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NANO BASED INTRAVENOUS AND TRANSDERMAL DRUG DELIVERY

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ABSTRACT

The collection of methods used to deliver a medication or pharmacologically active chemical to the target cell in order to treat a disease or other health concern is known as drug delivery. Oral, buccal, rectal, subcutaneous, intranasal, intramuscular, intravenous, pulmonary, and transdermal are the traditional drug delivery methods. These are the most widely utilized techniques for treating a variety of medical issues, but they have drawbacks, including instability, displacement danger, uncontrolled release, discomfort and irritation as side effects, sluggish absorption, enzymatic degeneration, and many more. One of the most effective ways to deliver a medicine in a targeted and sustained manner is by incorporating it into a nanocarrier. We talk about the use of nanocarriers including carbon nanotubes, solid nanoparticles, liposomes, dendrimers, polymeric nanoparticles, polymeric micelles, virus-like nanoparticles, and mesoporous silica nanoparticles.

Nucleic acid-based drug delivery systems, cell-based drug delivery systems, self-nano emulsifying drug delivery systems, self-micro emulsifying drug delivery systems, chemical and physical stimuli-based drug delivery systems, nanoneedles, patches, ultrasound drug delivery, and microchip technology are some examples of innovative delivery systems that are designed to overcome the limitations of drug delivery. These systems are commonly referred to as smart drug delivery systems. The fundamentals of drug delivery, pharmacokinetic research, new developments, and potential directions for the drug delivery system are the main topics of this article.

Keywords: Targeted Drug Delivery System, nanomedicine, Nanoparticles Drug Delivery System, Nanoparticles used in Drug Delivery System.

I. INTRODUCTION

"Designed for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "materials (other than food) designed to impact the structure or any function of the body of man or other animals" are two items that the FDA defines as drugs. With a precise therapeutic concentration, the medications should be able to effectively target the disease-causing cell. On the other hand, it has been noted that stability, release rate, and the capacity to target specific cells and tissues are uncontrollable and impossible to track [1]. The design of the drug delivery system is to overcome obstacles. A drug delivery system can control the pace of drug release and increase the drug's efficacy.

Studying technical principles, material design, implementation strategies, and clinical application are all part of the drug delivery system design process. Diffusion, erosion, degradation, shear, swelling, binding kinetics, passive cell uptake, surface area, and active cell uptake are the main topics of engineering concepts. The design of the material incorporates two systems: a self-emulsifying system and a controlled medication delivery system [2]. The following categories apply to controlled drug release systems: matrix, reservoir, hydrogel, osmotic pump, degradable material, and erodible material. Drug release in a matrix system occurs through linked pores. The semipermeable membrane in the reservoir system allows the medicine to pass through. The deterioration of the material creates a porous structure in the degradable material system, which causes the medicine to extrude. The hydrogel system uses a restrict mesh to release the medication. Drug release in an osmotic pump system occurs when the osmotic pressure changes through one or more pores in Oil, surfactant, co-surfactant, and medicine make up self-emulsifying drug delivery systems; when diluted with water, they form micro or nano emulsions [3].

There are a number of traditional approaches to getting a medicine into the target cell, but each one has drawbacks. This resulted in the creation of an intelligent medication delivery system that can overcome the drawbacks of traditional techniques. The mechanism underlying the drug's targeted delivery is the main topic of this review.

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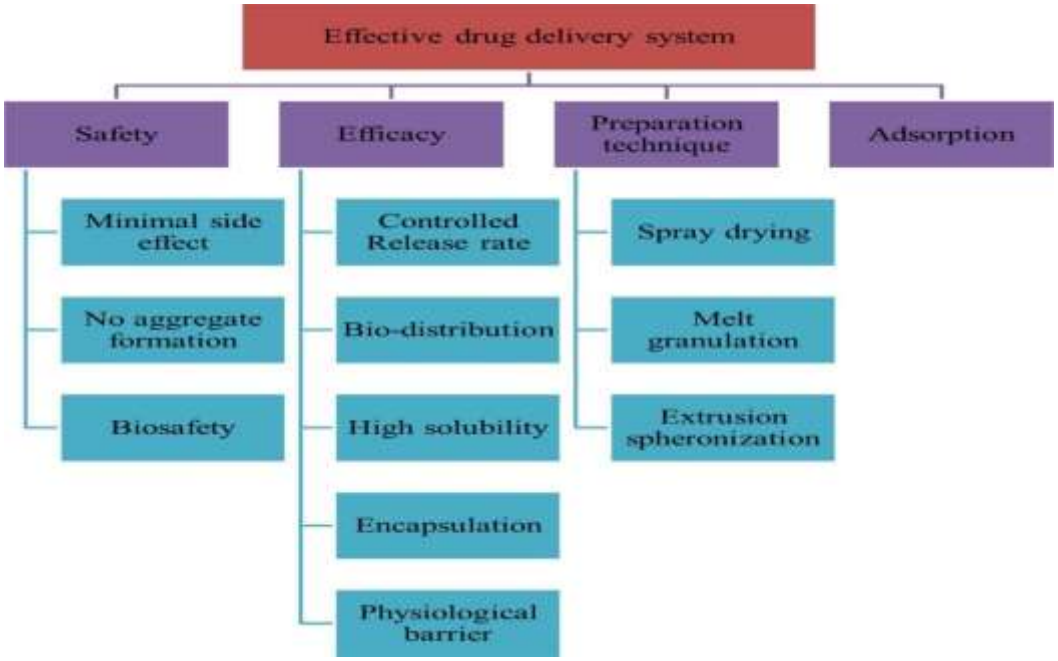

Fig 1:

II. MECHANISM OF TARGETED DRUG RELEASE

In order to limit side effects, a targeted drug delivery system transports the pharmacokinetic medication to the site of action while avoiding needless interactions with other healthy tissue [6]. Unwanted effects on healthy cells result from non-targeted drug administration, such as that of chemotherapeutic drugs used to treat cancer. Targeted drug administration lowers the dosage while increasing the consistency of the medicine's effect [7].

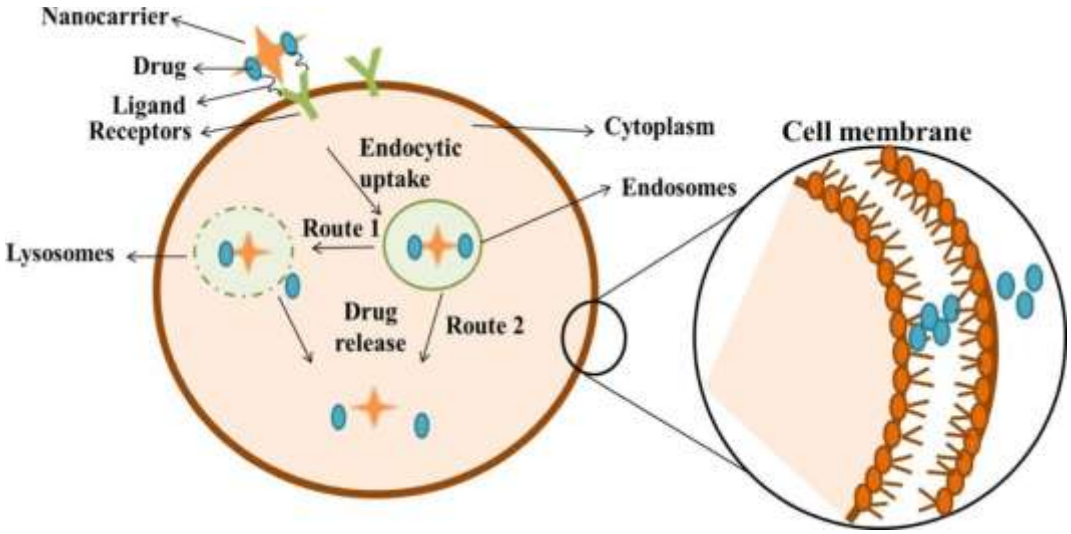

Fig 2: Schematic illustration of target drug release system in cytosol and cell membrane.

It shows that nanoparticles get linked to the receptors, then via endocytosis enters the cell and ultimately leads to release of drug.

The process of targeted medication release involves three steps: The drug nanocarrier enters the cell through endocytosis, (i) connects with the target cell's receptors through multivalent receptor–ligand interactions, and (ii) releases the drug in the final phase. By interacting with the lipid membrane, targeted drug delivery can occur in the cytosol and cell membrane (Fig. 2) [8].

Two techniques—linker cleavage and carrier control—can be used to release drugs; these are covered in more detail in this section [8].

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Linker cleavage

A linker is a component of fusion proteins that can separate several domains within a single protein [9], [10]. Cleavable and non-cleavable linkers are the two varieties. When the right conditions are present, cleavable linkers can readily break bonds. For example, endocytosis allows antibody–drug conjugates to enter the lysosome. Hydrolytic enzymes and a low pH environment within the lysosome facilitate cleavage. No chemical trigger can cause the cleavage of non-cleavable linkers [11]. Linker cleavage is essential for targeted drug delivery, which is covered in more detail in this section. Numerous processes, including ester hydrolysis, amide hydrolysis, hydrazone hydrolysis, disulphide exchange, hypoxia activation, mannich base, self-immolation, and others, can be used to release the medication through linker cleavages.

Ester linkers are also effective at basic pH, which is helpful for regulated release [12]. A drug conjugate with a nanocarrier can be formed using an amide linker. High temperatures and strong acids or bases are required for the chemical hydrolysis of amide bonds [13]. The ideal pH for cleavage is equivalent to or greater than five, and the hydrazone bond is stable at 7.4 pH [8]. A thiol group initiates the electrochemical or disulfide exchange reaction that causes disulfide bond breaking in the cytoplasm [14], [15], [16], and [17]. In hypoxic conditions, such as tumor microenvironments, the oxygen delivery to the tissue and cells is low [18], [19]. Mannich base functions as the parent drug's prodrug, aiding in includes an intervening linker. After the reaction is initiated, the triggering moiety is removed from the linker, which activates the free spacer and causes the medication to release on its own. By repeatedly releasing a large number of medication units each reaction cascade8, it has an advantage over other methods in that it increases the frequency of release. The process of photochemistry uses a photocleavable linker, and light triggers this reaction [20], [21]. In order to activate the anti-inflammatory group of azo- linked prodrugs of 5-aminosalicylic acid, the azo reaction entails the biological cleavage of the azo linker [22], [23]. The term "thermolysis" describes the breakage of a drug linker's chemical bond when temperature stimuli serve as a trigger [8].

Control of carrier

Drug loading and release can be accomplished through non-covalent mechanisms. Particle size, shape, and geometry have a crucial role in controlling biological mechanisms and can be accomplished through encapsulation or contact with the carrier [24], [25], [26], and [27]. The drug is put into the carrier and released through controlled diffusion in the encapsulation process [8].

III. NANO BASED DRUG DELIVERY SYSTEM

In order to cure a variety of illnesses, there have been significant advancements recently in the field of delivery systems that carry therapeutic agents or natural active substances to their intended region [33, 34]. Numerous drug delivery systems have been effectively used recently, but there are still some issues that need to be resolved and cutting-edge technology must be created in order to efficiently deliver medications to their intended locations. As a result, research is currently being done on nano-based drug delivery systems that will enable more sophisticated drug delivery systems.

1. FUNDAMENTAL NANOTECHNOLOGY BASED TECHNIQUE IN DESIGNING OF DRUG

Nanomedicine is the branch of medicine that utilizes the science of nanotechnology in the preclusion and cure of various diseases using the nanoscale materials, such as biocompatible nanoparticles [35] and nanorobots [36], for various applications including, diagnosis [37], delivery [38], sensory [39], or actuation purposes in a living organism [40]. Drugs with very low solubility possess various biopharmaceutical delivery issues including limited bio accessibility after intake through mouth, less diffusion capacity into the outer membrane, require more quantity for intravenous intake and unwanted after-effects preceding traditional formulated vaccination process. However all these limitations could be overcome by the application of nanotechnology approaches in the drug delivery mechanism. The ability to alter characteristics like solubility, drug release profiles, diffusivity, bioavailability, and immunogenicity makes nanoscale drug design the most advanced technology in the field of nanoparticle applications. It has been the subject of much research.

Convenient administration methods, reduced toxicity, fewer adverse effects, enhanced biodistribution, and a longer medication life cycle can all result from this [17]. Both targeted and controlled release of therapeutic substances at specific sites are features of the designed drug delivery systems. Their development entails self-

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assembly, in which building blocks spontaneously form well-defined shapes or patterns [41]. They also need to get past obstacles like the mononuclear phagcyte's opsonization or sequestration.

2. BIOPOLYMERIC NANOPARTICLES INDIGENOSIS, DETECTION AND IMAGING

The Integratio" of therapy and diagnosis is defined as theranostic and is being extensively utilized for cancer treatment [44, 45]. Theranostic nanoparticles can help diagnose the disease, report the location, identify the stage of the disease, and provide information about the treatment response. In addition, such nanoparticles can carry a therapeutic agent for the tumor, which can provide the necessary concentrations of the therapeutic agent via molecular and/or external stimuli [44, 45]. Chitosan is a biopolymer which possesses distinctive properties with biocompatibility and presence of functional groups [45,46,47]. It is used in the encapsulation or coating of various types of nanoparticles, thus producing different particles with multiple functions for their potential uses in the detection and diagnosis of different types of diseases [45, 47].For analytical purposes using near-infrared and magnetic resonance imaging (MRI) mechanisms, [48] encapsulated oleic acid-coated FeO nanoparticles in oleic acid- conjugated chitosan (oleyl-chitosan) to investigate the accretion of these nanoparticles in tumor cells through the penetrability and holding (EPR) consequence under the in vivo state. Following the intravenous injection of cyanine-5-attached oleyl-chitosan nanoparticles (Cyanine 5), both methods demonstrated a discernible improvement in the tumor tissues through a higher EPR consequence and signal strength, according to the in vivo evaluations. The physical conjugation of alginate with folic acid-modified chitosan results in the formation of nanoparticles with enhanced 5-aminolevulinic (5- ALA) release in the cell lysosome, which makes colorectal cancer (CC) cells visible.

Yang et al. [49] prepared highly effective nanoparticles for revealing CC cells via a light- mediated mechanism.

The findings showed that the CC cells used the folate receptor-based endocytosis pathway to voluntarily endocytose the designed nanoparticles. A decrease in the desirability strength between the 5-ALA and chitosan through deprotonated alginate subsequently caused the charged 5-ALA to be distributed into the lysosome, which in turn led to the accumulation of protoporphyrin IX (PpIX) for photodynamic detection within the cells. In order to enable endoscopic fluorescence monitoring, this study shows that chitosan-based nanoparticles combined with folic acid and alginate are excellent vectors for the specific delivery of 5-ALA to the CC cells. Cathepsin B (CB) is crucial for the detection of metastasis since it is highly linked to the metastatic process and is abundant in the pericellular regions where it takes place.

Nanoparticles used in Drug Delivery System

1. Biopolymeric nanoparticle

The drug delivery systems make use of a variety of biopolymeric materials. Below is a discussion of these materials and their characteristics.

2 Chitosan

Because of its mucoadhesive qualities, chitosan can be applied to tight epithelial junctions. For continuous drug release systems for several kinds of epithelia, such as buccal [109], intestinal [110], nasal [111], ocular [112], and pulmonary [113], chitosan- based nanoparticles are therefore frequently utilized. In order to provide the antibiotic ceftazidime to the eye, Silva et al. [114] produced and assessed the effectiveness of a 0.75% w/w isotonic solution of hydroxypropyl methylcellulose (HPMC) containing chitosan/sodium tripolyphosphate/ hyaluronic acid nanoparticles. The viscosity of the nanoparticles in contact with mucin in varying mass proportions was used to compute the rheological synergism parameter.

Pistone et al. [115] prepared chitosan, alginate, and pectin nanoparticles as possible candidates for drug administration into the oral cavity; the formulations' biocompatibility was estimated based on the nanoparticles' solubility in a salivary environment and their cytotoxicity potential was estimated in an oral cell line; alginate nanoparticles were the most stable in the artificial saliva for at least two hours, while pectin and particularly chitosan nanoparticles were unstable; however, the chitosan nanoparticles were the most cyto-competitive, while alginate and pectin nanoparticles demonstrated cytotoxicity under all tested conditions (concentration and time); the presence of Zn2+ (cross-linking agent) may be the cause of the observed cytotoxicity.

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3. Alginate

Alginate is another biopolymeric substance that has been utilized to transport drugs.

Compared to cationic and neutral polymers, this biopolymer exhibits higher mucoadhesive strength and is categorized as an anionic mucoadhesive polymer due to its terminal carboxyl groups [59, 118]. In order to increase blood insulin levels and decrease serum glucose levels in diabetic rats, Patil and Devarajan [119] created insulin-containing alginate nanoparticles using nicotinamide as a penetration agent. When nicotinamide was present, sublingually given nanoparticles (5 IU/kg) demonstrated high availability pharmacology (>100%) and bioavailability (>80%). The streptozotocin-induced diabetic mouse model has demonstrated that NPs are promising sublingual insulin carriers, as evidenced by their high pharmacological potential of 20.2% and bioavailability of 24.1% when compared to In order to treat depression, Haque et al. [120] also made alginate nanoparticles that release venlafaxine (VLF) intranasally. The superiority of the nano-formulation in directly conveying the VLF to the brain was demonstrated by the higher blood/brain ratios of the VLF concentration to the alginate nanoparticles given intra-nasally as opposed to the intranasal VLF and intravenous VLF solution. These nanoparticles show promise in treating depression in this way. To target non-small cell lung cancer cells, Román et al. [121] created alginate microcapsules with epidermal growth factor attached to their exterior. The nanoparticles also included the cancer medication cisplatin. EGF considerably improved carrier systems' selectivity and showed cell death kinetics (for the H460 lung cancer strain) more quickly than Consequently, they need to be further refined. Furthermore, in order to release intra- nasal carbamazepine (CBZ) without crossing the blood–brain barrier, Liu et al. [116] synthesized carboxymethyl chitosan nanoparticles. This improved treatment efficacy and increased the amount of medication in the brain, lowering systemic drug exposure. With a mean diameter of 218.76 ± 2.41 nm, the nanoparticles demonstrated 80% encapsulation efficiency and 35% drug loading. Over 240 minutes, the brain's CBZ concentrations were higher ($P<0.05$) than the plasma's. Using oral delivery, Jain and Jain [117] examined the discharge profile of 5-fluorouracil (5-FU) from chitosan nanoparticles coated with hyaluronic acid into the gut. Assays for release conducted under settings that replicate the passage from the stomach to the colon revealed the

4. Xanthum gum

Xanthomonas campestris produces xanthan gum (XG), a high molecular weight heteropolysaccharide. Being a polyanionic polysaccharide, it possesses strong bioadhesive qualities. Xanthan gum is a common pharmaceutical excipient due to its non-toxic and non-irritating properties [124]. To treat sialorrhea, Laffleur and Michalek [125] made a carrier out of xanthan gum that has been thiolated with l-cysteine to release tannin in the buccal mucosa. When compared to native xanthan gum, thiolation of xanthan gum increased adherence on the buccal mucosa. Furthermore, xanthan gum thiolate absorbs more saliva than tannic acid, which adstringently dries out the oral mucosa. In this sense, this device would be an effective means of lowering the salivary flow of sialorrhea sufferers. Angiogenesis is aHuang et al. [126] created injectable hydrogels with strong angiogenic factors (antivascular endothelial growth factor, or VEGF) that are made of carboxymethyl-modified chitosan and aldehyde- modified xanthan to enhance abdominal wall restoration. The hydrogel's releasing properties were mostly observed in open wounds and the digestive tract. The abdominal wall was able to be rebuilt and the angiogenesis process accelerated by the VEGF-containing hydrogel. A novel excipient was investigated by Menzel et al. [127] with the goal of using it as a nasal release method. The primary polymer in which the 2- amino-2-carboxyethyl) disulfanyl nicotinic acid (Cys-MNA) was linked was xanthan gum. The resulting conjugate's characteristics, including its durability against degradation, mucoadhesive qualities, and quantity of the associated binder, were examined. For every gram of polymer, 252.52 ± 20.54 µmol of the binder was used to ligate it.

5. Cellulose

The main reason cellulose and its derivatives are widely used in drug delivery systems is to change the solubility and gelation of the medicines, which in turn controls their release profile [128]. The use of chitosan nanoparticles and cellulose nanocrystals for the oral release of repaglinide (an anti-hyperglycemic—RPG) was examined by Elseoud et al. [129]. In contrast to the hybrid nanoparticles of chitosan and cellulose nanocrystals containing RPG, the chitosan nanoparticles displayed a mean size distribution of 197 nm. The mean diameter of RPG-containing oxidized cellulose nanocrystals and chitosan hybrid nanoparticles ranged from 251 to 310 nm.

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Hydrogen connections between the drug and the cellulose nanocrystals caused the drug to be released continuously, and as a result, the oxidized cellulose nanocrystal nanoparticles showed Have created a medication targeting mechanism that targets the colon and is based on the conjugation of calcium alginate beads with carboxymethylcellulose (CMC) loaded 5-fluoroacyl (5-FU). In the colonic environment simulation, the beads with reduced CMC fractions showed increased swelling and muco-adhesiveness. 90% of the 5-FU contained in the beads was released when intestinal enzymes were present. Four cellulose derivatives—meteylcellulose, hydroxypropyl methylcellulose, sodium carboxymethylcellulose, and cationic hydroxyethyl cellulose—were examined by Hansen et al. [131] for use in drug release into the nasal mucosa. It was also assessed how these cellulose derivatives interacted with another excipient. Acyclovir was the drug model used in this procedure. Additionally, the polymers' suitability as excipients for nasal release applications was examined for its

6. Liposomes

Alec Bangham made the discovery in 1960. Liposomes are one of the most researched drug delivery carrier systems and are utilized in the pharmaceutical and cosmetics industries to transport a variety of compounds. An established formulation technique to enhance medication distribution is the use of liposomes. They are spherical vesicles made of steroids and phospholipids that are typically between 50 and 450 nm in size [132]. Since their membrane structure is similar to that of cell membranes and because it makes it easier to incorporate pharmaceuticals into them, they are thought to be superior drug delivery vehicles [132]. Additionally, it has been demonstrated that they stabilize medicinal substances, enhance their biodistribution, work with both hydrophilic and hydrophobic medications, and are both biocompatible and biodegradable. There are four categories of liposomes: (1) Conventional type liposomes: these are composed of an aqueous core material encased in a lipid bilayer that can form either neutral, cationic, or anionic phospholipids and cholesterol. In this instance, hydrophobic or hydrophilic substances can be used to fill the lipid bilayer and the aqueous gap, respectively. (2) PEGylated types: To attain steric equilibrium, polyethylene glycol (PEG) is added to the liposome's surface. (3) ligand-targeted type: ligands such as peptides, carbohydrates, and antibodies are affixed to the liposome's surface or to the terminus of PEG chains that have already been attached. (4)

Theranostic Liposome Type: a combination of tvithe first three liposome kinds, it typically includes a nanoparticle in addition to a targeting, imaging, and Thin layer hydration, mechanical agitation, solvent evaporation, solvent injection, and surfactant solubilization are the standard synthesis processes for liposomes [134]. It is important to note that the medications that are encapsulated in liposomes are not accessible until they are released. In order to boost medication bioavailability within the therapeutic window at the appropriate rates and times, their accumulation in specific places is crucial. Both active (drug encapsulated after liposome formation) and passive (drug encapsulated during liposome formation) techniques are used to achieve drug loading in liposomes [135].

7. Polymeric micelles

Amphiphilic block copolymers are used to create polymeric micelles, which are nanostructures that self-assemble to form a core-shell structure in aqueous solution. While the hydrophilic shell stabilizes the core and renders the entire system soluble in water, the hydrophobic core can be loaded with hydrophobic medications (such as camptothecin, docetaxel, and paclitaxel). Because polymeric micelles are smaller than 100 nm and often have a restricted distribution to prevent rapid renal elimination, the EPR effect allows them to accumulate in tumor tissues. Furthermore, nonspecific interactions with biological components are inhibited by their polymeric coating.

Because of their internal core structure, which allows these medications to be assimilated and improve stability and bioavailability, these nanostructures offer a great potential for hydrophobic drug delivery. Two methods are used to create polymeric micelles: (1) the easy solvent-based direct dissolving of the polymer followed by the dialysis procedure, or (2) the solvent-assisted precipitation of a single block [142,143]. Micelle production is influenced by variables such as temperature, solvent system, amphiphile concentration, and the size of the hydrophobic chain of the amphiphilic molecule [144]. When the amphiphilic molecules reach the critical micelle concentration (CMC), a minimum concentration, the micelle construction process begins [143]. The amphiphilic molecules do actually arise independently and are tiny at lower concentrations [143].

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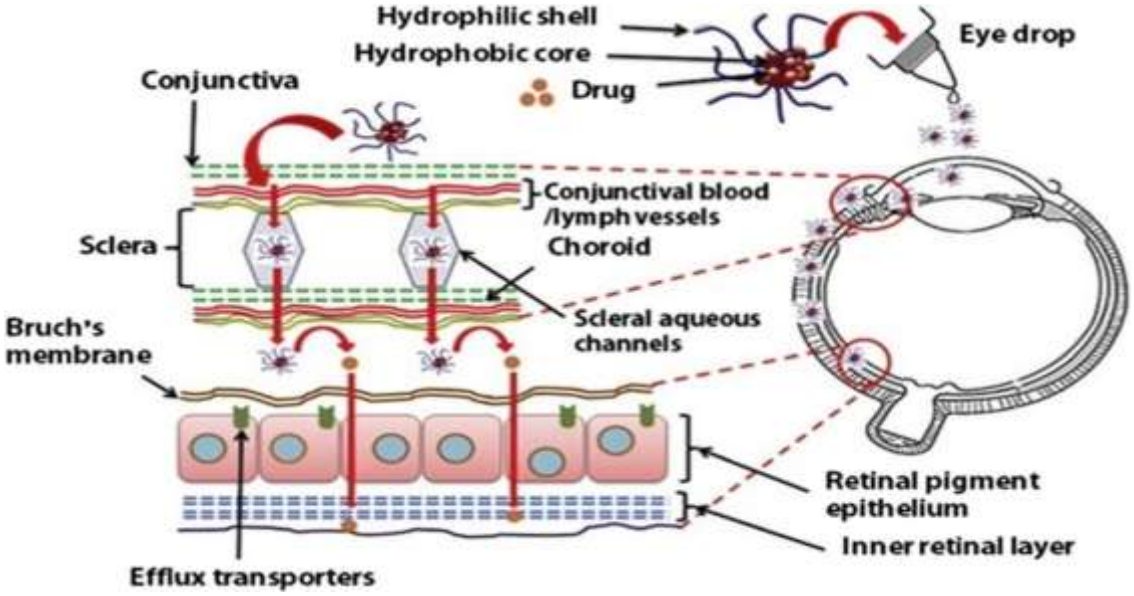

Fig 3:

8. Dendrimers

Dendrimers are three-dimensional, well-defined, monodisperse, and strongly bifurcated structures. Because of their globular form and easily regulated surface functionalization, these structures are great options for drug administration [149,150,151]. There are two methods for synthesizing dendrimers: The first is the divergent path, where the dendrimer begins to form from its core and subsequently extends outward, while the second is the convergent path, which begins from the dendrimer's exterior [152]. According to their functionalization moieties, dendrimers are classified into a number of types, including PAMAM, PPI, liquid crystalline, core-shell, chiral, peptide, glycodendrimers, and PAMAMOS. Of these, PAMAM is the most researched for oral drug delivery due to its water solubility and ability to penetrate epithelial tissue, which enhances its transfer.Dendrimers essentially deliver drugs in two ways: a) by breaking down the drug's covalent bonding in vivo based on the presence of appropriate enzymes or a favorable environment that could cleave the bonds, and b) by releasing the drug as a result of alterations in the physical environment, such as pH, temperature, etc. [154]. Dendrimers have been created for targeted drug delivery, oral, pulmonary, ophthalmic, and transdermal administration [155].

9. Inorganic nanoparticles

Silica, iron oxide, gold, and silver are examples of inorganic nanoparticles. Even though they have some potential uses, there aren't as many studies on them as there are on the other kinds of nanoparticles included in this area. Most of the nanoparticles are still in the clinical trial stage, but only a small number have been approved for usage in clinical settings. Silver and gold metal nanoparticles have unique characteristics, such as surface plasmon resonance (SPR), that liposomes, dendrimers, and micelles lack.

They demonstrated a number of benefits, including high surface functionalization adaptability and good biocompatibility.

Although two mechanisms—paracellular transport and transcytosis—have been proposed, there is insufficient information regarding their in vivo transport and uptake mechanism, and studies on their drug delivery-related activity have not been able to determine whether the particulate or ionized form is actually related to their toxicity [158]. Biological stimuli or light activation can be used to distribute and control the release of drugs that have been conjugated to the surfaces of gold nanoparticles (AuNPs) by ionic or covalent bonding and physical absorption [159].

10. Nanocrystals

Pure solid drug particles having a diameter of 1000 nm are called nanocrystals. These are pure drugs with no carrier molecules attached, and they are typically stabilized with surfactants or polymeric steric stabilizers. The use of a surfactant agent, referred to as nano-suspension, typically alleviates a suspension of nanocrystals in a

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marginal liquid medium. The dispersing medium in this instance is primarily water or any other aqueous or non-aqueous media, such as oils and liquid polyethylene glycol [162, 163].Certain characteristics of nanocrystals enable them to get around obstacles including enhanced solubility at saturation, accelerated rate of disintegration, and improved adhesiveness to cell membranes. There are two methods used to create nanocrystals: top-down and bottom-up methods. Sono-crystallization, high gravity controlled precipitation technology, multi-inlet vortex mixing techniques, and limited impinging liquid jet precipitation technique are all included in the top-down approach [162]. However, this procedure is highly costly due to the use of an organic solvent and its eventual cleanup. The bottom-up method includes greater pressure homogenization and grinding processes [162].

11. Metalic Nanoparticles

Metallic nanoparticles have gained popularity in recent years for use in a variety of medical applications, including photoablation treatment, target/sustained drug delivery, biosensors, bioimaging, and hyperthermia [35, 165]. Furthermore, these nanoparticles can bind to antibodies, medications, and other ligands after being modified and functionalized with particular functional groups, which increases the systems' potential for use in biomedical applications [166]. While gold, silver, iron, and copper are the most studied metallic nanoparticles, there has been increasing interest in other types as well, including zinc oxide, titanium oxide, platinum, selenium, gadolinium, palladium, and cerium dioxide [35, 165, 166].

12. Quantum Dots

With a diameter ranging from 2 to 10 nm, quantum dots (QDs) are semiconductor nanocrystals with size-dependent optical characteristics like absorbance and photoluminescence [167]. Since QDs exhibit emission in the near-infrared region (<650 nm), which is a highly desirable characteristic in the field of biomedical images due to their low absorption by tissues and reduction in light scattering, they have garnered a lot of attention in the field of nanomedicine, in contrast to conventional organic dyes [167, 168]. Furthermore, the same light source can excite QDs of varying sizes and/or compositions, producing distinct emission colors throughout a broad spectrum range [169, 170]. QDs are highly attractive for multiplex imaging in this regard. In the sphere of medicine, QDs have been. . There are now several research in the literature about the use of QDs as contrast agents for in vivo imaging [168, 171,172,173]. A new fluorophore for intravital cytometric imaging was created by Han et al. [172] using QDs-antibodies conjugates covered with polyimidazole ligands that display norbornene. Bone marrow cells were labeled in vivo using this fluorophore. The fluorophore was able to mark uncommon cell populations, including hematopoietic stem and progenitor cells, and diffuse throughout the bone marrow, according to the scientists' findings [172]. A multifunctional biocompatible graphene oxide quantum dot coated with a luminous magnetic nanoplatform was created by Shi et al. [171] to identify and diagnose a particular type of liver cancer tumor cell (glypican-3-expressing Hep G2). The authors claim that the binding of an anti-GPC3 antibody.

13. Protein and polysaccharide nanoparticles

Together, polysaccharides and proteins are referred to as natural biopolymers, and they are derived from biological sources such microbes, plants, animals, and marine life [178, 179]. In general, protein-based nanoparticles can be broken down, metabolized, and easily functionalized to connect to certain medications and other targeted ligands. They are generally synthesized by employing two separate techniques, (a) from water- soluble proteins like bovine and human serum albumin and (b) from insoluble ones like zein and gliadin [180]. Coacervation/desolvation, emulsion/solvent extraction, complicated coacervation, and electrospraying are the typical techniques used to create them.

Coacervation/desolvation, emulsion/solvent extraction, complicated coacervation, and electrospraying are the typical techniques used to create them. To enhance and improve their targeting mechanism, the protein-based nanoparticles undergo chemical modification to incorporate targeting ligands that pinpoint certain cells and tissues [180]. Similarly, sugar units (monosaccharides) joined by O-glycosidic linkages make up polysaccharides. These monomers' biological origin and composition can give these polysaccharides a number of distinct physical-chemical characteristics [126, 179, 181]. The deterioration (oxidation) properties of polysaccharides at high temperatures (beyond their melting point), which are frequently necessary in

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industrial operations, are one of the primary disadvantages of their usage in the field of nanomedicine. Additionally, the majority of polysaccharides dissolve in water, which restricts.

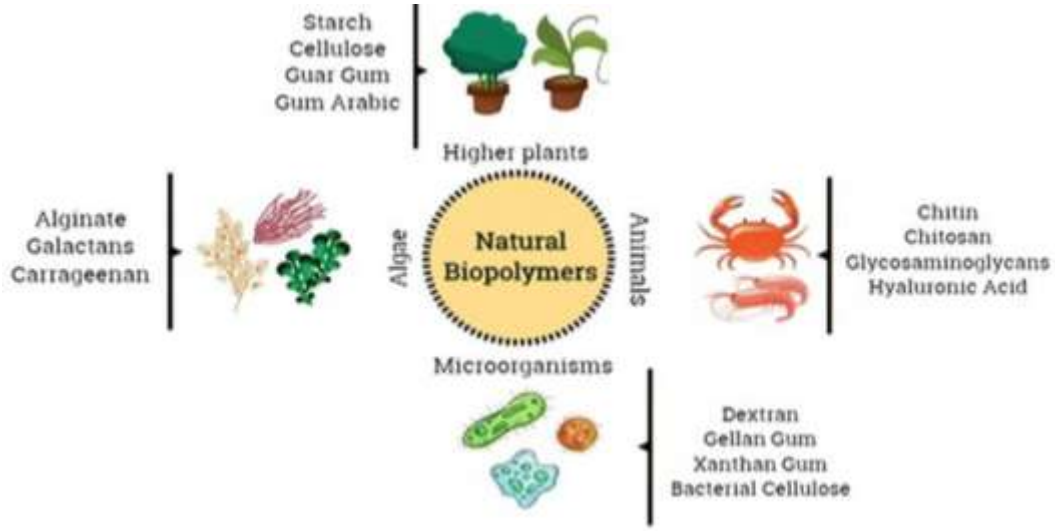

Fig 4:

IV. CONCLUSION

The present review discusses the recent advances in nanomedicines, including technological progresses in the delivery of old and new drugs as well as novel diagnostic methodologies. A range of nano-dimensional materials, including nanorobots and nanosensors that are applicable to diagnose, precisely deliver to targets, sense or activate materials in live system have been outlined. Initially, the use of nanotechnology was largely based on enhancing the solubility, absorption, bioavailability, and controlled-release of drugs. Even though the discovery of nanodrugs deal with high levels of uncertainties, and the discovery of pharmacologically active compounds from natural sources is not a favored option today, as compared to some 50 years ago; hence enhancing the efficacy of known natural bioactive compounds through nanotechnology has become a common feature.The therapeutic use of nanotechnology for resveratrol, curcumin, quercetin, ellagic acid, and berberine are excellent examples. Using nanocarriers made with polymeric nanoparticles of gold, silver, cadmium sulfide, and titanium dioxide in addition to solid lipid nanoparticles, crystal nanoparticles, liposomes, micelles, superparamagnetic iron oxide nanoparticles, and dendrimers has significantly increased the effectiveness of these natural products. Novel natural biomaterials have been in high demand because to their low toxicity, biodegradability, biocompatibility, availability, and renewable nature. Beyond identifying such proteins and polysaccharides as natural biopolymers, one of the most cutting-edge study areas nowadays is how to make them more stable in biological matrices and industrial processing environments via methods like crosslinking.Novel natural biomaterials have been in high demand because to their low toxicity, biodegradability, biocompatibility, availability, and renewable nature. Beyond identifying such proteins and polysaccharides as natural biopolymers, one of the most cutting-edge study areas nowadays is how to make them more stable in biological matrices and industrial processing environments via methods like crosslinking.

Additionally, polymeric nanoparticles (nanospheres and nanocapsules) produced using surfactant-free emulsion polymerization, solvent evaporation, and emulsion polymerization have been widely used. The integration of therapy and diagnosis (theranostic), as demonstrated by cancer as a disease model, is one of the main areas of focus in the recent development of nanomedicine. Synthetic polymer particles, liposome formulations, micellar nanoparticles, protein nanoparticles, nanocrystals, and many more, frequently in combination with medications or biologics, are among the astronomically growing list of FDA-approved nanotechnology-based products and clinical trials since the 1990s. Although safety/toxicity evaluations and regulatory mechanisms for nanomedicines may require more work in the future, nanomedicine has already completely changed how we find and deliver medications in biological systems. Advances in nanomedicine have made it possible for us to diagnose illnesses and even combine diagnosis and treatment.

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