NANOTECHNOLOGY ADVANCEMENT IN THE FIELD OF CURING CANCER

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

School of Pharmacy
Brac University
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Declaration

It is hereby declared that

1. The thesis submitted is my original work while completing my degree at Brac University.
2. 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.
3. The thesis does not contain material that has been accepted or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

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Ethics Statement

This study does not involve any human and animal trials.

Abstract

The ability to treat sickness is continually evolving. In this field, various approaches are being used. One of the deadliest diseases for which there are now no better treatments is cancer. There is a lot of utilization of conventional techniques such as chemotherapy, radiation, targeted therapy, and immunotherapy. However, they have detrimental side effects from which there is little chance of recovery. like cytotoxicity, specificity, drug resistance to multiple drugs, and so on. However, harsh treatment is now carried out in a laboratory setting. Such as nanotechnology. Different nanoparticles are employed in this technology to transport medications to the body's diseased areas to maximize therapeutic impact while reducing negative effects. Because of their unique benefits, Nanoparticles which are1-100 nm in size, can be utilized to treat cancer because of their better permeability, decreased toxicity, increased remarkable stability, biocompatibility, retention impact, and precision targeting. These particles make use of both the tumor's properties and its surrounding environment. These nanoparticle therapies help not just with cancer therapy but also with drug resistance to many medications. To lessen toxicity, increase permeability, lessen the effect of shielding, boost the retention effect, and other effects, numerous studies have already been conducted or are now being conducted. Many more studies are required to produce the best results. This review's objective is to inform readers about recent developments in cancer treatment using nanotechnology.

Keywords:

Nanoparticles, Cellular targeting, Multidrug resistance, Cryosurgery, Tumor microenvironment, Blood-brain barrier, Drug delivery, Protein corona.

Dedication

Dedicated to my Faculties & Family members.

Acknowledgment

First of all, I would like to thank the Almighty for the countless gifts has given me, and the will and motivation to complete this endeavor. It gives me great pleasure to express my sincere gratitude to my academic supervisor Dr. Sabrina Sharmin (Assistant Professor at the Department of Pharmacy at Brac University) for her tremendous support and encouragement throughout my study. She was a genuine source of guidance and support for me throughout my study and project writing. She provided me with a lot of useful feedback and suggestions when I was studying, and I am appreciative of that because it enabled me to finish my assignment on time. I also want to express my sincere gratitude to Professor Dr. Eva Rahman Kabir, dean of the school of pharmacy at Brac University, for everything that she does for the department and the students.

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List of Acronyms

NPs- Nanoparticles

ECM- Extracellular matrix

MDR- multidrug resistance

EPR- enhanced permeability and retention

ECM- extracellular matrix

PEG- polyethylene glycol

CVD- chemical vapor deposition

TME- tumor microenvironment

RES- reticuloendothelial system

MPS- mononuclear phagocyte system

ECF- extracellular fluid

MTD- maximum tolerated dose

EGFR- epidermal growth factor receptor

TK- tyrosine kinase

PNPs- Polymeric nanoparticles

PMMA- polymethylmethacrylate

IHC- immunohistochemical

CSCs- cancer stem cells

PDT- photodynamic therapy

PTT- photothermal therapy

CDT- chemo dynamic therapy

SDT- sonodynamic therapy

SPION- superparamagnetic iron oxide nanoparticles

NSTI- nanoscience, technology, and industry

EVs- extracellular vesicles

BBB- blood-brain barrier

FNPs- Fluorescent polymeric nanoparticles

mAbs- monoclonal antibodies

ADCs- antibody-drug conjugates

HER2- human epidermal growth factor receptor 2

exoDOX- exosomes loaded with DOX

SLNs- solid lipid nanoparticles

NLCs- nanostructured lipid carriers

MLV- multilamellar vesicles

SUV- small unilamellar vesicles

LUV- large unilamellar vesicles

MPS- mononuclear phagocyte system

CMCS- carboxymethyl chitosan

CL- cationic liposome

NE- Nano-emulsions

ABCs- ATP-binding cassette transporters

CDs- carbon dots

TRAIL- tumor necrosis factor-related apoptosis-inducing ligand

CNMs- Carbon nanomaterials

CNTs- carbon nanotubes

CNHs- carbon nano horns

CQDs- carbon quantum dots

GO- graphene oxide

rGO- reduced graphene oxide

PSMA- prostate-specific membrane antigen

GQDs- graphene quantum dots

ECM- extracellular matrix

IFP- interstitial fluid pressure

MMPs- matrix metalloproteinases

CAR- chimeric antigen receptor

FUS- focused ultrasound

MTX- methotrexate

AuNPs- gold nanoparticles

PC- protein corona

Chapter 01

1. Introduction

Cancer is one of the leading global killers therefore, advanced therapeutic procedures are urgently required. The advancement of nanotechnology has made it possible for a significant effort to enhance cancer treatment delivery. The primary goal of the majority of nanocarrier uses in nanotechnology has been to preserve the medicine from rapid breakdown after systemic distribution and to enable it to reach the tumor site at therapeutic concentrations, while minimizing drug delivery to normal areas to minimize side effects. They are designed to distribute medications either passively, making use of the leaky tumor vasculature, or actively, utilizing ligands that boost tumor uptake and may increase antitumor efficacy, resulting in a net improvement in therapeutic effects (Aslan et al., n.d.).

1.1. Background study

Cancer disease is a group of illnesses distinguished by invasiveness and irrational, uncontrolled cell division, and also tobacco use, smoking, stress, and a sedentary lifestyle all have a significant negative impact on the ability to predict cancer risk (Gavas et al., 2021). The second most frequent cause of mortality in the world is cancer. It is a set of disorders with aberrant cell proliferation rather than a single disease. Surgery, radiation, and chemotherapy are available as individual or combined cancer treatments. Only 5 to 10 percent of cancer cases have an inherited genetic component (Anand et al., 2008). It is the result of the mutation of the gene and this mutation can

occur for various reasons. The treatment of this disease is still limited. Researchers have been trying to overcome this problem and they are trying different types of technology.

Different statistics & research predict that new cases of cancer might be 18.1 million and cancer-related deaths could be 9.6 million. By 2030, GCO known as Global Cancer Observatory, predicts that 30 million people worldwide will die from cancer each year (Siegel et al., 2021). To address the rising rates of anticancer drug resistance develops, newer anticancer drug discovery is still a necessity in the hunt for novel targets for molecules and action-taking mechanisms. resulting from tumor heterogeneity, the creation of new medications against cancer is extremely difficult (Zitvogel et al., 2008). The traditional treatment is surgery, chemotherapy, hormone therapy, radiation therapy, and so on. But most of them have serious side effects & some time has high risk like hair loss, skin disorder, suppression of the bone marrow, fatigue, neuropathies, and so on. There are some drugs for cancer that have specific side effects like cardiotoxicity & pulmonary toxicity (Chan & Ismail, 2014). In light of all of these facts, the need for the development of fresh approaches to pursuing targeted cancer therapy has grown in the recent past. Nowadays, there have been attempts to use nanoparticles to overcome the shortcomings of current medicinal techniques.

In this nanotechnological system, the particles have a size of 1-100 nm & have unique properties. Depending on their general shape, they can be divided into 0 Dimensional, 1 Dimensional, 2 Dimensional, and 3 Dimensional (*(PDF) Magnetic Iron Oxide Nanoparticles: Synthesis, Stabilization, Vectorization, Physicochemical Characterizations, and Biological Applications | B A L U - Academia.Edu*, n.d.). The outermost layer, the innermost layer, and the core, which is the primary structural component of the NP, make up the basic composition of nanoparticles, which is highly complicated. EPR stands for increased permeability and retention which is increased by

NPs' deep tissue penetration, and their surface properties affect Biological activity and half-life by successfully overcoming fenestration of the epidermis (Shin et al., 2016). Let's look at an example, reduce opsonization and evade immune system clearance when NPs are coated with the hydrophilic polymer polyethylene glycol (PEG). Following the development of nanotechnology, some nanotherapeutic medications have been a lot of marketing and commercialized, and several more have since 2010 into the clinical phase. By facilitating the use of medication combinations and preventing drug resistance mechanisms, nanotherapeutic medicines have advanced the fields of delivery of drug techniques and multidrug resistance in anti-tumor therapy (MDR) (Gavas et al., 2021).

1.2. The rationale of The Study

A growing number of scholars are devoting their careers to studying cancer because it is one of the biggest health issues in the world. The few anti-cancer medications on the market are ineffective in resolving this problem. People are developing greater and greater resistance to the existing chemotherapy drugs. The world needs more modern anticancer medications. To combat the rising instances of anticancer drug resistance develops, scientists are working to identify novel molecular targets as well as improved and safer modes of action. Drug development and discovery are made more difficult by tumor heterogeneity. With the limited understanding of carcinogenesis, the key difficulties are the small structures' sizes and the image resolution in the discovery of anticancer drugs. Nanotechnology is a technique that can reduce the toxicity of drug delivery & can get the maximum therapeutic index. Though nanocarriers of this technology have some side effects also, researchers are trying to develop & modernize this technique so that the applications

of this technique can do easily marketized & people can get rid of cancer disease with minimum side effects or zero side effects.

1.3. Aim of this project

Knowing the state of cancer treatment now and what are the advancements of nanotechnology in this treatment recently is the goal of this study. Furthermore, this study intends to explore the negative impacts, benefits, and drawbacks of various nanotechnological techniques. So that this nanotechnology for the treatment of cancer treatment can be further extensively researched & can overcome the shortcomings as this study is a review, this study will focus overall current advancement of this nanotechnology in cancer treatment.

1.4. Study Objectives

The Objectives of this study are discussed below,

- To know the current advancement of nanotechnology for the treatment of cancer.
- To know the current treatment conditions of cancer.
- To discuss the errors, advantages & disadvantages of the treatment methods.
- To make better decisions about the techniques of nanotechnology throughout cancer treatment.

Chapter 02

2. Methodology

Recent and noteworthy research articles and papers from high-impact journals were used to generate this review study. The results of a thorough search through peer-reviewed journals, official papers, and articles have been obtained. Basic and supplemental information has been gathered from many books to enhance the review article.

The information for this study was gathered using the following search engines: Springer Open, BMC, ResearchGate, NIH, Cell Press, Google Scholar, PubMed, Elsevier, Science Direct, etc.; the major journals included in these search engines are Nature, Science, Molecular Biological Journal, Medicinal journal, Molecular Cell, Cancer Cell related Journal, etc.

Compared to traditional anti-cancer medications, diagnostics, radiation therapy, and imaging; nanotechnology offers many benefits. NPs can reduce systemic toxicity while enhancing treatment & this review will light on these nanotechnological advancements in cancer treatment.

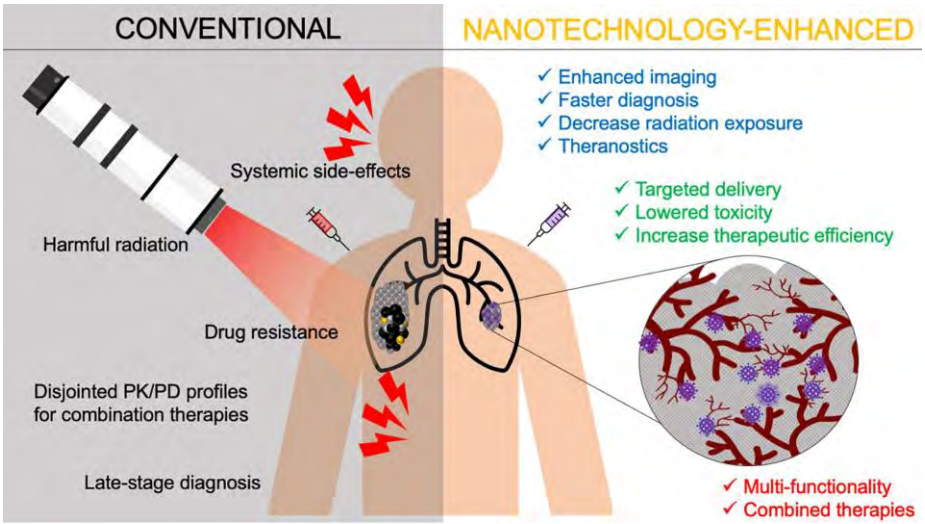

Figure-01: contrasts conventional and nanotechnology-based cancer treatment (Kemp & Kwon, 2021).

Statistical analysis of different research has shown the recent situation of cancer diagnosis & this review, will focus on the nano-technological treatment of cancer.

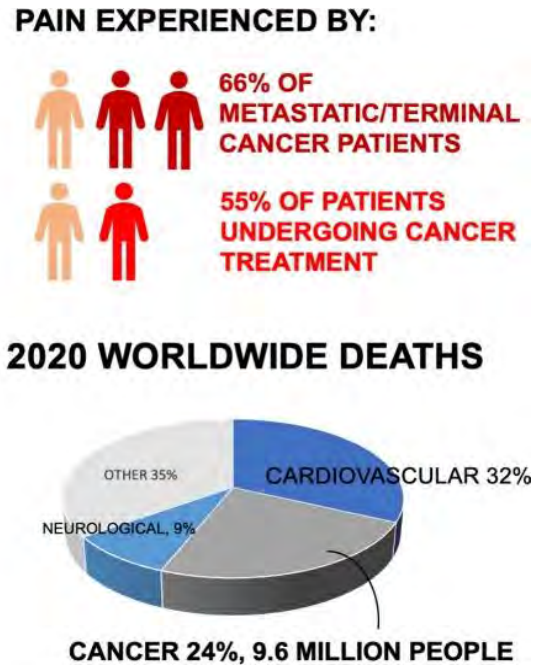

Figure-02: Cancer diagnoses at a late stage are associated with significantly greater patient expenses and lower 5-year survival chances (Kemp & Kwon, 2021).

An optimum quality evaluation was produced by carefully examining the journals, then focusing on those from the most recent and pertinent years for this review of the advancement of nanotechnology in the field of curing or in the treatment of cancer.

Chapter 03

3. Nanotechnology

With the development of nanotechnology, the negative effects of conventional cancer treatments like chemotherapy and radiotherapy may be lessened. Additionally, there has been a lot of research done in this area. Generally, the particles of nanotechnology are called nanoparticles and their size is normally less than 100nm. Besides this, the nanoparticles can be used in various sectors like gene therapy, cyro-surgery, immunotherapy, cellular targeting, and most important cancer therapy. Let's look at Figure 03, some information is illustrated here.

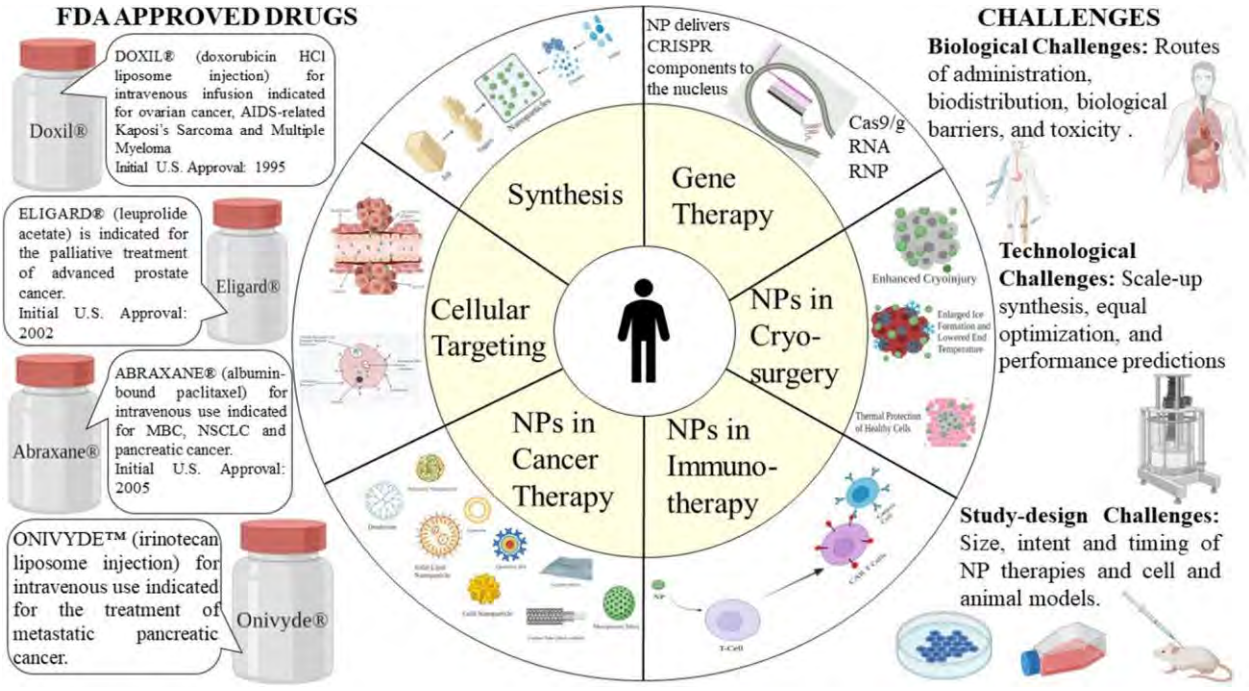

Figure-03: Nanoparticles for cancer therapy (Gavas et al., 2021).

3.1. Synthesis methods for the nanoparticles

They differ in their constructions, sizes, and shapes, and their methods are differently adopted. The methods of synthesizing of NPs are divided into 3 groups. They are-

- Physical methods,
- Chemical methods,
- Biological methods.

These two approaches can be further separated into many groups depending on the uses & terms-conditions (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

Let's look at figure 04 to understand those methods in detail.

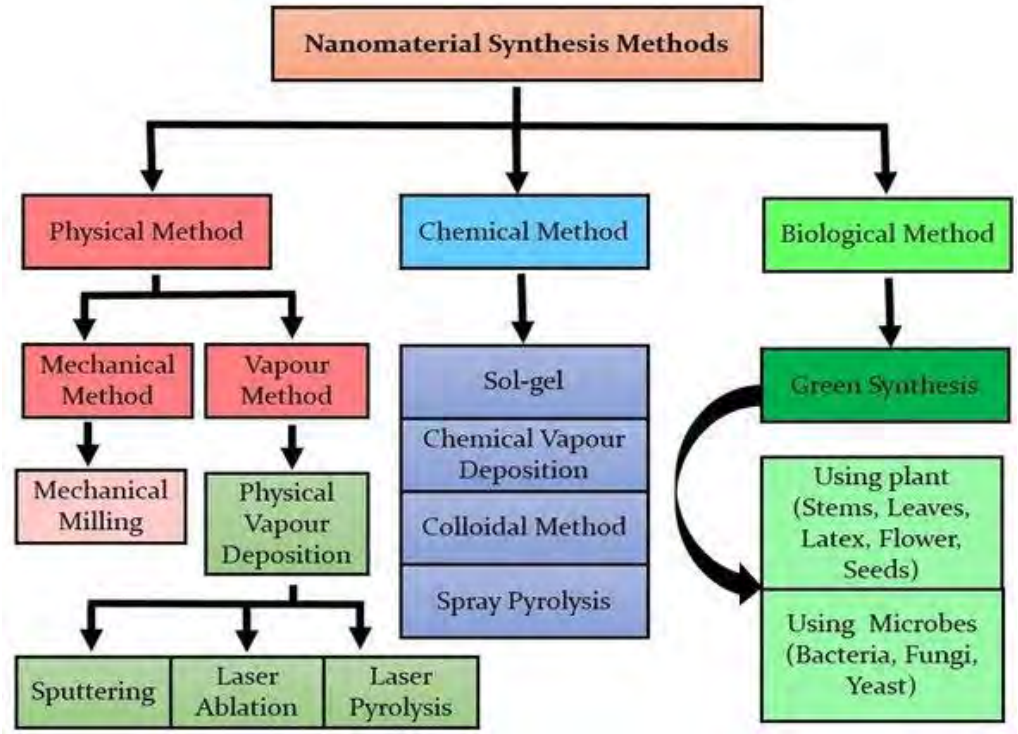

Figure-04: Methods of synthesis for nanoparticles (Goutam et al., 2020).

3.1.1. Physical methods

Small-scale production is ideal for physical approaches and they are further divided into some methods. Which are-

- Pulse laser ablation,
- Mechanical method,
- Laser pyrolysis,
- Chemical vapor deposition,
- Ionized cluster beam deposition,
- Pulsed wire discharge method

  (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.1.1. Pulse laser ablation

A vacuum chamber is filled with the desired sample. Plasma, which had previously been a colloidal solution of nanoparticles, is created when the high-pulsed laser beam is focused on the sample. In the creation of nanoparticles, the second-harmonic group type laser is widely employed. The type of laser, certain pulses, the type of solvent, and the pulsing time are all factors that determine the final product (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.1.2. Mechanical method

These methods are divided into 2 types which are- Ball milling & Melt mixing.

Ball milling

Innovative methods for producing nanoparticles. Planetary, vibratory, rod, and tumbler mill types are commonly employed. The container contains steel or carbide-based hard balls. Using this technique, nanocrystalline Co, Cr, W, and Ag-Fe are produced. Balls to materials are arranged in a 2:1 ratio. Inert gas or air is placed inside the container, which is then rapidly rotated around its axis. Between the container's walls and the balls, the materials are compressed. When creating nanoparticles of the ideal size, milling time and speed are crucial factors (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

Melt mixing

Turbulence and high-velocity metal molten streams combine to create nanoparticles. Nanoparticles in glass are captured. Glass is an amorphous substance with imperfect symmetry in the arrangement of atoms or molecules. When metals are cooled rapidly, amorphous solids and metallic glasses can develop. Ex: Nanoparticles of TiB2 are produced when a stream of heated and molten Cu-B combine (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.1.3. Laser pyrolysis

Laser pyrolysis is the term for the laser-assisted production of nanoparticles. When there is an inert gas present, such as helium or argon, an intense laser beam is concentrated to break down the mixture of reactant gases. The distribution and size of the particles are significantly influenced by the gas pressure (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.1.4. Chemical vapor deposition

At between 300 and 1200 °C, a thin coating of a gaseous reactant is applied to the substrate. A thin film of product is produced on the surface of the substrate as a result of a chemical interaction between the heated substrate and the combining gas. The applied pressure fluctuates between 100 and 105 Pa. There are numerous CVD variations, including Plasma Enhanced CVD, Atomic Layer Epitaxy, Vapor Phase Epitaxy, and Metallo Organic CVD. The advantages of this method include the production of stiff, homogeneous, and very pure nanoparticles (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.1.5. Ionized cluster beam deposition

The process was created in 1985. The primary goal of this technique is to produce excellent single-crystalline thin films. A source of evaporation, a nozzle through which material can expand into

the chamber, an arrangement to accelerate the clusters, an electron beam to ionize the clusters, and a substrate on which a nanoparticle layer can be formed are all included in the arrangement. Collections become ionized following contact with an electron beam. The clusters are concentrated close to the substrate because of the hastening voltage utilized. By keeping an eye on the accelerating voltage, it is probable to be able to regulate the energy with which the clusters impact the substrate. Since stable clusters of some materials would require a lot of energy to break their bonds, they would prefer to stay that way (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.1.6. Pulsed wire discharge method

The method used in the physical preparation of nanoparticles. The most used technique for creating metal nanoparticles. A pulsating current causes a metal wire to evaporate, producing a vapor that is then cooled by ambient gas to produce nanoparticles. It's possible that this plan will produce a lot of energy quickly. as in nanoparticles of nitride.

3.1.2. Chemical methods

This method is divided into several types which are-

- Sol-gel method,
- Sonochemical synthesis,

- Co-precipitation method,
- Inert gas condensation method,
- Hydrothermal synthesis.

3.1.2.1. Sol-gel method

Metal alkoxides or metal precursors in solution are condensed, hydrolyzed, and thermally decomposed. The result is the formation of a stable solution or sol. The gel's viscosity increases as a result of hydrolysis or condensation. By adjusting the precursor concentration, temperature, and pH levels, particle size can be observed. It may take several days for the solvent to be removed, for Ostwald ripening to occur, and for the phase to change, but this mature step is necessary to enable the growth of solid mass. Nanoparticles are created by detaching the unstable chemicals.

3.1.2.2. Sonochemical synthesis

In the presence of palladium and water, sonochemical fusion with copper salt has successfully created Pd-CuO nanohybrids. Switch metal salts could be converted into their oxides in the presence of palladium and water by using ultrasonic waves. The palladium supply is either the palladium salts or pure metallic palladium Pd(0) (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*).

3.1.2.3. Co-precipitation method

By sonochemically fusing copper salt with palladium in the presence of water, Pd-CuO nanohybrids were successfully created. Switch metal salts might change into their oxides in the presence of palladium and water. This was accomplished by using ultrasonic waves. Pure metallic palladium Pd(0) or palladium salts are the two sources of palladium (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*).

3.1.2.4. Inert gas condensation method

Metal nanoparticles are produced using this method in large quantities. It had been popular to make fine nanoparticles using the inactive gas compression approach, which creates nanoparticles by causing a metallic source to vanish in an inert gas. At a temperature that is attainable, metals evaporate at a tolerable pace. Copper metal nanoparticles are created by vaporizing copper metal inside a container containing argon, helium, or neon. By cooling the vaporized atom with an inert gas after it boils out, the atom quickly loses its energy. Liquid nitrogen is used to cool the gases, forming nanoparticles in a range of 2-100 nm (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*).

3.1.2.5. Hydrothermal synthesis

It is one of the techniques for making nanoparticles that is most frequently employed. It is primarily based on chemical reactions. For the synthesis of nanoparticles, hydrothermal synthesis uses a wide temperature range from ambient temperature to extremely high temperatures. Comparing this strategy to physical and biological ones has a number of benefits. Higher temperature ranges may make the hydrothermal synthesis-produced nanomaterials unstable (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.3. Biological methods

This method is also divided into some types which are-

- Synthesis using microorganisms,
- Synthesis using plant extracts,
- Synthesis using algae

  (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.3.1. Synthesis using microorganisms

Due to their affordability and environmental friendliness, microorganism-based nanoparticle production has attracted increased attention in recent years. Extracellular biosynthesis and

intracellular biosynthesis are the two processes used to create nanoparticles from microorganisms, respectively. Metal ions can be separated by some microorganisms. Pseudomonas stuzeri Ag295 can accumulate silver within or outside of cell walls, making it common in silver mines. Microorganisms have a variety of reductase enzymes that can store and detoxify heavy metals. CdS nanoparticles can be created using Klebsiella pneumonia (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.3.2. Synthesis using plant extracts

The production of nanoparticles demonstrates the critical role played by plant extracts. This method of producing nanoparticles is also known as green synthesis or a green technique. The geranium plant (Pelargonium graveolens) has leaves that have been utilized to make gold nanoparticles. To create silver nanoparticles, 1 ml of a 1 mmol aqueous silver nitrate solution is added to 5 ml of the plant extract. The same process is used to create compounds from alcoholic extract, The plant extract and silver nitrate are shaken in the dark at 150 rpm (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

3.1.3.3. Synthesis using algae

Preparation of algal extract in an organic or aqueous solvent through heating or boiling for a set amount of time. preparation of an ionic metallic complex molar solution. Algae solution and molar

solution of ionic metallic complexes are incubated under controlled circumstances, either with continuous stirring or without stirring for a predetermined amount of time. The method of creating nanoparticles is dose-dependent and depends on the kind of algae employed. Peptides, pigments, and polysaccharides are biomolecules that are responsible for the reduction of metals. Algae may produce nanoparticles more quickly than other types of living organisms (*View of OVERVIEW ON METHODS OF SYNTHESIS OF NANOPARTICLES | International Journal of Current Pharmaceutical Research*, n.d.).

Besides the three main methods of synthesis of NPs, the synthesis can also divide into 2 methods which can understand by looking at Figure 05.

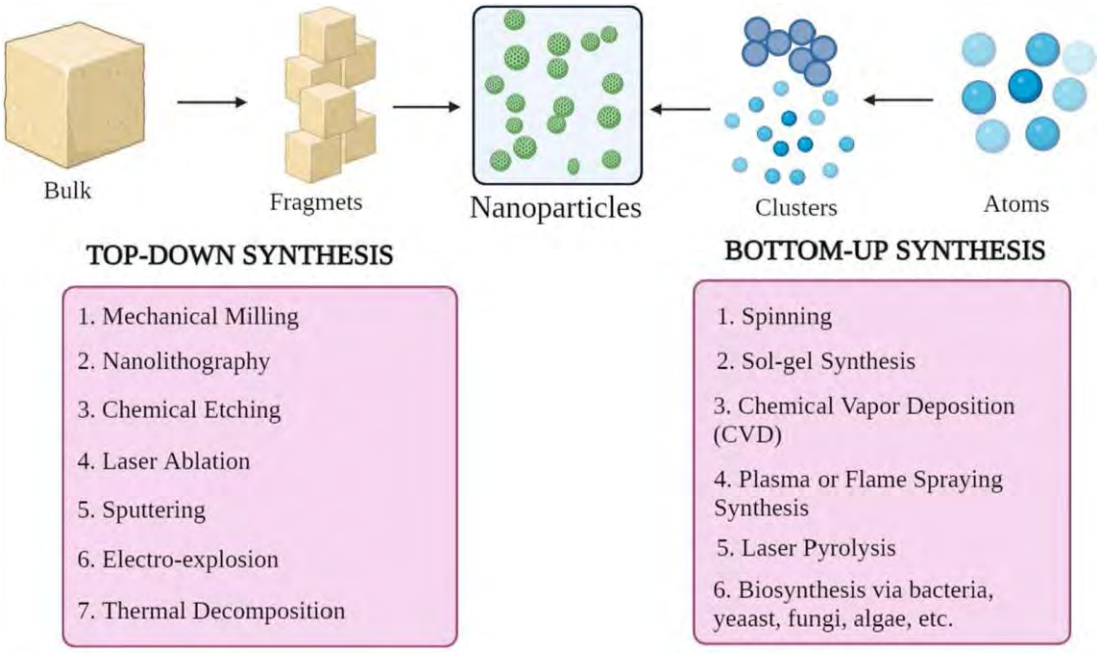

Figure-05: Classification of nanoparticle synthesis (1) top-down and (2) bottom-up approaches (Gavas et al., 2021).

Chapter 04

4. Mechanisms of Nanoparticle Cellular Targeting

To reduce toxicity in the treatment of cancer, the drug should be applied in a specific location. So that other healthy cells cannot get destroyed or harmed due to the treatment of the cancer-affected cells. That's why to get effective results nanoparticles are being used in the targeting drug delivery system. To find an NP-based medication targeting design, various studies have been conducted thus far, and more are under development. Typically, these nanocarriers ought to have a few basic qualities. They are-

- Insertion of high pressure into tumor fluid,
- Through the tumor vascular system, aggregate in TME,
- The capacity to stay steady in the bloodstream until they reach their target (TME),
- Reach the desired location and exclusively contact tumor cells,
- To circumvent the mononuclear phagocyte system (MPS),
- To circumvent the reticuloendothelial system's (RES) clearance

  (Gavas et al., 2021).

It is crucial to discuss the targeting mechanisms to comprehend the connection and tumor biology, cancer cells, and NP carriers interact. The two fundamental categories into which the targeting systems can be split into passive targeting and active targeting.

4.1. Passive Targeting

To target the nanoparticles passively, certain pathophysiological factors are exploited near the tumor, for example, pH, temperature, surface charge, and leaky vascular system. Nanoparticles take drugs to the cells which are affected by tumors or cancer indirectly and this depends on these factors.

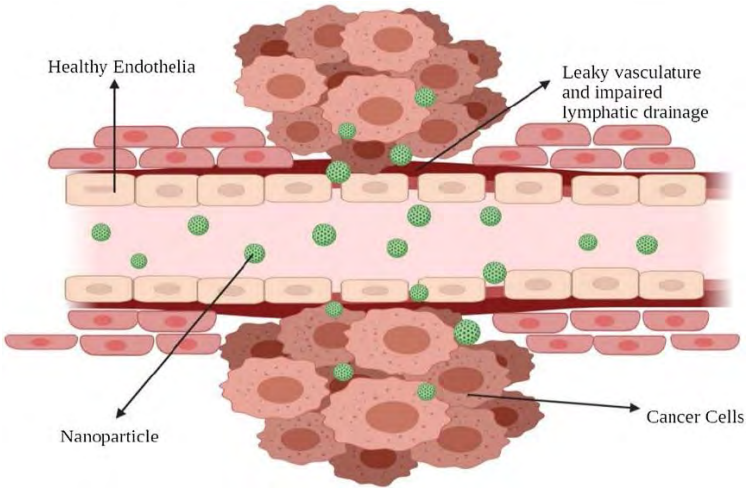

Figure 06: Passive cellular targeting (Gavas et al., 2021).

4.1.1. EPR effect, or enhanced permeability and retention

This passive distribution could be explained by the merger of inadequate lymphatic drainage and the formation of fenestrations within the clogged tumor blood vessels. The endothelial blood vessel layer becomes more porous in specific circumstances like hypoxia or inflammation and to keep up with their rapid growth, the hypoxic tumor cells often engulf or activate more blood vessels which is also known as neovascularization. Due to their wide pores, these new blood vessels leak and are less perm-selective for tumor blood than regular blood vessels (Torchilin, 2011);(Bates et al.,

2002). According to the cancer type, TME, and location, these enormous pores or fenestrations range in size from 200 to 2000 nm. Extracellular fluid (ECF) drainage into lymphatic arteries regularly occurs in normal tissues at an average flow rate of 0.1-2 m/s, maintaining continual drainage and regeneration. The lymphatic system is disrupted when a tumor develops, resulting in little interstitial fluid intake. Since they are not removed and accumulate in the tumor interstitium, this property helps with NP retention. The improved retention component of the EPR effect is indicated by this process (Hobbs et al., 1998; Swartz & Fleury, 2007). The fundamental aspects of tumor biology, including

- Intratumor pressure,
- Lymph angiogenesis and the level or amount of angiogenesis,
- Perivascular tumor invasion's degree or extent.

All play a significant role in the EPR effect. These elements evaluate the NP medication delivery system's efficiency along with the physicochemical properties of NPs. Let’s look at Figure 06.

4.1.2. Tumor microenvironment (TME)

Delivering drugs to the key component of passive aiming is TME. Glycolysis is A key component of passive aiming is TME which processes in tumor cells that reproduce quickly. It is the main source of energy for cell division & creates an acidic atmosphere around it. To take advantage of the TME's decreased pH, Low pH-sensitive pH-sensitive NPs that release medications can be used (Attia et al., 2019; Pelicano et al., 2006). Let’s look at Figure 06.

4.1.3. Neovascularization and angiogenesis

It affects NP diffusion and raises interstitial pressure, both of which prevent NP accumulation. Additionally, the proliferation of the tumor cells is unequal due to the diverse blood supply which means that cells near blood vessels divide more quickly than cells further inside the hypoxic or necrotic zone that makes up the tumor's core, or cells farther away from the blood vessels. Drug transport and accumulation are hindered by this irregular leakage, which raises interstitial pressure, and the neovascularization process is slowed down (Padera et al., 2004).

4.1.4. Examples of Passive Targeting NPs drug

Recently the drug products of NPs of passive targeting are developing under different research & laboratory. But some of them show the light of hope & they are used in the local market. They have some side effects also but they are very minor & research has been running to minimize them. Some of the drugs are approved by FDA & different organizations. Patients & doctors are getting positive results after using them. Some of them are-

- Taxanes-

  The three histologies most frequently treated with taxanes are cancer of the breast, non-small cell lung cancer, and cancer of the ovarian.

- Albraxane (Paclitaxel)-

  It is (albumin-bound paclitaxel, Abraxis BioSciences) used to treat advanced or metastatic breast cancer, and was given US-FDA approval in 2005. (MBC). By preventing depolymerization, this anti-microtubule medication stabilizes the

microtubules. When a medication promotes the formation of microtubules from tubulin dimers, it happens. It reduces pancreatic stroma either by itself or in combination with another cytotoxic substance for example pancreatic cancer, gemcitabine mouse xenograft models (Gavas et al., 2021; Li et al., 2020; Zhou et al., 2020).

- Genexol PM-

  It is a fresh, non-CrEL polymeric micellar formulation of paclitaxel in nanoscale. In addition, the biodistribution revealed two to three times larger quantities in cancer cells and organs like the liver, spleen, kidney, and lung.

  The decision to treat MBC in South Korea has been approved. Phase II clinical trials are still ongoing on pancreatic cancer patients in the USA (Gavas et al., 2021; Miele et al., 2009).

- DaunoXome-

  It is an anticancer drug that slows the development of tumor cells.

  Daunorubicin is an active chemical. Using a unique formulation of daunorubicin, Kaposi's sarcoma is a type of cancer that impacts the lungs, skin, and intestines, and is treated (in liposome form). In 1996, US-FDA gave its approval (Gavas et al., 2021; Kim et al., 2007).

4.2. Active Targeting or Ligand Based Targeting

It relies on particular chemicals or ligands, such as Transferrin and folate attach to molecules or receptors on the target cells that are particularly expressed or overexpressed (Mukwaya et al., 1998). Ligand targeting is another name for this form of targeting. To increase affinity, NPs have ligands with particular properties, such that the aim must be closely followed for retention and uptake. This process enhances the nanoparticle binding & also enhances drug penetration. In this process, the ligand like peptides, aptamers, antibodies, sugars, and small molecules like vitamins, nucleic acids, etc. are bound with different types of receptors to give a direct therapeutic effect. The nanoparticles stimulate the ligand or receptors to bind each other to the TME & also in the tumor cells so that proper therapeutic effects can get from the active targeting without harming other healthy cells. In 1980, For the first time, antibodies that were followed by different ligands were shown to graft on the surface of liposomes (Padera et al., 2004). The receptors that are most commonly studied are the receptor of transferrin, glycoproteins, receptor of folate, and EGFR which is known as the epidermal growth factor receptor (Byrne et al., 2008; Gavas et al., 2021).

4.2.1. Peptide-based targeting

This targeting is dependent on the ligand targeting system. owing to its ease of manufacture, small size, low immunogenicity, and reasonably inexpensive cost, this method is used. Finding peptide-based targeting ligands can be accomplished in several ways. Peptides are typically extracted from the protein of interest's binding areas. Finding peptide-based targeting ligands can also be done via phage display techniques (Trac & Chung, 2020).

4.2.2. Targeting based on aptamers

These are RNA or DNA oligonucleic acids with unique three-dimensional structures that can bind to different biological objectives, such as large proteins and small molecules. The technique comprises a series of the round of target-binding shots, distinguishing between binding and sequences which is non-binding, and increasing the number of sequences that are enriched in binding with the versions of the target proteins on the surface of the cell which are bioactive. They can be chosen from libraries of 10^{15} randomly chosen oligonucleotides because they have a high affinity and specificity for a target. More than 200 aptamers have so far been isolated (Hashemi et al., 2020).

4.2.3. Transferrin

It is a glycoprotein that binds non-heme iron in the serum that serves as the transporter, facilitating the blood's transport of iron to cells that are actively growing. It does this by attaching to the receptor that transfers iron. By receptor-mediated endocytosis, internalization of transferrin results in the release of iron in the environment of the cell which is acidic. The receptor is essential for controlling iron homeostasis and cell growth. For this reason, these receptors are overexpressed in metastatic and drug-resistant cancer cells because they have a higher iron requirement than normal cells, which makes them a prime target for nanoparticles (Amreddy et al., 2015; Saha et al., 2010; Santi et al., 2017).

To understand active targeting or Ligand-based targeting, let’s look into the Figure 07 illustration.

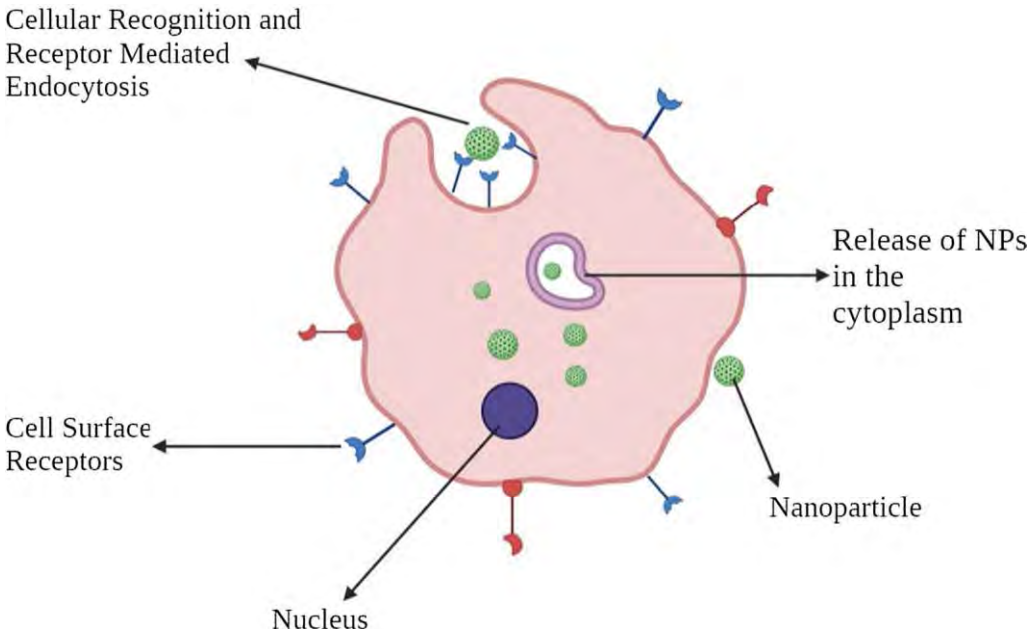

Figure 07: Active cellular targeting depicted visually (Gavas et al., 2021).

4.2.4. Examples of Active Targeting NPs drug

Like the passive targeting drug, active targeting drugs are also under the research & development sections. Some of them are used in the treatment of cancer curing. But most of them need to update properly so that the risk factor can reduce & can get the proper therapeutic effect or index. Let's look at some of the drugs from nanoparticle active targeting drugs,

- EGFR-

  It is related to the tyrosine kinase receptors and targets & treats human SCC. Moreover, useful gold nanoparticles include those with nanoparticles which are anti-EGFR-PEG-AuNPs and anti-IgG-PEG-Au (Gavas et al., 2021; Jiang et al., 2008).

- Herceptin-

  Human EGF receptor-2 (HER2), which is overexpressed on the surfaces of breast cancer cells, is the target of this therapeutic medication. Additionally, to lessen cardiotoxicity, HER2-targeted PEGylated Liposomal Doxorubicin was created (Gavas et al., 2021; Reuveni et al., 2011).

- VCAM-1

  It stands for vascular cell adhesion molecule-1 and is a glycoprotein that is expressed on the tumor endothelium's surface and takes part in the angiogenesis process. NPs that target VCAM-1 in the breast cancer model have been highlighted in a study, highlighting its potential function (Gavas et al., 2021; Reynolds et al., 2012).

- Folic acid-

  It is also referred to as vitamin B9 and is crucial for the synthesis of nucleotides. The cell-expressed folate receptor takes it up inside of itself. However, overexpression in tumor cells FR-α (an alpha isoform of folate receptor), while FR-β in liquid cancer cells is overexpressed (Gavas et al., 2021; Pan et al., 2013).

Chapter 05

5. Nanomaterials against the cancer cells

In nanotechnology, there are different types of particles or materials that are being used for the treatment of cancer. Different types of materials have different types of characteristics and they do work differently against cancer or tumor cells. Now different types of nanomaterials or particles will be discussed here and some of them are illustrated in Figure 08.

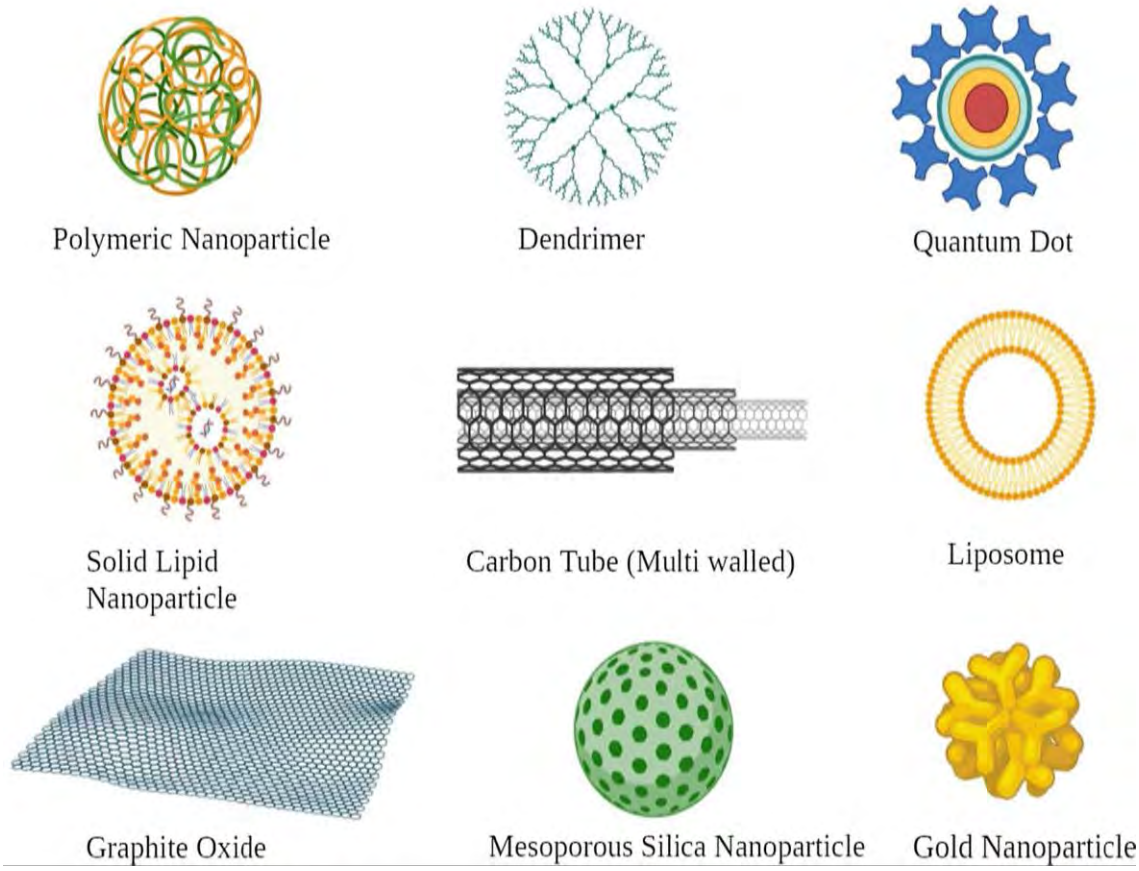

Figure-08: To cure cancer, a variety of different nanomaterials are used (Gavas et al., 2021).

5.1. Nanomaterials made of polymers

It is generally known that (PNPs) are "colloidal macromolecules" which has a specific structural architecture made up of several monomers. To offer the drug which is regulated to release in the target, the drug has either been encapsulated or attached to the exterior of nanoparticles which creates a nanosphere or a nanocapsule (Amreddy et al., 2018; Samadian et al., 2016). The non-biodegradable polymers used to make these PNPs included polyacrylamide, polymethylmethacrylate (PMMA), and polystyrene (Masood, 2016). Biodegradable polymers are now in use since they have a reputation for reducing toxicity and enhancing drug Releasing and being biocompatible. Chitosan, alginate, polylactic acid, albumin, and poly(amino acids) are among examples (Vijayan et al., 2013). The blood-brain barrier's endothelial cell membrane is better contacted by NPs when they are coated externally (BBB) (Elsabahy & Wooley, 2012). There are several instances, including modified dextran-camptothecin and PEG-camptothecin (Prothecan) (DE 310), HPMA copolymer-paclitaxel (PNU166945), HPMA copolymer-platinate (AP 5280), HPMA copolymer-DACH-platinate (AP5346), and HPMA copolymer-doxorubicin galactosamine (PK2) (Bernardi et al., 2009; Gavas et al., 2021).

5.2. mAb Nanoparticles

These are frequently utilized because of their unique targeting capabilities. NPs are now coupled with these nanoparticles to create antibody-drug conjugates (ADCs) (Kukowska-Latallo et al., 2005). A drug that is used as an antibody of NPs with paclitaxel core and trastuzumab which is surface modified demonstrated stronger efficacy of anti-tumor and their toxicity is lower than

Paclitaxel or trastuzumab as a single agent in the management of HER2-positive breast epithelial cells (Gavas et al., 2021; Sievers & Senter, 2013).

5.3. SLN-Solid Lipid Nanoparticles

They are nanomaterials (1 to 100 nanometers) that are colloidal in nature & zero-dimensional, made of a monolayer of a phospholipid, and an aqueous and an emulsifying agent (Hofheinz et al., 2005). In SLNs, the medication is contained in a "micelle-like structure" with a core that isn't watery. A good example is SLN which has been loaded with mitoxantrone and has been shown to have enhanced absorption & decreased toxicity (Ali et al., 2021; Gavas et al., 2021).

5.4. Cyclodextrin Nano-sponges

They are tiny, mesh-like structures that are generally added to NPs as stabilizers to increase their ability to carry drugs (Duchêne et al., 1999; Gavas et al., 2021; Gorain et al., 2020). B-cyclodextrin nanosponges containing paclitaxel demonstrated consistent cytotoxic activity in MCF-7 cell line culture (Subramanian et al., 2012).

5.5. Nano-emulsions

Heterogeneous oil droplet mixtures of nanoparticles that are colloidal in nature & their range of size are from 10 to 1000 nm are present in this aqueous medium. It is possible to create three types of nano-emulsions that are-

- Water-in-oil system,
- Oil-in-water system,
- Bi-continuous nano-emulsions.

Better anticancer effects were seen with Spirulina and Paclitaxel-loaded nanoemulsions that altered immune function through signaling pathways which are TLR4/NF-kB (Jaiswal et al., 2014). Nanoemulsions have greater advantages over others, for example, stability, optical clarity, and biodegradability, as they are unique from liposomes (Dianzani et al., 2020). Some difficulties include the high temperature and pressure involved, as well as the cost of the pricey homogenizers and microfluidizers.

5.6. Dendrimers

These polymeric macromolecules are spherical and have a characterized hyperbranched topology and an ammonia core and acrylic acid are reacted to begin the dendrimer production (Wang et al., 2008). The dendrimers typically have sizes between 1 and 10 nm. The size, however, could be as large as 15 nm. TEA, Polyamidoamine (PAMAM), PEG (poly(ethylene glycol)), and polypropylene imine (PPI) are some dendrimers that are frequently utilized (triethanolamine) (Gavas et al., 2021; Lim et al., 2013). When compared to animals receiving chemotherapy which is single-agent with the produced dendrimers dramatically inhibited the growth of xenografts with epithelial cancer and Initially a dendrimer known as PAMAM, was designed to accomplish the management of MDR (Gavas et al., 2021; Lo et al., 2013).

5.7. Liposomes

To enclose medicinal molecules, These vesicles are round and comprised of phospholipids which can be either unilamellar or multilamellar & Their distinctive qualities include biological inertness, weak immunogenicity, and minimal intrinsic toxicity (Gavas et al., 2021; Sun et al., 2019). In 1965, liposomes were started as nanoparticle drug delivery for cancer treatment. They are like the fluid-mosaic model because they have a hydrophilic core & a hydrophobic phospholipid bilayer. That's why they can entrap both hydrophilic & hydrophobic drugs. For example, Daunorubicin liposome-based formulations for the treatment of MBC, Doxil®, and Myocet®, are approved (Ferrari, 2005; Gavas et al., 2021; Wang et al., 2017).

5.8. Extracellular Vesicles

EVs are double-layered phospholipid vesicles that range in size from 50 to 1000 nm, bypass immune surveillance, and incorporate cancer cells very quickly (Abedin et al., 2021).

They are classified into 3 classes. They are-

- Exosomes,
- Microvesicles,
- Apoptotic bodies

  (György et al., 2011).

The finest example is exosomes that have been loaded with doxorubicin (exoDOX). Exosome NPs differ from synthetic NPs in that they have inherent biocompatibility properties, enhanced

chemical stability, and intracellular communications. ExoDOX, for instance, is used to reduce the effect of breast cancer (Raposo & Stoorvogel, 2013; Wei et al., 2021).

5.9. Carbon Nanoparticles

These are widely used because of some characteristics like mechanical, optical & electronic properties which are combined with biocompatibility. Because of their hydrophobic properties, carbon NPs entrap medicines by π-π stacking. They fit into a few different groups. Examples, are Fullerenes, Carbon Nano-Horns, Graphene, Carbon Nanotubes, Graphyne, and many more.

The graphene's carbon sheet, a two-dimensional material having high drug-loading properties, extraordinary mechanical, and electrochemical, is hybridized with two electrons. They can also be classified into further classes according to their properties, and composition.

They are; reduced graphene oxide (rGO), graphene oxide (GO), single-layer graphene, and multi-layer graphene (Gavas et al., 2021; Krishna et al., 2013).

“Due to its capacity to target hypoxia and erratic angiogenesis in TME, GO and rGOs are commonly employed. On tumor cells, PEG-modified fullerenes demonstrated positive photodynamic effects. On the other hand, Circular tubes known as carbon nanotubes (CNTs) are frequently compared to rolls of graphene and they are divided into 2 groups:

- Single-walled CNTs,
- Multi-walled CNTs.

They have traditionally been employed for thermal ablation therapy and as DNA delivery vectors. To target colon cancer cells, for instance, fluorescent single-walled CNTs with mAb encapsulating doxorubicin are utilized (Tabata et al., 1997)."

5.10. Magnetic Nanoparticles

These typically use MRI imaging and have a metal or metal oxide medicine delivery system. To increase biocompatibility and stability. Moreover, these are typically coated with materials that are organic, like fatty acids and polymers (Gavas et al., 2021). Targeting imaging breast cancer with Superparamagnetic iron oxide NPs linked to LHRH is successful and for the heat destruction of cancer cells, magnetic nanoparticles are employed during magnetic hyperthermia (Meng et al., 2009). Magnetic NPs are available for colon cancer and liver metastases & they are Feridex® and Resovist®.

5.11. Calcium Phosphate Nanoparticles

"It is biodegradable, compatible with biological systems, and has no serious side effects. They serve as a vehicle for the transfer of antibiotics, growth hormones, insulin, and contraceptives and are also utilized for plasmid DNA and oligonucleotide delivery (Maurya et al., 2019)."

5.12. Nanoparticles made of metal

Among the "biological imaging" and targeted DDS, gold, silver, iron, and copper NPs are frequently explored because of their excellent magnetic, optical, and photothermal properties. Because gold nanoparticles' size and surface characteristics are easily controllable, they are used as intracellular drug delivery systems (Bagalkot et al., 2007; Gavas et al., 2021). It is demonstrated that HER2-positive breast cancer cells are the target of anti-HER2 functionalized gold-on-silica nanoshells, and Feraheme®, an iron oxide NP formulation including ferumoxytol, is used to treat iron deficiency anemia. Additionally, these are used to treat testicular cancer, prostate, and nodal metastases, this had been granted by FDA & got approval in June 2009 (Mousa & Bharali, 2011).

5.13. Silica Nanoparticles

“By adding amino-silicones to the NP surface, silica NPs are frequently utilized to transport genes. It is now commercially possible to buy N-(6-aminohexyl)-3-aminopropyl-trimethoxysilane functionalized silica NPs, which have demonstrated great efficacy in the transfection of Cos-1 cells with little toxicity. Because of their superior pharmacokinetic characteristics, mesoporous silica nanoparticles are regarded as one of the best drug carriers. They are widely utilized in immunotherapy. In a study, camptothecin-loaded mesoporous silica NPs were successfully taken up by colorectal cancer cells (Gavas et al., 2021; Katragadda et al., 2010).”

5.14. Quantum Dots

These nanometer-scale semiconductors have narrow emission bands, a wide absorption spectrum, and good photostability, making them ideal for application in biological imaging. “They are divided into 2 types based on carbon and they are-

- Graphene quantum dots,
- Nanodiamond quantum dots,
- Carbon quantum dots.

Due to their innate biocompatibility and quick elimination, graphene quantum dots are the most often employed quantum dots. For instance, the prostate cancer cells are targeted by the drug conjugated with quantum dots aptamer (Gavas et al., 2021; Jamieson et al., 2007).”

Chapter 06

6. Benefits of Nanoparticle Therapy for Cancer

To establish and control the drug release, it is possible to produce and alter the targeted NPs so that they are either sensitive to pH or temperature. The acidic TME can receive medications through the pH-sensitive drug delivery mechanism. Similar to this, nanoparticles (NPs) are sensitive to temperature, when sources like magnetic fields and ultrasonic waves create temperature changes, the medications release at the target spot. Additionally, NPs can be altered for a specific target and applied to focus on a specific moiety. “Generally, the metabolism of drugs is an extremely intricate process. The medication must successfully cross the TME, RES, BBB, and renal infiltration under physiological conditions. "Blood monocytes, macrophages, and other immune cells" make up the RES or macrophage system, and MPS in the liver, spleen, or lungs reacts to drugs by activating "macrophages or leukocytes" that quickly remove the drug. As a result, the drug's half-life is reduced (Yona & Gordon, 2015).” NPs with surface modifications, like PEG, circumvent this and lengthen the drug half-life by doing so.

BBB known as the brain-blood barrier is a unique defense mechanism designed to shield the central nervous system (CNS) from poisonous and damaging substances. An ordered wall of "brain capillary endothelial cells" provides the brain with essential nutrients. Some NPs cross the BBB. Currently, peptide-modified endocytosis, the EPR effect, targeted ultrasound, and transcytosis are just a few of the ways NPs are administered (Tran et al., 2017). “Since NPs are transporters, they also prevent the enclosed cargo from degrading, which increases the drug's stability. Furthermore, a substantial number of pharmaceuticals can be enclosed without experiencing a chemical reaction. Nano liquid compounds are less stable than dry solid dose forms (Feng et al., 2017).”

The pathophysiology of tumors is distinct, with abnormal lymphatic drainage, excessive angiogenesis, and flawed vascular architecture. These characteristics enable the NPs to target tumor tissue. NPs are efficiently maintained because tumor tissue has a decreased venous return and a weak lymphatic clearance. EPR is the term for this phenomenon (Gavas et al., 2021; Wu et al., 2011). When used as drug carriers, nanoparticles are more efficient than microparticles and can enter the bodies through a variety of channels, including the oral, nasal, parenteral, intraocular, etc (Brigger et al., 2002; Gavas et al., 2021).

Table 01: FDA-approved list of nanomedicines for cancer treatment (Gavas et al., 2021).

Tradename	Material	Indication	Drug & Approval Year
Doxil®	Liposome-PEG	Metastatic ovarian cancer, or MBC	Doxorubicin in 1995
Eligard®	PLGA	Cancer for the Prostate	Leuprolide acetate in 2002
Abraxane®	Albumin	breast cancer that has spread	Paclitaxel in 2005
Genexol PM®	mPEG-PLA	breast cancer that has spread	Paclitaxel in 2007
Onivyde®	Liposome	Cancer for the Pancreases	Irinotecan in 2015

6.1. Immunotherapy using Nanoparticles

"Nano-vaccines," "aAPCs (artificial antigen-presenting cells)," and "immunosuppressed TME targeting" are all components of NP-based immunotherapy. Nano-vaccines are particularly good in providing "tumor-associated antigens" as well as "adjuvants" to antigen cells, like dendritic cells (DCs) (Gavas et al., 2021; Yan et al., 2020). Artificial APCs engage in direct interactions T cells are bound by MHC-antigen complexes. Additionally, these interact with the substances which are co-stimulatory in nature that attaches to receptors known for co-stimulatory and cause T-cells to become active (Fontana et al., 2017; Gavas et al., 2021).

Some of the crucial immunological checkpoints include "programmed cell death protein 1 (PD-1)" & "programmed cell death ligand 1 (PD-L1)". Immunological checkpoint inhibitors are used in conjunction with nanoparticles to target them (Bauleth-Ramos et al., 2017; Gavas et al., 2021).

6.2. Cryosurgery using Nanoparticles

Freezing cancerous tissue to death is a sophisticated technique. Nano-main cryosurgery's mechanism of action is the introduction of NPs with specific characteristics into cancer cells, which results in freezing. Ice is created inside the cells during this process, which harms them and can be accomplished with NPs. By utilizing a property of the NPs which is thermal conductivity can cause tumor damage and significantly freezes tumor tissue, it can regulate the "growth direction" and "direction of the ice ball." (Gavas et al., 2021; Liu & Deng, 2009). Reportedly, liposome-based microencapsulated phase change NPs have shown remarkable success in protecting the surrounding healthy tissue, making them ideal for cryosurgery. With their enormous latent heat and limited thermal conductivity, phase change materials (PMs) made of NPs have been

used in cryosurgery to shield the surrounding normal, healthy tissue (Chua et al., 2007; Di et al., 2012; Gavas et al., 2021).

For better understanding, let's look into Figure 09 and it would be useful to understand the importance of Nanoparticles in cryosurgery.

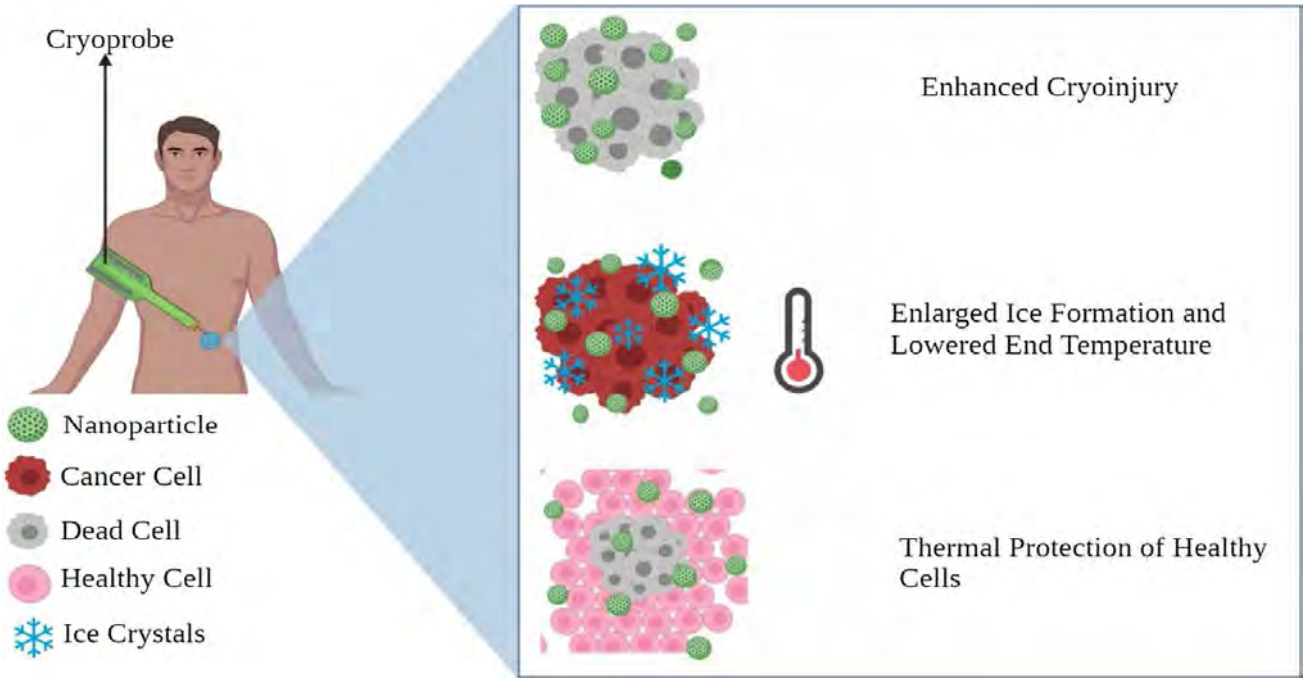

Figure 09: A diagram showing how NPs are used in cryosurgery (Gavas et al., 2021).

Chapter 07

7. Significant Obstacles in the Clinical Use of Nanoparticles

Even though interest in nanotechnology has grown recently, the research's and studies' proper outcomes still fall short. The majority of NPs experience the same issues or difficulties, which can be categorized into three categories: biological challenges, technological challenges, and study-design-related challenges.

7.1. Challenges in Biology

“This includes the absence of administration routes, limiting biodistribution, the passage of NPs via biological barriers, their breakdown, and their toxicity. NPs are often administered via intravenous injections into the circulation, which removes NPs and makes it difficult for NPs to remain at and interact with the target site. The use of 3D magnetic fields to control the movement of NPs against blood flow has been demonstrated in several in vivo and in vitro experiments, therefore magnetic nanoparticles can be utilized to overcome this. Studies show that NP-produced free radicals frequently harm healthy cells (Gavas et al., 2021).”

7.2. Technological challenges

“The majority of NPs utilized in vivo and in vitro investigations are often manufactured in small batches, and scale-up for enormous amounts is frequently not practical due to instrumentation and other factors. The best lead clinical prospects in animal models are not always systematically

conceived and optimized. To get around this, we can employ specific techniques that allow us to evaluate a variety of nano-formulations and choose one optimum formulation through careful iterations (Akinc et al., 2008; Dobrovolskaia et al., 2008; Gavas et al., 2021; Xia et al., 2020).”

7.3. Study-design challenges

“In clinical studies, factors including study size, purpose, and timing of NP therapies have a big impact on the outcome. The majority of studies use "cell and animal models," which might not produce clear outcomes in human trials. Therefore, it is difficult to replicate natural bodily processes using just one model. Additionally, as metastasis is one of the important characteristics of cancer, "models of cancer metastasis" should be actively explored. NPs are never employed as initial treatments. Although we have successfully authorized nano-formulations, they are often reserved for use in later stages of treatment if disease progression is discovered during a clinical trial (Love et al., 2010; Schork, 2015).”

Chapter 08

Discussion and Finding

Nanomedicine developments present fresh chances to enhance the arsenal against cancer. The preclinical and clinical stages of targeted and nontargeted nanoparticles show the influence of delivery mechanisms on the field. Additional research in nanomedicine will increase the therapeutic window for medications with far fewer side effects, improving patient outcomes (Aslan et al). As the days have been passing different types of study & research of different techniques are being developed. Though nanotechnology hasn't been used as the primary treatment, it will be used as a primary attempt treatment drug soon. The cancer cells can be destroyed with the nanoparticles if the research & studies have been gone through in further detail & try to minimize the side effects as the errors of the maximum nanoparticles are often the same. Different nano-drugs are already marketized & people are getting easy to take the nanoparticle treatment. So, it is hoped that despite all the errors & problems till now, soon a time will come when traditional chemotherapy & radiotherapy won't be necessary to take rather people will take the nanotechnology drug & people will get rid of cancer like other normal diseases.

Chapter 09

Conclusion

A promising new era of cancer treatment has emerged because of nanotechnology through the delivery of tiny molecules for the detection of cancer, and treatment plans of it. In comparison to traditional medications, the pharmacokinetics, biocompatibility, tumor targeting, and stability of NP-based DDS are all enhanced. Numerous NP forms, including polymeric, metallic, and hybrid NPs, have demonstrated enhanced delivery drugs & their effectiveness due to increased study. The characteristics of the suggested nanoplatforms and the characteristics of therapeutic drugs must be carefully studied by researchers.

It is anticipated that additional NP-based medications will be able to make use of this growing field as the study of "mechanism of cancer origin, MDR, incidence" in proteomics is still expanding. Only a small number of medications based on the nanoparticles are being used, a tiny number are in the phase of clinical trials, and the majority of the parts are still in the exploratory stage, in contrast to the vast number of investigations. More work needs to be put into "understanding toxicity, cellular and physiological parameters that influence NP-based medication delivery, EPR, and PC mechanism" for logical nanotechnology design, in the body of a human being.

The aforementioned information allows one to conclude that the development of nanotechnology and therapies involving nanoparticles will have a significant positive impact on the treatment of cancer.

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