International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 15, Issue 6, 2023

Review Article

NANOPARTICLES: THE FUTURE OF DRUG DELIVERY

SYED SAIF IMAM*

Department of Pharmaceutical Management, Jamia Millia Islamia, Jamia Nagar-110025, India
***Corresponding author: Syed Saif Imam; *Email: saifbehappy@gmail.com**

Received: 22 Aug 2023, Revised and Accepted: 05 Oct 2023

ABSTRACT

Material in the nanometric size are used as diagnostic instruments or even to administer therapeutic compounds to particular target regions in a controlled way in nanoparticles and nano delivery systems, which is a relatively young but fast-emerging discipline. By delivering accurate medications to specified locations and targets, nanotechnology provides numerous advantages in the treatment of chronic human diseases. The use of nanomedicine (including chemotherapy medicines, biological agents, immunotherapeutic agents, etc.) in the treatment of various illnesses has recently seen a number of notable uses. Through careful examination of the discovering and use of nanomaterials in enhancing the effectiveness of both new and old drugs (such as organic products) and preferential diagnosis through disease marker substances, the review article offers a comprehensive overview of recent developments in the field of nanoparticles and nano-based drug delivery. The advantages and disadvantages of using nanoparticles for the therapeutic delivery of drugs from natural or synthetic origins are also covered. Additionally, we have provided details on the developments and prospects in the field of nanotechnology.

Keywords: Novel drug delivery system, Drug delivery, Nanoparticles

DOI: https://dx.doi.org/10.22159/ijcpr.2023v15i6.3076. Journal homepage: https://innovareacademics.in/journals/index.php/ijcpr

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 about 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 retainment, 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.

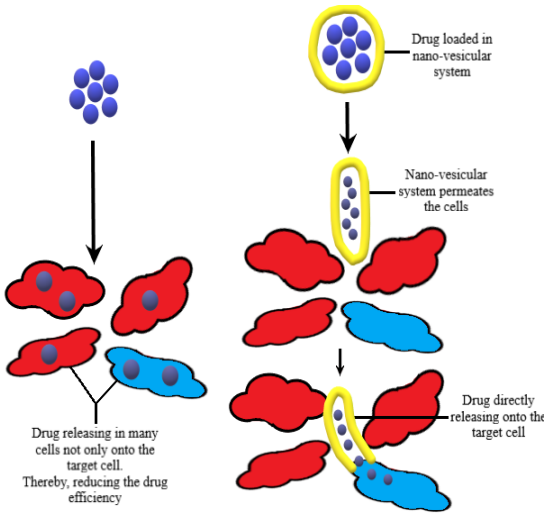

Fig. 1: Diagrammatic representation of novel drug delivery system

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].

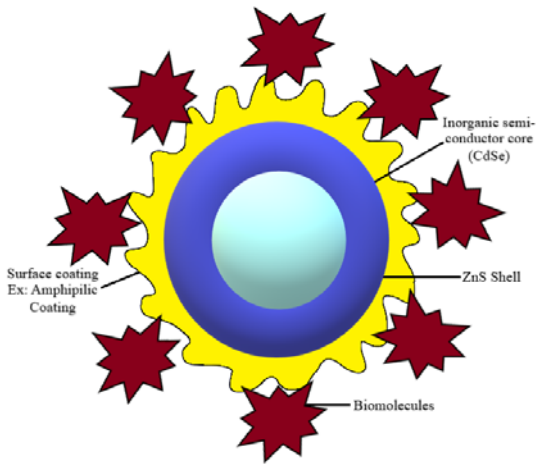

Fig. 2: Diagrammatic representation of quantum dots

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].

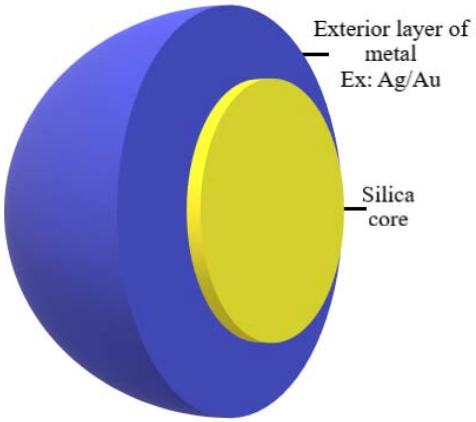

Fig. 3: Diagrammatic representation of nano-shells

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).

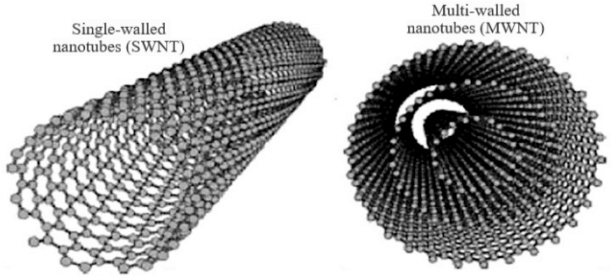

Fig. 4: Diagrammatic representation of carbon nanotubes

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 nano-spheres, 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) copolymers

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].

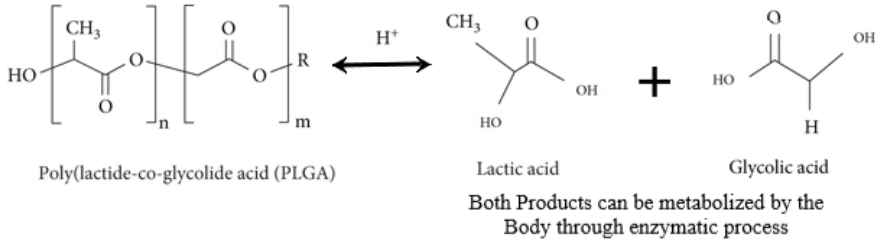

Fig. 5: Formation of poly lactic-co-glycolide (PLGA)

A significant drug loading is made possible by the PEG-PLGA copolymer's chemical conjugation, which is characterized by the drug's enforced concentration in the inner hydrophobic chains. In comparison to physically included DOX in PEG-PLGA micelles, recently developed doxorubicin (DOX) conjugated PLGA-PEG micellar nanocarriers with a greater DOX loading demonstrated a more prolonged drug release behaviour [29]. 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].

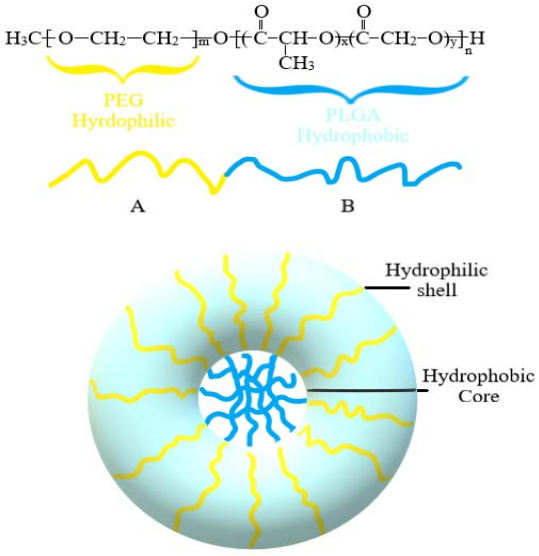

Fig. 6: Diagrammatic representation of poly lactic acid (PLA) and poly lactic-co-glycolide (PLGA) copolymers

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].

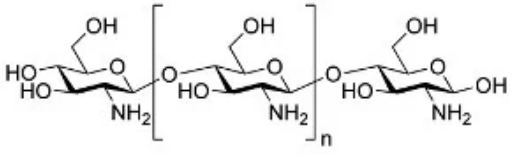

Fig. 7: Diagrammatic representation of Chitosan

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 the 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].

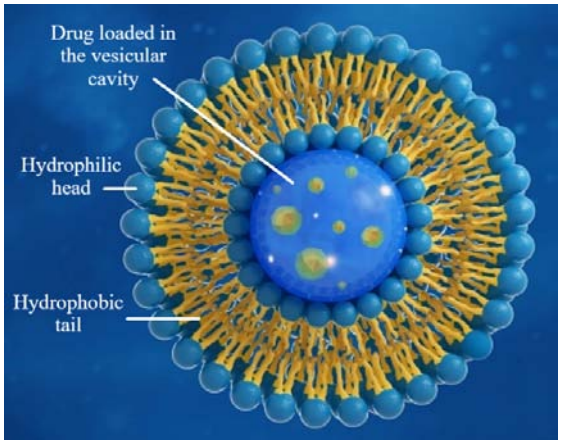

Fig. 8: Diagrammatic representation of liposomes

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 administer 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 circulatory 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.

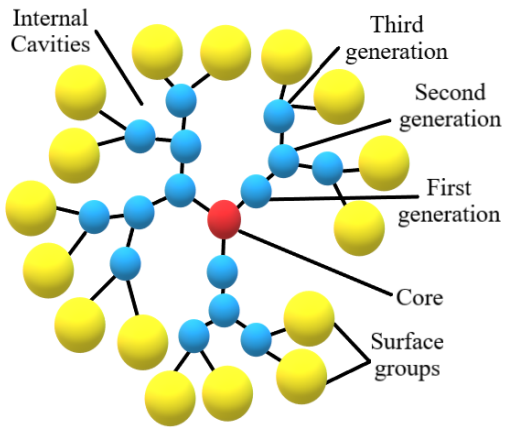

Fig. 9: Diagrammatic representation of dendrimers

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 utilised as tumour targeting techniques that can proactively target specific diseases and enhance drug delivery [43].

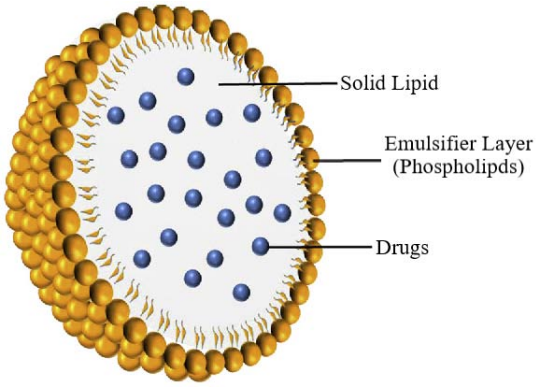

Fig. 10: Diagrammatic representation of solid lipid nanoparticles

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].

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 carboxyl groups, exhibits better muco-adhesive strength. Their benefits includes 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 polylactic 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 to 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 known 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.

ACKNOWLEDGEMENT

The authors are thankful to Department of Pharmaceutical Management, Jamia MilliaIslamia for providing kind guidance and excellent opportunity as well as necessary facilities for the research.

DATA AVAILABILITY

The original data that support the findings of this study are included in the article.

FUNDING

This research paper received no external funding.

AUTHOR CONTRIBUTION

All the work have been carried out by me.

CONFLICTS OF INTERESTS

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

REFERENCES

1. 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 Feb;2(2):85-120. doi: 10.1007/s12274-009-9009-8, PMID 20174481.
2. Razzacki SZ, Thwar PK, Yang M, Ugaz VM, Burns MA. Integrated microsystems for controlled drug delivery. Adv Drug Deliv Rev. 2004 Feb 10;56(2):185-98. doi: 10.1016/j.addr.2003.08.012, PMID 14741115.
3. Patra JK, Baek KH. Green nanobiotechnology: factors affecting synthesis and characterization techniques. J Nanomater. 2014 Oct;2014:1-12. doi: 10.1155/2014/417305.
4. Patra JK, Das G, Fraceto LF, Campos EVR, Rodriguez Torres MDP, Acosta Torres LS. Nano-based drug delivery systems: recent developments and future prospects. J Nanobiotechnology. 2018;16(1):71. doi: 10.1186/s12951-018-0392-8, PMID 30231877.
5. Duncan R. The dawning era of polymer therapeutics. Nat Rev Drug Discov. 2003 May;2(5):347-60. doi: 10.1038/nrd1088, PMID 12750738.
6. Jahangirian H, Lemraski EG, Webster TJ, Rafiee Moghaddam R, Abdollahi Y. A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine. Int J Nanomedicine. 2017;12:2957-78. doi: 10.2147/IJN.S127683, PMID 28442906.
7. Kohane DS. Microparticles and nanoparticles for drug delivery. Biotechnol Bioeng. 2007 Feb 1;96(2):203-9. doi: 10.1002/bit.21301, PMID 17191251.
8. Panyam J, Labhasetwar V. Biodegradable nanoparticles for drug and gene delivery to cells and tissue. Adv Drug Deliv Rev. 2003 Feb 24;55(3):329-47. doi: 10.1016/s0169-409x(02)00228-4, PMID 12628320.
9. Zhang J, Saltzman M. Engineering biodegradable nanoparticles for drug and gene delivery. Chem Eng Prog. 2013 Mar;109(3):25-30, PMID 25374435.
10. Lombardo D, Kiselev MA, Caccamo MT. Smart nanoparticles for drug delivery application: development of versatile nanocarrier platforms in biotechnology and nanomedicine. J Nanomater. 2019 Feb 27;2019:1-26. doi: 10.1155/2019/3702518.
11. Werner M, Auth T, Beales PA, Fleury JB, Hook F, Kress H. Nanomaterial interactions with biomembranes: bridging the gap between soft matter models and biological context. Biointerphases. 2018 Apr 3;13(2):028501. doi: 10.1116/1.5022145, PMID 29614862.
12. Amiot CL, Xu S, Liang S, Pan L, Zhao JX. Near-infrared fluorescent materials for sensing of biological targets. Sensors (Basel). 2008 May 8;8(5):3082-105. doi: 10.3390/s8053082, PMID 27879867.
13. Probst CE, Zrazhevskiy P, Bagalkot V, Gao X. Quantum dots as a platform for nanoparticle drug delivery vehicle design. Adv Drug Deliv Rev. 2013 May 1;65(5):703-18. doi: 10.1016/j.addr.2012.09.036, PMID 23000745.
14. Matea CT, Mocan T, Tabaran F, Pop T, Mosteanu O, Puia C. Quantum dots in imaging, drug delivery and sensor applications. Int J Nanomedicine. 2017;12:5421-31. doi: 10.2147/IJN.S138624, PMID 28814860.
15. Daou TJ, Li L, Reiss P, Josserand V, Texier I. Effect of poly(ethylene glycol) length on the *in vivo* behavior of coated quantum dots. Langmuir. 2009 Mar 3;25(5):3040-4. doi: 10.1021/la8035083, PMID 19437711.
16. Yao J, Li P, Li L, Yang M. Biochemistry and biomedicine of quantum dots: from biodetection to bioimaging, drug discovery, diagnostics, and therapy. Acta Biomater. 2018 Jul 1;74:36-55. doi: 10.1016/j.actbio.2018.05.004, PMID 29734008.
17. Kherlopian AR, Song T, Duan Q, Neimark MA, Po MJ, Gohagan JK. A review of imaging techniques for systems biology. BMC Syst Biol. 2008 Dec;2(1):74. doi: 10.1186/1752-0509-2-74, PMID 18700030.
18. Ghosh P, Han G, De M, Kim CK, Rotello VM. Gold nanoparticles in delivery applications. Adv Drug Deliv Rev. 2008 Aug 17;60(11):1307-15. doi: 10.1016/j.addr.2008.03.016, PMID 18555555.
19. Loo C, Lowery A, Halas NJ, West J, Drezek R. Immunotargeted nanoshells for integrated cancer imaging and therapy. Nano Lett. 2005;5(4):709-11. doi: 10.1021/nl050127s.
20. Reilly RM. Carbon nanotubes: potential benefits and risks of nanotechnology in nuclear medicine. J Nucl Med. 2007 Jul 1;48(7):1039-42. doi: 10.2967/jnumed.107.041723, PMID 17607037.

21. Saad MZ, Jahan R, Bagul U. Nanopharmaceuticals: a new perspective of drug delivery system. Asian J Biomed Pharm Sci. 2012 Jan 1;2(14):11.
22. Xu ZP, Zeng QH, Lu GQ, Yu AB. Inorganic nanoparticles as carriers for efficient cellular delivery. Chem Eng Sci. 2006 Feb 1;61(3):1027-40. doi: 10.1016/j.ces.2005.06.019.
23. Cuenca AG, Jiang H, Hochwald SN, Delano M, Cance WG, Grobmyer SR. Emerging implications of nanotechnology on cancer diagnostics and therapeutics. Cancer. 2006 Aug 1;107(3):459-66. doi: 10.1002/cncr.22035, PMID 16795065.
24. Karlsson J, Vaughan HJ, Green JJ. Biodegradable polymeric nanoparticles for therapeutic cancer treatments. Annu Rev Chem Biomol Eng. 2018 Jun 6;9:105-27. doi: 10.1146/annurev-chembioeng-060817-084055, PMID 29579402.
25. Elsabahy M, Wooley KL. Design of polymeric nanoparticles for biomedical delivery applications. Chem Soc Rev. 2012;41(7):2545-61. doi: 10.1039/c2cs15327k.
26. Tyler B, Gullotti D, Mangraviti A, Utsuki T, Brem H. Polylactic acid (PLA) controlled delivery carriers for biomedical applications. Adv Drug Deliv Rev. 2016 Dec 15;107:163-75. doi: 10.1016/j.addr.2016.06.018, PMID 27426411.
27. Cho H, Gao J, Kwon GS. PEG-b-PLA micelles and PLGA-b-PEG-b-PLGA sol-gels for drug delivery. J Control Release. 2016 Oct 28;240:191-201. doi: 10.1016/j.jconrel.2015.12.015, PMID 26699425.
28. Yoo HS, Park TG. Biodegradable polymeric micelles composed of doxorubicin conjugated PLGA–PEG block copolymer. J Control Release. 2001 Jan 29;70(1-2):63-70. doi: 10.1016/s0168-3659(00)00340-0, PMID 11166408.
29. Vu-Quang H, Vinding MS, Nielsen T, Ullisch MG, Nielsen NC, Kjems J. Theranostic tumor-targeted nanoparticles combining drug delivery with dual near-infrared and 19F magnetic resonance imaging modalities. Nanomedicine. 2016 Oct 1;12(7):1873-84. doi: 10.1016/j.nano.2016.04.010, PMID 27133191.
30. Din FU, Aman W, Ullah I, Qureshi OS, Mustapha O, Shafique S. Effective use of nanocarriers as drug delivery systems for the treatment of selected tumors. Int J Nanomedicine. 2017;12:7291-309. doi: 10.2147/IJN.S146315, PMID 29042776.
31. Jiang GB, Quan D, Liao K, Wang H. Preparation of polymeric micelles based on chitosan bearing a small amount of highly hydrophobic groups. Carbohydr Polym. 2006 Nov 23;66(4):514-20. doi: 10.1016/j.carbpol.2006.04.008.
32. Immordino ML, Dosio F, Cattel L. Stealth liposomes: review of the basic science, rationale, and clinical applications, existing and potential. Int J Nanomedicine. 2006;1(3):297-315, PMID 17717971.
33. Sackmann E. Physical basis of self-organization and function of membranes: physics of vesicles. Handbook of Biological Physics. 1995 Jan 1;1:213-304.
34. Lombardo D, Calandra P, Teresa Caccamo MT, Magazù S, Pasqua L, Kiselev MA. Interdisciplinary approaches to the study of biological membranes. AIMS Biophys. 2020;7(4):267-90. doi: 10.3934/biophy.2020020.
35. Torchilin VP. Recent advances with liposomes as pharmaceutical carriers. Nat Rev Drug Discov. 2005 Feb;4(2):145-60. doi: 10.1038/nrd1632, PMID 15688077.
36. Nekkanti V, Kalepu S. Recent advances in liposomal drug delivery: a review. Pharm Nanotechnol. 2015 Mar 1;3(1):35-55. doi: 10.2174/2211738503666150709173905.
37. Harris JM, Martin NE, Modi M. Pegylation: a novel process for modifying pharmacokinetics. Clin Pharmacokinet. 2001 Jul;40(7):539-51. doi: 10.2165/00003088-200140070-00005, PMID 11510630.
38. Moghimi SM, Hunter AC, Murray JC. Nanomedicine: current status and future prospects. FASEB J. 2005 Mar;19(3):311-30. doi: 10.1096/fj.04-2747rev, PMID 15746175.
39. Duncan R, Izzo L. Dendrimer biocompatibility and toxicity. Adv Drug Deliv Rev. 2005 Dec 14;57(15):2215-37. doi: 10.1016/j.addr.2005.09.019, PMID 16297497.
40. Lombardo D. Liquid-like ordering of negatively charged poly(amidoamine) (PAMAM) dendrimers in solution. Langmuir. 2009 Mar 3;25(5):3271-5. doi: 10.1021/la804234p, PMID 19437728.
41. Lombardo D. Modeling dendrimers charge interaction in solution: relevance in biosystems. Biochem Res Int. 2014;837651. doi: 10.1155/2014/837651, PMID 24719765.
42. Liu J, Gray WD, Davis ME, Luo Y. Peptide- and saccharide-conjugated dendrimers for targeted drug delivery: a concise review. Interface Focus. 2012 Jun 6;2(3):307-24. doi: 10.1098/rsfs.2012.0009, PMID 23741608.
43. Kayser O, Lemke A, Hernandez Trejo N. The impact of nanobiotechnology on the development of new drug delivery systems. Curr Pharm Biotechnol. 2005 Feb 1;6(1):3-5. doi: 10.2174/1389201053167158, PMID 15727551.
44. Yang SC, Lu LF, Cai Y, Zhu JB, Liang BW, Yang CZ. Body distribution in mice of intravenously injected camptothecin solid lipid nanoparticles and targeting effect on brain. J Control Release. 1999 Jun 2;59(3):299-307. doi: 10.1016/s0168-3659(99)00007-3, PMID 10332062.
45. Singh KK, Vingkar SK. Formulation, antimalarial activity and biodistribution of oral lipid nanoemulsion of primaquine. Int J Pharm. 2008 Jan 22;347(1-2):136-43. doi: 10.1016/j.ijpharm.2007.06.035, PMID 17709216.
46. Cai Z, Wang Y, Zhu LJ, Liu ZQ. Nanocarriers: a general strategy for enhancement of oral bioavailability of poorly absorbed or pre-systemically metabolized drugs. Curr Drug Metab. 2010 Feb 1;11(2):197-207. doi: 10.2174/138920010791110836, PMID 20384585.
47. Sosnik A. Alginate particles as a platform for drug delivery by the oral route: state-of-the-art. ISRN Pharm. 2014;2014:926157. doi: 10.1155/2014/926157, PMID 25101184.
48. Patil NH, Devarajan PV. Insulin-loaded alginic acid nanoparticles for sublingual delivery. Drug Deliv. 2016 Feb 12;23(2):429-36. doi: 10.3109/10717544.2014.916769, PMID 24901208.
49. Jung T, Kamm W, Breitenbach A, Kaiserling E, Xiao JX, Kissel T. Biodegradable nanoparticles for oral delivery of peptides: is there a role for polymers to affect mucosal uptake? Eur J Pharm Biopharm. 2000 Jul 3;50(1):147-60. doi: 10.1016/s0939-6411(00)00084-9, PMID 10840198.
50. Halder A, Shukla D, Das S, Roy P, Mukherjee A, Saha B. Lactoferrin-modified betulinic acid-loaded PLGA nanoparticles are strong anti-leishmanials. Cytokine. 2018 Oct 1;110:412-5. doi: 10.1016/j.cyto.2018.05.010, PMID 29784509.
51. Kwon HY, Lee JY, Choi SW, Jang Y, Kim JH. Preparation of PLGA nanoparticles containing estrogen by emulsification–diffusion method. Colloids Surf A Physicochem Eng Aspects. 2001 Jun 30;182(1-3):123-30. doi: 10.1016/S0927-7757(00)00825-6.
52. Hong JS, Srivastava D, Lee I. Fabrication of poly(lactic acid) nano-and microparticles using a nanomixer via nanoprecipitation or emulsion diffusion. J Appl Polym Sci. 2018 May 10;135(18):46199. doi: 10.1002/app.46199.
53. Bhatia S. Nanoparticles types, classification, characterization, fabrication methods and drug delivery applications. In: Natural polymer drug delivery systems. Berlin: Springer; 2016. p. 33-93.
54. Ubrich N, Bouillot P, Pellerin C, Hoffman M, Maincent P. Preparation and characterization of propranolol hydrochloride nanoparticles: a comparative study. J Control Release. 2004 Jun 18;97(2):291-300. doi: 10.1016/j.jconrel.2004.03.023, PMID 15196756.
55. Gharehbeglou P, Jafari SM, Homayouni A, Hamishekar H, Mirzaei H. Fabrication of double W1/O/W2 nano-emulsions loaded with oleuropein in the internal phase (W1) and evaluation of their release rate. Food Hydrocoll. 2019 Apr 1;89:44-55. doi: 10.1016/j.foodhyd.2018.10.020.
56. Sundar S, Kundu J, Kundu SC. Biopolymeric nanoparticles. Sci Technol Adv Mater. 2010 Feb 26;11(1):014104. doi: 10.1088/1468-6996/11/1/014104, PMID 27877319.
57. Lopez Lopez M, Fernandez Delgado A, Moya ML, Blanco Arevalo D, Carrera C, de la Haba RR. Optimized preparation of levofloxacin-loaded polymeric nanoparticles. Pharmaceutics. 2019 Jan 30;11(2):57. doi: 10.3390/pharmaceutics11020057, PMID 30704034.
58. Divya K, Jisha MS. Chitosan nanoparticles preparation and applications. Environ Chem Lett. 2018 Mar;16(1):101-12. doi: 10.1007/s10311-017-0670-y.

59. Chen D, Han S, Zhu Y, Hu F, Wei Y, Wang G. Kidney-targeted drug delivery via rhein-loaded polyethyleneglycol-co-polycaprolactone-co-polyethylenimine nanoparticles for diabetic nephropathy therapy. Int J Nanomedicine. 2018;13:3507-27. doi: 10.2147/IJN.S166445, PMID 29950832.
60. Hawkins M, Saha S, Ravindran E, Rathnayake H. Asol–gel polymerization method for creating nanoporous polyimide silsesquioxane nanostructures as soft dielectric materials. J Polym Sci Part A: Polym Chem. 2019 Feb 15;57(4):562-71. doi: 10.1002/pola.29295.
61. Arpagaus C, Collenberg A, Rutti D, Assadpour E, Jafari SM. Nano spray drying for encapsulation of pharmaceuticals. Int J Pharm. 2018 Jul 30;546(1-2):194-214. doi: 10.1016/j.ijpharm.2018.05.037, PMID 29778825.
62. Sun YP, Meziani MJ, Pathak P, Qu L. Polymeric nanoparticles from rapid expansion of the supercritical fluid solution. Chemistry. 2005 Feb 18;11(5):1366-73. doi: 10.1002/chem.200400422, PMID 15390139.