INTRODUCTION

Since bigger micro-molecules are less effectively absorbed by cells than nanoparticles, they may be used as efficient delivery and transport systems. Drugs may either be affixed to the particle surface or incorporated into the particle-matrix for therapeutic uses [1]. The outcome of a drug, after it enters the biological environment ought to be under the direction of a drug-targeting system [2]. Drug delivery nanoparticles typically measure less than 100 nm in at least one dimension and are made of a variety of biodegradable substances, including natural or manufactured polymers, lipids and metals [3]. Developing nanoparticles logically based on knowledge of their interactions with the physiological environment, cell surface population, specific cell receptors, changes in cellular receptors that occur as disease progresses, pathway and location of action of the drug, drug retention, multiple administration of drugs, molecular pathways, and microbiology of the disorder under considering would be an effective method for achieving effective drug delivery. It’s crucial to comprehend the obstacles to medication development, such as the therapeutic agents’ stability in a living cell environment [4].

Natural products display exceptional chemical variety, chemical and biological capabilities with macromolecular specificity, and lower toxicity, among other noteworthy traits. They mostly have special benefits, including reduced side effects and toxicity, low cost, and strong therapeutic potential [5]. Large-sized components in drug delivery pose significant challenges, poor absorption in the body, poor in vivo instability, and low bioavailability, problems with target-specific delivery, low solubility, tonic efficiency, and likely drug adverse effects. In contrast, many natural compounds are unable to pass the clinical trial stages [6].

Nanostructures allow the delivery of combined medications at the prescribed dose since they persist in the blood circulation system for a long time. They consequently result in fewer plasma fluctuations and worse side effects. Due to their nanoscale, these structures can easily enter the tissue system, make medication administration more effective, and assure that the medicine acts where it is intended [7, 8].

When creating target-specific drug delivery systems, metallic, organic, inorganic, and polymeric nanostructures, such as dendrimers, micelles, and liposomes, are commonly taken into account. These nanoparticles are specifically added to medications that have limited solubility and poor absorption. Thus, the site-specific and target-oriented administration of medications made possible by nanotechnology has many advantages in the treatment of chronic human diseases. However, the lack of knowledge regarding the toxicity of nanostructures is a significant concern and unquestionably calls for more study to increase the efficacy while maintaining better safety to permit better actual application of these medications [9].

Novel drug delivery system (NDDS)

To increase the intake of low-solubility medications, the localization of drugs to a specific region, and drug bioavailability, nanoparticles can be utilised in the targeted delivery of medications at the site of disease. Fig. 1 depicts a conceptual comparative of untargeted and targeted medication delivery methods.
Benefits of nanotechnology-based drug design

The advantages of using nanoparticles as medication delivery systems are due to their small size and, in most instances, the utilization of biodegradable materials. Particle size is discovered to play a significant role in the success of the majority of medicine delivery systems. Due to its vast surface area and small particle size, drug nanoparticles have a higher bioavailability and enhanced solubility. They also have added more value because of their capacity to penetrate the blood-brain barrier, the pulmonary system, tumour endothelium, and skin endothelial cell tight junctions. These particles’ average nano-range size enables efficient medication absorption by a variety of types of cells as well as targeted drug accumulation [10].

The advantages of targeted drug delivery, improved bioavailability, and sustained release behaviour of medications from a single dose at the target site across an extended period of time are achieved by employing both natural and synthetic biopolymers for nanoparticle preparation; by adapting the framework, intrinsic enzymes can be precluded from destroying the drug [11].

Types of pharmaceutical nanoparticles

Quantum dots

Semiconducting nanostructures, which are 2–10 nm in size, make up quantum dots. These are nanoparticles with an organic shell covered in zinc sulphide to improve optical properties and an inorganic semiconductor core that glows when exposed to light. The solubility of quantum dots in aqueous buffers is enhanced by the inclusion of a capping. Real-time monitoring, bio-imaging in vitro, and long-term monitoring of intracellular activities have all been linked to a number of benefits. Among these characteristics are brilliant fluorescence, strong photo-stability, broad UV excitation, and narrow emission [12, 13].

Among the diagnostic and therapeutic uses of quantum dots include cell labelling, biomolecule sensing and biological effectiveness, DNA hybridization, immunoassays, the formation of non-viral vectors for gene therapy, carriers for the treatment of cancer, and transporters for biological and non-biological agents [14-16].

Nano-shells

Nano-shells, which have a silica core and an exterior layer of metal, are modified prototypes for targeted therapy. By varying the ratio between both the core and shell, these particles’ properties can be altered [17]. In order to attain the proper morphology, particles with certain forms could be protected by a thin shell [18]. As precious materials may be added to affordable cores, these shells offer the benefit of being affordable. Because of this, less expensive material is required for creating nano-shells. Nano-shells serve a variety of purposes, including chemically stabilising colloids, enhancing luminescence properties, and medication development [19].

Carbon nanotubes

These tubes have a diameter range of 1 to 100 nm and are composed of graphite sheet cylinders which are capped at either one or both end by buckyballs. They are renowned because of being hollow and cage-like and are available in a number of graphite cylinder forms (nanotubes and fullerenes). Because of its size and surface characteristics, as well as important physical characteristics, they are appropriate for encapsulation [20]. Nanotubes enter cells through endocytosis or insertion from across cellular membranes. The architectures of fullerenes are able to target mitochondria both intracellularly and in tissues. It was also discovered that they have antioxidant and antibacterial activities [21]. It is of 2 types Single-walled nanotubes (SWNTs) and Multi-walled nanotubes (MWNTs).

Paramagnetic nanoparticles

Microscopic magnetic nanoparticles can be manipulated by a magnetic field and have a diameter of less than 100 nm. These nanoparticle materials are created using magnetic components [22]. These nanoparticles are categorised based on their sensitivity to magnetic fields. Paramagnetic nanoparticles have a higher magnetic susceptibility than conventional contrast versions. These nanoparticles are used in therapy and diagnosis plans. Targeting of magnetic nanoparticles is useful for identifying particular organs [23].

Polymeric nanoparticles

Scientists are interested in biodegradable polymeric nanoparticles as a medication delivery strategy since they are largely biodegradable and biocompatible [24]. Vesicular systems, also known as nano-capsules and matrix systems also known as nanospheres, are two categories of Polymeric nanoparticles. Researchers...
have recently investigated advanced modifications of natural polymers, including synthetic polyesters. Chitosan is one of the most well-known natural polymers. Numerous polymers mitigate hazardous problems associated with synthetic polymers [25].

Natural Polymeric nanoparticles won out over conventional distribution methods because of their greater efficacy and efficiency. They do, however, have significant shortcomings, such as low repeatability, issues with degrading, and significant antigenicity. The production process regulates the drug’s release behaviour when it is encapsulated. Potential intracellular and site-targeting systems are known as polymeric nanoparticles [26].

Polylactic acid (PLA) and poly lactic-co-glycolide (PLGA)

The hydrolyzing destruction of the polymers by de-esterification, that yields the monomeric constituents of lactic and glycolic acid, is the basis for PLGA’s biodegradability. These constituents are subsequently metabolised and eliminated by the body via natural processes [27]. The most common hydrophilic polymer for surface treatment of both (hydrophobic) PLA and PLGA to create an amphiphilic block copolymer is polyethylene glycol (PEG). Its uses have mostly centred on nanoparticle, micelle, and hydrogel-based drug-delivery methods [28].

Polylactic acid (PLA) and poly lactic-co-glycolide (PLGA) copolymers

The enormous possibility of these PLA and PLGA-based nanocarriers in the therapy of numerous diseases, including diabetes, cancer, cardiac dysfunction, bacterial infection, viral infection, autoimmune diseases, and cartilage damage, has also been demonstrated in a number of preclinical animal investigations [30].

Chitosan

Chitosan can be employed to function at the constrictive epithelial junctions since it has muco-adhesive qualities. As a result, continuing release of drug systems for many different types of epithelia, such buccal, intestinal, nasal, ocular, and pulmonary, are frequently made of chitosan-based nanoparticles [31]. Chitosan is a biocompatible and biodegradable polymer having molecular moiety that may be easily changed to carry out specific tasks, making it appropriate for a wide range of possible uses. These groups often have positive surface charges. Furthermore, amphiphilic chitosan derivatives made by coupling hydrophobic long acyl chains with polymeric micelle nanoparticles have been created through self-aggregation in water [32].
Liposomes

Amphiphilic phospholipids are used to create synthetic liposomes, which self-assemble. The diameter of the aqueous core domain can vary from 50 nm to several μm in diameter [Small uni-lamellar vesicles (SUVs, less than 100 nm), large uni-lamellar vesicles (LUVs, 100-1000 nm), and gigantic uni-lamellar vesicles (GUVs, more than 1 μm, multi-lamellar vesicles (MLVs) have an onion-like structure made of concentric bilayer surfaces (hydrated multilayers)], and they are composed of spherical, double-layered vesicles that surround it [33-35]. Biological properties of liposomes that are intriguing include their overall biocompatibility and biodegradable nature. The most frequently employed nano-systems as drug delivery systems in clinical studies are liposomes. It can be used to lessen adverse effects and toxicity as well as pharmaceutical clearance. Nano-sized altered liposomes possess good pharmacokinetic properties for the delivery of DNA, siRNA, proteins, and cancer therapies [36].

Fig. 8: Diagrammatic representation of liposomes

Lipid-based systems are simpler to produce than biopolymers since the basic phospho-lipid molecules are widely available.

The drawbacks of liposomes include their limited loading capacity, quick release of drug, and absence of programmable release of drug sequences. Since liposomes cannot enter cells, drugs are also released into extracellular fluid [37]. Surface treatment can be used to achieve stability and structural stability against with a harsh bio-environment after oral or parenteral delivery. Ammonium sulphate gradients can be used to integrate drugs into liposomes’ aqueous phase in order to slow down their fast drug release [38]. As a result, there will be constant drug entrapment and little drug loss during circulation. Additionally, liposomes and antibodies have been used to administrate drugs to specific sites.

The conjugation of appropriate hydrophilic polymers, including such dextran, alginate, and chitosan on their own surface, is indeed a key strategy for enhancing the associated with the occurrence of lipid nano-carriers. Other hydrophilic polymers include polyethylene glycol (PEG), polyvinyl alcohol (PVA), and polyvinyl pyrrolidone (PVP). With this strategy, it is possible to get beyond immune system interference, poor blood circulation half-life, toxic effects, and biodegradable polymeric problems. The most popular polymer conjugation method, PEGylation, results in a surface density of highly hydrated particles that sterically inhibit interactions to plasma proteins or cells through both hydrophobic and electrostatic means. This slows down the RES’s ability to absorb liposomes.

Dendrimers

Dendrimers are three-dimensional, hyperbranched nanoparticles which are structured in concentric rings (referred to as generations) and have several functional surfaces on the outside. They are made up of polymeric branch units which are covalently bonded to a core structure. These dendrimers’ amount of branching, which can be controlled, determines their size. Furthermore, dendrimer spherical branching produces gaps that can be utilized for delivery of drugs and trapping [39, 40]. Dendrimer-free ends, in contrast hand, can be modified for molecular conjugation.

The incorporation of appropriate compounds into the surfaces of dendrimers is among the most significant uses of these materials. This strategy encourages the creation of a new prototype that really can serve as an imaging agent, sensing affinity ligands, and targeting elements, while delivery of drugs applications show that dendrimers can effectively transfer genetic information into cells [41].

The main function in drug delivery procedures of Dendrimers appears to be played by charge effects and electrostatic forces. Various techniques that rely on the primary interaction among dendrimers and lipid bilayers, include adsorption on membrane, gap generation, and vesicles disruption, could be taking strategic on the dendrimer chemical composition, shape, and charge density [42]. The measured by total between charged dendrimers and zwitterionic lipids, which have a net dipolar charge, and the hydrophobic interface between both the arm of the dendrimers and the lipid hydrocarbon chains substantially influence the various interaction modes. Functional groups in the dendrimer’s surface also make it possible to add additional moieties, including folate and antibodies, which are now frequently used as target specific diseases and enhance drug delivery [43].

Solid lipid nanoparticles

Like a controlled alternative to emulsions, liposomes, and polymeric nanoparticles as a colloidal drug delivery system, solid lipid nanoparticles (SLN) were created. Solid lipids are used to create SLNs, which are stabilised by surfactant [44].

Fig. 9: Diagrammatic representation of dendrimers

Fig. 10: Diagrammatic representation of solid lipid nanoparticles
Over the other nanoparticle transporters, SLN has a number of advantages for delivery of drugs, including greater tolerability, biodegradability, high bioavailability through the ocular route, and a focused effect on the brain. In recent times, SLN research has proliferated, especially with the development of the high-pressure homogenization method, SLN has been created and researched for a number of uses. Due to their tiny size, SLN are ideal for intravenous injection and medication site-targeting [45].

Nano-emulsions

In recent times, there has been a significant amount of interest in using self-emulsified drug delivery systems (SEDDS) and nano-emulsions to improve the bioavailability of drugs with poor water solubility [46]. In non-homogeneous systems called nano-emulsions, immiscible liquids are mixed together and one is dispersed as droplets in the other. These systems enhance the oral bioavailability of medications that are only mildly water-soluble through a number of mechanisms. Additionally, because the oil droplets are so minute, there is less surface tension among them and the aqueous medium of a gastrointestinal system, enabling for a more even and thorough dispersion of drugs throughout the gut [47].

Alginate

When compared to cationic and neutral polymers, this anionic muco-adhesive polymer, which has final carb oxyl groups, exhibits better muco-adhesive strength. Their benefits include mucoadhesiveness, bio-compatibility, and biodegradation characteristics in addition to their adaptable physicochemical characteristics, which enable chemical alterations for site-specific targeting. Additionally, the combination of alginate nanoparticles with other polymers, surface customization utilising particular targeted groups, and physical or chemical cross-linking can all be used to modify mechanical properties, gel formation, and cell affinity [48, 49].

Methods to fabricate nanoparticles

The appropriate and adequate technique is determined by the physicochemical properties of the polymer and the chosen medication.

Salting out method

This technique has the benefit of lowering the stress on the protein involved in the synthesis of encapsulants, and it produced high efficiency and was simple to scale up. The extraction of water-miscible solvent from such an aqueous solution is what causes the salting-out phenomenon. The first phase involves dissolving the drug as well as the polymer in a vehicle, which would be subsequently emulsified into such an aqueous gel with a salting-out reagent and a colloidal stabiliser. Colloidal stabilisers and salting out agents, including electrolytes and non-electrolytes, have indeed been employed.

By using this method, an oil/water emulsion is created that is then diluted with additional water to improve solvent diffusion inside the aqueous phase and facilitate the production of nano-spheres. The manufacture of ethyl cellulose, PLA, and poly-methacrylic acids nano-spheres uses the salting out method [50].

Solvent evaporation method

This method depends on both how soluble the polymer is and how hydrophobic the organic solvent is. Ibuprofen’s better skin absorption and betulinic acid nanoparticles as an alternate treatment for visceral leishmaniasis are two examples [51].

The first step is the emulsification of a polymer solution in an aqueous phase, which is proceeded by the evaporation of the solvent of the polymer, which causes the polymer to precipitate as nano-spheres. The drug-polymer mixture is emulsified inside an aqueous solution that includes a surfactant or emulsifying agent to create oil in water (o/w) emulsion. Once a stable emulsion has been established, the organic solvent then is evaporated either by constant stirring or by lowering the pressure. To create tiny particle sizes, ultrasonication or high-speed homogenization may well be utilised. Nanoparticles are gathered by ultracentrifugation, and then any free drugs or stabiliser residue is removed by washing them in distilled water. For preservation, nanoparticles are even further lyophilized [52].

Emulsions-diffusion method

Excellent encapsulation efficiency, the absence of homogenization, high batch-to-batch repeatability, ease of scaling up, ease, and limited size range are just a few advantages of this method. This method was utilised to create polyactic acid and make PLGA nanoparticles that were loaded with oestrogen. The encapsulating polymeric is saturated with water after being mixed in a solvent that is partially water-miscible. Next, based on the oil-to-polymer proportion, the polymer-water saturated solvent phase is emulsion in an aqueous solution that contains a stabiliser, resulting in solvent diffusion to the outer phase as well as the creation of nano-spheres or nano-capsules. Based on the solvent’s boiling point, the solvent is eliminated in the final phase either through evaporation or filtration [53, 54].

Double emulsion and evaporation method

Examples of drug nano-formulations created using the double emulsion approach includes oleuropein with increased stability and Rose Bengal for the treatment of breast carcinoma.

The double emulsion method is used to load the lipophobic medication. Drug solutions are added to an organic solution that contains the polymer while being stirred constantly to create a w/o emulsion. The second aqueous phase then gradually incorporates the created emulsion. Continue spinning until the w/o/w emulsion forms. After the solvent has evaporated, high-speed centrifugation may be used to separate the nanoparticles [55, 56].

Coacervation or ionic gelation method

Two distinct aqueous phases have been prepared, one for the polymer and the other for the polyanion sodium tripolyphosphate, and it varies depending on the strong electrostatic attraction between both the positively charged amino group of chitosan and the negatively charged tripolyphosphate to shape coacervates-with-a-magnitude-in-the-nano-meter range [57-59].

Polymerization method

Diffusion in the polymerization medium or adsorption onto the nanoparticles after completion polymerization is the two ways that drugs are introduced during the polymerisation. An isotonic medium devoid of surfactants can be utilized to re-disperse the nanoparticle suspension after ultracentrifugation to remove the various stabilisers and surfactants that were employed throughout polymerization [60, 61].

Nano spray drying

A quick, easy, repeatable, and expandable drying method as spray drying provides for moderate ambient temperature that are ideal for heat-sensitive biopharmaceutical molecules. In contrast to certain other drying techniques, spray drying is a continual process that turns various liquids into solid particles while providing for alterations in dimension, distribution, structure, porosity, density, and chemical properties.

Four steps are involved in spray drying: heating the drying gas, producing droplets, drying the droplets, and collecting the particles [62].

Supercritical fluid technology

Although supercritical fluid technology is suitable for large-scale production and is ecologically beneficial, it requires specialised, expensive gear. Supercritical fluids are fluids that, even at temperatures higher than their critical temperature, maintain their homogeneity. Due to its moderately critical conditions, non-flammability, high cost, and safety, supercritical CO2 (SC-CO2) is the supercritical fluid that receives the most applications [63].

Future of nanomedicine and drug delivery system

Although nanoparticles and nano-drug delivery systems are widely understood, their actual impact on the healthcare system-including
in the treatment and diagnosis of cancer remains quite restricted. In the end, the use of nanoparticles will develop along with our growing understanding of diseases at the cellular scale or that reflect a nanomaterial-subcellular scale equivalent biomarker identification to open up new pathways for diagnosis and treatment. Therefore, developing nanoparticle applications for the future will require knowledge of the molecular fingerprints of disease.

Theoretical mathematical models of prediction, technologies for the evaluation of these processes, drug effect in tissues/cellular level, and the concept of controlled release of specific medications at the troubled locations are not yet reached their full potential.

Animal experiments and interdisciplinary study, which takes a lot of time and money, will yield valuable information that might be used in drug therapy and diagnostic studies. The search for more accurate treatments and diagnoses is an expanding worldwide trend, as well as the development of nanoparticles and nano-drug delivery system appears to be promising.

The creation of nanorobots and nanodevices that work in tissue diagnostic and repair mechanisms with full external methods of control has generated a significant amount of attention. But just as with their advantages, nanomedicines’ possible drawbacks must also be thoroughly investigated, both for humans and the ecosystem as a whole. Therefore, a thorough examination of the potential acute or long-term harmful consequences of novel nanomaterials on people and the environment is necessary. The accessibility of nanomedicines would be another topic of study that requires more study input as they become more and more widespread.

CONCLUSION

The application of nanotechnology to medicine, particularly more particularly to the administration of drugs, is expected to grow quickly. Pharmaceutical sciences have used nanoparticles to lessen the toxicity and adverse effects of drugs for many years. It wasn’t known until recent that the carrier systems itself could present dangers to the patient. Further than the typical risks given by compounds in the delivery matrix, new risks are added by the use of nanoparticles for medication administration. Unfortunately, there is currently no scientific framework for the potential (adverse) reaction of nanoparticles, and we know very little about the fundamentals of how nanoparticles react with living organisms, tissues, and animals.

For the future development and application of sustainable nanomaterials in medication delivery, a conceptual understanding of biological responses to nanoparticles is required. In order to advance this topic, strong cooperation between individuals involved in particle toxicology and drug delivery is required for the exchange of ideas, techniques, and knowledge.

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The authors confirm that the content of the article has no conflict of interest.

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