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# A Review on Genetically Targeting Drug Delivery System

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**Abstract**

Drug targeting is a modern drug delivery system. The goal of this review article is to introduce the basic conceptualization of drug targeting as it has advanced over previous decades. Deliver the drug to the targeted site without modifying or altering the other non-targeted site. The drug delivery system is to support the patient by designing an essential formulation. A drug delivery system is able to intensify the most important chemical features and biological properties of targeted drug delivery, sometimes called smart drug delivery. This method is a discrete dosage form that is applied to healthy skin in which there are no breaks, scrapes, cuts, or abnormal openings that allow pathogens to enter at a controlled rate to the systemic circulation. Genetically Targeted Drug Delivery System is an advanced technology for genetic disease management. The main purpose of a genetically targeted drug delivery system is to enhance therapeutic efficacy and minimize side effects by precisely delivering drugs to specific cells or tissues, particularly those affected by diseases like cancer, through genetic targeting mechanisms. This system aims to deliver drugs to the desired location (e.g., tumour cell) for genetically targeted drug delivery. Carriers like liposomes, nanoparticles (including polymers and solid lipid nanoparticle .and viral vectors are commonly used to transport genetic material (DNA or RNA) to specific cells or tissues and enhance the penetration of cell membranes or tissues more effectively. Also, these carriers can protect drugs or genetic material from degradation or premature release in the bloodstream. Active and passive targeting are two types of techniques used for targeted drug delivery. Targeted drug delivery improved pharmacokinetics, such as increased absorption and distribution, reduced side effects, avoidance of hepatic first-pass metabolism, lower doses compared to conventional drug delivery, reduced fluctuation in circulating drug levels, etc. A genetically targeted drug delivery system is a useful delivery system that uses techniques like gene therapy and nanotechnology, offers precise and targeted drug delivery, improves efficacy, and reduces side effects compared to traditional methods.

**Keywords**: - Gene, DNA, Amino Acid, targeted drug delivery, gene targeting, Nanoparticle, Viral vector, non -viral vector, Treatment.

## Introduction

A gene is a particular DNA sequence that houses the building blocks needed to make a given protein or RNA molecule. In the body, these molecules carried out a numbers of task, including controlling biological processes (like enzyme activity) and determining physical characteristics (like eye colour). The basic building blocks of heredity, genes are found on chromosomes in the cell nucleus and are passed down from parents to children. Also, genetic diseases are caused by genes. A DNA sequence can change or mutate, resulting in aberrant protein or RNA function and genetic disorders. A genetically targeted drug delivery system is a cutting-edge therapeutic strategy that precisely delivers medications to particular cells or tissues by using genetic information. These systems use gene-editing technologies, molecular profiles, or genetic markers to increase therapeutic efficacy, reduce adverse effects, and improve patient outcomes. They combine concepts from molecular biology, nanotechnology, and genomics to create carriers like liposomes, nanoparticles, or viral vectors that specifically target sick cells according to their molecular or genetic traits. workings, and possible uses of such systems are described in this introduction. Gene therapy is a medical treatment that uses genetic material to treat or prevent disease involving replacing a faulty gene with a healthy copy or inactivating a disease using a gene. Genes that aren't functioning correctly could be to responsible for the genetic disorder. Gene therapy targeting a drug delivery system is not just applicable for genetic deficiency; additionally, other chronic and complicated diseases like cancer and diabetes. (1) Gene therapy works by adding new copies of a gene that is broken or by replacing a defective or missing gene in patient cells with a healthy version of that gene. There is also other approach like gene editing There are many versions and approaches to gene therapy and gene editing on understanding how genes work and changes in gene effects on our health by targeting drug delivery systems. (2) These techniques use doctors to treat genetic disorders by inserting genes into patients within the nucleus of cells rather than using drugs or surgery.

Some approaches used in gene therapy include

I) replacing the mutant gene that causes disease with a healthy gene.
II) inactivating a faulty gene, which has an improper function;
III) introducing a new gene within the nucleus of the cell to protect from any disease.

This technique persists as risky and should be under examination to secure it until it is effective.
Genetic molecules (genetic information is carried in the linear sequence of nucleotides in DNA) penetrate the nucleus and reach the nuclei of host cells to induce gene expression (3,4, 5). Gene therapy has been derived to provide a patient's somatic cells (all the body cells except sperm and egg cells, containing a full set of chromosomes) along with genetic information for producing therapeutic protein to inflict genetic disease. In order to obtain a successful design of a gene delivery system, it is essential for complete understanding of the interaction between the targeting cell and the gene delivery system. These delivery systems comprise important components, such as plasmid-based gene expression systems, which control the activity of genes and deliver gene expression within the targeting cell gene encoded a specific therapeutic protein (6, 7). Effective gene delivery systems require exogenous genetic molecules to stay constant within the host cell (7, 8, 9). Viral-based vectors had first emerged (10).

**DNA:**

DNA is the reserve bank of genetics information. The DNA is organised into genes, the fundamental unit of genetic information the gene controlled the protein synthesis through the mediation of RNA. (11). It contains the blueprints needed to assemble every protein that makes up life as we know it. DNA is the genetic material found in humans and nearly all other species. It is kept in the nucleus of our cells and is passed down from generation to generation.instructions for making proteins through genes are encoded in DNA. The majority of cellular processes are carried out by proteins, including enzymatic activities and structural roles. Cell division ensures that each new cell obtains an identical copy of the DNA.

**Damage and Repair of DNA: _**

Being the carrier of genetic information the cellular DNA must be replicated maintained and passed down to the daughter cell accurately. It is estimated the approximately one error is introduced per billion base pair during each cycle of replication. The cell does possess the capability to repair damage done to DNA to a large extent. (11)

**DNA responsible for genetic disease**: - When faults or mutations in the DNA sequence interfere with the normal production or function of proteins, genetic disorders result.

**1Gene mutations**:

- **Point mutations:**
  the replacement of one base pair by another result in point mutation. there are 2 subtype

(a)Transition: -in this case, a purine (or pyrimidine) is replaced by another.
(b)Trans-version: -these are characterized by replacement of a purine by a pyrimidine or vice versa.

- **Frameshift mutation**: -
  these occur when one or more base pair are inserted in or deleted from the DNA, insertion **or deletion mutation** (11)

**Amino acid:**

Proteins, including structural proteins and enzymes, are made up of amino acids. Additionally, they serve as the structural foundation for important nitrogen-based substances such hormones, melanin, cytochromes, neurotransmitters, nucleotides, and nucleic acids, among others. The body uses amino acids effectively through a variety of processes, including energy production, transamination, and recycling. Only a small portion of protein intake is lost in urine or faeces in healthy people who eat a normal diet. The building blocks of proteins, amino acids, are essential for both healthy cellular operation and the emergence of hereditary illnesses. Defects in production, breakdown, or transport of amino acids can result in disorders in amino acid metabolism, which can cause a range of hereditary diseases. These conditions may be treated and impact several systems. Protein synthesis and amino acids: Protein synthesis, which is vital to cellular structure, function, and repair, depends on amino acids. Numerous genetic disorders can result from defective protein synthesis, which is frequently caused by imbalances in amino acids or mutations in genes related to protein structure. Proteins can be broken down to produce energy in addition to being structural or functional substances. In order to maintain plasma glucose levels or supply energy during fasting, the carbon skeletons can be utilised to create glucose or its derivatives (such as glycogen or fatty acids) when necessary

**How to occur genetic disease**

Amino acids are the building blocks of all proteins, and cancer alters .New cancer treatments may result from a greater knowledge of these changes. It was previously recognised that cancer could change how the body metabolises sugars to give rapidly expanding tumours more energy. Cancer also rewires the metabolism of amino acids, according to recent reports. Jiyeon Kim and colleagues at the University of Illinois at Chicago, USA, have examined the ways in which cancer appropriates amino acids. They state that in order to balance their generation of harmful reactive oxygen species, tumours need amino acids as an energy source and antioxidant precursor. Additionally, amino acids play a key role in annotating the epigenetic code to either promote or inhibit the production of genes linked to tumours and the tricarboxylic acid cycle (also known as the citric acid cycle or TCA cycle) are examples of central carbon metabolism that have historically been the focus of cancer metabolism. Our comprehension of oncology is still influenced by the metabolism of cancer (12). New findings, research directions, and therapeutic philosophies have emerged with every decade. Glycolysis the crucial part amino acids play in the metabolism of cancer. The vital functions of redox balance, energy regulation, biosynthesis support, and homeostatic maintenance are also fulfilled by amino acids. Amino acid metabolism has gained popularity in cancer research due to its broad range of metabolic activities. Amino acids are also significant fuels that assist the development of cancer, even though glucose is a well-known energy source for cancer growth. For instance, glutamine gives up both amine groups to promote the TCA cycle (13) and is primarily anaplerotic. Other amino acids, besides glutamine, can serve as cells' opportunistic fuel sources. Another source of organic molecules that can support the TCA cycle (14) are branched-chain amino acids (BCAAs), which include valine, leucine, and isoleucine. Derivatives made from amino acids also promote the growth and metastasis of cancer. Polyamines produced from arginine change the expression of genes via influencing the global chromatin structure and the growth of cancer cells. Immunosuppression (15,16) by attaching itself to and turning on the aryl hydrocarbon receptor (AhR) (17–18) transcription factor. This reduces the capacity of regulatory T cells and immune-tolerant dendritic cells (DCs) to identify and destroy cancer cells, (19). Reactive oxygen species build up as a result of cancer cell proliferation, which can harm macromolecules and ultimately cause cell death. Cancer cells use glutathione production from glutamate, glycine, and cysteine to mediate redox equilibrium in order to combat this (20-21). One significant family of enzymes for cancer is transaminases. Transaminases enable the utilisation of the many functionalities of amino acids from irregular sources by promoting the interconversion of amino acids. For pancreatic cancer cells to develop and maintain redox equilibrium, aspartate transaminase (AST) or glutamic oxaloacetic transaminase (GOT1 and 2) is necessary (22). Phosphoserine aminotransferase 1

(PSAT1) levels have been linked to a poor outcome in colorectal cancer (23). A common characteristic of many malignancies is the overexpression of EAA transporters to fulfil the high demand for essential amino acids (EAAs) to support cancer cell growth (24–25).

**Review Literature :-**

**Early Foundations: The Inception of Controlled Drug Delivery (1950s–1980s)**

The introduction of the Spansule sustained-release capsule technology in 1952 marked the beginning of modern drug delivery technology. This technology delivers a drug for 12 hours after oral administration by releasing the first dose immediately and the remaining dose gradually. **(26)**

**The Development of Molecular and Polymer-Based Targeting in the 1980s and 1990s**

Up until the 1980s, the market and drug delivery industry were dominated by oral and transdermal formulations that offered small molecules therapeutic durations of up to 24 hours. The era of PEGylating began in 1990 with the release of Adagen, the first PEGylated protein. This was followed by the release of Doxil (doxorubicin in PEGylated liposome) in 1995, used for cancer treatment. Movantik (PEGylated naloxone-naloxegol) in 2014, and Onpattro (Patisiran-siRNA in PEGylated lipid nanoparticle) in 2018. In 1974, InFed (iron-dextran complex injection) and in 2005, Abraxane (paclitaxel-albumin complex) improved drug solubility. Were two examples of drug-polymer complexes. Rapamune (a formulation of sirolimus nanocrystals).

Monoclonal antibodies and conjugates

MylotargTM (an antibody-drug combination containing gemtuzumab ozogamicin) were both released in 2000. Represent a leap in genetically targeted delivery. By linking cytotoxic drug to antibodies that bind specific cellular markers, these conjugates enabled selective targeting of cancer cells. The U.S. government also launched the National Nanotechnology Initiative in 2000, and the rest of the globe quickly followed suit.

The National Nanotechnology Initiative (NNI) is a new program that the US government launched in 2000. Nano medicine is the term used to describe its use in the field of drug delivery and discovery. Tumour-targeted medication delivery has been the primary focus of the Nano medicine field since its inception. However, the results have fallen short of expectations, and the quantity of newly approved anticancer compounds nanotechnology enabled the design of nanoparticle (egg. liposome, micelles and nanocrystal) that could exploit the enhance permeability and retention effect in tumour, through and clinical success was limited due to imprecise targeting and low drug accumulation at target site.

**Genetic Disease and Disorder**

Proteins are made up of amino acids, and genetic disorders frequently occur when DNA mutations change a protein's amino acid sequence, impairing its functionality.

DNA mutations:

A gene, which is a section of DNA that codes for a protein, is usually the source of a hereditary disease. These mutations may be insertions, deletions, point mutations (altering a single nucleotide), or more significant structural alterations.

Modified Amino Acid Sequence:

To create a protein, DNA is converted into mRNA, which is subsequently translated into an amino acid chain.

The mRNA codon may be altered by a DNA mutation, which could result in: A missense mutation occurs when one amino acid is swapped out for another (like in sickle cell anaemia, where haemoglobin's glutamic acid is swapped out for valine). A nonsense mutation results in a shortened, non-functional protein by changing a codon to a stop codon.

Protein Dysfunction:

The structure, stability, or function of the protein may be affected by the changed amino acid sequence. For instance, chloride transport is hampered in cystic fibrosis due to mutations in the CFTR gene that result in misfolded or non-functional CFTR proteins. Depending on the gene and mutation, genetic disorders brought on by alterations in amino acids are frequently inherited (e.g., autosomal recessive, dominant, or X-linked). Certain mutations develop on their own. cancer cells need a continual supply of nutrients that maintain aberrant growth and fast division during cancer advancement. For optimal development and function during cell-mediated immunity against pathogen attacks or during the battle against cancer, activated T cells also require a steady flow of nutrients (27). In regions like the tumour that have inadequate access to nutrients and oxygen.

**Genetic illnesses may include:**

Chromosomal:

This type has an impact on the chromosomes, which are the structures that house your genes and DNA in each cell. People with these diseases either have double chromosomal material or lack it altogether.

Complex (multifactorial):

A mix of gene mutations and other factors causes these illnesses. These consist of food, exposure to chemicals, usage of nicotine or alcohol, and some medications.

Single-gene (monogenic):

A single gene mutation causes this category of disorders.

**How Genetically Targeted Drug Delivery System Work**

Genetically targeted system use molecular tool to recognise specific genetic mutations or expression profile associated with disease. Key Strategies Include: -

- RNA-Based Targeting: -
  Small interfering RNA (siRNA)OR antisense oligonucleotides can silence muted genes. RNA-based therapeutics are subsequent due to their unique physiological and physicochemical properties. (28)

RNA plays a crucial role among the three essential biological macromolecule: DNA, RNA and Proteins.

Ribonucleic acid based molecule like antisense oligonucleotide, small interfering RNA(siRNA), and microRNA (miRNA) exert their function by specially binding to mRNA and noncoding RNA via Watson -crick base pairing (29). thus RNA can in theory target any desired gene by choosing the corresponding nucleotide sequence on the target. By contrast, only 0.05% of the human genome has been targeted by currently approved protein-based therapeutics (such as small molecule and antibodies), as the majority of genomic DNA is transcribed into noncoding RNA rather than protein-coding transcripts.' (30) Furthermore, in-vitro transcribed (IVT) m RNA can be utilized for protein replacement therapy or vaccination upon reaching the cytoplasm (31). This Process would not cause permanent genome alteration or pose genetic risk unlike DNA – based therapeutics. (32) RNA aptamers can inhibit protein

activity, much like small-molecule inhibitors and antibodies.as a result, RNA –based therapies expand the scope of drug gable target and are considered highly promising for therapeutic development. (33)

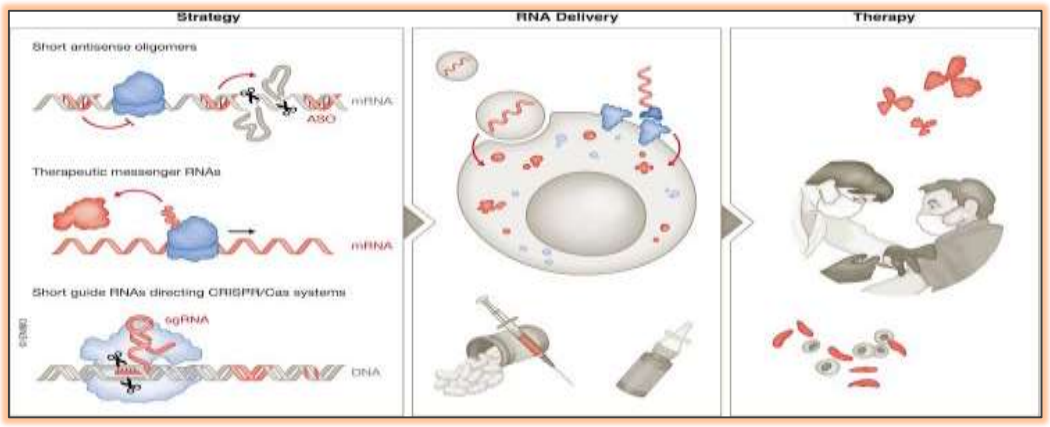


Figure No. 1 Illustrations of Gene targeting

- CRISPR (clustered regularly interspaced short palindromic repeats)/ Cas based delivery: -
  CRISPR-based genome editing allows for the direct modification of target RNA sequence, offering a potential treatment for specific disorder.'
- Ligand-receptor interaction: -Drug carriers ae modified due to certain genetic changes.
- **Technologies Use:**

**1.Nanoparticle in chemotherapy**

The utilization of nanoparticles as antitumor agent carriers is their most promising usage (Couvreur et al., 1990; Kreuter, 1991). The tumours exhibit leaky vasculature and increased endocytic activity**.**and this encourages the accumulation of nanoparticles given intravenously. The "stealth" behaviour that polyoxyethylene imparts can further facilitate and optimize medication delivery to tumour tissues by efficiently promoting extravasation. Using dialykyl polyoxyethylene, and phospholipids, or coating plain nanoparticles with soluble polyoxy-ethylene, can give them a stealthy appearanceNano-medicine identifies the site of disease within the human body and facilitate the targeted delivery of medication, diagnostics, and therapeutics to specific cells. (16)

**Particle Size:**

The fastest and most routine method for determining nanoparticle size is dynamic light scattering (DLS), also known as photon correlation spectroscopy (PCS). DLS measures the Brownian motion of nanoparticles in a suspension and correlates it to particle size via the Stokes-Einstein equation. It's widely used due to its speed, non-invasive nature, and ability to analyse a wide size range (typically 1 nm to 1 µm) in minutes. One potentially significant characteristic of synthetic gene delivery vectors is their complicated size. DNA complexes typically form particulate systems, which range in size from 0.05 to 1 µm.

**2.Viral Vector:**

To enhance protection, uptake, and effectiveness, viral carriers have been improved for targeted gene delivery. These vector are categorised based on how they enter cells: some penetrate the cell nucleus, while other remain in the cytoplasm to exert their effect. These carriers are derived from either from DNA or RNA. (34) Viral carriers that demonstrate gene-specific medication delivery benefit from the very complex viral infection mechanism while avoiding the declaration of an infected area, which causes viral multiplication and a lethal effect on the exposed individual. (35)

**Vectors of retro viruses**:

Retroviruses are among the most widely used viral vectors in gene therapy. system of retrovirus vectors They are using harmless retrovirus vectors with replication defects Plasmids are defined as plasmids that are associated with a retrovirus, a therapeutic gene, and a promoter. A therapeutic gene (DNA) smaller than 3.4 kb can be carried by the plasmovinus. The plasmovirus can produce virus particles with replication defects. Therefore, the target cells must be in a dividing stage in order for retroviral vectors to transmit genes. However, the vast majority of bodily cells are dormant. Viral vectors that infect non-dividing cells have been developed in recent years. Additionally, efforts are underway to include a DNA molecule that encodes for cell receptor protein into retroviral vectors through the creation of an env gene. (the env gene encodes a glycosylated polyprotein of about 160 kDa (160gp) that is subsequently cleaved by a host cell protease to generate the viral envelope protein gp120 and gp41. (11)

**Lentiviruses:**

A subclass of retroviruses known as lentiviruses has the capacity to incorporate itself into the genome of its host.
They are a flexible tool for gene therapy because of their well-known capacity to infect both proliferating and non-dividing cells.
Other Viral Vectors:

**Adeno-Associated Viruses (AAV):**

Human viruses that can integrate into chromosome 19 are known as adeno-associated viruses. It is a tiny, non-pathogenic, single-stranded DNA virus (4.7 kbp. The DNA becomes double-stranded, integrates into the chromosome, and expresses itself as the adeno-associated virus reaches the host cell. therapeutic gene delivery can be effectively facilitated by adeno-associated viruses. Two plasmids and an adenovirus (le helper virus) are used in a unique process to make recombinant viruses. Adeno-associated viruses have been used in some attempts to use therapeutic genes for the treatment of human diseases, such as haemophilia (for the manufacture of blood clotting factor IX) and cystic fibrosis (for the synthesis of cystic fibrosis transmembrane regulator protein) (11)

**2.Non-Viral Vectors: -**

Genes are delivered to different cells and cell populations using non-viral nucleic acid carriers.

Non-viral vectors have characteristics such as being simpler to identify, safe to accumulate, abundant, and potentially administered repeatedly, indicating that the body's defences against them are not very strong [36]. the majority of non-viral carrier's exhibit traits of condensation of positively charged DNA and RNA.

**Other Viral Vector:**

Although less frequent, other viral vectors such as vaccinia virus (VV) and herpes simplex virus (HSV) have also been investigated for use in gene therapy. A number of parameters, such as the target cell type, the desired amount of gene expression, and the possible dangers connected with the vector, influence the choice of viral vector to utilize in a given application

**Some non -viral vector carrier are as follows:**

- **Polymethyl-metha acrylates:**

PMMA nanoparticles function at temperatures that preserve heat-sensitive antigenic materials while maintaining their structure and nature, they have been regarded as the best polymeric systems for vaccination purposes in the presence of antigenic material. Copolymeric meth acrylic acid-based nanoparticles, in addition to PMMA nanoparticles, are also made by the dispersion polymerization method with mixtures of methyl methacrylate and one or more additional derivatives of acrylic acid (such as hydroxyethyl methacrylate, meth acrylic acid, (16) Polymethacrylates are vinyl-based cationic polymers that have been employed for gene delivery in both in vitro and in vivo model systems. The polymer has changed over time to become more poisonous, effective at distributing genes, and biodegradable. To increase the biodegradability of the polymer, it was coupled with a cationic side chain that could be hydrolyse (37).

- **PLGA (Lactic-co-glycolic acid,)**

Lactic-co-glycolic acid, or PLGA, has been considered one of the most effective vectors out of all the ones that could be used. It is a co-polymer of lactic and glycolic acids joined by an ester link. A polymer's weight, size, morphological shape, and components all have an impact on how long DNA entraps in it. A PLGA nanoparticle is helpful in gene silencing due to its efficient cellular absorption, quick endosomal escape, and continuous release of the therapeutic chemical [38]. It has been demonstrated that the PEI-based PLGA formulation has better serum stability and less cytotoxicity [39].

- **Dendrimers**

Dendrimer applications in pharmaceutical and medical chemistry are rapidly becoming popular. A wide range of applications have been investigated, particularly in gene transfection and medical imaging, as well as drug delivery. Dendrimers give a new platform for cellular transfection and manipulation. These are clearly defined, non-toxic, and provide very high efficacy of transfection in vitro. (16) RNA, plasmid DNA, antisense oligonucleotides, and other genomic material can all form complexes with dendrimers. They have a tight molecular structure and are synthetic macromolecules. Delivery systems based on dendrimers have demonstrated great potential as ways to enhance genetic treatments. (40)

- **Nano-carriers:**

Numerous organic and inorganic materials, such as metal, dendrimers, self-assembling amphiphilic molecules, lipids (liposomes, Nano emulsions and solid-lipid nanoparticles), non-degradable and biodegradable polymers, and inorganic semiconductor nanocrystals (quantum dots), can be used to create Nano particulate carriers. (41) (42) (26) It might be necessary for the Nano carriers to enter the targeted cells and transport the payload to subcellular organelles after they have been delivered to the particular sick organ or tissue (Fig. 3). Either specific or non-specific cell penetrating techniques must be used in this situation (43) The endocytosis process, in which the membrane envelops the Nano carriers to form a vesicle in the cell known as an endosome, is how non-specific cell uptake of Nano carriers takes place. The endosome then transports the material within the cell so that it can combine with lysosomes, which are extremely acidic organelles that are abundant in enzymes that break down things. Lysosomes are highly acidic organelles that are rich in enzymes that break down things. The endosome then transports the contents throughout the cell and can fuse with them. Typically, endocytosed Nano carriers follow a predetermined path before coming together at the nuclear membrane. The therapeutic chemicals in the Nano carrier are discouraged by the acidic endosomal environment. >99% of the internalised DNA may degrade as a result of this gene delivery restriction.By buffering the endosomes to allow for the safe release of their contents, efficient gene transport is accomplished. For instance, the polyatomic carriers' buffering ability may prevent the endosomes from becoming acidic, which would cause them to enlarge and rupture, allowing the contained contents to be safely released. (44,45)

**Passive and active targeting**

Targeting both passively and actively Both passive and active targeting techniques are used for systemic therapy. To avoid non-specific distribution and selectively accumulate the medicine at the place of interest, passive targeting depends on the characteristics of the disease pathology and the delivery mechanism For example, when administered intravenously, Nano carrier systems modified with poly (ethylene glycol) (PEG) or poly (ethylene oxide) (PEO) can preferentially accumulate near the tumour mass due to the hyper-permeability of the newly formed blood vessels. This phenomenon is called the enhanced permeability and retention (EPR) effect. (46) (47).

Compared to administering free drug, the EPR effect of polymer–drug conjugates can result in 10–100 times greater concentrations in the tumour (48). Other illnesses including persistent inflammation and infection have also been shown to exhibit the EPR effect.

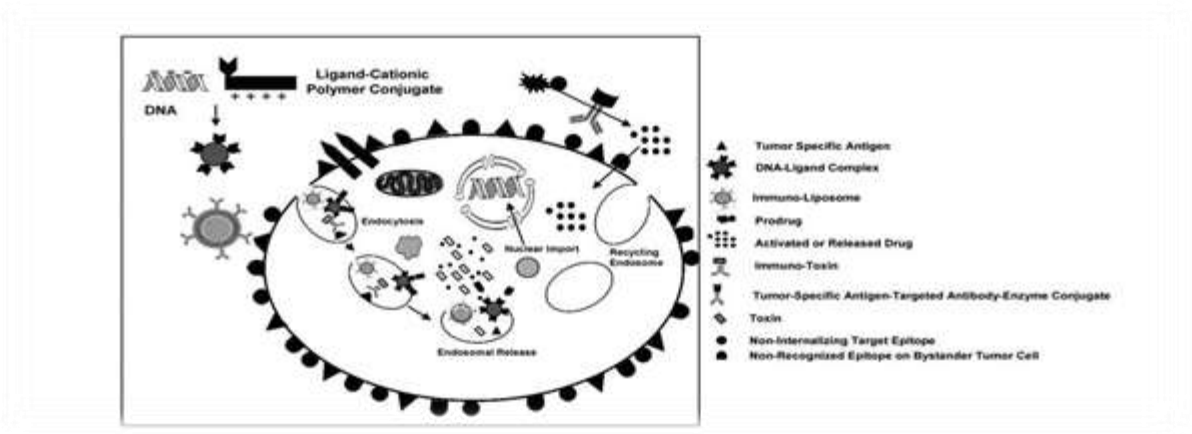


Figure Intracellular Delivery and sub cellular localization of nano carrier

Therefore, it is anticipated that using Nano carriers will also have therapeutic advantages for treating these illnesses (49) Type B gelatine-based nanoparticles delivered passively have proven to be highly successful in systemic gene delivery to solid tumours. (50) In vitro and in vivo transfection of reporter plasmid DNA encoding beta-galactosidase and green fluorescent protein was found to be more successful when the DNA was physically encased in PEG-modified gelatine nanoparticles (51), (52). In addition to PEG modification of Nano carriers to improve circulation time and accomplish passive targeting, active targeting to the illness site depends on coupling a particular ligand on the surface that will be recognised by the cells at the disease site. (53) Using a solid tumour as an example once more, there are a number of methods for altering the surface of Nano carrier systems to enable efficient targeted delivery to the tumour cells or the tumour blood vessel endothelial cells. Tumour cells overexpress certain receptors for improved absorption of nutrients, such as folic acid, vitamins, and carbohydrates, as a result of their fast proliferation. Folic acid-modified Nano carrier surfaces can be directed towards tumour cells that overexpress folate receptors. (54)

Genetically Targeted Drug Administration Agents used in chemotherapy:

An **anthracycline** medication used to treat cancer, **doxorubicin** is frequently delivered to tumour cells specifically using liposomes or nanoparticles. When administered via lipid-based Nano carriers, it has a lower toxicity and is effective against malignancies such as multiple myeloma and Kaposi sarcoma. Utilizing nanoparticles to enhance solubility and target tumour locations, **paclitaxel** is used to treat diseases like ovarian and breast cancer.

**5-Fluoro uracil:**

A chemotherapy medication that has been effectively administered via nanoparticles to improve absorption and bioavailability for colorectal and other malignancies.

**Cisplatin:** Used to treat tumours such as ovarian and lung cancer, however its effectiveness is increased by using nanoparticle delivery to get past resistance brought on by DNA methylation.

**Example of Diseases treated with genetically targeted drug delivery:**

Cancer:- Liposomes, nanoparticles, and virosomes are examples of targeted drug delivery systems that are essential for treating a variety of malignancies, including those of the brain, breast, prostate, and colon.

Cystic Fibrosis:-Gene therapy has been investigated for cystic fibrosis using gene-specific medication delivery methods.

Parkinson's Disease:-Research is being done on gene therapy and drug delivery that targets specific genes.

Huntington's disease:-Drugs that target certain genes are used to treat Huntington's disease.

Cardiovascular diseases: -Gene therapy can regulate the heart's development and function

**Treatment of cancer by using genetically targeting system:**

It is widely accepted that there is a certain amount of genetic predisposition for the development of cancer, but environmental variables also play a significant role. Indeed, several families have been shown to carry genes that are predisposed to cancer. For example, chromosomes 1 and 9 in humans include the genes for melanoma susceptibility. The gene p ^ 53 A protein with a molecular weight of 53 kd is encoded by the gene p ^ 53, hence the name. This gene is thought to create a protein that inhibits the growth of cancer and aids in DNA repair. Unrestricted replication and unchecked cell proliferation can result from specific DNA damage. Under such circumstances, the p-53 gene's encoded protein attaches itself to DNA and prevents replication. As a result, the growth and multiplication of the malignant cells are prevented. Therefore, p ^ 53 functions as a protector of cellular DNA and is a gene that suppresses cancer. The development of cancer is likely to result from any mutation that changes the tumour suppressor function of the p-53 gene. Indeed, the p-53 gene's preventive role against malignancies is confirmed by the changed forms of the gene that were retrieved

from the different tumour cells (breast, brain, colon, bladder, skin, and lung). Environmental variables are thought to be responsible for p-53 gene alterations, which can eventually result in cancer. Certain p-53 gene mutations may be inherited, which likely explains why some malignancies run in particular families.

**Colon cancer**

Colon cancer genes Given that it occurs in certain family; colon cancer seems to have a genetic component. A gene associated with hereditary nonpolyposis colon cancer, or HNPCC (also known as Lynch syndrome), has been discovered by some researchers. When DNA is damaged, the protein that this gene encodes serves as a protector and repairs it. But when this protective gene is mutated, a changed protein is created that is unable to repair the DNA damage. HNPCC is the result of this. One in every 200 members of the general population is thought to have this mutated gene. (11)

**Drug used for colon cancer by genetically targeting system**

Krazati (adagrasib): The KRAS-G12C mutation is the target and is found in approximately 4% of colorectal tumours.

**Mechanism:** The KRAS-G12C mutation, which promotes the proliferation of cancer cells, is the target of the KRAS inhibitor adagrasib. By targeting two genetic pathways at once, cetuximab, an EGFR inhibitor, is used in conjunction with it to increase efficacy**.**

**Conclusion:**

With improved selectivity and fewer adverse effects, genetically targeted drug delivery system have long term benefit are in precision medicine. Although advancements in genetic engineering, synthetic biology, and nanotechnology are propelling advancement, issues with scalability, safety, and biological constraints still exist. Realising their full promise in the treatment of genetic abnormalities, malignancies, and chronic diseases will require ongoing research and regulatory development justified heightened efforts and ongoing optimism to incorporate this treatment into our standard toolkit for treating serious human illnesses. the advancements in understanding the roles of miRNAs in cancer. Delivering genetic information to tissues in vivo is the foundation of clinical gene therapy, a widely utilised scientific technique. Compared to previous drug delivery methods, genetically targeted drug delivery systems exhibit increased efficacy, monitoring, medication availability, and distribution. Because it incorporates many carriers and several techniques for plasma membrane penetration, this review emphasises how the genetically targeting delivery system offers a wide range of therapeutic applications and can be superior to alternative therapies. To get better and more desired results, all of these elements can be changed as needed.

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