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# Combination of Nanoparticles and Smart Drug Delivery Systems.

***Anjali Kumari [a*], Akshay Kumar [b], Dev Raj Sharma [c], Dr. Pravin Kumar [d], Dr. M. S Ashawat [e]***

**[a*]Student M. Pharmacy Deptt of Pharmaceutics Laureate Institute of Pharmacy Kathog Jawalaji H.P India**
**[b] Student M. Pharmacy Deptt of Pharmaceutics Laureate Institute of Pharmacy Kathog Jawalaji H.P India**
**[c] Assistant Professor Deptt of Pharmaceutics Laureate Institute of Pharmacy Kathog Jawalaji H.P India**
**[d] HOD Deptt of Pharmaceutics Laureate Institute of Pharmacy Kathog Jawalaji H.P India**
**[e] Director cum Principal Deptt of Pharmaceutics Laureate Institute of Pharmacy Kathog Jawalaji H.P India**

Drug delivery methods have long been a focus of study in the pharmaceutical business. The ultimate goal is to create new formulations for clinical use in order to cure diseases and enhance treatment outcomes. Novel drug delivery systems are designed to improve the delivery and efficacy of existing medications over old systems. Many pharmaceutical treatments have been developed as a result of drug delivery methods, which improve patient health by improving therapeutic delivery to the target location, minimising off-target accumulation, and simplifying patient compliance. Significant progress has been made in drug delivery system research in recent years, including improvements in allied domains such as pharmaceutical sciences, material sciences, and biological sciences. To maximise the potential advantages for patients, advanced drug delivery methods are required for the targeted and regulated release of new compounds in tissues and cells. The pharmaceutical industry is constantly evolving due to continued research, technological break throughs, and novel discoveries. Innovative drug delivery techniques with several benefits have been created thanks to the development of smart drug delivery systems and nanotechnology. These methods have completely changed how drugs are delivered by fusing the special qualities of nanoparticles with the accuracy of smart drug administration.

## Nanotechnology-based drug delivery systems:

Nanotechnology has grown in prominence in recent years, with nanoparticles serving as its fundamental building components. Nanoparticles are extremely small particles that are less than 100 nm in size and can be made of a variety of materials, including carbon, metals, metal oxides, and organic compounds. Liposomes, solid lipid nanoparticles, dendrimers, polymers, silicon or carbon materials, and magnetic nanoparticles are examples of drug delivery system nanocarriers. [1]. Many different types of nanoparticle medication delivery systems are being researched at various levels. These particles were created from various materials with unique architectures to act as a potential drug vehicle to cure a certain ailment [2],[3]. Nanoparticles with a hydrodynamic diameter of 10-100 nm are widely regarded to have good pharmacokinetic properties for in vivo applications. Smaller nanoparticles are prone to tissue extravasation and renal clearance, but bigger particles are promptly opsonized and eliminated from the bloodstream by reticuloendothelial system macrophages [4]. Following types of Nano carriers are used in different disease :

1. Cancer

The potential of nanoparticles in the delivery of tailored drugs for the treatment of cancer has been thoroughly investigated. The following are some essential details concerning various nanoparticle types and how they are used in cancer treatment:

- Liposomes: Self-assembling, polyvalent nanoparticles known as liposomal nanoparticles are useful as medication delivery systems. They can deliver chemotherapeutic medications to tumour cells only, lowering systemic toxicity and improving treatment effectiveness [5]. As "smart" pharmaceutical nanocarriers, liposomes have been investigated and have showed promise for enhancing drug delivery in the treatment of cancer [6].
- Polymeric nanoparticles: Through passive or active targeting strategies, anticancer drugs have been delivered to tumour tissues using polymer-based nanoparticles. The enhanced permeability and retention (EPR) effect, where nanoparticles aggregate in tumour tissues as a result of leaky blood arteries and compromised lymphatic outflow, is used in passive targeting. Active targeting entails coating nanoparticles' surfaces with cancer-site-specific ligands, such as folate receptors or monoclonal antibodies, to interact with over expressed receptors or antigens on tumour cells. The potential of polymeric nanoparticles to enhance drug delivery and targeting in cancer therapy has received extensive research [7].
- Gold nanoparticles: Targeting ligands can be functionalized on gold nanoparticles to use them in a variety of cancer treatment procedures. They can be used in photothermal therapy, which targets cancer cells specifically by absorbing light and converting it into heat. Gold nanoparticles can be functionalized with targeting ligands to be employed for the delivery of medication to cancer cells. They appeal for use in cancer treatment due to their special qualities [7].

- Quantum dots: Quantum dots have been researched as fluorescent probes for cancer detection and imaging. They can be utilised for early cancer detection and diagnosis and have the potential to deliver high-resolution tumour imaging.

These several nanoparticles have been thoroughly researched for their potential to enhance drug delivery and targeting in cancer therapy. They each have distinct advantages. The number of approved nano-drugs is still small, despite the fact that there have been sizable developments in the field of nanomaterial-based drug delivery for the treatment of cancer. To fully realise the potential of nanoparticles in cancer therapy, more study and development is required [8].

- Iron oxide nanoparticles: Using MRI to diagnose cardiovascular disorders, iron oxide nanoparticles have been used as contrast agents. These nanoparticles are capable of being functionalized and injected into the bloodstream, where they gather in areas affected by disease or inflammation. Iron oxide nanoparticles can aid in the diagnosis and monitoring of cardiovascular problems by improving the contrast in MRI images [9].

2. Cardiovascular diseases:

- Lipid-based nanoparticles have been investigated for therapeutic delivery in the management of atherosclerosis and restenosis. These nanoparticles can carry therapeutic agents to the desired site and encapsulate them. Lipid-based nanoparticles are thought to be less dangerous and appropriate for drug administration because of their biodegradable nature. They provide a potential method of administering medications to particular body parts in illnesses involving the heart [10].
- Iron oxide nanoparticles: Using contrast agents for magnetic resonance imaging (MRI), iron oxide nanoparticles have been used to identify cardiovascular disorders. These nanoparticles can support the detection and monitoring of cardiovascular problems by improving contrast in MRI images. Targeted molecular imaging of cardiovascular disorders has showed potential for them [11].

3. Neurological disorders:

- For their potential to carry drugs to the brain for the treatment of neurological illnesses including Alzheimer's and Parkinson's disease, polymeric micelles have been thoroughly researched. Amphiphilic block copolymers make up the micelles, which self-assemble into nanoscale structures in aqueous liquids. The hydrophilic shell of the micelles offers stability and biocompatibility, while the hydrophobic core of the micelles can encapsulate hydrophobic medicines. Polymeric micelles are a viable option for enhancing therapeutic efficacy and minimising side effects because of their capacity to cross the blood-brain barrier (BBB) and target particular brain areas. Additionally, they can be made to release medications gradually and steadily, extending their therapeutic efficacy and lowering the frequency of administration [12].
- Nanogels: For targeted therapy in brain tumours, nanogels have been investigated as drug carriers. These cross-linked polymer networks, which make up the nanoparticles, can encapsulate medications and release them gradually. By focusing on particular cells or receptors and minimising off-target effects, nanogels offer the potential to enhance medicine delivery to brain tumours. They can also be functionalized with ligands that target specific brain cells to increase their focus on those cells [12].

4. Infectious diseases:

- Nanoliposomes: These lipid-based nanoparticles can contain antibacterial compounds enabling specialised drug delivery to diseased tissues. The hydrophilic surface offers stability and biocompatibility, and the lipid bilayer allows for the encapsulation of hydrophobic medicines. Treatment for numerous bacterial and fungal diseases, as well as the delivery of anti-cancer, anti-biotic, gene, anaesthetic, and anti-inflammatory medications, have all showed promise when using nanoliposomes [13].
- Dendrimers: For the purpose of treating infections, dendrimers are a class of polymeric nanoparticle that can be functionalized with antiviral or antibacterial substances. They are highly branched, monodisperse macromolecules that may be precisely controlled in terms of size, shape, and surface characteristics throughout the synthetic process. Dendrimers have demonstrated promise in the treatment of bacterial infections like methicillin-resistant Staphylococcus aureus (MRSA), as well as viral diseases like HIV and herpes simplex virus [14].

5. Diabetes:

- Insulin can be contained and released under control using nanoporous materials because of their porous structure. In order to precisely regulate blood glucose levels, nanoporous materials can be created to release insulin in a regulated manner.

Insulin may be shielded from deterioration and given greater stability during circulation by being encapsulated in nanoporous materials.

With an emphasis on improving their design, stability, and drug-loading capacity, research on nanoporous materials for the treatment of diabetes is still ongoing.

The development of new and existing medications in nanoporous carriers holds the potential to address a number of difficulties in the treatment of diabetes, such as low on-target bioavailability, sub-therapeutic drug accumulation in the pancreas, and low patient adherence because of drug-related side effects and lengthy therapeutic regimens [15].

6. Autoimmune diseases:

    - As a treatment for autoimmune illnesses, nanoparticles can be used to inhibit the immune system. Additionally, they can be created to stimulate the immune system in order to cure autoimmune diseases.

Numerous autoimmune disorders, including rheumatoid arthritis and inflammatory bowel disease, have been researched in relation to the therapeutic potential of nanoparticles. Nanoparticles must have their properties optimised for targeting, internalisation, and cross-presentation while minimising negative effects in order to be used in immunomodulation. The topic of nanoparticle-based immunomodulation for autoimmune illnesses is still under investigation, with a particular emphasis on improving nanoparticle design and assessing their long-term effects [16].

7. Gene therapy:

    - The delivery of therapeutic genes to target cells for gene therapy can be accomplished via viral vectors, such as adenoviral vectors. In order to deliver medications to specific areas, virus-like nanoparticles are delivered as tailored viral vectors. Polymer-coated viral vectors are hybrid nano systems for gene therapy that have been documented thus far, and the following information discusses their potential. The host environment, such as macrophages, the reticuloendothelial system, and magnetic nanoparticles, can interact with viral vectors in a non-specific way. Compared to viral vectors, nanoparticles are less likely to trigger immunological reactions, and they are simpler to create and modify for specific applications [17].

## Smart drug delivery system

An innovative method called a "smart drug delivery system" tries to distribute medications in a targeted and controlled way, maximising their therapeutic effects while reducing their adverse effects and systemic toxicity. These systems provide on-demand drug release or delivery to the appropriate site since they are built to react to particular bodily triggers or stimuli [18]. Some essential aspects of intelligent medication delivery systems include:

1. Targeting: The design and deployment of medication delivery systems that selectively target sick tissues or cells is referred to as smart targeting, also known as targeted drug delivery or smart drug delivery. In order to maximise therapeutic efficacy while minimising adverse effects, this strategy seeks to raise the concentration of drug in particular bodily regions relative to others.

There are two main strategies employed in smart targeting:

- Passive Targeting: Passive targeting makes use of the EPR effect. This result is brought on by the abnormal lymphatic drainage and leaky vasculature that are frequently present in tumours. Drugs can aggregate preferentially in tumour tissues by using nanoparticles or drug carriers, improving drug delivery to the intended target [19].

- Active targeting: Using ligands or antibodies that precisely bind to receptors or markers that are overexpressed on the surface of target cells is known as "active targeting." Drugs can be delivered to particular cells or tissues by attaching these ligands or antibodies to drug carriers or nanoparticles. This method increases the concentration of medications at the desired site while reducing off-target effects, improving the specificity and selectivity of drug delivery [20].

2. Stimuli responsiveness: Drug delivery methods that respond to numerous internal or external stimuli, such as pH, temperature, enzymes, light, magnetic fields, or electric fields, are known as stimulus-responsive drug delivery methods. The medicine is released at the desired spot by the drug delivery mechanism when exposed to the trigger. Direct application of external stimuli, including heat, light, magnetic fields, and ultrasound, can promote drug release in the target region. A stimuli-responsive drug delivery system has the advantage of being able to stop premature drug release, which is a typical issue with conventional drug delivery systems. Drug release can be accurately controlled by external influences, and exogenous stimuli-responsive systems have the potential to overcome interpatient variability. Smart medication delivery strategies can offer the required spatiotemporal resolution and complex release profile [21].

3. Drug release can be prolonged throughout time with the use of smart drug delivery systems'-controlled release kinetics. By reducing the requirement for frequent dosage, this feature can assist in maintaining therapeutic medication levels. According to how the drug is released from the dosage form, controlled release drug delivery systems are divided into dissolution controlled, diffusion controlled, water penetration controlled (osmotic pressure controlled and swelling controlled), chemical controlled, and nanoparticle-based systems. The essential spatiotemporal resolution and intricate release profiles can be provided by smart medication delivery systems. Smart polymer-based drug delivery systems have a number of advantages, including decreased dose frequency, simplicity in preparation, maintenance of optimal therapeutic levels, and increased patient compliance [22]. Additionally, diagnostic tools such as PET scanning and MRI-CAs can be created using smart drug delivery methods [23].

4. Personalization: Smart drug delivery systems have controlled release kinetics that enable prolonged medication release. Smart medication delivery systems with the ability to be customised for each patient's needs include personalised drug delivery systems (PDDS). Solid dosage forms known as PDDS are those that contain a drug's precise, patient-tailored dose. Personalised medicine in drug delivery systems has evolved as a strategy to increase the effectiveness of treatments by creating personalised therapy[24]. A focus area in NDDS has been smart drug delivery systems, which offer the potential to improve medication delivery and efficacy and provide targeted specificity and controlled

release. Several aspects and criteria, including biomaterial qualities, administration route, pharmacokinetics, and stability enhancement, must be taken into account while building a controlled release drug delivery system [25].

There are various advantages of combining nanoparticles with smart delivery systems[26],[18][27].

Increased drug stability: Nanoparticles help keep pharmaceuticals from degrading while they are being circulated throughout the body.

Targeting is improved thanks to active targeting ligands on nanoparticles, which increase the site-specificity of drug delivery.

Controlled release: With the help of smart drug delivery systems, drug release can be precisely managed, resulting in the best possible drug concentrations at the target site.

Reduced side effects: Targeted drug delivery reduces unwanted effects by decreasing exposure of healthy tissues to the drug.

Therapeutic synergy: The use of various medications in a single nanoparticle during combination therapy can boost the therapeutic effects.

Conclusion: Drug delivery systems based on nanoparticles have been utilised to increase the bioavailability of a variety of medications, especially those that are poorly soluble. Smart drug delivery systems can offer controlled release, precise targeting, and the capacity to enhance drug delivery and efficacy. In order to circumvent the drawbacks of free therapies and get over biological barriers that vary among patient populations and diseases, nanoparticles have been developed. A new technological foundation for customised, environmentally sensitive, and multifunctional drug delivery systems has evolved in the form of polymer nanoparticles. Overall, the use of nanoparticles in conjunction with intelligent drug delivery systems offers the potential to increase drug distribution and effectiveness while lowering side effects.

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