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A Comprehensive Review On Nanoparticles As Drug Targets And Their Applications In Targeted Drug Delivery Systems

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ABSTRACT

The creation of medication formulations composed of nanoparticles has made it possible to target and cure difficult diseases. Although their sizes differ, nanoparticles typically range in size from 100 to 500 nm. By modifying the substance, nanoparticles may be formed into intelligent devices that contain diagnostic and therapeutic chemicals and have stealth characteristics. These systems also offer controlled administration of treatment and the capacity to administer drugs to particular regions. By delivering the medication in a targeted and sustained manner, the toxic effect associated with the treatment is reduced, and patients comply with fewer doses. In addition to improving diagnostic tests, nanotechnology has demonstrated potential in the treatment of several diseases, including, cancer, diagnostic testing, Alzheimer's disease, Neurological Disorders, Infectious Diseases, Diabetes, Cardiovascular Diseases, Organ Transplantation and Gene Therapy.

KEY WORDS: - Nanoparticles, Targeted drug delivery system, cancer, diagnostic testing, Alzheimer's disease, Neurological Disorders, Infectious Diseases, Diabetes, Cardiovascular Diseases, Organ Transplantation, Gene Therapy.

INTRODUCTION

Targeted drug administration may be a perfectly reasonable drug delivery method that works wonders in getting the medication into the patient. In contrast to the targeted unharness system, which discharges the medication in an infinite amount form, the normal drug delivery method involves the drug being absorbed through a biological membrane. Framework Because of the high level of integration in the drug delivery system, scientists, engineers,and chemists must collaborate to improve this method.

Following the implementation of a targeted release system, the following criteria had to be considered by the system: the medication's qualities, side effects, distribution method, targeted website, and also the patient's condition. A targeted medication delivery method is better than a traditional one.

The first is due to pharmaceuticals. Targeted drug delivery technologies exhibit higher drug stability and lower solubility in contrast to conventional medicines. Even their poor absorption, short half-lives, and high volume of dispersion are characteristics of conventional medications. Its pharmacokinetic characteristics are comprised of these. The pharmacodynamic qualities of medications make up the third justification. When comparing standard medications to targeted drug delivery systems, the former have lower therapeutic index and lower specificity. These factors make tailored medication delivery systems superior to traditional drug delivery methods.

NANOPARTICLES

In terms of illness diagnosis, treatment, and prevention, the scientific landscape is starting to shift with the invention of an array of nanoscale technologies. The National Institutes of Health refers to these technical advancements as "nanomedicines" because they have the capacity to transform molecular findings from proteomics and genomics into broad benefits for patients. Biochemical processes (such as infection, tissue engineering, de novo synthesis, etc.) can be mimicked or changed using nanoparticles. Functionalized carbon nanotubes, self-assembling polymeric nano constructs, nanofibers, nanomachines (e.g., made of replaceable DNA components and DNA scaffolds), nanomembranes, and nano-sized silicon chips for drug, protein, nucleic acid, or peptide delivery and release are a few examples of these devices. Biosensors and laboratory diagnostics are also included.

A lot of research has been done on polymers that decompose in recent years in an effort to create medication delivery methods. A lot of attention is being paid to the development of biodegradable polymeric nanoparticles for tissue engineering and pharmaceutical delivery because of their potential uses in controlling drug release, stabilizing labile molecules (like proteins, peptides, or DNA) from degradation, and targeting specific sites for drug delivery. In the late 1960s and early 1970s, acrylamide micelle polymerization was used to create polymer microparticles.

NECESSITY FOR NANOPARTICLE BASED DRUG FORMULATION

The use of nanoparticles as pharmacological and medical devices, as well as to improve medication delivery, is crucial and urgent for a number of reasons. One of them is that conventional medications that are now marketed for injection or oral use aren't always produced in the best possible formulation for each product. More creative carrier systems are needed for products comprising proteins or nucleic acids in order to increase their effectiveness and shield them from unintended destruction.

Due to their tiny dimensions and extensive area of coverage, drug nanoparticles have better bioavailability and increased solubility.

- They also demonstrate the capacity to penetrate the respiratory tract, penetrate the blood-brain barriers (BBB), and permeate via the close proximity of cutaneous endothelial cells.
- The ability to modify natural and synthetic polymer-based tiny particles for delivery of medications, improve accessibility, and deliver a precise dispensing of drugs via an individual dose—as well as the system's ability to prevent natural digestive enzymes from breaking down the drug—has drawn increased interest in these nanoparticles, both biodegradable and non-biodegradable.
- Second, the creation of novel medication delivery methods is giving pharmaceutical sales still another reason to expand. Pharmaceutical firms are developing new formulations of their existing medications due to innovative drug delivery. Although the patients will benefit from these novel formulations, they will also generate a strong market force that will push the creation of ever more efficient delivery systems. In addition, once patents expire, the corporations will be motivated to create new formulas for their own "intellectual property" in addition to thriving in this regard. Pharmaceutical businesses can gain from using this new technology by realizing that medications that were previously deemed unmarketable owing to low solubility and bioavailability as well as high.

MAJOR APPROACH OF NANOPATICLES

The two primary types of nanotechnology techniques are known as

- **Top-down** - method involves removing metal from the tiniest components to create nanoscalestructures.

Process includes: - sputtering, thermal processing, mechanical, optical, and chemical etching.

- **Bottom-up** - a variety of unique techniques were used to create the nanoparticles.

Process includes: - chemical, vapour deposition, molecular condensation, sol–gel, andelectrochemical methods.

TYPES OF NANOPARTICLES

NANOTECHNOLOGY	**NANODEVICES**	**NANO-STRUCTURED**
Supramolecular chemistry, surfacescience	Nanoelectronics	Nanotubes, Nanowires,
Nanolithography, Synthetic approach	Spintronics	Nanoparticles, Nanocomposites
Computer modelling	Nano sensors	Nano patterned

FIG 1 – Three main types of nanoparticles

CHARACTERISTICS OF NANOPARTICLES IN DRUG FORMULATION

Prior to precisely specifying the components of an optimal medication delivery system based on nanoparticles, itis necessary to comprehend how the body responds to external particulates.

Three basic routes exist for nanoparticles to reach the human body: oral ingestion, inhalation, and direct injection. Particle-protein interaction occurs initially after they reach systemic circulation and then they are

distributed to different organs.

- The lymphatic system can disperse and remove the particles once they are absorbed from the blood capillaries. Two of the three primary purposes of this system are related to the delivery of drugs.
- The lymphatic system removes fluids from blood capillaries in the first step, known as fluid
- recovery. The second is maybe the most pertinent to this subject as it deals with immunity. As the system removes extra fluid from the body while also removing chemicals and foreign cells from the tissues.
- The lymph nodes identify any foreign material going through when the fluids are filtered back into thecirculation.
- Macrophages will take up and remove everything that they identify as foreign from the body.
- This is often the challenge with drug administration via nanoparticles; however, the size and surface properties of the particles can affect clearance, as will be discussed in more detail in the subsections.

DRUG LOADING AND RELEASE

In order to improve the dimension and coating characteristics of nanoparticles to enhance stability, minimize clearance, and optimize bioavailability. By adjusting these characteristics, the drug is now able to enter body tissues that it was not before able to. Nevertheless, if the drug cannot be released from the colloidal matrices, this process is pointless. The amount of drug released from the nanoparticle-based formulation depends on a number of variables, including pH, temperature, solubility of the medicament, removal of the medicine that is consumed or surface-bound, drug diffusion through the small particle's matrices, bruising and destruction of the small particle's matrix, and the interaction of deterioration and diffusion reactions. Depending on the type of nanoparticle being used, the release of medicine will change.

Depending on their makeup, the produced polymeric nanoparticles may be referred to as nanospheres or nano capsules. The arrangement of the polymer chains in nanospheres is homogenous, like the way surfactants generate micelles (which are phase-separated from the bulk solution). However, because nano capsules are heterogeneoussystems, the medication is contained inside a polymer-like vesicle-like reservoir.

Drug release occurs by matrix erosion in nanospheres, which are matrix systems in which the drug is evenly and physically disseminated. Due to the enormous surface area of the nanoparticle and the weakly bound drug, there is a quick burst of drug release followed by a persistent release. Conversely, in the case of nano capsules, drug release is regulated by drug diffusion via the polymeric layer; hence, the drug's diffusion through that polymer unquestionably determines its deliverability. medication and polymer that interact ionically will produce complexes that prevent the medication from releasing from the capsule. By using additional auxiliary agents, suchas polyethylene oxide-propylene oxide, this can be prevented.

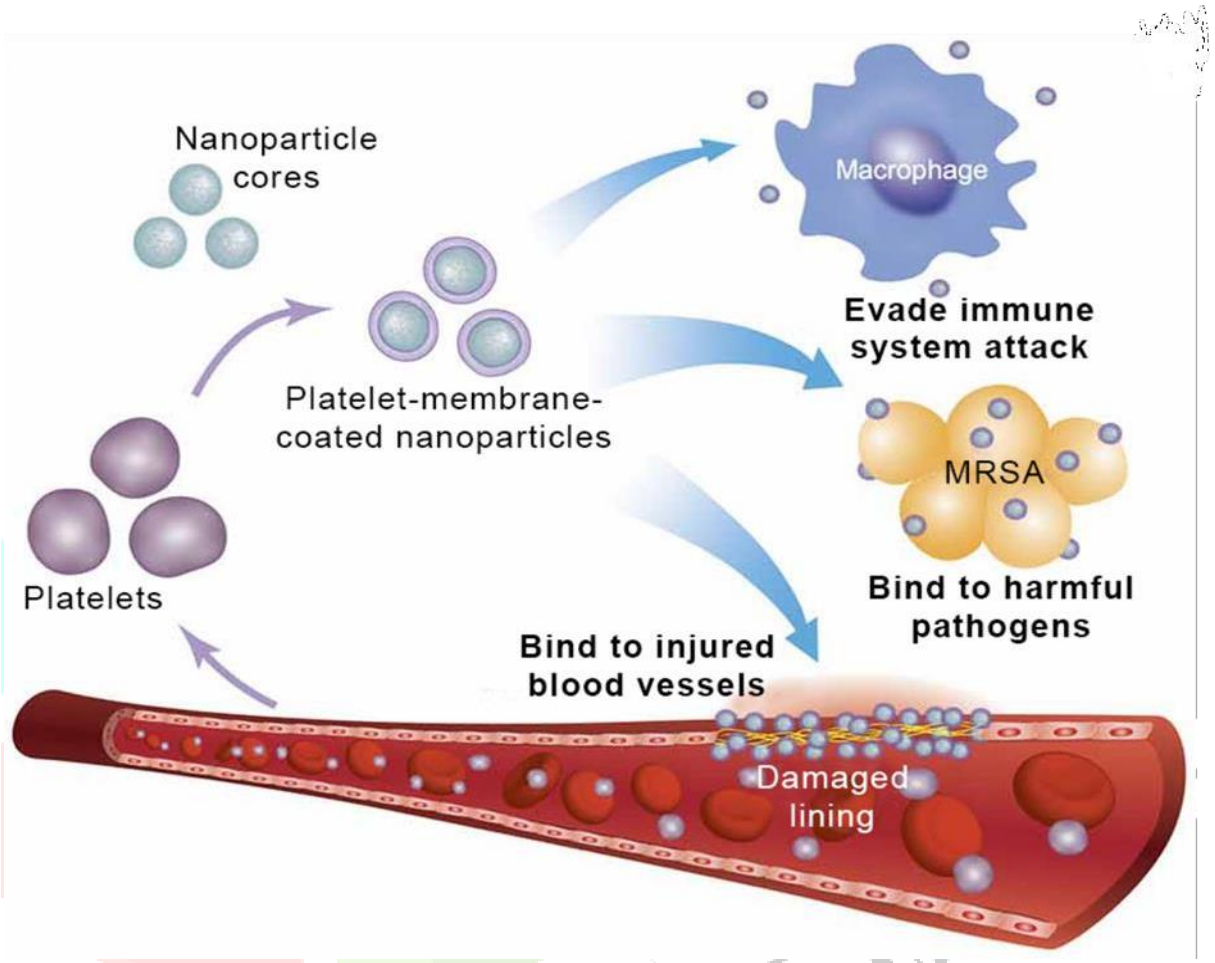

FIG 2- Nanoparticles drug loaded at targeted binding site.

TARGETED DRUG DELIVERY IN NANOPARTICLES

The creation of targeted medication delivery makes sense after realizing how crucial it is to manipulate nanoparticles in order to produce an efficient drug delivery system. Because of their bigger epithelial connections, the nanoparticles can penetrate tissue that is irritated or injured. This infiltration might happen in an active or passive manner. Passive targeting occurs when a nanoparticle enters the target organ because of leaky junctions, whereas active targeting occurs when the nanoparticles penetrate is coupled to a tissue- or cell-specific ligand.

A perfect nanoparticle drug delivery system (Fig. 1) should be able to reduce or completely prevent drug-induced harm to healthy tissues while being able to approach, identify, bind, and distribute its load to certain diseased tissues. The most popular tactic is to encapsulate a particular targeted ligand or ligands on the surface of nanoparticles. These targeting ligands may be nucleic acid aptamers, tiny compounds, peptides, antibodies,engineered proteins.

The most often used targeting agents are small organic compounds because of their relative stability, simplicity of synthesis, and controllability over conjugation chemistry. It's possible that the targeted ligands lack the appropriate affinity and specificity. Because of its strong affinity for streptavidin, biotin

(vitamin H) is frequently utilized in conjugation with nanoparticles. Due to its strong affinity for the endogenous folate receptor, folic acid (vitamin B9) has been studied as a potential treatment for a variety of tumours where high levels of folate receptor expression are present. Similar to this, several additional task-specific tiny compounds, short peptides, polysaccharides, and antibodies have been created and used.

Liposomes are another helpful finding to help with medicine distribution that is targeted. Because they resemble the cell membrane, some lipid monomers may be designed to modify physicochemical characteristics like size and charge. Surface targeting ligands, as previously mentioned, can also be included. Because the liposomal composition of this system is identical to that of the targeted cell membrane, there is an improved lipid-lipid exchange. This is an additional benefit. This accelerates the lipophilic drug's convective flow into the targeted cellmembrane from the liposomal lipid layer.

APPLICATION OF NANOPARTICLES

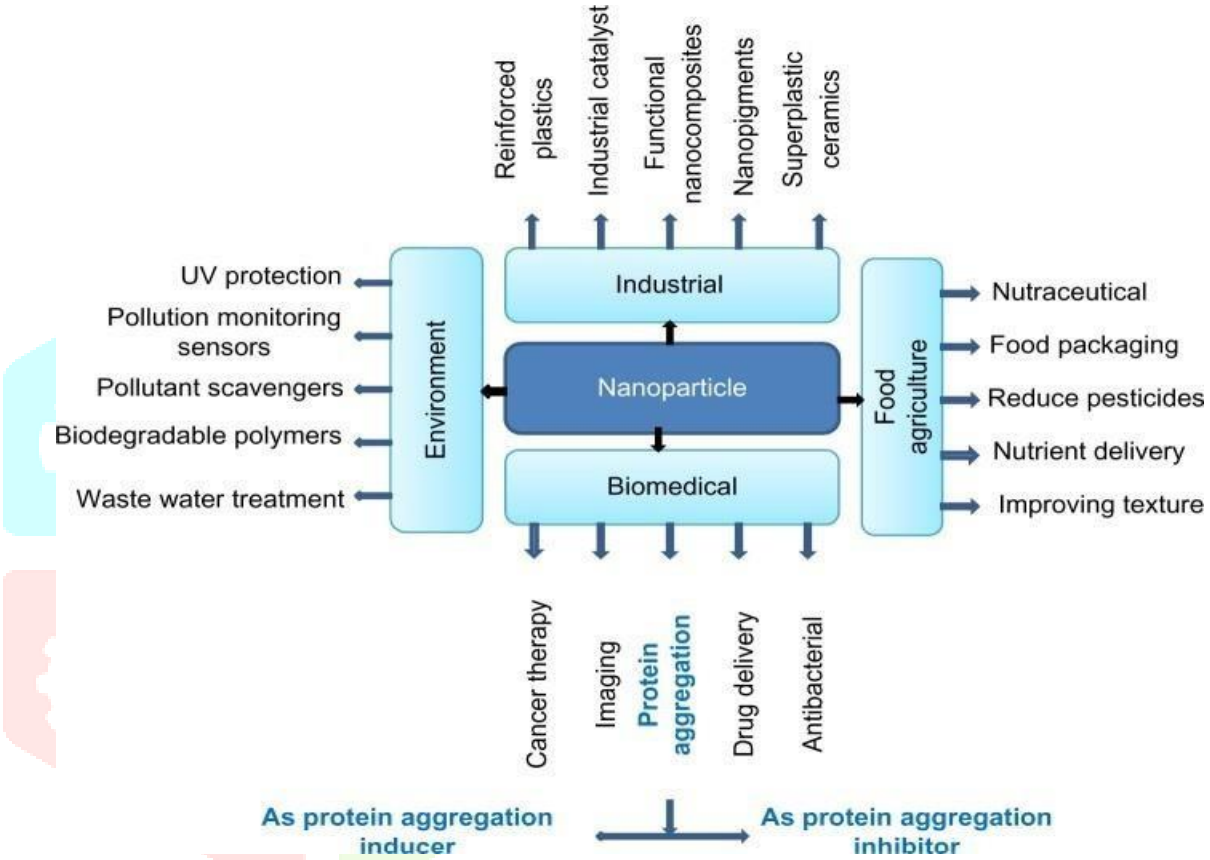

FIG 3 - Various application of nanoparticles

BIOMEDICAL APPLICATION

1. Cancer therapy

Many lives have been spared by the sort of medication utilized to treat cancer patients today, but the severe side effects of the treatment affect every part of the body since the chemotherapeutic drugs are non-specific. Because of its complexity, cancer is sometimes referred to as a sickness of many illnesses. Rapid and uncontrollably dividing and multiplying cells is one of the characteristics of malignant cells. The primary goal of modern chemotherapy is to eliminate any cells that divide quickly. The drawback of this treatment is that it also kills off the body's other fast-growing cells, such those in the intestinal epithelium and hair follicles, leaving the patient to deal with potentially fatal side effects. The evolution of Chemotherapy now offers an additional option because of the creation of nanoparticles. Tailored medication delivery at the tumour site or to a specific cell population can mainly prevent adverse effects on other normal tissues and organs when using cleverly engineered nanoparticles. This kind of treatment has been tested on a number of systems.

Another method for delivering chemotherapy drugs is by the use of liposomes and micellar particles. Additionally, because of its hydrophobic core and hydrophilic exterior, micelles are a wonderful method to make medications that are intractable and soluble. Higher drug concentrations in tumours can be achieved if the micelle's surface is further PEGylated, since this will improve the nanocarriers' capacity to passively carry drugs across the fenestrated vasculature of tumours and inflammatory tissue. Currently, clinical trials are being conducted on a number of polymeric micelles carrying anticancer medicines, including NK012, NK105, NK911, NC-6004, and SP1049C. One such system is authorized for use in patients with breast cancer.

The absorption, distribution, metabolism, and elimination (ADME) profile of dendrimers—which are highly branched macromolecules with numerous functional groups available for the attachment of drug, targeting, and imaging agents—depends on a variety of structural feature, a polyfunctional dendrimer system has been successfully used for methotrexate administration, imaging, and localization (using fluorescein). By utilizing biocompatible nanoparticle delivery vehicles can play a role in multiple steps of activation of the immune system to suppress cancer. Nanoparticle-based therapeutics can induce tumour cell death and in turn increase neo-antigen release from this tumour. Nanoparticles can be utilized to improve antigen presentation and T cell activation. They can also deliver pro-immune/pro-inflammatory agents to tumours and tumour microenvironments to enhance thecancer immunotherapy response.

components and surface derivatization with PEGylation, acetylation, glycosylation, and different amino acids, dendrimer-based nanoparticle therapies might enhance the therapeutic index of cytotoxic medications.

Although several other types of nanoparticles have demonstrated potential in cancer treatment, carbon nanotubes are one of the most recent systems to do so. Single-walled carbon nanotubes (SWCNTs) and multiwalled carbon nanotubes (MWCNTs) are two types of carbon nanotubes (CNTs), which are allotropic forms of carbon with a cylindrical framework and deepening on a number of sheets in concentric cylinders. The hollow core of carbon nanotubes makes them extremely hydrophobic, making it easy to load water-insoluble medications within. The broad surface area enables outer surface functionalization, which may be tailored for specific cancer receptors andcontrast agents.

Lastly, the spherical molecule Buckminsterfullerene C60 and its derivatives are investigated for use in cancer treatment. Reactive oxygen species (ROS) are effectively scavenged by fullerene C60, which has the ability to bind up to six electrons. Fullerene nanocrystals, or Nano-C60, have been shown to increase the cytotoxicity of chemotherapeutic drugs; as a result, additional research may be done on Nano-C60 adjunct chemotherapy. Another investigation employing the Fullerene C60 and Doxorubicin combination was carried out by. They observed that the tumour volumes of the treated rats (C60 + Dox) were 1.4 times smaller than those of the control group (untreated rats). Moreover, the C60 + Dox complex's mode of action.

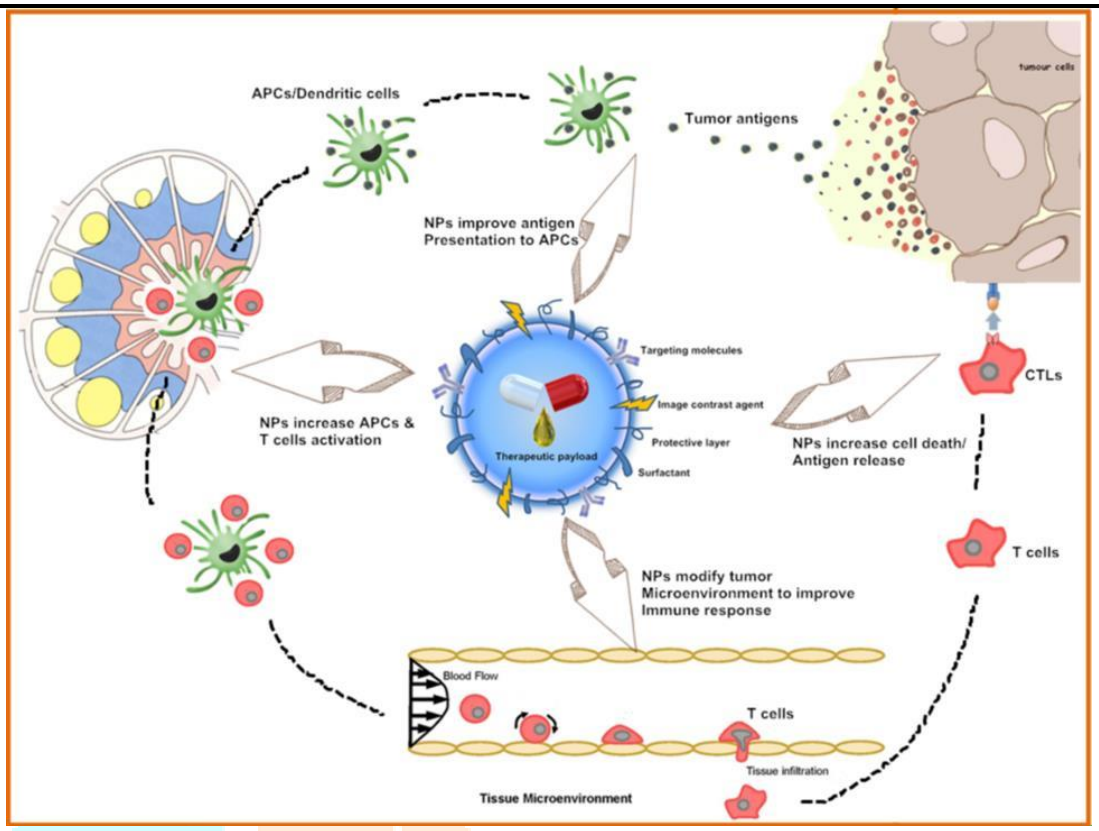

FIG 4 - The immunological mechanism's numerous stages of stimulation in order to combat malignancy can be aided by nanoparticle carriers. Therapy centred around nanoparticles have the ability to kill tumour cells, which increases the release of neo-antigens from the tumour. Antigen distribution and activated T cells can both be enhanced by the use of nanoparticles. To improve the body's reaction to immunotherapy for carcinoma, they can also introduce harmful and pro-immune substances into tumours and the surroundings surrounding them.

2. Diagnostic testing

Although not yet ready for clinical usage, the use of nanoparticles for diagnostics is a field that has received a lot of attention in academics fluorescent nanoparticles offer researchers a way around the shortcomings of fluorescent markers, which limit the use of dyes due to bleeding effects, colour matching issues, and fluorescence fading after a single use. These drawbacks impede the current diagnostic testing technology. The discovery of quantum dots, which can be produced on demand in a wide range of precisely specified colours, was one significant advancement. Their high quantum yield, adjustable emission spectrum, and photostability are all provided by their absorption spectrum, which stretches from the ultraviolet to a wavelength in the visible spectrum. Where a particular particle lands in the spectrum depends on the size of the nanodot. Longer wavelengths and narrower emission are characteristics of larger particles. Quantum dot tagging has several benefits. They are first made excited by white light. Second, they may be connected to biomolecules that can stay in a biological system for a considerable length of time in order to study different bio-mechanisms. Additionally, this technology makes it possible to tag different biological occurrences and keep an eye on many ones at once.

Recently, theragnostic nanoparticles, nanoparticles that can be used for treatment as well as diagnoses have gained much. This strategy has been realized in many classes of nanoparticles including, drug conjugates, dendrimers, surfactant aggregates (micelles and vesicles), core-shell particles, and carbon nanotubes. By combining both drug and imaging agent in one smart formulation, it is possible to monitor the pathway and localization of these nanoparticles at the target site as well as drug action to assess therapeutic response.

3.Alzheimer's Disease (AD)

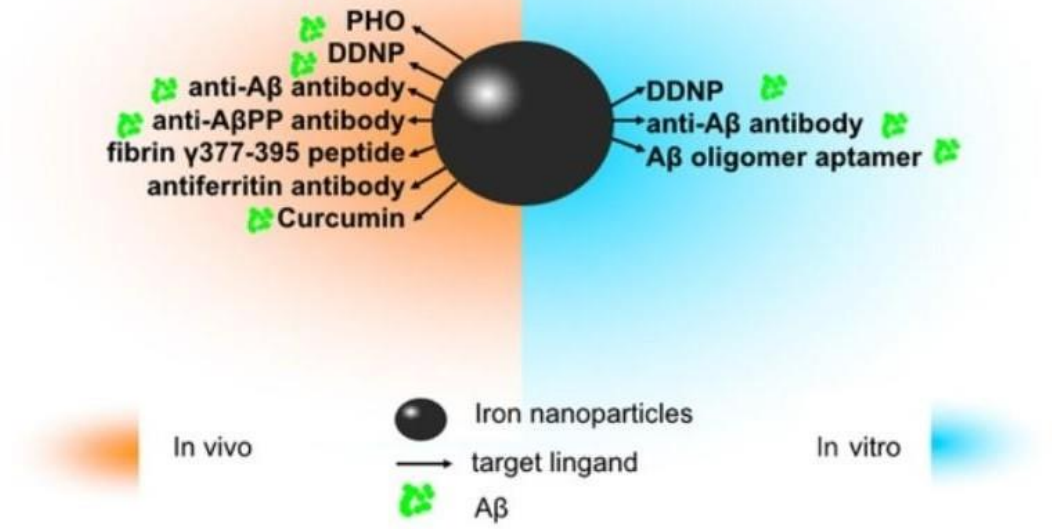

FIG 5 – Alzheimer's disease diagnosis in nanoparticles.

Alzheimer's disease (AD) diagnosis and therapy using iron oxide nanoparticles (IONPs). Since amyloidβ (Aβ) has now been found to be the best visualization evidence of AD, IONPs can be utilized to identify Aβ to aid in AD evaluation and treatment using the technique of magnetic resonance imaging (MRI). To identify Aβ in blood, magnetic nanoparticles (MNPs) tagged with antibodies against Aβ-40 and Aβ-42 can be used in vitro. Measurements of the Aβ oligomer in synthetic cerebral spinal fluid (CSF) may be made using IONPs, which are conjugated with the Aβ oligomer aptamer and its corresponding oligonucleotide. Fluor photometry may be used to identify DDNP-superparamagnetic iron oxide nanoparticles (SPIONs) with strong affinities to Aβ (1-40) aggregates. In vivo, amyloid plaques in the brains of NMRI mice may be marked by ultrasmall superparamagnetic iron oxide (USPIO)-PHO; in AβPP/PS1 transgenic mice, the quantity of lesions can be seen using anti-Aβ protein precursor (AβPP) antibody-conjugated SPIONs. In the rat AD framework, DDNP-SPIONs nanoparticle dramatically reduce the signal intensity (SI) in the hippocampus region Superparamagnetic iron oxides (SPIOs) coupled with curcumin may identify amyloid plaques in the brains of Tg2576 mice. Nanoparticles of fibrin γ377– 395 peptide-conjugated γ-Fe2O3 may selectively suppress the number of microglial cells in tau-mutant rTg4510 mice, offering a potential treatment approach for neurodegenerative tauopathies. Furthermore, in the brain of a transgenic AD mouse model, ferrous proteins were detected in regions with a high concentration of amyloid plaques using magnetic IONPs linked to an anti- ferritin antibody. Blood-Brain Barrier, or BBB.

4. Neurological Disorders: Nanoparticles can be engineered to cross the blood-brain barrier, allowing drugs to reach the central nervous system for the treatment of conditions like brain tumours, neurodegenerative diseases, or infections.

5. Infectious Diseases: Nanoparticles can be used to target specific pathogens or infected cells. This approach is particularly useful in the treatment of viral infections, bacterial infections, and other microbial diseases.

6. Diabetes: Nanoparticles can be employed for targeted insulin delivery. Surface modifications can be designed to respond to glucose levels, releasing insulin when needed to maintain blood sugar levels.

7. cardiovascular diseases: Nanoparticles can target specific cells in the cardiovascular system to deliver drugs forconditions such as atherosclerosis, hypertension, or restenosis.

8. Organ Transplantation: In organ transplantation, nanoparticles can be used to modulate the immune response and prevent organ rejection. They can be designed to selectively deliver immunosuppressive drugs to immune cells.

9. Gene Therapy: Nanoparticles can deliver genetic material (DNA or RNA) to target cells for gene therapyapplications. This is a promising approach for treating genetic disorders or inducing therapeutic

CONCLUSION

As a genuinely interdisciplinary field of study, nanotechnology has benefited greatly from the contributions of pharmacists, physicists, scientists, and pharmaceutical experts in the development of innovative therapeutic and diagnostic approaches. This analysis makes it clear that the use of nanotechnology in healthcare and medication delivery has created new avenues for individualized and secure treatment options. The application of nanotechnology has advanced safe examinations. nutraceutical delivery, cancer diagnostic and Alzheimer's treatment, and more. In the end, researchers are able to administer medications for longer periods of time with less frequent doses (long-term release), higher accuracy, and absorption in difficult-to-access tissues through thealteration of molecule size and surface features.

FUTURE ASPECTS

Nanoparticles have gained significant attention in the field of medicine, particularly in targeted drug delivery systems. The unique properties of nanoparticles, such as their small size and large surface area-to-volume ratio, make them ideal for delivering drugs in a controlled and targeted manner. The use of nanoparticles in targeted drug delivery systems offers the potential to improve the therapeutic efficacy of drugs while minimizing side effects. However, challenges such as biocompatibility, stability, and scalability must be addressed for widespread clinical application. Ongoing research is focused on optimizing nanoparticle design and understanding their interactions within the biological system.

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