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# TARGETTED DRUG DELIVERY SYSTEM

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**ABSTRACT**:

Nanomedicine is an advanced version of Paul Ehrlich's "magic bullet" concept. Targeted drug delivery is a system of specifying the drug moiety directly into its targeted body area (organ, cellular, and subcellular level of specific tissue) to overcome the specific toxic effect of conventional drug delivery, thereby reducing the amount of drug required for therapeutic efficacy. To achieve this objective, the magic bullet concept was developed and pushed scientists to investigate for more than a century, leading to the envisioning of different nanometre-sized devices — today's nanomedicine. Different carrier systems are being used and investigated, which include colloidal (vesicular and multiarticulate) carriers, polymers, and cellular/subcellular systems. This review addresses the need for and advantages of targeting, with its basic principles, strategies, and carrier systems. Recent advances, challenges, and future perspectives are also highlighted.

**KEYWORDS:** Nanomedicine, Magic bullet concept, Targeted drug delivery Drug carriers' Colloidal carriers, Vesicular systems, Multiarticulate systems, Polymers, Nanoparticles, Nanosome Cellular carriers, Subcellular delivery, Therapeutic efficacy, Toxicity reduction, Advances and challenges in nanomedicine.

## INTRODUCTION:

Drug delivery (DD) refers to the methods, formulations, technologies, and processes involved in transporting a pharmaceutical substance in the body to achieve the desired therapeutic effect.1 It encompasses the approaches of administering medicinal compounds in humans and animals to attain therapeutic effectiveness. Recent developments in drug delivery systems (DDSs) are primarily been focused on smart DD, which focuses on drug administration at the appropriate time, dosage, and location with maximum safety and efficacy.2 The advancement

of novel DDSs (NDDSs) has attracted pronounced attention in recent years. These systems enhance the therapeutic effectiveness of new and existing drugs with targeted, managed, and sustained delivery while meeting real and appropriate drug demand.1 DD is a growing field in pharmaceutical science. There are five generations of DDSs, and targeted delivery belongs to the fourth generation.3 Figure 1 illustrates the generations of DDSs. Over the last few decades, developing sustained or controlled DDSs has been a focus, with the objective of controlling and/or sustaining drug release, reducing dose frequency, or increasing drug efficacy compared to conventional delivery. Bilayer tablets are one example of an NDDS, used with modification of conventional drug-preparation and -delivery approaches.

**Basic Principles and Applications of Targeted Drug-Delivery Systems:**

The basic principle behind drug targeting is delivering a high concentration of drug to the targeted site while minimizing its concentration to the nontargeted region. This principal aids in optimizing the drug's therapeutic effects while decreasing the side effects due to multitarget interactions, higher doses, and nontarget concentrations. The carrier is a specially engineered molecule or system essential for effective transportation of the loaded drug toward preselected sites. Ideally, a drug-targeting complex is expected to be toxic, nonimmunogenic, biochemically inert, biodegradable, biocompatible, and physiochemically stable in vivo and in vitro.

**The advantages of drug targeting:**

1. The protocol of drug administration becomes simpler
2. The toxicity of the drug is decreased by targeting a specific site.
3. The desired drug response can be reached by a small dose.
4. Avoid the first-pass effect. 5. Improvement in the drug absorption from the target site.

**The disadvantages of drug targeting:**

1. Rapid drug elimination from the body results in high dose frequency.
2. The carrier of the targeted drug delivery system may result in the immune response.
3. The drug delivery system is not localized at the tumour tissue for sufficient time.
4. The diffusion and redistribution of released drugs.

**DIFFERENT TYPES OF CARRIERS APPLIED FOR DRUG TARGETING:-**

**Colloidal carrier systems**: -

Colloidal dispersant tablets (NDDSs) are nanoscale particle targeting vesicles or vesicular dosage forms. They consist of numerous emulsions, liposomes, noisome, nanospheres, and

ceramics. These kinds of drug vectors have the capacity to change the distribution profile by sequestering, transporting, and holding onto the active medication as it elutes or is delivered within or close to the target. They are frequently divided into two groups: microparticulate and vesicular systems.

**Niosomes**: -

Arguably these carriers, niosomes are among the best. Researchers working in the cosmetics business initially reported on the self-assembly of non-ionic surfactants into vesicles in the1970s. Niosomes, also known as non-ionic surfactant vesicles, are tiny lamellar structures that are created when cholesterol and non-ionic surfactant belonging to the alkyl or di-alkyl polyglycerol ether class are combined. Because non-ionic surfactants are amphiphilic, they need energy, such as heat or physical agitation, to create a closed bilayer vesicle in aqueous fluids. Consequently, liposomes' drug entrapment effectiveness declines relative to that of niosomes. In addition, liposomes are costly and their constituents, such phospholipids, are chemically unstable due to their propensity for oxidative destruction; therefore, these need particular treatment and storage, and the quality of natural phospholipids varies. This may lower the cost of manufacture. Niosomes and liposomes are not as suitable for transdermal distribution due to their poor skin permeability, aggregation and fusion of vesicles, shattering of vesicles, and drug leakage.

**Liposomes**:-

Liposomes are drug-based, self-assembling phospholipid-based vesicles that surround a core aqueous compartment in the shape of a concentric sequence of several bilayers (multilamellar) or a bilayer (uni-lamellar). Liposomes are between 30 and micrometres in size, having a phospholipid bilayer that is 4-5 nm thick British scientist Alec Bangham and associates at Babraham Cambridge established the science of liposomology in the middle of the 1960s, publishing the structure of liposomes for the first time in 1964. Since then, liposomes have been thoroughly studied for their potential as delivery systems for imaging agents, proteins, nucleic acids, and small molecules. To increase treatment effectiveness and patient compliance, several delivery methods, including parenteral, pulmonary, oral, transdermal, ocular, and nasal routes, have been devised. Moreover, liposomes can use passive or active targeting to deliver their payload to the sick site selectively, reducing systemic adverse effects, increasing the maximum tolerated dose, and enhancing therapeutic

benefits. Sphingomyelin (SM), cholesterol (Chol), and glycerophospholipids (GP) are the main

**Transferosomes:**

Transferosomes are a unique kind of liposome that are made up of an edge activator and phosphatidylcholine. These are flexible, soft vesicles designed to improve the delivery of active drugs. IDEA AG, a German business, registered them and uses them to refer to its own unique medication delivery technique. The Latin term "transfer," which means "to carry across," and the Greek word "soma," which means "body," are the sources of the name, which means "carrying body." An artificial vesicle called a transferosome carrier is made to resemble a cell vesicle or a cell undergoing exocytosis, making it appropriate for targeted and controlled drug administration. Using vesicle formulations as skin delivery systems is one of the most contentious approaches of medication administration via the skin. This high flux rate is caused by "transdermal osmotic gradients," which are naturally existing gradients that are available across the skin but are significantly more pronounced. The skin penetration barrier creates an osmotic gradient that keeps the viable portion of the epidermis (75% water content) and the almost dry stratum corneum (15%) close to the skin's surface from losing water. This gradient also keeps the skin from drying out.

**Spanlastics**: -

Spanlastics are a unique drug delivery device that traps the medication as a bilayer in the core cavity. The phrase "Spanlastics" (Span + Elastic) was initially used in 2011. These carriers resemble transferosomes in that they are elastic and extremely malleable. Compared to drug solution, these deformable vesicular carrier systems exhibit enhanced permeability. They are amphiphilic, meaning that the drug is contained in a vesicle formed by a non-ionic surfactant. Spandex is quite tiny and minuscule in size. These unique nanovesicles eliminate the drawbacks of liposomes, namely their tendency to become unstable chemically. The inclusion of edge activators in their structure is responsible for the vesicles' elastic character

**Nanotubes**:

These are a type of drug delivery system which is a hollow cylindrical tube made of carbon that can be easily filled and sealed with the required drug.18,19 They are usually used for delivering the drug to the cancer cell.20,21Liu et al. applied carbon nanotube for targeting the tumour in mice.22 Also, Mc Devitt et al. achieved tumour targeting with antibody-functionalized, radiolabelled carbon nanotubes.23

**NANOWIRES**:

It is a wire with a very small diameter made of metal or other organic compounds. It possesses a large surface area, so the surface can be treated to allow the nanowire to bind with specific biological molecules when inserted inside the body. It can be used for detecting the causes and treatment of brain diseases, such as seizures, parkinsonism and similar diseases.24,25 This system can treat Parkinson's and similar diseases.26 Also, it can be used for the detection and localization of tumors.27Hong et al. used fluorescent zinc oxide nanowires for molecularly targeted imaging of cancer cells.28

**Nanoshells:**

Nanoshells are new strategies of nanoparticles, consisting of a hollow dielectric core of silica covered by a shell of gold29,30 It may be used for diagnostic or therapeutic purposes. Nanoshells can be attached with antibodies on their surfaces, allowing them to conjugate certain areas such as cancer cells.31 This technique is very effective in targeting the antineoplastic drug.32 Loo et al. studied the ability of Nanoshells in imaging and treatment of cancer.33

**Quantum dots:**

Quantum dots are nanocrystalline semiconductor particles that possess distinctive optical characters which import them the ability to be used in imaging of tumors.34-36 This carrier is effectively used for targeting cancer drugs.37Pardo et al. used quantum dots and nanotubes for cancer targeting and drug delivery.38

**Nanopores:**

They have very tiny holes that allow the passage of DNA molecules in one strand at a time. So, allow highly exact and effective DNA sequencing.39,40 This technique has potential in genetic engineering40,41 and biotechnology.42 Schneider et al. reported DNA translocations through nanopores created in graphene membranes.43

**Gold nanoparticles:**

The gold nanoparticles are used by scientists to develop an ultrasensitive detection system for DNA44 and the protein markers associated with the presence of different types of cancer,45 like breast and prostate cancer.46 Penget al. used gold nanoparticles in the diagnosis of lung cancer.

**Dendrimers**:

Dendrimers are synthetic nanoparticles with a specific diameter.48 They consist of a control core surrounded by layers of polymers.49 There are several sites at the surface of the dendrimers to which the drug may be attached.50 They are used in gene transfection and medical imaging.

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