MINI REVIEW

Recieved: March 2015
Accepted: July 2015

A review on application of gold nanostructures in cancer therapy

Maryam Heidari[1,2], Naghmeh Sattarahmady[*,1,3]

1. Department of Medical Physics, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
2. Student Research Committee, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran
3. Nanomedicine and Nanobiology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

***Corresponding Author:**
Naghmeh Sattarahmady
Department of Medical Physics, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
Phone: 987132349332
Fax: 987132349332
E-mail: nsattar@sums.ac.ir
sattarahmady@yahoo.com

ABSTRACT

Today, use of nanotechnology for cancer therapy is an active field of research. Early detection, accurate diagnosis, and individual treatment are the aims which have turned nanotechnology to an attractive area for research. Among metallic nanomaterials, gold nanostructures have unique properties which make them remarkable candidates for biomedical approaches. Surface plasmonic resonance (SPR) effect of gold nanostructures leads to maximum absorption at particular electromagnetic wave length. This wavelength changes with the shape and size of the particles, so optical properties of gold nanostructures are adjustable. In this review, we will summarize the application of gold nanostructures in the treatment of cancer especially as the agent in Plasmonic photothermal therapy (PPTT) and photosensitizer in photodynamic therapy (PDT).

Key words: Cancer, Gold Nanostructures, Photothermal Therapy, Photodynamic Therapy

BCCR
2015; 7(2&3): 32-36
www.bccrjournal.com

Introduction

Cancer is a consequence of cells growth out of control in a particular part of the body. Generally, it follows from DNA damage of normal cells. The body is often able to repair the damaged DNA, but in cancer cells, this damage is not restored. Some types of cancer cells transfer to other organs by blood vessels or lymphatics and begin to grow in new locations, which is called metastasis[1]. Treatment of cancer in its early stages is often effortless, but when metastasis occurs, it becomes complicated. So, finding new methods for the early diagnosis of cancer is an active field of research.

Common methods for cancer therapy including surgery, chemotherapy, and radiotherapy are not comprehensive and each of them has their special indications[1]. Although surgery is the best strategy for cure at the early stage of cancers, when metastasis occurs, it is not the best option any more. In addition, the removal of some tumors in sensitive areas will not be a viable method. In radiotherapy, ionization radiation causes damage to DNA of cancer cells to remove them, but it may have long-term side effects, such as damage to normal surrounding cells, formation of scar tissue, and immune suppression. Chemotherapy is a systemic therapy which has advantages for metastasized cancers, but it has undesirable systemic toxic side effects as well[2,3].

Today, nanotechnology is an active field of cancer-related research. Early detection, accurate diagnosis, and individual treatment could be achieved using different nanomaterials[4].

Another technique for cancer therapy is heat induction in the specific target region, termed as hyperthermia, to destroy cancer cells through heat sources, such as near infrared or visible light, radiofrequency waves, microwaves, and ultrasound waves[5]. In this technique, cancer cells are eliminated when their temperature reaches above 41°C[6].

Plasmonic photothermal therapy (PPTT) and photodynamic therapy (PDT) are two strategies of hyperthermia. In PPTT, as a minimally-invasive method, photon energy is transformed to thermal energy; consequently, ablation of malignant cells occurs[5]. In order to avoid overheating of the tumor and its surrounding normal cells and have localized hyperthermia, nanoparticles are demonstrated to absorb the light and act as local heat sources[7]. In PDT, three components including photosensitizer drug and the drugs activating light and oxygen are involved. In this technique, photosensitizer drug is activated through light with specific wavelength and, eventually, the generation of cytotoxic reactive oxygen species (ROS) causes necrosis and apoptosis in cancer cells[2]. In 1978, Dougherty et al. performed the first modern demonstration of this mechanism in cancer therapy[8].

PDT has some advantages over conventional chemotherapy and radiotherapy. In the absence of light, PDT drug itself is minimally toxic, so drug accumulation in normal tissues does not make toxicity, unlike chemotherapy drugs. By focusing the light on the target area, treatment is performed locally. Unlike radiotherapy, non-ionizing radiation used in PDT does not make destructive effects on healthy tissues[2].

There are some materials that have the potential to be used as agents or sensitizers in PPTT and PDT, among which gold nanostructures and carbon nanostructures are the best candidates[9-13].

Optical properties of gold nanoparticles

Gold nanostructures have unique optical properties and what causes gold particles to have the potential to be used in this field is a phenomenon known as surface plasmon resonance (SPR) related to the oscillation of surface free electrons in the gold particles. If the frequency of this oscillation is equal to that of incidence electromagnetic radiation,

resonance occurs and electromagnetic radiation energy is converted into heat energy[14]. Regularly, UV-visible absorption spectroscopy is used to characterize the optical properties and electronic structure of nanoparticles. Absorption band depends on the diameter and aspect ratio of gold nanoparticles[14], so by optimizing the particle diameter and adjusting the wave length of electromagnetic wave with it, adequate heat could be induced in the particles. In gold nanospheres, there is a single absorption peak in the visible range (510- 550 nm), which undergoes a red shift by increasing the particle size. Thus, gold nanostructures are tunable particles for hyperthermia approaches[15].

Source of light

For in-vivo study, there is a need to use the wavelength of light that has satisfactory penetration into the body. Hemogolobin and water are two major light absorbers in the body which have the minimum absorption in the range of 650-900 nm. So, in order to achieve optimum penetration in the body, NIR light as well as agents with SPR peaks in this range can be used[16]. Approximately in all studies on PPTT, diode lasers with the wavelength range of 805- 810 nm have been used as a light source[7,17-20].

Other gold nanostructures

The SPR peak of small gold nanospheres is in the visible region which does not have maximum penetration into the body. Other types of gold nanostructures, including nanorods, nanoshells, and nanocages, have remarkable optical properties in biomedical applications[15]. The SPR peak of gold nanoshells varies from visible to NIR regions through changing the ratio of the core diameter and shell thickness; therefore, by designing this ratio, gold nanoshell can be constructed with desired SPR peak in NIR region[21].

Source of light

To obtain temperature distribution, magnetic resonance temperature imaging (MRTI) which applies proton resonance frequency shift method can be used. In this technique, the temperature resolution is less than 1°C and, unlike IR thermography, data in depth can be obtained as well as the surface data[7]. Thermal imaging is another method that is used for in-vivo temperature measurement[18].

In-vivo study

An in-vivo investigation by Hisch et al. in 2003 revealed that, after the administration of gold nanoshells and NIR light irradiation in the solid tumor, irreversible tissue damage occurred due to the significant temperature increase, while control subjects did not show any damage[15]. In 2008, Melancon et al.[22] used hollow gold nanoshells with an average diameter of 30 nm for in-vitro and in-vivo studies. In the NIR region, this structure exhibited effective photothermal results. Also, Melancon et al.[17] showed that SPIO@silica-Au nanoshells under 810 nm of continuous-wave diode laser irradiation (power= 1 W) caused a temperature increase of 16°C after 15 min. Robinson et al. in 2010[18] used single-walled carbon nanotubes (SWNTs) and gold nanorods, separately, in terms of the effect of diode laser in 808 nm for photothermal therapy outcome. Ke et al. in 2014[19] acquired nanoscale capsules (SPIO-embedded perfluorooctylbromide nanocapsules) in order to increase the enhanced permeability and retention (EPR) effect by avoiding the rapid clearance of NPs from the bloodstream. For obtaining comprehensive diagnostic information, this theranostic nanocapsule combined real-time ultrasound and high-resolution MR imaging agents. In 2011, Melancon et al.[20] examined the magnetic/optical properties of SPIO@ AuNS through in-vitro and in-vivo studies. They used this material as an

MRI contrast agent and an agent in phototherapy in the presence of NIR light; finally, they suggested multimodal SPIO @ AuNS as a promising theranostic nanoplatform.

Acknowledgments

We would like to thank Research Consultation Center, Shiraz University of Medical Sciences.

References

1. Sudhakar A. History of cancer, ancient and modern treatment methods. J Cancer Sci Ther. 2009; 1(2): 1-4.

2. Master A, Livingston M, Sen Gupta A. Photodynamic nanomedicine in the treatment of solid tumors: Perspectives and Challenges. J Control Release. 2013; 168(1): 88-102.

3. Darzynkiewicz Z, Traganos F, Wlodkowic D. Impaired DNA damage response--an Achilles' heel sensitizing cancer to chemotherapy and radiotherapy. Eur J Pharmacol. 2009; 625(1-3): 143-50.

4. Cai W, Chen X. Nanoplatforms for targeted molecular imaging in living subjects. Small. 2007; 3: 1840–54.

5. Huang X, El-Sayed MA. Plasmonic photo-thermal therapy (PPTT). Alexandria Journal of Medicine. 2011; 47: 1–9.

6. Bettge M, Chatterjee J, Haik Y. Physically synthesized Ni-Cu nanoparticles for magnetic hyperthermia. Biomagn Res Technol. 2004; 2: 4.

7. Terentyuk GS, Maslyakova GN, Suleymanova LV, Khlebtsov NG, Khlebtsov BN, Akchurin GG, Maksimova IL, Tuchin VV. Laser-induced tissue hyperthermia mediated by gold nanoparticles: toward cancer phototherapy. J Biomed Opt. 2009; 14(2): 021016.

8. Dougherty T, Dougherty TJ, Kaufman JE, Goldfarb A, Weishaupt KR, Boyle D, Mittleman A. Photoradiation therapy for treatment of malignant tumors. Cancer Res. 1978; 38: 2628–2635.

9. Sassaroli E, Li KC, O'Neill BE. Numerical investigation of heating of a gold nanoparticle and the surrounding microenvironment by nanosecond laser pulses for nanomedicine applications. Phys. Med. Biol. 2009; 54: 5541–5560.

10. Huang X, Jain P, El-Sayed I, El-Sayed M. Plasmonic photothermal therapy (pptt) using gold nanoparticles. Laser Med. Sci. 2008; 23: 217–228.

11. O'Neal DP, Hirsch LR, Halas NJ, Payne JD, West JL. Photo-thermal tumor ablation in mice using nearinfrared-absorbing nanoparticles. Cancer Lett. 2004; 209: 171–176.

12) Xiao Y, Gao X, Taratula O, Treado S, Urbas A, Holbrook RD, Cavicchi RE, Avedisian CT, Mitra S, Savla R, Wagner PD, Srivastava S, He H. Anti-her2 igy antibody-functionalized single walled carbon nanotubes for detection and selective destruction of breast cancer cells. BMC Cancer. 2009; 9: 351.

13. Zhou F, Xing D, Ou Z, Wu B, Resasco DE, Chen WR. Cancer photothermal therapy in the near-infrared region by using single-walled carbon nanotubes. J. Biomed. Opt. 2009; 14: 021009.

14. Abdelhalim MA, Mady MM, Ghannam MM. Physical properties of different gold nanoparticles: ultraviolet-visible and fluorescence measurements. Nanomed-Nanotechnol. 2012; 3(3): 1-5.

15. Weibo Cai, Ting Gao, Hao Hong, Jiangtao Sun. Applications of gold nanoparticles in cancer nanotechnology. Nanotechnol Sci Appl. 2008; 2008(1): 10.2147/NSA.S3788.

16. Weissleder R. A clearer vision for in vivo imaging Nat. Biotechnol. 2001; 19: 316-317.

17. Melancon M, Lu W, Li C. Gold-Based Magneto/Optical Nanostructures: Challenges for in vivo applications in cancer diagnostics and therapy. Mater Res Bull. 2009; 34(6): 415-421.

18. Robinson JT, Welsher K, Tabakman SM, Sherlock SP, Wang H, Luong R. High performance in

vivo near-ir (>1 μm) imaging and photothermal cancer therapy with carbon nanotubes. Nano Res. 2010; 3(11): 779-793.
19. Ke H, Wang J, Tong S, Jin Y, Wang S, Qu E, Gang Bao, Zhifei Dai. Gold nanoshelled liquid perfluorocarbon magnetic nanocapsules: a nanotheranostic platform for bimodal ultrasound/magnetic resonance imaging guided photothermal tumor ablation. Theranostics. 2014; 4(1): 12-23.
20. Melancon MP, Elliott A, Ji X, Shetty A, Yang Z, Tian M, Taylor B, Stafford RJ, Li C. Theranostics with multifunctional magnetic gold nanoshells: photothermal therapy and t2* magnetic resonance imaging. Invest Radiol. 2011; 46(2): 132-40.
21. Oldenburg SJ, Westcott SL, Averitt RD, Naomi J Halas. Surface enhanced Raman scattering in the near infrared using metal nanoshell substrates. J Chem Phys. 1999; 111: 4729–35.
22. Melancon MP, Lu W, Yang Z, Zhang R, Cheng Z, Elliot AM. In vitro and in vivo targeting of hollow gold nanoshells directed at epidermal growth factor receptors for photothermal ablation therapy. Mol Cancer Ther. 2008; 7(6): 1730-9.