GOLD NANOPARTICALS USE IN CANCER TREATMENT

By

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Declaration

1. It is hereby declared that
2. The thesis submitted is my/our own original work while completing degree at Brac University.
3. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
4. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
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Ethics Statement

This study does not involve any human and animal trial

Abstract/Executive Summary

Cancer is a serious illness that necessitates a more effective, non-invasive treatment, linked to the least possible adverse effects. Now a days various nanoparticles are constantly use for various cancer diagnosis. Some studies show many potential applications in treatment of cancer disease by using gold nanoparticles. This Coagulated gold has been extensively researched in the direction of its possible use in medicine for many decades. Nevertheless, the composite and assessment of different gold nanoparticles have recently garnered significant attention from experts. Contemporary research validates the many benefits of nanogold compared to other nanomaterials, mostly attributed to well optimized procedures for manufacturing gold nanoparticles of various area, which possess distinct functionalities. By modifying the superficial of nanogold crump with abundant targeting as well as functional chemicals, the potential biological applications of these particles are greatly expanded, especially in the field of various cancer treatment. The biocompatibility and controlled biodistribution patterns of functionalized gold nanoparticles make them very suitable for the foundation of novel therapeutics.

Keywords -nanotechnology, nanotherapeutics, cancer therapy, cancer diagnosis

Acknowledgement

First and foremost, I would like to express my gratitude to the Almighty for his endless gifts, which have been given to me in an effort to provide me with the strength and determination to complete this project.

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Finally, I'd like to convey my thanks to my parents, who never cease to inspire me to push myself beyond my comfort zone. I would not have made it this far without the daily prayers and unconditional love of my family and loved ones. I'd also want to express my gratitude to all of the folks who, whenever they were called upon, went above and beyond to assist me.

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List of Acronyms

GNPs	Gold Nanoparticles
CSC	Cancer Stem Cell
MQ	Mefloquine
PE	Phosphatidyl ethanolamine
TK	Tyrosine Kinase
TEM	Transmission Electron Microscope
DMF	Dimethylformamide
CAR-T	Chimeric-Antigen Receptor
GEM	Gemcitabine
AC-NPs	Antigen-Capturing Nanoparticles
PTT	Photothermal therapy
RFA	Radiofrequency Ablation
CTAB	Cetyltrimethylammonium bromide
MPS	Multifunctional Phagocyte System
SPR	Surface Plasmon Resonance
EGFR	Epidermal Growth Factor Receptors
MRI	Magnetic Resonance Imaging
NHL	Non-Hodgkin lymphoma

CHAPTER 1

Introduction

Around 1–100 nm, the word is most commonly used to refer to biologically relevant particles in biology laboratories. Nanoparticle arrangements consist of core natural In modern times, the term cancer has become a common approach to refer to a classification of inherited libciouses. Abnormal cell division, or uncontrolled cell division. In genetics, most carcinogenesis is explained by genetic mutations. It is well established that cancer is one of the leading global causes of death. In 2012, there were an estimated 14 million new cases of cancer and 8.2million cancer-related deaths worldwide [NCI. National Cancer Institute [accessed July 29, 2018]. The updated number of new cases per year is likely to increase to 24 million in the next two decades, and approximately 40% of people are predicted to develop cancer during their life.Given all this, there is a strong case for novel strategies to enhance the efficacy of cancer treatments. A very significant development is occurring in the area of nanotechnology and nano science that has led to optimisms on overcoming the classic limitations of cancer modalities. These days a greater deal of interest is on nanoparticles, which are composed of noble metals.

1.1. what are nanoparticles

Nanoparticles represent another class of intermediate atoms and bulk materials wherein selective optical, electrical, catalytic and medicinal properties are exhibited.35 In organic molecules and inorganic molecules (e.g., iron oxide, gold, and carbon nanotubes), hybrid matrices (composed of more than two of the previous elements). Nanoparticles are also referred to as magnetic nanoparticles and nanobubbles. They are highly effective for medical imaging, drug distribution and in vivo tracking of cells in living animal models [1]. For some recent years, their notable characters, including bacteria-killing activity, excellent anti-oxidative ability, and abundant thermal conductivity, have attracted much attention.

1.2. various forms of nanoparticles

Some novel nanoparticles are-

Alloy: The nanoparticles of alloy have distinct structural attributes than their respective parent bulk materials. Because silver (Ag) is the most conductive metal filler of all metals, and its oxides are very much better conducting than many other metals. Ag flakes are widely used. The physical chemical properties of these bimetallic alloy nanoparticles, which are controlled by both of the two metals, are significantly improved compared to their mono metallic nanoparticle counterparts. [2]

Magnetic: The magnetic nanoparticles included magnetite (Fe_3O_4) and maghemite (Fe_2O_3) which have been recognized due to their use in various biosystems. This treatment type is used in the treatment of cancer (magnetic hyperthermia), processing (separation) of stem cells, targeted drug delivery, gene therapy, DNA analysis, and magnetic resonance imaging (MRI).

Silver: When it comes to killing bacteria, viruses and other eukaryotic microbes, nothing compares to the power of silver nanoparticles. It is the most abundant nanomaterial type. They are also used as an antibacterial agent in sunscreen creams, other skin care products and the textile industry.

1.3 Gold nanoparticles in cancer therapy

More recently, AuNPs have drawn significant attention in the medical mix with the field of oncology. Gold was one of the first metals to be identified thousands of years ago. This is a bright yellow, very dense, not very hard, malleable metal in its elemental form, solid at room temperature, and displays a wide variation of geometric shapes and sizes, gold nanoparticles (AuNPs) are likewise tunable by straightforward synthetic techniques… The size, shape, and surrounding environment of AuNPs can be tuned to control various physical and chemical properties such as catalysis, melting temperature, electric conductivity, and hue. The design flexibility is severely limited by the performance pursuit and application specificity in organic nanoparticles. One of the unique optical properties of AuNPs is size and shape dependent76,77. This property is related to the surface plasma resonance (SPR) phenomenon, which is the coherent oscillation of free electrons. Due to its optical property, gold nanoparticles (AuNPs) have been demonstrated to be very suitable for many applications as nano-objects. Applications include biosensors, imaging agents, and photothermal agents for medical diagnosis, imaging, and therapy. In the field of other inorganic nanomaterials, this application was quite rare. Simultaneously, the high surface area and strong surface activity of AuNPs underscore the potential for functionalization and high loadings on NP. It is well recognized that AuNPs can conjugate directly or indirectly as well as come in contact with a plethora of molecules (Table 1) [4,5]. These may include drugs, nucleic acids (DNA or RNA), proteins or peptides, antibodies, particular ligands, as well as other types of molecules. Both of such interactions can occur. The ability to associate with other molecules and the diversity of these molecules greatly increase their biochemical activity and expand the possibilities of use of anticancer drugs.

Modification of amphiphilic materials has been shown to provide gold nanoparticles (AuNPs) with high stability under physiological conditions. Another unique work property that metallic gold has is inert, which makes it biocompatible. These properties of AuNPs have led to the basis of increasing interest in the use of AuNPs as nano-vectors in oncology. [6-9]

1.4 Aim of the project

Nanoparticles are now amenable to testing for various therapeutic environments that do not fall under the typical auspices of oncology. But in this article, I'm going to focus on cancer, which according to DMG accounted for more than 10 million deaths in 2020, or over one in six people. There is a huge type of treatment for cancer patients, but the outcome is not good. For such diseases, there is always a process of having everything done for medicines or treatment paradigms. GNPs are one of those. We aim to address this significant clinical challenge in cancer therapeutics by investigating the intervention modalities that might be applicable here.

1.5 objective of this study

The aim of this study is –

- To know how do gold nanoparticles affect cancer treatment
- To realize the effects of nano medicines for the elimination of cancer
- Improving decisions about nanotechnology tailoring across cancer-therapeutics

CHAPTER 2

methodology

methodology

This article provides a comprehensive overview of several cancer treatment options. This includes gold nanoparticles. The information for this review forum article is compiled from peer-reviewed studies, news, published academic articles, and websites. Additionally, for this study article from prestigious journals such as Springer, Nature, Cells, The Lancet, MDPI, Frontiers, Biopharma, Taylor and Francis have been reviewed. A large number of articles were consulted to obtain information which helped to determine the importance and future direction of autophagy. All information is carefully and appropriately referenced. As a result, there will be more understanding. A few times I have tried to find gaps or hidden information in the existing literature. Meanwhile There are approximately 120 clinical studies investigating autophagy mechanisms initiated at a specific time or period [10]. Most research has focused on therapeutic autophagy. cancer and it has shown promising results, for example when chloroquine or hydroxychloroquine are used separately or in combination with other agents. Autophagy can be controlled by the development of nanoparticles. in which some surrounding protein aggregates or organelles are damaged by the activity of the nanoparticle's two membrane receptors. By eliminating abnormal accumulations of proteins in cells This mechanism in nerve cells protects against cognitive decline. Recently, gold nanoparticles have been recognized as a potential treatment for various diseases, including cancer. Many studies indicate that nanoparticle thickeners can inhibit the growth of cancer cells in precancerous lesions (Galluzzi et al. 2015). However, in advanced cancers Increased suppression of autophagy has been proposed for both.[11]

Chapter 3

properties and applications-

Through well-matched synthesis techniques, AuNPs may be finely tuned on the nanometer scale in terms of size, shape, and dimension, endowing them unique features. NP size & shape are major characteristics that influence many of the particulate properties such as stability, mobility, compatibility. Hence the properties of the biofilm need to be customized for the specific biomedical applications. Drug-delivery–type nanoparticles must be within certain size ranges to cross physiologic barriers or enter into the destination cells, and the size of the nanoparticles must also be large enough to deliver an adequate mass of therapeutic agents to the site. Gold of Nanotubes Biological Synthesis from Bacillus Licheniformis [12]

Indeed, at the nano scale the physical and chemical properties (including its fluorescence, its electrical conductivity or chemical reactivity, etc.) of an element can be drastically different to those of its bulk equivalents. Gold has a characteristic yellow color in bulk form and AuNPs (of less than 100 nm particle) show red/yellow and blue/purple (for larger, greater-100 nm, particles) color depends on their shape and composition [13-15], one of the greatest physical properties of gold. The believed reactivity of colloidal gold much larger than the bulk gold, thus transferring its area of applicability [13, 14] with optoelectronic, catalytic and antioxidant properties besides the possibility of surface modification.

3.1. Biological distribution, toxicity and functionalization

This gives rise to the fact that biodistribution and toxicity are seminal parameters to be determined before application of gold nanoparticles into anticancer treatment and diagnosis. These factors might also impact the reliability of patient-specific AuNPs. Some concerns exist about the inflammatory response or potential retention of metal in the organism, but these have not been fully characterized in long-term in vivo studies. Now that these tests are finally being factored into the equation, this issue is getting studied up one side and down the other by scholars. Additionally, with variations in doses, different animal or cellular models, differences in the models used for particle preparation and experiments, and possible aggregation of the AuNPs in physiological conditions, the results remain inconsistent [16,17].

3.2 Applications of gold nanoparticles –

Application areas for gold nanoparticles continue to expand, including:

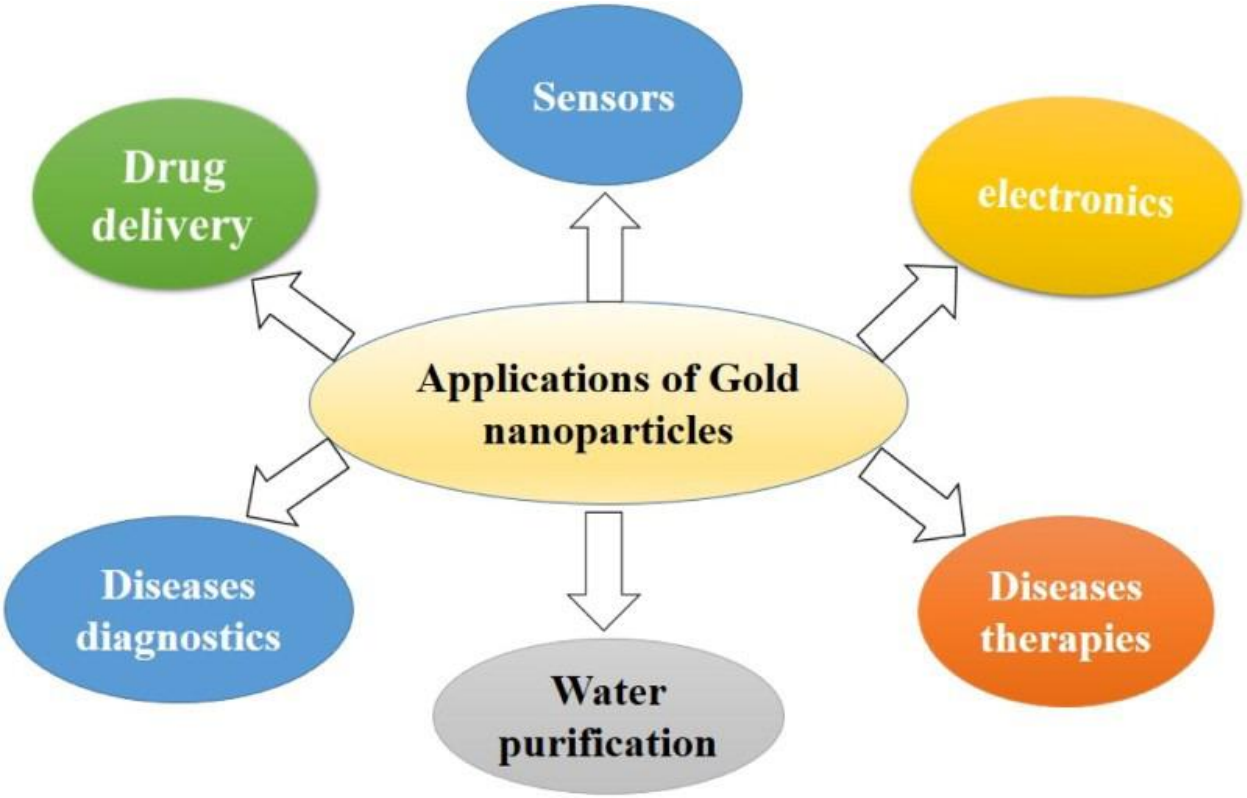

Figure 1- application of gold nanoparticles

[Dhal, N.K. A Review on Gold Nanoparticles. Int. J. Pharm. Bio. Sci. 2015].

- **Electronics** – Gold nanoparticles are used bridge conductors from printable inks to electronic chips Nanoparticles, Electronic world shrink, 1 The nanoparticle acts as whatever piece of chip you would require. Now they use nanoscale gold nanoparticles to make connections between the resistors, conductors, and other electronic components on a chip.

- **Therapeutics delivery** – There are therapeutic agents that can also be attached to the surface of gold nanoparticles. Due to a high surface area-to-volume ratio, gold nanoparticles can coat their surfaces with hundreds of molecules (therapeutics, targeting agents, anti-fouling polymers, etc).
- **Sensors** – Different types of sensors can be developed using gold nanoparticles. For example, a colorimetric sensor can determine the edibility or inedibility of food with the help of gold nanoparticles. Other methods, such as surface enhanced Raman spectroscopy, employ gold nanoparticles as a substrate to detect vibrational energies of chemical bonds. This is also a strategy that may be applied for proteomics, computing toxins and other molecules, without any labels.
- **Probes** – Gold Nanoparticles not only scatter light, but also produce a wide range of gorgeous colours on dark-field microscopy. Currently, the dispersed hues of gold nanoparticles are applied in biological imaging applications. 5 Gold nanoparticles are also relatively dense particles, which is why they can serve as probes for transmission electron microscopy as well.
- **Diagnosis** – For the diagnosis of heart diseases, cancers and infectious agents, Golden nanoparticles are used for detected biomarkers. They are also found in lateral flow immunoassays, the fairest of which is the home pregnancy test.
- **Catalysis** –Gold nanoparticles can catalyze numerous chemical reactions. The catalysis of a reaction (e.g. the oxidation or in some cases, the reduction of nitrogen oxides) can be controlled at the surface of the gold nanoparticle. Abstract: Finally, the article covered the making of gold nanoparticles for fuel cell applications. These applied to both automotive and the display industry.

- **Protein, Peptide and Nucleic Acid Delivery**-Their tunable size [21] can be used as a carrier for delivery of peptides, proteins and nucleic acid like DNA Cationic 4° [22] ammonium group functionalized gold nanoparticles can electrostatically bind to the DNA plasmid and protect DNA from exchange reaction of thiol enzymatic digestion Peptide carriers. polyethylene glycol at both ends, and proteins at the other, have reported that the cationic tetra alkyl gold half binaries. Gold nanoparticles also as an insulin carrier Chitosan coated gold nanoparticles have also been shown to readily adsorb insulin Therefore gold nanoparticles can conjugate two the surface of their PEG spacer and to improve transmucosal particulate dosage and insulin delivery.
- **Photo-Physical Property** -GNPs induce local heating upon irradiation with light within 800 to 1200 nm.[23] destroy tumors by their photo thermal interaction high surface area, photo physical and optical characteristics gives special class because these have high significance in chemotherapy, cancer diagnosis and drug delivery.

Chapter 4

Cancer

Cancer is a term used for diseases in which abnormal cells divide without control and can invade nearby tissues and has the potential to spread to other parts of the body. In healthy development, cells have a carefully regulated cycle of growth, division, and death. But abnormal cancer cells proliferate uncontrollably, leading to malignant and benign tumors. Malignant tumors are made up of tumor cells that do not just penetrate surrounding tissues but also have the potential to metastasize or spread to other parts of the body. Cancer is a global health challenge associated with a high risk that can result in one in six deaths in the world. The cancer experience has for too long been a maddeningly complex dance. Conventional approaches that previously performed on melanoma are surgery, chemotherapy, and radiotherapy, but in recent years some remarkable progress has been made on the approaches such as stem cell therapy, targeted therapy, ablation therapy, nanoparticles, natural antioxidants, radionics, chemo dynamic therapy, sonodynamic therapy and ferroptosis-based therapy. Nanomedicine for Cancer: Current strategies in technology have focused on polymeric nanoparticles employed for the targeted delivery of bioactive agents to desired tissues in the field of oncology and development of safe and efficient cancer nanomedicines. Stem cell treatment indicated multiple therapeutic potentials to regenerate and repair the diseased/damaged tissues such as targeting both primary and metastatic foci of cancer, whereas nanoparticles have gained interest as unique diagnostic and therapeutic modalities. It showed breakthrough potential targeted therapy suppressed the growth and spread of the targeted cancer cells, with minimal damage to the healthy cells. Ablation therapy has emerged as a skin-sparing procedure that burns or freezes cancers without performing open surgery. So, among the components, the antioxidants were shown to be the primary molecule that can scavenge the free radicals and neutralize them to prevent or treat cancer. Several promising new technologies are being explored in clinical trials, and some have even been approved. [24-27]

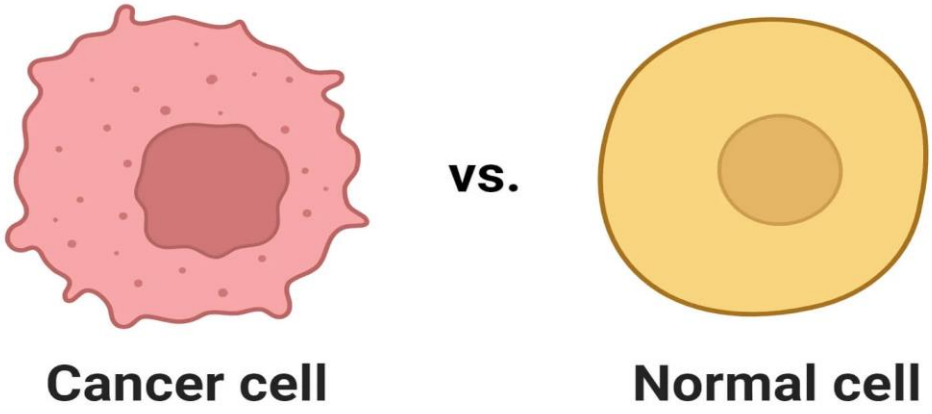

Figure 2 – normal cell vs cancer cell

[Fuchs, E., Tambar (2004)]

4.1Cancer stem cells

Epigenetic mutations lead to the generation of cancer stem cells (CSCs) in normal stem/ precursor/progenitor cells. They play an important role in the tumor carcinogenesis, metastasis and recurrence, providing hope for the potential application of solid tumors treatment. [28] Stem cells have several action mechanisms in treating the tumor. E.g., the horming, a rapid trafficking of HSCs to their own specialized stem cell niches in the BM, leads to engraftment before first giving rise to specialized blood cells on subsequent transplants. In addition to Matrix Degradative enzyme (MMP-2/9) secretion [29–33], this mechanism is based on the mediating action of stem cells CXCR4 receptor and their interaction with endothelial cells by latching LFA-1, VLA-4/5, and CD44. The second mode is the migration of mesenchymal stem cells (MSCs) to the tumor microenvironment (TM) after they are recruited by the CXCL16, SDF-1, CCL-25, and interleukin-6 released by tumor cells. The third mode is the differentiation of MSCs in tumor cells and the contribution of these cells to the development of the tumor stroma. [34–37] As a transplant, these stem cells can not only act by releasing paracrine factors, including EVs and soluble materials, but also have the capacity to differentiate to give rise to all blood cell types. There are different methods to use stem cell therapy against cancer, including HSC transplantation, MSC infusion, therapeutic carriers, immune effector cells, and vaccine [38,39]. However, some breakthroughs, such as therapeutic dose control, low cell targeting, and retention at tumor sites, will need to be further studied and resolved. The existing results of stem cell technologies are very promising for the treatment of tumors, but to prove safety and efficacy is still a challenge before clinical trials.

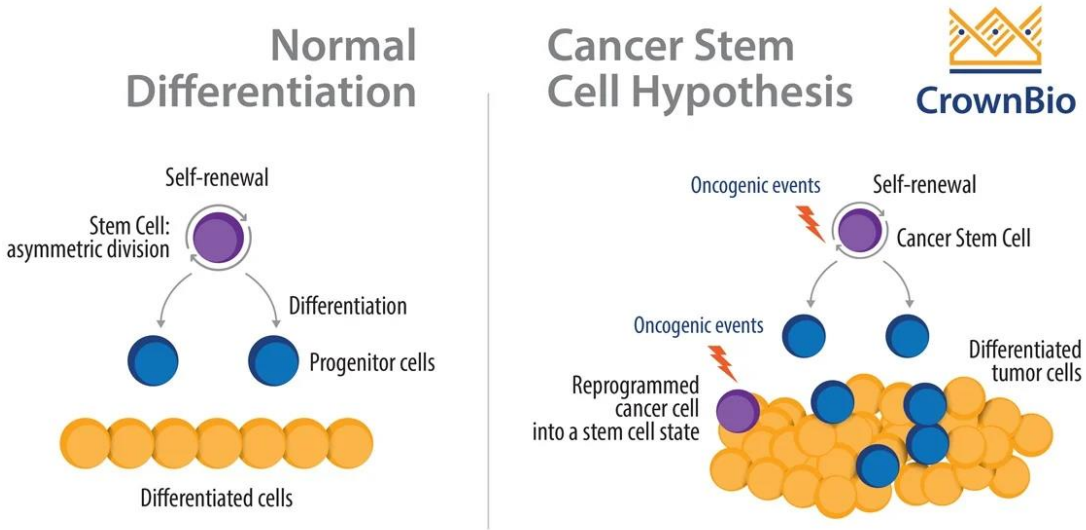

Figure-3 cancer stem cell

[Peyton A .et .al 2023)]

4.2 cancer cell development

The only potential of the metastasizing cancer cell is repetition! These abnormal and over proliferating cells infiltrate into malignant carcinoma process and inevitably invade to the biological tissue in the body, and are responsible for the development of metastasis. Aberrant versions of all of these proteins that participate in cell-cell attachment antiregulation are implicated in cancer metastatic spread by regulating migratory behavior of cancer cells. MMPs: Matrix metalloproteases play a significant role in metastasis initiation and metastasis progression and thus tumor dissemination. [40] They fail attachment of cancer cells: Receptors for cell-cell attachment are dysregulated. It encourages the ability to diffuse throughout the body through the blood and establish itself within other organs and tissues—the unregulated process by which cells divide and grow and develop produces cancer. The initiation of cancer requires two basic changes in the original cell, i) Genetic change and ii) A change in the cellular point of view, which later followed more changes started to the point of view of the cancer cell. Discusses the days-based genetic or cellular mechanism in cancer instances. Genetically speaking, those are mainly oncogenes and tumor suppression genes, which are considered key cancer genes during the early stage of cancer development. In general, the activation and deactivation manage inContact in the initiation and development of various "tumor repressors" genes. [41-44]

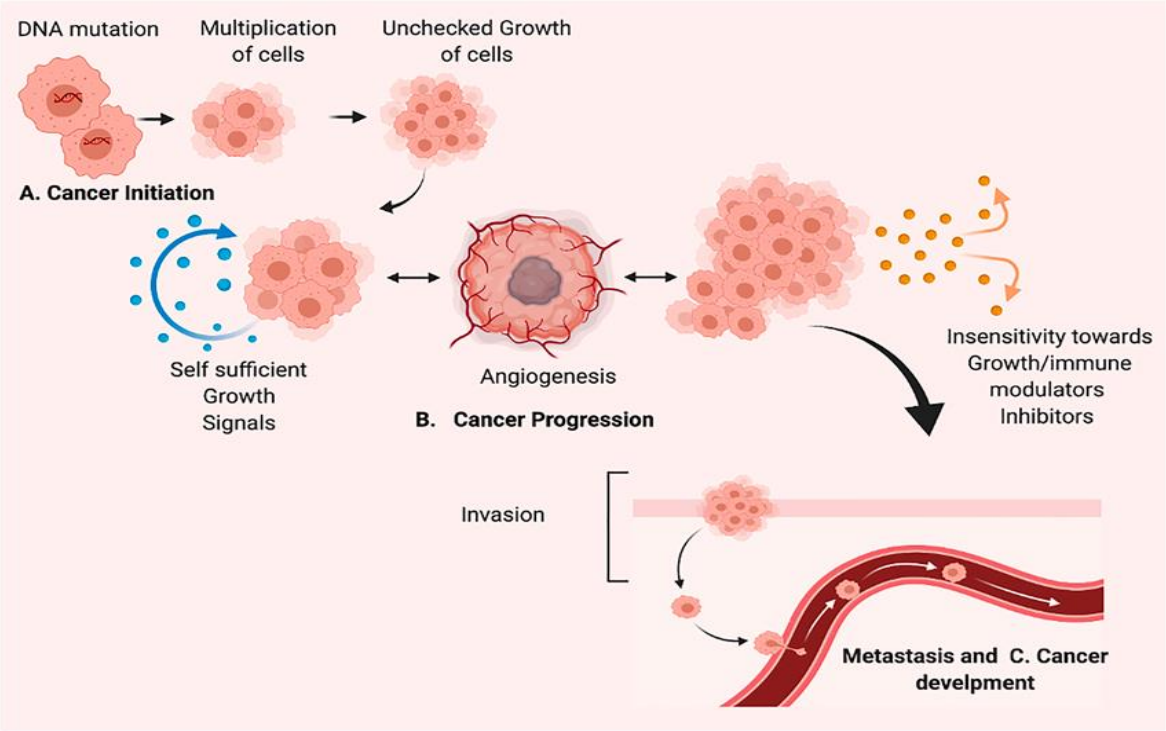

Figure-4 development of cancer cell.

(Hassan et al., 2014)

In addition, these complex genetic mechanisms range, genetic mutation, chromosomal abrasion or variation, i.e, addition or deletion, and differences in cell cycling. Alteration of the dysregulated signaling pathways in the regulatory mechanism of dividing cells: The cellular alteration includes the dysregulated signaling pathways involved in the regulatory mechanism of dividing cells. But also, the 8 hallmarks of cancer cells: Selective proliferative advantage i) Vascularization, immunomodulation. ii) Metabolic rewiring. iii) An exacerbating microenvironment (iv) Invasion/metastasis of tissue. v) Altered stress response. Process of cancer development Carcinogenesis, is predominantly a multi-step-up process. [45-47] Since it does not have the growth regulation, it gets started dividing very fast and hence it takes the form of several cells or tumors and travels to the other places by means of metastasis. In addition to genomic and cellular changes, several epigenetic changes, including hypomethylation and hypermethylation of oncogenes and tumor suppresser genes, depletion of hydroxy methylation, changes in histone acetylation patterns and cellular profiles of DNA methylation and miRNA have been associated with the vast majority of human cancers. Apoptosis is a type of programmed cell death that is involved predominantly in the control of cell growth and cell division in order to prevent uncontrolled tumorigenesis [48,49]. Meaning That Carcinogenesis is Damage, Insult, or Induction of a Change By a Variety of Modes — Physical, Chemical, Genetic and Pathogenic. The three broad stages of cancer development and establishment are initiation, promotion, and progression (Figure 1). The cancer initiator carcinogens with the help of various promoter molecules result in the formation of cancer. Similar to initiation of cancer, most carcinogens make irreversible damage in DNA. This damage is followed by a mutation in a specific genetic code that can be inherited to daughter cells and fast-dividing cells with a mutated pattern. Whatever the way of triggering, it can be internal or external, as in direct interact with surface receptors on cell or some what's indeterminate means. Hence, genetic alterations through a considerably irreversible genetic impact are required for cancer initiation by several mechanisms with the aid of: simple mutations, small deletions, transitions, and transversions in DNA molecules. These genetic alterations are often not structural changes in the DNA. We have irreversible and have upregulated cancer that is reversible but rather in genome-interactions mediated by the receptor domain. The protein that assists in the subduction of the cancer is actually based on the evolution of the cancer. The extrachromosomal environment (ECM) of cells is a reservoir of materials which can be inducers which can be specifically stimulate & active the cancer initiation or promotion mechanisms. Karyotypic instability is an irreversible phase; the advanced stage is defined by cancer evolution and progression [50-52]. But the old stage clearly shows the role of molecular variation, mutations in various tumor suppressor genes, oncogenes, proto-oncogenes and chromosomal deviations. Thus, deeper understanding of cancer etiology, initiation and progression of cancer has important implication towards clarity in cancer biomarkers for directing therapeutics and conceptual chemicals as carcinogens. Soissons the Thing which regulates organ engineering is seen fast, but invoked oncogenes and dyes-regulatory tumor spend is turned on most cancers. Mitosis and without apoptosis most cancers fetal types are certainly one of the qualities of various cell division and can't bear essentially the process cell loss of life. [53]

4.3 types of cancer cells

Cancer cells that start from other parts of the body as well. Some common types of cancer cells depending upon the cells of origin are-Carcinoma: Carcinoma starts in the cells that make up the tissue that cover the exterior of the body and some internal organs. It can also affect other organs, including the skin, lungs, breast, prostate and colon. Carcinomas Types: Adenocarcinoma begins in epithelial cells that secrete fluids or mucus, present in glandular tissues such as the breast, colon and prostate. Basal cell carcinoma develops in the lowest layer of skin's epidermis, the outer skin layer. Squamous cell carcinoma type of cancer found in squamous epithelial cells below the skin and in other organs. Because they originate in supportive tissues in the body — connective tissues like muscles, fat, blood vessels, bone or cartilage — these tumors are known as sarcomas. E.g.: The most common bone tumor, osteosarcoma, originates in and responds to a variety of drugs. Leiomyosarcoma is a rare, slowly growing tumor that arises from smooth muscle tissue. Kaposi Sarcoma appears on skin and in the lymph nodes and organs. [54-57] What are the types of leukemia We have: As mentioned earlier leukemia forms blood-forming cells. Most commonly, leukemia is a malignant transformation of white blood cells (although some leukemia types can as well arise from other types of blood cells). They are generally described as acute or chronic, and can originate from myeloid or lymphoid blood cell lineages. [58] Lymphoma–Blood cancer of lymphatic system. This affects lymph glands or some part of the lymphatic system related organs. Lymphoma is mainly classified into two categories: Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). [59] Multiple myeloma, or plasma cell myeloma, is about plasma cells, immune cells that make antibodies. "It is originated in the bone marrow and creates tumors in bones. Maturity Onset Diabetes of the Young (MODY) [60]

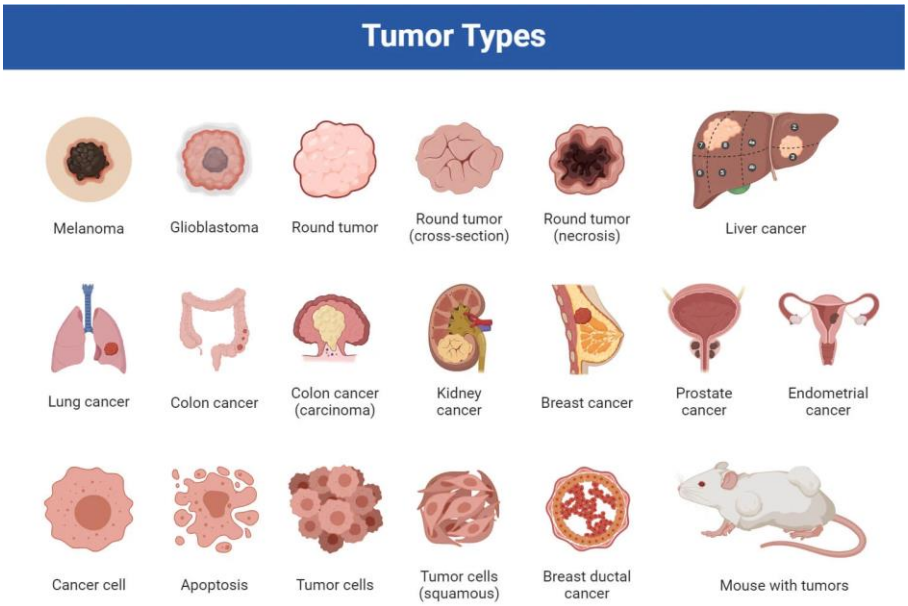

Figure-5 types of tumor cells

[Weinstein, JN Drug discovery: cell lines battle cancer Nature (201

4.4 different cancer treatment

The utilization of gold nanoparticles (AuNPs) in cancer therapy has attracted significant attention, largely due to their unique physicochemical properties. These properties include a small size, compatibility with biological systems, ease of functionalization, and the phenomenon of surface plasmon resonance (SPR). Such attributes facilitate the deployment of gold nanoparticles in a range of applications pertaining to cancer diagnosis and therapeutic interventions. This document offers a summary of the role of gold nanoparticles in diverse cancer treatment modalities**.** [61-63]

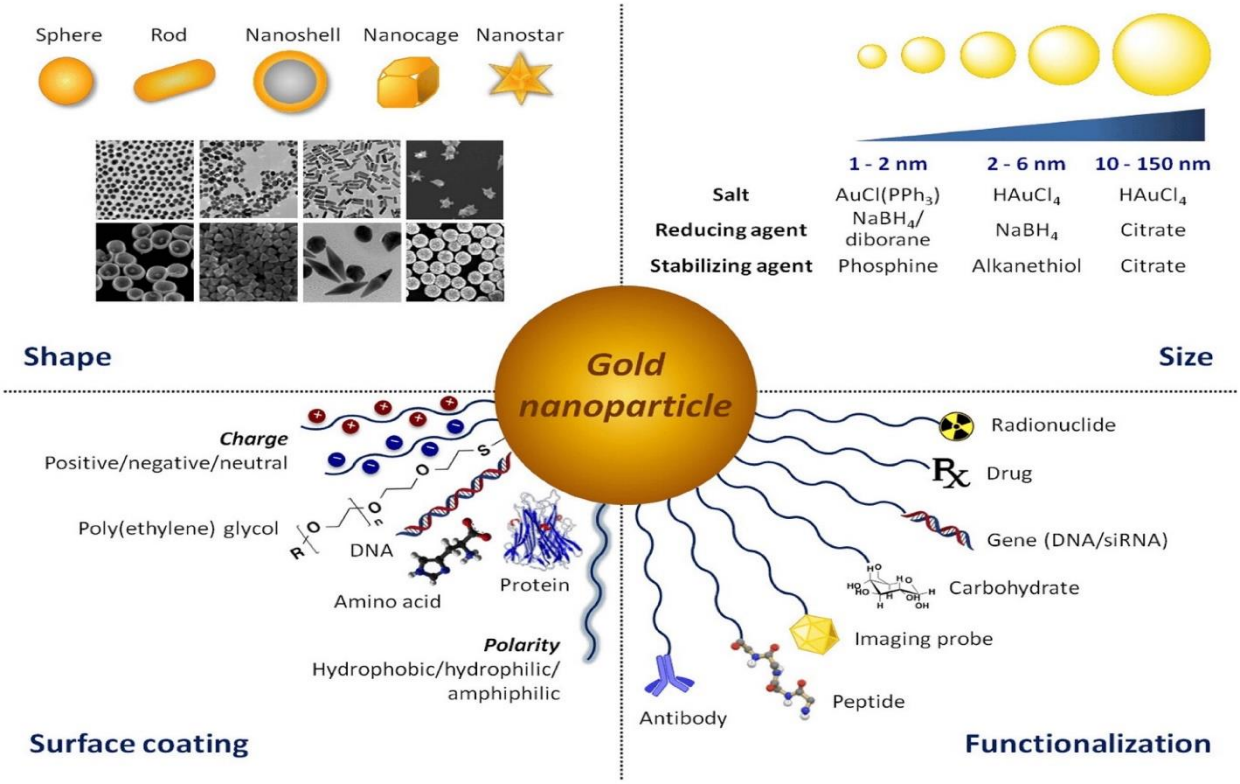

Figure – 6 This represents the synthetic versatility and functionalization properties of AuNPs. Various synthetic procedures and reducing or stabilizing agents allow fine-tuning of AuNP size and shape.

[Waldman, A.D.; Fritz, J.M.; Lenardo, M.J. A guide to cancer immunotherapy (2014)]

The utilization of gold nanoparticles (AuNPs) in cancer therapy has attracted significant attention, largely due to their unique physicochemical properties. These properties include a small size, compatibility with biological systems, ease of functionalization, and the phenomenon of surface plasmon resonance (SPR). Such attributes facilitate the deployment of gold nanoparticles in a range of applications pertaining to cancer diagnosis and therapeutic interventions. This document offers a summary of the role of gold nanoparticles in diverse cancer treatment modalities.[64]

4.5. lung cancer (A549) cell

Gold Nanoparticles (AuNPs) have been a subject of considerable interest as a potential tool in oncology, especially in lung cancer therapy. In lung cancer treatment, gold nanoparticles have emerged as promising vehicles for the usage of targeted medicines. Certain surface ligands, such as antibodies, peptides, or aptamers can be used to modify their surfaces, allowing for these nanoparticles to specifically bind to a malignant cell. These targeted modifications significantly improve delivery potency in relation to the administered drug and reduce adverse impacts on healthy tissues. This methodological strategy enables targeted application of various therapeutic modalities including chemotherapeutic agents, RNA-based therapies, or small molecular compounds directly to the tumor site. As a result, treatment outcomes are improved, showing the advantages of using gold nanoparticles in the context of cancer treatments. [65,66]

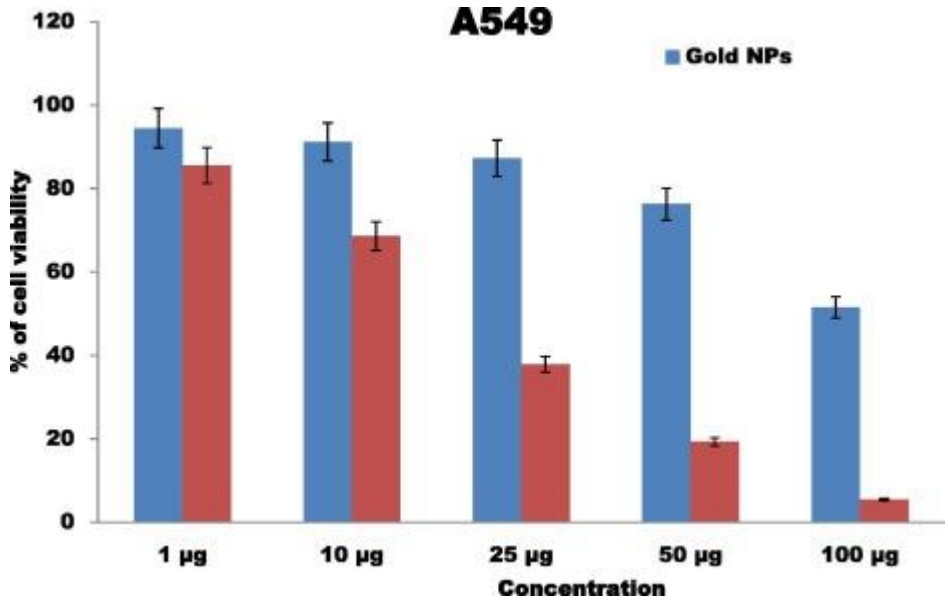

Figure 7 -Anticancer activity of gold nanoparticles against lung cancer (A549) cells.
[S.S. Dash, B.G. Bag, Appl. Nanoscience. (2012)]

A549 cell line was used to assess the cytotoxicity profile selectively according to the dosage and compared to standard anti-cancer agent cyclophosphamide. Anticancer activities of gold

nanoparticles were systematically analyzed at various concentrations such as: 1 μg, 10 μg, 25 μg, 50 μg and 100 μg.[67]

The antitumor activity of the gold nanoparticles against the A549 lung cancer cell lines was assessed, and the obtained data show a real cytotoxicity effect on the cancer cells, (Figure 7). The study showed that gold nanoparticle concentration significantly affects their anticancer property. Among the studied nanoparticles, the interaction with A549 cells was favorable at a concentration of 100 μg as can be seen in the table, while concentrations of 50 μg, 25 μg, and 1 μg exerted less effect. Moreover, a slight inhibitory effect was observed at the rate of 10 μg. In cancer therapy. [68]

4.6 liver cancer cell

Liver Cancer is the 7th most prevalent cancer in the world and the 4th leading cause of cancer mortality [68,69] Globally, incidence rates have consistently been on the rise. The most common ones are regions of Africa and Asia. Global estimates suggest that 70–80% of hepatocellular carcinoma (HCC) cases are attributable to chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV). [70] The antiproliferative efficacy of synthesized nanoparticles was evaluated using Hep2 liver cancer cell line. Wirtgen was obtained from Kings Institute, Guindy, Chennai. Logarithmically growing cells (1 × 10^4) were plated on 96-well plates and incubated overnight. Subsequently, the cells were treated 24 hours with varying concentrations of both gold nanoparticles (AuNPs) at 37 °C in CO2 incubator [71].

5 mg/ml MTT solution was added to each well (10 μl). The cells were then incubated for ~3 h to allow for formazan crystals to form. Afterward, 100 μl of DMSO was added for solubilization of formazan crystals produced, and after 1 hour incubation, the plates were read. Optical density was recorded at 540 nm, the reference filter being set at 620 nm. Percentage of live cells was calculated as follows for cell inhibition: Cell inhibition = (OD of treated cells / OD control) x 100. Viability = (100 - cell inhibition) [72-75]

4.7 brain cancer

Gold nanoparticles (GNPs) have exceptional potential for targeted therapeutic brain cancer treatment due to their specific physical, chemical, and biological properties. The unique inherent properties, small size, increased surface area, and functionalization properties make GNPs promising for a number of medical applications. Such applications include targeted therapy, diagnostic procedures, and imaging of brain tumors. The investigation into GNPs for the treatment of brain cancer is multifarious, seeing a varied repertoire of approaches and methodologies. [76,77] One such promising strategy that addresses the limitations a metastasis or penetration of the blood-brain barrier (BBB) pose is the direct delivery of chemotherapy and other therapeutic agents utilizing gold nanoparticles (GNPs) targeted towards brain tumor cells. The BBB presents a major obstacle for drug delivery into brain tissues and therefore, GNPs could act as novel carriers to translocate drugs across this barrier. Specificity towards tumor cells is achieved by utilizing engineered nanoparticles, thus minimizing the adverse effects on non-cancerous tissues. GNPs are

functionalized with several ligands, antibodies, or peptides that specifically target a specific marker on the cancer cell. These modifications not only guarantee that the therapeutic agents are localized and released at the tumor site, but they also significantly improve the overall efficacy of the treatment while reducing systemic toxicity at the same time.

Moreover, it is possible to chemically design the surface properties of GNPs to regulate the release profiles of the therapeutics. For instance, environmental stimuli (pH and temperature changes, or presence of specific enzymes found in tumor microenvironment) can be used to trigger the release of the encapsulated drugs. The controlled release capability also allows for an optimized therapeutic profile for the treatment, which is critical for enhancing clinical outcome. Gold nanoparticles (GNPs) have been widely recognized as contrast agents for different imaging modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), and optical imaging. [78] Here, the size, shape and surface characteristics of GNPs play a great role in the improvement of brain tumor sensitivity and sensitivity. The high atomic number of gold nanoparticles makes them suitable for enhancing CT imaging and improving the contrast of CT images. This property allows better visualization of brain tumors and facilitates tracking of disease progression through time. Moreover, GNPs can be combined with other imaging agents, such as fluorescent dyes or MRI contrast agents, as a multimodal imaging system. The resulting methodology provides a global understanding of tumors, accounting for both their structural and spatial characteristics, and in turn improving the diagnostic ability and accuracy of imaging techniques. Despite their promising therapeutic potential, there are several barriers to the clinical application of gold nanoparticles in the treatment of brain cancer [79]. First, we need to be clear about toxicity issues. Even though gold is generally considered non-toxic, the long-term effects of the usage of gold nanoparticles in the human body, especially in brain tissues, must be thoroughly studied. Nanoparticle build-up in different tissues could potentially have negative effects. Second major challenges include the ability of gold nanoparticles (GNPs) to cross the blood-brain barrier (BBB) efficiently. [80,81] Although GNPs has been engineered to penetrate the BBB, delivery to brain tumors in a highly controllable and efficient manner continues to be a significant challenge, particularly when the tumors reside deep within the brain. Finally, the regulatory approval pathway must be regarded as an essential component of the integration of gold nanoparticle treatment approaches into clinical practice. All new technology in medicine faces a rigorous process of regulation which seeks to establish the safety and efficacy of new approaches. In summary, it is important to consider these multiple barriers to the successful clinical use of gold nanoparticles in the management of brain cancer. [82-84]

4.8 breast cancer

Gold nanoparticles however has certain drawbacks as in the recent studies gold nanoparticles have been used as evidence in clinical treatments as well as formulations [85] Gold nanoparticles (AuNPs) have been identified as a potential medical therapeutic agent that can be used in treating breast cancer. Their unique physical, chemical, and biological properties enable them to be used in a wide variety of therapeutic modalities. This review describes about the contribution of gold nanoparticles in breast cancer treatment, starting with targeted drug delivery.

Gold nanoparticles can be modified or engineered for direct delivery of chemotherapy agents or other therapeutic compounds to cancerous cells of clinical importance. This knowledge in the

mechanism of delivery aims towards avoiding unwanted side effects, in addition to using the administered medicines much more efficiently. By functionalizing the surface of the nanoparticles with specific molecules, it is possible to preferentially target receptors that are over-expressed on the membranes of the tumor. Thereby, this allows drug-loaded nanoparticles to attach to the tumor cells and, in turn, permit the controlled release of the therapeutic agent. Not only does this technique increase the amount of drug at the tumor site; it also lowers the exposure of surrounding healthy tissues, thereby reducing the overall toxicity of the treatment. Gold Nanoparticles have immense potential for use in diagnostic imaging, especially in the early detection of breast cancer. These nanoparticles have benefited that stem from their high-specific surface area, customizable size, and simple surface modification with different imaging agents like MRI contrast agents and fluorescence probes. Such properties enable a more sensitive characterization of imaging methods. Combined with imaging modalities like MRI, ultrasound, or X-ray, gold nanoparticles allow for a more accurate visualization of tumors, and as a result, more accurate diagnosis and earlier detection. [86-88]

Besides their uses in imaging, gold nanoparticles have been used in gene therapy delivery as a breast cancer treatment as well. These nanoparticles are capable of delivering genetic materials, such as small interfering RNA (siRNA) or plasmids, that target specific genes involved in cancer progression. [89] This approach makes it possible either to silence specific genes thought to be involved in tumor growth, or to insert agents of therapy into malignant cells. The surface of these nanoparticles can be easily modified to optimize the binding of DNA or RNA molecules and enable targeted delivery of genetic material to breast cancer cells.

4.9 colon cancer

Gold nanoparticles (AuNPs) have attracted considerable attention in the treatment of colon cancer. Because of varying physical, chemical and biological properties. From 1 to 100 nm, these nanoparticles have unique properties on the surface that enhance their interaction with biological systems. [90,91] This is unattainable for larger particles. Gold Nanoparticles: Applications in Colon Cancer. This is particularly true in targeted drug delivery systems. Gold nanoparticles act as the multiple molecules like antibodies, peptides or other specific ligands that aid in precise capture of the cancer cells. in the context of colon cancer Specifically, these nanoparticles are engineered to target receptors or markers with higher expression levels on colon cancer cells' surfaces, including (but not limited to) folate and epidermal growth factor receptors (EGFR). There are two implications of this solution. [92] Hence, there is clarity on the possibility of more localized non-tumor treatment. I can be a ferry for chemotherapy agents gold nanoparticles provide targeted drug delivery in cancer therapy. Speaker reduce systemic side effects and improve treatment efficiency at the same time, as the drug concentration in the drug delivery system is a considerable improvement. And secondly, the capacity to release controlled drug is an integral component of this technique. Drugs can be encapsulated in nanoparticles and then released in a controlled way to target cancer cells. This release mechanism does not only optimize the therapeutic effect. but additionally enhances the overall treatment effect. Application of gold nanoparticles in colon cancer treatment development specifically targeted drug delivery and controlled drug release Shows progress in cancer treatment. It emphasizes the possible usefulness of nanotechnology in

enhancing treatment's effectiveness. [93,94] In magnetic resonance imaging (MRI), X-rays and other medical imaging modalities, gold nanoparticles are utilized as contrast agents. and computed tomography (CT), owing to its high atomic number and substantial X-ray scattering capability. [95-97] The functionalization of gold nanoparticles provides a number of enhanced beneficial properties, including but not limited to [98] Enhanced Tumor Imaging: The accumulation of these nanoparticles at tumor sites results in improved contrast delineation of neoplastic and adjacent healthy tissues. This improvement helps to detect and keep track of colonic cancer that leads to more accurate diagnoses. Tracking drug delivery gold nanoparticles can also track distribution and accumulation of drug-loaded nanoparticles in vivo to evaluate the therapeutic efficacy and delivery mechanisms. Gold nanoparticles are also being tested in gene therapy for treatment of colon cancer in addition to their roles in photography and drug delivery. These nanoparticles are effective at loading pearls (nucleic acids) that comprise small interfering RNA (siRNA) or plasmid DNA. that can control the expression of genes implicated in cancer development. The gene therapy approach yields various prominent outcomes. [99] Further, by employing targeted gene silencing strategies, such as with the use of RNA interference, selective oncogenes involved in colon cancer pathogenesis, including the mutant variants of mutant p53 or APC,[100] can be inhibited with efficacy and thus, reduce tumor proliferation. Gold nanoparticles also serve as vehicles for gene delivery that can regulate important cellular pathways such as those associated with apoptosis, growth arrest, and DNA repair [101,102]. Such strategies might encourage augmented apoptosis rates within colon cancer cells and would boost clinical outcomes.

CHAPTER 5

nanotechnology use for Cancer treatment

Due to different properties of gold nanoparticles, they were really good candidates for cancer treatment. Gold nanoparticles (GNPs) display unique optical behaviors and high absorption efficiency without photobleaching. Meanwhile, the increased surface area at nanoscale affords them superior light absorption and scattering ability [103,104]. Such a characteristic makes them a highly efficient system for cancer imaging and investigation. Gold nanomaterials, through specific geometries like nanocages, nanorods, and nano stars demonstrate localized surface plasmon resonance properties. They are also found useful in the targeted killing of cancer due to the surface plasmon resonance (SPR) phenomenon, which increases their therapeutic significance. [105] The SPR phenomenon initiates oscillation in the valence electron of a solid material under the incidence of light with a particular wavelength. At this time, the integrated absorption of light and release of photons at a similar frequency induce close/thermally devastation of the extent plasmon reverberation (SPR) impact afterward accumulating at the target site. [106] Commonly used anti-cancer drugs tend to be low in molecular weight, and have a median HLB index that makes them easily distributed throughout lipid membranes. [107,108] This quality can be ascribed to prompt dispersion of anticancer medications all through the body, with both target and non-target connective tissue, high primary pass digestion system by the organ of liver and expeditious disposal into kidneys. For that reason, nanocarrier systems containing an anticancer drug must not be readily cleared from the body and thus previously experience the ideal interaction between drug substrates and location. Arterial compartment parameters influencing nanoparticle activity include, but are not limited to quantity, structure, and surface morphology. These parameters control the alteration of blood circulation time and the pathway of nanocarrier's entry into the targeted cellular compartment. Thus, these parameters must be taken into consideration in the process of synthesizing metal nanoparticles like gold nanoparticle (GNPs).

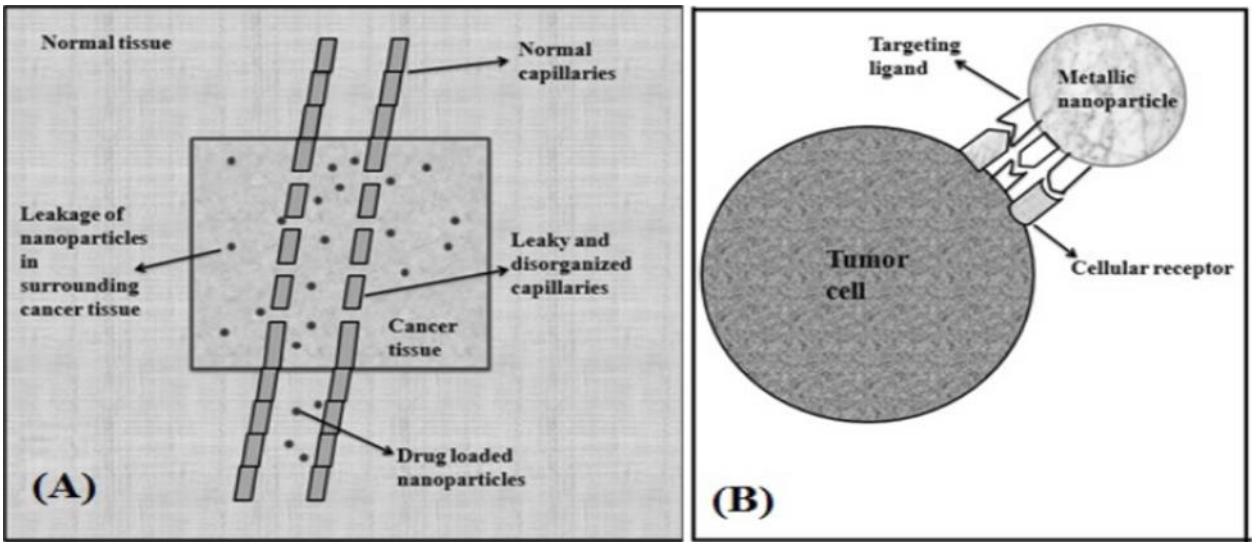

Figure 8- Gold nanoparticles are used to target cancerous tissue. The notion of active targeting comprises ligand receptor-mediated communication between the nanocarrier as well as target cell (B), whereas the concept of passive targeting involves determining the location of nanocarrier that will system in target tissue through the use of increased transparency and subsequent retention (EPR) effect (A).

[M.C. Daniel, D. Astruc, Chem. Rev. 104 (2004)

Gold-based nanoparticles allow for selective targeting of malignant areas using combination active and passive targeting methods. Only when the ability of nanocarriers to be entered by the multifunctional phagocyte system (MPS) phagocytes is >= Knowledge that such behavior is a process of competition to establish an effective and efficient targeting [47] Nanoparticles are mainly absorbed through reticuloendothelial system (RES) diffusion and rapidly excreted from the body. Modification of metallic NPs' exterior hydrophilic properties to prevent RES absorption Their high surface hydrophilicity prevents recognition by the RES system, which makes them invisible to macrophages. [48] For this purpose, nanoparticles are typically conjugated with polyethylene glycol (PEG) or its copolymers, PEG moieties prevent the interaction between blood opsonin's and nanoparticles, thus sterically prolonging their circulation time in the blood and increasing their retention time in neoplastic cells. Studies have shown that the upper limit of phagocytosis is between 1 and 2 μm. [109–111] It is thus reasonable to keep the sizes of metallic nanoparticles like GNPs below 100 nm. [112] Also, a non-polar surface can allow entity blast generated by a PV power stockpiling framework. Passive targeting uses the pathological characteristics inherent to malignant tissue to guide nanoparticles to their intended target area. [113] Enzymes such as alkaline phosphatase that break down are found in malignant tissues and assist in the release of medicines from nanoparticles at targeted sites. That is, normal cells are pushed out as oncogenic tissue develops. Angiogenesis is also referred to as the formation of new blood vessels from existing blood vessels. [114] The bottom of the membrane in tumor vasculature is strikingly abnormal. Abnormal blood vessels are formed in malignant tissues due to insufficient vasculature, and leaky blood capillaries are formed. The tumor tissues are also naturally vascularized, which helps facilitate access between nanocarriers and malignant cells. This lack of

lymphatic drainage causes an accumulation of fluid in the tumor's unstuck tissue. This increased EPR effect (i.e., elevated permeability and retention) is depicted in (Figure 1A). Nanoparticulate technological advancements aim at tumor cells indirectly, but lack target specificity to tumor cells. [115-117] Thus, with this idea that particular types of molecule ligands that target can be used to downright abolish cancerous cells. Cancer cells might express numerous surface receptors that are capable of selective targeting with metal derived nanoparticles (GNPs) (figure 1B).

A concise summary of the research conducted on gold nanoparticles for the purpose of diagnosis tumors is provided in Table 1-

Drug Name	Targeting Type/ Ligand Used	Animal Model/Route of Administration	Key Findings	Reference
5-Fluorouracil (5-FU)	Active targeting/ thioglycolic acid (TGA) and glu-tathione (GSH)	----------	5-FU/GSH-gold nanoparticles exhibited pH-dependent controlled drug release and demonstrated a twofold increase in cytotoxic efficacy in vitro compared to the free drug.	[115]
Temozolomide (TMZ)	Passive targeting/--------	Male BALB/c mice/ intratracheal route	TMZ-loaded gold nanoparticles (GNPs) and liposome-embedded gold nanoparticles (LGNPs) exhibited comparable stability and safety profiles in vitro; however, the in vivo lung antitumor efficacy was superior in LGNPs.	[116]
TGF-β1 antibody and methotrexate	Active targeting/ folic acid	----------	The combination of folate, methotrexate, and gold nanoparticles (GNPs) at a ratio of 5:5:9 exhibited the most significant in-vitro cytotoxicity against MDA-MB-231 (breast cancer) cells, while the conjugation of TGF-β1 antibody to the GNPs decreased the extracellular concentration of TGF-β1 by 30%.	[117]
Doxorubicin hydrochloride	Active targeting/ thiol-terminated polyethylene glycol (PEG)	Female BALB/c mice/intravenous	Targeted magnetic nanoparticles measuring 22 nm, loaded with a medication, demonstrated superior in-vivo accumulation in malignant tissues and reduced toxicity to normal tissues in comparison to passive drug delivery systems.	[117,118]

5.1. Gold Nanorods in Cancer Therapeutics

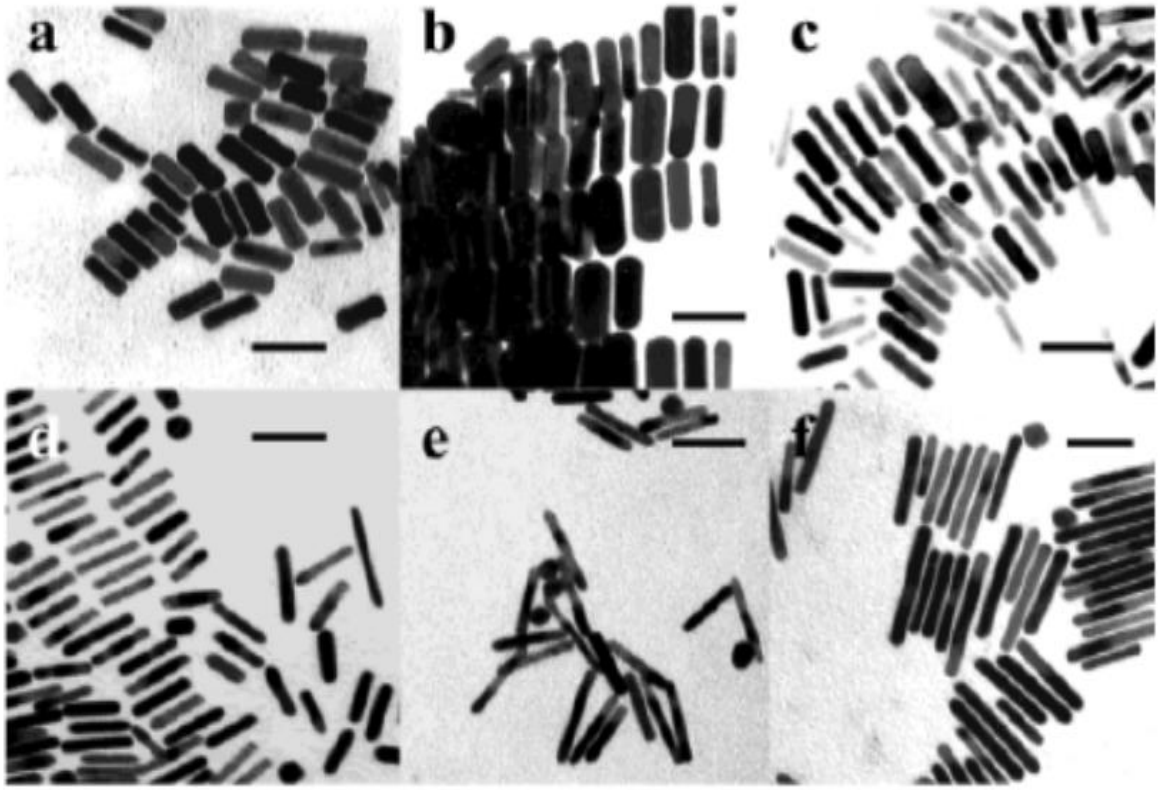

Figure 9 -displays that the electron transfer microscope (TEM) images of gold nanorods exhibiting different plasmon band energies.

[Abadeer, N. S.Chem. C 2016]

Gold nanorods are an engineered carrier system utilizing gold, designed for medication delivery applications. This approach involves a two-stage manufacturing procedure, with the initial step being the formation of a seed solution using sodium borohydride, gold salt, and cetyltrimethylammonium bromide (CTAB). In the second stage, the current suspension is added to a growth solution comprising the antioxidant ascorbic acid, gold salt, CTAB, and differing quantities of silver nitrate to synthesize gold nanorods.[119]

The significance of gold nanorods in cancer treatment in Table 2

Drug name	Targeting Type/ Ligand	Animal Model/Route of Administration	Key Findings	Reference
Nutlin-3	Active targeting/ folicacid (FA)		Gold nanorods functionalised with α,β-poly(N-2-hydroxyethyl)D,aaspartamide and folic acid exhibited significant in vitro absorption in U2OS cancer cells and demonstrated a dual drug release at acidic pH, mimicking the conditions of cancer cells, in contrast to traditional systems.	[120]
Doxorubicin (DOX)	Active targeting/ Low density lipopro-tein receptor (LDLR) targeted peptide-RLT (R)	BALB/c-nu male nude mice/ intrave-nous	DOX/DNA/PEG/R coupled gold nanorods shown a 1.7-fold increase in apoptosis rate in vitro and exhibited significant efficacy against PC-3 tumour cells in vivo upon application of near-infrared (NIR) laser, in comparison to free DOX.	[121]
Doxorubicin (DOX)	Active targeting/ transferrin (Tf)		DOX-Tf-gold nanorods exhibited cytotoxic effects of 48% and 46% against A549 and HCC827 cells, respectively, surpassing the non-targeted system, DOX-gold nanorods, which shown 36% cytotoxicity for A549 and 39% for HCC827 cells.	[122]
Cisplatin (Pt)	Active targeting/ folic acid (FA	Nude mice/ intra-venous	Pt/Fa-gold nanorods exhibited an in-vivo increase in temperature upon 655 nm NIR irradiation, resulting in significant reduction of the growth of aggressive triple-negative breast cancer cells, demonstrating superior efficacy compared to the conventional system (Pt-gold nanorods).	[123]

5.2. Gold Nanostars in Cancer Therapeutics-

Gold nanostars, a type of gold-based carrier system, are made by mixing chloroauric acid (HAuCl4) with an N,N-dimethylformamide (DMF) solution which has high quantities of poly(vinylpyrrolidone) (PVP) and gold nanoparticle seeds. As you can see the shape of his images come from a transmission electron microscope (TEM) of gold nanostars. Evaluation of the efficacy of the nucleolin-targeted genomic aptamer AS1411 (Apt) encapsulated in gold nanostars (AuNS) in different types of cancer cell lines. This proposed method proved effective at internalising malignant cells and reducing antiapoptotic Bcl-2 mRNA levels by 200%. [124] The light-activated release of aptamers to cytochrome led to a 2fold increase in enzyme activity and a 40% decrease in cell viability. [125-127]

Table 3 outlines the efficacy of gold nano stars in cancer-

Drug name	Targeting Type/ Ligand Used	Animal Model/Route ofAdministration	Key Findings	Reference
Gemcitabine -5 monophosphate (GMP)	Passive targeting/------	Female athymic nude mice/ intravenous	The gold nanostar (AuNS) core, encased in a metal-drug coordination polymer (CP) shell, demonstrated efficacy in MRI (magnetic resonance imaging) for tumour analysis and exhibited optimal anticancer effects when the tumour location was treated with an 808 nm NIR laser.	[128]
Mitoxantrone (MTX)	Passive targeting/------	Female athymic nude mice/ intravenous	MTX-conjugated gold nanorods demonstrated significant accumulation at the lung tumour site 5 hours post-administration of a 200 μg/ml dosage, as evidenced by in vivo surface-enhanced Raman scattering (SERS).	[129]
Resveratrol	Passive targeting/----------		Resveratrol-conjugated gold nanoparticles exhibited a greater inhibitory effect on treatment of breast cancer.	[130]

CHAPTER 6

Gold nanoparticles in anticancer therapy

Over the last few years, nanotechnology has progressed significantly and there has been growing interest in its applications, particularly in areas related to nanoparticle research and medical applications. An exponentially growing canon driven by increasing understanding of the characteristics of gold nanoparticles (AuNPs), and limitlessly noted experimentation suggests that the frontiers of nanotechnology are in a dynamic state of enlargement. As a result, currently there is growing interest in using AuNPs to treat cancer disease, including cancer disease diagnosis, monitoring and therapy. The ultimate goal behind the works of many others in this area is also to be able to do a paradigm shift change in a field, which is therapy and therapy strategy of multifactorial disease like cancer. Hence the limits of cancer science are consistently stretched to give way for the best approaches for cancer diagnostics, monitoring and treatment modalities. The fruits of cancer research would inescapably redound to the benefit of man and save tens of thousands of lives.

In the current model, cancer is treated with surgery, chemotherapy and radiation therapy, among other therapies. But these methods have limitations and side effects, and they've been evaluated and put into practice for decades. Only large, respectable and operable one can be treated through surgical removal of tumors.

6.1. Chemotherapy-

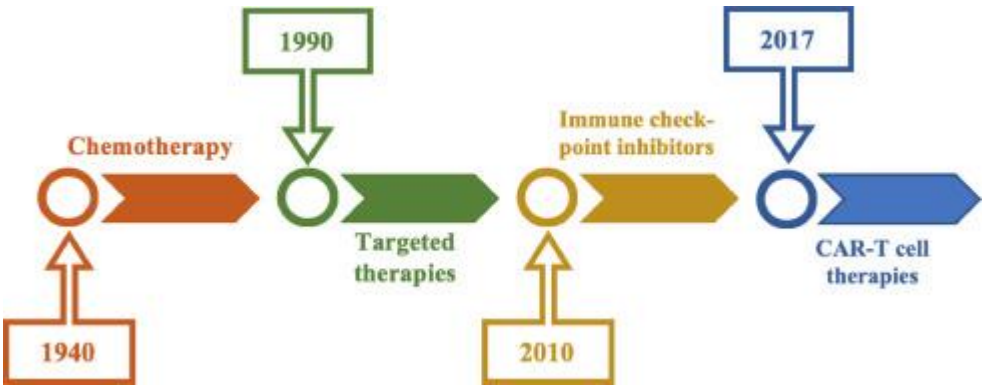

Figure 10-chemotherapy start to use in cancer treatment.

[Rai M., Yadav A. and Glade A.(2010)]

Found in 1940, [131], the earliest antibiotic that was also demonstrated to exhibit any cytotoxic activity. The discovery of new target specific malignancy treatment with activity to describe molecular intentions These may be small chemical molecules biotechnological macromolecules (especially monoclonal antibodies) that bind specific receptors or proteins with a role in the pathologic pathways of cancers. The therapeutic strategies based on immunotherapy were initiated after 2010[132] used for the initial investigation and made way for more medicines as ipilimumab, which is a monoclonal antibody recognized for use in 2011 and works as immune-checkpoint inhibitor [133,134]. As one of the most recent cancer therapies, CAR-T cell therapies (Chimeric-Antigen Receptor) have gained a lot of attention. These cells are T-lymphocytes that were genetically modified to express a chimeric (i.e., hybrid or artificially constructed) protein on their cell surface. Which then allows them to hone in to areas of cancer, and to re-activate to lyse these same cancer cells [135] CAR-T based products were approved in 2017 and 2018 respectively [136]. One of the most common cornerstones of anticancer therapy is chemotherapy. Post cancer treatment includes mainly surgical interventions and therapies such as irradiation hormone therapy and cell therapy. Chemotherapy works by targeting some of the tumor biology and thereby overcoming its selective constraints to produce additive or potentially synergistic antagonistic therapeutic effects. This initiated a chemotherapy-based combinatorial strategy using a synthesized medicinal drug [137] In mice with tumors, a ROS-sensitive component saturated hydrogel scaffold showed that we could exactly target the administration of gemcitabine (GEM) and an anti-programmed passing away the ligand antibody (αPDL1), with special kinetics. Notably, this could induce the immunogenic tumor phenotype and lead to immune-mediated tumor rejection. [138-141]

Antigen-capturing nanoparticles (AC-NPs) of engineered sustainable and biodegradable properties led to enhancement of cancer immunotherapy effects. Treatment with AC-NPs carrying tumor-specific antibodies induced a significant improvement of PD-1 therapy in the B16F10 melanoma model, with a 20% increase of cure rate when compared with control group. AC-NPs promoted the expansion of CD8+ cytotoxic T cells and increased the ratio of CD4+/Treg and CD8+/Treg. This is a new strategy to enhance cancer chemotherapy using nanotechnology. [142-145]

6.2. Photothermal therapy-

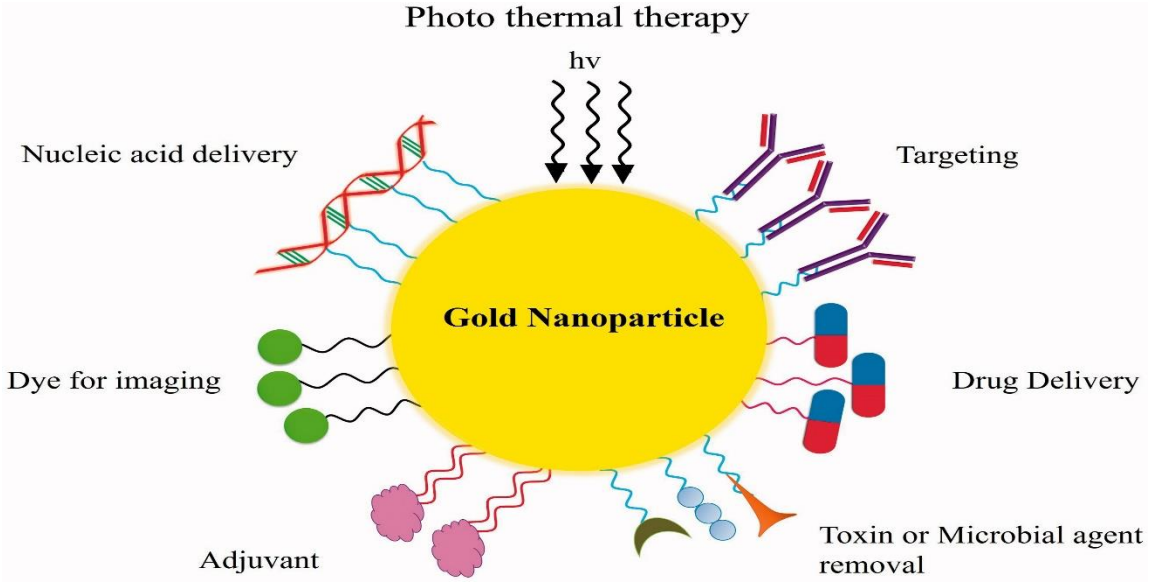

Figure 11 - photo thermal therapy uses in cancer diagnosis.

[Lewinski NA, et al. A new era (2013)]

As the structure has a strong impact on the photothermal features, the photothermal effect of gold nanoparticles in photothermal therapy (PTT) is mediated by size shape and structure. Since they possess unique properties, like electromagnetic energy absorption and scattering, gold nanoparticles are particularly fascinating for applications in photothermal therapy (PTT) [146]. This therapeutic modality uses electromagnetic radiation to create heat to thermally ablate neoplastic cells. Localized heating also known as hyperthermia or thermal exposure has been used in tumor therapy back to the 18th century [147,148] Localized and systemic hyperthermia disrupts cellular membranes and denatures proteins, thus promoting cellular apoptosis. However, healthy tissues are also affected during this process, which is the main limitation of PTT and restricts its therapeutic applications. The progressive expansion of this restriction helped a little by the utilization of laser therapy radiation which provides topographic and accurate ablation of the plagues with the malignant tissue. Photothermal therapy (PTT) techniques with enhanced specificity, limited range of malignancy, and precise spatio-temporal specificity have provided an exciting alternative strategy for treating chemotherapy-resistant cancers. [149-150]

6.3. Radiofrequency therapy-

Radiofrequency is one of the invasive cancer treatment methods. It involves thermal ablation of affected tissue via temperature generation by intermediate stability changing present. For the radiofrequency ablation (RFA), a needle-like probe is inserted in the tumor mass to heat it. The below ultimately helps to destroy the tumor by radiofrequency diathermy. Radiofrequency ablation (RFA) is a particularly effective technique for managing primary and metastases respiratory tract and other small-kidney implants. Moreover, it has been proven effective in the management of duodenal and bile duct malignancies. The utilization of RFA compared with surgical methods enables the careful and precise surgical resection of benign bone neoplasms that ultimately leads to less destructive harm to the bone and reduced risk of recurrence. Microwave therapy is more organism than surgical excision and does not invade patient skin. Besides, you can achieve the required results more easily. It is relatively safe, not threatening overall well-being of the patients, as well as being also no threat principle, because heart muscles or nerves are not directly stimulated, thus its usage is possible without general anesthesia. This is a recurrent approach in case of tumor incidence and helps to treat difficulties in malignancies that are impossible or difficult to remove. Some limitations of RFA include the requirement of precise positioning of the needle, the size and distance of tumor(s) from other organs, poor neoplastic tissue destruction (usually 5–40%), [107] and low specificity. Thus, a safe and precise approach for the selective heat production induced by radiofrequency is required. Gold nanoparticles have the ability to reflect x-rays making them able molecules of interest to use to produce heat inside malignant cells with an external radiofrequency field. [151-152]

As noted earlier, visible light and near-infrared ray can induce surface plasmon resonances in nanogold particles, which can be exploited for photothermal heating using already established technology. However, the underlying mechanism behind this phenomenon of nanoparticles-enhanced heating for infrequent irradiation is still poorly understood. Three proposed mechanisms of action include Joule heating, otherwise known as inductive heating, magnetically heating, or electrophoretic warmth. Furthermore, not only does the frequency of the delivered irradiation significantly influence each mechanism, but the size and the appearance of the gold nanoparticles does as well. In radiofrequency-based anticancer therapy, spherical AuNPs are most widely studied. Several human cancer cell lines were used to evaluate the nanoparticles in vitro. Bandwidth, adhesion loss, and even apoptosis due to heating can increase due to exposure to the radiofrequency field. Other studies also observed a temperature damage elevation in animal models when a selected field and a power level of 35 W were applied in gold nanoparticles administration here. While gold may be beneficial in some cases, leading to the development of applications with nanogold. [153]

Chapter-7

current challenges and Future Outlook

7.1 current challenges

Another formation of gold nanoparticles has been used in the 10 years from now different morphology and properties {AuNPs}[154]. Multiple articles have been published under diverse plants and organisms for the similar purpose from around the world. However, despite few of the advantages over other methods, there are many restrictions and disadvantages, which limits their scale-up to commercial applications that hinders their downstream application in biotechnology and nanomedicine. Current challenges are as follows:

- Insufficient data to control size and shape of nanoparticles: a lot of literatures has demonstrated in the synthesis process various AuNPs morphologies will result [155]. Uniform morphology and narrow size distribution: Prerequisites for the pharmacological and biological applications It is possible to solve this problem through the adequate knowledge of optimizing the reaction mixture, with experimental time, pH, temperature, rotational speed, chloroauric acid concentrations, etc.
- Absence of uniform protocols for the production of NPs having similar characteristics: for instance, even from the same plant, one instance AuNPs generated using different plant parts display multiple degrees of cytotoxicity [156], forces of the antioxidant/metabolite (s) content.
- First and foremost, one could contend that insufficient knowledge regarding the mechanism of NP biosynthesis is a major limitation and a critical finding has been elucidating which portions of their derived metabolites from distinct plant and microbial source stimulate NP biosynthesis still difficult.
- Even the separation and purification of NPs from the complex reaction mixture is another important mandatory task that encounters one of the biggest holes that in spite of the synthesized NPs can be productively scaled up form a laboratory-based approach meeting the huge demands in terms of industrial and pharmaceutical scale is a major concern.
- This is a field that requires thorough exploration of biosynthesized NPs, toxicokinetic and toxicodynamic, which will broaden their use in multiple areas. There are technical obstacles and corresponding regulatory policies that must be matched to overcome commercial NP synthesis limitations.
- Stability and functionalization: While scientists have extensively investigated green synthesis, very few studies have surface-functionalized the synthesized NPs to increase their stability in the biological media and functionalized NPs specifically against antibodies or peptides for better applications in drug delivery and cancer therapy.
- While the green synthesis method is highly popular, the resolution of the challenges cited could lead to better global acceptability and adaptability of the commercial synthesis of AuNPs. The current challenges faced in this sector can be tackled in upcoming research and developmental studies by designing next-generation standard established routing and protocols, developing smart and safe effective functionalized AuNPs using different kinds of biomolecules and targeted moieties for multimodal applications. [157-159]

7.2 future outlook

Because of nontoxicity and biocompatibility gold NPs are known in many fields of nanotechnology. Their higher antibacterial activity characteristics makes the plant synthesized gold NPs a helpful and a potential material that may play a major role in the combat against antimicrobial resistance. NPs exhibit several antimicrobial mechanisms, paving a way for a new class of antimicrobial drugs between bacteria and NPs with antimicrobial activity, including peptides and lipids, for broad-spectrum antimicrobial agents, with examples of commercial formulations. The worldwide gold NPs businesses calculated to grow at a compound annual growth rate of 18.84 percent for the year and by 2021 [160]. Sustainable or bio-based manufacturing offers a practical, cost-effective route to industrial scale gold NPs for diverse market applications, such as point-of-care assessment, large-scale diagnoses, and immunization and domestic uses [161]. Recently a variety of NPs, including gold NPs, were granted FDA approval for nanomedical application, while even more are in a phase of clinical or preclinical trial concerning the promotion of human health. Only standardized synthesis and characterization procedures can provide quality assurance throughout gold NP technologies manufacturing. Collaboratively, researchers, industry stakeholders, and regulatory bodies could establish standardized frameworks to assess the toxicity, biocompatibility, and long-term stability of golds. Currently, there are health issues and long-term safety evaluation that need to be concerning regarding preclinical studies. Cheap and Cost Competitive Downstream Use of Nanoparticle Technology Upstream Investing in Environmentally Friendly Production Techniques [162,163] Transparent regulatory pathways can optimize approvals and safeguard public trust in drug or device systems. However, such product has different physicochemical and optical properties and potential bio application, thus the international community needs to establish specific protocols for preclinical development as well as the characterization of such products. Gold NPs have been employed primarily for anticancer application. Thus, they can be utilized as multifunctional agents for imaging and/or targeted drug delivery in anticancer therapy [164]. It has long been recognized that anticancer profiling suffers from a lack of rigorous methodology and breakthrough agents. Among a variety of approaches, surface modification by metal NPs represents one of the most effective methods, and Golds are alternative candidates for this purpose. Cantinas, already applied in anticancer research and capable of cuddling with antibodies [165,166], are expected to be the first trend for anticancer drug delivery and patient-based anticancer treatment needing specific drug delivery in a few years. Gold NPs are expected to be the most valuable nanomaterial in anticancer research in the coming days mainly due to the significant role alternative treatments play in anticancer research for which low toxicity needs to be integrated with environment friendly synthetic methods [167,168].

CHAPTER 8

Conclusion-

Researchers have now an abundance of particles of different sizes, shapes, and architectures that emerged in the last few decades with the fast-growing field of nanotechnology and nanoscience. Gold nanoparticles have a distinctive structure that makes them highly essential for medicinal applications, particularly for anticancer treatment. Various synthesis methods available for preparation of nanogold particles with specific design and properties according to application requirements. In addition, Due to its reactivity allowing them to further qualify and operationalize (there by enhancing bioactivity and widening the range of therapeutic application of AuNPs. The myriad and mixed physical and chemical characteristics of nanogolds, stressed in this article, distinguish them from other nanoparticles and harbor potential for applications like drug delivery systems, heat-on delivery agents for escarpment ablation. Opportunities to the higher Future now provide hope to present generation of cancer treatments as well, while also providing an opportunity to increase the likely viability of the leading modes chemotherapeutics.

Last but not least, there are many questions about the outcome of drugs or induced by AuNPs have some complexes and conjugates as well. The therapeutic exodus and he strands with the golden must undergo the testing in this juncture. Several data prove getting one with the reduction in the either compound handling into the presence of the nanocarrier to perhaps considerably correspond both the staying with in addition to the arrangement strength of the nanogold. Such formulations must also be carefully evaluated for their stability across a range of environmental conditions. And it took intensive long-time as well as work to obtain final results in the area of healing. So, this work was focused on a comprehensive analysis of the current landscape concerning the possible application of AuNPs in several anticancer treatments.

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