

Application of Nano Particles in a Cancer Treatment

Sakshi Anant Tathe, Dr. Shivshankar Mhaske, Prof. Miss. Sanjana Bali
Satyajeet College of Pharmacy, Mehkar

Abstract:- Undifferentiated cell mass can arise as a result of abnormal, unregulated, and aimless cell division. It's referred to as cancer. When malignant cells divide unchecked to create new tumors known as neoplasms, cancer damages the body. It is currently one of the leading causes of death. Anywhere in the body, tumors can form, and not all of them are malignant. There are numerous forms of cancer; some can be cured, while others cannot. Globally, cancer continues to be the top cause of death. Nanoparticles have become a potentially useful cancer treatment technique. Because they improve medicine delivery and minimize adverse effects, nanoparticles are transforming the treatment of cancer. The interdisciplinary fields of biology, chemistry, physics, food, medicine, electronics, aerospace, and nanotechnology are all fast evolving.

Keywords:- Nanoparticles, Cancer, Synthesis, Chemotherapy.

INTRODUCTION

Cancer is characterized by aberrant, aimless cell division and unchecked proliferation in reaction to several tumorigenic stimuli. As an expansionist illness, cancer spreads by invading tissues, establishing colonies in adverse environments, and first finding "sanctuary" in one organ before moving to another. Oncologists are medical professionals and researchers who focus on the investigation, diagnosis, treatment, and prevention of cancer. The term oncology refers to the study of cancer. Neurons and heart cells do not get cancer. Hyperplasia refers to an increase in the number of malignant cells, whereas hypertrophy refers to an increase in the size of cancerous cells. Cancer is a widespread illness that has a high death rate. With 10 million fatalities from the disease in 2020, cancer is one of the top causes of mortality globally. An estimated 1,461,427 new cases of cancer were reported in India in 2022. According to the International Agency for Research on Cancer (IARC), 8.2 million people died from cancer globally in 2012, and by 2030, that number is expected to rise to 13 million. According to the American Cancer Society, cancer is the second leading cause of death in the United States; an estimated 571,905 Americans are predicted to lose their lives to the disease in 2011. Unquestionably, technological advancements have

been made to improve cancer treatment, particularly in relation to the finding that chemotherapy and radiation therapy have limited anti-cancer therapeutic benefits. The frequency and extent of cell division during the 20th century are mostly determined by cell signaling pathways. When these signaling pathways malfunction, cells may multiply uncontrollably and develop into a tumor. It is possible to describe the physiology of a cancer tumor as intricate and dynamic. The presence of several kinds of malignant cells, including cancer stem cells, within a tumor. The creation of nanodrugs, nanodevices, drug delivery systems, and nanocarriers is greatly aided by nanomedicine. Multidrug resistance (MDR), a limited therapeutic window, and undesirable side effects are some of the main problems in cancer treatment. Adverse effects of currently available anticancer medications. Numerous nanotechnology centers have been built globally in the past ten years (Kawasaki and Player 2005; Horton and Khan 2006). Over six billion dollars have been spent on nanotechnology research in the US alone. According to National Institutes of Health (NIH) criteria, a nanoparticle is any substance employed in therapeutic formulation that produces a finished product that is less than one micron in size. Every year, an estimated 550,000 new instances of bladder cancer are reported worldwide, making it one of the most prevalent cancers of the urinary tract. Nanoparticles have been used in several scientific fields in recent years, and they have frequently been shown to be important in contemporary medicine cancer mortality as a result of the use of therapy; the development of nanotechnology made it possible for treatments utilizing nanoparticles to be very beneficial. An estimated 550,000 new instances of bladder cancer are reported worldwide each year, making it one of the most prevalent cancers of the urinary system. In addition to standard cancer care, complementary therapies are employed. They are helpful strategies that manage symptoms, improve health, and advance patient care in general.

REVIEW LITERATURE

1. Anish Babu (2013): Worldwide lung cancer is the leading cause of cancer-related deaths with a dismal 5-years survival rate of only 15%. First-line chemotherapy regimens for lung cancer include platinum-based drugs such as cisplatin and carboplatin. Nanoparticle-based medicine has infinite potential with novel applications continuously being developed for use in cancer diagnosis, detection, imaging, and treatment.
2. Thais P. Pivetta: Cancer is a leading cause of death worldwide, with an estimated 19.3 million new cases and nearly 10 million deaths caused by cancer in 2020. This review shows that nanoparticles are being extensively investigated for phototherapies nowadays.
3. Sangiliyandi Gurunathan: Cancer represents a group of heterogeneous diseases characterized by uncontrolled growth and spread of abnormal cells, ultimately leading to death. The use of NPs in combination with other anticancer agents regulates multiple pathways involved in the various stages of cancer cell, including growth, progression, metastasis and drug resistance. The use of nanomedicine leads to an unsurpassed opportunity to move forward for the treatment of a variety of diseases, including cancer.
4. Weibo Cai: Gold nanospheres, nanorods, nanoshells, nanocages, and surface enhanced Raman scattering nanoparticles will be discussed in detail regarding their uses in in vitro assays, ex vivo and in vivo imaging, cancer therapy, and drug delivery.
5. Dr Stefanos Mourdikoudis: The variety of nanostructures he prepares are either directed for specific applications or simply inspired from curiosity to explore new protocols and characterize the resulting products.

Types : cancer can be named according to tissue from which they arise

Carcinoma = cancer that arises from epithelial tissue coverings or linings .

Examples : breast cancer, Prostate cancer ,lung cancer ,skin cancer.

1 .breast cancer : The most prevalent cancer in the world to harm women is breast cancer. As a metastatic malignancy, breast cancer frequently spreads to distant organs such as the liver, lungs, and bones. In certain patient categories, magnetic resonance imaging and ultrasound have emerged as

helpful diagnostic adjuncts, but mammograms are still the gold standard for breast cancer screening and diagnosis .

Risk factors :

Life style

Estrogen

Reproductive factors

Family history

Aging

Prevention : cancer can be prevented by following methods

*screening = it includes mammography and MRI

*chemoprevention = includes SERMs: TAM (Raloxifene) and AIS (Exemestane)

*biological prevention = Hereceptin, pertuzumab and PDI/PDLI inhibitors

2 colorectal cancer : One of the most common tumors of the gastrointestinal tract is colorectal cancer (CRC). It has a tendency to be malignant and highly aggressive. According to GLOBOCAN 2020 data, colorectal cancer is the second leading cause of cancer-related mortality worldwide and the third most common type of cancer diagnosed.(13,14). Lung, prostate, and colorectal cancer account for around one half (39%) of all incidence cases in men. However, 32% of women develop lung, breast, and colorectal cancer.

Risk factor :

Age (more common over 50)

family history

personal history of colorectal issues

certain genetic mutations

poor diet

lack of physical activity

smoking and high alcohol consumption

prevention :

1 screening

- Colonoscopy

- Fecal occult blood test (FOBT)

2 Diet

- Omega 3 fatty acid
- Low fat dairy products
- Antioxidant – rich food

3 medication

- Aspirin
- NSAIDs

*Sarcoma = cancer that arise from connective tissue

Examples : osteosarcoma ,ewings sarcoma .

1 osteosarcoma or bone cancer : The direct development of juvenile bone or osteoid tissue by tumor cells is the hallmark of osteosarcoma, a primary malignant tumor of the skeleton. Osteosarcoma is classified as a central or surface tumor, with several subtypes identified within each group.

Risk factor :

ionizing radiation

radiation and chemotherapy treatments

Paget disease of bone, or osteitis deformans

Prevention :

- Surgical treatment
- Systemic treatment
- Immunomodulatory agents
- Tyrosine kinase inhibitor
- HER2
- Microenvironment
- Novel antifolates

2 Ewings sarcoma : Ewings sarcoma is a tiny, round-to-oval cell sarcoma that resembles a primary osseous tumor in both radiologic and clinical features. It mostly happens in the first three decades of life and is slightly more common in males. Diagnosing Ewing's sarcoma can be quite challenging.

Risk Factors :

Age

Viral infection (HHV6)

Genetic predeposition

Sex

Prevention :

Roentgenographic Findings

Operative and gross findings

radiation and chemotherapy

*Lymphoma = Cancer that arise from lymphatic tissue

Examples: Hodgkin lymphoma, follicular lymphoma, mantle cell lymphoma.

1 Hodgkin lymphoma : alter "Hodgkin's disease" for "lymphosarcomatosis." According to Oliver 3's 1913 conclusion that "all constitute a series of neoplastic processes of the lymphatic glands, which differ not so much qualitatively as quantitatively" it is the predominant cell type that allows one to distinguish the tumor as a lymphosarcoma, endothelioma, or Hodgkin's disease.

Risk factors :

Genetic factors (genetic mutation,family history)

Infectious agents(HIV,HCV,EBV)

Environmental factors (air pollution ,radition,chemical exposure)

Immunological factors(weak immune system)

Life style (smoking,obesity)

Demogeaphic factors (age,sex)

Prevention :

Primary prevention

- EBV Vaccination
- HIV treatment

Secondary prevention

- Screening
- Early detection

Tertiary prevention

- Surveillance (regular follow up appointments)

*Peadiatric Carcoma = The population affected is predominantly children, teenagers, and young adults aged 10–30 years.

Examples: neuroblastoma,wilms tumor.

1 Neuroblastoma : A juvenile neoplasm originating from neural crest cells, neuroblastoma (NB) is the most common extracranial solid tumor in children. Its

clinical behavior varies from spontaneous remission to rapid tumor development and mortality.

*Risk factors :

Genetic factors

-Family history

- Genetic mutation

Environmental factors

-Tobacco

-Alcohol

-pesticides

-Radition

-Chemicals

*Prevention

Histopathologic evaluation

surgery

*Gynecologic Cancer : Any type of cancer that originate in female reproductive organs

Examples : ovarian cancer,cervical cancer,vaginal cancer.

1 Ovarian Cancer : The several tumor forms that comprise ovarian cancer share similarities with the endometrial, gastrointestinal, urinary tract, fallopian tube, and endocervix epithelia. However, there are no characteristics of a normal ovary that resemble these tumors.

Risk factors:

-Genetic factors

Family history

Lunch syndrome

-Hormonal factors

Early menarche

Late menopause

Nullparitl (never having child)

-Reproductive factors

Breast feeding

Age at first pregnancy

Number of pregnancy

-Medical history

Endometriosis

PCOS

PID

Oral contraceptive

Prevention :

Transvaginal ultrasonography

Targated theripies

Combination therapies

Immunotherapy

Drug delivery system

Biomarker identificatio

Treatment of Cancer

Conventional Treatment

1 Chemotherapy - For conditions like primary breast cancer, adjuvant chemotherapy has resulted in modest but significant increases in cure rates. Chemotherapy is frequently given intravenously as a first-line treatment for advanced-stage lung cancer. It travels throughout the body, eventually identifying and eliminating both malignant and healthy cells.

2. Immunotherapy: This treatment has ushered in a new age for cancer patients. Immunocheckpoint inhibitor-based medications have significantly improved the survival rate of cancer patients by bringing about significant advancements in the treatment of a variety of solid malignancies.

3 Combination therapy: In order to improve the clinical outcome, combination therapy has long been used as the first-line standard treatment for a number of cancers.It has been demonstrated that anticancer medication combination therapy typically results in synergistic drugactions and prevents the development of drug resistance.

4. Surgery: When there are no known metastases, surgery is a better option for accomplishing this goal than other types of tumor reduction therapy. A condition of antigen decrease but not clearance would result from incomplete tumor excision, causing the antitumor immunity to wane without the ability to develop a memory mechanism.

Importance of Nanoparticles in Cancer

1 Diagnosis

-Early detection: nps can detect cancer biomarkers at early stages

-Imaging :nps enhance imaging technique for diagnosis of cancer (MRI,CT)

-Liquid biopsy: nps can isolate tumor cell .

2 Treatment

- targeted therapy :nps deliver drug selectively to cancer cell

-controlled release : nps release drug over time ,reduce side effects

-Combination therapy: nps deliver multiple therapeutic agents

-Photothermal therapy : nps absorb light ,generate heat to destroy cancer cell

3 Nanomedicine has tremendous prospects for the improvement of the diagnosis and treatment of human diseases

4 Nanotechnology has potential to revolutionize a wide array of tools in biotechnology

5 Nanoparticle technologies have great potentials, being able to convert poorly soluble, poorly absorbed and labile biologically active substance into promising deliverable substances.

6 provide potential applications in medical imaging or drug delivery (c49)

7 The electromagnetic radiation used in magnetic hyperthermia

8 The potential strategy to treat brain cancer is the local administration of nanoparticles at the resection site during surgery.

9.NPS used in the biomedical field for purposes such as protection from harmful microorganisms, bio-imaging, drug transport, cancer treatment.

10. NPS used in the industrial field due to their catalytic activity

11 . NPS use in deferent fields as catalysis, electronics, and photonics.

12 .tremendous prospects for the improvement of the diagnosis and treatment of human diseases. 5. 5. Use

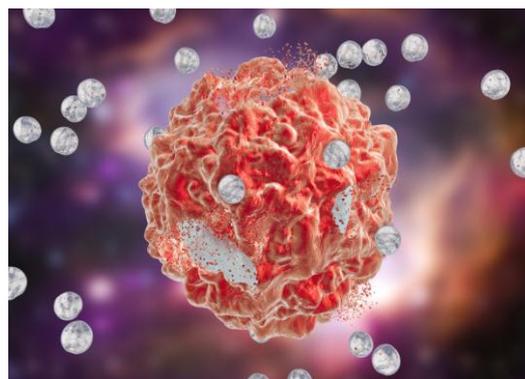
of microbes in biosynthesis of nanoparticles is an environmentally acceptable procedure. 6.Nanotechnology has potential to revolutionize a wide array of tools in biotechnology so that they are more personalized, portable, cheaper, safer, and easier to administer.

13. Very few nanoparticle-based agents are in clinical testing or commercialized for cancer diagnosis or treatment

14. MNPs are an optimal choice for drug delivery owing to their low toxicity levels, great targeting efficiency, and large surface area to volume ratio

15. Additionally, MNPs can be utilized in magnetic hyperthermia to destroy cancer cells and decrease tumour volume via a targeted approach .

Nanoparticles – Nanoparticles (NPS) are minuscule particles with dimensions measured in nanometers (1-100nm). The word "NPS" is highly generic and frequently used to cover materials. NPS has special chemical, biological, and physical characteristics . It is occasionally used to refer to dendrimers, which are globular polymers. NPS are also known as nanocrystals and are frequently crystalline.Numerous changes in physical attributes may result from the transition from microparticles to NPs. The interdisciplinary fields of biology, chemistry, physics, food, medicine, electronics, aerospace, and nanotechnology are all fast evolving.



Properties of Nps

1 physical properties

(i)size

- size range from 1-100 nm

(ii)shape

-spherical,rod like,irregular

| | |
|------------------------------------|---|
| (iii) surface area | - Nps cross biological membrane |
| -nps having high surface area | 3 reduced toxicity |
| (iv) volume | - Minimize side effects |
| -having small volume | Cancer Targeting Strategies |
| 2 chemical properties | 1 passive targating mechanism |
| (i) reactivity | 2 active targating mechanism |
| - catalytic nps | Types of Nps |
| (ii) stability | 1 Organic Nps |
| -inert nps | 2 Inorganic Nps |
| (iii)solubility | 1 Organic Nps : organic NPS are the most used system to encapsulate molecules which can be used in PDT.there are several categories based on different materials and respective organization |
| -hydrophobic\hydrophilic nps | |
| 3 optical properties | |
| (i) absorption | - Liposomes |
| -uv-visible ,NIR | - Dentrimers |
| (ii) fluorescence | - Miscelles |
| -quantum dots | - Nanocapsule |
| 4 biological properties | - Cyclodextrins |
| (i) biocompatibility | 1 liposomes : Liposomes are formed by auto-organization of phospholipids in bilayers ,in an aqueous medium tend to fold on themselves ,creating vesicles the vesicles are employed as a model in the study of cell membrane . Due to the lipid's amphiphilic nature, hydrophilic and hydrophobic drugs can be stored in different compartments of liposomes . |
| -NPS are biodegradable | |
| (ii)targeting | 2 dentrimers : it is highly branched 3D nanoparticle with a well defined structure .it have uniform size and shape ,having high surface area ,it can improve the solubility and stability ,reduce toxicity |
| -active \passive targeting | |
| Application of Nanoparticles | 3 miscelles : Similar to the previous description of liposomes formation, micelles are also formed by the self-organization of amphiphilic molecules, and the resultant particle is different from the vesicles because of the different packing parameters . |
| - Use in the treatment of cancer | |
| - Gene therapy | 4 nanocapsules : nanocapsules are type of nanoparticles that consist of core shell structure where a payload (API,therapeutic agent) is encapsulated within a thin,protective layer. |
| - Vaccine development | |
| - Air purification | 5 Cyclodextrins (CD) are biodegradable and biocompatible structures composed oligosaccharides of D(+)-glucose that are able to form nanosized particles by self-organization in aqueous medium |
| - Cosmetics | |
| - Propulsion system | |
| - 3D printing | |
| - Medical implants | |
| - Tissue engineering | |
| - Wound healing | |
| - Food packaging | |
| Advantage of Nps | |
| 1 improve solubility | |
| - Nps solubilize hydrophobic drugs | |
| 2 inhance permeability | |

2 Inorganic Nps

- METAL

Examples : gold ,silver,copper.

- Ceramic

Examples : silica,alumina

- Carbon based

Eamples : carbon nanotubes

Metal

1 gold nps : Gold (Au) is unique compared to other metals because of its resistance to tarnishing. gold nanoparticles (AuNPs) have been used for the treatment of diseases like rheumatoid arthritis. The combination of unique optical, electronic, and magnetic properties exhibited at nanoscale level can be exploited in a systematic manner to design more advanced materials and might be possible to attract the NPs

Properties of gold nps

1 Magnetic Resonance Properties

- CT-MRI
- MRI-contrast agent
- Diagnosis of malignant

and solid tumors

2 Surface Plasmon Resonance

- Ligand-receptor interaction
- DNA hybridization
- Antibody characterization
- Epitope mapping

3 Fluorescence Behavior of Gold Nanoparticles Imaging

- Analytical genomic and proteomic studies
- drug screening
- Immunological assay

2 Silver : Silver nanoparticles have proved to be most effective because of it's good antimicrobial efficacy against bacteria, viruses and other eukaryotic micro-organism.They are undoubtedly the most widely used nanomaterials among all, thereby being used as antimicrobial agents, in textile industries, for water treatment, sunscreen lotions etc, Studies have already reported the successful biosynthesis of silver

nanoparticles by plants such as Azadirachta indica²⁰, Capsicum annum²¹ and Carica papaya²²

3 Iron Oxide : Iron oxide based nanoparticles with superior magnetic properties and properly surface functionalized are being intensively investigated to achieve highly efficient carcinogenic celldestruction through hyperthermia treatments. In particular,it is difficult to find a definition for hyperthermia not linked to cancer therapy.

4 Magnetic Nps : MNPs are one of the most extensively researched nanomaterials, owing to their potential uses in various areas of research MNPs have already been used for the detection of cancer by localising the sentinel node, as well as molecular imaging .MNP are extensively being researched for usage in various industrial and scientific areas,varying from mass data storage to catalysis MNPs ranging from 10 to 100 nm are favourable for use in-vivo, considering they do not present with rapid renal clearance. The synthesis of MNPs is a multistep process that requires great attention in order to obtain its desired results . There are various approaches to synthesizing MNPs. ,MNPs can either be produced via “top-down” or “bottom-up” techniques .

Route of Administration

1 Invasive routes

- Intravenous injection (directly into blood stream)
- Intramuscular (into muscle tissue)
- Subcutaneous injection (under skin)
- Intra peritoneal (into abdominal cavity)
- Intrathecal injection (into spine)

2 Non-invasive routes

- Topical administration (skin application)
- Transdermal administration (through skin using microneedles)
- Inhalation (via aerosol)
- Oral administration (capsules or tablets)

3 Targated routes

- Tumor-targated delivery (using ligands or antibodies)
- Brain -targates delivery (using nose-to-brain or bbb-penetrating NPS)
- Lymph node-targated delivery (for immunotherapy)

Coating And Chemical Modification Of Nanoparticles

Coating or chemically modifying a variety of nanoparticles is common practice and an area where, valuable, innovations are likely to be seen.

Silicate nanoparticles are hydrophilic and need to be chemically modified to make them more hydrophilic, for example with larger molecules such as polyhedral oligomeric silsesquioxanes (POSS), which is popular both for coating silicate nanoparticles and as filler for composites on their own. The customizable side group on POSS can assist in making polymers easier to graft to each other and hold promise for initiating protein adhesion in biomaterial. At about 1.5 nm in radius, POSS are themselves sometimes classified as nanoparticles.

METHODOLOGY

1. Physical Method
- 2 Biological Method
- 3 Chemical Method
- 4 Mechanical Method

1 Physical Method :

(i) Inert gas condensation (IGC)

Inert gas condensation is one of the primitive methods for the NP synthesis that employ inert gases (e.g. He or Ar) and liquid nitrogen cooled substrate holder for the preparation of NPs. The evaporated materials are transported with inert gases

(ii) Physical vapor deposition (PVD)

Physical vapour deposition is a collective set of processes commonly used to produce NPs and to deposit thin layers of material, typically in the range of few nanometers to several micrometers. PVD is an environment friendly vacuum deposition technique consisting of three fundamental steps

- (1) vaporization of the material from a solid source
- (2) transportation of the vaporized material
- (3) nucleation and

Most commonly used PVD methods for NPs synthesis are

- (i) Sputtering
- (ii) Electron beam evaporation

(iii) Pulsed laser deposition

(iv) Vacuum arc

2 Chemical Method :

(i) Sol-gel method

In the sol-gel processing method, there are two types of components viz., 'sol' which is a colloidal suspension of solid particles in a liquid and 'gel' which are polymers containing liquid. Thus, this process includes the creation of 'sols' in the liquid that lead to the formation of a network of discrete particles or network polymers by the connection of sol particles. Formation of NPS occurs in four stages.

1 Hydrolysis

2 Condensation

3 Growth of particles

4 Agglomeration of particles

3 Biological Method :

(i) GREEN SYNTHESIS METHOD

The biological method, which is represented as an alternative to chemical and physical methods, provides an environmentally friendly way of synthesizing nanoparticles. Moreover, this method does not require expensive, harmful and toxic chemicals. Metallic nanoparticles with various shapes, sizes, contents and physicochemical properties can be synthesized. Thanks to the biological method actively used in recent years. Synthesis can be done in one step using biological organisms such as bacteria, actinobacteria, yeasts, molds, algae and plants, or their products. Molecules in plants and microorganisms, such as proteins, enzymes, phenolic compounds, amine

4 Mechanical Method :

(i) mechanical attrition

produces its nanostructures not by cluster assembly but by the structural decomposition of coarser grained structures as a result of plastic deformation. High energy mill involve

1 Attrition Ball Mill

2 Planetary Ball Mill

3 Vibrating Ball Mill

4 Low Energy Tumbling Mill

5 High Energy Ball Mill

Technique For Characterization Of Nps

(size, shape, and surface properties) Two of the main parameters studied in the characterization of NPs are size and shape. We can also measure size distribution, degree of aggregation, surface charge and surface area, and to some extent evaluate the surface chemistry.

1 Size Determination :

TDM (Transmission electron scattering)

DLC (Dynamic electron microscopy)

SEM (scanning electron microscopy)

XRD (x-ray diffraction)

2 Shape Determination :

SEM (surface morphology and shape)

AFM(surface topography and shape)

3 Surface Determination

zeta potential

FTIR (fourier transformation infrared spectroscopy)

Current on Going Research

- NPS design
- Nanomedicine use in treatment of cancer

Future prospects :-

Since the inception of NPs over half a century ago, scientists are continuously exploring advanced novel methods of synthesizing NPs with the optimal size and morphology that would be beneficial for various disciplines. To engineer and fabricate an ideal size and morphology of NPs, depending upon their application/use, diverse range of physical, chemical or biological methods are already available. In this review, we provided a comprehensive overview of the commonly employed/explored strategies for the synthesis of NPs in terms of their working principle, NP designing strategy and relevant literature. It is anticipated that this review will act as a guide article for the researchers to selectively choose particular synthesis strategy for designing the desired NPs with particular material type, size, surface properties, targeted application, etc.

CONCLUSION

The application of nanoparticles in cancer treatment has revolutionized the field of oncology, offering unprecedented opportunities for improved diagnosis, therapy and patient outcomes. Nanoparticle-based drug delivery systems not only improve the targeting and effectiveness of treatment but also address critical challenges such as drug resistance and systemic toxicity.

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