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"A review on application of gold nanoparticles in biomedical sciences"

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Abstract

Ongoing advances in nanotechnology are because of the improvement of built nanoparticles. Effectively, metallic nanoparticles have been broadly abused for biomedical application and among them, gold nanoparticles are exceptionally surprising. Resulting upon their huge nature, circular and gold nanorods nanoparticles draw in extraordinary consideration. Their natural highlights, for example, optical, electronic, physicochemical and, surface plasmon reverberation; which can be adjusted by changing the portrayals of particles, for example, shape, size, viewpoint proportion, or condition; simplicity of union and functionalization properties have come about to different applications in various fields of biomedicine, for example, detecting, directed medication conveyance, imaging, photothermal and photodynamic treatment just as the regulation of a few applications. This article evaluated the prominent combination strategies and referenced their built up applications in different requests, particularly in natural detecting.

1. Introduction

For centuries gold nanoparticles (AuNPs) in colloidal form have been used by painters because of their prominent colors which they produce on interaction with visible light. Currently, these particles were extensively studied and used for numerous technical purposes such as sensory probes, electronic conductors, photovoltaics (organic in nature), therapeutic agents, and drug delivery in medical and biological applications. AuNPs can influence the optical and electronic properties by adjusting their surface chemistry or aggregation, size and shape [1].

2. History

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AuNPs are colloidal suspension of colloidal gold. It was used to make Lycurgus cup for stained glasses in the 4th century, which changed colors based on the location of a light source. Solution of gold salt was considered to be a cure for various diseases.

Various books were published describing the medical uses of colloidal gold like *Panacea Aurea* by Francis Anthony in 1618 and *Treatise of Aurum Potabile* written by Nicholas Culpepper in 1656.

Johann Kunckel in his book *Valuable Observations or Remarks About the Fixed and Volatile Salts-Auro and Argento Potabile* told that the pink color of the Aurum Potabile was due to the presence of small metallic gold particles which were not visible to human eyes.

John Herschel designed a technique for photography that involved the use of colloidal gold to print image on paper.

The real work on colloidal gold began when Faraday accidentally formed ruby red solution when he was mounting the gold leaf on the microscopic slide. He became fascinated about the optical properties of colloidal gold and noticed that colour was attributed to the tiny gold particles and that the phenomenon was first detected and documented so that it was recognised as the Faraday-Tyndall effect. He was able to prepare first colloidal gold sample in 1857 [2].

The research on AuNPs has increased with the new technologies in the current century. With the use of newer microscopy methods such as electron microscopy and atomic force microscopy has been proved to be very useful in nanoparticle research. As they are easy to synthesize and have high stability they are generally used for practical studies. They are already being used in various industries such as electronics and medicines and various FDA approved drugs made up of nanoparticles are used to deliver drugs [3].

3. Gold nanoparticles (AuNPs) :

Gold nanoparticles (AuNPs) are highly useful for controlled cancer treatment, drug delivery, biomedical imaging, diagnosis, etc. because of their higher compatibility with the human body, tunable stability and low toxicity, possible interaction with a diversity of substances and small

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dimensions. These possess optical properties, are able to absorb infrared light, and have exhibited greater potential for the use of drug delivery system because of their wider surface and their ability to be protected by various therapeutic agents. They have been studied carefully in areas such as biomedicine, and recent studies have shown that they are able to overcome the blood brain barrier. They can interact with DNA in order to produce genotoxic outcomes. It has the ability to produce heat that can be used to target and kill tumors and often it is used in photodynamic treatment. In several ways that can be synthesized, from which two methods are more common biological and scientific methods, but with a better control of the size or the form of nanoparticles the chemical method provides more advantage over the biological method [4].

3.1. General fabrication technique of AuNPs

AuNPs are generally generated by chloroauric acid reduction in liquid. Firstly, we dissolve the acid, then the solution is mixed rapidly by the addition of reducing agents. This leads to the formation of normal gold atom from its Au^{3+} form. Supersaturation occurs due to the excessive formation of the gold atoms. Sub-nanometer form of gold is seen to precipitate in the solution. Now these precipitates are collected which can be used as gold nanoparticles. The particles tend to be uniform in size when the solution is vigorously mixed. In order to avoid particle aggregation, stabilizing agents may be employed [5].

3.2. Types of AuNPs

Different types of AuNPs are used in nanotechnology such as SERS (Surface Enhanced Raman Scattering) nanoparticles, gold nanospheres, gold nanoshells, gold nanorods and gold nanocages.

3.2.1. Gold Nanospheres

These range from two nm to over 100 nm in diameters, which can be fabricated using different reduction agents that vary depending on the condition with the technology of controlled reduction of an aqua $HAuCl_4$ solution. Citrate is the most common reduction agent that produces almost monodisperse gold nanospheres and its size can be controlled by a different citrate or gold ratio. Overall, small quantities of citrate tend to produce larger nanospheres [6].

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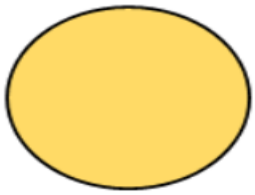

Figure 1- Gold Nanosphere

3.2.2. Gold Nanorods

They are synthesized using the template method which is based on the electrochemical deposition of gold particles within the alumina template membranes or pores of nanoporous polycarbonate. Their diameter is determined by the pore diameter of the template membrane, while their length can be controlled through the amount of gold deposited within the pores of the membrane [7].

Figure 2- Gold Nanorod

3.2.3. Gold Nanoshells

These are used in optical imaging, golden nanoparticles are used as contrast agents and are very limited in human studies, but biomolecules are absorbed in the almost infrared range from 700 – 900 nm and that gives a comparatively visible picture for optical imaging. Gold nanoshells can be produced and designed with surface plasm resonance (SPR) whose peaks range from the visible

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region to the NIR by a slight modification in the size and composition of the layers. A modification of the core and shell thickness ratio will alter the Gold nanoshell composition of the SPR peak [8].

Figure 3- Gold Nanoshell

3.2.4. Gold Nanocages

They have a controllable characteristic pores which are present on the surface and synthesized between aqueous HAuCl4 and truncated silverside nanocubes through a galvanic replacement reaction. Such silver nanostructures are produced via polyol-controlled morphologies that reduce AgNO3 to produce silver atoms and then nanocrystals or seeds. By integrating sufficient silver atoms in the seeds the desired nanostructures are created in the presence of polyvinylpyrrolidone that can selectively bundle to at least 100 surfaces by regulating the crystalline silver seed structures. These nanostructures are used as sacrificial template that may then be transformed by galvanic replacement into golden nanostructures with hollow interior. By changing the molar ratio of HAuCl4 to silver, the wall width and dimension of the resulting gold nano-cages can be easily controlled to high precision [9].

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Figure 4- Gold Nanocages

3.2.5. SERS (Surface Enhanced Raman Scattering) Nanoparticles

It is an optical method that has many benefits over conventional techniques, such as chemiluminescence and fluorescence, including higher multiplexing rates, blood and robustness, high sensitivity and improved biological matrices quality. Gold nanospheres with a diameter of 13 nm modified with Cy3 labels and capsulated by alkylthiol oligonucleotide strands can be used as samples to monitor the presence of specific target DNA strands. Due to its large Raman cross section, the Cy3 group was selected [10].

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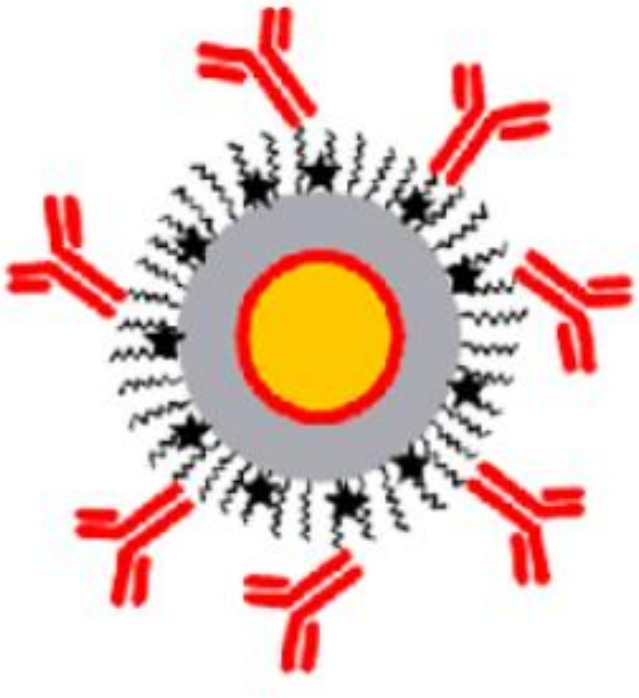

Figure 5- SERS Nanoparticles

The red layer surrounding the gold core is Raman dye and antibodies are represented in red as this is used to delivery antibodies.

4. **Gold Nanoparticles in Biomedical Sciences: -**

Biomedical science describes us that how cells, organs and systems function in the human body. It is an interesting area which deals with the knowledge, understanding and treatment of human diseases. Biomedical sciences are a combination of natural and formal sciences and applying its knowledge, technology in public health care system.

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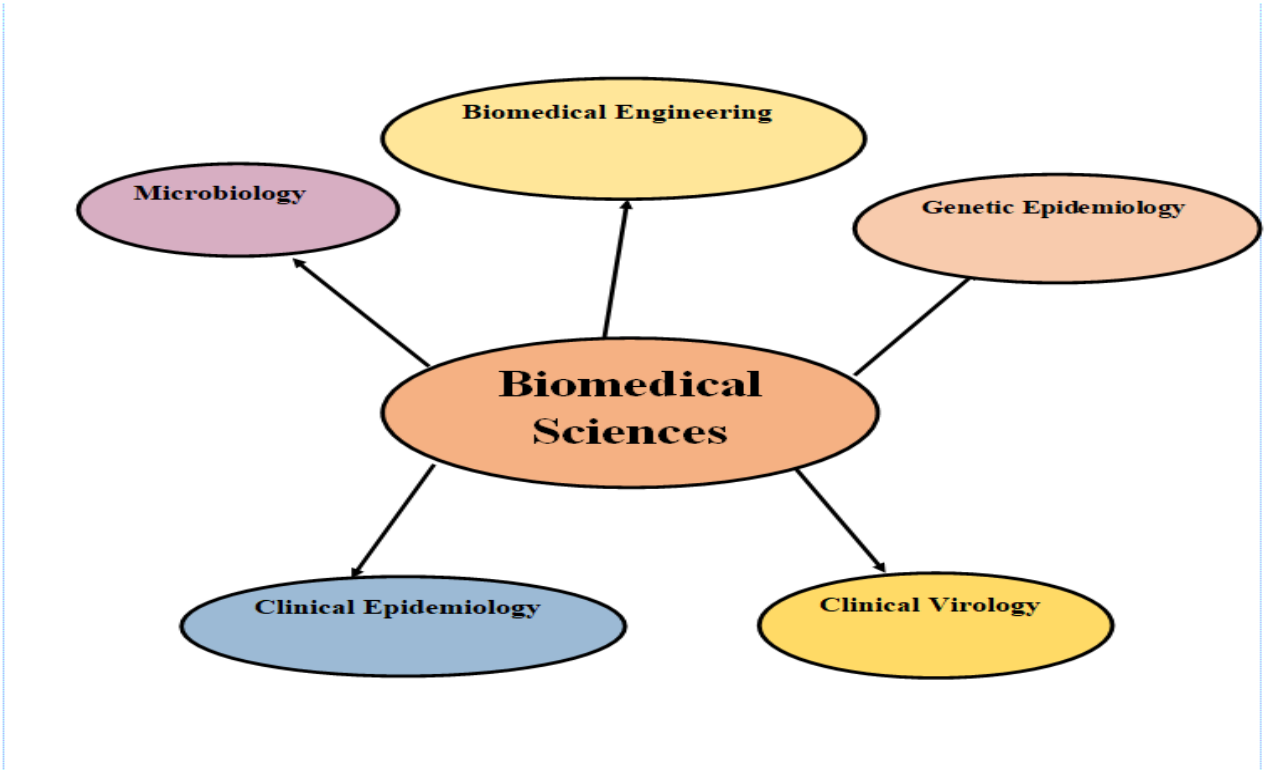

Figure 6- Parts of Biomedical Sciences.

Its main focus is the biology of diseases, human health which ranges from the biomedical sciences and human biology to the more specific subject as that of pharmacology, human nutrition and physiology. It is also supported by bioinformatics, microbiology, anatomy and physiology, immunology, molecular biology and mathematics and statistics. They are on the major focus list for funding and research in this century [11].

With the establishment of Institute of Biomedical Science in the United Kingdom in 1912 created proper place for the progress of biomedical sciences. Major breakthrough came for the field with the discovery of penicillin in 1928 by Alexander Fleming which was helpful in the treatment of bacterial infections. 1930s was a big decade for the field as it saw the rise in the use of antibiotics and the development of vaccines were also seen and in 1935 the polio vaccine was introduced by Dr. Maurice Brodie. World war II saw the new age of biomedical sciences were new technology and treatments were introduced for example in 1941 hormonal

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treatment for prostate cancer was introduced by cancer researcher and urologist Charles B. Huggins. In 1949 first bone marrow transplant was done and they are still saving many lives.

5. Recent Advancements

Most of the use of nanoparticle are induced in the diagnosis and treatment of cancer as these are small and are perfect for diagnosis and site release of medication. By the development of nanoparticles various methods to treat cancerous cell have been developed which include thermal therapies as these therapies causes minimal damage to the healthy cells. The most prominent challenge to treat cancer is the identification of diseased cell and the development of its efficient treatment so that side effects are minimal. Thermal therapy and integrated imaging are used for the diagnosis and treatment of diseased tissue as these image treatments might be useful for the diagnosis and identification of the source. The use of the Surface Plasmon Resonance (SPR) in near-infrared region and Alternative Magnetic Fields (AMF) is also used for heat induced treatments [12].

5.1. Cancer Diagnosis and Treatment

Treatment of cancer is carried out via surgery, radiation therapy and chemotherapy but these have few setbacks such as tumor reoccurrence, damage to healthy cells, side effects etc. Scientists are trying to find new ways to eliminate these effects of treatment of cancer and they used hyperthermia to destroy tumor cells. For thermal imaging and therapy, nanoparticle-composed organic material was investigated but photobleaching is one of the major disadvantages, which has led to research on inorganic materials. Their imaging properties including fluorescence, magnetic resonance, near Photo acoustic image, infrared absorption, and raman enhancements are typically studied in the field of therapy for heat induced cancer and they still undergo clinical trials. By the surface modification of nanoparticles by molecules like polyethylene glycol would change the in vivo circulation and it would be excreted without showing potential toxicity and by the modification of carbon-based materials such as carbon nanotubes and graphene by polyethylene glycol toxicity is reduced and when tested in mice they were excreted gradually. Thus, these nanoparticles can be carefully formulated to kill cancer cells through therapy [13].

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Surface Plasmon Resonance is the physical characteristics of nanoparticles and when their size exceeds the nanoscale, the surface properties of noble metals are increased. They have a higher cross-sectional absorption compared to organic dyes, leading to less energy intake for laser treatment and also to no photobleaching of metallic compounds and to a greater degree of photostability and effective laser treatment [14].

Since 1957 Magnetic Hyper-Thermia (MHT) has been used for the treatment of cancer. In this tumor cells are given heat using magnetic field alternating in nature and magnetic nanoparticles [15].

Alternating Magnetic Fields (AMF) effectively kills the cancer cells by keeping the temperature between 42-46 ^{o}C. It has several advantages such as deep penetration and tumor temperature regulation. At the surface level of metallic nanoparticles large electric fields are induced and these excited electrons undergoes rapid relaxation which produces heat and is utilized in thermal therapies for killing cancerous cells [16].

anoscale Gold Particles (NGP), which are plasmonic, are the widely studied nanomaterials used for thermal therapy. It improves light-to-heat conversion efficiency, photostational plasm resonance, and enhances biocompatibility within a close infrared region. They also have a higher emission and light absorption properties than organic dyes. There are three major class of NGP's namely: -

a. Gold Nanocages.
b. Gold Nanorods.
c. Gold Nanoshells.

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Figure 7- Gold Nanocages

Figure 8- Gold Nanorod

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Figure 9- Gold Nanoshell

They are mainly depended upon their photothermal properties of shape, size and medium's di-electric constant. They also have a strong absorbance in UV region. The hydrophobic forces and the Vander Waals forces tend to aggregate AuNPs. It has significant drawback that they have a low disintegration rate and also their clearance is relatively low which causes toxicity. Nanorods has a higher SPR absorption when compared to the spherical particles because of their aspect ratio. When aspect ratio is increased the SPR reaches maximum and when the reduction of the thickness of nanoshells are done then SPR enhances greatly [17].

Gold Nanoparticle's different morphologies are being studied to achieve higher therapeutic outcome, one of the examples is when amorphous SiO_2 was coated on gold nanoparticle to form nanoaggregates. This was greater than 1.4 nm and showed better biocompatibility and used as dielectric spacer for tuning of Photo Thermal Therapy (PTT) [18].

5.2. In Vitro Diagnostic

It is one of the major component of clinical care used for diagnostic purpose on biological samples which includes urine, blood and tissue. They are done to determine the presence of a particular disease in an individual. They are widely popular because of their importance in medical profession as they do not interact with humans directly and is done without any surgery and hence reducing pain.

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As they are performed on samples rather than humans, the chances of biological harm is not present. They provide quick information on patient's healthcare. It makes the treatment of serious diseases easier as it enables early detection and treatment. It plays an important role for managing outbreaks of acute infectious diseases as they are simple and highly desirable and all this makes IVD's extremely desirable [19-21].

6. Summary

It describes gold nanoparticles, as these particles are extensively studied and used for a variety of technical applications, such as sensory probes,biological and medical uses, photovoltaics (organic in nature), therapeutic agents, electronical conductors and catalyse. Solution of gold salt was considered to be a cure for various diseases. AuNPs are highly useful for controlled cancer treatment, drug delivery, biomedical imaging, diagnosis, etc. because of their higher compatibility with the human body, tunable stability and low toxicity, possible interaction with a variety of substances and small dimensions.

Most of the use of nanoparticle are induced in the diagnosis and treatment of cancer as these are small and are perfect for diagnosis and site release of medication. By the development of nanoparticles various methods to treat cancerous cell have been developed which include thermal therapies as these therapies causes minimal damage to the healthy cells. The most prominent challenge to treat cancer is the identification of diseased cell and the development of its efficient treatment so that side effects are minimal. Thermal therapy and integrated imaging are used for diagnosing and treating diseased tissue because this image therapy could be extremely useful in the diagnosis and identification of the source.

References

[1].M. E. Ali, U. Hashim, S. Mustafa, Y. B. Che Man, and Kh. N. Islam, "Gold Nanoparticle Sensor for the Visual Detection of Pork Adulteration in Meatball Formulation", Journal of Nanomaterials 7, 2012.

ISSN: 0971-1260

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[2]. K. E. Sapsford, W.R. Algar, L. Berti, K. B. Gemmill, B. J. Casey, E. Oh, M. H. Stewart and I. L. Medintz , "Functionalizing nanoparticles with biological molecules: developing chemistries that facilitate nanotechnology", *Chemical Reviews*, 113 (3), 1904–2074, 2013.

[3]. C. N. Rao, G. U. Kulkarni, P. J. Thomas and P. P. Edwards, "Metal nanoparticles and their assemblies", Chemical Society Reviews, 29(1), 27–35, 2000.

[4]. P. Singh, S. Pandit, V. R. S. S. Mokkapati, A. Garg, V. Ravikumar and I. Mijakovic, "Gold Nanoparticles in Diagnostics and Therapeutics for Human Cancer", Int. J. Mol. Sci, 19 (7) 2018.

[5]. Y. Panahi, M. Mohammadhosseini, K. Nejati-Koshki, A. J. Abadi, H. F. Moafi, A. Akbarzadeh and M. Farshbaf, "87Preparation, Surface Properties, and Therapeutic Applications of Gold Nanoparticles in Biomedicine", Drug Res, 67 (2) 77, 2017.

[6]. J. Turkevich, P. C. Stevenson and J. Hillier, "The nucleation and growth processes in the synthesis of colloidal gold", Discuss Faraday Soc, 11, 55–75, 1951.

[7]. Y. Y. Yu, S. S. Chang and C. L. Lee, "Gold nanorods: electrochemical synthesis and optical properties", J Phys Chem B., 101, 6661–4, 1997.

[8]. S. J. Oldenburg, S. L. Westcott and R. D. Averitt, "Surface enhanced Raman scattering in the near infrared using metal nanoshell substrates", J Chem Phys., 111, 4729–35, 1999.

[9]. J. Chen, F. Saeki, B. J. Wiley, H. Cang, M. J. Cobb, Z. Y. Li, L. Au, H. Zhang, M. B. Kimmey, X. Li and Y. Xia, "Gold nanocages: bioconjugation and their potential use as optical imaging contrast agents", Nano Lett. 5(3), 473-7, 2005.

[10]. M. Y. Sha, H. Xu, S. G. Penn and R. Cromer, "SERS nanoparticles: a new optical detection modality for cancer diagnosis", Nanomedicine (Lond)., 2 (5), 725-34, 2007.

[11]. N. Elahi, M. Kamali, and Md. H. Baghersad, "Recent biomedical applications of gold nanoparticles: A review", Talanta, 184, 537-556, 2018.

[12]. X. Zheng, D. Xing, F. Zhou, B. Wu and W. R. Chen, "Indocyanine green-containing nanostructure as near infrared dual-functional targeting probes for optical imaging and photothermal therapy", Mol. Pharm., 8, 447–456, 2011.

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Vol-22-Issue-17-September-2019

[13]. Z. Liu, C. Davis, W. Cai, L. He, X. Chen and H. Dai, "Circulation and long-term fate of functionalized, biocompatible single-walled carbon nanotubes in mice probed by Raman spectroscopy", PNAS, 1410–1415, 2008.

[14]. M. K. Yu, J. Park and S. Jon, "Targeting strategies for multifunctional nanoparticles in cancer imaging and therapy", Theranostics, 2, 3–44, 2012.

[15]. R. K. Gilchrist, R. Medal, W. D. Shorey, R. C. Hanselman, J. C. Parrott and C. B. Taylor, "Selective inductive heating of lymph nodes", Ann. Surg., 146, 596–606, 1995.

[16]. M. A. El-Sayed, "Some interesting properties of metals confined in time and nanometer space of different shapes, "Acc. Chem. Res., 34, 257–264, 2001.

[17]. . S. Link, M. B. Mohamed and M. A. El-Sayed, "Simulation of the optical absorption spectra of gold nanorods as a function of their aspect ratio and the effect of the medium dielectric constant," J. Phys. Chem. B, 103, 3073–3077, 1999.

[18]. A. Polakiewicz, H. Dodiuk and S. Kenig, "Super-hydrophilic coatings based on silica nanoparticles," J. Adhes. Sci. Technol., 28, 466–478, 2014.

[19]. Z. Jin and N. Hildebrandt, "Semiconductor Quantum Dots for in Vitro Diagnostics and Cellular Imaging", Trends Biotechnol., 30, 394–403, 2012.

[20]. A. P. F. Turner, B. N. Chen and S. A. Piletsky, "In Vitro Diagnostics in Diabetes: Meeting the Challenge", Clin Chem., 45, 1596–1601, 1999.

[21]. Y. Xing and J. Rao, "Quantum Dot Bioconjugates for in Vitro Diagnostics & in Vivo Imaging", Cancer Biomarkers, 4, 307–319, 2008.