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STUDY AND ANALYSIS ON APPLICATIONS OF NANOTECHNOLOGY DURING DRUG DELIVERY

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ABSTRACT: Nanotechnology is the study of materials at the nanoscale and the utilization of their unique features. Many sectors are turning to nanotechnology because it promises better-built and smarter products. Details are provided on the use of nanotechnology in different industries, including health and medical, electronics, energy and the environment. Drug delivery, protein delivery, and cancer treatment applications of nanoparticles are described here. Nanotechnology's usage in medicine administration and in vivo imaging is a rapidly increasing field. Drug delivery and imaging platforms, as well as the biological features that enable these platforms to target wounded and diseased tissues, are the focus of this study. It highlighted the types and targeting tactics of NDDSs, as well as the current advances in CVD diagnosis and therapy. Gene therapy is a prospective use for nano-carriers in CVD drug delivery that could bring further ideas for enhancing cardiovascular treatments.

Key Words: Nanotechnology, Drug, Nanomaterials, Nanoscale.

1. INTRODUCTION

The use of nanoscience to produce or change novel products is known as nanotechnology. Nanoscience is the study of materials having unique properties that range in size from 1 to 100 nanometers in size. Nanomaterials can be created by manipulating structures at the atomic scale. There are a wide range of applications for nanomaterials, including electronics and medical. In contrast to conventional materials, nanomaterials have a high surface-to-volume ratio.

Nearly all industries and areas of society have benefited from nanotechnology, which offers i) better built, ii) safer and cleaner, iii) longer lasting and iv) smarter goods for medical, communications, everyday life and agriculture. Nanomaterials are used in everyday items in two different ways.

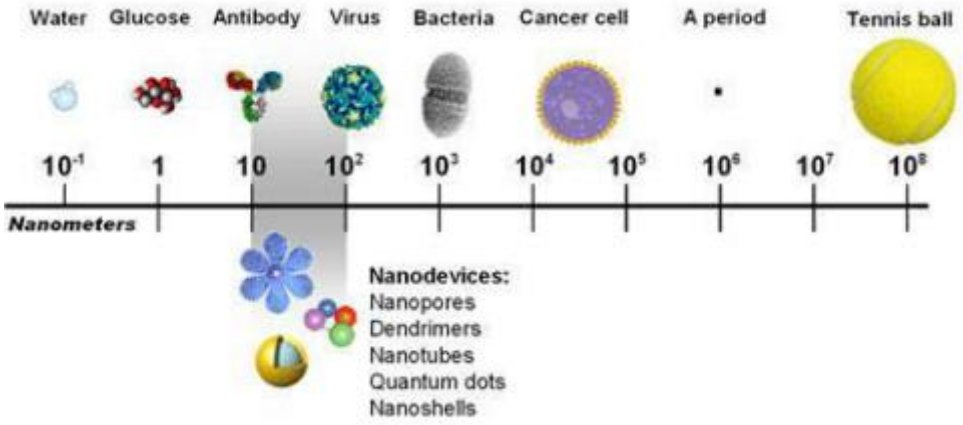

Figure 1: Nanoscale and nanostructures

On the one hand, nano materials can be incorporated into pre-existing objects and increase their overall performance by imparting some of their unique qualities onto them. The unique features of nanomaterials such as nanocrystals and nanoparticles, on the other hand, allow them to be directly utilised to develop innovative and powerful electronics.

Mortality and morbidity rates for cardiovascular diseases (CVDs) are the highest of any disease in the world, according to the World Health Organization (WHO). With such an urgent need for medications to treat cardiovascular diseases, drug development has taken on a new level of importance. It has become possible to treat cardiovascular disease more effectively with nanotechnology due to the rapid growth of nanoscience and the exceptional performance of nanomaterials. As a class of nanomaterials, they have the ability to increase drug stability and water solubility as

well as lengthen cycle times, increase target cell or tissue absorption rates, and block enzyme breakdown. As a result of its bioavailability, NDDSs can be delivered by inhalation, oral administration, and intravenous injection. During the past few years, more researchers have been working on developing nano-drug carrier systems for the diagnosis and treatment of cardiovascular diseases.

2. TARGETED DRUG DELIVERY AND IMAGING

2.1 Passive targeting

Microvasculature at the sick location leaks nanoparticles, resulting in passive targeting. Tumors and inflammatory tissues are examples of disorders where passive targeting of nanocarriers can be achieved. Cancer-associated vascular leakiness results from angiogenesis and other vasoactive stimuli that promote permeability. Arterioles, capillaries, and venules are not present in tumors with angiogenesis, which is characterized by vessels with uneven sizes and branching.

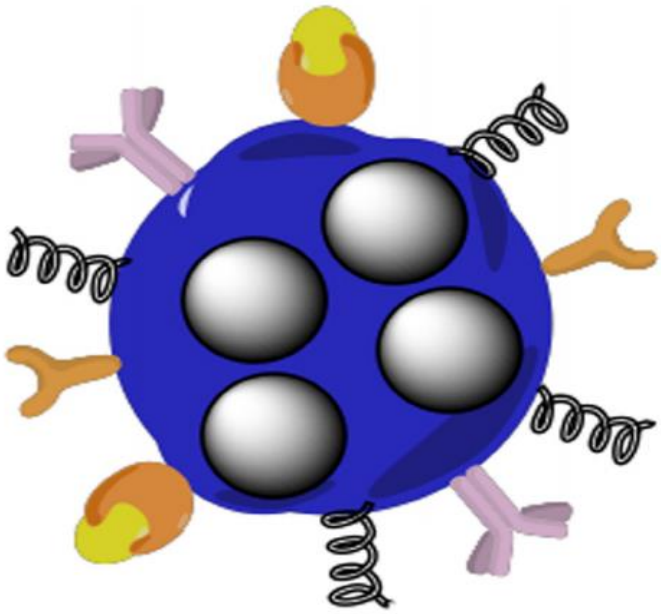

Figure.2. Multifunctional smart nanoparticle coated with diverse moieties for targeting, imaging, and stealth.

Drug-delivery nanoparticles should be able to bind and distribute their drug load to specific diseased tissues while minimising or avoiding the drug's adverse effects on healthy tissues (Figure 2). As a result, covering nanoparticle surfaces with specific targeted ligands is the most prevalent technique.

Small organic compounds are the most commonly used targeting agents due to their relative simplicity in synthesis, stability, and ability to control conjugation chemistry. The specificity and affinity of these targeted ligands may not be as high as wanted. Due to its strong affinity for streptavidin, biotin (vitamin H) has been widely employed in nanoparticle conjugation. A strong affinity for folate receptors exists in folic acid (vitamin B9) and it has been examined as a cancer treatment for a number of cancer types. There have also been a number of additional task-specific carbohydrate molecules developed and used in the past.

They are essential in maintaining the balance between the leakiness associated with the faulty endothelial linings of tumor vessels and the growth, maturation, and regression of vascular structures. In addition to causing vasodilatation, elevated levels of bradykinin also encourage the extravasations of big molecules and their retention in tumors. Nitric oxide is responsible for VEGF and bradykinin's increased vascular permeability.

2.2 Proteins and Peptide Delivery

Macromolecules, such as proteins and peptides, are known as biopharmaceuticals. As a result of their diverse biological activities in the human body, these drugs have been identified for the treatment of a variety of diseases and disorders. Nano biopharmaceuticals, including as nanoparticles and dendrimers, are employed for targeted or regulated distribution.

3. APPLICATIONS

Tolerance to myelin antigens was achieved in a mouse model of relapse MS by administering nanoparticles. Myelin sheath peptide-coated polystyrene micro particles reset the mouse's immune system, preventing disease recurrence and reducing symptoms as the protective myelin sheath builds coating on the nerve fibers of the central nervous system, according to this

treatment method. It is possible that this form of treatment could be utilized to treat additional autoimmune illnesses.

3.1 The applications of various nano systems in cancer therapy are summarized as:

• To detect DNA mutations and disease protein biomarkers, researchers are using carbon nanotubes that have a diameter of 0.5–3 nm and a length of 20–1000 nm.

• Dendrimers with a size of fewer than 10 nanometers are useful for controlled release drug administration and as image contrast agents.

• Breast cancer marker HeR2 can be labelled on cancer cells using nano crystals, which have a size of 2-9.5 nm.

• 10-1000 nm nanoparticles are employed as contrast agents in MRI and ultrasound images as well as for drug delivery and permeation enhancement. They are also used as reporters of apoptosis, angiogenesis, and permeation.

• Nanoshells are used in tumor-specific imaging and thermal ablation of deep tissues.

• In addition to illness protein biomarker detection, nano wires are excellent for detecting DNA mutations and gene expression.

3.2 Nanotechnology in drug delivery

The delivery of medications to a specified target place is typical in therapy. An external therapeutic approach, such as radiotherapy or surgery, is employed if a drug delivery channel within the body cannot be accessed. There's nothing unusual about combining these tactics when it comes to combating illness. A permanent cure for tumors or disease is the goal of therapy. Developing innovative medication delivery systems is a major contribution of nanotechnology to this area of research. They are currently being used in therapeutic settings where some of them have proven to be effective.

3.3 Diagnostic testing

While currently not ready for clinical usage, the use of nanoparticles for diagnostic purposes has been extensively studied in academia. Fluorescent nanoparticles present researchers with a solution to solve current diagnostic technology's shortcomings, including fading fluorescence after a single use, color matching, and dye use restrictions due to a bleeding impact.

Quantum dots, which can be custom-made in a variety of colors that are clearly defined, were one of the most important discoveries. Absorbing from UV to visible wavelengths, they have high quantum yield, variable emission spectrum and good photo stability, among other properties. The size of the nanodot dictates where it falls in the spectral spectrum. Longer wavelengths and narrower emission are associated with larger particles.

4. APPLICATION OF THE NDDSs IN THE DIAGNOSIS OF CVDs

In order to effectively prevent and treat CVDs, early, quick, and precise detection is essential. In recent years, the use of molecular imaging in the diagnosis of cardiovascular disease has gained increasing interest. Diagnostics that are real-time, rapid, sensitive, and high-resolution require new contrast agents, in addition to the ongoing improvement of imaging technologies. These advantages of nano contrast agents are superior to those of conventional contrast agents

1. This includes stability in vivo, controllable dispersion, and an extended half-life.
2. Chemical composition, size, and imaging performance are all examples of controllable physical and chemical attributes.
3. A method for the precise identification of biomolecules
4. Realization of multimodal imaging capability is possible.
5. Expectations are high for tailored diagnosis and therapy to provide positive results.

When disease is in its early stages, pathologists can use nanoprobes that contain the unique chemical signal molecules of diseased tissues for MRI, X-ray, fluorescence, and contrast enhanced ultrasound (US) (Figure 3).

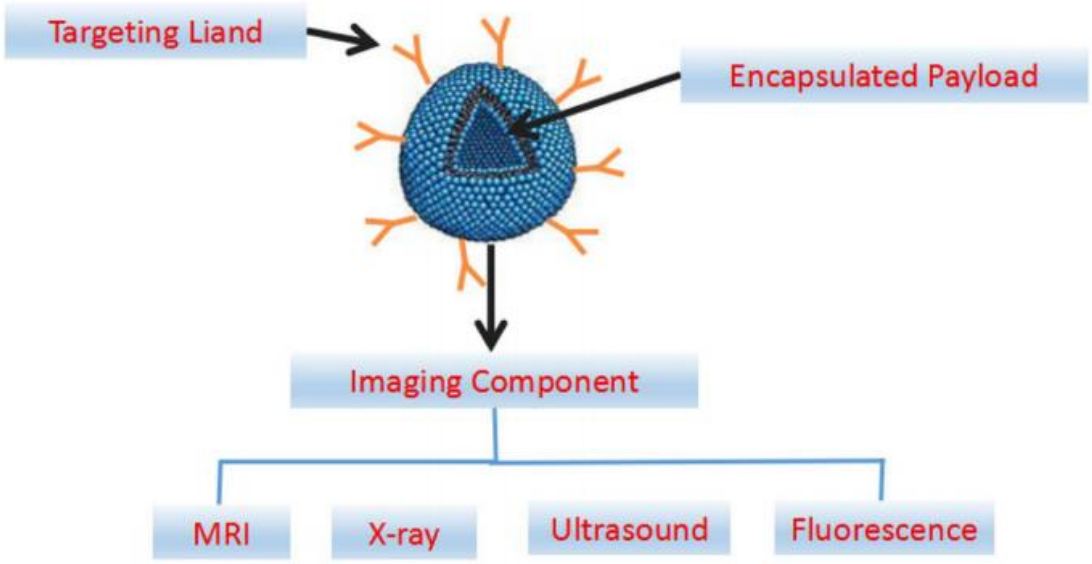

Figure 3: Nanoparticles developed for imaging and medication delivery are shown in a simplified general perspective on a map.

It contains a cell-targeting ligand and therapeutic drugs that are contained in its payload. Nanoparticle shells, targeting ligands and internal payloads can all be used as imaging components.

4.1 Magnetic Resonance Imaging

For soft tissue imaging, magnetic resonance imaging is a popular imaging approach because it is noninvasive, safe, and high-resolution. MRI's sensitivity, on the other hand, is low (103 -109 M). In clinical practice, these compounds are commonly used as T1-weighted imaging contrast agents, and gadolinium is nephrotoxic. As T2-weighted MRI contrast agents, Fe3O4 nanoparticles are believed to be nontoxic.

4.2 X-Ray Imaging

Nuclear medicine relies heavily on imaging with radio nuclides. In addition to being sensitive, radio nuclides are also measurable. PET and SPECT are the two most prevalent kinds of tomography. In the current state of the art, radiation-labelled nanoparticles can be used to monitor embolization and nanomedicine distribution for targeted imaging.

4.3 Fluorescence Imaging

It has the advantages of being radiation-free, non-intrusive, having a high resolution and being easy to manipulate, but its penetration is weak. Fluoresce in is typically used to generate fluorescence signals for fluorescence imaging. Due to its high penetration power and safety, NIRF probes are widely employed. In imaging systems for small animals and in clinical tumor transformation, they have proven to be highly effective and safe. As of today, nanoparticles and liposomes can be employed to monitor blood vessels using NIRF.

4.4 Ultrasound Imaging

It is safe and convenient, and it is real-time, compared to fluorescence. It has been designed to target vascular markers with nano-ultrasound imaging materials. VEGFR2-targeted ultrasound nanoparticles, for example, not only improve ultrasound imaging of tumor blood vessels, but also aid in medication localization in blood vessels.

5. METHODOLOGY

5.1 Vesicular nanocarriers

5.1.1 Nanoliposomes

Medicines, imaging agents, and peptide, protein, and nucleic acid molecules with lower molecular weights can be delivered through these bilayers. With multiple bilayers, particle sizes can range from 25 nm to several micrometers in size. These carriers are suitable for drug delivery due to their versatility in terms of particle size, bilayer charge and composition, as well as their encapsulating properties. A substance enclosed in smaller liposomes can be released over a longer period of time, resulting in increased efficacy. Nanoliposomes, on the other hand, degrade quicker than liposomes and are taken up by liver macrophages, making them ideal for active targeting.

5.1.2 Solid lipid nanoparticles (SLNs)

Aqueous emulsions of solid lipids are used to form SLNs. They are similar to nanoemulsions, but the liquid lipid has been replaced with a solid lipid in these formulations. As shown in Figure 2, SLNs are commonly prepared using the hot melt method. Oil phase increases drug mobility while solid lipids reduce it significantly. SLNs do not have the advantages of other carrier systems, such as polymeric nanoparticles, liposomes, ethosomes, and lipid emulsions. An excellent study was recently analysed and that is discussed about the major challenges and applications of lipid-based nanocarriers, as well as their safety aspects.

5.1.3 Dynamic light scattering

In terms of particle size determination, DLS is the most widely used method. Photon correlation spectroscopy is a technique for calculating particle size in suspension (PCS). When the particle size is less than 1/10th of the incident light wavelength (i.e. k/10), elastic scattering occurs (Rayleigh scattering). Once particle diameter exceeds k/10, Mie scattering replaces Rayleigh pattern. There is a result of this inelastic scattering, which results in a beam with a different energy from the incident light. Yet many manufacturers insist on a range of 0.3 nanometers to 10 micrometers. A polydisperse nanoparticle dispersion may be challenging to size using DLS, despite its many applications. To estimate the size of unimodal nanoparticles, DLS is the most appropriate technique. Using a photon detector, the DLS device detects a dispersed laser light beam whose strength is proportional to the size of the nanoparticles being measured.

5.2 Surface morphology

Electron microscopy

A nanoparticle's toxicity profile can be determined by examining its overall morphology with an electron microscope. Nano-pharmaceutical nanocarriers are primarily used to modulate medication release and drug targeting. When employing light, it is exceedingly difficult to examine tiny particles with diameters >1 mm because diffraction effects limit the resolution of optical microscopy. Therefore, higher resolution electromagnetic radiation of shorter wavelength is desired.

Scanning Electron Microscopy (SEM). After being turned into a dry powder and placed on a sample stand, nanocarriers are then sputter-coated with gold or platinum or gold/palladium alloys using SEM sputter coaters. The results of this study will be published in the journal Nano Letters.

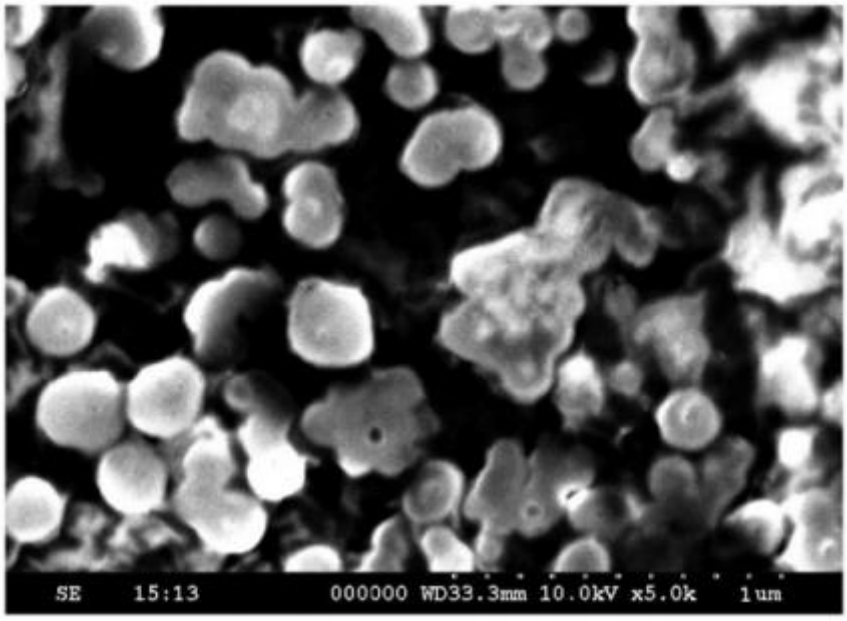

Figure 4. SEM image of insulin nanoparticles with starch.

External X-ray maps, backscattered electron images, and secondary electron images are the three primary types of images produced by the scanning electron microscope (SEM). Secondary electrons were emitted from the sample surface, which were used to determine the surface properties of particles. In order to prevent particle destruction, nanocarriers must be able to maintain a vacuum. As a result of its similarity to the DLS approach in terms of average diameter, SEM analysis is more time-consuming and expensive, and requires the

addition of size distribution patterns on a regular basis. As may be seen in Figure 4, insulin-containing starch nanoparticles were observed under scanning electron microscope. Destructive sample preparation was required for the majority of EM techniques, including SEM, which restricted the sample's capacity to be examined by other techniques. In ESEM, the sample compartment is kept at 10–50 Torr of low-pressure gaseous environment, and particles do not need to be coated with conductive compounds.

Salting Out Method

The salting-out method separates the solution from the water-soluble solvent. When separating a water miscible solvent from an aqueous solution, the salting-out action is used. Polymer and drug are first dissolved in a solvent, which is then emulsified into an aqueous gel containing salting-out agents (electrolytes, such as magnesium chloride and calcium chloride, or nonelectrolytes, such as sucrose) and colloidal stabilizers such as polyvinylpyrrolidone or hydroxyethanolcellulose. When the oil/water emulsion is diluted with enough water or aqueous solution to facilitate solvent diffusion into the water phase, these nanospheres are generated. Several manufacturing parameters, including stirring rate, internal/external phase ratio, polymer concentration in the organic phase, electrolyte type, and stabilizer type in the aqueous phase, can be modified throughout production.

Emulsions- Diffusion Method

Preparation of nanoparticles is also carried out in this way. Encapsulating polymer is dissolved in partially water-miscible solvent for the first thermodynamic equilibrium of both liquids (such as propylene carbonate or benzyl alcohol). To achieve nanosphere or nanocapsule formation after polymer water and solvent phase emulsions, the solution is stabilized by stabilizers. Evaporation or filtration are the ultimate methods for removing the solvent, based on its boiling point. In addition to its high encapsulation efficiency (usually 70 percent), no homogenization is required, batch-to-batch consistency is excellent, scaling up is simple and the size distribution is restricted.

CONCLUSION

By offering a platform for biotechnological, medical, and pharmaceutical developments, nanotechnologies have unquestionably contributed to improving the quality of life for patients worldwide. For the diagnosis and treatment of cardiovascular disease (CVD), the nano-carrier has proven distinct advantages as an efficient, specific and regulated intracellular drug delivery technique. Diagnostics and therapy are evolving in a multifunctional and integrative direction. In the last two decades, the scope of nanomedicine has expanded rapidly. Inorganic or organic nanocarriers can be used to manipulate particle size, shape, morphology, surface characteristics, drug encapsulation, and drug release to an incredible degree. Liposomes and micelles are the only commercially available compounds that have undergone a clinical transition.

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