International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

Nano based drug delivery systems: Emerging trends and future prospects

[1]Tapas Kumar Mohapatra, [2]Priyanka Behera, [3]Pratibha Patel, [4]Rajesh Pothal
Department of Pharmaceutics, Gayatri College of Pharmacy, Sambalpur, Odisha,India

Date of Submission: 25-10-2024 Date of Acceptance: 05-11-2024

ABSTRACT:
Drug delivery systems based on nanotechnology have enormous potential to transform medicine by improving therapeutic efficacy, lowering side effects, and facilitating precision medicine. Liposomes, solid lipid nanoparticles, polymeric nanoparticles, and dendrimers are examples of nanocarriers that have shown notable benefits in terms of drug solubility, bioavailability, site-specific and controlled delivery to diseased cells. By providing controlled and sustained release mechanisms, these systems minimise systemic toxicity and enable optimal dosing schedules. Through ligand functionalisation, responsive release to environmental stimuli (such as pH or temperature), and integration with diagnostic imaging for theragnostic applications, future developments seek to enhance targeted delivery. Biocompatibility, decreased immunogenicity, and scalability for broad clinical application are other emerging trends. The opportunities and challenges of nanomedicines in delivering drugs from natural or synthetic sources to clinical use. In the field of nanotechnology, there are numerous drug delivery systems based on nanotechnology. Additionally, gene therapy, cancer treatment, and overcoming multidrug resistance are being investigated using nanocarriers, which could lead to a shift towards more individualised and efficient treatments for a variety of illnesses. In the field of nanotechnology, there are numerous drug delivery systems based on nanotechnology. Because of its exceptional ability to get around the restrictions and disadvantages of conventional drug delivery, the pharmaceutical and biotechnology industries might focus research on nanotechnology applications in drug delivery.

Keywords: Nanotechnology, Nanoparticles, Drug Delivery, Personalized medicine, Different disease. Nanomedicine.

I. INTRODUCTION:

Humans have been using natural plant-based products as treatments for a wide range of illnesses since ancient times. Based on customs and knowledge from the past, modern medications are mostly made from herbs. Natural resources provide around 25% of the main medicinal chemicals and their derivatives that are now on the market [1, 2]. Natural products have many amazing qualities, including decreased toxicity, astonishing chemical variety, and chemical and biological capabilities with macromolecular precision. Because of this, they are beneficial leads in the search for new medications [3]. Target-based drug delivery and other next-generation drug developments, as well as the understanding of drug interactions at the molecular level, have been made possible by computational studies. In the past, a variety of illnesses have been treated by drug delivery systems (DDSs). In order to find new treatments, pharmaceutical corporations are reluctant to invest more in drug delivery and natural product-based drug discovery [4]. Instead, they are looking into the libraries of chemical compounds that are now available. Natural medications provide benefits like reduced toxicity and adverse effects, affordability, and promising therapeutic outcomes. **Fig-1**

To treat illnesses, all medications rely on pharmacologic active metabolites, or pharmaceuticals [5]. Certain medications are intended to be inactive precursors that the body must change into active forms [6]. Large-sized material distribution presents a number of significant hurdles, including as in vivo instability, low solubility and bioavailability, poor absorption in the body, problems with target-specific delivery and tonic effectiveness, and potentially harmful pharmacological side effects. Conventionally administered medications caused injury to unaffected areas, were excreted early, had a lower absorption rate, and required longer to heal the illness [7]. Numerous obstacles, including their enzymatic breakdown or pH difference, numerous mucosal barriers, off-target effects, and their rapid release that increased toxicity in blood, made them less effective [8]. Recently, DDSs have been designed to regulate the release of drugs [9].

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

By working with traditional disciplines like applied health, molecular chemistry, molecular science, pharmaceutical science, optics, and even engineering, nanoscience is the only platform to uncover new features of matter. Over the past few decades, science and technology have come together to provide more effective healthcare systems, treatment techniques, and nano-medical technologies to address difficulties in the medical and health sciences. By applying nanostructures and nanophases to a variety of scientific domains, nanotechnology has been demonstrated to bridge the gap between the biological and physical sciences [10]. This is particularly true in the fields of nanomedicine and nano-based drug delivery systems, where these particles are of great interest [11, 12]. The first recorded use of the phrase "nanotechnology" dates back to 1974 and was made by Professor N. Taniguchi. The first idea of nanotechnology (Feynman's theories) was soon expanded and published by Drexler in the 1986 book "Vehicles of creation: the arrival of the nanotechnology era" [13]. The effects of nanotechnology on people and animals may open up new research directions and revolutionise the field of health science, making it a crucial topic to be taken into account as a therapeutic tool.

In order to engineer biological materials, such as atoms, molecules, and supramolecules, at the nanoscale range of approximately 1–100 nm, nanotechnology is a very dubious multidisciplinary field that holds promise against current challenges by developing new devices and characterising material structure technologies with unique properties to study and comprehend the deadly biological problems followed by disease diagnosis and cure [14,15]. The components of living cells are incredibly important pieces of very small machinery, or nanoscale. They play a significant role in nearly every biological process, including nutrition delivery, energy synthesis, metabolism, and cell signalling. Numerous clinical benefits are associated with the invention of various nanoscale materials, and nanomedicine is quickly becoming the gold standard in the health sciences [16, 17]. There are various strategies that tissue-specific drug targeting techniques can employ to improve the prognosis of the disease [18]. To create nanomedicines, nanotechnology uses therapeutic molecules at the nanoscale level. Nanoparticles have been the driving force behind the discipline of biomedicine, which includes tissue engineering, medication delivery, nanobiotechnology, and biosensors [19]. Since nanoparticles are made of materials with atomic or molecular structures, they are often tiny nanospheres [20]. As a result, they have greater mobility within the human body than larger materials do.Particles at the nanoscale have special biological, mechanical, chemical, electrical, magnetic, and structural characteristics. The use of information and methods from nanoscience to medical biology, disease prevention, and treatment is a rapidly developing discipline known as nanomedicine. It involves using materials with nanoscale dimensions for things like nanorobots, nano sensors for delivery, diagnosis, and sensing, and materials that actuate living cells. Therefore, by delivering medications in a site-specific and target-oriented way, nanotechnology offers several benefits in the treatment of chronic human diseases. But a significant concern is the lack of understanding regarding the toxicity of nanostructures, which surely calls for more study to increase safety and efficacy and allow for the safer, more practical use of these medications. Thus, cautiously creating these nanoparticles may assist address the issues related to their application. The purpose of this review is to describe various nano-based drug delivery methods, important uses of nanomedicines based on natural compounds, and the bioavailability, targeting locations, and controlled release of nano-drugs, in addition to other issues related to nanomaterials in pharmaceuticals.

[Fig-1- Examples of naturally occurring substances taken from higher plants and applied to various nanomedicine techniques.]

Drug delivery based on nanotechnology:

Nanoparticles are used in nano-based drug delivery systems (NDDS), a cutting-edge

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

therapeutic approach, to enhance the administration of medications to particular bodily locations. Through more accurate targeting and release control, these systems are intended to improve the safety, bioavailability, and effectiveness of medications. Drugs that are poorly soluble in water may become more soluble as a result, improving distribution and absorption. By functionalising nanoparticles with ligands that attach to receptors on the target cells, NDDS can target particular tissues or cells (like cancer cells). They minimise negative effects and decrease the frequency of dose by delivering regulated medication release over time. NDDS lowers the total toxicity of treatments by precisely targeting sick cells with medications, minimising harm to healthy tissues. By avoiding biological barriers such as the gastrointestinal tract or blood-brain barrier, nanoparticles can increase the bioavailability of medications. Drug formulation and delivery have undergone a radical change because to NDDS, which enables more individualised and efficient therapies. [**Fig-2]**

[Fig-2, Drugs were previously administered without nanocarriers, causing damage healthy organs or cellsToday, procedures use nanomedicines to deliver drugs directly to the target site.]

Nanoparticles used in personalized medicine:

Now FDA-approved lipid systems like liposomes and micelles were part of the first generation of nanoparticle-based therapies [21]. Inorganic nanoparticles such as magnetic or gold nanoparticles may be present in these liposomes and micelles [22]. Due to these characteristics, inorganic nanoparticles are being used more often, with a focus on therapeutic, imaging, and drug delivery applications. Additionally, it has been observed that nanostructures help carry medications that are only partially water soluble to their intended place and prevent pharmaceuticals from tarnishing in the gastrointestinal tract. Oral bioavailability of nanodrugs is increased due to their usual absorptive endocytosis absorption methods.Because of its ability to target, nanomedicine makes it possible to reach far higher doses than the non-formulated drug's maximum tolerated dose. Therefore, the dosage can be modified in accordance with the specific needs of each patient [23]. Ultimately, two key factors that influence a person's unique medication response can be avoided by using nanomedicine. These factors are associated with the variations in cytochrome-P enzymes (CYP) and drug transporters among various ethnicities **[Figure 3].**

Drug designing methods based on nanotechnology:

The goal of nanotechnology-based drug design methodologies is to develop new drug formulations with enhanced qualities for disease detection, therapy, and prevention by modifying materials at the nanoscale, usually 1–100 nanometres. This strategy makes use of nanoparticles' distinct physical, chemical, and biological properties to increase medication efficacy, lessen adverse effects, and enhance patient outcomes. Using nanoscale materials, such as biocompatible nanoparticles [27] and nanorobots [28], nanotechnology can prevent and cure a variety of diseases for a range of uses, such as diagnosis [29], delivery [30], sensing [31], or actuation in a living body [32].Numerous nanoscale materials have been developed with a range of clinical applications, such as medication delivery, illness diagnostics, and molecular medical imaging. Some of these items are currently undergoing clinical trials [33, 34]. Atomic or molecular components are used to create nanoparticles for the Bottom-Up Approach approach. Polymerisation, precipitation, and self-assembly are some of the techniques used in this procedure. Top-Down Approach methods such as high-energy ball milling, etching, and milling reduce larger materials into nanoparticles. To improve selectivity towards sick cells or tissues, targeting ligands (such as aptamers, peptides, or antibodies) can be functionalised into nanoparticles.

Liposomes, proteins, polymers, micelles, emulsions, nanocapsules, dendrimers, and nanoparticles are among the many varieties of nanomedicines.

Nanoscale drug design has been thoroughly researched and is by far the most sophisticated technology in the field of nanoparticle applications due to its potential benefits, which include the ability to alter characteristics like

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

solubility, drug release profiles, diffusivity, bioavailability, and immunogenicity. Convenient administration methods, reduced toxicity, fewer adverse effects, enhanced biodistribution, and a prolonged drug life cycle can all result from this [35].Drugs are chemically bound to the surface of nanoparticles for targeted administration and controlled release, and they are physically confined within nanoparticle matrices (such as liposomes, dendrimers, or polymeric nanoparticles). The Enhanced Permeability and Retention (EPR) effect, in which nanoparticles gather in tumour tissues as a result of leaky vasculature and inadequate lymphatic drainage, is exploited by passive targeting. In order to provide a greater medication concentration at the sick region, active targeting entails functionalising nanoparticles with ligands that attach to particular receptors that are overexpressed on the surface of target cells (such as cancer cells).

Drug targeting is another important area that employs active and passive drug delivery devices made of nanomaterials or nano formulations. Active targeting involves attaching moieties, including peptides and antibodies, to the receptor structures expressed at the target region by coupling them with a drug delivery system. The produced drug carrier complex travels through the bloodstream during passive targeting, where it is drawn to the target site by affinity or binding that is regulated by factors such as pH, temperature, molecular site, and shape. Cell membrane receptors, lipid components of the cell membrane, and antigens or proteins on the cell surface are the primary targets in the body [36]. Nowadays, the majority of drug delivery systems mediated by nanotechnology are focused on cancer and its treatment. Techniques based on nanotechnology provide substantial benefits in medication design by enhancing treatments' safety, effectiveness, and delivery. These methods have the potential to improve treatment outcomes, particularly for complicated illnesses including cancer, neurological conditions, and infectious infections.

Different nano-carriers/ Nanotechnology based on drug delivery:

Liposome: Liposomes are tiny, spherical vesicles that contain one or more aqueous compartments. Liposomes are frequently utilised in pharmaceutical formulations because of their biocompatibility and capacity to encapsulate both hydrophilic (water loving) and hydrophobic (water hating) substances. They might exist alone or in several bilayers. Depending on their size, those with a single bilayer membrane are referred to as small or large uni-lamellar vesicles. Multilamellar vesicles are those that contain more than one bilayer.As model cells or carriers for a variety of bioactive substances, such as medications, vaccines, cosmetics, and nutraceuticals, liposomes are frequently employed. When compared to free drugs in solution, drugs associated with liposomes exhibit significantly different pharmacokinetic characteristics. Moreover, liposomes can lessen systemic toxicity and stop the encapsulated medication from degrading too soon after administration. [76] **[Table-][fig-4]**

Solid lipid nanoparticles: Solid lipid nanoparticles (SLNs) are a kind of nanocarrier that combines nanotechnology and solid lipid matrices to deliver drugs.Their capacity to encapsulate both hydrophilic drugs and lipophilic drugs medications makes them especially noteworthy.SLNs is made by melting solid lipids in water and adding an emulsifier by using high-pressure homogenization, solvent evaporation, ultrasonication methods to create a stabilised solution. It has a diameter of 50–1000 nm. A promising method for improving drug delivery is the use of solid lipid nanoparticles, which have advantages like increased bioavailability and minimize adverse effects. Their distinct qualities make them a desirable choice for a variety of pharmaceutical applications. [77-78]**[Table-2][Fig—5]**

Carbon-based nanoparticles:

Carbon atoms make up the majority of these tiny particles. These particles have a variety of shapes and sizes, and each one has special qualities that make it useful in fields including materials science, electronics, medicine, and energy. Fullerenes and carbon nanotubes (CNTs) are the two primary forms of carbon-based nanoparticles. Carbon Nanotubes (CNTs) Carbon atoms grouped in a lattice pattern inside cylindrical tube. They can be used to strengthen materials, make lightweight yet sturdy components, and create high-performance electrical conductors because of their extraordinary strength and conductivity. They are categorised as either single-walled carbon nanotubes (SWCNTs) or multiwalled carbon nanotubes (MWCNTs). CNTs are an allotropic type of carbon with a cylindrical framework and an increasing number of sheets in concentric cylinders. CNTs' physical characteristics, which are applied in biomedical fields. For example, carbon nanotubes doped with

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

nitrogen have been created for use in medication delivery. However, the question of CNT cytotoxicity has already garnered a lot of attention from researchers and has yet to yield a conclusive response [79]. Fullerenes are spherical molecules, sometimes referred to as "buckyballs," are made up of only carbon atoms organised in the shape of a football. Due to their special electrical characteristics, fullerenes find use in solar cells, superconductors, and medication delivery. Allotropes of carbon with a hollow cage structure made up of sixty or more carbon atoms are called fullerenes. Buckminsterfullerene, the structure of C-60, resembles a hollow football. Fullerenes were being researched for a number of medical applications, including as light-activated antibacterial agents and for attaching particular antibiotics to their structure to target resistant bacteria and even some cancer cells like melanoma [80]. Additionally, there aren't many studies on fullerene toxicity that show these carbon nanoparticles are dependent on a variety of other elements in addition to dose and time [81]. The structural variety, chemical stability, conductivity, and biocompatibility of these carbon-based nanoparticles make them valuable. They offer promising answers to difficult technological problems in a variety of fields, from advanced medicine to environmental protection. **[Fig-6]**

Nano crystal:

These are nanoscale crystalline particles, usually with sizes between 1 and 100 nanometres. These are pure drugs with no carrier molecules attached, and they are often stabilised by surfactants or polymeric stabilisers. Because they have distinct physical, chemical, and visual characteristics that set them apart from bulk materials, nanocrystals are very remarkable. Metal nanocrystals, oxide nanocrystals, and semiconductor nanocrystals (such as quantum dots) are important kinds of nanocrystals. In order to overcome challenges such as higher saturation solubility, increased dissolution velocity, and increased glueyness to surface/cell membranes, nanocrystals have certain characteristics [82]. Nanocrystals are extremely reactive and helpful as catalysts in chemical reactions, environmental cleanup, and energy storage systems because of their small size and high surface-to-volume ratio. **[Fig-7]**

DENDRIMERS

Dendrimers are artificial macromolecules that resemble trees and have many branches. They have a central core and a well-defined, symmetrical structure. The absorption, distribution, metabolism, and elimination (ADME) profile of dendrimers, which are highly branched macromolecules with several functional groups available for drug attachment, targeting, and imaging agents, depends on a number of structural characteristics. Dendrimers have great potential in nanotechnology because of their accuracy, high surface functionality, and flexibility, especially in areas like environmental science, materials science, and medicine. Their adaptability enables very effective and tailored delivery systems in situations where conventional techniques might not be sufficient. Because of their globular form and easily regulated surface functionalisation, these structures are great options for drug delivery [83]. **[Fig-8]**

HYDROGEL

Large volumes of water or biological fluids can be absorbed and retained by these three-dimensional, hydrophilic polymer networks. These encapsulate and transport drugs, therapeutic proteins, or vaccination antigens using hydrophobic polysaccharides. There is a lot of potential in a new approach that uses cholesterol pullulan, an extracellular polysaccharide that is released by the fungus Aureobasidium pullulans. Pullulan surrounds the hydrophobic core of cholesterol molecules, which self-aggregate. Hydrogels are prized for their adaptability, especially in the medical domain where they promote tissue repair, cell survival, and long-term medication release. They are an essential component of sophisticated biomedical and ecological applications due to their capacity to replicate natural tissues and adapt to changes in their surroundings. Monoclonal antibodies can be encapsulated and released by larger hydrogels [84]. **[Fig-9]**

Polymeric Nano-particles: The size of polymeric nanoparticles (PNPs) ranges from 1 to 1000 nanometres. They are composed of polymers that have many uses, particularly in nanotechnology and medicine.which comes in two forms: nanospheres and nano capsules.The drug is dissolved or dispersed in a liquid core (oil or water) and then encased in a polymeric membrane to create a nano capsule.To create a nanosphere, a drug is encapsulated in a polymeric matrix.Among other applications, their structure, biocompatibility, and capacity to transport therapeutic agents make

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

them perfect for targeted drug delivery, medical imaging, and diagnostics.[85]**[Table-3] [Fig-10]**

Polymeric micelles:

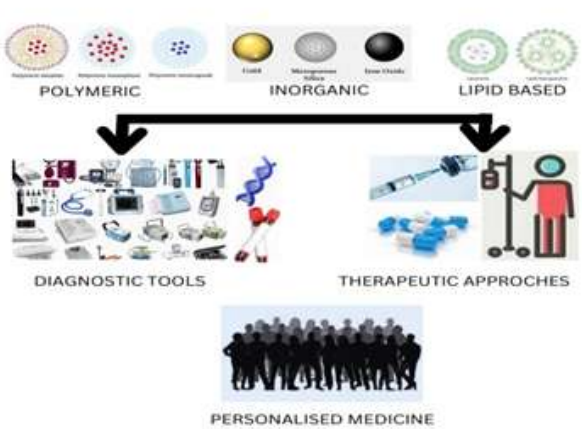
In aqueous environments, amphiphilic block copolymers self-assemble to form nanoscale spherical structures known as polymeric micelles, particles size ranging from 10- 100 nanometers.They resemble surfactant-formed micelles but provide more stability and adaptability. Applications of polymeric micelles in imaging and diagnostics, as well as drug delivery especially for poorly soluble drugs are being extensively studied.[86]**[table-4][Fig-11]**

The method and mechanism of medication drug design and drug delivery:

To guarantee that therapeutic agents are not only powerful but also safely and effectively reach their intended site of action, two essential components of pharmaceutical science—drug delivery and drug design—cooperate. A thorough explanation of these two procedures, their workings, and how they combine to provide successful treatments is provided below. Finding and creating compounds that can alter biological targets in order to treat illnesses is known as drug design. In order to maximise the therapeutic impact while minimising side effects, the procedure frequently uses a number of clearly defined steps and a variety of computational and experimental methodologies.

Drug delivery refers to the techniques and tools utilised to deliver a medication to the body's place of action. By making sure the medication reaches the target site in the right concentration and for the intended amount of time; while minimising adverse effects, the goal is to obtain the best possible therapeutic result. The medical system has recently used a variety of drug delivery methods. Nonetheless, there are still several issues that require attention and investigation in order to successfully transport medications to a specific location.

As nanomedicine has developed and drug delivery and discovery/design techniques have improved, many therapeutic approaches and conventional clinical diagnostic techniques have been researched in an effort to improve drug specificity and diagnostic precision. In order to decrease their toxicity and increase their bioavailability in the body, new drug administration methods are being investigated, with an emphasis on guaranteeing their targeted effect in particular locations [37].



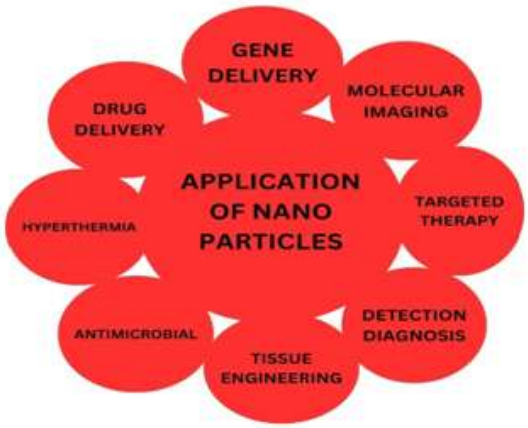
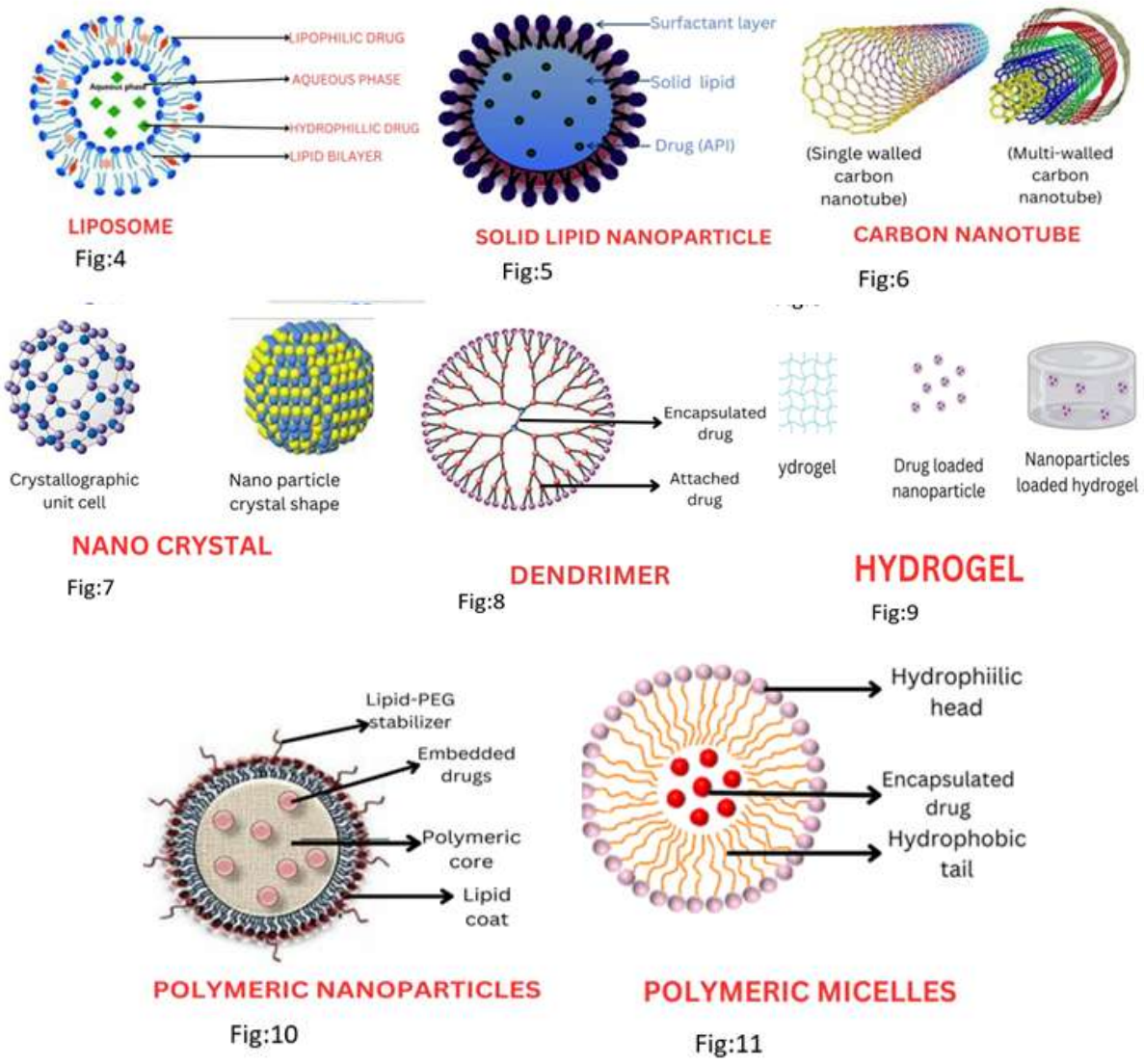


Fig-12

[Fig-3– It represents nanotechnology apply in personalized medicine] and [Fig- 12 represents applications of nanoparticles]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494



[Different types of Nano carriers/ Nanotechnology formulations in below]

Table-1, List of drugs incorporated in liposomes for effective drug delivery

Drugs	formulation	Therapeutic effect
Doxorubicin	Thioether phosphatidylcholines liposomes	• Cancer treatment, particularly for breast cancer. • Reduces cardiotoxicity and improves targeting to tumor cells.
Paclitaxel	Glutamic oligopeptides-RGD peptide (PTXGlu6-RGD-Lip)	• Various cancers, including ovarian and lung cancer.
Bupivacaine	Unilamellar	• Sustained drug release was recorded for 6 days
Cytarabine	Liposome	• Treatment of lymphomatous meningitis. • Prolonged release and improved delivery to the central nervous system

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

Table-2 List of drugs loaded SLNs for effective drug delivery

Drugs loaded in SLNs	Therapeutics effect
Enrofloxacin	By facilitating targeted, controlled-release delivery and maintaining the effectiveness of enrofloxacin againstSalmonella, enrofloxacin-loaded SLNs have the potential to enhance treatment outcomes.
Insulin	SLNs are explored for oral insulin delivery to improve stability against gastrointestinal degradation.
Ritonavir	SLNs can enhance oral bioavailability and provide sustained release.

Table-3 List of medications that have been successfully delivered by polymeric nanoparticles.

Drugs	Polymeric nanoparticle type	Delivery of action
Curcumin	Poly (lactic-co-glycolic acid)-poly (ethylene glycol) (PLGA-PEG)	Compared to PLGA, drug-loaded polymeric nanoparticles have a 14-fold greater diffusivity in the brain parenchyma. For drug-loaded PLGA-PEG, the median area loss was 12.3%.
Doxorubicin triphenylphosphine	Polylactic-co-glycolic acid (PLGA) wrapped with bovine serum albumin	After 12 hours of treatment, MCF-7 cell, at pH 6.5 caused 74% of cell apoptosis. Tumor volume was reduced from 26 mm3 to 23 mm3.
Ofloxacin	Polycaprolactone	The drug's continuous release for six hours was noted.

Table-4 List of different polymeric micelles that are used to deliver drugs effectively.

Drugs	Copolymer	Delivery of action
Doxorubicine	Diselenide-crosslinked micelles (DCM)	In tumor-bearing mice, drug-loaded micelles delivered a 3.73-fold greater quantity of drug than free drug.
Doxorubicine	Poly (ethylene glycol)	Drug release was found to increase twofold at pH 5.

Utilising nanoparticles in a medication delivery system:

These days, scientists and medical experts are interested in drug delivery systems that are focused on nanotechnology. When creating a target-specific drug delivery system, liposomes, micelles, dendrimers, and other organic, inorganic, metallic, and polymer-based NPs are frequently taken into account. These NPs cause drug delivery in medications with low absorption capacity and poor solubility. However, the size, shape, and other intrinsic biophysical/chemical characteristics of these NPs affect how effective they are as drug delivery vehicles. NP is referred to by a number of other names, such as nanocarriers, nanospheres, nanostructures, and nanovehicles. Gregory Gregoriadis created the liposome, the first NPs for a drug delivery method. NP is referred to by a number of other names, such as nanocarriers, nanospheres, nanostructures, and nanovehicles. A number of commercially marketed nano-based medications, including Abraxane®, Doxil®, Transdrug®, and Caelyx®, are used to treat cancer.

Drug delivery systems are simple to create and can facilitate the body's altered release of active chemicals. For instance, reviewed the therapeutic effects of nanocarrier systems and provided an intriguing evaluation of their use in imaging and sensory applications. Furthermore, addressed fresh prospects and difficulties for the field of nanomedicine while offering a current summary of various nanocarrier uses. These drug delivery systems have unique morphological, chemical, and physical properties. They may also

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

have a preference for various drug polarities through physical or chemical interactions, such as electrostatic and van der Waals interactions or covalent and hydrogen bonding.Each of these elements affects how nanocarriers interact with biological systems and how quickly the active ingredient is released within the body.

Strategies are currently being developed to reduce immunogenicity by coating or chemically functionalising the nanostructures with various substances, including polymers, natural polysaccharides, antibodies, cell membrane, tenable surfactants, peptides, and others, and to increase the specificity of the nanostructures to target regions of the organism. These ligand-modified nanocarriers have been utilised to get through the cell membrane and enable a planned drug delivery in a specific setting in situations where medications do not exhibit binding and affinity with a particular target or do not flow through specific barriers (such as the blood–brain barrier or the blood–cerebrospinal fluid barrier).

The interaction between the ligand-appended in nanocarriers and cell membranes has not been well studied, and it is still unknown how they are absorbed. However, using external factors like ultrasound, heat, magnetism, light, pH, and ionic strength, stimuli-responsive nanocarriers have demonstrated the ability to control the release profile of drugs (as a triggered release), which can improve targeting and allow greater dosage control.

A number of advantages are provided by nanoparticles in drug delivery systems, such as enhanced bioavailability, targeted distribution, controlled release, and fewer adverse effects. Scientists can create extremely effective and customised drug delivery systems to treat a variety of illnesses, especially cancer, neurological conditions, and infections, by utilising several nanoparticle kinds, including polymeric, lipid-based, metal, and hybrid nanoparticles. [38-61] [**Fig-12]**

Implementation of nanoparticles in various diseases:

Although they improve medicine delivery, increase targeting accuracy, and decrease adverse effects, nanoparticles have completely changed the way many diseases are treated. They are used to treat a variety of illnesses, such as cancer, neurological conditions, heart conditions, infectious diseases, and more. Here is a thorough examination of the various disorders that nanoparticles are used to treat:

Cancer:

Globally, cancer is the biggest cause of mortality. Because of the difficulties in properly and successfully administering chemotherapeutic medications, cancer treatment is one of the most developed fields for nanoparticle applications. Traditional cancer treatments like radiotherapy and chemotherapy have seen many advancements, but they still seem to be far from effective. Due to some drawbacks, including significant side effects and chemoresistance [61-63]

Nanoparticles are functionalized with ligands (antibodies, peptides) that bind to specific receptors overexpressed in cancer cells (e.g., HER2 in breast cancer), ensuring that the drug is delivered directly to the tumor.Nanomedicine has an enormous capacity to transform cancer treatment and diagnosis by developing innovative biocompatible nanoparticles that are the most crucial feature of nanoparticles for drug delivery purposes.Quantum dots, dendrimers, nanoshells, nanocantilevers, nanoprobes, nanocrystals, nanopolymers, and nanotechnologies can all be employed to cure cancer [64-65]. These nanoparticles stand out from conventional cancer treatments due to their special qualities [66]. Because the vasculature of tumour tissues leaks, nanoparticles can passively collect at the tumour site while preventing drug accumulation in healthy tissues, which contributes to the increased permeability and retention (EPR) effect. For instance,

- Doxil® (doxorubicin) and other liposomal formulations enhance chemotherapeuticmedication delivery while lowering cardiotoxicity.
- Abraxane®, or albumin-bound paclitaxel, is a polymeric nanoparticle that improvespaclitaxel's solubility and targeting in pancreatic, lung, and breast cancer.
- Gold nanoparticles used in photothermal therapy, which produces heat and kills cancercells by exposingthem to near-infrared light.

One important factor in cancer therapy is the interchangeability of antiangiogenic medicines and chemotherapy. Her-2 was employed as a target group for breast cancer treatment, and it was created by encapsulating hydrophilic and hydrophobic anticancer medications as double-drug delivery approach [67]. A biomedical strategy known as theragnostic is emerging that combines diagnosis and treatment in a single step. To make

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

treatment quicker, simpler, and more effective, theranostics will be used to integrate the key components of medical care, including diagnosis and therapy. Shim et al. have successfully diagnosed and treated cancer together (theranostics). They discovered the potential for both stimulation enhanced gene silencing and stimulus-responsive optical imaging using tiny gold nanoparticles that contained Si RNA [68].

Ophthalmic Disorder:

One of the primary issues with topical ophthalmic medication administration is poor eye absorption, which makes it challenging to maintain a suitable drug concentration in the precorneal area. Age-related macular degeneration (AMD), diabetic retinopathy, and glaucoma can all be treated with nanoparticles. Lipid and polymeric nanoparticles enhance eye drop delivery by boosting medication penetration and extending drug retention on the surface of the eye. In order to reduce the frequency of injections for chronic illnesses like AMD, intraocular injections employ nanoparticles to enable prolonged drug release. Since nanoparticles exhibit greater durability and a longer half-life (t1/2) in tear fluids (up to 20 min) than conventional drugs (t1/2 = 1–3 min), they are attractive substitutes for standard ocular topical medications. Drug delivery methods using nanoparticles have demonstrated promise for improved bioavailability, sustained intraocular dose levels, reduced side effects, and higher absorption of therapeutic agents. Flurbiprofen and ibuprofen-loaded nanoparticles effectively prevented post-operative inflammatory responses brought on by trauma. In addition, compared to conventional eye drop devices, the nanoparticle device generated more medicines in vitreous humour [68-69].

Heart Disorder:

Atherosclerosis, myocardial infarction, stroke, hypertension, and heart failure are among the conditions collectively referred to as cardiovascular diseases (CVDs). For cardiovascular illnesses to be prevented and effectively treated, early detection is essential. because it has the potential to be the world's leading cause of death. This is addressed by a number of novel methods, including molecular imaging and cardiac immunoassays. To identify CVDs, quick, precise, sensitive, and targeted methods are required [71-72].

To enhance medication delivery, imaging, and the therapeutic efficiency of treatments for disorders like atherosclerosis, heart attacks, and hypertension, nanoparticles are used in the treatment of cardiovascular diseases.

Disorders of the nervous system:

The most delicate and intricate organ in the human body that is protected by the Blood-Brain Barrier (BBB) barrier is the brain. CNS disorders pose a serious risk to human health since the BBB is a significant treatment barrier. One of the biggest challenges in treating neurological illnesses has been getting medications past the blood-brain barrier (BBB). There are few alternatives for particular future therapeutic and diagnostic techniques because the BBB can only pass via lipophilic substances or molecules with a molecular weight of less than 400–600 Da. Nanoparticles provide fresh approaches to this problem.

Since polymeric nanoparticles like butyl cyanoacrylate (PBCA), poly (isohexylcyanoacrylate) (PIHCA), poly (lactic acid) (PLA), or copolymer (lactide-co-glycolide) (PLGA), and human serum albumin (HSA) have been shown to cross tight cell junctions, bypass the blood-brain barrier, encapsulate higher drug content, and can be combined with ligands to achieve site-specific drug release, they make up the majority of drug delivery systems used to treat neurological diseases. To improve their capacity to penetrate the blood-brain barrier and target the central nervous system (CNS), nanoparticles can be coated with surfactants, ligands, or antibodies. When coupled with transferrin, NPs containing anti-cancer medications, including taxols, may have enhanced brain endothelial cell aggregation in brain cancer. One of the neurodegenerative disorders that affects the older population the fastest is Alzheimer's disease. Clinically, it is classified by a loss of spatial skills and reasoning, linguistic access impairment, and abstraction [73]. Liquid crystals, liposomes, solid lipid nanoparticles, polymeric nanoparticles, nano-emulsions, and micro-emulsions are all utilised to treat Alzheimer's disease. Drugs that lessen the production of amyloid plaque, a defining feature of Alzheimer's disease, can be delivered using nanoparticles that are designed to pass the blood-brain barrier. Anti-inflammatory, antioxidant, and neuroprotective medications can be delivered to the brain using lipid-based nanoparticles.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

Diabetes:

Because they improve blood glucose monitoring and allow for the controlled release of insulin, nanoparticles are important in the management of diabetes.

Because polymeric nanoparticles shield insulin from enzymatic breakdown in the gastrointestinal tract, they can give insulin orally, eliminating the need for injections. On the other hand, glucose-responsive insulin delivery systems that release insulin in response to elevated blood glucose levels are developed using nanogels. Glucose monitoring systems that provide real-time, extremely sensitive blood sugar level readings use nanoparticles like gold nanoparticles and quantum dots.

Nanomedicine's perspective for the future:

The application of nanotechnology in healthcare, or nanomedicine, has demonstrated great promise in enhancing drug delivery, diagnosis, and treatment results. But in order for nanomedicine to realise its full potential, a number of upcoming issues need to be resolved, even with its notable breakthroughs. These difficulties include logistical, ethical, legal, and scientific concerns. Numerous developments in the field of nanomedicine demonstrate its significance in clinical and other medical contexts. Numerous researchers have looked into the role that nanomedicine plays in curing cancer and lowering rates of death and morbidity. But there are still issues that nanomedicines will have to deal with in the future [74].

One of the most exciting fields of study at the moment is nanomedicine. Over the past 20 years, a great deal of research in this area has already resulted in the completion of several dozen clinical trials and the filing of 1500 patents [75]. The application of nanomedicine and nano-drug delivery systems is undoubtedly the trend that will continue to be the future area of research and development for decades to come since it uses different types of nanoparticles to deliver the precise amount of drug to the affected cells, such as the cancer/tumor cells, without interfering with the physiology of the normal cells.

In healthy tissues, certain nanoparticles, namely those based on metals (such as gold, silver, and iron oxide), can induce inflammation, oxidative stress, and cytotoxicity. Long-term exposure to certain nanoparticles might cause unexpected side effects, such as kidney, lung, or liver damage. On the other hand, certain nanoparticles are difficult for the body to eliminate and can build up in organs or tissues over time, which raises questions regarding long-term toxicity. It is crucial to make sure that nanoparticles can be biodegraded or effectively eliminated. Unwanted immunological reactions, such as hypersensitivity, inflammation, or allergic reactions, can be brought on by nanoparticles. It is still difficult to maintain therapeutic efficacy while making sure that nanoparticles don't trigger negative immunological reactions. Since nanomedicines frequently work differently from conventional medications, new evaluation procedures are needed for preclinical research, clinical trials, and production. It might be necessary for regulatory agencies like the FDA and EMA to create new standards that take into account the distinct pharmacokinetics and biodistribution of nanoparticles. Assessing the therapeutic and diagnostic components of a single nanomedicine can make the licensing process more difficult. Nanoparticles are frequently employed for theranostics, which combines therapy and diagnostics on a single platform. The liver and spleen are examples of non-target tissues where nanoparticles can still collect despite improvements in focused delivery. Targeting tactics need to be further refined in order to reduce off-target effects while retaining effective drug delivery to sick cells.

The production of nanomedicine frequently entails intricate, multi-step procedures that are expensive and challenging to scale. Creating economical, scalable manufacturing processes is essential to introducing nanomedicines to the market at a reasonable cost. It is challenging to reliably create nanoparticles on a large scale with constant size, shape, and surface features. Safety and effectiveness may be impacted by the unpredictable behaviour that slight changes in nanoparticle characteristics can produce in biological systems.

The behaviour of nanoparticles can vary according on the disease state, metabolism, and genetic makeup of the patient. Personalised nanomedicine necessitates more accurate diagnostic and customisation techniques, which are still in their infancy, and designing "one-size-fits-all" nanomedicines might not work. We are still in the early stages of developing prediction models that can precisely forecast how a patient's body will react to nanoparticles. Customising nanomedicine treatments requires an understanding of individual variations in nanoparticle absorption, distribution, metabolism, and excretion (ADME).

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

II. CONCLUSION:

In a variety of medical applications, nano-based drug delivery systems (NDDS) have demonstrated revolutionary potential in improving therapeutic efficacy, specificity, and patient outcomes. Utilising nanoscale materials such as polymeric carriers, liposomes, and solid lipid nanoparticles, these systems tackle important issues in traditional drug delivery, including low solubility, restricted bioavailability, and lack of targeted specificity. The controlled release, extended circulation time, and tissue-specific targeting offered by nano-based drug delivery greatly enhances the therapeutic index and lowers unfavourable side effects, particularly in complex treatments like cancer therapy and the management of chronic diseases. In the future, NDDS will probably be pushed into more individualised, accurate, and adaptive medicine frameworks by the creation of stimuli-responsive nanocarriers, integration with diagnostic tools for theragnostic applications, and developments in bio-safe and biodegradable materials. Furthermore, better prediction and control over drug release profiles, which improve patient outcomes and treatment adherence, are promised by the integration of artificial intelligence and machine learning into NDDS design. To fully realise the clinical potential of NDDS, however, issues with long-term safety, regulatory approval, and large-scale production must be resolved. All things considered, NDDS have the potential to completely transform pharmacotherapy by facilitating individualised and minimally invasive treatments that may soon completely change the way healthcare is delivered. As long as researchers, physicians, and regulatory agencies continue to innovate and work together, nano-based delivery systems will play a crucial role in the development of next-generation medical treatments.

BIBLIOGRAPHY:

[1]. Swamy MK, Sinniah UR. Patchouli (Pogostemoncablin Benth.): botany, agrotechnology and biotechnological aspects. Ind Crops Prod. 2016; 87:161–76.

[2]. Mohanty SK, Swamy MK, Sinniah UR, Anuradha M. Leptadenia reticulata (Retz.) Wight &Arn. (Jivanti): botanical, agronomical, phytochemical, pharmacological, and biotechnological aspects. Molecules. 1019;2017:22

[3]. Siddiqui AA, Iram F, Siddiqui S, Sahu K. Role of natural products in drug discovery process. Int J Drug Dev Res. 2014;6(2):172–204.

[4]. Beutler JA. Natural products as a foundation for drug discovery. Curr Prot Pharmacol. 2009;46(1):9–11.

[5]. Li, S.; Zhang, H.; Chen, K.; Jin, M.; Vu, S.H.; Jung, S.; He, N.; Zheng, Z.; Lee, M.S. Applicatio of chitosan/alginate nanoparticle in oral drug delivery systems: Prospects and challenges. Drug Deliv. **2022**, 29, 1142–1149. [CrossRef] [PubMed]

[6]. Vlachopoulos, A.; Karlioti, G.; Balla, E.; Daniilidis, V.; Kalamas, T.; Stefanidou, M.; Bikiaris, N.D.; Christodoulou, E.; Koumentakou, I.; Karavas, E.; et al. Poly (Lactic Acid)-Based Microparticles for Drug Delivery Applications: An Overview of Recent Advances. Pharmaceutics **2022**, 14, 359. [CrossRef] [PubMed]

[7]. Builders, P.F.; Arhewoh, M.I. Pharmaceutical applications of native starch in conventional drug delivery. Starch-Stärke 2016, 9–10, 864–873. [CrossRef]

[8]. Alshammari, M.K.; Alshehri, M.M.; Alshehri, A.M.; Alshlali, O.M.; Mahzari, A.M.; Almalki, H.H.; Kulaybi, O.Y.; Alghazwni, M.K.; Kamal, M.; Imran, M. Camptothecin loaded nano-delivery systems in the cancer therapeutic domains: A critical examination of the literature. J. Drug Deliv. Sci. Technol. 2022, 79, 104034. [CrossRef]

[9]. Marco-Dufort, B.;Willi, J.; Vielba-Gomez, F.; Gatti, F.; Tibbitt, M.W. Environment Controls Biomolecule Release from Dynamic Covalent Hydrogels. Biomacromolecules 2021, 22, 146–157. [CrossRef]

[10]. Liu Z, Tabakman S, Welsher K, Dai H. Carbon nanotubes in biology and medicine: in vitro and in vivo detection, imaging and drug delivery. Nano Res. 2009; 2:85–120.

[11]. Orive G , Gascon AR , Hernández RM , Domínguez-Gil A, Pedraz JL. Techniques: new approaches to the delivery of biopharmaceuticals. Trends Pharmacol Sci. 2004; 25:382–7.

[12]. Razzacki SZ, Thwar PK, Yang M, Ugaz VM, Burns MA. Integrated microsystems for controlled drug delivery. Adv Drug Deliv Rev. 2004; 56:185–98.

[13]. S. Bayda, et al., The history of nanoscience and nanotechnology: from chemical-physical applications to nanomedicine, Molecules 25 (1) (2019).
[14]. Coil embolization for intracranial aneurysms: an evidence-based analysis, Ont. Health Technol. Assess. Ser. 6 (1) (2006) 1–114.
[15]. J.A. Sichert, et al., Quantum size effect in organometal halide perovskite nanoplatelets, Nano Lett. 15 (10) (2015) 6521–6527.
[16]. S.M. Moghimi, Z.S. Farhangrazi, Nanomedicine and the complement paradigm, Nanomedicine 9 (4) (2013) 458–460.
[17]. P. Zarrintaj, et al., Can regenerative medicine and nanotechnology combine to heal wounds? The search for the ideal wound dressing, Nanomedicine 12 (19) (2017) 2403–2422.
[18]. D.L. Stirland, et al., 3 - targeted drug delivery for cancer therapy, in: K. Park (Ed.), Biomaterials for Cancer Therapeutics, Woodhead Publishing, 2013, pp. 31–56.
[19]. Mirza AZ, Siddiqui FA. Nanomedicine and drug delivery: a mini review. Int Nano Lett. 2014; 4:94.
[20]. Rudramurthy GR, Swamy MK, Sinniah UR, Ghasemzadeh A. Nanoparticles: alternatives against drug-resistant pathogenic microbes. Molecules. 2016; 21:836.
[21]. Shi X, Sun K, Baker JR Jr. Spontaneous formation of functionalized dendrimer-stabilized gold nanoparticles. J Phys Chem C. 2008; 112:8251–8.
[22]. Park S-H, Oh S-G, Mun J-Y, Han S-S. Loading of gold nanoparticles inside the DPPC bilayers of liposome and their effects on membrane fluidities. Coll Surf B. 2006; 48:112–8.
[23]. Maeda, H. SMANCS and polymer-conjugated macromolecular drugs: Advantages in cancer chemotherapy. Adv. Drug Deliv. Rev. 2001, 46, 169–185. [CrossRef]
[24]. Su, Y.; Xie, Z.; Kim, G.B.; Dong, C.; Yang, J. Design strategies and applications of circulating cell-mediated drug delivery systems.ACSBiomater. Sci. Eng. 2005, 4, 201–217. [CrossRef] [PubMed]
[25]. MaHam, A.; Tang, Z.; Wu, H.; Wang, J.; Lin, Y. Protein-based nanomedicine platforms for drug delivery. Small 2009, 5, 1706–1721. [CrossRef] [PubMed]
[26]. Harrington, K.J. Phase II study of pegylated liposomal doxorubicin (CaelyxTM) as induction chemotherapy for patients with squamous cell cancer of the head and neck. Eur. J. Cancer 2001, 37, 2015–2022. [CrossRef] [PubMed].
[27]. McNamara K, Tofail SA. Nanosystems: the use of nanoalloys, metallic, bimetallic, and magnetic nanoparticles in biomedical applications. Phys Chem Chem Phys. 2015; 17:27981–95.
[28]. Saadeh Y, Vyas D. Nanorobotic applications in medicine: current proposals and designs. Am J Robot Surg. 2014; 1:4–11.
[29]. Oliveira ON Jr, Iost RM, Siqueira JR Jr, Crespilho FN, Caseli L. Nanomaterials for diagnosis: challenges and applications in smart devices based on molecular recognition. ACS Appl Mater Interfaces. 2014; 6:14745–66.
[30]. De Jong WH, Borm PJ. Drug delivery and nanoparticles: applications and hazards. Int J Nanomed. 2008; 3:133.
[31]. Holzinger M, Le Goff A, Cosnier S. Nanomaterials for biosensing applications: a review. Front Chem. 2014; 2:63.
[32]. Golovin YI, Gribanovsky SL, Golovin DY, Klyachko NL, Majouga AG, Master AM, Sokolsky M, Kabanov AV. Towards nanomedicines of the future: remote magneto-mechanical actuation of nanomedicines by alternating magnetic fields. J Control Release. 2015; 219:43–60.
[33]. B. Pelaz, et al., Diverse applications of nanomedicine, ACS Nano 11 (3) (2017) 2313–2381.
[34]. S. Chen, et al., Nanomaterials in medicine and pharmaceuticals: nanoscale materials developed with less toxicity and more efficacy, Eur. J. Nanomed. 5 (2) (2013) 61.
[35]. Mirza AZ, Siddiqui FA. Nanomedicine and drug delivery: a mini review. Int Nano Lett. 2014; 4:94.
[36]. Kumari A, Kumar V, Yadav S. Nanotechnology: a tool to enhance therapeutic values of natural plant products. Trends Med Res. 2012; 7:34.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 1198-1213 www.ijprajournal.com ISSN: 2456-4494

[37]. Mignani S, El Kazzouli S, Bousmina M, Majoral JP. Expand classical drug administration ways by emerging routes using dendrimer drug delivery systems: a concise overview. Adv Drug Deliv Rev. 2013; 65:1316–30.
[38]. A.Z. Mirza, F.A. Siddiqui, Nanomedicine and drug delivery: a mini review, Int. Nano Lett. 4 (1) (2014) 94.
[39]. G. Gregoriadis, Liposomes in drug delivery: how it all happened, Pharmaceutics 8 (2) (2016) 19.
[40]. Chen G, Roy I, Yang C, Prasad PN. Nanochemistry and nanomedicine for nanoparticle-based diagnostics and therapy. Chem Rev. 2016;116:2826–85.
[41]. Pelaz B, Alexiou C, Alvarez-Puebla RA, Alves F, Andrews AM, Ashraf S, Balogh LP, Ballerini L, Bestetti A, Brendel C, Bosi S. Diverse applications of nanomedicine. Acs Nano. 2017;11:2313–81.
[42]. Kinnear C, Moore TL, Rodriguez-Lorenzo L, Rothen-Rutishauser B, Petri-Fink A. Form follows function: nanoparticle shape and its implications for nanomedicine. Chem Rev. 2017;117:11476–521.
[43]. Wong PT, Choi SK. Mechanisms of drug release in nanotherapeutic delivery systems. Chem Rev. 2015;115:3388–432.
[44]. Torchilin VP. Multifunctional nanocarriers. Adv Drug Deliv Rev. 2012;64:302–15.
[45]. Pelaz B, del Pino P, Maffre P, Hartmann R, Gallego M, Rivera-Fernandez S, de la Fuente JM, Nienhaus GU, Parak WJ. Surface functionalization of nanoparticles with polyethylene glycol: effects on protein adsorption and cellular uptake. Acs Nano. 2015;9:6996–7008.
[46]. Almalik A, Benabdelkamel H, Masood A, Alanazi IO, Alradwan I, Majrashi MA, Alfadda AA, Alghamdi WM, Alrabiah H, Tirelli N, Alhasan AH. Hyaluronic acid coated chitosan nanoparticles reduced the immunogenicity of the formed protein corona. Sci Rep. 2017;7:10542.
[47]. Martens TF, Remaut K, Deschout H, Engbersen JFJ, Hennink WE, van Steenbergen MJ, Demeester J, De Smedt SC, Braeckmans K. Coating nanocarriers with hyaluronic acid facilitates intravitreal drug delivery for retinal gene therapy. J Control Release. 2015;202:83–92.
[48]. Kolhar P, Anselmo AC, Gupta V, Pant K Prabhakarpandian B, Ruoslahti E, Mitragotri S. Using shape effects to target antibody-coated nanoparticles to lung and brain endothelium. Proc Natl Acad Sci USA. 2013;110:10753–8.
[49]. Muller J, Bauer KN, Prozeller D, Simon J, Mailander V, Wurm FR, Winzen S, Landfester K. Coating nanoparticles with tunable surfactants facilitates control over the protein corona. Biomaterials. 2017;115:1–8.
[50]. Gao H, Yang Z, Zhang S, Cao S, Shen S, Pang Z, Jiang X. Ligand modified nanoparticles increases cell uptake, alters endocytosis and elevates glioma distribution and internalization. Sci Rep. 2013;3:2534.
[51]. Jain A, Jain SK. Ligand-appended BBB-targeted nanocarriers (LABTNs). Crit Rev Ther Drug Carrier Syst. 2015;32:149–80.
[52]. Anirudhan TS, Nair AS. Temperature and ultrasound sensitive gatekeepers for the controlled release of chemotherapeutic drugs from mesoporous silica nanoparticles. J Mater Chem B. 2018;6:428–39.
[53]. Al-Ahmady Z, Kostarelos K. Chemical components for the design of temperature-responsive vesicles as cancer therapeutics. Chem Rev. 2016;116:3883–918.
[54]. Bai Y, Xie FY, Tian W. Controlled self-assembly of thermo-responsive amphiphilic h-shaped polymer for adjustable drug release. Chin J Polym Sci. 2018;36:406–16.
[55]. Zhang Z, Zhang D, Wei L, Wang X, Xu YL, Li HW, Ma M, Chen B, Xiao LH. Temperature responsive fluorescent polymer nanoparticles (TRFNPs) for cellular imaging and controlled releasing of drug to living cells. Coll Surf B. 2017;159:905–12.
[56]. Guo Y, Zhang Y, Ma J, Li Q, Li Y, Zhou X, Zhao D, Song H, Chen Q, Zhu X. Light/magnetic hyperthermia triggered drug released from multifunctional thermo-sensitive magnetoliposomes for precise cancer synergetic theranostics. J Control Release. 2017;272:145–58.
[57]. Hervault A, Thanh NT. Magnetic nanoparticle-based therapeutic agents for

thermo-chemotherapy treatment of cancer. Nanoscale. 2014;6:11553–73.

[58]. Mathiyazhakan M, Wiraja C, Xu CJ: A Concise Review of Gold Nanoparticles-Based Photo-Responsive Liposomes for Controlled Drug Delivery. Nano-Micro Letters 2018, 10.

[59]. Xu L, Qiu LZ, Sheng Y, Sun YX, Deng LH, Li XQ, Bradley M, Zhang R. Biodegradable pH-responsive hydrogels for controlled dual-drug release. J Mater Chem B. 2018;6:510–7.

[60]. Ma GL, Lin WF, Yuan ZF, Wu J, Qian HF, Xua LB, Chen SF. Development of ionic strength/pH/enzyme triple-responsive zwitterionic hydrogel of the mixed l-glutamic acid and l-lysine polypeptide for site-specific drug delivery. J Mater Chem B. 2017;5:935–43.

[61]. S. Russi, et al., Adapting and surviving: intra and extra-cellular remodeling in drug-resistant gastric cancer cells, Int. J. Mol. Sci. 20 (15) (2019).

[62]. H.K. Verma, et al., Micro RNA facilitated chemoresistance in gastric cancer: novel biomarkers and potential therapeutics, Alexand. J. Med. 56 (1) (2020) 81–92.

[63]. H.K. Verma, Exosomes facilitate chemoresistance in gastric cancer: future challenges and openings, Precis. Radiat. Oncol. 3 (4) (2019) 163–164.

[64]. J. Larocque, D.J. Bharali, S.A. Mousa, Cancer detection and treatment: the role of nanomedicines, Mol. Biotechnol. 42 (3) (2009) 358–366.

[65]. J.K. Patra, et al., Nano based drug delivery systems: recent developments and future prospects, J. Nanobiotechnol. 16 (1) (2018) 1–33.

[66]. R. Misra, S. Acharya, S.K. Sahoo, Cancer nanotechnology: application of nanotechnology in cancer therapy, Drug Discov. Today 15 (19–20) (2010) 842–850.

[67]. A. Singh, et al., Composite polymeric magnetic nanoparticles for co-delivery of hydrophobic and hydrophilic anticancer drugs and MRI imaging for cancer therapy, ACS Appl. Mater. Interfaces 3 (3) (2011) 842–856.

[68]. M.S. Shim, et al., Combined multimodal optical imaging and targeted gene silencing using stimuli-transforming nanotheragnostics, J. Am. Chem. Soc. 132 (24) (2010) 8316–8324.

[69]. S.A.A. Rizvi, A.M. Saleh, Applications of nanoparticle systems in drug delivery technology, Saudi Pharmaceut. J. 26 (1) (2018) 64–70.

[70]. R. Pignatello, et al., Flurbiprofen-loaded acrylate polymer nanosuspensions for ophthalmic application, Biomaterials 23 (15) (2002) 3247–3255.

[71]. Mandal A, Bisht R, Rupenthal ID, Mitra AK. Polymeric micelles for ocular drug delivery: from structural frameworks to recent preclinical studies. J Control Release. 2017;248:96–116.

[72]. C. Shi, et al., Nanoscale technologies in highly sensitive diagnosis of cardiovascular diseases, Front. Bioeng. Biotechnol. 8 (June) (2020) 1–18.

[73]. Y. Deng, et al., Application of the nano-drug delivery system in treatment of cardiovascular diseases, Front. Bioeng. Biotechnol. 7 (January) (2020) 1–18.

[74]. Nazıroˇglu, M.; Muhamad, S.; Pecze, L. Nanoparticles as potential clinical therapeutic agents in Alzheimer's disease: Focus on selenium nanoparticles. Expert Rev. Clin. Pharmacol. 2017, 16, 73–782. [CrossRef].

[75]. Tewabe, A.; Abate, A.; Tamrie, M.; Seyfu, A.; Siraj, E.A. Targeted drug delivery—From magic bullet to nanomedicine: Principles, challenges, and future perspectives. J. Multidiscip. Healthc. 2021, 14, 1711. [CrossRef]

[76]. Pandit A, Zeugolis DI. Twenty-five years of nano-bio-materials: have we revolutionized healthcare? Fut Med. 2016;11(9):985–7.

[77]. Mozafari MR. (2005). Liposomes: An overview of manufacturing techniques. Cell Mol Biol Lett. 10: 711-719

[78]. Alvandi N, Rajabnejad M, Taghvaei Z, Esfandiari N. New generation of viral nanoparticles for targeted drug delivery in cancer therapy. J Drug Target 2021:1–5.

[79]. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery–a review of the state of the art. Eur J Pharm Biopharm 2000;50:161–77.

[80]. Rastogi V, Yadav P, Bhattacharya SS, Mishra AK, Verma N, et al. (2014). Carbon nanotubes: An emerging drug

carrier for targeting cancer cells. J Drug Deliv. 2014: 670815.

[81]. Tegos GP, Demidova TN, Arcila-Lopez D, Lee H, Wharton T, et al. (2005). Cationic fullerenes are effective and selective antimicrobial photosensitizers. Chem Biol. 12: 1127-1135.

[82]. Lalwani G, Sitharaman B. (2013). Multifunctional fullerene and metallofullerene based nanobiomaterials. Nano LIFE. 3: 1342003.

[83]. Junyaprasert VB, Morakul B. (2015). Nanocrystals for enhancement of oral bioavailability of poorly water-soluble drugs. Asian J Pharm Sci. 10: 13-23.

[84]. Somani S, Dufes C. (2014). Applications of dendrimers for brain delivery and cancer therapy. Nanomedicine. 2014; 9: 2403-2414.

[85]. Kesharwani P, Jain NK. (2014). Dendrimer as nanocarrier for drug delivery. Prog Polym Sci. 39: 268-307.

[86]. Singh R, Lillard JW. (2009). Nanoparticle-based targeted drug delivery. Exp Mol Pathol. 86: 215-223.

[87]. Prabhu RH, Patravale VB, Joshi MD. Polymeric nanoparticles for targeted treatment in oncology: current insights. Int J Nanomed 2015;10:1001.