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A DETAILED REVIEW ON TARGETED DRUGS DILIVERY SYSTEM

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ABSTRACT

Targeted drug delivery is a method of delivering medication to a patient in a manner that increases the concentration of the medication in some parts of the body relative to others. Targeted drug delivery seeks to concentrate the medication in the tissues of interest while reducing the relative concentration of the medication in the remaining tissues. This improves efficacy of the while reducing side effects. It is very difficult for a drug molecule to reach its destination in the complex cellular network of an organism. Targeted delivery of drugs, as the name suggests, is to assist the drug molecule to reach preferably to the desired site. The inherent advantage of this technique has been the reduction in dose & side effect of the drug. Research related to the development of targeted drug delivery system is now a day is highly preferred and facilitating field of pharmaceutical world. A quantum dot is a semiconductor nanostructure which is particularly significant for optical applications due to their theoretically high quantum yield. Transdermal devices allow for pharmaceuticals to be delivered across the skin barrier. Molecules as diverse as small radiodiagnostic imaging agents to large DNA plasmid formulations have successfully been delivered inside FR-positive cells and tissue.

I. 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. 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.

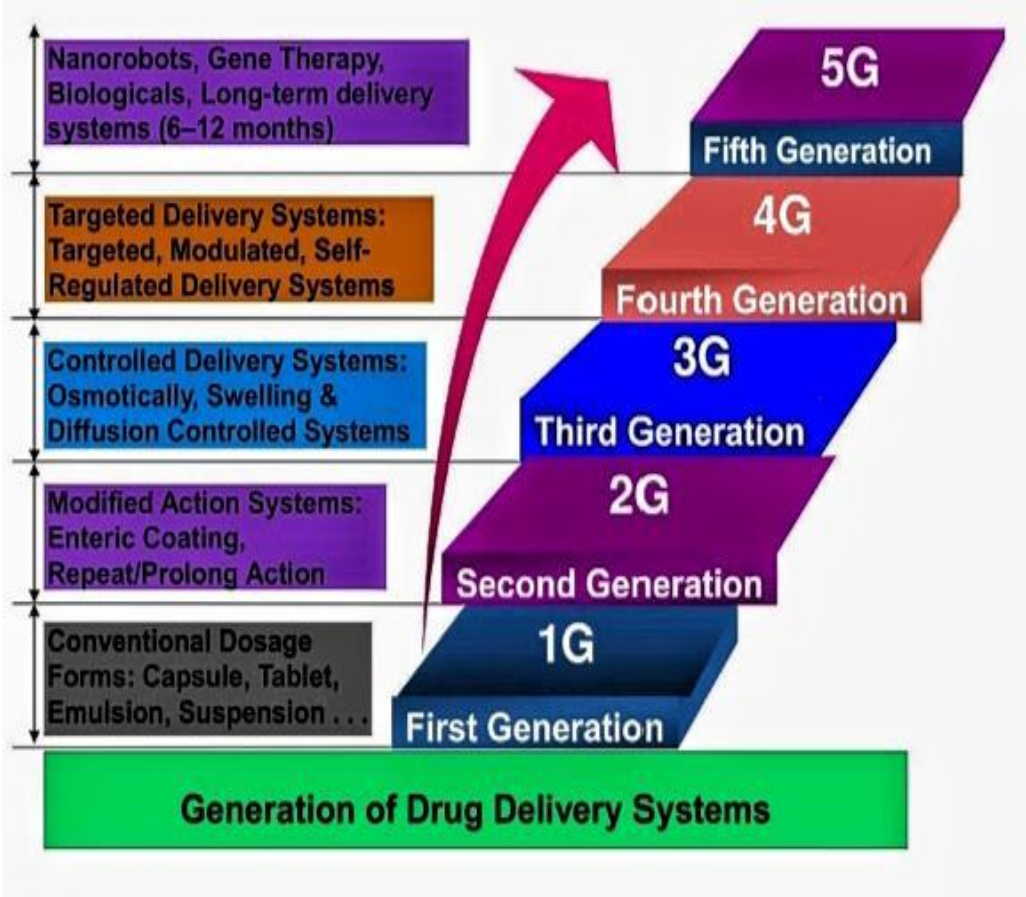

Figure 1: Generation of drug-delivery systems.

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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. DD is a growing field in pharmaceutical science. There are five generations of DDSs, and targeted delivery belongs to the fourth generation. 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. They are composed of two of the same drug or different drugs fixed in a single dose for sequential release of the combined drugs or sustained and mediate release of the same drug, one as a loading dose and other as a maintenance dose. Such modifications in all forms of traditional DD can represent promising advancements, but there are still types of DDSs that need to be refined, such as delivery of poorly soluble drug formulations, protein delivery, self-regulated insulin delivery, and targeted DDSs (TDDSs). Targeted delivery to tumors is another potential advance that can be achieved with nanotechnology-based DSs. Nanoparticle(NP)-based DD brings an opportunity for controlled release of drugs, allowing sufficient time for drugs to act with enhanced therapeutic action and respond to specific stimuli, such as pH, light, heat, or enzymes.

The Need for Targeted Drug Delivery

1. The need for TDD over conventional DSs is fourfold: unsatisfied peformance of drugs in terms of pharmacodynamic, pharmacokinetic, pharmaceutical, and pharmacotherapeutic features with conventional delivery.

2. To enhance therapeutic effectiveness.

3. To reduce the toxicity associated with a small therapeutic index and high doses.

4. Targeting is needed to achieve solutions to these constraints and innate disadvantages of conventional DDSs.

5. The effectiveness of drug–target interactions is compromised unless the drug is delivered to its site of action at a dosage and rate that produces minimal side effects while maximizing therapeutic effects.

6. In addition, simpler drug-administration procedures, decreased drug quantity, which reduces therapeutic costs, and the potential to sharply increase drug concentration in target compartments without adverse effects on nontarget compartments are promising benefits of TDD.

7. Generally, drug targeting results in increased efficacy, modulated pharmacokinetics, controlled biodistribution, increased specificity of localization, decreased toxicity, reduced dose, and improved patient compliance.

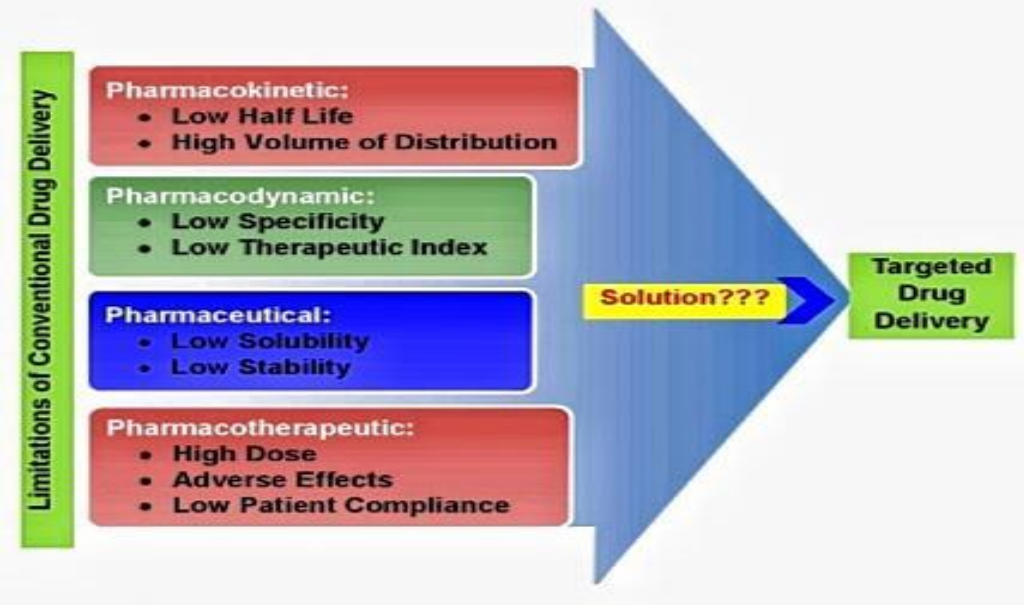

Figure 2: The need of targeted drug delivery.

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Basic Principles of Targeted Drug-Delivery Systems

- Delivering a high concentration of drug to the targeted site.
- Minimizing its concentration to the nontargeted region.
- Optimizing the drug's therapeutic effects.
- Decreasing the side effects due to multitarget interactions, higher doses, and nontarget concentrations.
- Ameliorates unwanted interactions of the drug with bioenvironmental factors that affect drug access to targeted sites in the body.
- Ideally, a drug-targeting complex is expected to be atoxic, nonimmu-nogenic, biochemically inert, biodegradable, biocompatible, and physicochemically stable in vivo and in vitro.
- It should also have a predictable and controllable pattern of drug release, reasonably simple, reproducible, and cost-effective preparation, be easily and readily eliminated from the body, and minimal drug leakage during transit.

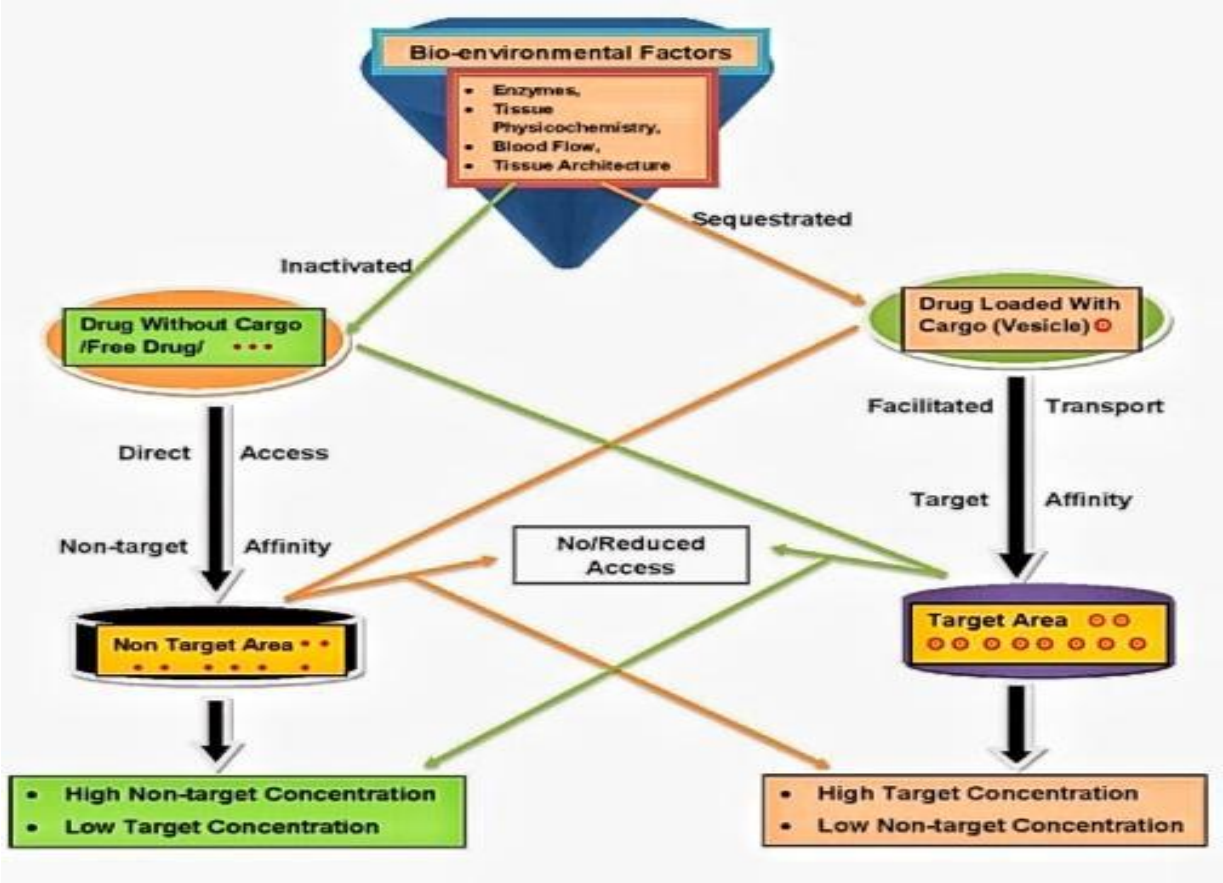

Figure 3: Principles drug delivery.

Types of Targeted Drug-Delivery System

Various approaches are used to help target specific body sites.

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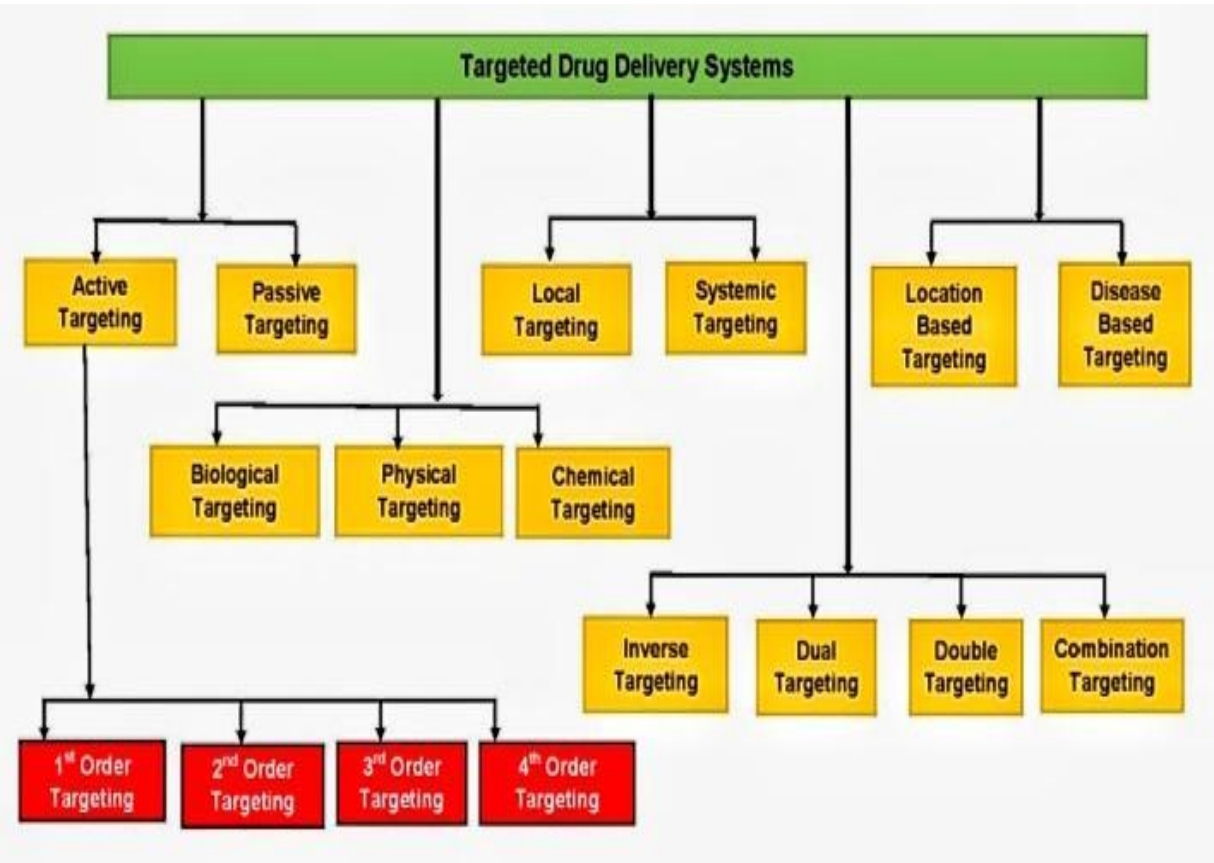

Figure 4: various categories of drug targeting.

Passive Targeting :-

1. Passive targeting is DD that targets systemic circulation.

2. In this technique, drug targeting occurs because of the body's natural response to physico chemical characteristics of the drug or drug-carrier system.

3. This is based on the accumulation of drug(s) at areas targeting the site of interest, such as in the case of tumor tissue.

4. NPs are used as carriers in passive targeting, and they are directed to enter blood vessels more at the disease site, which provides the opportunity for significant drug accumulation at the target.

5. This process is aided by slow lymphatic drainage — the EPR effect.

6. Small nanocarriers with those tumor properties are believed to be suited for passive targeting of anticancer drugs.

7. recent studies have demonstrated that interendothelial gaps on tumors are not responsible for NP transport and accumulation into solid tumors.

Active Targeting :-

1. Active targeting is a particular ligand receptor type interaction that occurs after blood circulation and extravasation.

2. It mainly relies on the biological interface between target cells and the ligands attached to NPs.

3. Various types of ligands have been employed for this purpose, including proteins, polysaccharides, nucleic acids, peptides, and small molecules.

4. Active transport mechanisms are predicted to be better for uptake of targeted NPs from the bloodstream into the tumor micro-environment than more passive transport mechanisms like the EPR effect.

5. First-, Second-, Third-, and Fourth-Order Targeting Drug targeting can further be classified into different orders of targeting.

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- In first-order targeting, there is limited distribution of the drug-carrier system to the capillary bed of the target site.
- Second-order targeting refers to the selective provision of drugs to specific cell types, such as tumor cells.
- Third-order targeting indicates targeting intracellular sites specifically.
- fourth-order targeting is sometimes nominated for drugs targeting macromolecules, such as DNA and proteins.

Inverse, Dual, Double, and Combination Targeting:-

- If the normal activity of reticuloendothelial system is inhibited by a blank colloidal carrier to minimize its passive drug uptake, the system will be saturated with suppression of its defense mechanisms, an approach known as inverse targeting.
- Dual targeting is the delivery of carrier molecule with its own therapeutic activity and thus increasing the (synergistic) therapeutic effect of the drug.
- In double targeting, temporal and spatial methodologies are combined, ie, spatial placement to specific sites and temporal delivery at a controlled rate.
- Combination targeting is a way of targeted delivery equipped with carriers, polymers, and homing devices of molecular specificity that provide a direct approach to a target.

Physical, Chemical, and Biological Targeting:-

- Physical targeting describes systems that localize agents to target areas because of their size, composition.
- Chemical targeting involves the localization of agents to targeted areas through the use of site specific prodrugs.
- Biological targeting allows localizedagents to target areas through the use of antibodies (Abs), peptides, proteins, or other biomolecules that have affinity with receptors, sites, or other biological targets in a specific manner.

Local and Systemic Targeting:-

- Locally targeted systems are noninvasive targeting strategies with the pricipal goal of delivering the drug to the local site for the management of local pathologies.
- systemic targeting, delivery of such therapeutic systems occurs through an invasive route, such as intravenous administration of nanotechnological systems.

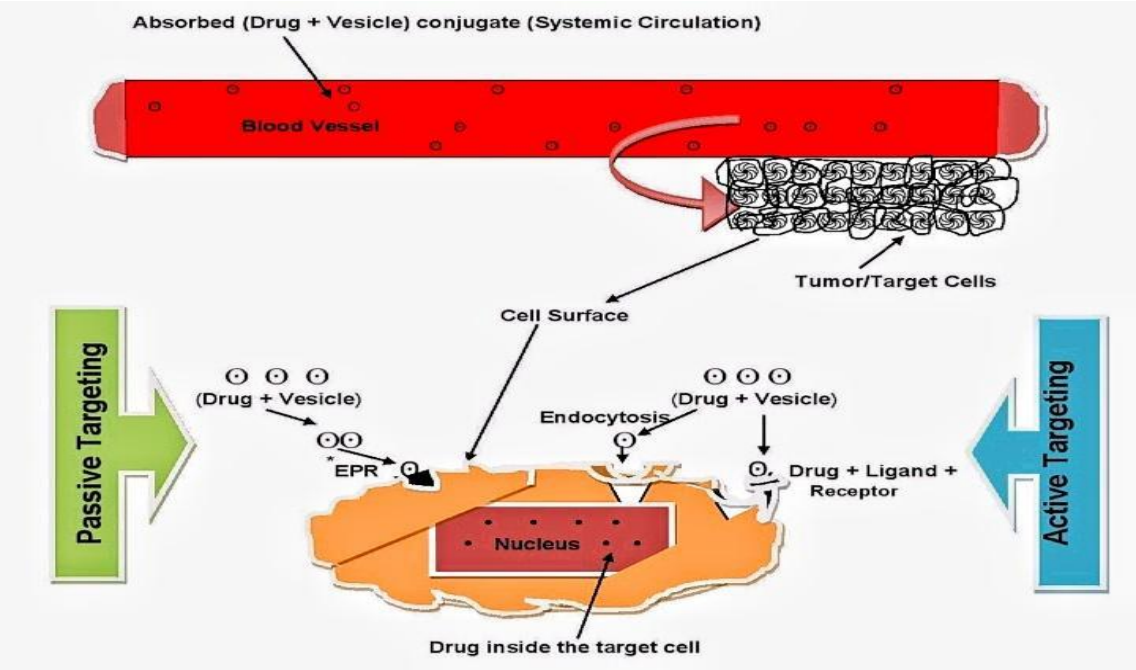

Figure 5: Active vs Passive targeting.

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EPR* Enhance Permeability and Retention

Vehicle/Carrier Systems for Targeted DD

Drug carriers, sometimes called drug vectors. They transport, retain, and deliver the drug within or at the localion of the target. Depending on the type of targeting mechanism, TDDSs require specific carrier systems. Ideally, carriers for TDD must be atoxic, stable, non-immunogenic, biocompatible, and biodegradable, readily eliminated from the body, and unrecognizable by the host's defense mechanisms. They should successfully transport the drug to the target site, cross barriers and tumor vasculatures as needed, be of acceptable size and shape (for nanocarriers), and have optimum release properties at the target site, but no or minimum drug leakage before that target site.

Commonly Used Carriers for Targeted Drug Delivery

1. Colloidal Carrier Systems:-

Colloidal DDSs are nanoscaled targeting vesicles of particulate or vesicular dosage form. They include liposomes, niosomes, nanospheres, multiple emulsions, and ceramics.

a. Vesicular Carrier Systems

Vesicular DDSs are used to improve the therapeutic index, solubility, stability, and rapid degradation of drug molecules.

Nanosomes are the best-known advance in vesicular carrier systems. They are available in different forms, eg:- liposomes, niosomes, transferosomes, and ethosomes.

- Liposomes are simple, microscopic, nanoscaled lipoidal vesicles that have a lipid-bilayer structure.
- Niosomes are nanometric NDDSs in which the medication is encapsulated in vesicles composed of a bilayer of nonionic active surface agents.

b. Microparticulate Systems

Microparticles are DDSs on the micrometer–millimeter scale. This microencapsulation technology allows protection of the drug from the environment, stabilization of sensitive drug substances, elimination of incompatibilities, and masking unpleasant taste.

They play an important role as DDSs, aiming at improved bioavailability of conventional drugs and minimizing side effects.

Microparticulate systems includes microparticles, NPs, and magnetic microsphere.

2. Polymeric Carriers for TDDSs:-

Polymers are the backbone of pharmaceutical DDSs.

Polymer-based drug nanocarriers can significantly increase the solubility of hydrophobic drugs, reduce their cytotoxicity toward normal tissue, prolong the circulation time of drugs in blood, facilitate the entry of NPs, and improve utilization efficiency.

Though natural polymers, such as chitosan and dextran, have been well investigated in the last few decades, research on using synthetic polymers, such as polyesters, polyamides, and polypeptides, has been more prevalent in the field of DD.

Amphiphilic polymers that contain both hydrophilic and hydrophobic blocks have been extensively studied for use in DD as polymeric carriers, such as micelles, nanomicelles, and dendrimers.

Polymeric micelles are composed of a hydrophobic internal core and hydrophilic external surface in which physical entrapment of drug molecules occurs in the hydrophobic core, escaping the need for encapsulation functional groups.

Dendrimers are the other types of polymeric carriers for drug targeting. They are monodispersed macromolecules with well-articulated and structurally multibranched globular units. Dendrimers consist of three main parts with particular functions: focal point, interior branching units, and exterior surfaces with functional groups.

Table 2 Structural components of dendrimers****

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3. Monoclonal Antibodies and Fragments:-

Monoclonal Abs (mAbs) are getting attention as therapeutic agents in targeting for the treatment of various chronic conditions, such as cancer and infectious diseases.

They can be conjugated with chemotherapeutic drugs, radioisotopes, bacterial toxins, cytokines, and enzymes for targeting of tumors in order to potentiate their cytotoxic effects.

Nowadays, human mAbs are being formulated as antitumor agents. For example, adalimumab is the first human mAb officially approved for clinical use.

II. CONCLUSION

Nanomedicine is the advanced version of Paul Ehrlich's magic bullet concept. A large variety of NPs can be used to prepare targeted-delivery nanomedicines. TDD is advancing as one ofhe brightest prospects within the medical sciences for the diagnosis and treatment of lethal diseases. Drugs for targeting can easily be attached to conjugated polymers, polymeric micelles, liposomes, dendrimers, and polymeric NPs, due to their characteristic structural features. Many problems related to drug-targeting strategies for clinical application have been identified, analyzed, and solved, especially in the treatment of cancer. Combining expertise with technological developments and interdisciplinary research might help to introduce safer way nanomedicine.

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