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A REVIEW: NANOPARTICLES USED IN ANTICANCER THERAPY

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ABSTRACT

Nanotechnology is the study and use of structures between 1 nanometer and 100 nanometers in size. Cancer is the leading cause of death among most of people. Nanoparticles that deliver chemotherapy drugs directly to cancer cells. Nanomedicine application areas include drug delivery, therapy, diagnostic, imaging and antimicrobial techniques. This article aims at giving an overview of the present use of nanotechnology in cancer therapy. Conventional treatment methods, such as chemotherapy or radiotherapy, suffer from a lack of specific targeting and consequent off-target effects. Therefore there is need of development of smart nanosystems which can effect specific regional and temporal activation. In this review, we will discuss the synthesis of different nanoparticles, principle of nanotechnologies in cancer treatment. These can be divided into mechanisms which take advantage of the differences between healthy cells and cancer cells to trigger activation, and those which activate by a mechanism extrinsic to the cell or tumour environment.

KEYWORDS: Nanotechnology, Nanoparticles, Synthesis of nanoparticles, Nanoparticles for cancer, Advancement of Nanotechnology.

INTRODUCTION

Cancer is one of the most serious diseases in today's world that kills many people every year. It is one of the major health concerns of the 21st century which affect any organ of people from any place.[8] Cancer, the uncontrolled proliferation of cells where apoptosis is greatly disappeared, requires very complex process of treatment. Because of complexity in genetic and phenotypic levels, cancer shows clinical diversity and therapeutic resistance. Various

treatments are being practiced for the recovery of cancer each of which has some si limitations and side effects.[8] Cancer treatment includes surgical removal, chemotherapy, radiation, and hormone therapy.

Chemotherapy is very common treatment of cancer, delivers anticancer drugs systemically to patients for preventing the uncontrolled growth of cancerous cells.[8] Unfortunately, due to nonspecific targeting by anticancer agents, many side effects occur. Also poor drug delivery of those agents cannot give the desired result in most of the cases. Cancer drug development involves a very complex Procedure which is associated with advanced polymer chemistry and electronic engineering. The main challenge of cancer therapy is to differentiate between the cancerous cells and the normal body cells. That is why the main objective becomes providing the drug in such a way as it can identify the cancer cells to prevent their growth and proliferation. Conventional chemotherapy fails to target the cancerous cells selectively without interacting with the normal body cells. Thus they cause serious side effects including organ damage resulting in impaired treatment in low dose.[8]

Nanotechnology

It has been claimed as a new smart technology that produces system with the ability of targeting drugs to specific sites in the body. This systems include submicron Nanoparticles (NPs) composed of several materials (e g., polymers, lipids, virus, metals), or devices (e g., carbon nanotubes and nanowires).[1]

Nanoparticles (NPs) are defined as a small object that behaves as a whole unit in term of its transport and properties

Nanotechnology deals with the design, production and characterization on ultra small particles which is extended to broad area in pharmaceutical, medical, chemical and engineering application due to its unique properties. The development of technology occurs at the atomic, molecular or macromolecular range of approximately 1 nm - 100 nanometre's (nm) to create and use structures that have novel properties.[1]

Size of Nanoparticles

They can be further classified according to the size and diameter. Fine particles have the range of 100 to 2500 nm or ultrafine particles having the size of 1 to 100 nm. Nano clusters have one dimension between 1 and 10 nm and narrow size distribution and Nano powders which are agglomerates of ultrafine particles.[9]

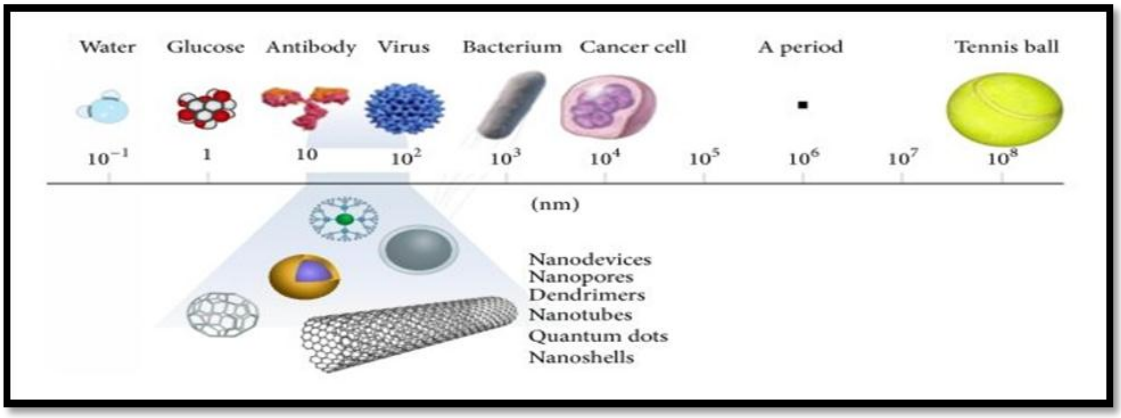

Fig no 1: a size comparison of nanoparticles with other larger molecules.

Specialized Nano technological approaches like dendrimers, quantum dots, monoclonal antibodies and integrin's which are extensively researched for diagnostic and targeted delivery of therapeutic agents. Nanorobotics centres on self-sufficient machines of some functionally operating at the Nano scale. These are hopes for applying nanorobots in medicine. The advance of contemporary materials and methodologies have to be manifested with some patients granted about new Nano devices which will help in establishing NPs with the use of embedded Nano bioelectronics concept in future. Nanomedicine access to drug delivery on development of nanoscale molecules which can improve drug bioavailability. It was disclosed that this can potentially be achieved by molecules targeting by Nano engineering devices.[8]

Nanotechnology is the science that usually deals with the size range from a few nanometers (nm) to several hundred nm, depending on their intended use.[5] It has been the area of interest over the last decade for developing precise drug delivery systems as it offers numerous benefits to overcome the limitations of conventional formulations.[6,7]

❖ TYPES OF CANCER TREATMENT

Following are the two types of treatment used in anticancer therapy

1. Conventional Cancer Treatment

Conventional cancer therapies are limited to surgery, radiation, and chemotherapy. All three methods cause damage to healthy tissues or incomplete eradication of cancer. Conventional chemotherapy suffers the lack of aqueous solubility of the drugs, lack of selectivity for the cancer cells and multidrug resistance developed after repeated administration of the same drug. Nano therapeutics is a rapidly progressing field of cancer research aimed to solve several limitations of conventional drug delivery systems. The nonspecific target of cancer

chemotherapy leads to the damage of rapidly proliferating normal cells. These adverse effects can be significantly reduced through the administration folate and transferrin-mediated Nano therapeutics which are aimed to target cancerous cells. Multidrug resistance is a challenge in cancer chemotherapy that can be managed effectively by using solid lipid nanoparticles, mesoporous silica nanoparticles, nanoparticulated chemosensitizer, nanoparticulated poloxamer, polymeric nanoparticles, and magnetic nanoparticles.[2]

➢ **Limitations of Conventional Chemotherapy**

- Conventional chemotherapeutic agents work by destroying rapidly dividing cells, which is the main property of neoplastic cells. This is why chemotherapy also damages normal healthy cells that divide rapidly such as cells in the bone marrow, macrophages, digestive tract, and hair follicles.[2]
- The main drawback of conventional chemotherapy is that it cannot give selective action only to the cancerous cells. This results in common side effects of most chemotherapeutic agents which include mylo suppression (decreased production of white blood cells causing immunosuppression), mucositis (inflammation of the lining of the digestive tract), alopecia (hair loss), organ dysfunction, and even anaemia or thrombocytopenia.[2]
- These chemotherapeutic agents often cannot penetrate and reach the core of solid tumours, failing to kill the cancerous cells.[7]
- Traditional chemotherapeutic agents often get washed out from the circulation being engulfed by macrophages. Thus they remain in the circulation for a very short time and cannot interact with the cancerous cells making the chemotherapy completely ineffective.[7]
- The poor solubility of the drugs is also a major problem in conventional chemotherapy making them unable to penetrate the biological membranes.
- Another problem is associated with glycoprotein, a multidrug resistance protein that is over expressed on the surface of the cancerous cells, which prevents drug accumulation inside the tumour, acting as the efflux pump, and often mediates the development of resistance to anticancer drugs. Thus the administered drugs remain unsuccessful or cannot bring the desired output.[7]

2. Modern Cancer Treatment

The immune system has significant natural capacity to identify and destroy abnormal cells. This may prevent the development of many cancers but not all cancers. Some cancer cells

escape the anticancer effect of the natural immune system by reducing the expression of tumour antigens on their surface, inactivating the immune cells by expression of certain proteins, or modifying the cells in the surrounding microenvironment to release substances to suppress the immune response. Immunotherapies either stimulate the activities of specific components of the immune system or counteract signals produced by cancer cells that suppress immune responses.[2]

Following are the Different types of modern cancer treatment using nanoparticles

a. Immune checkpoint modulators

There are certain natural proteins called immune checkpoint proteins that normally keep immune responses in check by preventing intense responses that might damage normal cells as well as abnormal cells. Blocking the activity of immune checkpoint proteins stimulate the immune system and increase its ability to destroy cancer cells. Several immune checkpoint inhibitors have been approved by the Food and Drug Administration (FDA). The first FDA approved drug was ipiliumab for the treatment of advanced melanoma, blocks the activity of a checkpoint protein known as CTLA4, which is expressed on the surface of activated cytotoxic T lymphocytes.[2]

b. Adoptive cell transfer (ACT)

Infiltrated T-cells from a patient's tumour are collected from samples of the tumour. The T-cells that show the greatest recognition of the patient's tumour cells in laboratory tests are selected, and large populations of these cells are grown in the laboratory. The cells are then activated by treatment with immune system signalling proteins called cytokines and infused into the patient's blood stream.[2]

c. Therapeutic antibodies and Cancer treatment vaccines

Therapeutic antibodies are made in the laboratory that is designed to destroy the cancer cells. One class of therapeutic antibodies, called antibody–drug conjugates (ADCs), has proven to be particularly effective to kill cancer cells. ADCs are created by chemically linking antibodies, or fragments of antibodies, to a cytotoxic substance. The antibody portion of the ADC allows it to bind to a target molecule that is expressed on the surface of cancer cells. The toxic substance can be a poison, such as a bacterial toxin; a small-molecule drug; or a radioactive compound. Once an ADC binds to a cancer cell, it is taken up by the cell and the toxic substance kills the cell. Cancer treatment vaccines are usually prepared from a patient's

own tumour cells or from substances produced by tumour cells. They are designed to treat already developed cancers by strengthening the body's natural defences against the cancer.[2]

d. Chimeric antigen receptor T-Cell therapy (CAR-T Cell Therapy)

It is an advanced version of Adoptive Cell Transfer techniques. After collection, the T cells are genetically engineered to produce special receptors on their surface called chimeric antigen receptors (CARs). CARs are proteins that allow the T cells to recognize a specific protein (antigen) on tumour cells. These engineered CAR-T cells are then grown in the laboratory until they expand their population in billions. The expanded population of CAR T-cells is then infused into the patient. After the infusion, the T cells multiply in the patient's body and, with guidance from their engineered receptor, recognize and kill cancer cells that harbor the antigen on their surfaces. Despite the promising clinical results, CAR-T cell therapy also involves several deleterious types of toxicity due to the inability to control T cell activity and some tumour-associated antigens that are presented by both diseased and healthy tissue. The prominent toxicity of CAR-T cell therapy involves cytokine release syndrome (CRS) and "on-target, off- tumour" toxicity.[2]

e. Stem cell transplant

The types of stem cell transplant includes autologous (stem cells collected from the donor before initiating high dose chemotherapy) allogeneic (stem cells from a donor is used), and syngeneic (stem cells collected from an identical sibling). The harvested marrow is filtered, stored in a special solution in bags, and then frozen. When the marrow is to be used, it's thawed and then put into the patient's blood through a vein, just like a blood transfusion. The stem cells travel to the bone marrow, where they engraft and start to make blood cells. Signs of the new blood cells usually can be measured in the patient's blood tests in about two to four weeks.

❖ Principles of Nanotechnology in Cancer Treatment

1. Nanocarriers

Conventional chemotherapy utilizes drugs that are able to kill cancer cells effectively. But these cytotoxic drugs destroy healthy cells in addition to tumour cells, leading to many unintended adverse side effects. Nanoparticles are used as drug carriers for chemotherapeutics to deliver medication directly to the tumour while sparing healthy tissue. Nanocarriers have several advantages over conventional chemotherapy. Nanomaterial's offer manifold advantages as drug carriers.[2] Evidently, the drug particles that are large cannot

reach the remote, secluded areas of the body. Because of the small size of the cell, the particles should be small enough with nanoscale dimensions to penetrate and cross the cell boundary. The tiny capillaries have 5-6 micron diameter, and most of the microparticles cannot pass through them. So nanoparticles are more suitable than microparticles for intravenous delivery. For systemic circulation, the particle diameters should lie in the range of 10-100 nm to have access to various parts of the body.[11]

Secondly, nanomaterials raise the drug effectiveness since they are consumed by cells efficiently than comparatively larger micro molecules. The drug is integrated into a matrix of nanoparticle or attached to the particle surface. As nanoparticles possess very high surface to volume ratio, the dissolution rate is increased Nanoparticles are formulated to adsorb preferentially on organs or tissues depending on the particle charge, surface properties, and relative hydrophobicity, fourthly, nanomaterials help in the lessening of undesirable side effects by a controlled release.[2]

Nanosphere encapsulation of the drug safeguards against degradation and prolongs exposure of the drug by restricted release, a preferred quality of any chemotherapeutic agents Therefore, use of nanomaterial's in the pharmaceutical sector improves therapeutic index, providing solutions for delivery problems. Nanomaterial-based drug carriers can protect drugs from being degraded in the body before they reach their target, and increase bioavailability to obtain the best effect from it. It also enhances the absorption of drugs into tumours, and the cancerous cells. Themselves thus prevent drugs from interacting with normal cells and avoids side effects.[2]

2. Passive targeting

Because of their size and surface properties, certain nanoparticles can escape through blood vessel walls into tissues. Nanoparticles accumulate in tumours since tumours have leaky blood vessels and defective lymphatic drainage. This feature enables conticles accumulate in tumours since tumours have leaky blood vessels and defective lymphatic drainage. This feature enables concentrating the attached cytotoxic drug where it's needed, protecting healthy tissue and significantly reducing adverse side effects. Examples of such diseases where passive targeting of can be achieved are the tumour tissues and inflamed tissues. There are several nanocarrier-based drugs in the market, which rely on passive targeting through a process known as enhanced permeability and retention. Because of their size and surface properties, certain nanoparticles can escape through blood vessel walls into tissues.[2]

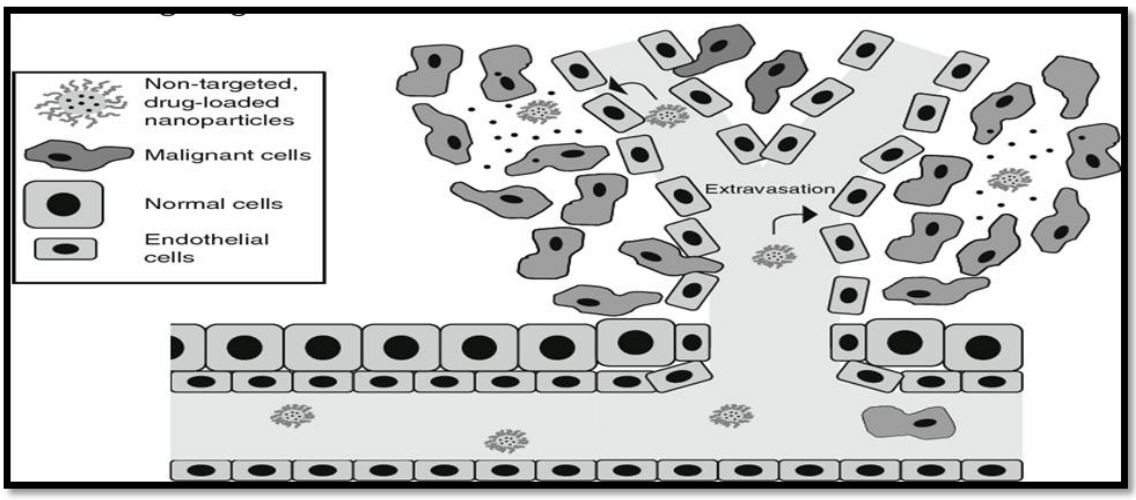

Fig no 2: Passive targeting via ESR.

3. Active targeting

Active targeting is based on the molecules expressed by cancerous cells on their surfaces and the selective targeting by nanoparticles. Attaching a molecule to a nanoparticle enables targeting of the molecule to a cell that expresses a particular receptor. Active targeting principle is used to deliver drugs into the cancerous cell, by inducing the cell to absorb the nanocarrier. Active targeting can be combined with passive targeting to reduce further the interaction of carried drugs with healthy tissue. Nanotechnology-enabled targeting can also increase the efficacy of a chemotherapeutic, achieving greater tumour reduction with lower doses of the drug.

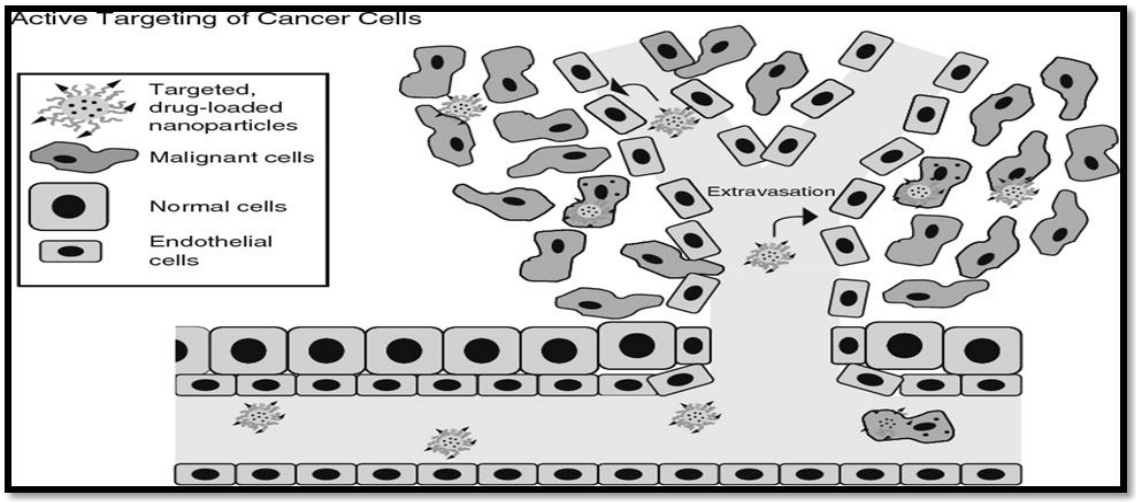

Fig no 3: Active targeting.

4. Destruction from inside the cell

Nanoshells are a form of nanoparticles that are used in the laboratory to destroy tumours from the inside by its thermal properties. Nanoshells can be designed to absorb light of different frequencies, generating heat (hyperthermia). The multifunctional gold nanoshells could be a more efficient cancer treatment because of its ability to target cancer cells specifically and spare healthy cells. After the nanoshells get into the cancer cells (via active targeting), scientists apply near-infrared light that is absorbed by the nanoshells. It creates an intense heat inside the cancer tissue that selectively kills the tumour cells without disturbing neighbouring healthy cells.[8]

Newer targeted magnetic nanoparticles that are in development will be visible through Magnetic Resonance Imaging (MRI) and can destroy cells by hyperthermia. Features of improved targeting ability, guiding the nanoshells to specific cancer cells and attaching to markers on the surface of the cells are attributed to the small peptides situated on the surface of the nanoshells. Cancer cells maintain an acidic environment, and that triggers the offloading of the anticancer drugs. The specific nanostructure of the gold nanoshells could also allow nearinfrared light to be absorbed and converted into heat whereby cancer cells are exposed to slightly higher temperatures than usual to destroy them.[2] Toxicity can cause significant complications, such as neutropenia or heart failure that necessitate cessation of treatment. The tissue damage inflicted by some nanoshell therapies can even be fatal. In spite of all disadvantages, there are many significant benefits of the nanoshell therapy too. Nanotechnology-based therapeutics have exhibited clear advantages compared to unmodified drugs, including improved half-lives, retention, and targeting efficiency, and fewer patient side effects.[2]

❖ **Common Nanoparticles Used in Cancer Medicine**

Nanotechnology has opened a window for the development of diverse organic and inorganic drug carriers, known as nanoparticles. Source materials include phospholipids, lactic acid, chitosan, dextran, polyethylene glycol (PEG), cholesterol, carbon, silica, and some metals. The surface of nanoparticles is further modified by covalent conjugation with small functional groups that increase their targeting potential. Functional groups that improve the nanoparticle specificity include follate, antibodies, aptamers, and the tripeptide. In this section, we will discuss the characteristics of the major nanoparticle platforms used as drug delivery systems.[4]

Following are the some common nanoparticles used in anticancer therapy

1. Polymeric Nanoparticles

Polymeric nanoparticles are colloidal solid particles prepared from biodegradable polymers such as chitosan and collagen or non-biodegradable polymers such as polylactic acid (PLA) and polylactic co-glycolic acid (PLGA). Their small size (50–300 nm) allows these particles to penetrate capillaries and to be taken up by the cells, increasing the accumulation of the drug at the target site of action. The majority of these compounds are formulated through a spontaneous self-assembly process using block polymers of two or more polymeric chains with different hydrophilicity. They are considered promising nanocarriers for drug delivery because they can improve the specificity to the target site of action by changing their physicochemical properties and pharmacokinetics. The stability of PLGA nanoparticles can be further improved by coating them with PEG.[4]

A different very promising polymeric nanoparticle is the chitosan based-nanoparticles. Chitosan is a natural polymer obtained by the partial N- deacetylation of chitin, the second most abundant polysaccharide in Nature. A modified PLGA nanoparticle containing chitosan through physical adsorption and chemical binding methods has also been described.[4]

2. Polymeric Micelles

Polymeric micelles are made by amphiphilic block copolymers such as polyethylene oxide, poly β-benzyl-L-aspartate and poly N-isopropylacrylamide-polystyrene. Micelles of less than 100 nm assembled with a hydrophobic core and hydrophilic shell are commonly used as drug carriers. The small size of micelles, allows the specific accumulation in the pathologic tissue.[4]

Their hydrophobic core and hydrophilic shell make micelles potent nanocarriers for poorly water soluble anticancer drugs, including paclitaxel and docetaxel. One particular feature of micelles is that the amount of drug released can be controlled by an external stimulus like pH, temperature, ultrasound or certain enzymes. Other unique properties of polymeric micelles are that they are easily modified with small functional groups that increase their targeting potential.[4]

3. Dendrimers

Dendrimers differ from traditional polymers in the sense that they are highly branched synthetic polymers made of macromolecules such as poly (N-isopropylacrylamide)-

polystyrene and polyethylene oxide-polyβ-benzyl-L-aspartate with an inner core diameter of less than 15 nm. Dendrimers possess perfect nano-architecture composed of three different parts; a focal core, repetitive units of several interior layers, and multiple peripheral functional groups. Because dendrimers are synthesized from branched monomers in a stepwise manner; it is possible to control some of their molecular properties including the shape, size, dimension, and, polarity.[4]

Dendrimers offer enormous capacity for solubilization of hydrophobic compounds, and can be modified with guest molecules. Therefore, dendrimers have shown enormous potential as anticancer drug delivery systems. Limited number of preclinical or clinical studies of dendrimers as drug carriers is currently available. Thus, it is not possible to make any conclusions about the safety and/or efficacy of dendrimers for human use.[4]

2. Quantum Dots

Quantum dots (QD) are small (2–10 nm) colloidal fluorescent semiconductor nanocrystals composed from 10–50 atoms of groups II–IV or III–V of the periodic table. Their structure consists of a metalloid crystalline core and a shell that protects the core and renders the QD available for in vivo applications. The size and shape of quantum dots can be controlled precisely, properties that determine their absorption and light emission. One of the most valuable properties of QD is their fluorescence spectrum, which make them optimal fluorophores for biomedical imaging.[4]

Fluorescent QD can be conjugated with bioactive moieties or specific ligands (e.g., receptor ligands and antibodies). QD are stable for months without degradation or alteration. QD are mostly used as long-term, high-sensitivity and multicontrast imaging agents for detection and diagnosis of cancer in vivo. Other examples of QD applications include transistors, solar cells, and quantum computing. Nevertheless, because they are composed of hazardous heavy metals, it is important to be cautious about their toxicity.[4]

5. Fullerenes

Carbon nanotubes and buckyball clusters belong to the fullerenes, a family of structures composed entirely of carbon. Carbon nanotubes are carbon coaxial graphite sheets of less than 100 nm rolled up into cylinders.

They can be classified in to two categories based on their structure

1. single-walled carbon nanotubes (SWNT) (one graphite sheet)
2. multi-walled carbon nanotubes (MWNT) (several concentric graphite sheets)

They have been applied in biology as biosensors for detecting protein and DNA, diagnostics, and carriers. This type of nanoparticle is insoluble in several solvents, provoking toxicity problems and some health concerns. fullerense can be chemically modified to make them soluble in water, and functionalized so that they can be linked to active molecules such as nucleic acids, proteins, and therapeutic agents. They have unique electronic, structural, and thermal characteristics that made them appropriate vehicles for drug delivery systems.[4]

6. Polymeric Nanofibers

Polymeric nanofibers describes fibres with diameters from 1 nm to 1m, closely matching the size scale of extracellular matrix (ECM) fibres. Polymeric fibres are derived of inorganic (i.e., titanium, silicon or aluminum oxides) or organic (polyvinyl alcohol, gelatine, poly(N-isopropyl acrylamide, poly caprolactone, or polyurethane) materials. There are three available techniques for the synthesis of nanofibers: electrospinning, phase separation and self-assembly; however, the most commonly used is electrospinning. Nanofibers consist of large surface area, low density, high pore volume, and tight pore size. In addition, these properties can be easily changed by voltage, capillary collector distance, and polymer flow rate. The surface tension and viscoelasticity of nanofibers in solution can also be modified. Nanofibers are used for several applications such as medical (tissue engineering), filtration, barriers, wipes, personal care, composite, insulation, garments, and energy storage. They have also been used as drug delivery systems.[4]

7. Metal-Based Nanoparticles

Metal-based nanoparticles of different shapes, sizes (between 10 to 100 nm) have also been investigated as diagnostic and drug delivery systems. Most common metallic nanoparticles include gold, nickel, silver, iron oxide, zinc oxide, gadolinium, and titanium dioxide particles. The large surface area of metallic nanoparticles enable the incorporation of high drug doses. Qian et al. demonstrated the utility of gold-based nanoparticles in human cancer cells and in xenograft tumour mouse models. They reported the use of biocompatible and nontoxic PEG-gold nanoparticles for in vivo tumour targeting which were spectroscopically detected by surface-enhanced Raman scattering (SERS). Even though metallic nanoparticles are

biocompatible and inert vehicles, a significant fraction of metal particles can be retained and accumulated in the body after drug administration, possibly causing toxicity.[4]

8. Nanoliposomes

Liposomes and particularly nanoliposomes are one of the most used delivery systems for small molecules, peptides, small and long nucleic acids, and proteins. Liposomes were the first nanoparticle platform applied in medicine since Bangham described them in 1961. Nanoliposomes are nanometric (30–100 nm) versions of liposomes formed by expontaneous self-organization of phospholipids such as phosphatidylcholine, phosphatidyl ethanolamine, phosphatidylglycerol and phosphatidylserine, and other molecules such as cholesterol. Importantly, many of the lipids used for liposome preparation are major components of naturally occurring bilayers. The key common characteristic of bilayer-forming molecules is their defined polar and nonpolar regions that allows hydrophobic drugs to be embedded in the lipid bilayer, or be encapsulated in the central aqueous cavity when the molecule is hydrophilic. Nanoliposomes have been used in medicine, biology, biochemistry, and in food and cosmetics industries.[4]

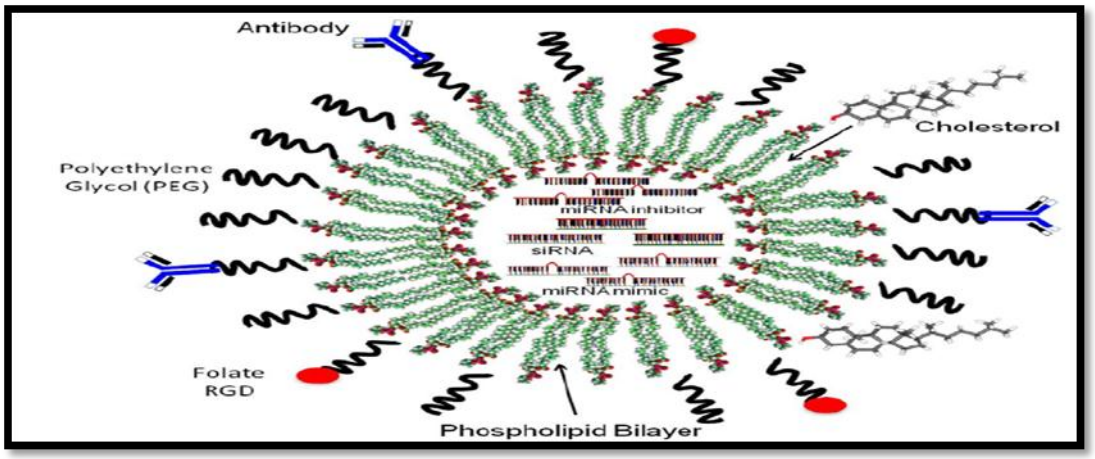

Fig no 4: Nanoliposomes for drug delivery.

A liposome is a vesicle composed of a lipid bilayer. Liposomes are made of phospholipids and small amounts of other molecules as cholesterol and/or PEG (PEGylated or stealth liposomes Functional groups (targeted liposomes) improve the specificity of the nanoparticle. Functional groups are generally covalently bound to PEG. Nab-paclitaxel (Abraxane) represents one of the new strategies to overcome the solvent-related problems of paclitaxel, and was recently approved by the US Food and Drug Administration (FDA) for pretreated metastatic breast cancer patients.[4]

❖ **Advancement of Nanoparticle Based Drug Delivery System**

- The important technological advantages of Nanoparticles used drug carrier are high stability, high carrier capacity, feasibility of incorporation of both hydrophilic, hydrophobic substances and feasibility of variable routes of administration including oral application and inhalation.[3]
- The NPs can also be designed to allow controlled sustained drug release from the matrix. These properties will enhance to improve the drug bioavailability and reduces of dosing frequency and prevent non adherence to prescribed therapy. Micelles so called core shell structure in which the core of the micelles which is either the hydrophobic part or the ionic part of the NPs can contains small or bigger therapeutic drug.[3]
- The novel intracellular pH sensitive polymeric micelles drug carrier which control the systemic and sub cellular distribution of pharmacologically active drug. The micelles can be prepared from self assembling amphiphilic block copolymers, poly (ethylene glycol), poly (aspirate hydrazone adriamycin) to which the Adriamycin (anticancer drug) is conjugated to the hydrophobic segments by acid sensitive hydrazone linkers. Therefore micelles can preserve drug under pH 7.4 and can release them by sensing the intracellular pH of the endosomes and lysosomes when they decreases to pH 5-6. Nanometer sized semiconductor particles can be covalently linked with biorecognition molecules such as peptides, antibodies, nucleic acid, and small molecules ligand as biological labels.[3]
- The new approach of quantum dots technology with anticancer drug therapy called ZnQ Quantum dots which is loaded with anticancer agents and encapsulated with biocompatible polymer represent a potential platform to deliver tumour targeted drugs and document the delivery process.[3]
- The nontoxic water dispersed ZnQ quantum dots with long term fluorescence stability can be synthesized by a chemical hydrolysis method encapsulated with chitosan and loaded with anticancer drug. Chitosan enhanced the stability of quantum dots for its hydrophilicity and cationic charge of chitosan.[3]
- NPs are being developed as delivery vehicles for therapeutic pharmaceuticals such as liposomal NPs (LNPs), encapsulated therapeutic agents for cancer therapy, pegylated form of liposomal encapsulated doxorubicin for breast cancer, layered double hydroxide (LDHs), nanoscale polymer carrier therapy for targeting tumor cells, water soluble polymers drug conjugate to increases half life with potent antitumor effect, 5-flurorouracil

loaded iron/ ethyl cellulose NPs for active targeting of cancer cells can be used in nanomedicine. NPs play a vital role in developing new drugs to neural disorders.[3]

- It is more challenging for delivery of drugs to central nervous system (CNS) and brain but NPs and neuropeptides can over comes these problems and the drug can be delivered in the brain successfully through the carrier such as hexapeptide dalargin, dipeptide kyotorphin across blood brain barriers (BBB) through endocytosis by endothelical cell lining of the brain blood capillaries.[3]
- The Nano sized carriers like micro nanosuspension, liposome, dendrimer, ocular inserts, Hydrogels are useful in ocular drug delivery which improves the release profile and reduced toxicity. This method of approach will also increase the efficiency of drug delivery than conventional delivery system.[5]

❖ **Challenges of NPs for cancer therapy**

Although development of Nanoparticles has been considered as a promising strategy for cancer therapy, it also contain various drawbacks which limit their successful application. First of all, nanocarrier-mediated drug delivery to cancer cells could develop drug resistance due to the insufficient and delayed drug release from the nanocarriers. Strategies, including development of multifunctional targeted nanocarriers for tumor selectivity, endosomal disruption for quick drug release in the cytoplasm as well as delivering combination therapy using multiple drugs or drug/nucleic acids have been adopted to overcome multiple drug resistance.[6]

Along with the development of multiple drug resistance, changes in the physico-chemical properties of the nanocarriers in the systemic circulation such as change in particle size, aggregation behaviour and premature drug release could limit their successful therapeutic application.[6]

Nanocarriers made out of novel materials, including organic polymers, and inorganic materials such as gold, silver oxide, silica nanoparticles, carbon nanotubes pose problem for clinical application due to the toxicity of the nanocarrier forming materials. In addition to developing new materials or selecting appropriate materials for each specific treatment, other parameters need to be registered in order to design efficient nanocarriers for cancer targeted drug delivery.[6] These factors include the particles size, shape, sedimentation, drug encapsulation efficacy, desired drug release profiles, distribution in the body, circulation and

cost. For instance, clearance rate of small nanoparticles of particle size less than 10nm is high.[6]

In addition, majority of nanoparticles in the systemic circulation are recognized by reticulo-endothelial system and gets accumulated in the liver and spleen leading to toxicity to other organs. On the other hand, nanocarriers with larger diameters would not get accumulated in the tumour by EPR effect depending on the leakiness of the tumour vasculature. Thus, selecting the right materials and particle size is another important aspect in targeted NPs for cancer therapy.

The major drawback for the slow development of effective targeted nanocarriers could be the lack of knowledge about the distribution and location of targeted nanoparticles after oral or intravenous administrations. Most studies have not examined the targeting efficiency of nanoparticles real time in vivo, thus precise bio-distribution and subsequently therapeutic effects are not well-known. Therefore, detecting cancer (malignant) cells in the body and monitoring treatment efficacy in real time is a challenge that needs to be overcome to develop efficient targeted nanocarrier system for cancer therapy.[6]

❖ **Advantages of using nanoparticles technology in cancer treatment**

1. Nanoscale devices have the potential to radically change cancer therapy for the better.
2. To dramatically increase the number of highly effective therapeutic agents.
3. Nanotechnology may also be useful for protect drugs from being degraded in the body before they reach their target enhance the absorption of drugs into tumours and into the cancerous cells themselves.[10]

❖ **Disadvantages of using nanoparticles technology in cancer treatment**

1. Cancer targeting is highly dependent on surface chemistry. Not just any nanoparticles will work.
2. The need for biocompatible and stable nanoparticles.
3. Side effects and toxicity of nanoparticles are found.[5]

CONCLUSION

Nanotechnology has already revolutionized cancer therapy in many aspects and is radically changing the treatment pattern. It has made a great impact on selective recognizing of the cancerous cells, targeted drug delivery, and overcoming limitations of the conventional

chemotherapies. Some nanotechnology based formulations have already been launched in the market and many are undergoing research and clinical trials. The side effects of the traditional chemotherapies can greatly bere moved by these novel active or passive targeting which can substantially increase the survival rate. As cancer is one of the most serious lethal diseases, the contribution of nanotechnology in precise treatment avoiding the life threatening side effects can potentially contribute to a positive movement in clinical practice for life saving approach.

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