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Development and Optimization of Novel Drug Delivery Systems for Targeted Therapy: An Analytical Perspective

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ABSTRACT
Pharmaceutical research is driving innovation in targeted drug delivery systems, aiming for precise therapy with reduced side effects and enhanced efficacy. Strategies involving ligands, antibodies, peptides, or nanoparticles are enhancing targeting capabilities, facilitated by nanotechnology. Refinement techniques improve stability and biocompatibility, while smart materials enable controlled-release systems responsive to environmental triggers. These advancements promise improved treatment across diseases like cancer, cardiovascular issues, and neurodegenerative disorders, by extending drug activity and enhancing targeting precision. Novel Drug Delivery Systems (NDDS) offer advantages including prolonged drug activity and precise targeting, with various advanced approaches showcasing superior properties over conventional therapies. This article provides a comprehensive overview of these innovative drug delivery systems.

Keywords: Nanoparticles, Controlledrelease, Active targeting, Drug release, Dosage forms, Hydrogel, Cancer therapy, Novel drug delivery system, Nanoparticles, Liposomes, Microspheres, Microemulsion.

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Contents

1. Introduction

Medical practice has undergone a revolution, especially in targeted therapy, because of the creation and improvement of innovative drug delivery methods. To maximize effectiveness while minimizing negative side effects on healthy tissues; targeted therapy seeks to deliver therapeutic molecules to cells, tissues, or organs. This strategy has a great deal of potential for the treatment of numerous illnesses, such as cancer, cardiovascular problems, neurological illnesses, and autoimmune disorders. Poor bioavailability, a lack of specificity, a lack of stability, and insufficient control over drug release are common problems with traditional drug delivery systems. Due to these restrictions, researchers are investigating novel methods to improve drug delivery and boost therapeutic results. Significant progress has been made recently in the creation of innovative drug delivery systems that may precisely target diseased tissues or cells, provide therapeutic chemicals in a regulated manner, and enhance treatment effectiveness [1]. The utilization of nanotechnology-based medication delivery systems is one of the most promising strategies in targeted medicine. Due to the small size and high surface area-to-volume ratio, nanoparticles, which are typically1 to 100 nanometers in size, have special advantages. These characteristics allow for the effective encapsulation, defense, and controlled release of medicinal substances. Numerous forms of nanoparticles, including liposomes, polymeric nanoparticles, dendrimers, and metallic nanoparticles, have been thoroughly studied for applications in targeted therapy. As medication transporters, vesicles made of lipid called liposomes have drawn a lot of attention. Within the watery core and lipid bilayer, they can contain both hydrophilic and hydrophobic medications.

Targeting ligands can be added to liposomes' surface to enable them to recognize and bind to receptors that are overexpressed on sick cells. By selectively accumulating therapeutic molecules at the appropriate region, thisactive targeting strategy reduces off-target effects. Polymeric nanoparticles are becoming increasingly popular as adaptable medication delivery methods. By adjusting the polymer composition, molecular weight, and surface changes, these nanoparticles can be engineered to produce the desired drug release kinetics. Small molecules, proteins, peptides, and nucleic acids are just a few of the many medications that can be packaged into polymeric nanoparticles [2].

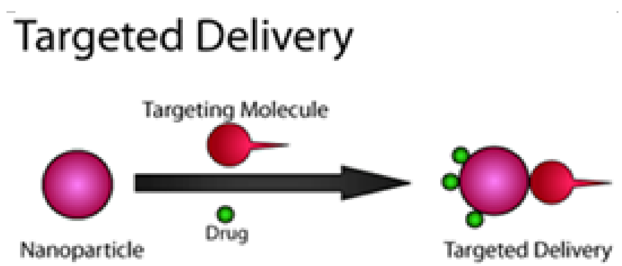

Fig.1: Targeted Drug delivery

Another option for focused therapy is provided by dendrimers, which are highly branched macromolecules. Size, shape, and surface capabilities are all precisely under control. Drugs can either be conjugated to the surface of dendrimers or encapsulated within the cavities. Dendrimer surfaces that have been functionalized allow for more precise targeting and easier passage across biological barriers. Dendrimers have also demonstrated the ability to deliver numerous medicines simultaneously, which can work in concert to affect various targets or pathways to produce stronger therapeutic effects. The unique physicochemical characteristics of metallic nanoparticles ,such as gold nanoparticles and magnetic nanoparticles, have attracted attention. Gold nanoparticles can be used for targeted medication delivery and imaging because of the high biocompatibility, simplicity in manufacturing, and surface Plasmon resonance [3,4].

Cancer is one of the major public health causes in the world. Cancer therapy still remains great challenges[5-7]. Because of the great potential application of NDDS in cancer therapy we are enabled the development of novel therapeutic and diagnostic strategies[8-10]. The particular technique by which drug is conveyed can have an impressive result on its adequacy. A few medications have an ideal focus range which maximum advantage is derived, and above or below concentration of drug from this range can be harmful or didn't produce therapeutic benefit [11,12].

Advanced drug delivery carriers should fulfill mainly two conditions. Firstly, delivery should be rate specific. Secondly, it should be site-specific. Conventional dosage forms can't meet any of these. NDDS can be divided into classes. 1) Sustained release drug delivery system. 2) Controlled release drug delivery system[12-14]. Drug delivery system is designed to produce delayed therapeutic effect over a prolonged period of time [12]. The principle objective of treatment is to accomplish consistent state blood level that is powerful and non-lethal for an extended period of time.

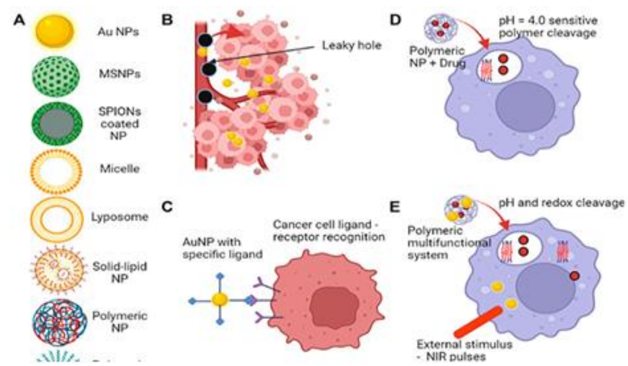

Fig.2: Drug delivery strategies for cancer therapy

Advantages:

- Improved patient convenience and compliance due to less frequent drug administration
- Increase safety margin
- Maximum utilization of drug
- Less frequency of dosing etc.

Disadvantages:

- Poor in-vivo, in-vitro correlation
- Decreased systemic availability
- Possibility of dose dumping etc.
- Controlled drug delivery follows delivery of the drug at a predetermined rate, for locally or systemically. Controlled release is splendidly zero order drug release.
- Reduced dose concentration and dosing frequency
- Reduced GI toxicity
- Better patient acceptance.

Oral, parenteral, Transdermal and Inhalation route of administration are defined as most preferable route of administration [15-17]. NDDS strategies for local medication like nanoparticles, microspheres, polymeric micelles, liposomes, and hydrogel systems for targeting and controlled release have been examined with biodegradable and non-biodegradable polymers, comprising polyether's, polyesters, polysaccharides, poly amino-acids and proteins. These polymers are mostly utilized in cancer therapy for parenteral drug delivery system [12]. These polymers are actively known for their reduced harmful reactions and enhanced carcinostatic pharmaceutical impacts.

2. Different Drug Delivery System

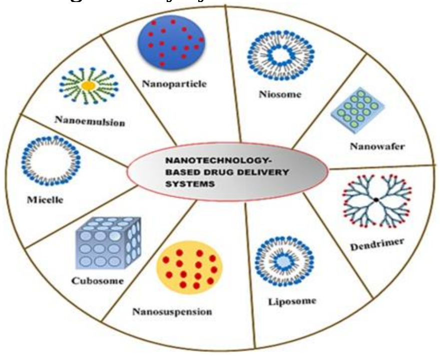

Fig.3: Different drug delivery systems

Lipoprotein

In any ideal drug delivery system, an acceptable amount of active therapeutic drug must be assimilated and transported to the site of activity at the favorable time and rate [18]. Lipoprotein as a medication system for malignancy therapy, Lipoprotein can be utilized as a Targeted drug delivery system in malignancy therapy which helps to improve therapeutic index of anticancer agents, either by expanding the concentration of medication in tumor cells or by diminishing the interaction in normal host tissues [19, 20]. Low density lipoprotein is potential transporter for chemotherapeutic mediators. They are utilized for targeted delivery of anticancer because several types of malignant cells display higher level of receptor mediated uptake of low density lipoprotein [12]. For clinical malignancy therapy liposomes and phospholipid vesicles, have been known as a potential drug delivery system [21-23]. This system protecting healthy cells from toxic effect and keep their concentration in susceptible tissues for example in patient kidneys and their liver [24-28].

Nanoparticle

Nanoparticles are in the solid state and are either amorphous or crystalline in nature with size range (from 10 to 200 nm) [29,30]. It secures drug against chemical and enzymatic dilapidation [31-33]. Biodegradable polymeric nanoparticles have few applications in the controlled release of therapeutic medications in targeting specific tissue or organs as carriers in gene therapy [34]. Nanomaterial classified as Nanotubes, Nanowires, Nano shells, Quantum dots, Nano pores, Gold nanoparticles [35-38].

Nanoemulsion

Nano emulsions can be characterized as oil-in-water (o/w) emulsions with mean droplet size from 50 to 200 nm and the particles can exist as both water-in-oil and oil-in water forms, where the core of the particle is whichever water or oil [12,39-43]. Nano-emulsions like microemulsion may have high optical transparency and kinetic constancy[44-47].

Microcapsules

Numerous anticancer agents (such as paclitaxel, PCT; camptothecin, CPT; and certain porphyrins like meso tetraphenylporphine, TPP, utilized as a part of photodynamic treatment, PDT) with stumpy aqueous solubility affect their application and makes direct parenteral administration more complicated [48-50]. Novel drug delivery strategies based on the drug carrier systems approaches have been advised to overwhelmed their reduced solubility, little stability, and dangerous symptoms [12,51]. PEG diacyllipids conjugates have attracted much consideration towards their easily controlled properties and great pharmacological features [52-55].

Microemulsion

Microemulsion are defined as liquid scatterings of water and oil that are prepared thermodynamically stable formulation which is homogenous, transparent or translucent in nature by the addition of relatively huge concentration of a surfactant and a surfactant [14,56]. Microemulsion droplets diameter having range of 10-100 nm and have been extensively considered for targeted drug delivery system to the brain [57-60]. It is a cost effective strategy and enhances the bioavailability of the poorly dissolvable medications [61-63].

Microspheres

Microsphere technology is the newest development in cancer chemotherapy. Microsphere is solid porous particles with diameters 1 - 100 μm [12,64]. It can focus on their medication load by physical trapping in blood veins known as chemoembolization and sustain therapeutic agent action through controlled release. Biodegradable microspheres are used for direct delivery of drugs to organ(s) by lodging therapeutic drug in the end organ vessels [65-68]. Its effect depends on the size and mode of administration of the microsphere either intravenous or intra-arterial [69-71].

Dendrimers

Dendrimers are highly branched-three-dimensional, monodisperse molecules with highly controlled structures [12]. Its monodispersed, encapsulation ability, water solubility and huge number of peripheral functional groups, make them perfect candidates for assessment as medication delivery system [72-73]. Recently, Dendrimers used as drug delivery system for anticancer drugs in variety of cancer therapies [74-80].

Mainly there are three methods used for drug delivery through Dendrimers (a) attachment of drug to periphery of the Dendrimers through covalent bond to form Dendrimers pro-drugs, (b) the drug is synchronized to the outer functional groups through ionic interactions, or (c) host-guest supramolecular assembly [81-85].

Hydrogels

Hydrogels are three-dimensional networks of water-swollen polymers [11-13]. It usually comprises crosslinked hydrophilic polymers which cross-linked either through covalent bonds or composed by physical intramolecular and intermolecular attractions that swell readily without dissolving in aqueous solution [86-90]. Because of hydrogel unique ability to swell under biological conditions makes them an ideal class of materials for biomedical applications, for example drug delivery and tissue engineering [91-98].

Hydrogels are highly hydrophilic in nature due to the presence of some hydrophilic moieties such as carboxyl, amide, amino, and hydroxyl groups [99-102].

3. Literature Review

To increase the effectiveness and lessen the negative effects of traditional medicines, targeted therapy has become a promising strategy in the field of drug delivery. On the creation and improvement of innovative drug delivery systems for targeted therapy, significant research efforts are done throughout the years. By increasing the selectivity and specificity of therapeutic activity, targeted therapy provides important advantages over traditional drug delivery techniques. Therapeutic chemicals are delivered directly to the target region, decreasing systemic exposure and off-target consequences.

Nanoparticles as Drug Delivery Systems: Due to the distinctive characteristics and powers, nanoparticles have become viable medication delivery methods. They can interact with biological systems at the cellular and molecular levels since they are extremely small particles with sizes ranging from 1 to 100 nanometers. Biocompatible and biodegradable polymers like poly (lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), and chitosan make up polymeric nanoparticles. Small compounds, proteins, and nucleic acids are just a few of the many medications that these nanoparticles can enclose. They have several benefits, including high drug-loading capacity, prolonged release kinetics, and defense against drug degradation. For improved targeting of cells or tissues, the surfaces of polymeric nanoparticles can be modified with ligands or antibodies. Metal-based nanoparticles with distinctive physicochemical features, such gold, silver, and iron oxide nanoparticles, are desirable for drug delivery applications. With careful control over the size, shape, and surface characteristics, they can be synthesized. For targeted medication delivery and in-flight monitoring, metal nanoparticles can have the surfaces functionalized with imaging and targeting ligands. They can also be used for photothermal therapy, which kills cancer cells by targeting them with heat instead of light[104].

Liposomes for Targeted Therapy: The spherical vesicles known as liposomes are made of lipid bilayers and can encase a variety of compounds, including pharmaceuticals, in the aqueous compartments. Due to the capacity to increase therapeutic efficacy and lessen adverse medication reactions, they have attracted considerable attention in the field of drug delivery. Numerous benefits of liposomes include the biocompatibility, biodegradability, and capacity to encapsulate both hydrophilic and hydrophobic medicines. The phospholipids and cholesterol that make up conventional liposomes give the lipid bilayer stability and mobility. These liposomes can also be divided into large unilamellar vesicles (LUVs) and small unilamellar vesicles (SUVs) according to the size. Although conventional liposomes have shown effective at delivering a variety of medications, they have drawbacks like quick bloodstream clearance and low accumulation at the target region. Long-circulating liposomes, also known as stealth liposomes, were created to address the drawbacks of ordinary liposomes[105] .

Micelles for Targeted Drug Delivery: Micelles are colloidal structures made of amphiphilic block copolymers that self-assemble in aqueous liquids. These copolymers have segments that are both hydrophilic and hydrophobic. The hydrophilic blocks stay on the micelle's outside shell while the hydrophobic blocks gather in the center to form a stable nanostructure when it is submerged in water. Hydrophobic medications, which have problems with solubility and stability, can be effectively encapsulated in micelles because of the hydrophobic core. During or after micelle production, the drug molecules can be loaded into the hydrophobic core. By supplying steric hindrance and electrostatic repulsion, the hydrophilic shell of the micelles improves the stability and prevents aggregation.

Hydrogels as Targeted Drug Delivery Systems: Water or biological fluids can be absorbed and retained in huge quantities by hydrogels, which are three-dimensional cross-linked networks of hydrophilic polymers. Hydrogels have drawn a lot of interest as therapeutic drug delivery systems for targeted and sustained release because of the high-water content and soft, gel-like nature. Compared to traditional drug delivery systems, they have several benefits, including increased bioavailability, improved drug stability, and controlled release kinetics. Hydrogels come in two primary categories: natural and artificial hydrogels. Natural hydrogels come from biological materials including proteins (such as collagen and gelatin) and polysaccharides (such as alginate and hyaluronic acid). These hydrogels are excellent for a variety of biological applications because they frequently include in heren't biocompatibility, biodegradability, and bioactivity. Contrarily, synthetic hydrogels are produced by chemical processes and can be customized to fulfil unique needs[106].

Challenges and Future Perspectives: Navigating the intricate regulatory environment is one of the biggest obstacles to the development of tailored medication delivery systems. With considerable preclinical and clinical evidence needed to prove safety and efficacy, the regulatory approval procedure for innovative drug delivery systems can be drawn out and rigorous. For researchers and developers, complying with these regulatory standards can be difficult because it calls for significant time, money, and skill commitments. The abilityof drug delivery systems to scale are another issue. In the lab or small-scale investigations, it is possible to get encouraging results, but it can be challenging to apply those findings to manufacturing procedures that are carried out on a big scale. For targeted drug delivery systems to be successfully commercialized, consistency, repeatability, and quality control must be ensured throughout the scale-up process. Exciting possibilities exist for targeted medicine delivery thanks to nanotechnology. Researchers can create systems that enable real-time monitoring of medication release, distribution, and therapeutic response by combining imaging and diagnostic tools into nanoscale drug carriers.

Personalized medical techniques aremade possible by this integration, which improves precision and offers insightful feedback on treatment efficacy. By customizing therapies for individual patients, targeted drug delivery systems have the power to completely transform personalized medicine. Drug delivery systems can target diseased cells specifically while reducing off-target effects by using certain biomarkers or molecular signatures. With this strategy, treatment outcomes are enhanced, side effects are minimized, and therapeutic efficacy is increased[107].

4. Conclusion

In conclusion, significant strides have been made in the development and refinement of new drug delivery systems for targeted therapy since 2017. These advancements have revolutionized medication delivery to specific body locations, enhancing therapeutic efficacy while minimizing adverse effects. Researchers have explored diverse strategies, including nanotechnology-based systems, biomaterials, and intelligent drug carriers, to optimize targeted medication delivery. These innovations enable precise drug delivery to specific cells or tissues, amplifying drug concentration at the target site while sparing healthy areas. Overall, the evolution of novel drug delivery methods for targeted therapy holds immense promise for personalized medicine and improved patient outcomes. Future advancements in this domain, coupled with progress in nanotechnology and biomaterial science, are poised to yield even more sophisticated and efficient drug delivery systems. Novel drug delivery systems offer formulation researchers an avenue to overcome challenges associated with conventional systems, particularly in areas such as cancer chemotherapy. Lipoproteins, nanoparticles, microspheres, and other advanced drug delivery systems emerge as compelling fields of research, showing great potential in the realm of novel drug delivery systems.

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