INJ INTERNATIONAL NEUROUROLOGY JOURNAL

The Advanced Approach in The Development of Targeted Drug Delivery (TDD) With Their Bio-Medical Applications: A Descriptive Review

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Abstract

Currently, a significant proportion of dosage forms exhibit suboptimal pharmacokinetic and biopharmaceutical properties. Consequently, there is a pressing requirement to devise an appropriate drug system that selectively delivers the active drug molecule solely to the intended site of action. Drug delivery refers to the technique employed to transport drugs to patients at the specific targeted site or site of action. This approach enhances the effectiveness of treatment by mitigating the adverse effects associated with drug administration. The main highlights of this review article to focus of the basics of targeted drug delivery (TDD) with their several merits and demerits. Secondly, the recent approaches in TDD including liposome, niosome (non-ionic surfactant vesicles), nanoparticles (NPs) and monoclonal antibody and their production. Lastly, the several bio-medical applications of the each and every approaches of the TDD.

Key-words: Targeted drug delivery (TDD), niosome (Non-ionic surfactant vesicles), Antibody, Nanoparticles (NPs).

Introduction

Targeted Drug Delivery (TDD)

Targeted drug delivery (TDD) is a method of delivering medication to specific cells or tissues in the body. This is in contrast to traditional methods of drug delivery, such as oral or intravenous administration, which can expose the entire body to the drug, including healthy cells. Targeted drug delivery (TDD), also known as targeted therapy or precision medicine, is a medical approach that involves delivering medication or therapeutic agents specifically to the site of a disease or a particular target within the body [1].

TDD has been particularly significant in the treatment of cancer, where it has enabled the development of drugs that specifically target cancer cells while sparing healthy ones. This approach has the potential to increase the efficacy of treatments, reduce side effects, and improve the overall quality of patient care [1-2]. It is also being explored in various other medical fields, including the treatment of autoimmune diseases and infectious diseases.

TDD continues to be an active area of research, with ongoing efforts to develop new and innovative targeting approaches for improved therapeutic outcomes. The vehicles or advance approach in TDD shown in the **Fig. 1** for the delivery of drug.

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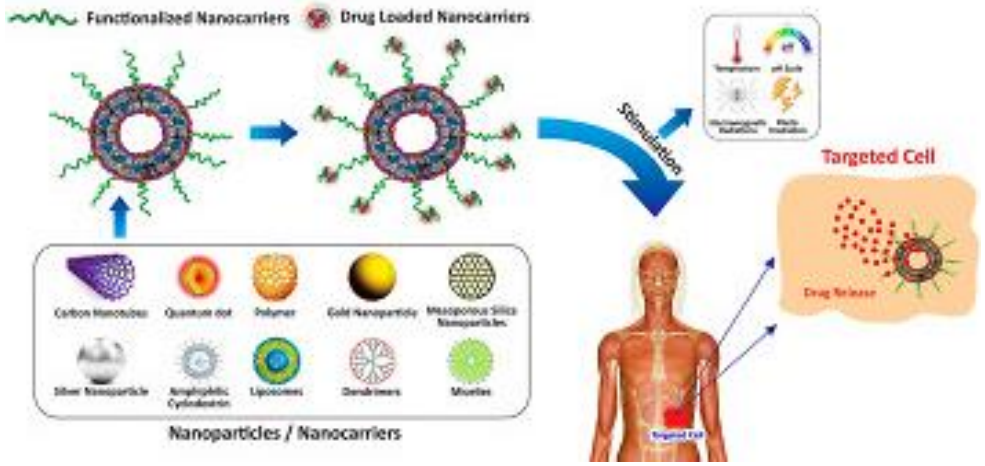

Figure. 1: The representation of nano vehicles in TDD with advance approaches

Targeted Drug Delivery (TDD) is a novel and innovative approach in the field of medicine and pharmacology. TDD can be achieved using a variety of methods, including:

- ***Nanoparticles:*** Nanoparticles can be designed to carry drugs and deliver them to specific cells. The nanoparticles can be targeted to specific cells by binding to receptors on the surface of the cells.
- ***Monoclonal antibodies:*** Monoclonal antibodies are proteins that can bind to specific cells. They can be used to deliver drugs to specific cells by attaching the drug to the antibody.
- ***Gene therapy:*** Gene therapy involves delivering a gene to a cell. This gene can then produce a protein that can deliver a drug to the cell [1-3].

TDD is still in its early stages of development, but it has the potential to revolutionize the way that drugs are delivered. It has the potential to reduce the side effects of drugs, improve the effectiveness of drugs, and make it possible to treat diseases that are currently difficult or impossible to treat.

Characteristics of targeted drug delivery (TDD) systems:

a) **Specificity:** Targeted drug delivery systems are designed to interact with specific molecules or cells at the target site. This specificity is achieved by attaching a targeting ligand to the drug carrier system. The targeting ligand is a molecule that binds to a specific receptor on the target cell or tissue.
b) **Biocompatibility:** Targeted drug delivery systems must be biocompatible, meaning that they must be non-toxic and non-immunogenic. This is important to ensure that the drug carrier system does not cause any harm to the patient.
c) **Controlled release:** Targeted drug delivery systems should be able to release the drug at a controlled rate once it has reached the target site. This is important to ensure that the drug is effective and to minimize side effects [2,3].

Need of targeted drug delivery (TDD): Targeted drug delivery is needed for a number of reasons, including:

- **To improve the efficacy of drugs:** Targeted drug delivery can deliver a higher concentration of drug to the target site, which can improve the therapeutic effect of the drug. This is especially important for drugs with a narrow therapeutic index, meaning that there is a small difference between the effective dose and the toxic dose.
- **To reduce the side effects of drugs:** By minimizing the distribution of drug to non-target tissues, targeted drug delivery can reduce the risk of side effects. This is especially important for drugs that have serious side effects, such as chemotherapy drugs.
- **To increase patient compliance:** Targeted drug delivery systems can often be administered less frequently than conventional drug delivery methods, which can improve patient compliance. This is important because patients are more likely to take their medications as prescribed if they are easy to take [1-3].

DOI: 10.5123/inj.2023.4.inj6
ISSN:2093-4777 | E-ISSN:2093-6931
Vol. 27 Iss. 4 (2023)

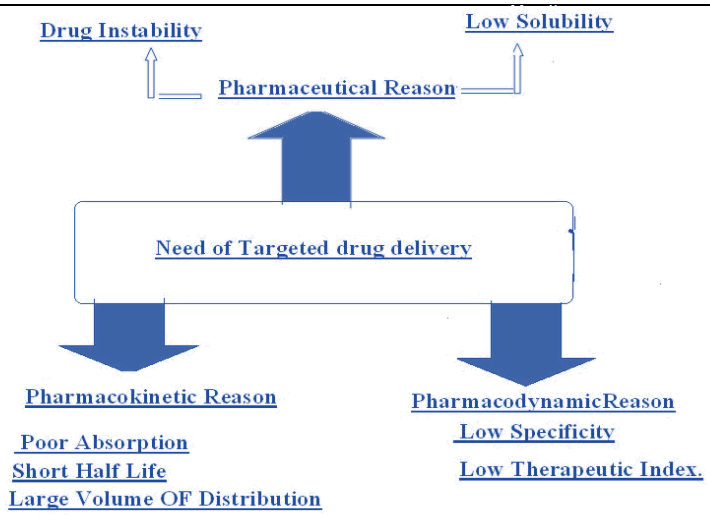

Figure. 2: The need of targeted drug delivery (TDD) for drug delivery

In addition to these general benefits, targeted drug delivery is also needed for the treatment of specific diseases. For example, targeted drug delivery is essential for the treatment of cancer, as it allows cancer drugs to be delivered directly to tumor cells while minimizing the exposure of healthy cells to the drug.

THE TYPES OF DRUG TARGETING IN TARGETED DRUG DELIVERY (TDD)

Targeted drug delivery employs various strategies and mechanisms to deliver drugs to specific sites or targets within the body. These targeting methods aim to enhance the therapeutic efficacy of drugs while minimizing off-target effects. The types of drug targeting delivery (TDD) shown in the given (**Fig. 3**). The types of drug targeting in TDD:

Active Drug Targeting:

- ***Receptor-Mediated Targeting:*** This approach involves designing drug carriers or therapeutic agents that can bind specifically to overexpressed receptors on the surface of target cells. For instance, in cancer therapy, monoclonal antibodies or ligands may be used to target receptors on cancer cells, increasing drug delivery to the tumor.
- ***Antibody-Drug Conjugates (ADCs):*** ADCs combine a monoclonal antibody that recognizes a specific target on the surface of cells with a cytotoxic drug. Once the antibody binds to the target, it delivers the drug directly to the cell, enhancing specificity and reducing systemic toxicity.
- ***Peptide-drug conjugates (PDCs):*** PDCs are formed by conjugating a peptide to a cytotoxic drug. Peptides can be designed to bind to specific receptors on the surface of target cells.
- ***Aptamers:*** Aptamers are short, single-stranded oligonucleotides that can bind to proteins and other molecules with high affinity. They can be used to deliver drugs to specific cells or tissues [3-4].

Passive Drug Targeting: Passive drug targeting in TDD (Target Drug Delivery) is a strategy that relies on the physical and chemical properties of the drug and the target tissue to deliver the drug to the desired site. This can be achieved through a variety of mechanisms, such as:

- ***Enhanced Permeability and Retention (EPR) effect:*** This effect occurs in tumor tissue, which has leaky blood vessels and poor lymphatic drainage. This allows large molecules, such as nanoparticles, to accumulate in the tumor tissue.
- ***Affinity-based targeting:*** This involves attaching a targeting ligand to the drug delivery system. The ligand binds to a specific receptor on the target cell, which allows the drug to enter the cell.
- ***Cell surface targeting:*** This involves targeting specific cell surface markers on the target cell. This can be achieved using antibodies, aptamers, or other targeting ligands [2,4].

Passive drug targeting can be used to improve the efficacy and safety of TDD. By delivering the drug directly to the target tissue, it is possible to reduce the dose required and minimize side effects. Generally, passive drug targeting involves the some example such as *liposome, nanoparticles (NPs) and monoclonal antibodies* for drug delivery at the site of action.

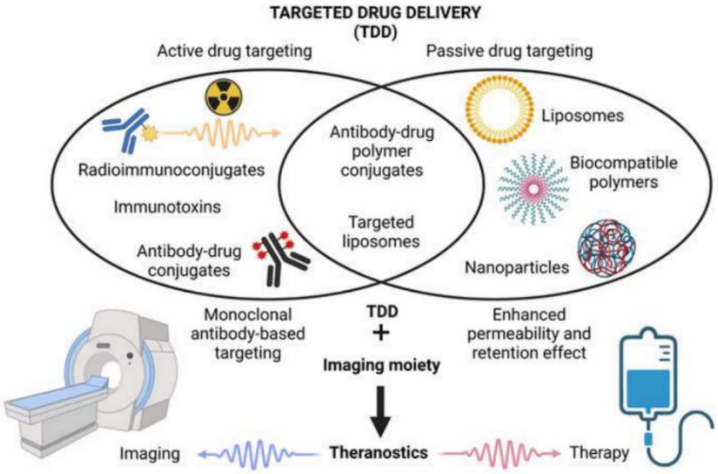

Figure. 3: The basic targeted drug delivery (TDD) via several targeting

The several types of TDD to deliver the drug at the site of action with their active and passive targeting discuss in the given **Table. 1** as below description.

Table. 1: The list of types of TDD with their suitable example

Type of drug targeting	Description	Examples
Passive targeting	Passive targeting relies on the physicochemical properties of the drug delivery system to deliver the drug to the target tissue.	Nanoparticles, liposomes and Monoclonal Antibody.
Active targeting	Active targeting uses a targeting ligand to deliver the drug to the target cell or tissue. The targeting ligand can be an antibody, peptide, or other molecule that binds to a specific receptor on the target cell or tissue.	Antibody-drug conjugates (ADCs), peptide-drug conjugates (PDCs), and aptamers [5-7].

The choice of targeting method depends on the specific disease, the characteristics of the target, and the nature of the drug being delivered.

Merits and Demerits of targeted drug delivery: TDD is a method of delivering a therapeutic agent to a specific site in the body, while minimizing its distribution to non-target tissues. This is achieved by using a drug carrier system that is designed to interact with specific molecules or cells at the target site. Targeted drug delivery systems offer a number of advantages and disadvantages (**Table. 2**) including as below followings:

Table. 2: The list of merits & demerits of Targeted drug delivery (TDD)

Merits	Demerits
Increased therapeutic efficacy	High cost
Reduced side effects	More complex to develop and manufacture
Controlled drug release	May be less effective in certain tissues
Improved patient compliance	May require specialized administration equipment
Potential to reduce drug dosage	May not be suitable for all drugs or diseases [6,7]

TDD is a promising technology with the potential to revolutionize the way that drugs are delivered. By delivering drugs directly to the target cells or tissues, TDD can improve the efficacy of drugs and reduce their side effects. TDD has the potential to make it possible to treat diseases that are currently difficult or impossible to treat.

DOI: 10.5123/inj.2023.4.inj6
ISSN:2093-4777 | E-ISSN:2093-6931
Vol. 27 Iss. 4 (2023)

INJ INTERNATIONAL NEUROUROLOGY JOURNAL

RECENT ADVANCE APPROACHES OF TARGETED DRUG DELIVERY (TDD)

Targeted drug delivery (TDD) is a rapidly evolving field, and several recent approaches have emerged to enhance the precision, efficacy, and safety of drug delivery. These recent approaches in targeted drug delivery are continually evolving, offering innovative solutions to enhance the effectiveness of therapies, reduce side effects, and improve patient outcomes across various medical fields. The various recent approaches for the TDD of drug delivery as first one, ***liposome*** is a spherical vesicle made up of a phospholipid bilayer. Liposomes can be used to encapsulate a variety of drugs, including small molecules, proteins, and nucleic acids. Liposomes can be passively or actively targeted to the target site [8]. Secondly, ***niosome*** is a spherical vesicle made up of a non-ionic surfactant bilayer. Niosomes are similar to liposomes, but they are more stable and less expensive to produce. Niosomes can also be passively or actively targeted to the target site [17]. Thirdly, ***nanoparticles*** are small particles with a diameter of less than 100 nanometers. Nanoparticles can be made from a variety of materials, including polymers, lipids, and metals. Nanoparticles can be passively or actively targeted to the target site [24]. Lastly, ***monoclonal antibodies*** are highly specific antibodies that are produced by a single clone of B cells. Monoclonal antibodies can be used to bind to specific proteins or cells, which can be used to deliver drugs to the target site or to kill the target cells [32].

The various advance approach for targeted drug delivery (TDD) shown in the below following **fig. 4** for their all components.

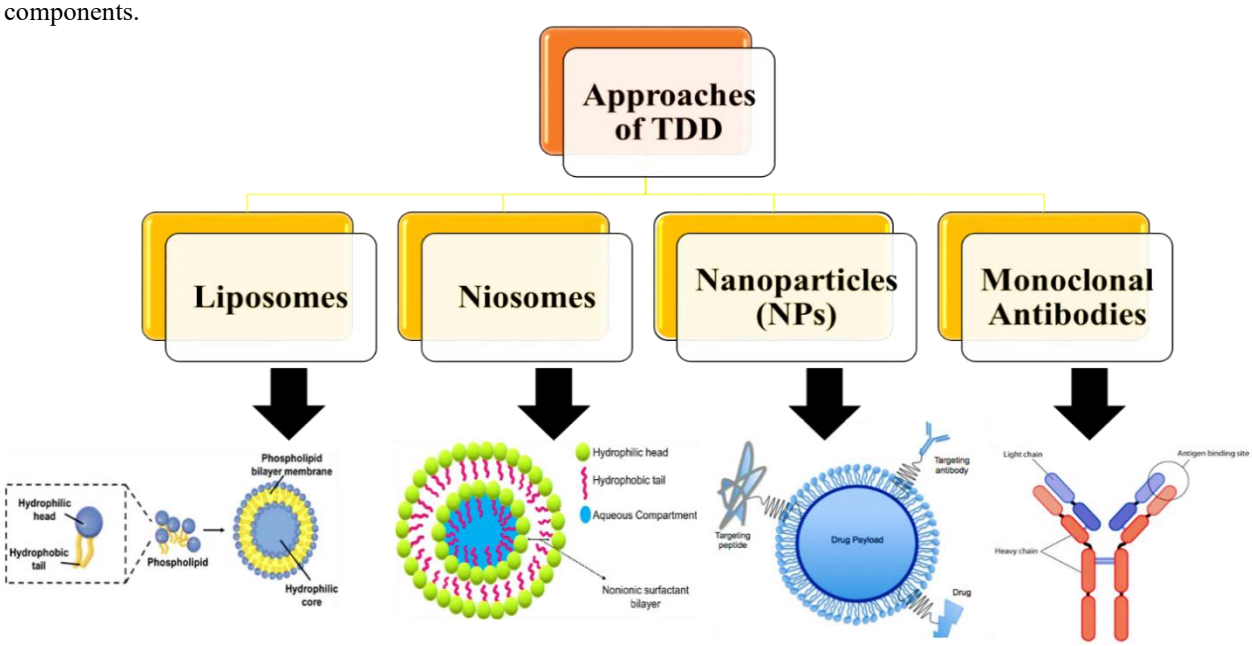

Figure. 4: The basic structure of novel approaches in TDD for the drug delivery

Targeted drug delivery is a field of research that focuses on delivering drugs specifically to the site of action, minimizing side effects and maximizing therapeutic efficacy. There several advanced and novel approaches in targeted drug delivery discussed in the given **Table. 3** as below:

Table. 3 The list of advance novel approach in TDD for the drug delivery

Approach	Description	Examples
Liposomes	Liposomes are spherical vesicles composed of a phospholipid bilayer. They can be used to encapsulate drugs and deliver them to the target tissue.	Doxil is a liposome-encapsulated form of doxorubicin, a chemotherapy drug. Doxil is targeted to cancer cells by binding to a receptor on the surface of the cells [8].
Niosomes	Niosomes are similar to liposomes, but they are made from non-ionic surfactants instead of phospholipids. This makes them more stable and less expensive than liposomes.	Ambisome is a niosome-encapsulated form of amphotericin B, an antifungal drug. Ambisome is used to treat severe fungal infections, such as invasive aspergillosis [17].

DOI: 10.5123/inj.2023.4.inj6
ISSN:2093-4777 | E-ISSN:2093-6931
Vol. 27 Iss. 4 (2023)

NPs	NPs (Nanoparticles) are small particles that can be made from a variety of materials, such as polymers, lipids, and metals. They can be designed to target specific cells or tissues in the body.	Abraxane is a nanoparticle-encapsulated form of paclitaxel, a chemotherapy drug. Abraxane is used to treat breast cancer and non-small cell lung cancer [24].
Monoclonal antibodies	Monoclonal antibodies are proteins that can bind to specific cells or tissues in the body. They can be used to deliver drugs to specific cells.	Herceptin is a monoclonal antibody that targets the HER2 receptor, which is overexpressed on some breast cancer cells [32].

This paper discusses the latest advancements in the field of targeted drug delivery (TDD) utilizing advanced nano-vehicles, including liposomes, niosomes, nanoparticles (NPs), and monoclonal antibodies. These cutting-edge approaches aim to enhance the delivery of drugs directly to the desired site of action.

LIPOSOME (PHOSPHOLIPID VESICLES)

Liposomes can encapsulate a wide range of substances, such as drugs, genetic material (DNA or RNA), and other bioactive molecules. They are versatile delivery vehicles that can protect their cargo, improve its stability, and enable targeted release. Liposomes can be engineered to have specific properties, including size, surface charge, and composition, which allow for precise control over drug release and targeting. This versatility makes liposomes a valuable tool in pharmaceuticals and biotechnology for enhancing the efficacy and safety of drug delivery systems.

Liposome is a spherical vesicle composed of one or more phospholipid bilayers. Phospholipids are the main components of cell membranes, and they have a hydrophilic head and a hydrophobic tail. This allows them to form a bilayer, with the hydrophilic heads facing the outside and the hydrophobic tails facing the inside [8].

Structure and Composition of the Liposome:

Liposomes are spherical, microscopic vesicles composed of one or more lipid bilayers that enclose an aqueous core. They are widely used in pharmaceutical and biomedical research for drug delivery, as well as in various cosmetic and industrial applications. The basic structure and composition of liposomes (**Fig. 5**) are as follows:

Structure of Liposome:

1) ***Lipid Bilayer:*** The fundamental structure of a liposome consists of a lipid bilayer. This lipid bilayer is composed of phospholipids, which are amphipathic molecules with a hydrophilic ("water-attracting") head and two hydrophobic ("water-repelling") tails. In an aqueous environment, these lipids self-assemble into a bilayer structure, with the hydrophobic tails orienting toward the interior and the hydrophilic heads facing outward. This bilayer mimics the structure of cell membranes.
2) ***Aqueous Core:*** The lipid bilayer encloses an aqueous (water-based) core. This core can hold a variety of substances, including drugs, proteins, nucleic acids, or other molecules, depending on the specific application of the liposome [8,9].

Composition of Liposome:

The composition of liposomes can vary depending on the desired characteristics and applications. The primary components of liposomes include:

1) ***Phospholipids:*** Phospholipids are the essential building blocks of liposomes. Common phospholipids used in liposome composition include phosphatidylcholine, phosphatidylethanolamine, and phosphatidylserine. These phospholipids are responsible for forming the lipid bilayer.
2) ***Cholesterol:*** Cholesterol is often added to the liposome composition to improve the stability and rigidity of the lipid bilayer. Cholesterol molecules are integrated into the bilayer, reducing membrane permeability and preventing leakage of encapsulated substances.
3) ***Additional Lipids:*** In some cases, other lipids, such as cationic lipids or PEGylated lipids (lipids modified with polyethylene glycol), may be included to alter the surface charge, enhance stability, or provide stealth properties, which reduce immune system recognition.

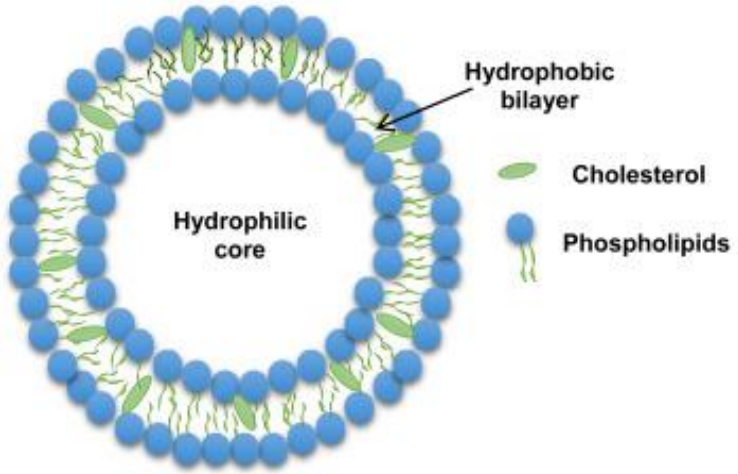

Figure. 5: The basic structure of liposome as advance drug nano-carrier

1) ***Aqueous Phase:*** The aqueous core of the liposome contains the payload, which can be a drug, a contrast agent for imaging, or other therapeutic or diagnostic substances. The aqueous phase can also include buffer solutions to maintain a desired pH or ionic strength.
2) ***Stabilizers and Preservatives:*** Depending on the intended use and storage conditions, stabilizers and preservatives may be added to the liposome formulation to extend shelf life and maintain the integrity of the liposomal structure [7, 8, 10].

The composition and structure of liposomes can be customized to meet the requirements of a particular application, such as drug delivery, gene therapy, or diagnostic imaging. This versatility makes liposomes a versatile tool in pharmaceutical and biomedical research. The structural composition shown in the given **Table 4** as below:

Table. 4: The structure of composition of liposome in brief

Feature	Description
Structure	Liposomes are spherical vesicles composed of one or more concentric bilayers of phospholipids, surrounding an aqueous core.
Composition	The phospholipid bilayer is composed of two layers of phospholipid molecules, arranged with their hydrophilic heads facing the outside and their hydrophobic tails facing the inside. The aqueous core of a liposome can contain a variety of substances, such as drugs, proteins, and nucleic acids.
Commonly used phospholipids	Phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylglycerol (PG), sphingomyelin (SM)
Other materials	Cholesterol, polyethylene glycol (PEG), targeting ligands
Preparation methods	Thin-film hydration method, reverse-phase evaporation method, microfluidics method [8-10]

THE TYPES OF LIPOSOME IN TDD

Liposomes are a versatile drug delivery system that can be used to deliver a variety of drugs to specific cells or tissues. Liposomes have the potential to improve the efficacy of drugs and reduce their side effects. There are many different types of liposomes, which can be classified based on their size, structure, and composition. The types of liposome **Fig. 6** shown in the **Table. 5** as below followings:

Table. 5: There are many different types of liposomes, which can be classified based on their size, structure, and composition

Classification based on	Types	Description
Size	Multilamellar liposomes (MLVs)	Have multiple concentric layers of phospholipid bilayers. Are the largest type of liposome and can be used to deliver a variety of drugs, including chemotherapy drugs, antibiotics, and vaccines.
	Unilamellar liposomes (ULVs)	Have a single phospholipid bilayer. Can be further divided into two types: small unilamellar vesicles (SUVs) and large unilamellar vesicles (LUVs). SUVs are used to deliver drugs to specific cells or tissues, while LUVs are used to deliver drugs that are difficult to dissolve in water [9].
Structure Based	Conventional liposomes	Are made with phospholipids and cholesterol. Are relatively simple to prepare and can be used to deliver a variety of drugs.
	Stealth liposomes	Are coated with a layer of polyethylene glycol (PEG). This coating makes the liposomes less visible to the immune system, which can help to increase their circulation time.
	Targeted liposomes	Are conjugated to a targeting ligand, such as an antibody or peptide. This allows the liposomes to bind to specific cells or tissues and deliver their payload directly to the target [10].
Compositional based	Liposomes with pH-sensitive membranes	Are designed to release their payload at a specific pH, such as the acidic pH of tumor cells.
	Liposomes with temperature-sensitive	Are designed to release their payload at a specific temperature, such as the elevated temperature of tumor cells.
	Liposomes with light-sensitive	Are designed to release their payload when exposed to light [11].

The various classification of liposome like *conventional, theranostics, PEGylated and Ligand* targeted liposome shown in the **fig. 6** for the brief discussion.

DOI: 10.5123/inj.2023.4.inj6
ISSN:2093-4777 | E-ISSN:2093-6931
Vol. 27 Iss. 4 (2023)

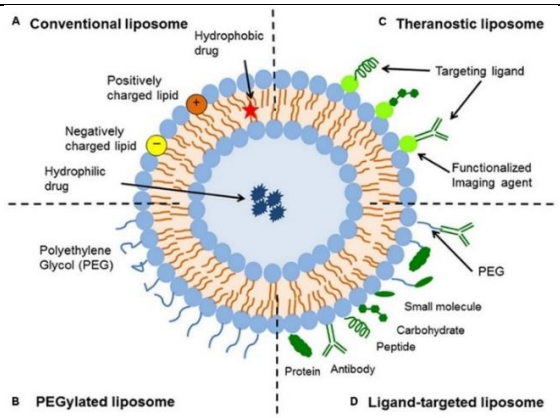

Figure. 6: The various types of liposome in targeted drug delivery system

The aforementioned classification of liposomes is depicted in **Fig. 6** and summarized in **Table 5**, accompanied by a concise discourse on liposomes as carriers of phospholipids.

LIPOSOMAL BIO-APPLICATIONS IN TDD: Liposomes are a versatile drug delivery system that can be used to deliver a variety of drugs to specific cells or tissues. Liposomes have the potential to improve the efficacy of drugs and reduce their side effects. The several liposomal applications in TDD:

1) ***Cancer treatment:*** Liposomes can be used to deliver chemotherapy drugs directly to cancer cells. This can help to reduce the side effects of chemotherapy drugs, such as hair loss and nausea. For example, Doxil is a liposome-encapsulated form of the chemotherapy drug doxorubicin. Doxil is used to treat breast cancer, non-small cell lung cancer, and ovarian cancer [13].
2) ***Infectious disease treatment:*** Liposomes can be used to deliver antibiotics and antifungals directly to infected cells. This can help to improve the efficacy of these drugs and reduce their side effects. For example, Ambisome is a liposome-encapsulated form of the antifungal drug amphotericin B. Ambisome is used to treat severe fungal infections, such as invasive aspergillosis.
3) ***Gene therapy:*** Liposomes can be used to deliver genes to specific cells. This can be used to treat genetic disorders or to develop new vaccines. For example, Myocet is a liposome-encapsulated form of the antiviral drug doxorubicin. Myocet is used to treat patients with HIV/AIDS who have developed cytomegalovirus retinitis [13-16].

Liposomes can also be used to deliver a variety of other drugs, including proteins, vaccines, and imaging agents.

NIOSOME (NON-IONIC SURFACTANT VESICLES)

Niosomes are spherical vesicles made up of a non-ionic surfactant bilayer. They are similar to liposomes, but they are more stable and less expensive to produce. Niosomes can be used to encapsulate a variety of drugs, including small molecules, proteins, and nucleic acids.

Niosomes are a promising new technology for drug delivery [17]. They are stable, inexpensive, and compatible with a wide range of drugs. Niosomes have the potential to revolutionize the way that drugs are delivered to patients.

Structure and composition of the niosome:

The structure of a niosome is similar to that of a liposome. The bilayer is formed by the self-assembly of non-ionic surfactant molecules in an aqueous solution. The hydrophilic heads of the surfactant molecules face the outside of the vesicle, while the hydrophobic tails face the inside. This creates a closed vesicle with a hydrophilic interior and a hydrophobic exterior.

DOI: 10.5123/inj.2023.4.inj6
ISSN:2093-4777 | E-ISSN:2093-6931
Vol. 27 Iss. 4 (2023)

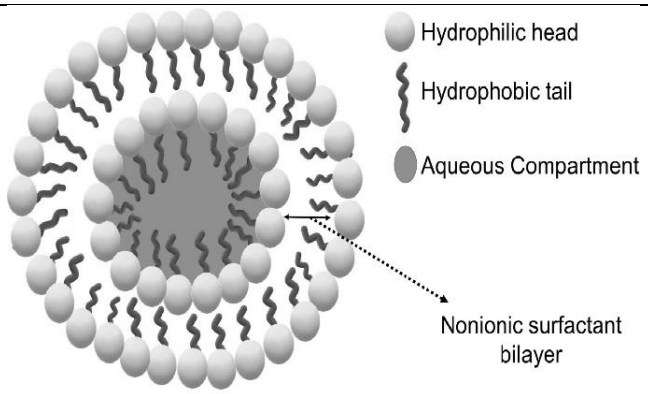

Figure. 7: The basic compositional structure of niosome

The composition of a niosome can vary depending on the desired properties. The most common non-ionic surfactants used to make niosomes are alkyl ether polyglycerols, such as sorbitan monostearate and polysorbate 80. Cholesterol is often added to the bilayer to improve stability. Other components that may be added to niosomes include charge-inducing agents, such as dicetyl phosphate, and drugs.
Niosomes are artificial vesicles or liposomes composed of non-ionic surfactants. They are used as drug delivery systems, especially for hydrophobic drugs, and share some structural and compositional features with liposomes [17, 18]. The basic structure and composition of niosomes include:

- ***Non-Ionic Surfactants (Amphiphiles):*** Niosomes are primarily composed of non-ionic surfactants, which are amphiphilic molecules. These surfactants have a hydrophilic ("water-attracting") head group and a hydrophobic ("water-repelling") tail.
- ***Cholesterol:*** Similar to liposomes, niosomes often contain cholesterol. Cholesterol helps stabilize the niosome structure by inserting itself into the lipid bilayer, improving rigidity and reducing permeability.
- ***Drug or Cargo Molecules:*** Niosomes can encapsulate various types of cargo molecules, including drugs, nucleic acids, or imaging agents. The hydrophobic nature of the lipid bilayer allows for the encapsulation of hydrophobic drugs.
- ***Aqueous Core:*** The hydrophilic head groups of the surfactants create an aqueous core within the niosome. This core can encapsulate hydrophilic drugs or maintain a medium for drug release.
- ***Stabilizers:*** In some formulations, stabilizers such as polymeric stabilizers or carbohydrates may be added to enhance niosome stability and prevent aggregation [17-19].

The primary difference between niosomes and liposomes lies in the nature of the surfactants used. Liposomes are composed of phospholipids, which are zwitterionic, while niosomes use non-ionic surfactants, which do not carry a charge. Niosomes are advantageous in certain applications due to their stability, biocompatibility, and versatility, especially for encapsulating hydrophobic drugs.

THE TYPES OF NIOSOME IN TDD

Niosomes can be classified into three groups based on their size, which influences their characteristics and potential applications. The present figure, **Fig. 8**, and accompanying **Table. 6** provide a discussion on size classifications of niosomes. As per the aforementioned sources, niosomes are classified based on their sizes, which are presented in the following section of **Fig. 8.**

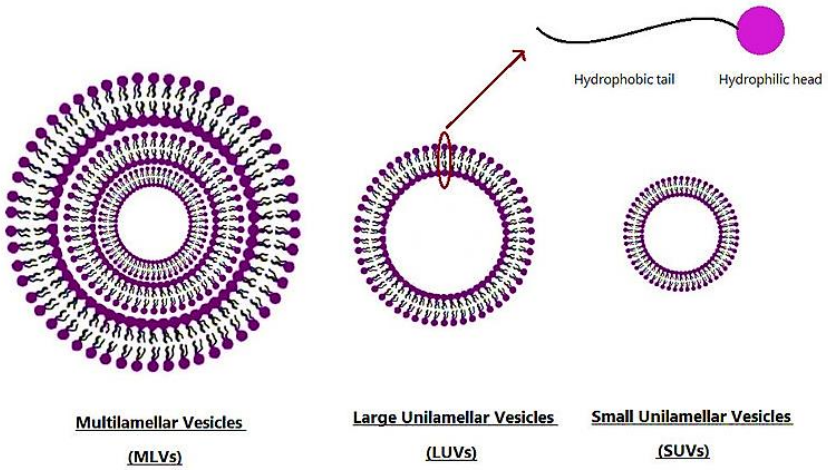

Figure. 8: The various types of niosome based on their size

The choice of niosome size is often made based on the specific drug or payload being delivered, the route of administration, and the desired drug release profile. Smaller niosomes are typically preferred for enhanced bioavailability, while larger niosomes may be favored for controlled and sustained release of drugs [19]. The versatility in size and structure makes niosomes a valuable tool in drug delivery and various biomedical applications.

Table. 6: The list of types of niosome with their examples

Type of niosome	Description	Example
Multilamellar niosomes (MLNs)	MLNs have multiple concentric layers of non-ionic surfactant bilayers. They are the simplest type of niosome and can be used to deliver a variety of drugs, including chemotherapy drugs, antibiotics, and vaccines.	Span 60:Cholesterol (9:1)
Unilamellar niosomes (ULNs)	ULNs have a single non-ionic surfactant bilayer. They can be further divided into two types: small unilamellar vesicles (SUVs) and large unilamellar vesicles (LUVs). SUVs are used to deliver drugs to specific cells or tissues, while LUVs are used to deliver drugs that are difficult to dissolve in water.	Span 60:Cholesterol (9:1)
Stealth niosomes	Stealth niosomes are coated with a layer of polyethylene glycol (PEG). This coating makes the niosomes less visible to the immune system, which can help to increase their circulation time in the body.	Span 60:Cholesterol (9:1) coated with PEG [18-21]

NIOSOMAL BIO- MEDICAL APPLICATIONS OF TDD

Niosomes are a type of lipid-based vesicle that can be used in various applications, including drug delivery. Niosomes offer several advantages and have found applications in this field. The several potential applications of niosomes in Targeted Drug Delivery discussed in **Table. 7** as below following description:

Table. 7: The list of various disease and niosomal formulation with example

Disease	Niosomal formulation	Example
Cancer	Niosomes loaded with anticancer drugs	Doxorubicin-loaded niosomes, paclitaxel-loaded niosomes
Autoimmune diseases	Niosomes loaded with immunosuppressive drugs	Methotrexate-loaded niosomes, cyclosporine A-loaded niosomes

DOI: 10.5123/inj.2023.4.inj6
ISSN:2093-4777 | E-ISSN:2093-6931
Vol. 27 Iss. 4 (2023)

Infectious diseases	Niosomes loaded with antibiotics or antiviral drugs	Amphotericin B-loaded niosomes, acyclovir-loaded niosomes
Neurological disorders	Niosomes loaded with drugs for the treatment of neurological disorders	Amantadine-loaded niosomes, levodopa-loaded niosomes
Other diseases	Niosomes loaded with drugs for the treatment of other diseases	Insulin-loaded niosomes, gene therapy-loaded niosomes [21-23]

These are the some biomedical applications in TDD for the drug targeting at the site of action as per the **Table. 7** above description.

NANOPARTICLES (NPs)

Nanoparticles (NPs) are small particles that range between 1 and 100 nanometers in size. They can be made from a variety of materials, including metals, polymers, and lipids. NPs have unique properties that make them ideal for targeted drug delivery (TDD). In TDD, NPs are used to deliver drugs directly to the target cells or tissues [24]. This can be done by designing the NPs to be specific to the target cells or tissues, or by using external stimuli, such as light or magnetic fields, to guide the NPs to the target.

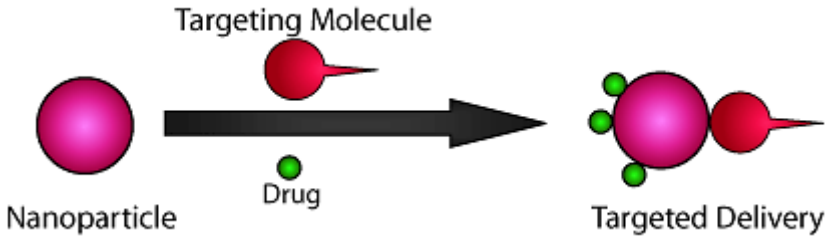

Figure. 9: The NPs delivery at the target delivery with carrier of drug

Advantages: NPs have a number of advantages over traditional drug delivery methods:

- ***Increased drug delivery efficiency:*** NPs can deliver drugs directly to the target cells or tissues, which can increase the efficacy of the drug and reduce its side effects.
- ***Reduced side effects:*** NPs can protect drugs from degradation and excretion, which can reduce the side effects of the drug.
- ***Controlled drug release:*** NPs can be designed to release drugs in a controlled manner, which can improve the efficacy of the drug and reduce its side effects.
- ***Targeting ability:*** NPs can be conjugated to targeting ligands, such as antibodies and peptides, to direct them to specific cells or tissues [24-26].

NPs are a rapidly developing field, and new NP-based drugs are being developed all the time. NPs have the potential to revolutionize the way that drugs are delivered and to make it possible to treat diseases that are currently difficult or impossible to treat.

TYPES OF NANOPARTICLES (NPs) IN TDD: Nanoparticles (NPs) are tiny particles with a diameter of less than 100 nanometers. They can be made from a variety of materials, including metals, polymers, and ceramics [27]. NPs have unique properties that make them useful for a variety of applications, including drug delivery, imaging, and energy storage.

They have a wide range of applications in fields such as medicine, materials science, electronics, and environmental science. Nanoparticles can be classified into various types based on their composition, properties, and applications. The various common types of nanoparticles (NPs) as below mentioned:

NPs are a promising drug delivery system for TDD. They have the potential to improve the efficacy and safety of drugs for a variety of diseases. The **Table 8** and **Fig. 10** provide a comprehensive depiction of the diverse examples and types of nanoparticles (NPs) employed in Targeted drug delivery (TDD) [26-29].

Metal Nanoparticles:

- ***Gold Nanoparticles:*** Known for their biocompatibility and unique optical properties, gold nanoparticles are used in drug delivery, imaging, and diagnostic applications.
- ***Silver Nanoparticles:*** Often used for their antimicrobial properties, silver nanoparticles are found in wound dressings, textiles, and water purification.
- ***Iron Nanoparticles:*** Used in magnetic resonance imaging (MRI) contrast agents and for drug delivery in cancer therapy.

The several types of nanoparticles (NPs) as mentioned in the given below description and **Fig. 10:**

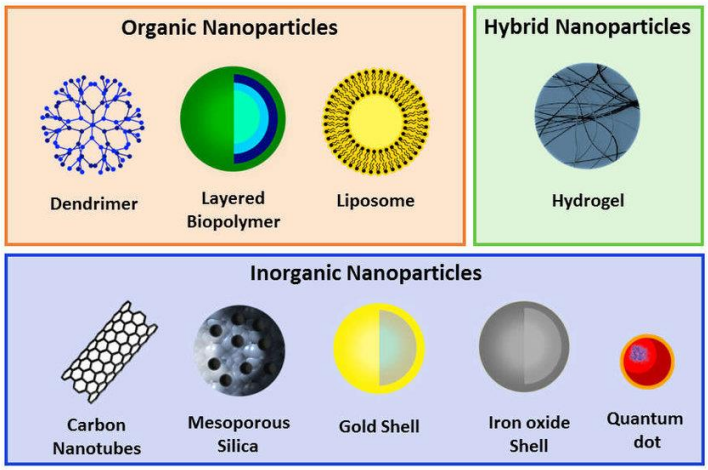

Figure. 10: The types of nanoparticles in TDD as drug delivery vehicles

Metal Oxide Nanoparticles:

- ***Titanium Dioxide (TiO2) Nanoparticles:*** Widely used in sunscreens and cosmetics for their UV-blocking properties.
- ***Zinc Oxide (ZnO) Nanoparticles:*** Used in sunscreens and as antibacterial agents in various applications.
- ***Iron Oxide (Fe3O4) Nanoparticles:*** Utilized as contrast agents in MRI and for hyperthermia cancer treatment [26-29].

The alternative categorization of NPs, as outlined in the subsequent description, is presented in **Table 8**, as discussed below.

Table. 8: The list of different types of nanoparticles (NPs) used in TDD

Type of nanoparticle	Material(s)	Examples	Applications
Liposomes	Phospholipids	Doxil, Ambisome, Myocet	Cancer treatment, infectious disease treatment, gene therapy
Polymeric nanoparticles	Polymers, such as poly(lactic-co-glycolic acid) (PLGA) and poly(ε-caprolactone) (PCL)	Abraxane, Genexol	Cancer treatment, gene therapy
Metallic nanoparticles	Metals, such as gold, silver, and iron oxide	Auristatin E-conjugated gold nanoparticles, Doxorubicin-loaded silver nanoparticles, Feridex	Cancer treatment, imaging

Ceramic nanoparticles	Ceramics, such as silica and mesoporous silica	Doxil, Ambisome, Myocet	Cancer treatment, infectious disease treatment, gene therapy
Carbon nanotubes	Carbon	Carbon nanotube-loaded doxorubicin	Cancer treatment [29-31]

These are just a few examples of the many types of nanoparticles with unique properties and applications. The choice of nanoparticle type depends on the intended use, including drug delivery, imaging, materials development, electronics, and more.

MONOCLONAL ANTIBODIES AS TDD APPROACH

Antibodies were primarily reported as a nullifying matter floats in blood introduced via Behring and Shibasaburo in year 1890 at their research on animal models for diphtheria. Monoclonal antibodies (mAbs) are proteins that can bind to specific cells or tissues. They are produced by immune cells in response to infection or vaccination. mAbs (**Fig. 11**) can also be produced in the laboratory using a process called hybridoma technology. mAbs are a promising drug delivery system for targeted drug delivery (TDD). They can be used to deliver drugs directly to the target cells or tissues, which can improve the efficacy of the drug and reduce its side effects [32]. mAbs can also be used to target cancer cells and deliver chemotherapy drugs directly to the tumor.

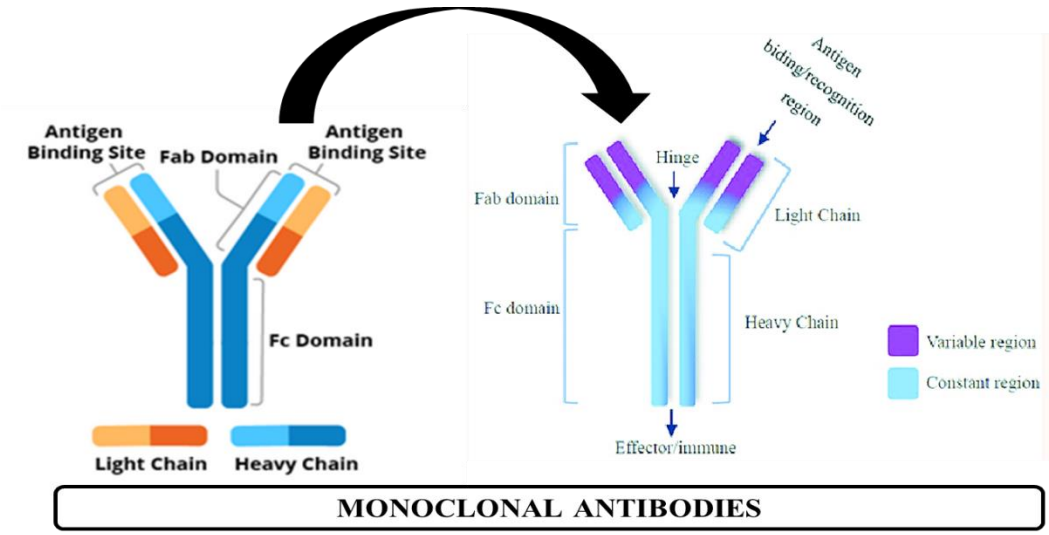

Figure. 11: The structural representation of monoclonal antibodies

The various advantages of using mAbs for TDD:

- ***High specificity:*** mAbs can bind to specific cells or tissues with high specificity. This allows mAbs to deliver drugs directly to the target cells or tissues, which can improve the efficacy of the drug and reduce its side effects.
- ***Low toxicity:*** mAbs are generally low in toxicity and are well-tolerated by patients.
- ***Long half-life:*** mAbs have a long half-life in the bloodstream, which allows them to circulate in the body for an extended period of time [32-34].

mAbs are a promising drug delivery system for TDD. They have the potential to improve the efficacy and safety of drugs for a variety of diseases. The various monoclonal antibodies with their diseases and example including in **Table. 9.**

Table. 9: The list of monoclonal antibodies with their disease and examples

Monoclonal Antibody	Disease or condition treated	Example
Adalimumab	Rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis	Humira
Bevacizumab	Metastatic colorectal cancer, non-small cell lung cancer, glioblastoma	Avastin
Cetuximab	Colorectal cancer, head and neck cancer	Erbitux
Infliximab	Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriasis	Remicade
Rituximab	Non-Hodgkin lymphoma, chronic lymphocytic leukemia	Rituxan
Trastuzumab	Breast cancer	Herceptin [33-34]

PRODUCTION OF MONOCLONAL ANTIBODIES:

Monoclonal antibodies (mAbs) are proteins that can bind to specific cells or tissues. They are produced by immune cells in response to infection or vaccination. mAbs can also be produced in the laboratory using a process called hybridoma technology.

Hybridoma technology: Hybridoma technology is a method for producing monoclonal antibodies. Monoclonal antibodies are highly specific antibodies that are produced by a single clone of B cells. Hybridoma technology was developed in 1975 by Georges Kohler and Cesar Milstein, who were awarded the Nobel Prize in Physiology or Medicine in 1984 for their work. Hybridoma technology is a process that fuses a B cell, which produces mAbs, with a myeloma cell, which is a cancerous cell that can grow indefinitely. The resulting hybrid cell, called a hybridoma, can produce large quantities of mAbs that are specific to the antigen that the B cell was originally exposed to.

Hybridoma technology is a powerful tool for producing monoclonal antibodies that are used for research and therapeutic purposes.

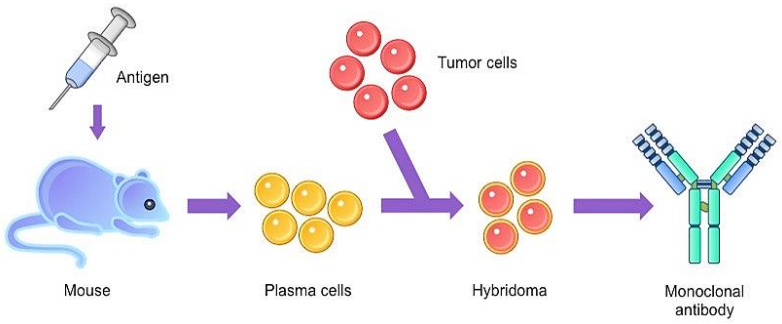

Figure. 12: The steps of production of monoclonal antibodies from antigen

The production of mAbs using hybridoma technology typically involves the following steps:

- Immunize a mouse with the antigen of interest.
- Collect the mouse's spleen and isolate the B cells.
- Fuse the B cells with myeloma cells.
- Select the hybridomas that produce mAbs that are specific to the antigen of interest.
- Clone the hybridomas.
- Grow the hybridomas in culture and collect the mAbs.

Purification of monoclonal antibodies: Once the mAbs have been collected from the hybridoma culture, they need to be purified to remove any impurities. This can be done using a variety of methods, such as chromatography and immunoaffinity filtration [34-35].

Hybridoma technology has revolutionized the field of immunology and has led to the development of a wide range of monoclonal antibodies that are used for research and therapeutic purposes. Monoclonal antibodies are

used to diagnose and treat a wide range of diseases, including cancer, autoimmune diseases, and infectious diseases.

TYPES OF MONOCLONAL ANTIBODIES: Monoclonal antibodies (mAbs) are a class of antibodies produced by identical immune cells that are clones of a single parent cell. They have become important tools in both research and medical treatment. The various types of monoclonal antibody used in the targeted drug delivery (TDD) for the treating of the disease.

Table. 10: The list of types of monoclonal antibodies with their example of drug in disease treating

Type of monoclonal antibody	Description	Example
Murine monoclonal antibodies	Murine monoclonal antibodies are produced from mouse B cells. They are the most common type of monoclonal antibody used in research and clinical applications.	Rituximab, Avastin
Chimeric monoclonal antibodies	Chimeric monoclonal antibodies are produced by fusing the variable regions of a murine monoclonal antibody with the constant regions of a human monoclonal antibody. This makes the antibody less likely to trigger an immune response in the patient.	Herceptin
Humanized monoclonal antibodies	Humanized monoclonal antibodies are produced by modifying the amino acid sequence of a murine monoclonal antibody to make it more similar to a human antibody. This makes the antibody even less likely to trigger an immune response in the patient.	Adalimumab, Infliximab
Fully human monoclonal antibodies	Fully human monoclonal antibodies are produced from human B cells. They are the least likely type of monoclonal antibody to trigger an immune response in the patient.	Dupilumab, Pembrolizumab [35-36]

APPLICATIONS OF MONOCLONAL ANTIBODIES:
Monoclonal antibodies (mAbs) have a wide range of applications in various fields, including medicine, research, and diagnostics. mAbs can be used to deliver a variety of therapeutic agents, including drugs, toxins, and radioactive isotopes. They can also be used to target specific cells and tissues, which can help to minimize the side effects of treatment [36]. The notable applications of monoclonal antibodies in several diseases including in

Table. 11 as followings:

Table. 11: The list of monoclonal antibodies (Autoimmune Disease) with their disease and examples [34-37]

Monoclonal Antibody	Disease or condition treated	Example	Year
Adalimumab (Human)	Rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis {tumor necrosis factor-alpha (TNF-α)}	Humira	2002
Alemtuzumab (Humanized)	Multiple sclerosis, Chronic Lymphoblastic Leukemia and for relapsing-remitting multiple sclerosis (RRMS) in 2014.(CD52 receptor)	Lemtrada, Camptah	**2001**
Belimumab (Human)	Systemic Lupus Erythrematous (B-cell activating factor (BAFF))	Benlysta	2011

DOI: 10.5123/inj.2023.4.inj6
ISSN:2093-4777 | E-ISSN:2093-6931
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Infliximab (Chimeric)	Crohn's disease, ulcerative colitis, rheumatoid arthritis, psoriasis { tumor necrosis factor-alpha (TNF-α)}	Remicade	1998
Rituximab (Chimeric)	Non-Hodgkin lymphoma, chronic lymphocytic leukemia (CD20- B-lymphocyte antigen)	Rituxan	1997
Trastuzumab	Breast cancer (HER-2 - human epidermal growth factor receptor)	Herceptin	1998
Natalizumab (Humanized)	Multiple sclerosis, Chronic Lymphoblastic Leukemia (Alpha 4 subunit)	Tysabri	2004
Rituximab (Chimeric)	Rheumatoid arthritis, Chronic Lymphoblastic Leukemia, Wegner's granulomatosis, microscopic polyangitis (CD20)	Entyvio	2014
Tocilizumab (Human)	Rheumatoid arthritis (IL-6 receptor)	Actemra	2010
Vedolizumab (Humanized)	Crohn's disease, Ulcerative colitis (Integrin alpha 4 beta 7)	Entyvio	2014
Basiliximab (Chimeric)	Prophylaxis of renal transplant rejection (IL-2 receptor antagonist)	Simulect	1998
Muromonab (Murine)	Acute graft versus host disease (CD3)	Orthoclone OKT3	1992

Anti-cancer mAbs represents to suppress the growth of human melanomas in nude mice and in 1980 the first human trial of mAb therapy against cancer was conducted in a lymphoma patients. The monoclonal antibodies (malignancy) shown in the given **Table. 12** in brief.

Table. 12. The list of monoclonal antibodies (malignancy) with their disease and examples [37-39]

Monoclonal Antibody	Disease	Example
Rituximab	B-cell malignancies, including chronic lymphocytic leukemia (CLL), non-Hodgkin lymphoma (NHL), and diffuse large B-cell lymphoma (DLBCL)	MabThera
Trastuzumab	HER2-positive breast cancer	Herceptin
Cetuximab	Epidermal growth factor receptor (EGFR)-positive colorectal cancer and head and neck cancer	Erbitux
Bevacizumab	Metastatic colorectal cancer, non-small cell lung cancer (NSCLC), and renal cell carcinoma (RCC)	Avastin
Pembrolizumab	Melanoma, lung cancer, head and neck cancer, and other malignancies	Keytruda
Ipilimumab	Melanoma	Yervoy
Daratumumab	Multiple myeloma	Darzalex
Alemtuzumab	B-cell chronic lymphocytic leukemia (CLL)	Campath
Ofatumumab	Relapsed or refractory chronic lymphocytic leukemia (CLL)	Arzerra

mAbs are used to detect and quantify specific proteins in complex mixtures, making them valuable research tools. Monoclonal antibodies are used to purify specific proteins or protein complexes from cell lysates or biological samples. Monoclonal antibodies are versatile tools and therapies with the potential to impact a wide range of fields, from medicine and diagnostics to scientific research and beyond 40-41]. The development of new monoclonal antibodies continues to expand their applications in various areas of healthcare and beyond.

Conclusion

Targeted drug delivery is currently undergoing rapid development due to its ability to deliver drugs directly to specific sites. This advancement not only allows for the administration of lower drug doses but also significantly reduces the occurrence of side effects. Previously, the inefficiency of drug delivery systems in accurately targeting the site of action resulted in more pronounced side effects. The delivery of a drug molecule to its specific site presents a significant challenge. As the name suggests, targeted delivery of drugs aims to facilitate the drug molecule's arrival at the desired site. This technique offers the advantage of reducing the drug's dose and side effects. Various studies have demonstrated that the science of site-specific or targeted drug delivery has

become more sophisticated. The manifestation of these strategies in clinical practice appears to be a possibility in the near future.

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