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Concept of Magic Bullet: An Advanced Drug Delivery

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ABSTRACT

Drug Delivery Systems refer to the science of utilization of technologic advancements and biological polymer materials to deliver drug or gene to the body in clinical time and dose. Targeted drug delivery ensures increased concentration of medication in specific receptors in the body inherently being advantageous with respect to reduction in dose and side effects of drug. This paper discusses about the concept of magic bullet proposed by Paul Ehrlich as well as about the challenges of targeted drug delivery. The basic principle of targeted delivery is coordination of drug behavior, targeting the site and pharmaceutical carrier to bring out the maximum therapeutic success with the least toxic effects. The various nanocarriers being extensively exploited in targeted delivery are discussed in detail including quantum dots, mesoporous silica materials, metallic nanocarriers, and carbon nanotubes. The area of advancements in targeted drug delivery is vast enough to cater to the demands of ever-growing technology.

INTRODUCTION

Targeted drug delivery is the method of treatment that involves the transportation of the therapeutic agent to specific tissue without reaching the remaining parts of the body. It may involve scientific site-targeting within the body, or it might involve facilitating systemic pharmacokinetics, in any case it is typically concerned with both quantity and duration of drug's presence. The goal of targeting sites of drug delivery is to prolong, localize, target, and have a protected drug interaction with the diseased tissue. This helps maintain the required plasma and tissue drug levels in the body, thereby preventing any damage to the healthy tissues via the drug. This improves the efficacy of the drug while reducing side effects. The desired differential distribution of the drug to targeted sites would spare the rest of the body while maintaining its therapeutic benefits, enhancing the therapeutic index of the drug. The inherent advantages of this technique are reduction in dose, avoidance of hepatic metabolism and enhancement of bioavailability with better patient compliance. Various carrier systems with specific benefits are developed for targeting GIT, lymphatics, respiratory tract, brain, and tumor tissues. Products are carefully developed with high expertise by considering the specific properties of target cells, the nature of markers or transport carriers, receptors, route of administration and the disease to be treated. The drug delivery system is highly integrated and requires various disciplines such as chemists, biologists, and engineers to join forces to optimize the system.

GENERATION OF DRUG DELIVERY SYSTEMS (DDS) [1,2]

There are five generations of DDS and targeted delivery belongs to fourth generation.

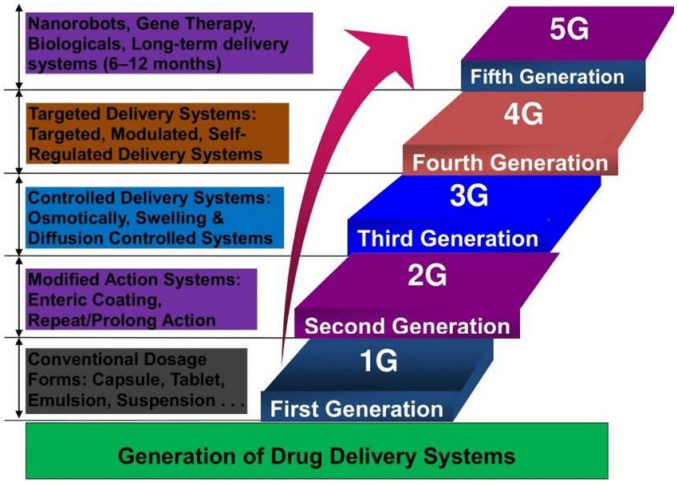


Figure: Generation Of DDS

a. First generation (1G): Conventional dosage form (Tablets, capsules, suspension, ointments, suppositories)

b. Second generation (2G): Modified action system (Prolonged action tablet, Repeat action tablet)

c. Third generation (3G): Controlled drug delivery (Diffusion controlled, osmotically controlled, Swelling controlled system)

d. Fourth generation (4G): Targeted drug delivery (Modulated systems, Self-regulated system)

e. Fifth generation (5G): Nanorobots, Gene therapy, Biologics with advancements.

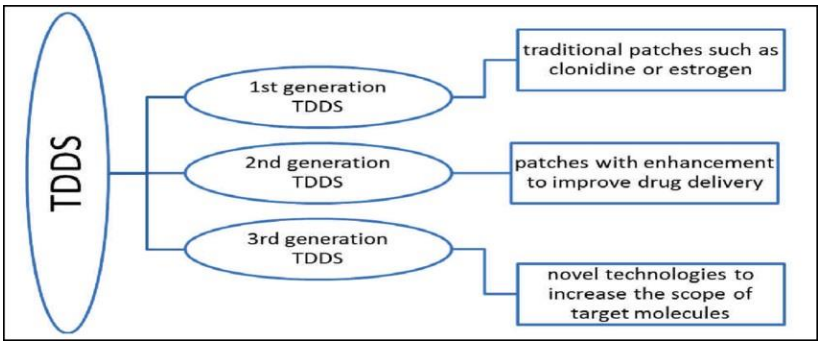


Figure: Generation of Targeted DDS

NEED FOR TARGETED DDS (TDDS) [1,3]

The need for targeted delivery is four-fold: unsatisfied performance of drugs in terms of pharmacodynamic, pharmacokinetic, pharmaceutical, and pharmacotherapeutic features with conventional delivery, as shown in Figure.

Targeting is needed to overcome the disadvantages of other conventional methods of delivery. Parenteral delivery is highly invasive, oral delivery of protein and peptide is not possible, topical delivery of creams and ointments is limited to local effects, and above all, drug-target interactions compromise the effectiveness of the drug.

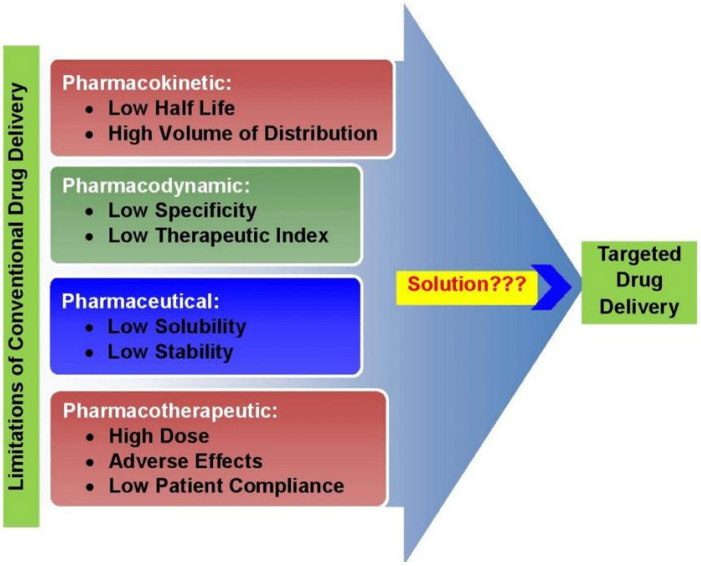


Figure: Need for TDDS

ADVANTAGES OF TARGETED DELIVERY[2,3,4]

- Targets diseased tissue or specific types of cells or parts of the body without affecting healthy tissue.
- Controlled release of drugs for longer period.
- Reduced fluctuation of drug plasma level.
- Reduction in dose and side effects.
- Reduced inter- and intra-patient variability.
- Protocol of drug administration becomes simpler.
- Avoids first pass effect.
- Non-target site-based toxicity is eliminated.
- A smaller dose of drug can elicit desired drug response.
- Improvement in therapeutic efficacy and therapeutic index of drug.

DISADVANTAGES OF TARGETED DELIVERY SYSTEMS [2,3]

- The stability of products is difficult to attain.
- The carrier of the targeted drug delivery system may elicit an immune response.

- Drug deposition at the target site may lead to toxicity.
- Required high expertise in manufacturing, storage, and administration.
- Diffusion and redistribution of released drugs.
- Non-localisation of TDDS at the tumor site for sufficient duration of time.
- Costlier formulation as compared to conventional dosage forms.
- Rapid clearance of drugs is required to avoid side effects at site of action.
- Skilled personnel are required to handle and control drug delivery to the site of action.
- Quite complex and delicate processes of manufacturing and storage needs advanced techniques.

IDEAL FEATURES OF A TDDS [3,5]

An ideal Targeted drug delivery system should possess the following features:

- Biochemically inert, bio-degradable
- Non-immunogenic and chemically stable in-vivo and in-vitro
- Should have restricted drug distribution.
- Should have uniform capillary distribution.
- Controllable and predictable rate of drug release
- Drug release should not affect drug action.
- Minimal drug leakage during transit
- Should have the therapeutic amount of drug release.
- Preparation process should be simple, easy, and cost-effective.

COMPONENTS OF A TDDS [1,2,5]

Any targeted delivery system has two components Target and drug carriers.

(i) **Target** can refer to any specific organ or a cell or tissue which need treatment or repair, in acute or chronic condition.

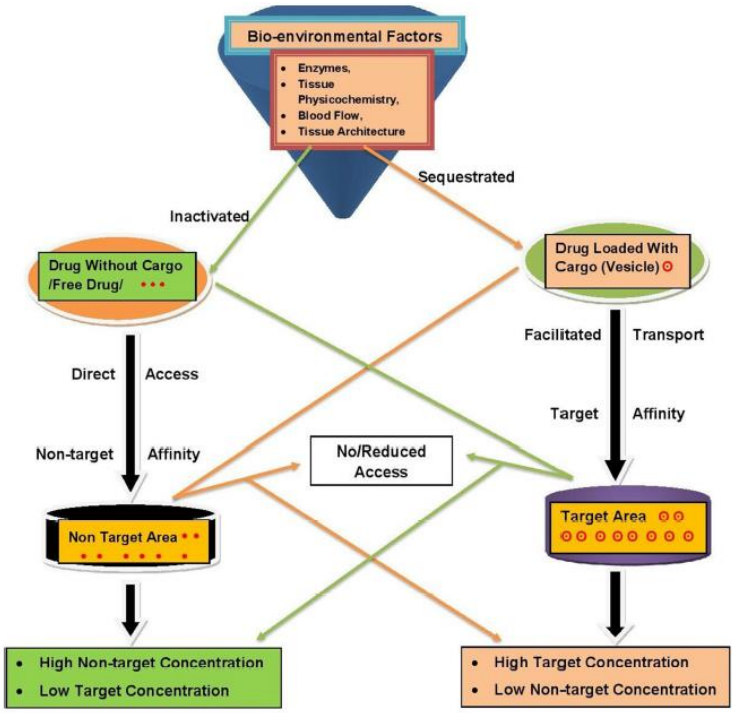
(ii) **Drug-carriers** (Markers) play an important role of the site-specific delivery of drug and

preventing the delivery of drug to non-targeted sites.

Drug carriers are engineered vectors that entrap, retain, transport, and deliver the drug within or at the target site.

BASIC PRINCIPLES OF TARGETING [1,3]

The basic principle is to deliver a high concentration of drug to targeted sites, while minimising the concentration to non-target regions. This optimises the therapeutic effects, and decreases the side effects due to multitarget interactions, higher doses, and non-target concentrations. Coordination of drug behaviour, targeting the site and pharmaceutical carrier to bring out the maximum potential treatment.



The process of drug targeting requires four principles, **first,** the ability to load the drug to the target site, **second,** avoid the degradation by body fluid, **third,** reach the target site, and **fourth,** release the drug at the specific site at the predetermined time.

CONCEPT OF MAGIC BULLET[1]

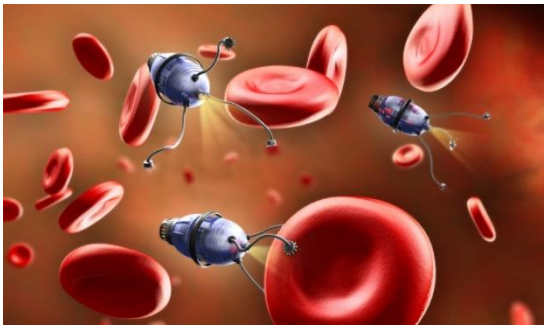
Paul Ehrlich postulated the concept of the magic bullet a century ago. He envisioned the concept of selectively targeting a pathogen without harming the host organism, using "Magic bullets". Ehrlich had a "Two consecutive steps" approach towards magic bullets:

1. Screening for toxic drugs.
2. Modifying toxic drugs to be more specific and less toxic.

He proposed the idea that the process of cure would be more pronounced if the drug moiety had exclusive affinity towards the causative bacteria alone and not to the host. By this, he implied, that the least harmful effect on the human body by exerting an exclusively lethal action on the parasite (pathogen) within the host would be exerted. Hence coined the term "Magic bullets".

Nanomedicine is the advanced and refined version of magic bullets. The various factors posing a challenge to this concept include finding the

- the right target for a specific disease,
- medication that efficiently cure the disease,
- way to deliver the drug in a stable form to specific sites while preventing immunogenic and aseptic interactions.



According to Ehrlich's philosophy of magic bullet, the drug should go unhindered and straight to its anticipated targets and interact only with the target molecule. Unfortunately, the ideal DDS which could directly reach the bodily target without any pathway interaction has not yet been developed. This interference with several targets makes the drug a "magic shotgun" rather than a "magic bullet".

PARAMETERS TO BE CONSIDERED FOR THE DESIGN OF TDDS [2]

a. Bio-environmental factors

- Enzymes
- Co-enzymes

- Structure of ligands, receptors, and tissues
- Blood flow
- Active and passive diffusion

b. Drug and Carrier related factors

- Drug concentration
- Location of target site
- The molecular weight of drug and carrier
- Distribution
- Physiochemical properties of molecules
- Particle size
- Physiological environment pH
- Electrical field
- Surface properties (charge, shape, density)
- Stability of drug

c. Biological parameters

- Rate of drug absorption through GIT
- Volume of distribution of drug
- Metabolism rate
- Elimination rate
- Peak drug-plasma concentration
- Half-life
- Pathological conditions
- Permeability and structure of capillary wall
- Bioavailability

- Toxic dose

d. Parameters concerned with Tumor Targeting [1]

- Clinically enhanced permeability and retention (EPR) effect.
- Extravasation
- Intra-tumoral distribution
- Tumor heterogeneity
- Overexpression characteristics

CANDIDATES SUITABLE FOR TARGETED DELIVERY [3]

Drugs with following characteristics are suitable for targeted delivery:

- Low drug solubility
- Poor drug absorption
- The short half-life of drug
- Large volume of distribution
- Low drug specificity
- Narrow therapeutic index of drug

TYPES OF TARGETING[2,6]

I. Based on Target:

a. First order targeting: Delivers the drug to a desecrated organ or tissue.

b. Second-order targeting: targeting a specific cell type(s) within the tissue or organ.

c. Third-order targeting: delivery to specific intracellular compartments in the target site such as lysosomes.

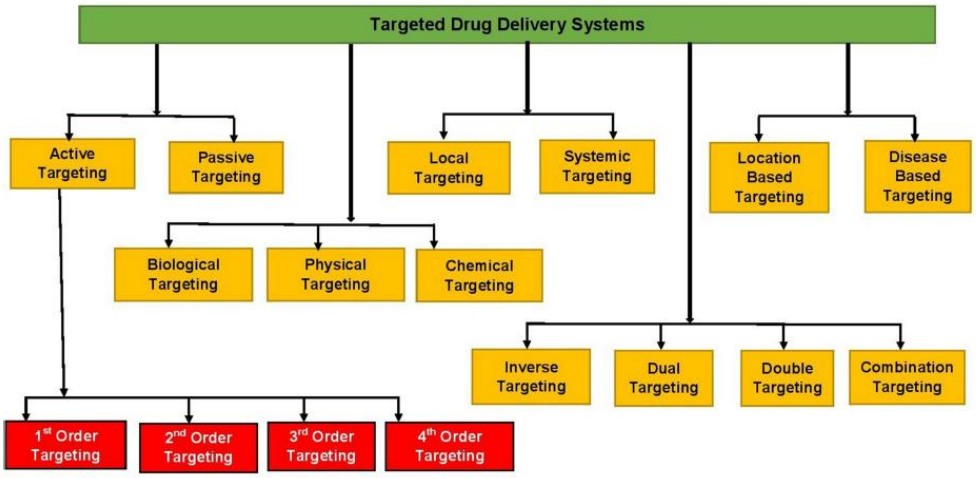
II. Based on Approach:

a. Magic bullet approach: use of biologically active agents that are both potent and selective to a particular site in the body.

b. Prodrugs approach: preparation of a pharmacologically inert form of active drugs that

gets activated upon reaching the target site.

c. Carrier approach: makes use of a biologically inert macromolecular carrier system that transports the drug moiety to the target site.



III. Based on Drug Carrier:

a. Active targeting: receptor-mediated targeting that acts via receptor-ligand interaction. This method involves surface modification of target molecules and is widely used in tumor targeting in cancer therapy.

b. Passive targeting: It targets the body's natural immune system and is possible through the EPR mechanism. It does not require surface alteration of drug-carriers. Common techniques include nano-sizing and PEGylation.

c. Local targeting: A non-invasive technique that manages local delivery to cell or tissue sites for treating local pathologies.

d. Systemic targeting: An invasive targeting strategy that delivers the drug to systemic circulation via intravenous injection.

e. Biological targeting: Use of antibodies, peptides, proteins, etc. that bind to the receptor's sites in a specific and controlled manner.

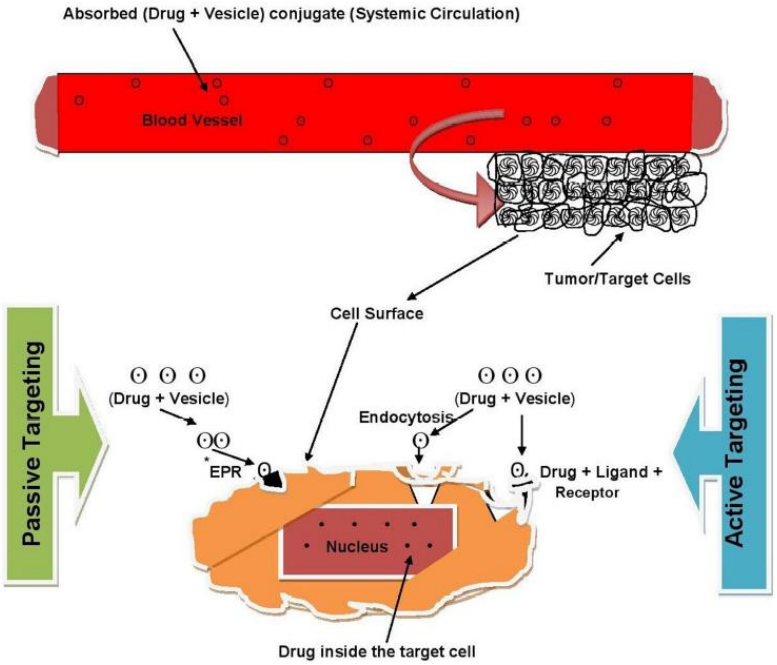


Figure: EPR (Enhanced Permeability & Retention) Effect

f. Chemical targeting: used in repeat-action and delayed-action formulations. This involves the use of site-specific prodrugs, enzymes, or chemical reactions.

g. Physical targeting: Targeting is achieved by environmental changes such as pH, size, temperature, ionic strength, external stimuli, composition, light intensity, etc.

h. Inverse targeting: Most suited method for targeting non-ERS organs in the body. This approach targets the specific site by avoiding the uptake by the Reticulo-Endothelial System (RES) which reduces the defense mechanism.

i. Dual targeting: Drug carriers possess their own therapeutic activity as employed in this approach. The synergistic effect increases the therapeutic effectiveness of the drug.

j. Double targeting: Combination of temporal and spatial methods for effective targeting to specific organs, tissues, cells, and sub-cellular compartments.

k. Combination approach: A direct targeting method that combines the use of polymers, homing devices and carriers having molecular specificity.

CARRIER SYSTEMS USED IN TARGETING

I. Colloidal carrier systems [1,3,5,7]

These are nano-scaled targeting vesicles of the particulate or vesicular dosage form. These systems sequester, transport, and retain the active drug *en* route, while they elute or deliver it within or in the vicinity of the target. They are classified into vesicular and microparticulate systems.

(a) Vesicular carriers:

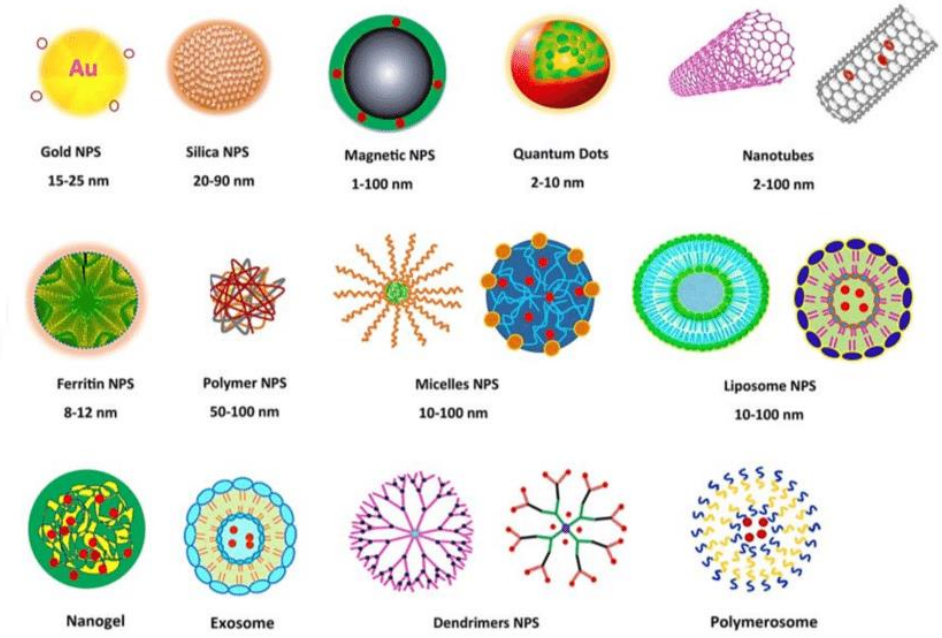
- **Liposomes:** nano-scaled lipoidal vesicles with a lipid-bilayer structure consisting of an aqueous core entirely enclosed by a lipid membrane. Phospholipid elimination in the blood is relatively slow which prolongs the action time of drugs.[8] Liposomes were developed to treat bacterial infections in cystic fibrosis regarding enhanced bactericidal activity of entrapped antibiotics which overcame the problem of antibiotic resistance.

- **Niosomes:** nanometric systems in which the medication is encapsulated in vesicles composed of a bilayer of nonionic surfactants. They are quite stable compared to liposomes, and hence require no special conditions for preparation. Being nonionic in nature, they are less toxic and have an improved therapeutic index.

- **Transferosomes:** They are structures that are self-optimizing, self-regulating, ultra deformable, and ultra flexible. These vesicular structures comprise an inner aqueous core surrounded by complex lipid bilayer comprised of “edge activators”. These edge activators are surfactants that allow transferosomes to squeeze through pores from 5 to 10 times less than their diameter. This enables avoidance of complete rupture of the vesicle and the drug remains intact after penetrating the skin. [9 - 11]

- **Ethosomes:** Ethosomes are used as replacements of liposomes, mainly for transdermal route of administration and can be used for delivery of hydrophilic and impermeable drugs.[12] They have comparatively low penetration through biological membranes but relatively higher penetration through skin.

- **Ufasomes:** Ufasomes are dispersions of unsaturated fatty acid vesicles prepared from fatty acid and ionic surfactant (soap) and cholesterol. They consist of lipid membranes which get attached to the stratum corneum – the major barrier in transdermal delivery. This property makes Ufasomes a good carrier for the topical application of drugs. [13]



- **Pharmacosomes:** The term Pharmacosome comes from Pharmakon and soma, meaning drug carriers. They are neutral molecules that possess both hydrophilic and lipophilic carriers with optimum ratio of polyphenol with phospholipids in the form of a complex. The drug is conjugated to the complex by electrostatic force or by hydrogen bond. The conjugate may be in the form of micelles or hexagonal aggregates. [14]

- **Virosomes:** They are unilamellar vesicles prepared from phospholipids, the surface of which contains sites to which virus-derived glycoproteins are attached to facilitate recognition and targeting of the virosomes. [15-17]

- **Cubosomes:** They are liquid crystalline nanoparticles having cubic structure suitable for injection. They are mainly used in brain targeting. [18]

(b) Microparticulate systems [1]

Microparticles are DDSs on the micrometer-millimeter scale. Microencapsulation technology allows the protection of drug from the diverse environmental conditions, adds stability of drug, eliminates incompatibility problems, masking unpleasant taste. Microparticulate systems include the following categories of systems:

- Microparticles
- Nanoparticles

- Microsponges
- Magnetic microspheres
- Solid-Lipid-Nanoparticles (SLNPs)

II. Polymeric carriers [1,3,5,7]

- **Amphiphilic polymers:** Polymers that contain both hydrophilic and hydrophobic blocks. By controlling the hydrophilic-hydrophobic balance, various nanostructures can be formed with better stability.

- **Polymeric micelles:** they are new-generation nanomedicine with structures that are composed of a hydrophobic internal core and hydrophilic external surface wherein physical entrapment of drug molecules occurs in the internal core. Chemical conjugation of drugs with micelles prevents early drug release. They are known for decreased chances of rapid drug clearance and prolonged circulation in-vivo, the property exploited for targeting tumor cells.

- **Polymeric nanovesicles:** structures that possess a bilayer with internal aqueous core, isolating the core from external medium, where hydrophilic drugs can be encapsulated within the aqueous interior, integrating the hydrophobic molecules within the membrane.

- **Dendrimers:** Popularly used in gene transfection and medical imaging, these synthetic nanoparticles with a control core surrounded by layers of polymers and specific diameters. They possess several sites on their surface to which the drug or ligand can be attached for targeted delivery. [19-21] They are well-articulated and structurally multibranched globular units. The covalent linkage offers greater stability to dendrimers. [22]

III. Monoclonal Antibodies and Fragments [1,5]: More specifically utilized in cancer therapy, these are very efficient in targeting the drug to tumor tissues and infectious diseases. Monoclonal antibodies are based on the principle of antigen-antibody recognition. The strategy is aimed at tumor-associated antigens expressed by tumor cells. Antibody-drug conjugates (ADC) is complex of a drug with monoclonal antibody that provides selective targeting for lymphomas.[23] Monoclonal antibodies can be conjugated with chemotherapeutic agents, radioisotopes, bacterial toxins, cytokines, and enzymes which potentiate their cytotoxic effects. [24] The drug is released by enzymatic cleavage of the linker under physiological conditions.

IV. Modified (Plasma) Proteins [5]: These are categorized as intelligent vehicles, due to their

solubility and relatively smaller molecular weight. They are vehemently used as carriers for drug transportation and are modified by mere attachment of molecules such as peptides, sugars, and other ligands to suit as a mode of targeted drug delivery. They are exploited as effective carriers for liver cell targeting, by extensive modifications of albumin backbone.[25]

V. Quantum Dots [3-5]: Quantum dots are nanocrystalline semiconductor particles that possess distinctive optical characteristics which is exploited in imaging of tumors.[26-28] A quantum dot is a semiconductor nanostructure that confines the motion of conduction band electrons, valence bond holes or excitons (bond pairs of conduction band electrons and valence band holes) in all three spatial directions. The confinement can be due to electrostatic potentials generated by external electrodes, doping impurities), the presence of an interface between different semiconductor materials, the presence of semiconductor surface or a combination of these. [4] They are characterised to possess theoretically high quantum yield. This offers the highly advantageous potential of the ability to tune the size of quantum dots.

VI. Mesoporous Silica Materials[7]: These are uniformly sized, porous, and dispersible nanoparticles using colloidal chemistry and evaporation-induced self-assembly. They are known for their loading capacities. They can be loaded with diverse drugs and drug combinations at levels exceeding those of common drug carriers such as liposomes and polymer conjugates. This property is attributed to non-covalent electrostatic, hydrogen-bonding and van der Waals interactions of the drug to the mesoporous silica materials that allow preferential drug adsorption.[29] Silica nanoparticles within reconfigurable supported lipid bilayers are used to develop new classes of responsive nanocarriers. [30-32]

VII. Metallic Nanomaterials[7]: Gold and silver nanocrystals, iron oxide nanocrystals and nano rods fall under this category. They are shown to generate localized hyper thermal heating through the absorption of incident optical radiation and surface Plasmon relaxation to treat the disease. They all differ from magnetic particles in the aspect of production of heat generated. Metallic nanomaterials offer the advantages of low cost, ease of synthesis, high thermal stability, and pharmacokinetic improvement in the blood circulation time. Enhanced permeation across the vascular endothelium and improved accumulation in the tumor are the therapeutic advantages of these systems. [33,34]

VIII. Nanocarriers[3,7]:

- **Nanotubes:** Carbon Nano Tubes (CNTs) have recently been studied as novel and versatile drug and gene delivery vehicles. They are hollow cylindrical tubes made of carbon

that can be easily filled and sealed with the required drug. [35,36] Shorter multi-walled CNTs penetrate the cell membrane more efficiently while longer CNTs inhibit their uptake by self-arranging into a coiled or bundled shape.[37] Antibody-functionalized and radiolabeled CNTs are utilized in cancer therapies.

- **Nanowires:** Nanowires are wires with a very small diameter made of metal or other organic compounds with large surface area, which is modified suitably that facilitates the binding of nanowires with specific biological molecules when inserted inside the body. This system is potentially exploited in treatment and diagnosis of brain diseases such as parkinsonism and seizures. These are also used for localization of tumors and targeted imaging of cancer cells[38,39].

- **Nanopores:** Nanopores have very tiny holes that allow the passage of DNA molecules in one strand at a time. Thus, allowing a highly exact and effective DNA sequencing.[40,41] Reports of application of nanopores in DNA translocations in graphene membranes. [42]

- **Nanocrystals:** They are materials of dimension less than 100nm and are crystalline in nature.[43] These are different from nanoparticles in the aspect that nanoparticles are less than 1000nm in dimension.[44] Nanocrystals are efficient in solubility improvisation and tumor targeting studies.

- **Nanobots:** Nanobots are nanoscale machines with a diameter of 10^{-9} m. Nanorobotics is a new technology concerned with the design and application aspects of nanobots in drug delivery. Self-propelling targeted magneto-nanorobots are among the advanced nanobots designed for deep tumor penetration. [45]

- **Nanoshells:** Nanoshells are a new strategy of nanoparticles comprising a hollow dielectric core of silica covered by a shell of gold. The surface of Nanoshells is conjugated with antibodies complexed with antineoplastic agents and are targeted to tumor sites for chemotherapy. [46,47]

CHARACTERISTICS OF VEHICLE[1,5]

A drug carrier (also known as a vehicle) is expected to possess the following characteristics for successful targeted delivery of drug moiety:

- Non-toxic, non-immunogenic and stable
- Bio-compatible and bio-degradable

- Eliminated readily from body.
- Successfully transport the drug to target site.
- Cross barriers and tumor vasculatures
- Be of acceptable size and shape
- No or minimum drug leakage during transit.
- Reasonably simple, reproducible, and cost-effective preparation process.
- Optimal target selectivity and specificity
- Stable in plasma, intestinal and other biofluids.

TRANSDERMAL APPROACH[4,5]

Topically administered medicaments in the form of patches deliver the drugs for systemic effects at a predetermined and controlled rate. The patch provides an alternative route for drug administration, allowing drug delivery across the skin barrier, either actively or passively. A drug loaded in a relatively high dosage within the inner side of the patch, worn on the skin for an extended duration of time, will allow the drug to diffuse through the skin layers, enter the bloodstream directly, avoiding the first pass effect encountered in conventional delivery systems. Sustained delivery is ensured due to the sink conditions between the outermost skin layer and the bloodstream where the concentration of drug is always maintained lower than that at the surface of the skin.

Folate Targeting

Folate targeting is an advanced technology utilized in biotechnology for several purposes. This method involved attachment of Folic Acid (Vitamin B9) to drug molecule which is termed the “folate conjugate”. This method utilizes the naturally high affinity of folate to the folate receptor protein (FR) expressed on the surface of the cancerous cells, facilitating the tight binding of the drug-folate conjugate to the FR. This binding triggers cellular uptake via endocytosis. Folic acid also displays high affinity to glycosylphosphatidylinositol-linked protein that captures its ligands from the extracellular milieu and transports them into the cell via a non-destructive recycling endosomal pathway. The folate receptor protein is also a recognized tumor antigen biomarker. This has led to a revolutionary exploitation of the FR’s function to develop diagnostic and therapeutic methods in cancer therapy.

CHALLENGES IN TARGETED DELIVERY [1]

Despite being an advanced and focused method for drug delivery, targeted delivery suffers from several challenges in various regards. Some of them are discussed below:

- Challenges Specific to Receptors, Ligands, and Carriers
- Misconceptions
- Complex Manufacturing Process
- Tumor Heterogeneity
- Barely Predictable Practical Outcomes
- Clinical Translation related barriers
- **Challenges specific to receptors, ligands, and carriers**

Receptors: Difficulties in the identification of receptors,

Variable expression characteristics,

Accessibility and availability of receptors, and,

Shedding of receptors.

Ligands: Appropriate selection of a ligands,

Conjugation strategies developed,

Release characterization of drug from ligands, and,

Selection of linker.

Carrier: Carrier selection,

Physiochemical & pharmacokinetic characterization of carrier.

- **Misconceptions:**

There are a few misconceptions that imply a negative effect on the success of targeted drug delivery systems. They are, in general, categorized into four types:

a) Targeting is not precise but is a random distribution.

b) Theory of receptor over-expression has not yet fully correlated targeted delivery.

c) There is improved delivery from the EPR effect, but not as exact as with targeted delivery.

d) There may be drug release before reaching the target site, and reaching the tumor tissue does not guarantee improved delivery.

➢ **Complex Manufacturing Process**

There are a certain number of additional steps incorporated in the manufacturing process of targeted delivery systems as compared to the conventional delivery systems, that need to be handled and processed by expert and highly skillful manpower to ensure complete success of the process. This in turn mandates more quality control and regulatory steps, increased cost, and longer timelines.

Design challenges associated with the design and development of nanocarriers include scalability, sensitivity, biocompatibility, and toxicity.

➢ **Tumor Heterogeneity**

The immense heterogeneity within and between tumors poses an additional challenge to targeted delivery. There is also the existence of tumor- and metastasis- associated stroma, eg, tumor-associated macrophages and fibroblasts.

➢ **Barely Predictable Practical Outcomes**

- Lack of clinically translatable models and completely specific targets,
- Selection of targets with specific spatial and temporal expression,
- Appropriate alignment of targets to interventional requirements,

are the major factors that bear the challenge flag to the success of predictability in outcomes and success of targeted delivery.

➢ **Barriers in Clinical Translation**

The clinical translation of nanomedicine into human medicine faces the following challenges that poses a problem in the success of targeted delivery of tumor-targeted drugs:

- Unproven EPR effect in human oncology cases,
- Lower nanocarriers accumulation (than expected levels) within tumors with active targeting mechanisms,

- Factors that should be considered, modified, and controlled during the preparation and delivery.

CONCLUSION

Targeted drug delivery is emerging as the brightest advancement in medical sciences in the diagnosis and treatment of lethal and severe contagious diseases. Magic bullets are the growing roots that form the basis for site-specific and tissue-specific delivery. The two major advantages of targeting the drug delivery include a promising curative effect with reduced dose and frequency, and smaller side effects as compared to conventional dosage forms are encouraging factors for the instillation of the thrive to design, develop, and discover the unleashed potential magic bullets. Nanomedicine is the advanced version of magic bullet concept of Paul Ehrlich. Combining the expertise with technological advancements and interdisciplinary research will greatly help to promote safer use of nanomedicine. Apart from polymers of natural and synthetic origin, metallic nanoparticles in various forms such as shells, tubes, wires, spheres and pores are also the targets for carrier or linker molecules that could bring success to the concept of magic bullet.

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