of the Therapeutic Effect at the Cellular Level of Bismuth Sulfide Nanoflowers

For further biomedical applications, it is necessary to evaluate the biocompatibility of Bi2S3 nanoflowers. The cytotoxicity of Bi2S3 nanoflowers to 4T1 was detected by CCK-8 method. The results showed that the viability of 4T1 cells was almost unaffected after different concentrations of bismuth sulfide nanoflowers were treated with bismuth sulfide nanoflowers for 24 h, indicating that bismuth sulfide nanoflowers had no obvious cytotoxicity and had biological safety, as shown in Table 3.

*Table 3. The survival rate of 4T1 cells incubated with different concentrations of Bi2S3 nanoflowers for 24h (Bi2S3:μgmL-1)*

| Different concentrations of bismuth sulfide nanoflowers | Cell viability (%) |
|---|---|
| Ctr | 100 |
| 6.25 | 97.45 |
| 12.5 | 97.92 |
| 25 | 96.88 |
| 50 | 98.48 |
| 100 | 98.29 |
| 200 | 97.12 |

In order to evaluate the photothermal treatment effect of bismuth sulfide nanoflowers at the cellular level, and to further confirm the biological safety of bismuth sulfide nanoflowers.

We further verified the photothermal treatment effect of bismuth sulfide nanoflowers by staining with live and dead cells (green represents live cells and red represents dead cells). As shown in Fig. 3, the different treatment groups exhibited green fluorescence similar to the control group, which indicated that the bismuth sulfide nanoflowers had good biocompatibility. Moreover, the results of live and dead staining of 4T1 cells were consistent with the flow cytometry results. With the increase of the concentration of bismuth sulfide nanoflowers and the laser power, the activity of 4T1 decreased significantly. These results also indicate that bismuth sulfide nanoflowers have the potential of photothermal therapy.

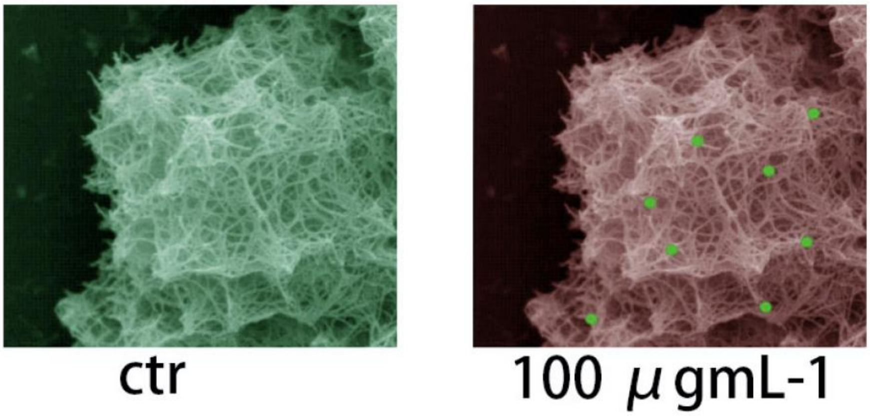


*Figure 3. In vitro hyperthermia of bismuth sulfide nanoflowers*

## 5.Conclusions

At present, due to the limited sensitivity of tumor detection methods, poor targeting of therapeutic drugs, insufficient accumulation of therapeutic drugs in tumor sites, and non-specific distribution, it is often difficult to achieve early diagnosis and real-time monitoring of tumors. Treatment results are not expected. Therefore, the development of new methods for high-sensitivity diagnosis and effective treatment of tumors has become a research hotspot in the current biomedical field. This paper firstly reviews the applications of nanoparticles in the biomedical field, and then proposes the main idea of this paper on this basis. According to the research results in this paper, targeted modification or modification of nanoparticles can be carried out according to different experimental purposes, or to increase the uptake of nanoparticles or prevent them from entering cells, so as to be better applied in various fields.

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