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Review Article

The Impact Of Nanotechnology On Drug Delivery System

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ABSTRACT

Nanotechnology supramolecular scale in the range of 1-100 nanometers. Nanotechnology is a modern science that is gaining immense popularity and applications in multiple scientific fields such as surface science, micro fabrication, semiconductor, molecular biology, electronics, medicine, consumer products and many other industrial and military applications. Nanotechnology also raises various issues like the impact of nanoparticles on the environment, toxicity, regulation of nanotechnology and nanoparticles and the overall impact of nanotechnology on global economics. The present article focuses on the past, present and future of nanotechnology with a special focus on the application of nanotechnology in various fields of medicine. Nanotechnology is the exploitation of the unique properties of materials at the nanoscale. Nanotechnology has gained popularity in several industries, as it offers better built and smarter products. The application of nanotechnology in medicine and healthcare is referred to as nanomedicine, and it has been used to combat some of the most common diseases, including cardiovascular diseases and cancer. The present review provides an overview of the recent advances of nanotechnology in the aspects of imaging and drug delivery.

INTRODUCTION

The engineering and production of materials at the atomic and molecular scale is known as nanotechnology. According to the National Nanotechnology Initiative, structures roughly in the 1−100 nm size range in at least one dimension are referred to be nanotechnology. Despite this limit on size, structures as small as a few hundred nanometers are frequently referred to as nanotechnology. These structures are created through top-down or bottom-up engineering of individual components. In this work, we primarily address the use of nanotechnology in medication delivery and identify a number of promising areas where new and developing nanotechnologies may open up whole new therapeutic avenues. [1] Nanotechnology is the application of such research to build or change innovative materials. Nanoscience is the study of the special properties of materials between 1-100 nm. and the use of such

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research to produce or alter novel objects is known as nanotechnology. Nanomaterials can be created through the manipulation of atomic-scale structures. Among other applications, the domains of electronics and health can make advantage of nanomaterials' distinctive optical, electrical, and/or magnetic capabilities at the nanoscale. Because they have a high surface area to volume ratio, nanomaterials are special. Nanomaterials are regulated by the principles of quantum mechanics rather than the traditional laws of physics and chemistry, in contrast to typical large-scale constructed objects and systems. Nanotechnology can be defined as the engineering of functional systems and useful objects at the molecular or atomic scale. [2], Nearly all sectors and fields have been significantly impacted by nanotechnologies. society has to offer.

i) More robust,

ii) Cleaner and safer,

iii) more durable

iv) Smarter goods for the medical, telecom, daily living, agricultural, and other industries. [3] There are two main categories into which nanomaterials are used in common products. Initially, incorporating nanoparticles into an already-existing product can enhance the composite goods' overall efficacy by contributing a couple of its unique attributes. Otherwise, nanomaterials such as nanoparticles and nanocrystals can be directly used to create powerful and advanced electronics because of their special characteristics. The benefits of nanoparticles may have an impact on practically every industrial area in the future. [4] Nanomaterials are useful in a variety of common products, including electronics, tyres, sporting goods, cosmetics, and sunscreens. Furthermore, nanotechnologies have transformed medical advancements, particularly in the areas of medication distribution, imaging, and diagnostic techniques. Nanomaterials enable the mass production of goods with improved functionality at much reduced costs, as well as cleaner, greener manufacturing processes that improve healthcare and lessen the environmental effect of manufacturing. [5]

Literature review:

1. Tushar Madan et al.: Thoroughly examines the critical role that nanotechnology plays in contemporary healthcare as an intelligent drug delivery method. Madaan probably studies the complex characteristics of nanoscale materials and their use in targeted medication delivery systems with an eye toward enhancing treatment outcomes and minimizing side effects. Through the utilisation of nanoparticles' distinct features, including their elevated surface area-to-volume ratio and modifiable surface characteristics, scientists can create intricate drug delivery systems that exhibit accurate targeting and regulated release. It is anticipated that Madaan's review would showcase current developments in medication delivery facilitated by nanotechnology, examining creative approaches to improve drug solubility, stability, and bioavailability. Furthermore, the review might clarify how nanotechnology can support personalized medicine strategies that meet the demands of specific patients and maximize the effectiveness of treatments. Taken together, Madaan's. All things considered Madaan's research offers a thorough summary of the revolutionary effects of nanotechnology on contemporary healthcare delivery.

2. Sneh Lata, et.al: By increasing medication solubility, stability, and targeting—all of which improve therapeutic efficacy and minimize side effects—nanotechnology has completely changed the way drugs are delivered. Due to their capacity to encapsulate medications, shield them from deterioration, and transport them to certain locations inside the body, liposomes, dendrimers,

and nanoparticles are among the most studied nanocarriers. By targeting and regulating the release of nanoparticles to sick tissues, their surface modification reduces systemic toxicity. Furthermore, co-delivery of several medications or therapeutic agents is made possible by nanotechnology, which strengthens their synergistic effects. However, further research is needed to address issues like scalability, regulatory obstacles, and potential toxicity. Overall, medicine delivery has a great deal of promise thanks to nanotechnology.

Drug Delivery System:

Drugs have been used for millennia to cure illnesses, enhance well-being, and prolong the lives of both people and animals. The concoctions of therapeutic herbs and other chemicals found in antiquity have substantially changed into the substances utilized as medications today. Drug delivery methods have changed along with the science of medicine, becoming the extensively studied and refined chemical substances that pharmaceutical corporations manufacture today.[6] However, until the last several decades, there was little discussion on how patients would receive these treatments. The field of medicine effectiveness has seen significant changes due to advancements in drug delivery, and further significant developments are expected in the near future.[7]

- **What is Drug Delivery?**

The technique of giving medication or other pharmacological chemicals to produce a therapeutic effect is known as drug delivery. Over the past few decades, drug delivery has gained prominence in the pharmaceutical business due to the discovery that a medicine's efficacy can be affected by its distribution method. Therefore, it is feasible to optimize the drug throughout the body by determining which delivery method is most appropriate for a given treatment.

- **What is a Drug Delivery System?**

A formulation or apparatus that presents a drug to the body for administration and absorption is called a drug delivery system. By regulating the location, rate, and time of release of a specific medicine within the body, drug delivery systems aim to improve safety and efficacy while delivering a therapeutic dose of medication. Over the past 60 years, drug delivery techniques have seen significant change. Particularly in the past 12 years, there have been significant advances in medication delivery technology. For example, more sophisticated drug delivery technologies, such transdermal patches, can target a specific area with a medicine more precisely, which often results in simpler, more precise, and lower overall dosages. These kinds of drug delivery systems can also result in a medication absorption that is more in line with the place and mode of action. Different patient needs led to the development of different medication delivery systems that are utilized in both medical and home care settings, and researchers are always coming up with novel techniques.[8]

- **What Are Drug Delivery Devices?**

The physical agents that are a part of the drug delivery system are called drug delivery devices. This category includes the vast array of devices that individuals use on a daily basis. Novel drug delivery systems and combination products are being developed in the pharmaceutical industry today for a variety of purposes, one of which is to enable patients to self-administer some prescriptions at home, thereby improving adherence to prescribed regimens. Modern medicine and technology are changing the market for combo products. All combination devices, particularly those for drugs, have to adhere to tight regulations. [9] It is fairly usual to use these kinds of gadgets both inside and outside of healthcare settings. Here are a few instances:

Prefilled needles and auto-injectors
• Pumps for infusion
• MDIs, or measured dosage inhalers
• Nebulizers
• Sprays for the nose
• Eyedroppers
• IUDs, or intrauterine devices
• Patches applied topically

- **How Does Drug Delivery Work?**

Medication or drugs are delivered to the body so they can be absorbed. However, not every delivery technique is made equally. Particularly in the domain of how medications flow through cells and tissue, biomedical engineers have made a substantial contribution to our understanding of the physiological barriers that might result in ineffective drug delivery. These scientists and engineers have also made enormous contributions to our understanding of drug delivery mechanisms. Modern drug delivery systems and gadgets are made to do more than just deliver a medication to the patient. Certain systems, for instance, are made to deliver medication locally as opposed to systemically. Using a topical ointment on a skin rash or administering a lidocaine injection prior to a dental operation are examples of common localized delivery techniques. While there are alternative methods for delivering localized therapy, some medications can only be administered systemically. Drug administration techniques have evolved in the modern era to accommodate a variety of user needs.

- **What Are the Types of Drug Delivery Routes?**

Depending on the demands of the patient and the drug's intended use, there are differences in the way medications are absorbed by the body and how they are delivered. A medication can enter the body through a variety of pathways. The most popular method of medicine delivery is oral. Oral drug administration is generally safe, easy, and cost-effective for a wide range of pharmaceuticals that can be taken as liquids, tablets, or capsules. Additional typical delivery routes consist of:

- **Injection**: administered intravenously, intramuscularly, intrathecally, subcutaneously, or into a vein or muscle.
- **Nebulization**: The process of breathing in air through the nose and mouth (inhaled) or both.
- **Topical**: applied topically to the skin for a localized effect; • Transdermal: applied through the skin via a patch for a systemic impact; • Nasal: sprayed into the nostril(s) and absorbed via the nasal membranes.
- **Rectal:** inserted to absorb into the bloodstream by passing through the rectum
- **Sublingual**: positioned beneath the tongue to enter the bloodstream quickly

Every medicine delivery method has benefits and drawbacks. The fact that every treatment must be administered via the most suitable and efficient method contributes to the importance of continuous improvements in medication administration.[10]

- **What Are the Four Drug Delivery Methods?**

The time it takes for a drug to be released into the body is another crucial aspect of medication delivery. There are various ways that medication transfer might take place since diverse qualities have the ability to alter and regulate drug delivery.

• **Immediate Release:** A dose form intended to provide a quick and thorough release of the medication.

• **Non-Immediate Release:** This dose type is used for medications that need some time to fully release after being administered. By improving the efficacy, safety, and patient compliance surrounding the drug, these and other delivery techniques may improve its performance and eventually improve patient outcomes.[11]

Nanotechnology in Medicine and Healthcare

The word "nanomedicine" describes the use of nanotechnologies in healthcare and medicine. In particular, nanomedicine prevents, detects, tracks, and treats illnesses using nanoscale technologies and nanoenabled methods. Medical nanotechnologies have shown great promise in imaging and diagnostic tools, drug delivery, tissue engineering, implants, and pharmaceutical therapeutics. They have also improved the treatment of a number of diseases, including cancer, diabetes, musculoskeletal disorders, mental and neurological disorders, bacterial and viral infections, and cardiovascular disorders.[12]

Types of Nanoparticles

Numerous nanomaterials and nanoparticles have been studied and authorized for use in medicine. We'll talk about a few popular kinds of nanoparticles below. Lipids and other amphiphilic molecules combine to form micelles, which are amphiphilic surfactant molecules. Hydrophobic therapeutic drugs can be included into micellar spherical vesicles, which spontaneously aggregate and self-assemble into a hydrophilic outer monolayer and a hydrophobic core in water conditions. Because of the special qualities of micelles, hydrophobic medications can be made more soluble, increasing their bioavailability. Micelles have diameters ranging from 10 to 100 nm. Micelles can be used as therapeutic, imaging, contrast, and delivery agents, among other purpose.[13]

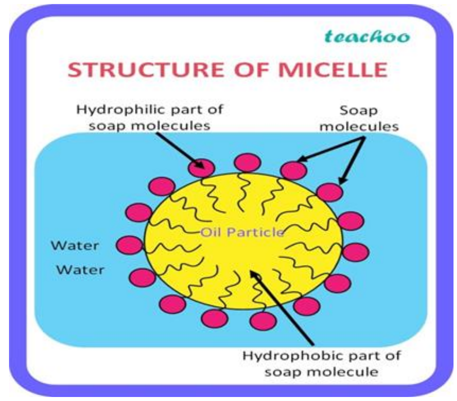


Fig.1

Liposomes

Liposomes are spherical vesicles made of lipid bilayers that range in size from 30 nm to several microns. Hydrophilic therapeutic compounds can be incorporated into the liposomal membrane layer of liposomes, while hydrophobic agents can be incorporated into the aqueous phase. Because liposomes can have their surface features changed by adding polymers, antibodies, or proteins, liposomes can be used to incorporate macromolecular medications such solid metals and nucleic acids. The first FDA-approved nanomedicine for the treatment of breast cancer is poly (ethylene glycol) (PEG)ylated liposomal doxorubicin (Doxil), which increases the effective drug concentration in malignant effusions without requiring an increase in the total dosage.[14]

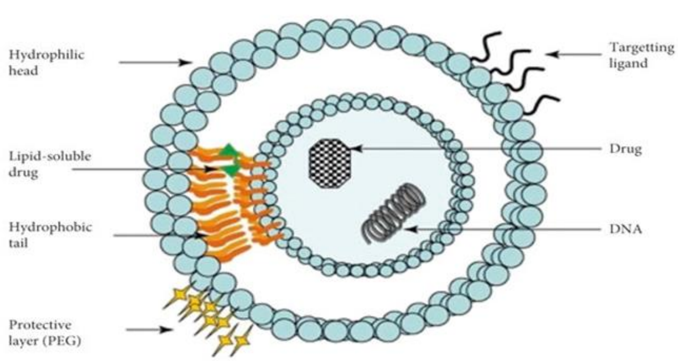


Fig.no.2

Dendrimers

Dendrimers are macromolecules made up of external functional groups and branched repeating units that extend from a central core. These functional groups, which can be anionic, neutral, or cationic terminals, can change the structure's overall composition as well as its chemical and physical characteristics. Dendrimers are highly bioavailable and biodegradable because therapeutic substances can be enclosed within the inner space of dendrimers or bonded to the surface groups. It has been demonstrated that dendrimer conjugates containing saccharides or peptides have better antibacterial, antiprion, and antiviral qualities as well as increased solubility and stability when therapeutic medications are absorbed. Because of their transformable properties, polyamidoamine dendrimer-DNA complexes, also known as dendriplexes, have been studied as gene delivery vectors and show promise for improving drug efficacy, targeted drug delivery, and successive gene expression. Dendrimers are also promising particulate systems for biomedical applications, including imaging and drug delivery.[15]

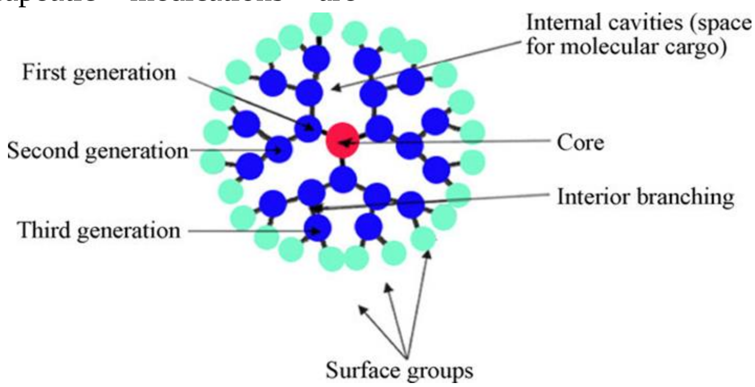
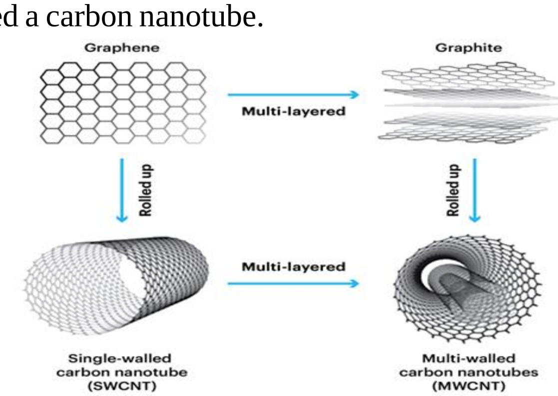


Fig.no.3

Carbon nanotubes

Carbon nanotubes are spherical molecules made of sheets of carbon atoms wrapped up into a single layer (graphene). They may consist of many concentrically connected nanotubes or have one or more walls. Carbon nanotubes can reach remarkably high loading capacities as drug carriers because of their large exterior surface area. Additionally, carbon tubes are attractive as biological sensors and imaging contrast agents due to their special optical, mechanical, and electrical capabilities. An allotrope of carbon that resembles a tube of carbon atoms is called a carbon nanotube. Despite being incredibly strong and hard to break, carbon nanotubes are nonetheless rather light. One of the most studied nanomaterials is carbon nanotubes because to their remarkable mechanical, electrical, and thermal capabilities. For radios and other electromagnetic devices, CNTs can serve as antennas. Commercial electric motor brushes are made of conductive carbon nanotubes. They take the place of conventional carbon black. Because the nanotubes can extend through the brush's plastic matrix, they increase thermal and electrical conductivity.[16]

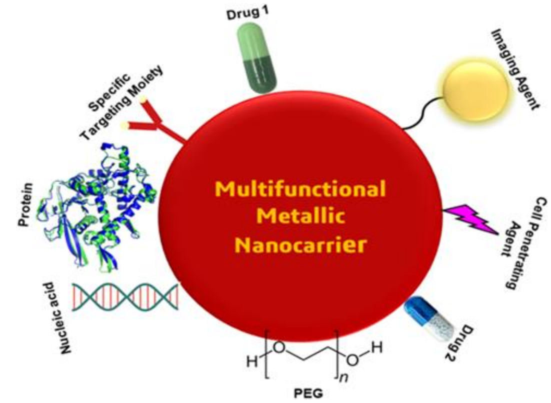


Fig, no.4

Metallic nanoparticles

Metallic nanoparticles include iron oxide and gold nanoparticles. Iron oxide nanoparticles consist of a magnetic core (4-5 nm) and hydrophilic polymers, such as dextran or PEG. Conversely, gold nanoparticles are composed of a gold atom core surrounded by negative reactive groups on the surface that can be functionalized by adding a monolayer of surface moieties as ligands for active targeting. Metallic nanoparticles have been used as imaging contrast agent in laser-based treatment as optical biosensors and drug delivery vehicles.

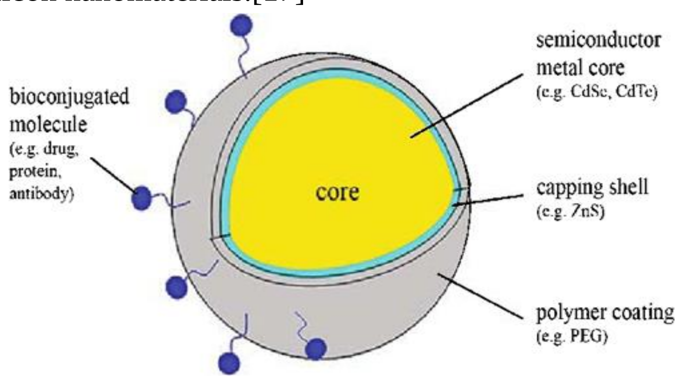
CNTs can act as antennas for radios and other electromagnetic devices. Conductive CNTs are used in brushes for commercial electric motors. They replace traditional carbon black. The nanotubes improve electrical and thermal conductivity because they stretch through the plastic matrix of the brush. The metallic nanoparticles include silver, copper, gold, zinc, platinum, and palladium nanoparticles, whereas the nonmetallic nanoparticles are titanium dioxide, zinc oxide, and cadmium oxide. Carbon-based nanomaterials include multiwalled carbon nanotubes and carbon–silicon nanomaterials.[17]



Fig, no.5

Quantum dot

Quantum dots (QDs) are fluorescent semiconductor nanocrystals (1-100 nm) and have shown potential use for several biomedical applications, such as drug delivery and cellular imaging. Quantum dots possess a shell-core structure, in which the core structure is typically composed of II-VI or III-V group elements of the periodic table. Due to their distinctive optical properties and size, with high brightness and stability, quantum dots have been employed in the field of medical imaging.[18]



Nanotechnology in drug delivery

Drugs are usually administered to a specific target place as part of therapy. External therapeutic approaches, such radiation therapy and surgery, are used when there is no internal channel for drug administration. These techniques are frequently applied singly or in concert to fight illnesses. Therapy's constant objective is to eradicate tumors or the source of disease in a persistent way. By creating new drug delivery mechanisms, nanotechnologies are making a significant contribution to this field. Several of these techniques have been shown to be useful in clinical settings and are currently in use. For instance, doxorubicin, a medication with a high level of toxicity, can be given directly to tumor cells via liposomes (Doxil) without harming the kidneys or heart. Furthermore, paclitaxel combined with polymeric mPEG-PLA micelles (Genexol-PM) is utilized in the chemotherapeutic management of breast tumors that have spread. The enhanced reticuloendothelial system evasion, favorable pharmacokinetics, and improved in vivo distribution are the main reasons for the success of nanotechnologies in drug administration.[19]

Both the capacity to target and control drug release are essential components of an ideal drug delivery system. By properly targeting and eliminating dangerous or malignant cells, side effects can be greatly decreased and treatment efficacy can be guaranteed. Furthermore, medication side effects might be lessened with controlled drug release. Because of their small size, which enables intravenous and other delivery methods, nanoparticle drug delivery systems have the advantage of reduced irritating reactions and improved penetration within the body. Adhesing nanoscaled radioactive antibodies complementary to antigens on the cancer cells with pharmaceuticals enables the specificity of nanoparticle drug delivery systems.

i) medication delivery to the intended location

ii) uptake of low solubility drugs summarizes the advantages of nanoparticles over conventional fine particles.[20]

At many different levels, including materials, systems, and devices, nanotechnology is being developed. Nanomaterials represent the most innovative level of information currently found in research and commercial applications. A small entity that functions as a single, cohesive unit in terms of its attributes and mobility is referred to as a particle in nanotechnology. It can be divided into fine and ultrafine particle categories based on size. Fine particles range in diameter from 100 to 2500 nanometers, and ultrafine particles are smaller, falling between 1 and 100 nanometers. Like ultrafine particles, nanoparticles are likewise sized between 1 and 100 nanometers. It is possible for nanoparticles to have size-related characteristics that are purposefully different from those seen in bulk materials and fine particles. As a result, nanoparticles are smaller than a few hundred nm. Their physical characteristics significantly alter as a result of this size decrease when compared to bulk material qualities. They may consist of a mixture of materials, minerals, metals, or polymers. Nanoparticle research is currently a hot topic in science because to its many potentiale uses in optical, electronic, and biological domains. The attraction of nanoparticles stems from their distinct and significant characteristics, including a surface to mass ratio significantly greater than that of other materials and particles, the capacity to adsorb and transport other substances like drugs, probes, and proteins, and the ability to catalytically promote reactions.[21]

➢ **Advantages**

It is possible to simply modify the particle size and surface properties of nanoparticles after parenteral delivery to accomplish both passive and active medication targeting.

• By attaching targeting ligands to particle surfaces or using magnetic guidance, site-specific targeting can be achieved. This leads to high drug therapeutic efficacy and fewer side effects.

• During transportation, they control and sustain release of the drug and at the localization site, altering distribution of the drug and subsequent clearance of the drug. Oral, intraocular, parenteral, and nasal administration are among the modes of administration that the system can be utilized for.[22]

Preparation of nanoparticles

Based on the medicine to be loaded and the physicochemical characteristics of the polymer, the best preparation technique for nanoparticles is chosen. The following are the main techniques for preparing nanoparticles:

a. Emulsion-Solvent Evaporation Method;

This approach is usually used to prepare the nanoparticles. This procedure mostly involves two steps. Emulsification of the polymer solution is necessary as the initial step in an aqueous phase. In the second stage, however, the polymer solution evaporates and the precipitation of the polymer is induced, resulting in the formation of nanospheres. Ultracentrifugation is used to collect the nanoparticles, which are then lyophilized for storage after being cleaned with distilled water to eliminate any remaining medication or residue. 18High pressure emulsification and the solvent evaporation method are other names for this process. 19 To remove organic solvent, this procedure entails homogenization under high pressure and general stirring.20 The size can be regulated by varying the temperature, the kind and quantity of the dispersion agent, the rate of stirring, and the viscosity of the organic and aqueous phases. 21 However, this technique can be used with lipid-soluble medications, and scale-up concerns impose limitations. PLGA24, cellulose acetate phthalate25, EC26, Poly (β-hydroxybutyrate) (PHB)22, Poly (caprolactone) (PCL)23, and PLA are the polymers employed in this process.[23]

b. Double Emulsion and Evaporation Method:

The primary shortcoming of this approach is the poor trapping of hydrophilic medicines. Consequently, the double emulsion method is used to encapsulate hydrophilic drugs. This method involves vigorously churning an organic polymer solution and adding aqueous drug solutions to create water-in-oil emulsions. After creating a mixed emulsion (w/o/w) by constant stirring, this w/o emulsion is introduced to another aqueous phase. The solvent is then eliminated by evaporation, and nanoparticles can be separated by rapidly centrifuging the mixture. The produced nanoparticles need to be cleaned before lyophilization. The amount of polymer, the volume of the aqueous phase, the concentration of the stabilizer, and the amount of hydrophilic medication included are the variables used in this approach. These factors also have an impact on how nanoparticles are characterized.[24]

c. Salting Out Method:

This method of separating the water-miscible solvent involves salting-out from an aqueous solution. Polyvinylpyrrolidone (PVP) or hydroxyethyl cellulose as a colloidal stabilizer are first dissolved in a solvent, which is then followed by the addition of the saltingout agent (electrolytes, such as calcium chloride, magnesium chloride, or sucrose as non-electrolytes) and the drug to create an aqueous gel that is emulsified. To enhance the solvent diffusion, which signals the creation of an aqueous phase, this oil in water emulsion is diluted with water. nanospheres. Numerous variables can be changed, including the concentration of the electrolyte, the amount of polymers in the organic phase, the kind of stabilizer, the velocity of stirring, and the ratio of the internal to exterior phases. This method produces PLA, poly(methacrylic) acids, and ethyl cellulose with great efficiency and ease of scaling up. nanospheres Since salting out doesn't require a rise in temperature, it might be helpful for materials that are sensitive to heat. The limitations of this approach include a limited application to lipophilic drugs and the need for lengthy washing procedures for nanoparticles.[25]

d. Emulsions Diffusion Method

To prepare nanoparticles, emulsions diffusion method is another method which iscommonly used. The encapsulating polymer is dissolvedin a solvent which is partially miscible with water such as propylene carbonate, benzyl alcohol and the initial thermodynamic equilibrium of both liquids saturated with water should be ensured.

Subsequently, The polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer, leading to solvent diffusion to the external phase and according to the oil-topolymer ratio nanospheres or nanocapsules are formed. Finally, according to boiling point the solvent is removed by evaporation or filtration. This technique has several advantages, such as high reproducibility (batch-to-batch), no requirement of homogenization, high encapsulation efficiencies (generally 70%) simplicity, narrow size distribution and ease of scale-up However, this approach has significant disadvantages, such as large amounts of water that must be removed from the suspension and decreased encapsulation efficiency during emulsification due to water-soluble drug leakage in the saturated-aqueous exterior phase. Cyclosporine (cy-A-), loaded sodium glycolate nanoparticles, mesotetra (hydroxyphenyl) porphyrin-laden PLGA (p-THPP) nanoparticles, and doxorubicin-loaded PLGA nanoparticles are a few examples of drug-loaded nanoparticles that were created using this technology.[26]

e. Solvent Displacement/Precipitation method

The precipitation of a preformed polymer from an organic solution and the diffusion of the organic solvent in the aqueous medium, either with or without a surfactant, are examples of solvent displacement. Polymers, drugs, and lipophilic surfactants are dissolved in a semi-polar water miscible solvent, like ethanol or acetone. The solution is then injected or poured while being stirred magnetically.into an aqueous solution-containing stabilizer. Rapid solvent diffusion causes the formation of nanoparticles. Subsequently, the solvent is extracted from the suspension under low pressure. The pace at which the organic phase is added to the aqueous phase has an impact on the size of the particles as well. It was found that drug entrapment and particle size both decreased with increased mixing rate. The majority of medications that are poorly soluble can be effectively treated using nano precipitation. The size of the nanospheres and the release of the drug can be efficiently regulated by varying the production conditions. While varying the polymer's concentration produces good yields of nanospheres with lower sizes.[27]

f. Polymerization method

In this approach, the medication is integrated either by adsorption onto the nanoparticles or by dissolving in the polymerization medium after the monomers are polymerized in an aqueous solution. By using ultra centrifugation, the stabilizers and surfactants used in the polymerization process are eliminated from the nanoparticle suspension. The particles are then re-suspended in an isotonic solution that is surfactant-free. This method has been published for the production of polybutyl cyanoacrylate or poly(alkylcyano acrylate) nanoparticles. The concentration of the stabilizers and surfactants utilized influences the formation of nanocapsules and their particle size.[28]

g. Coacervation or ionic gelation method

Much study has been done on the creation of nanoparticles employing hydrophilic biodegradable polymers like gelatin, chitosan, and sodium alginate. a technique created by Calvo and associates for ionic gelation to produce hydrophilic chitosan nanoparticles.39, 40 Two aqueous phases comprise the procedure: one phase comprises the polymer chitosan, while the second phase contains a polyanion, such as sodium tripolyphosphate. This approach creates coacervates with an anometer size range by interacting the positively charged amino group of chitosan with the negatively charged tri polyphosphate. Coacervates are formed when two aqueous phases interact electrostatically, and ionic gelation, which occurs at room temperature ionic interaction circumstances, causes a liquid to turn into a gel.[29]

Different Routes of Drug Delivery System:

The technique of delivering a pharmaceutical ingredient to produce a therapeutic effect in either people or animals is known as drug delivery. The importance of using nasal and pulmonary medication delivery channels for treating human diseases is growing. These delivery methods offer viable substitutes for parenteral medication administration, especially in the case of peptide and protein therapies. Numerous drug delivery methods have been developed for this reason, and pulmonary and nasal delivery are now being researched. These comprise, among other things, cyclodextrins, liposomes, proliposomes, microspheres, gels, and prodrugs. Biodegradable polymer-based nanoparticles provide certainty in meeting the strict specifications imposed on these delivery methods.characteristics, including the capacity to transform into an aerosol, stability against forces produced during aerosolization, biocompatibility, targeting of particular lung cell populations or places, controlled release of the medication, and disintegration within a reasonable amount of time.[30]

A. Beaded Delivery Systems:

Beaded delivery formulations are a further technique to provide long-acting drug levels associated with the ease of once-daily dosing, albeit they are not utilized in conjunction with oxybutylin. This system is marketed under the name Detrol LA (Pharmacia, Peapack, NJ) and has been effectively linked to tolterodine tartrate. The beaded system is basically made up of several tiny, inert beads made of polystyrene or some similar material. The delivery capsule containing the active medication is placed on top of the beads. This system's drug delivery is acid sensitive since the drug's release from the drug levels depends on the acidity of the stomach. A pharmacokinetic pattern that is akin to a zero-order pattern is produced by this procedure; C max is attained 4–6 hours after consumption, and sustained levels are shown for 24 hours following the initial dose. Detrol LA exhibits comparative advantages to immediate-release tolterodine in terms of both efficacy (improved rates of incontinence) and tolerability. The LA formulation produced 18% fewer incontinence episodes than the immediate-release tolterodine in a double-blind, placebo-controlled, randomized study involving 1529 patients. Both formulations, however, were statistically better than the placebo in terms of decreasing frequency of urination and increasing volume of urine that was voided.[31]

B. Liposomal and Targeted Drug Delivery System

In theory, drug delivery systems can give anticancer medications increased efficacy and/or decreased toxicity. The "enhanced permeability and retention" effect can be used by long-circulating macromolecular carriers, like liposomes, to achieve preferential extravasation from tumor arteries. Liposomal anthracyclines, which include forms with much extended circulation such liposomal daunorubicin and pegylated liposomal doxorubicin, have achieved highly effective drug encapsulation, leading to considerable anticancer activity with reduced cardiac toxicity. Treatment for breast cancer with tigelated liposomal doxorubucin has demonstrated significant success when used alone or in conjunction with other chemotherapeutics. More liposome structures are being created to deliver different medications. True molecular targeting will be a feature of the next generation of delivery systems; immunoliposomes and other ligand-directed structures are examples of how biological elements with tumor identification capabilities might be integrated with delivery technology.[32] As was previously said, the liposomal drug delivery methods that are now approved offer stable formulation, enhanced pharmacokinetics, and a certain amount of "passive" or "physiological" targeting to tumor tissue. These carriers do not, however, specifically target tumor cells. In addition to shielding liposomes from unfavorable interactions with cell membranes and plasma proteins, the design changes that set them apart from reactive carriers like cationic liposomes also stop interactions with tumor cells. Rather, liposomes stay within the tumor stroma as a drug-loaded depot following their extravasation into the tumor tissue. Eventually, phagocytic or enzymatic destruction of liposomes results in the release of medication, which diffuses into tumor cells. The upcoming generations of drug carriers are being developed with the ability to directly target cancer cells molecularly through interactions mediated by antibodies or other ligands.[33] A method for delivering drugs with molecular targeting is immuno liposomes, which are made of conjugated mAb fragments and liposomes. Fab' or scFv fragments attached to long-circulating liposomes have been used to create anti-HER2 immunoliposomes. Anti-HER2 immunoliposomes bound and internalized in HER2-overexpressing cells with efficiency in preclinical trials, leading to effective intracellular delivery of encapsulated drugs. In addition to demonstrating a markedly superior efficacy over all other treatments tested (free doxorubicin, liposomal doxorubicin, free mAb [trastuzumab], and combinations of trastuzumab plus doxorubicin or liposomal doxorubicin), anti-HER2 immunoliposomes loaded with doxorubicin also demonstrated potent and selective anticancer activity against HER2-overexpressing tumors. Scaling up of anti-HER2 immunoliposomes for clinical trials is presently underway.[34]

C. Lung-specific drug delivery

Compared to alternative administration methods, pulmonary medication delivery has a number of benefits for the treatment of respiratory disorders. It is possible to provide medication directly to the lungs by inhalation therapy. Without requiring high dose exposures through alternative modes of administration, the local pulmonary deposition and distribution of the supplied drug allows for a tailored therapy of respiratory illnesses, such as pulmonary arterial hypertension (PAH). For the past ten years, the preferred course of treatment for individuals with PAH has been the intravenous administration of short-acting vasodilators. The relative severity of side effects prompted the creation of novel prostacyclin analogs as well as alternate delivery systems. Iloprost (Ventavis), one such equivalent, is a medication that has been licensed for use in all countries to treat PAH. Because of this compound's pulmonary selectivity, inhaling it is an appealing idea for limiting adverse effects. Unfortunately, iloprost's short half-life necessitates repeated inhalation maneuvers—up to nine times daily. Consequently, a patient's convenience and compliance would be enhanced by an aerosolized controlled release formulation. The use of controlled drug delivery systems in inhalation therapy is becoming more and more appealing. Numerous carrier systems, such as drug-loaded lipid and polymer-based particles, have been created and explored as potential controlled drug delivery formulations to the lung. In nanomedicine, the application of colloidal carrier systems for pulmonary medication administration is gaining attention. [35]

D. Targeting to brain

The fact that mucosal surfaces serve as a primary point of entry for numerous infections is the reason for the increased interest in mucosal vaccination administration. Nasal administration is particularly appealing for vaccination among other mucosal sites because the nasal epithelium has a significant number of immunocompetent cells, low enzymatic activity, and relatively high permeability. Together with these benefits, the nasal route may also provide vaccination procedures that are easier to follow and more affordable while also improving patient compliance. Using nano carriers, antigenic substances can be efficiently transported into the nasal passage. In addition to enhancing defense and expediting antigen transportation, nanoparticulate delivery technologies may enhance immune cell antigen recognition. These are important elements in the best possible presentation and processing of the antigen, and consequently in the formation of an appropriate immune response. Thus, the development of highly effective vaccine nanocarriers presents a viable approach to nasal mucosal immunization.[36]

E. Nano particulate systems for brain delivery of drugs

Using nanoparticles is one method of delivering medication to the brain. Polymeric particles known as nanoparticles are composed of synthetic or natural polymers and range in size from 1 mm to around 1000 nm. Drugs can be chemically bonded, adsorbed to the surface, or bound inside a solid solution or dispersion. To yet, only poly (butylcyanoacrylate) nanoparticles have shown effective in the in vivo administration of pharmaceuticals to the brain. The first medication to be administered to the brain via nanoparticle delivery was hexapeptidedalargin (Tyr-D-Ala-Gly- Phe-Leu-Arg), an opioid-active counterpart of leu-enkephalin. Drug delivery systems utilizing nanoparticles and nanoformulations have previously been used with remarkable effectiveness, and there is yet more promise for these systems involving the use of radiation treatment, anti-tumor, gene. [37]

F. Transdermal delivery

Bioadhesive liposomes containing levonorgestrel have been studied as a controlled drug delivery system.[26] The mesophasic proliposomal system of levonorgestral was developed. Most of the vesicles were unilamellar, however a small number of them were multilamellar. Zero order kinetics applied to the release. Alcohol affected transdermal flux more than oils did. Research carried out in vivo demonstrated the requirement for a loading dose due to a discernible latency period prior to the achievement of therapeutic levels. Proliposome technology was found to function better than the PEG-based ointment approach for topical delivery that is controlled and localized, a liposomal reservoir system containing the local anesthetic benzocaine was developed [33]. A gel and ointment basis was combined with the liposomal suspension. Unlike regular ointment, which releases the medication at a rapidly dropping rate every 24 hours, the systems delivered the medication at a consistent pace every day. Drugs did not absorb through human cadaver skin very quickly. Research carried out in vivo revealed that liposomal formulation has a longer-lasting effect. [38]

G. Colon-specific drug delivery:

The development of dosage forms with site-specific release is required due to the increasing number of protein and peptide medications under research. Colonic absorption is a novel approach to delivering peptide and protein therapeutic molecules, together with pharmaceuticals that are poorly absorbed through the upper gastrointestinal (GI) tract, into the systemic circulation. Oral colon-specific drug delivery techniques have definite advantages over parenteral administration. It goes without saying that colon targeting is advantageous for the topical treatment of colon conditions such as ulcerative colitis, Crohn's disease, and colorectal cancer. Medication administered by chronic colonic release may be useful in the treatment of angina, arthritis, and nocturnal asthma.[39] Colon-specific drug delivery systems have been demonstrated to be beneficial and required. Prodrugs, pH- and time-dependent systems, and microflora-activated systems were the main approaches used to achieve colon-specific delivery in the past. These approaches had varied degrees of success. The triggering mechanism of the delivery system must only respond to the physiological conditions specific to the colon in order for colon medicine administration to be accurate. Ongoing efforts have been focused on creating colon-specific delivery systems with improved site specificity and flexible drug release kinetics in order to achieve a range of therapeutic goals. In terms of achieving in vivo site specificity, design rationale, and manufacturing feasibility, four of the most recently developed colon-specific delivery systems—pressure-controlled colon delivery capsules (PCDCs), CODES, colonic drug delivery system based on pectin and galactomannan coating, and Azo hydrogels—were exceptional. In addition to offering thorough explanations of each of the four systems in particular, this study seeks to evaluate colon-specific drug delivery techniques generally both in vitro and in vivo.[40] The potential for administering therapeutic proteins and peptides as well as drugs for the treatment of localized colon illnesses has made colonic drug delivery increasingly important. For a medication to properly undergo colonic administration, it must be protected against absorption and/or the environment of the upper gastrointestinal tract (GIT). This is followed by a rapid release of the medication into the proximal colon, which is considered to be the optimal site for colon-targeted drug delivery. Colon targeting, of course, is helpful for the topical management of colon diseases like Chron's diseases, ulcerative colitis, amebiasis, and colorectal cancer. Candidates for colon-targeted drug delivery include proteins, oligonucleotides, vaccines, and peptides.[41]

Target Drug Delivery System:

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.[42] The pharmacological characteristics of a medication determine its biological effects in a patient The interactions between the drug and the receptors at the drug's site of action result in these effects. Until the medicine is delivered to its site of action at a concentration and pace that results in the fewest negative effects and the greatest number of beneficial benefits, the effectiveness of this drug-target interaction has been compromised. Targeted medication delivery is a therapeutic approach in which a therapeutic material is delivered to a particular tissue while avoiding contact with other bodily parts. As a result, it exclusively administers the drug to the body's targeted regions. The drug delivery system's superior technology regulates the pharmacokinetic parameters, drug absorption, and drug bioavailability. Four fundamental principles are needed for drug targeting: (1) the drug must be able to be loaded at the target location; (2) it must not be broken down by bodily fluids; (3) it must reach the target site; and (4) it must be released at the designated place at the scheduled time. Depending on the route to be taken, different drug delivery mechanisms must be used at different body areas of interest. [43]

➢ **The advantages of drug targeting**

1. The drug administration regimen gets easier to follow
2. By focusing on a single spot, the drug's toxicity is reduced.
3. A modest dosage can produce the required pharmacological effect.
4. Prevent the effect of first pass.
5. An increase in the medication's absorption from the intended spot.
6. There was no peak or dip in plasma concentration as a result of drug targeting

➢ **The disadvantages of drug targeting**

1. Rapid drug elimination from the body results in high dose frequency.

2. The carrier of the targeted drug delivery system may result in the immune response.
3. The drug delivery system is not localized at the tumor tissue for sufficient time.
4. The diffusion and redistribution of released drugs.

Carries applied for drug targeting a. Carriers systems can be used to target drugs. b. The carriers are the systems needed to deliver entrapped drugs to their intended locations. c. The drug moiety is entrapped by the carriers, who then transfer it to the target site without letting it escape into the non-target site.[44]

➢ **6.1 Different types of carriers for drug targeting**

- **Quantum dots:**

Conduction band electrons, valence band holes, or excitons—bound pairs of conduction semiconductor nanostructure. The presence of an interface between distinct semiconductor materials (as in core-shell nanocrystal systems), the presence of the semiconductor surface (as in semiconductor nanocrystals), electrostatic potentials (produced by external electrodes, doping, strain, and impurities), or a combination of these can all be responsible for the confinement.

Because of their theoretically high quantum yield, quantum dots are especially important for optical applications. One of the most intriguing options for use in solid-state quantum computation and diagnosis, drug delivery, tissue engineering, catalysis, filtration, and textile band electrons and valence band holes—can only move in certain three spatial directions within a quantum dot, a Technology is the capacity to alter the size of quantum dots.[45]

- **Transdermal Approach:**

Transdermal drug delivery system is topically administered medicaments in the form of patches that deliver drugs for systemic effects at a predetermined and controlled rate. A transdermal drug delivery device, which may be of an active or a passive design, is a device which provides an alternative route for administering medication. These devices allow for pharmaceuticals to be delivered across the skin barrier. In theory, transdermal patches work very simply. A drug is applied in a relatively high dosage to the inside of a patch, which is worn on the skin for an extended period of time. Through a diffusion process, the drug enters the bloodstream directly through the skin. Since there is high concentration on the patch. and low concentration in the blood, the drug will keep diffusing into the blood for a long period of time, maintaining the constant concentration of drug in the blood flow.[46]

- **Folate Targeting:**

Folate targeting is a method utilized in biotechnology for drug delivery purposes. It involves the attachment of the vitamin, folate (folic acid), to a molecule/drug to form a "folate conjugate". Based on the natural high affinity of folate for the folate receptor protein (FR), which is commonly Folate-drug conjugates, which are expressed on the surface of numerous human malignancies, bind firmly to the FR and cause endocytosis to occur, which initiates cellular uptake. It has been successfully accomplished to deliver a wide range of molecules inside FR-positive cells and tissues, from huge DNA plasmid formulations to small radio diagnostic imaging agents.[47]

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