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NANOMEDICINE AND IT'S APPLICATIONS IN CANCER TREATMET

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ABSTRACT

Nanotechnology, although not a new concept, has gained significant momentum in recent years. The prefix 'nano' is derived from a Greek word, which means dwarf. The term nanotechnology describes the fabrication of new materials with nanoscale dimensions between 1 and 100nm. One of the most promising application of nanotechnology is in the field of medicine. A new field of nanomedicine is emerging. Nanomedicine has been defined as monitoring, repair, construction and control of human biological systems at the molecular level using engineered nanodevices and nanostructures. Cancer is a leading cause of morbidity and mortality worldwide. Recent advances in nanotechnology offered a new hope for cancer detection, prevention and treatment. Chemotherapy is a powerful adjuvant therapy, but undesirable side effects remain a significant challenge. Nanomedicine can overcome this challenge by its unique properties like small particle size, targeted drug delivery, reduced side effects and low cost.

KEYWORDS: Nanomedicine, Nanoparticles, Drug delivery, Green nanoparticles.

1. INTRODUCTION

Nanotechnology is defined as the "intentional design, characterization, production, and application of materials, structures, devices, and systems by controlling their size and shape in the nanoscale range. The nanoscale ranges from 1 to 100nm. The first ever concept of nanomedicine was presented in 1959 by Dr. Richard P. Feynman. He is the father of nanotechnology.[1]

The term Nanotechnology was coined by Norio Taniguchi in 1974. The discovery of fullerene C60 in 1985 sparked great interest in the field of nanotechnology. Laboratory synthesized and pilot-level, plant produced nanomaterials include fullerenes, nanoparticles, nanotubes, nanowires, nanorods, quantum dots, dendrimers, nanoclusters, nanocoatings and nanocomposites.

2. Nanoparticles

Nanoparticles are defined as particulate dispersions or solid particles with a size in the nanorange. It can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. Depending upon the method of preparation, nanoparticles, nanospheres or nanocapsules can be obtained. Nanocapsules are systems in which the drug is confined into a cavity surrounded by a unique polymer membrane. While nanospheres are matrix systems in which the drug is physically and uniformly dispersed.[2]

The major goals in designing a nanoparticle as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site specific action of the drug at the therapeutically optimal rate and low dose.

3. Preparation of nanoparticles

Nanoparticles have been prepared mostly by three methods. The selection of matrix materials is dependent on many factors which includes; the size of nanoparticle required, the inherent properties of the drug like aqueous solubility and stability, surface characteristics like charge and permeability, degree of biodegradability, biocompatibility and toxicity.

Dispersion of performed polymers is the common technique. This is used to prepare biodegradable nanoparticles from polymers like poly lactic acid (PLA), poly D,L-glycolide (PLG) and poly cyanoacrylate (PCA). This technique can be used in various ways. They are solvent evaporation method, spontaneous emulsification or solvent diffusion method.

In solvent evaporation method, the polymer is dissolved in an organic solvent such as dichloromethane. This solvents can also be used for dissolving the hydrophobic drugs. The mixture of polymer and drug solution is then emulsified with the help of emulsifying agent and after the formation of stable emulsion the organic solvent is evaporated. This can be done by either reducing the pressure or by continuous stirring. If we want to produce small sized particle high speed homogenization or ultrasonication may be employed.

In spontaneous emulsification or solvent diffusion method, the water miscible solvent along with a small amount of the water immiscible organic solvent is used as an oil phase. This method is a modified version of solvent evaporation method. Due to the spontaneous diffusion of solvents an interfacial turbulence is created between the two phases leading to the formation of small particles.

In Polymerization method, monomers are polymerized to form nanoparticles in aqueous solution. Drug is incorporated either by being dissolved in the polymerization medium or by absorption onto the nanoparticles after polymerization is completed. The nanoparticle suspension is then purified to remove various stabilizers and surfactants employed for polymerization by ultracentrifugation. This method is used to prepare polybutylcyanoacrylate and polyalkylcyanoacrylate nanoparticles.

The third method is Coacervation or ionic gelation method. This is used for the preparation of nanoparticles from biodegradable hydrophilic polymers such as chitosan, gelatin and sodium alginate. Much research has been focused on this method. The chitosan nanoparticles are prepared by this ionic gelation method. Here the positively charged amino group of chitosan interacts with negatively charged tripolyphosphate to form coacervates with a size in the range of nanometer.[1]

4. Properties of nanoparticles

In contrast to atoms and macroscopic materials, nanomaterials have a high ratio of surface area to volume. As well as tunable optical, electronic, magnetic and biologic properties. They can be engineered to have different sizes, shapes, and chemical characteristics and hollow or solid structures. These properties are being incorporated in to new generations of drug delivery vehicles, contrast agents and diagnostic devices.

5. Applications of nanoparticles

Nanomaterials are being applied in ever increasing applications in the fields of electronics, optics, photonics, optoelectronics, displays, logic devices, magnetics, dot circuits, cantilevers, tooling, aerospace, catalysis, water filtration, biotechnology, biosensors, coatings, robotics and medicine.

In medicine

- ✓ The use of polymeric micelle nanoparticle to deliver drugs to tumors
- ✓ The use of polymer coated iron oxide nanoparticles to break up clusters of bacteria for effective treatment of chronic bacterial infections
- ✓ Cerium oxide nanoparticles act as an antioxidant
- ✓ Nanodiamonds with protein molecules attached can be used to increase bone growth around dental or joint implants
- ✓ Chemotherapy drugs attached to nanodiamonds used to treat brain tumors and leukemia

Manufacturing materials

- ✓ Ceramic silicon carbide nanoparticles dispersed in magnesium produce a strong light weight material
- ✓ Synthetic skin is produced by using nickel nanoparticles and a polymer
- ✓ Silicate nanoparticles can be used to provide a barrier to gases in a plastic film used for packaging of food
- ✓ Zinc oxide nanoparticles can be dispersed in industrial coatings to protect wood, plastics and textiles from exposure to UV rays
- ✓ Silicon dioxide crystalline nanoparticles can be used to fill gap between carbon fibers
- ✓ Silver nanoparticles in fabric are used to kill bacteria, making clothing odour- resistant

Environment

- ✓ Gold nanoparticles embedded in a porous manganese oxide as a room temperature catalyst to break down volatile organic pollutants in air
- ✓ Iron nanoparticles are being used to clean up carbon tetrachloride pollution in ground water
- ✓ Iron oxide nanoparticles are being used to clean arsenic from water wells

In energy and electronics

- ✓ Nanoparticles called nanotetrapods studded with nanoparticles of carbon to develop low coast electrodes for fuel cells
- ✓ Silver nanoparticle ink was used to form the conductive lines needed in the circuit boards
- ✓ Silicon nanoparticles coating anodes of lithium-ion batteries can increase battery power and reduce recharge time
- ✓ Semiconductor nanoparticles are being applied in a low temperature printing process that enables the manufacture of low cost solar cells

- ✓ Palladium nanoparticles are used in hydrogen sensor.[3]

6. Nanomedicine

Nanomedicine is defined as applications of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems by the National Institute of Health. The term nano means very small. Nanomedicine deals with drug formulations that have sizes in the nanorange. Devices built with the help of nanotechnology are used in the monitoring, repair, construction and control of human biological systems. The goal of nanomedicine is to develop safer and more therapeutic and diagnostic modalities. Because of the size and supramolecular structure of nanoparticle, technologies utilizing nanomedicine have much potential for improving cancer therapy.[4]

The major applications of nanomedicine are diagnosis, drug delivery and treatment.

7. Diagnosis

Nanomedicine can be used for diagnosis of diseases at nanoscale. The main objective of nanomedicine is to identify a disease in the earliest stage possible. It is working in the direction of making possible the detection of a single ill cell and curing or eliminating it. *In vivo* imaging devices and tools using nanotechnology are constantly being developed. Following are the techniques used which help in the detection of tumors in the body.

- **Nanowires**

There is a microfluidic channel across which the nanosized sensing wires or nanowires are arranged. When particles pass through this channel, the sensors on the nanowires pick up the specific molecular signatures of these particles. This information is then transmitted instantly through a system of electrodes. They detect the presence of transformed genes associated with cancer.

- **Cantilevers**

These are beams coated with molecules capable of binding specific substrates. Such micron sized devices, can detect single molecules of DNA or protein. The cancer cell secretes proteinaceous molecular products, the antibodies bound on the surface of the cantilever fingers selectively combine with the secreted proteins. These antibodies can pick up one or more distinctive molecular expressions from a malignant cell. The binding event results in change in the conductance of the cantilevers, thus helping in rapid and sensitive detection of cancer-related molecules.

- **Nanoparticles**

Nanoparticles are directed to cancer cells to aid in the imaging of a cancerous tumor at the molecular level. Large numbers of radio labelled nanoparticles are safely injected into the body. And this bind favorably to the cancer cell, thus making it visible. This method is better than conventional imaging. Because nanoparticles gives us the ability to see cells that cannot be otherwise detected through conventional imaging. This capability to gather what happens inside the cell is crucial to the effective diagnosis and treatment of the disease.

Nanoparticles may be of biological or chemical origin. Particles like phospholipids, lipids, chitosan, dextran and lactic acids are examples for biological nanoparticles. The chemical origin nanoparticles are, carbon, silica, polymer or metals and cadmium or iron.

Carbon nanotubes are long, needle-like, C-60 fullerene-based tubes that act as bio-persistent fibers. They help to identify the exact location of the cancer-related DNA changes, thereby aiding in diagnosis of the disease. The mutated areas linked with cancer are tagged with bulky molecules that are Fullerens.

- **Quantum dots**

Nanoscale, coated crystals that are made of a semiconductor material. The size ranges from 2.5 to 100nm. This varies with the thickness of coating. The crystals glow when activated by ultraviolet light and the emitted color depends on their size. When they are connected to a molecule that can bind to the substance of interest, they light up when such binding does occur. Because of the various colours and intensities of light that can be emitted by quantum dots, they can be combined to create probes that simultaneously detect several substances. For example, they have been used for the concurrent imaging of multiple proteins.

8. Drug delivery

One of the key properties of nanomedicine research is using nanotechnology in delivery of drugs. This is being achieved by developing nanoscale particles or molecules to improve the pharmacokinetic and pharmacodynamic properties of a drug. Bioavailability is one of the key pharmacokinetic property of drugs. It is approximated that about 65 billion dollars are being wasted per year because of the poor bioavailability of drugs.

Nanotechnology can be used to overcome the poor bioavailability of drugs. When the drug is administered in a dose, the part of the drug reaches the systemic circulation is unchanged, this is called bioavailability.Sothe nanodrug delivery system significantly improves drug delivery. Unlike other bigger elements, which are discarded that could force a patient to take high doses.

The other goals of nanodrugs are, prolonged, targeted action of the drug, smaller drug doses, faster dissolution of drugs and diminished toxicity.

The established platforms for drug delivery are,

- **Nanoshel**l

A type of spherical nanoparticles consists of dielectric center which is covered by a thin metallic shell, which is usually gold. This can be injected without harm. They collect favourably in cancer wound sites because of their size. Tumor cells express antigens themselves. Nanoshells can be modified to carry molecular conjugates to these antibodies.

Then externally energy can be supplied to these cells and this creates an intense heat that kills only the tumor cells. The external energy whether it be mechanical, radio frequency or optical. Tumor and not to adjoining healthy cells. Nanoshells are very specific to preferentially link to the tumor and not to adjoining healthy cells. The use of nanoshells thus reduces side effects and increases the efficacy of the treatment.

- **Dendrimers**

Nanosized radially symmetric molecules. They are well-defined, homogeneous structure consisting of tree-like arms or branches. The branches containing voids provide protection where in drug molecules can be physically trapped. And these flexible branches of a dendrimer provides protection from the outside environment. This trapped drug is then released at the tumor site.

- **Micelle**

They are aggregates of amphipathic molecules in water. Hydrophobic drug can be trapped in the core of such micelles, which effectively protect the drug from the environment. And polar drug will be adsorbed at the micellar surface.

- **Liposomes**

The liposomal spherical, bilayered vesicles and amphipathic in nature. The drug is carried either in the aqueous compartment. These vesicular carriers can pass through the smallest arterioles and can penetrate endothelium as they are small, flexible and bio-compatible.

- **Niosomes**

Niosomes are non-ionic surfactant vesicles are an alternative to liposomes. They overcome the limitations of liposomes such as chemical instability, inconsistent purity of phospholipids and high price. They have potential use in controlled and targeted drug delivery.

- **Fullerenes**

Also called bulky balls and are composed of carbon. They are natural hollow balls which have 1nm in diameter. In fullerenes, active pharmacophores can be coupled to the surface in three-dimensional arrangement to target the compounds to biological sites.[5]

9. Nanomedicine in cancer chemotherapy

Cancer is a leading cause of morbidity and mortality worldwide with recent advancements resulting in modest impacts on patient survival. The more harrowing fact is that several significant achievements towards the treatment of disease have failed to profoundly impact patient survival. Nanomedicine represents an innovative field with immense potential for improving cancer treatment. The last century witnessed the maturation of chemotherapy as a viable, adjuvant therapeutic modality for the treatment of cancer.

Novel and traditional chemotherapeutics suffer from non-specific distribution with only a small fraction of drug reaching the tumor. It is well known that injected materials suffer from sequestration by the reticuloendothelial system (RES). The RES is comprised of monocytes and macrophages that clear foreign materials. As a result drugs accumulate in healthy organs, with their inherent toxicity drawing a lifeline between tolerability and severe morbidity. The factors preclude the curative potential of anticancer drugs warranting more effective ways to deliver them to tumors. With these limitations in mind, and in attempts to apply Paul Ehrlic's magic bullet concept to chemotherapy.

Liposomes and polymer drug conjugates were developed in the 1960s and 1970s. these are mainstay platforms within the field of nanomedicine. These carriers assist in drug solubilization and protect the drug from degradation. These nanoscale particles on the surface aids in evasion of the RES allowing drugs to accumulate in tumors through the enhanced permeability and retention effect, the result of tumor blood vessel leakiness.[6]

10. Advantages of nanomedicine

\Recently targeted therapeutics in nanomedicine have been widely explored. Drug targeting by nanoparticles or nanocapsules offers the following enormous advantages as example, advanced therapies with reduced degree of invasiveness, reduced negative effects of drugs and surgical procedures, Faster, smaller and highly sensitive diagnostic tools, cost effectiveness of medicines and disease management procedures as a whole, protects drugs against degradation and enhances drug stability, reduced mortality and morbidity rates and increased longevity in return.

11. Disadvantages of nanomedicine

Lack of proper knowledge about the effect of nanoparticles on biochemical pathways and processes of human body. Scientists are primarily concerned about the toxicity, characterization and exposure pathways associated with Nano medicine that might pose a serious threat to the human beings and environment**.** The society's ethical use of Nano medicine beyond the concerned safety issues, poses a serious question to the researchers.

12. Green nano particles

Plant mediated synthesis of nanoparticles is a green chemistry approach that connects nanotechnology with the plants. Novel methods of ideally synthesizing nanoparticles are thus thought that are formed at ambient temperatures, neutral pH, low costs and environmentally friendly fashion. Keeping all these in mind nanoparticles have been synthesized using various routes. Among these alternatives, plants and plant extracts seem to be the best option. Plants are natures chemical factories.

The use of plant extracts for the formation of nanoparticles is being favoured due its salubrious nature towards the environment. The plants supplement both the reducing as well as stabilizing agents for the nanoparticles which otherwise have to be externally added in other methods. In plant method maintenance cost is much less and the waste disposal requires less effort among other factors. This method is even better because the maintenance of whole plant system is much less than a culture of bacteria.

Recent studies have shown that the therapeutic effects of plants, from which the nanoparticles are being derived, can also be used as perfect vehicles to the therapeutic materials. This eliminating the need to artificially develop a drug for that particular ailment.

For example *Azadirachtaindica*is commonly known as neem is used for the synthesis of green nanoparticles.[7]

13. Future of nanomedicine

Nanotechnology is beginning to change the scale and methods of vascular imaging and drug delivery. National Institute of Health sciences says that nanoscale technologies will begin yielding more medical benefits within the next 10 years. This includes the development of nanoscale laboratory-based diagnostic and drug discovery platform devices such as; nanoscale cantilevers for chemical force microscopes, microchip devices, nanopore sequencing etc.

The National Cancer Institute has related programs too, with the goal of producing nanometer scale multifunctional entities that can diagnose, deliver therapeutic agents, and monitor cancer treatment progress. Design and engineering of targeted contrast agents that improve the resolution of cancer cells to the single cell level. Nanodevices capable of addressing the biological and evolutionary diversity of the multiple cancer cells that make up a tumor within an individual cell, for the full in vivo potential of nanotechnology in targeted imaging and drug delivery to be realized, nanocarriers have to get smarter.

Clear understandings of both physicochemical and physiological processes form a basis of complex inherent to the fingerprint nanovehicle. Examples of which include carrier stability, extracellular and intracellular drug release rates in different pathologies, interaction with biological milieu, and other barriers enroute to the target site. Inherently, carrier design and targeting strategies may vary in relation to the type, developmental stage, and location of the disease.

Toxicity issues are of particular concern but are often ignored. Nanotechnology is, in fact, helping to realize mankind's dream of fighting against many complex illnesses like cancer, multiple sclerosis, cardiovascular diseases, Alzheimer's and Parkinson's diseases.

REFERENCES

1. Betty YS, Kim MD, James TR ,Warren andChan CW. Nanomedicine, N Engl J Med, 2010; 363: 2434-43.
2. V.J.Mohanraj and Y Chen. Nanoparticles, Trop J Pharm Res, 2006; 5: 561-573.
3. Www.understandingnano.com/ nanomaterials.html
4. S.Moein Moghimi, A Christy Hunter, and J. Clifford Murray. Nanomedicine: current status and future prospects, The FASEB journal, 2005; 19: 311- 330.
5. KwatraS. Nanotechnology and medicine –The upside and the downside, Int J Drug Dev Res, 2013; 5(1): 1-10.
6. Elvin B, Angela H, Aman P, Matthew GL, Funda, Meric Bernstem and Mauro F. Nanomedicine in cancer therapy: Innovative trends and prospects, J JCA, 2011; 102: 1247- 1252.
7. Khadeeja Parveen, Viktoria Banseand Lalita Ledwani. Green synthesis of nanoparticles: Their advantages and disadvantages, AIP Conf Proc, 2016; 1724(1).