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Nanomedicine on Cancer

Mr. Ajay R. Deshmukh, Mr. Akshay G. Dongardive, Mr. Aniket N. Jagtap, Dr. Gopalkrishna R. Sitaphale, Dr. Prafulla R. Tathe

Samarth College of Pharmacy, Deulgaon Raja, Maharashtra India.

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ABSTRACT

Nanomedicine is the application of nanotechnology, often described as technologies under 1000nm, in the health sciences. Over the past years, researchers have been using nanomedicine to target microbes, with promising results in vitro and as a potential innovation to the field of antimicrobials. In the studies that followed, clinical trials started to appear, and it seems that a movement of clinical translation is initiating in the field of antimicrobial nanomedicine. Although the clinical trials have tended to be initial and small studies, they represent an important achievement for the field, stimulating further clinical research and basic science, and generating novel questions and scientific enquiries. Trials addressing nano particles on catheters, hand gels, therapeutic vaccines, safety, and other issues have been conducted. For their financial and bureaucratic restrictions, the presence of clinical trials is a great indicator of the potential of the field and is a necessary step for a great leap in the fight against microbes proposed by nanomedicine.

Keywords: Nanotechnology, Nanomedicine, 1000nm, nanoparticles, nanocarrier, nano vectors, biodistribution, Tumour.

1.INTRODUCTION

Cancer is a leading cause of death and a global health burden. It was estimated that there would be 18.1 million new cancer cases and 9.6 million cancer-related deaths by 20181. Cancer is a disease characterized by uncontrolled cell proliferation that spreads from an initial focal point to other parts of the body to cause death. For these reasons, it is key to ensure earlier detection and treatment of cancers to reduce disease spread and mortalities. Amongst the widely used strategies, today in cancer research is nanotechnology. Nanotechnology has led to several promising results with its applications in the diagnosis and treatment of cancer, including drug delivery, gene therapy, detection and diagnosis, drug carriage, biomarker mapping, targeted therapy, and molecular imaging. Nanotechnology has been applied in the development of nanomaterials, such as gold nanoparticles and quantum dots, which are used for cancer diagnosis at the molecular level. Molecular diagnostics based on nanotechnology, such as the development of biomarkers, can accurately and quickly detect the cancers. Nanotechnology treatments, such as the development of nanoscale drug delivery, can ensure precise cancerous tissue targeting with minimal side effects. Due to its biological nature, nanomaterials can easily cross cell barriers.

Over the years, nanomaterials have been used in the treatment of tumours, due to their active and passive targeting. Although many drugs can be used to treat cancers, the sensitivity of the drugs generally leads to inadequate results and can have various side effects, as well as damage to the healthy cells. In view of that, several studies have examined different forms of nanomaterials, such as liposomes, polymers, molecules, and antibodies, with the conclusion that a combination of these nanomaterials in cancer drug design can achieve a balance between increasing efficacy and reducing the toxicity of drugs. However, due to the potential toxicity of nanomaterials, there is still a lot of advancement to be done on them. Before their readily acceptance in the clinic for cancer management. With the rapid development of nanotechnology, this paper will review its application in cancer diagnosis and treatment with focus on their benefits and limitations during use.

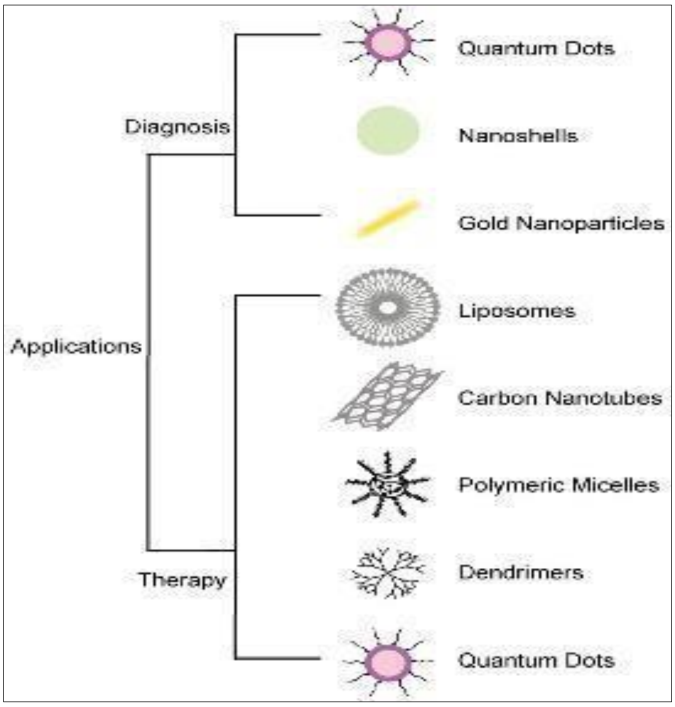

Fig.no.1 Application of nanomedicine in cancer diagnosis and therapy.

Nanomedicine:

Nanomedicine is the medical application of nanotechnology. Nanomedicine ranges from the medical applications of nanomaterials and biological devices, to nanoelectronics biosensors, and even possible future applications of molecular Nanomedicine is the medical application of nanotechnology. Nanomedicine ranges from the medical applications of nanomaterials and biological devices, to nanoelectronics biosensors, and even possible future applications of molecular nanotechnology such as biological machines nanotechnology such as machines.

According to the EC recommendation, nanomaterial refers to a natural, incidental, or manufactured material comprising particles, either in an unbound state or as an aggregate wherein one or more external dimensions is in the size range of 1–100 nm for ≥50% of the particles, according to the number size distribution. In cases of environment, health, safety or competitiveness concern, the number size distribution threshold of 50% may be substituted by a threshold between 1 and 50%. Structures with one or more external dimensions below 1 nm, such as fullerenes, graphene flakes, and single wall carbon nanotubes, should be considered as nanomaterials. Materials with surface area by volume in excess of 60 m2/cm3 are also used.

Medical Benefits of Nanotechnology

Nanotechnology has the potential to bring major advances in medicine. Nanobots could be sent.

into a patient's arteries to clear away blockages. Surgeries could become much faster and more accurate. Injuries could be repaired cell-by-cell. It may even become possible to heal genetic conditions by fixing the damaged genes. Nanotechnology could also be used to refine drug production, tailoring drugs at a molecular level to make them more effective and reduce side effects.

Manufacturing Advantages of Nanomaterials

Nanotechnology is already making new materials available that could revolutionize many areas of manufacturing. For example, nanotubes and nano particles, which are tubes and particles only a few atoms across, and aerogels, materials composed of very light and strong materials with remarkable insulating properties, could pave the way for new techniques and superior products. In addition, robots that are only a few nanometres in length, called nanobots, and nano factories could help construct novel materials and objects.

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Advantages of Nano Medicine:

1. Advanced therapies with reduced degree of invasiveness.

2. Reduced negative effects of drugs and surgical procedures.

3. Faster, smaller and highly sensitive diagnostic tools.

4. Cost effectiveness of medicines and disease management procedures as a whole.

5. Unsolved medical problems such as cancer, benefiting from the Nano medical approach.

6. Reduced mortality and morbidity rates and increased longevity in return.

Disadvantages of Nano Medicine:

1. Lack of proper knowledge about the effect of nanoparticles on biochemical pathways and processes of human body.

2. Scientists are primarily concerned about the toxicity, characterization, and exposure pathways associated with Nano medicine that might pose a serious threat to the human being and environment.

3. The society's ethical use of Nano medicine beyond the concerned safety issues, poses a serious question to the researchers.

4. Included in the list of disadvantages of this science and its development is the possible loss of jobs in the traditional farming and manufacturing industry.

5. You will also find that the development of nanotechnology can also bring about the crash of certain markets due to the lowering of the value of oil and diamonds due to the possibility of developing alternative sources of energy that are more efficient and won't require the use of fossil fuels. This can also mean that since people can now develop products at the molecular level, diamonds will also lose its value since it can now be mass produced.

All kinds of nano under the microscope.

1) DNA-based origami robots

One of the most forward–thinking experiments proved that DNA–based nanorobots can be inserted into a living cockroach and later perform logical operations upon command such as releasing a molecule stored within it. Such nanorobots are also called origami robots since they can unfold and deliver drugs, could eventually be able to carry out complex programs including diagnoses or treatments. One of the most astonishing feats is the accuracy of delivery and control of these nanobots, which are equivalent to a computer system. The other one is that the same basic design principles that apply to typical full-size machine parts can also be applied to DNA.

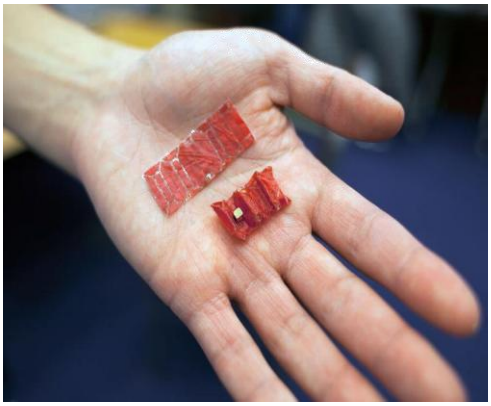

Fig. No.2 Origami Robot Made from Pig Tissue Offers Non-Invasive Way to Retrieve Swallowed Batteries

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2) Scallop-like microbots and nanoswimmers

Researchers from the Max Planck Institute have been experimenting with exceptionally microsized – smaller than a millimetre – robots that literally swim through your bodily fluids and could be used to deliver drugs or other medical relief in a highly-targeted way. These scallop-like microbots are designed to swim through non-Newtonian fluids, like your bloodstream, around your lymphatic system, or across the slippery goo on the surface of your eyeballs.

ETH Zurich and Technion researchers have developed an elastic "nanoswimmer" polypy role (Ppy) nanowire about 15 micrometers (millionths of a meter) long and 200 nanometers thick that can move through biological fluid environments at almost 15 micrometers per second. The nanoswimmers might be programmed to deliver drugs and magnetically controlled to swim through the bloodstream to target cancer cells, for example.

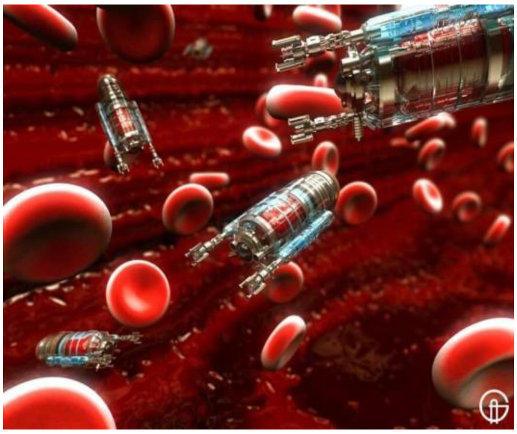

Fig. No.3 Scallop-like microbots and nanoswimmers

3) Ant-like nano engines

Ant–like robots are controlled magnetically, are very fast, can locate, and use tools. Moving through even flexible surfaces they can construct three–dimensional structures at an amazing pace.

They could revolutionize both biotechnology and electronics manufacturing.

University of Cambridge researchers have developed the world's tiniest engine, made of gold nanoparticles bound together with temperature-responsive gel polymers, capable of a force per unit weight nearly 100 times higher than any motor or muscle. Researchers named the Nano machine ANT, since as real ants, they produce large forces for their weight.

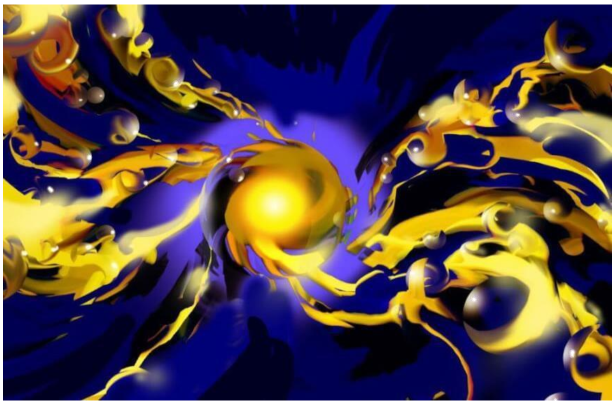

Fig. No. 4 Exploding polymer-coated gold nanoparticles in the world's tiniest engine

Cancer:

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. Cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and multiply (through a process called cell division) to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply when they shouldn't. These cells may form tumours, which are lumps of tissue. Tumours can be cancerous or not cancerous.

Cancerous tumors spread into, or invade, nearby tissues and can travel to distant places in the body to form new tumors (a process called metastasis). Cancerous tumors may also be called malignant tumors. Many cancers form solid tumors, but cancers of the blood, such as leukemias, generally do not. Benign tumors do not spread into, or invade, nearby tissues. When removed, benign tumors usually don't grow back, whereas cancerous tumors sometimes do. Benign tumors can sometimes be quite large, however. Some can cause serious symptoms or be life threatening, such as benign tumors in the brain.

How does cancer develop :

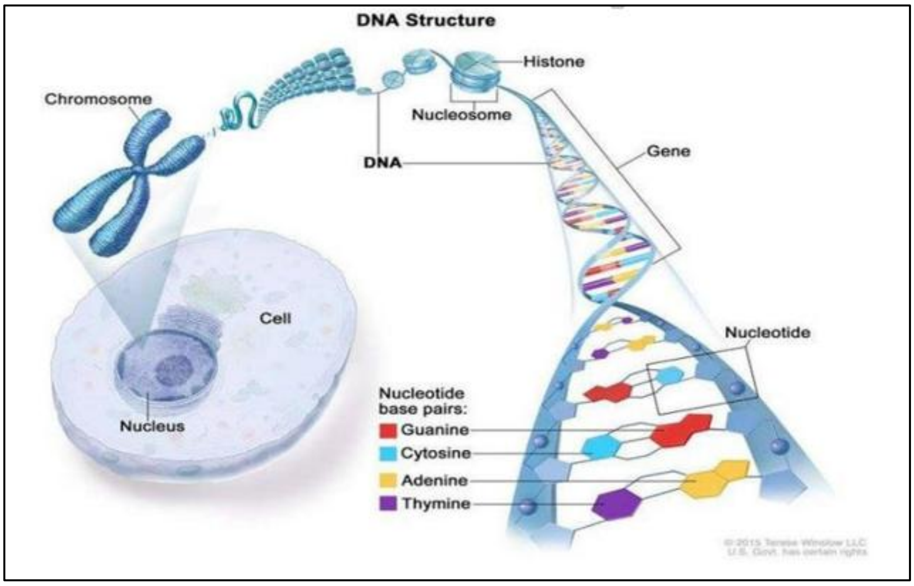

Fig.no. 5 Cancer is caused by certain changes to genes, the basic physical units of inheritance.

Genes are arranged in long strands of tightly packed DNA called chromosomes

Cancer is a genetic disease that is, it is caused by changes to genes that control the way our cells function, especially how they grow and divide.

Genetic changes that cause cancer can happen because of errors that occur as cells divide.

of damage to DNA caused by harmful substances in the environment, such as the chemicals in tobacco smoke and ultraviolet rays from the sun. They were inherited from our parents.

The body normally eliminates cells with damaged DNA before they turn cancerous. But the body's ability to do so goes down as we age. This is part of the reason why there is a higher risk of cancer later in life.

Each person's cancer has a unique combination of genetic changes. As the cancer continues to grow, additional changes will occur. Even within the same tumour, different cells may have different genetic changes.

Types of cancer :

- Bladder Cancer
- Breast Cancer
- Colorectal Cancer
- Kidney Cancer
- Lung Cancer - Non-Small Cell
- Lymphoma
- Melanoma
- Oral and Oropharyngeal Cancer
- Pancreatic Cancer
- Prostate Cancer
- Thyroid Cancer
- Uterine Cancer

NANOTECHNOLOGY IN CANCER DIAGNOSIS :

Cancer diagnostic and therapeutic strategies are targeted at early detection and inhibition of cancerous cell growth and their spread. Notable among the early diagnostic tools for cancers is the use of positron emission tomography (PET), magnetic resonance imaging (MRI), computed tomography (CT) and ultrasound. These imaging systems, however, are limited by their inadequate provision of relevant clinical information about different cancer types and the stage. Hence it makes it difficult to obtain a full evaluation of the disease state based on which an optimum therapy can be provided.

Nanotechnology aids in tumour imaging:

In the past few decades, the application of nanoparticles in cancer diagnosis and monitoring has attracted a lot of attention with several nanoparticle types being used today for molecular imaging. Due to their advantages including small size, good biocompatibility, and high atomic number, they have gained prominence in recent cancer research and diagnosis. Nanoparticles used in cancer such as semiconductors, quantum dots and iron oxide nanocrystals possess optical, magnetic or structural properties that are less common in other molecules . Different anti-tumour drugs and biomolecules including peptides, antibodies or other chemicals, can be used with nanoparticles to label highly specific tumors, which are useful for early detection and screening of cancer cells.

For cancer diagnostics, imaging of tumour tissue with nanoparticles has made it possible to detect cancer in its early stages. In lung cancer, the detection of metastases can be determined by developing immune superparamagnetic iron oxide nanoparticles (SPIONs) that can be used in MRI imaging with the cancer cell lines as the target for the SPIONs. Recent studies have shown a high specificity of SPIONs with no known side effects, making them suitable building blocks for aerosols in lung cancer MRI imaging.

Magnetic powder imaging has also been used in tomographic imaging technology where it has shown a high resolution and sensitivity to cancer tissues. In animal experiments, nebulization of the lungs have been achieved using magnetic nanoparticles (MNPs) with Epidermal growth factor receptor (EGFR), a commonly expressed protein in non-small cell lung cancer (NSCLC) cases as a target. Further, in vitro studies using nanosystem for positron emission tomography (PET) has also been developed based on self-assembled amphiphilic dendritic molecules.

These dendritic molecules spontaneously assemble into uniform supramolecular nanoparticles with abundant PET reporting units on the surface. By taking advantage of dendritic multivalence and the enhanced penetration and retention (EPR) effect, the dendritic nanometre system effectively accumulates in tumors, resulting in extremely sensitive and specific imaging of various tumors while reducing treatment toxicities.

Nanotechnology Tools Used in Cancer Diagnosis:

In current research, nanotechnology can validate cancer imaging at the tissue, cell, and molecular levels. This is achieved through the capacity of nanotechnology applications to explore the tumour's environment, for instance, pH- response to fluorescent nanoprobes can help detect fibroblast activated protein-a on the cell membrane of tumour-associated fibroblasts. Hereon, we will discuss some nanotechnology-based spatial and temporal techniques that can help accurately track living cells and monitor dynamic cellular events in tumors.

Near Infrared (NIR) Quantum Dots

The lack of ability to penetrate objects limits the use of visible spectral imaging. Quantum dots that emit fluorescence in the near-infrared spectrum (i.e., 700-1000 nanometers) have been designed to overcome this problem, making them more suitable for imaging colorectal cancer, liver cancer, pancreatic cancer, and lymphoma.

A second near-infrared (NIR) window (NIR-ii, 900-1700 nm) with higher tissue penetration depth, higher spatial and temporal resolution has also been developed to aid cancer imaging. Also, the development of a silver-rich Ag2Te quantum dots (QDs) containing a Sulphur source has been reported to allow visualization of better spatial resolution images over a wide infrared range.

Nano shells

Another commonly used nanotechnology application is the use of nano shells. Nano shells are dielectric cores between 10 and 300 nanometers in size, usually made of silicon and coated with a thin metal shell (usually gold).

These nano shells work by converting plasma-mediated electrical energy into light energy and can be flexibly tuned optically through UV-infrared emission/absorption arrays. Nano shells are desirable because their imaging is devoid of the heavy metal toxicity even though their uses are limited by their large sizes.

Colloidal Gold Nanoparticles

Gold nanoparticle (AuNPs) is a good contrast agent because of its small size, good biocompatibility, and high atomic number. Research shows that AuNPs work by both active and passive ways to target cells. The principle of passive targeting is governed by a gathering of the gold nanoparticles to enhance imaging because of the permeability tension effect (EPR) in tumour tissues. Active targeting, on the other hand, is mediated by the coupling of AuNPs with tumour-specific targeted drugs, such as EGFR monoclonal antibodies, to achieve AuNP active targeting of tumour cells. When the energy exceeds 80kev, the mass attenuation rate of gold becomes higher than alternative elements like iodine, indicating a greater prospect gold nanoparticle. Rand et al. mixed AuNPs with liver cancer cells and found that using X-ray imaging, the clusters of liver cancer cells in the gold nanocomposite group were significantly stronger than those in the liver cancer cells alone. These findings have important implications for early diagnosis, with the technique allowing tumors as small as a few millimetres in diameter to be detected in the body.

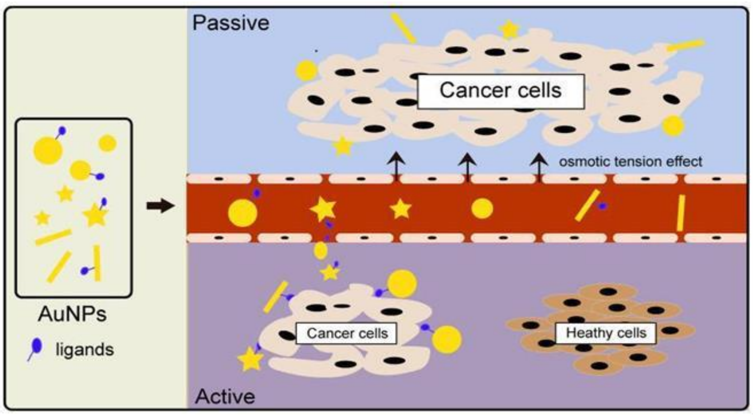

Fig.no. 6 Nanotechnology Tools Used in Cancer Diagnosis Various types of gold nanoparticles.

NANOTECHNOLOGY IN CANCER THERAPY

Tools of Nanotechnology for Cancer Therapy

The development of nanotechnology is based on the usage of small molecular structures and particles as tools for delivering drugs. Nano-carriers such as liposomes, micelles, dendritic macromolecules, quantum dots, and carbon nanotubes have been widely used in cancer treatment.

1.Liposomes

Liposomes are one of the most studied nanomaterials, which are nanoscale spheres composed of natural or synthesized phospholipid bilayer membrane and water phase nuclei. Because of the amphiphilicity of phospholipids, liposomes form spontaneously, allowing hydrophilic drugs to preferentially stay in the monolayer liposome while hydrophobic one's form before the multilayer liposome. Some drugs could be incorporated into liposomes by exchanging them from acidic buffer to the neutral buffer. Neutral drugs can be transported in liposomes also, but due to a poor avidity for acidic environments, they are not readily released from the inside of the liposomes. Other mechanisms of drug delivery are the combination of saturated drugs with organic solvents to form liposomes. Under the influence of the EPR effect, the vesicle of size around 4000 or 500 nm can be allowed into the tumour by the gaps in vessels. In tumors they can fuse with cells, are internalized by endocytosis, and release drugs in the intracellular space. In the case of the appropriate pH, redox potential, ultrasonic and under the electromagnetic field, the liposome can also release the drug through passive or active ligand-mediated activity. The targeted therapy has an advantage in the vascular system, micro metastases, and blood cancers. It has been shown that the half-life of liposome is affected by size. The liposome up to 100 nanometers easily penetrate the tumour and stay longer, while the half-life of the bigger liposome is shorter because they are easily recognized and cleared by the mononuclear phagocyte system. Liposome-bound antibodies target tumour-specific antigens to ensure active targeting and then transport drugs to the tumour. With a lot of pharmacokinetic benefits, some liposomal drugs are approved for clinicaltherapy.For instance, liposomal forms of Adriamycin have been used for the management of metastatic ovarian cancer where they have shown appreciable clinical benefit.

2.Carbon Nanotubes

Based on the structure and the diameter, Carbon nanotubes (CNTs) can be categorized into two kinds, the single-walled CNTs (SWNTs) and the multiwalled CNTs (MWNTs). The SWNTs are composed of monolithic cylindrical graphene, and the MWNTs are composed of concentric graphene. Because of the physical and chemical properties of carbon nanotubes, that include surface area, mechanical strength, metal properties, electrical and thermal conductivity, it is a candidate well suited for large-scale biomedical applications. Carbon nanotubes also possess a property that allows them to absorb light from the near-infrared (NIR) region, causing the nanotubes to heat up by the thermal effect, hence can target tumour cells. The natural forms of carbon nanotubes promote non-invasive penetration of biofilms and are regarded as highly competent carriers for the transport of various drug molecules into living cells. Due to the suitability of carbon nanotubes, drugs such as paclitaxel are assembled with them and administered both in vitro and in vivo for cancer treatment.

3.Quantum Dots

Quantum dots (QDs) are small particles or nanocrystals of semiconductor materials between 2 and 10 nanometers in size. The ratio of the height of the surface to the volume of these particles gives the QDs the intermediate electron property which is between a mass semiconductor and a discrete atom. Over the years, various QDs based techniques such as modification of QD conjugates and QD immunostaining have been developed. With the improvement of multiplexing capability, QDs conjugation greatly exceeds the monochromatic experiment in both time and cost-effectiveness. Moreover, at low protein expression levels and in a low context, QD immunostaining is more accurate than traditional immunochemical methods. In cancer diagnosis, QD immunostaining is a potential tool for the detection of various tumour biomarkers, such as a cell protein or other components of a heterogeneous tumour sample. Quantum dots can gather in specific parts of the body and transfer the drugs to those parts. The ability of the QDs to concentrate in a single internal organ makes them a potential solution against untargeted drug delivery, and possibly avoid the side effects of chemotherapy. The latest advancement in surface modification of QDs, which combine with biomolecules, including peptides and antibodies, in vivo, can be used to target tumors and make possible their potential applications in cancer imaging and treatment. Some studies combine QDs with prostate-specific antigen to label cancer, while others use QDs to make biomarkers that speed up the process with such immune markers having a more stable light intensity than traditional fluorescent immunomarkers.

High sensitivity probes based on quantum dots have been reported for multicolour fluorescence imaging of cancer cells in vivo and can also be used to detect ovarian cancer marker cancer antigen 125 (CA125) in different types of specimens (such as fixed cells, tissue sections, and xenograft). Besides, the light stability of quantum dot signals is more concrete and brighter than that of traditional organic dyes. Chen et al. successfully detected BC using quantum-dot-based probes, confirming that unlike traditional immunohistochemistry, quantum dot immunohistochemistry (IHC) can detect the very low expressions of Human Epidermal Growth Factor Receptor 2 (HER2) as well as multichannel detection.

Conclusion

Nanotechnology has shown a lot of promise in cancer therapy over the years. By their improved pharmacokinetic and pharmacodynamic properties, nanomaterials have contributed to improved cancer diagnosis and treatment. Nanotechnology allows targeted drug delivery in affected organs with minimal systemic toxicities due to their specificities. However, as with other therapeutic options, nanotechnology is not completely devoid of toxicities and comes with few challenges with its use including systemic and certain organ toxicities, hence, causing setbacks with their clinical applications. Given the limitations with nanotechnology, more advancements must be done to improve drug delivery, maximize their efficacy while keeping the disadvantages to the minimum. By improving the interactions between the physicochemical properties of the nanomaterials employed, safer and more efficacious derivatives for diagnosis and treatment can be made available for cancer management. In sum, we sought to highlight the key advantages of nanotechnology and the shortfalls in their use to meet clinical needs for cancer. Adding to that, the therapeutic benefits of nanotechnology and future advancements could make them a therapeutic potential to be applied in other disease conditions. These may include ischemic stroke and rheumatoid arthritis which would require targeted delivery of a suitable pharmacologic agent at the affected site.

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