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Gold Nanoparticles for Detection of Cancerous Cell: A Review

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Subject: Nanotechnology

Abstract
In nanotechnology, a particle is defined as a small object that behaves as a whole unit in terms of its transport and properties. It is further classified according to size: In terms of diameter, fine particles cover a range between 100 and 2500 nanometers, while ultrafine particles, on the other hand, are sized between 1 and 100 nanometers. Similarly to ultrafine particles, nanoparticles are sized between 1 and 100 nanometers. Nanoparticles may or may not exhibit size-related properties that differ significantly from those observed in fine particles or bulk materials1. Although the size of most molecules would fit into the above outline, individual molecules are usually not referred to as nanoparticles. The use of metallic nanoparticles in the treatment of cancer is a promising, relatively recent development in this field. At present, gold is a favored material for this purpose. Formed into spheres, shells, cages or wires on the scale of ten to one thousand nanometers, gold can be bound to a wide variety of biochemical functional groups and made to target specific types of cells. Once there, the nanoparticles may be used for imaging or, in conjunction with an external energy source such as an infrared laser, to concentrate lethal doses of energy in the target cancer cells. Many re- searchers believe that nanoparticles-based techniques could prove to be more effective than current chemical- or radiation-based treatments, with fewer adverse side effects.

Keywords: *Nanoparticle, Gold nanoparticle, cancer cell*

Introduction:
Nanoparticle research is currently an area of intense scientific research, due to a wide variety of potential applications in biomedical, optical, and electronic fields. Nanoparticles are of great scientific interest as they are effectively a bridge between bulk materials and atomic or molecular structures. [#].

Type of Nanoparticle:-

1.Nanocluster
2.Nanopowder
3.Nanocrystal

• **Nanocluster:-** Nanoclusters have at least one dimension between 1 and 10 nanometers and a narrow size distribution.

• **Nanopowder:-** Nanopowders are agglomerates of ultrafine particles, nanoparticles, or nanoclusters.

• **Nanocrystal:-**
Nanometer sized single crystals, or single-domain ultrafine particles, are often referred to as nanocrystal

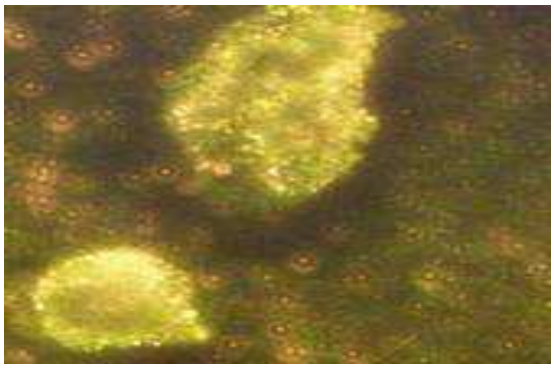

Fig.1 Gold Nanoparticles

Since the concept of nanotechnology was first formed, the possible medical applications of nano-scale materials and devices have drawn considerable interest. The use of metallic nanoparticles in the treatment of cancer is a promising, relatively recent development in this field1. At present, gold is a favoured material for this purpose. Formed into spheres, shells, cages or wires on the scale of ten to one thousand nanometers, gold can be bound to a

wide variety of biochemical functional groups and made to target specific types of cells. Once there, thenanoparticles may be used for imaging or, in conjunction with an external energy source such as an infrared laser, to concentrate lethal doses of energy in the target cancer cells. Many researchers believe that nanoparticle-based techniques could prove to be more effective than current chemical- or radiation-based treatments, with fewer adverse side effects[2].

Nanoparticle-based techniques have the potential to offer many advantages over more conventional forms of cancer treatment[3]. At present,the most common cancer treatment methods are based on chemotherapy, radiation therapy, or surgery, all of which can be successful, but have substantial disadvantages. Chemotherapy often induces severe side effects and can cause damage to healthy cells, and radiation is only useful on localized, well-defined tumours. Surgical removal also requires that the tumour be well localized, and is often impossible if the tumour is surrounded by sensitive tissues such as the brain.

Hyperthermic treatment has been tried in many forms, but conventional techniques tend to cause substantial damage to surrounding tissues. Modern nanotechnology, though, offers the possibility of materials that selectively bind to particular types of cancer cells, sensitizing them to light without affecting surrounding healthy tissues[4]. As a diagnostic tool, these nanoparticle techniques can be used to greatly enhance image contrast when studying a tumour. As a treatment tool, they may take several forms: photodynamic therapy (PDT) if the cancer is destroyed chemically by the light-activated sensitizer particles, or photothermal therapy (PTT) if it is destroyed by heating the nanoparticles with an external energy source (often an infrared laser) [5].

Properties of Cancer Cells :

• Epidermal Growth Factor Receptor (EGFR) over expression and over activity have been associated many different types of Cancer

• Cancer cells have a unique properties that can be exploited by nanoparticles

• Their rapid rate of growth causes them to intake an abnormal amount of nutrients (i.e., folic acid)

• Nanoparticles can be used to target bio-markers or antigens that are highly specific to Cancer cells

Following difficulties arrises in cancerous cell detection:

• Ineffectiveness of many Cancer treatments

• numerous side effects

• Difficulties in early Cancer detection

• No immunization

Mechanism:

Since the development of medical lasers, scientists have been turning to electromagnetic radiation to treat cancer. This can be done in several ways. Photodynamic therapy (PDT) involves a photosensitizer which becomes excited and generates singlet oxygen and other free radicals. The combination of the generated heat and the interaction of the cells with the oxygen cause irreparable damage to the cancerous cells6. This method requires short wavelengths of light, reducing the depth to which the light can penetrate and making deep tumour treatment unachievable. Another method of cancer treatment using electromagnetic radiation is photothermal therapy (PTT) [7]. Using this method, near infrared (NIR) radiation from a laser may be used to penetrate through the skin to a deeper extent because the light will undergo less absorption from tissue chromophore and water. Heat absorbed from the radiation will cause thermal denaturation and coagulation of affected cells. In addition, heating will cause vaporization of surrounding fluids, producing cavitation bubble formation and what may be compared to underwater explosion, but on a very small scale. This sudden formation of bubbles cause mechanical stress on the cells which lead to cell destruction. When a PTT sensitizer is specifically designed to make use of the surface plasmon resonance of a metallic nanoparticle, the techniqueis sometimes referred to as plasmonic photothermal therapy (PPTT).While it is possible to photothermally kill cells using electromagnetic radiation, it is crucial that neighbouring healthy cells are not destroyed in the process. A localized high intensity field is required to selectively kill the malignant cells. This is where nanotechnology and nanophysics meet complex chemistry and biology to play an essential role. Gold nanoparticles (GNPs) may be programmed to bind with malignant cells using self-assembly methods. A NIR laser operating at an intensity too low to damage cells is imparted on an area containing healthy cells as well as cancerous cells bound to goldnanoparticles. The intense evanescent field throughout the NP will excite surface plasmons on the goldnanoparticles. If the frequency of the laser is tailored to the resonance frequency of the surface plasmons, the oscillations in the free electron density

will generate a strong field, much stronger than the incident field. This condition is called surface plasmon resonance. GNPs-Ab-1 and GNPs-Ab-2 represent the two types of gold nanoparticles bearing different antibodies, and Ag represents the CEA antigen. When mixed , a dimer is formed reducing the total number of nanoparticles in the sample[8]. The scattering and absorption of the light cause a great enhancement in the local field[9]. This essentially results in a very strong field within close proximity of the NPs (i.e. where the malignant cells are) as well as significant absorption which leads to thermal heating. During the absorption process the heated electron gas transfers energy to the metal lattice resulting in phonon-phonon interactions. The energy is then transferred to the surrounding medium. The energy transferfrom the hot electron gas to the lattice takes approximately 1ps where as the phonon-phonon interactions occur over the course of approximately 100ps. These are the effects sought after for selective destruction of malignant cells.

Colloidal gold nanoparticles may be grown and produced in various shapes and sizes[10]. The scattering and absorption properties of the NPs will depend on their geometry and dimensions. A NP is most useful and effective when it has a strong peak in absorption in the NIR region. It is also important that the peak is tunable based on the dimensions of the NP so that the system can be optimized. In addition, it is important that the NPs may be manipulated to target cancer cells. The NPs that have been studied most extensively for these purposes are nanospheres, nanoshells and nanorods. It has been found that the NPs the most effective for this method of photothermal therapy are nanorods with a minor length that is 15 to 20nm and a major length 50 to 70nm which have a peak in absorption around 800nm. This peak may be tuned by the aspect ratio of the rods. The main drawback to these rods is that it is fairly difficult to attach them to biomolecular labels. The nanoshells may also be tunable, with the resonance peaking in the NIR spectrum. The optimal silica core diameter and shell thickness are 50 to 100nm and 3 to 8nm respectively. The main problem faced with the nanoshells is that heating can destroy the particles due to the nature of the thin shells[11]. For larger shells thicknesses (>10nm) the scattering dominates over the absorption and the photothermal effects are reduced. Nanospheres are the least attractive of the three because they cannot be tuned well in the NIR spectrum and have weak absorption peaks in this region.

This form of cancer therapy is dependent on the tendency of cancer cells to absorb substantially higher concentrations of nanoparticles than the surrounding tissue. Much of the current research in the field involves biochemical functionalization of the nanoparticles with a cancer antibody. Some recent research, however, has indicated that specific cell lines may preferentially absorb unfunctionalized GNPs based on purely geometric factors. In the case of cancer cells, one functional group that has been found to selectively bind to the target tumour is the anti-epithelial growth factor receptor (EGFR) antibody. EGFR is strongly expressed by some cancer cell lines, such as oral squamous carcinoma, but is not a prominent feature of healthy cells from similar tissues. Thus, nanoparticles bound to anti-EGFR are preferentially absorbed by the cancerous cells. The conjugated gold NPs will bind with canerous cells 600% more than with noncancerous cells. Different types of cancer cells express different protein groups on their surface; for example, many breast cancers overexpress seprase and Her2, both of which have corresponding antibodies that can be bound to the gold nanoparticles. A light scattering imaging technique is used here where the light is tuned to the surface Plasmon resonance of the NPs to get the enhanced scattered light effects.

The sample with malignant cells have well defined cells whereas for the non-cancerous sample the nanoparticles appear to be spread fairly haphazardly. In order to improve biocompatibility, unfunctionalized GNPs are sometimes coated with a passivating layer, often polyethylene glycol. These passivated nanoparticles are still susceptible to the same surface plasmon effects as uncoated ones (albeit at a slightly different resonance, due to the dielectric constant of the coating). However, they are not as affected by some chemical effects, such as the aggregation of salt ions that can be problematic for uncoated nanoparticles.

Current Limitations:

1. Cancer targeting is highly dependent on surface chemistry. Not just any nanoparticles will work.
2. The need for biocompatible & stable nanoparticles.
3. Side-effects and toxicity.
4. Environmental impact.
5. Uncharted territory

Future:

1. Human clinical trials within the next 2-3 years.
2. Highly specific team of communicating

multifunctional nanoparticles used in the discovery, treatment and prevention of Cancer growth.
3. Safer, more consistent & highly specific nanoparticles production.
4. Turning Cancer into a chronic, but manageable disease within the next 15-20 years.

Summary:

Different types of Cancer cells have unique properties that can be exploited by nanoparticles to target the Cancer cells.Nanoparticles can be used to detect/monitor (by utilizing or adding optic, magnetic, and fluorescent properties) and to treat Cancer (by Heat ablation, chemotherapy, gene therapy). No human trials have been performed yet and human trials are still at least a few years away. (Unknown side effects, toxicity, difficulty in manufacturing and harmful byproducts, need for highly specific nanoparticles)

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