NANOPARTICLES IN EMERGING PARENTERAL DRUG THERAPY: AN OVERVIEW

***[1]Ramandeep Kaur, [2]Pushpendra Singh, [3]Rita Yadav**

Author (s) affiliations-

[1]Assistant Professor, Pharmacy Academy, IFTM University Moradabad, UP, IN

[2]Research Scholar, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur Rajasthan, IN

[3]Assistant Professor, School of Pharmaceutical Sciences, IFTM University Moradabad, UP, IN

Corresponding author's details-

Ramandeep Kaur

Assistant Professor, Pharmacy Academy, IFTM University Moradabad, UP, IN

Email id: asifkhanpcol@gmail.com

Abstract

Aim: *The aim of the study was to discuss the recent researches done over the nanoparticles and types of nanoparticles being useful in the parenteral delivery of drugs.*

Materials and methods: *Different types of nanoparticles are developed i.e., liposomes, polymeric nanoparticles, nano-capsules, dendrimers, nanotubes, nanowires, nanocrystals and nanobots. Nanoparticles are very beneficial in pharmacy and health sciences as in cancer therapy, biological binders, drug carriers, targeted therapy etc. to boost the healthcare system. It aids in the improvement of medication solubility and bioavailability, as well as the reduction of toxicity, improved release, and better formulation options. It's worth noting that various commercial oral medications have been created using nanoparticle technology to improve API absorption. Nano-milling process is used to increase absorption of nano-parenteral.*

Conclusion: *Active targeting is useful in oncology, especially for the treatment of malignancies, because it can reduce side effects. Consider tiny miniature robots that your doctor will inject into vein to look for cancer cells or administer a medicine. We anticipate that this system will modify cancer immunotherapy and provide novel therapeutic options in the near future.*

Keywords: *Nanoparticles, Nanowires, Nano-parenteral, Therapy, Liposomes*

Introduction

Nanoparticles are such solid particles those have a size b/w 10-1000nm. To entrap/ attach the drug, a nanoparticle matrix is used. Nanospheres are matrix systems in which the drug is contained within a hollow limited by a single polymer membrane, while nano capsules are matrix systems in which the medication is dispersed physically and uniformly. Biodegradable nanoparticles, especially those wrapped in hydrophilic polymers such as polyethylene glycol, have been studied as potential drug delivery devices in recent years due to its capability to circulate for extended periods of time, in target organ and deliver proteins, peptides, and genes [1][4].

Nanoparticles (NP) are appealing for such applications because of their valuable & unique features i.e., surface to mass ratio which is greater than other particles and allowing for catalytic reaction with power to adsorb other compounds [2]. Liposomes were used as potential carriers with specific advantages such as protecting drugs from degradation, targeting to the action site, and reducing toxicity or adverse reactions, but their techniques are limited due to inherent issues such as low encapsulation efficiency, quick spillages of liquid drugs, and poor storage stability [3]. Polymeric nanoparticles, on the other hand, have certain distinct benefits over liposomes. They, for example, aid in drug/protein stability and have important controlled release features. The following are some of the benefits of employing nanoparticles to deliver drugs [5][6]:

1. After parenteral delivery, nanoparticle size and surface features can be easily altered to accomplish passive and active drug targeting.
2. They modulate medication organ distribution and subsequent clearance to promote therapeutic efficacy while reducing negative effects throughout transit and at the place of delivery.
3. Matrix elements can readily control controlled release and particle degrading attributes. Pharmaceuticals can be transported into tissues without suffering any chemical changes, which is important for medication activity maintenance.
4. Targeting ligands can be added to the surface of particles to provide site-specific targeting.
5. It can be used for oral, nasal, intravenous, intra-ocular, and other modes of administration.

Nanoparticles, while their benefits, have limits due to their tiny size and huge surface area, nanoparticles can clump together, making physical handling problematic in both liquid and dry forms. [5][23] The current research looks at the most recent advancements in nanoparticulate drug delivery systems & surface modification issues and nanoparticle applications.

Types of nanoparticles

Liposomes

Liposomes are bi-layered spheres with an aqueous volume entirely contained by a membranous lipid bilayer consisting primarily of natural or synthetic phospholipids [7]. Liposomes are classed according to their size, surface charge, and number of bilayers. It offers a number of advantages, including amphiphilicity, biocompatibility, and ease of surface modification, making it an attractive option for biotech drug delivery. These have a significant impact on the pharmacokinetic profile of loaded pharmaceuticals, particularly

proteins and peptides, and can be easily changed by adding PEG to the drug's surface, transforming it into stealth liposomes with a prolonged circulation half-life [9][10][11].

Polymeric nanoparticles

Unlike nanosuspensions, polymeric nanoparticles are comprised of a fragile polymer. The most important advantage of using polymeric nanoparticles in medication delivery is that they improve the stability of any volatile pharmacological substances and may be produced in vast quantities in a variety of methods. Polymeric nanoparticles may also have been produced with customised preference allowing them to produce a rich concentration of therapeutic substance to a specific site [12][13]. Vesicular (nanocapsules) and matrix nanoparticles are both included in the category of polymeric nanoparticles (nanospheres).

Nano-capsules

Nanospheres are platforms wherein the drug is distributed all across the polymer matrix, while nanocapsules are drug-delivery systems that contain the medicine in a hollow enclosed by a polymeric membrane. The nanoparticles are made from natural polymers such as gelatin, albumin, and alginate, but they have several drawbacks, including poor batch-to-batch repeatability, vulnerability to degradation, and potential antigenicity. [14]. Inside the polymeric shell/matrix, the candidate medicine is dissolved, entrapped, connected, or encapsulated. The release characteristics of the integrated medicine can be modified depending on the technique of manufacture [15]. Their surface is easily customizable and functionalized.

Dendrimers

Dendrimers are highly branched macromolecules with precise control over size and form, making them a distinct class of polymers. Dendrimers are created from monomers utilising polymeric processes called convergence or divergence step growth. [16] Due to their well-defined morphology, monodispersity of size, surface functionalization ability, and stability, dendrimers are excellent drug carrier candidates. Drug compounds can be loaded onto dendrimers by complexation or encapsulation. [17] Dendrimers are being researched as drug and gene delivery vehicles, as well as potential penicillin transporters for anticancer treatment.

Nanotubes

Nanotubes (sometimes called buckytubes) are carbon allotropes having a cylindrical nanostructure. They are extremely strong, have good electrical properties, and are excellent heat conductors. Nanotubes are part of the heterocyclic structural category, which also contains spherical bucky balls. Chemical bonding in nanotubes is described by applied quantum chemistry, particularly orbital hybridization. Nanotubes are entirely made up of sp2 bonds, which are similar to those in graphite. These connections, which are strong than the sp3 bonds found in diamonds, give nanotubules their unique strength. Nanotubes also form "ropes" that are held together by themselves [18].

Nanowire

At these scales, quantum mechanical phenomena is crucial, hence the term quantum wires. Metallic, semiconducting, and insulating nanowires are only a few of the many options. Organic or inorganic repeating molecular units make up molecular nanowires. In the near future, nanowires may be used to connect microscopic components into exceedingly small circuits. Nanotechnology could be utilised to produce such components out of chemical compounds [19].

Nanocrystals

A nanocrystal is a single-crystalline nanostructure with at nanometer scale of less than 100 nanometers. A nanoparticle, not a nanocrystal, is any substance having a dimension with less than 1 micrometre, or 1000 nanometers. For example, every particle with crystallinity regions should be classified as a nanoparticle or organizational design based on its size. Because many of their electrical and thermal characteristics are size dependent and hence controllable through precise production methods, these materials are of great technological importance [20][21] Quantum dots are semiconductor nanocrystals with a size of less than 10 nanometers. At an ExxonMobil oil refinery in Louisiana, crystalline nanoparticles formed of zeolite are employed as a filter to convert crude oil into diesel fuel, a technology that is less expensive than the traditional approach. A coating of crystalline nanoparticles is employed in Nanosolar's SolarPly,[22] a novel form of solar panel. It is less expensive, more adaptable, and boasts a 12 percent efficiency rating. (Organic solar panels, which are often affordable, convert 9% of the sun's energy into electricity.) Photons are converted into electricity by crystal tetrapods 40 nanometers wide, albeit at just 3% efficiency. (National Geographic Magazine, June 2006) Elan Pharma International Limited (Ireland) owns the trademark NanoCrystal, which is used to describe the company's patented milling technique and nanoparticulate medication compositions.

Nanobots

Nanorobotics is the science of building machines and robots on or near the minuscule scale of nanometer (109metres). Nanorobotics, in particular, refers to the largely speculative nanotechnology engineering subject of building and producing nanorobots, which are nanoscale or molecular devices ranging in size from 0.1 to 10 micrometres [23].

Nanoparticles applications in Healthcare and Medicine

- Alternative medication and vaccine delivery techniques
- Targeted drug delivery
- Cancer therapies
- Facilitate Bone growth
- Biocompatible implants
- Bio labelling and detection (e.g., Au)
- Drug carriers with less hydrophilicity
- Fungicides
- MRI contrast agents
- Dental composites

- Biological binders
- Non-chemical lotions and powders that are antiviral, antibacterial (Ag), and anti-spore

Nanoparticles as drug carrier vehicle

It aids in the improvement of medication solubility and bioavailability, as well as the reduction of toxicity, improved release, and better formulation options.

Nano-sizing has several major advantages, including

- *Increased solubility,*
- *Increased surface area,*
- *Increased dissolution rate,*
- *Increased oral absorption,*
- *Faster onset of drug effects,*
- *Less dose required,*
- *Reduced fed/fasted variations, and*
- *Decreased patient care variability*

Nanocarriers in parenteral drug delivery

It's worth noting that various commercial oral medications have been created using nanoparticle technology to improve API absorption. For example, API dissolution is critical for improved absorption and pharmacokinetics, and this is precisely what nanomilling technologies are doing. The possibility for enhanced therapeutic targeting to tumour sites as well as increased solubility/partition in the circulating blood without the need of several excipients has sparked significant interest in nanoparticle preparations on the parenteral side. In comparison to their free-drug equivalents, nanocarrier systems have been explored for parenteral drug administration because they offer superior drug protection, controlled release, and longer circulation.

Parenteral administration of various compounds has been widely investigated using nanotechnology. Some of these compounds are harmful due to uncontrolled systemic dispersion or non-target effects, or they need to be delivered locally using nanoparticles. For example, doxorubicin, a very powerful anticancer medication, has major adverse effects such as cardiotoxicity, which limits its usage [8][24].

Types of nanocarriers

The medication is encased in polymeric nanocarriers in a spherical polymeric matrix. A good example is polymer-based particles formed of poly (lactic acid-co-glycolic acid). Different types of nanoparticles, on the other hand, have been explored for medical targeting [25][26]. Dendrimers, for example, are now being developed. The medicine is typically spread evenly throughout the nanoparticle matrix and administered slowly via diffusion and/or nanocarrier breakdown [27].

However, because most modern polymeric nanocarriers are biodegradable and have a reducing surface area, significant adjustments to the Higuchi equation are necessary [28]. Furthermore, it has been proposed that solvation of the pharmacological treatment (once on the membrane or outside the nanoparticle) is more significant than diffusion [29].

Passive tumor targeting with nanocarriers

Using aberrant tumour physiology and passive targeting of nanocarriers carrying therapeutic compounds to tumour tissues. Nanotherapeutics for parenteral medication delivery that use nanoparticle technology. Anesthesia after surgery 2011 Liposomes Marqibo/vincristine sulphate Acute lymphoblastic leukaemia with no Philadelphia chromosome Advanced (metastatic) pancreatic cancer, 2012 Onivyde Liposomes/Irinotecan vasculature has been studied in preclinical models, with malignancies showing preferential accumulation of nanoparticles [30][31]. Matsumura and Maeda demonstrated in an early investigation that proteins with molecular weights ranging from 15,000 to 70,000 g/mol may accumulate efficiently in solid tumours [32].

Tumor accumulation and prevention of diffusion back into the systemic circulation are influenced by tumour size. Particles smaller than 400 nm are eliminated from the circulation more slowly than bigger ones [27]. Polymeric micelles, for example, are unstable in blood and discharge completely after 15 minutes [28]. An editorial [21] published recently questioned our notion of increased permeability, pointing to additional extravasation mechanisms as a major contribution to nanoparticle deposition in malignancies.

Nanoparticles in gene delivery

The use of targeted delivery (peptides, tiny molecules, or antibodies) that link with receptors on the surfaces of cancer cells to transport medications to the right tissue region has been investigated using active targeting of nanocarriers. The receptor and ligand interact to allow absorption by endocytosis once a nanocarrier containing active chemical enters the tumour location via systemic circulation. Active targeting is useful in oncology, especially for the treatment of malignancies, because it can reduce side effects. The pharmacokinetic features of traditional instant release (red) and extended-release formulations are investigated (blue). The dosing time for standard and sustained release formulations is indicated by red and blue arrows, respectively. During active release, interfacial diffusion constraints in nanoparticle formulations.

Conclusion

If nanomedicines are to attain their full potential, a few hurdles must be overcome right now. Dr. Bernard L. Nobel, the 2016 Nobel Laureate in Chemistry, saw a wide range of biological uses for molecular machines, stating, "Of course, it's early days, but once you're there, you're there." Everything is possible when you have control over your movement. Consider tiny miniature robots that your doctor will inject into vein to look for cancer cells or administer a medicine. We anticipate that this system will modify cancer immunotherapy and provide novel therapeutic options in the near future.

Conflict of Interest

Authors declare there is no conflict of interest.

Funding

Nil

Acknowledgement
All the authors contributed equally in the study.

References

[1] Guidance for Industry: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology, Food and Drug Administration (Accessed 02 Fig. 4. Schematic showing flexibility for developing immunotherapy combinations based on patient parameters such as tumor phenotype and tumor biomarker information. P. Tyagi, J.A. Subramony Journal of Controlled Release, 2018; 272:159-168.
[2] E. Merisko-Liversidge, G.G. Liversidge, Nanosizing for oral and parenteral drug delivery: a perspective on formulating poorly-water soluble compounds using wet media milling technology, Adv. Drug Deliv. Rev. 63 (2011) 427-440.
[3] P.R. Khadka, H. Kim, I. Kim, J.T. Kim, H. Kim, J.M. Cho, G. Yun, J. Lee. Pharmaceutical particle technologies: an approach to improve drug solubility, dissolution and bioavailability, DOAJ 9 (2014) 304-316.
[4] L. Liu, Q. Ye, M. Lu, Y.C. Lo, Y.H. Hsu, M.C. Wei, Y.H. Chen, S.C. Lo, S.J. Wang, D.J. Bain, C. Ho, A new approach to reduce toxicities and to improve bioavail- abilities of platinum-containing anti-cancer nanodrugs, Sci. Rep. 5 (2015) 10881.
[5] C.H. Choi, C.A. Alabi, P. Webster, M.E. Davis, Mechanism of active targeting in solid tumors with transferrin-containing gold nanoparticles, Proc. Natl. Acad. Sci. U. S. A. 107 (2010) 1235–1240.
[6] J. Shi, P.W. Kantoff, R. Wooster, O.C. Farokhzad, Cancer nanomedicine: progress, challenges and opportunities, Nat. Rev. Cancer 17 (2017) 20–37.
[7] Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate-Release Solid Oral Dosage Forms Based on a Biopharmaceutics Classification System, Food and Drug Administration, 2015.
[8] P.R. Khadka, H. Kim, I. Kim, J. Kim, H. Kim, J. Cho, G. Yun, J. Lee, Pharmaceutical particle technologies: an approach to improve drug solubility, dissolution and bioavailability, Asian J. Pharm. Sci. 9 (2014) 304–316.
[9] V.B.M. Junyaprasert, Nanocrystals for enhancement of oral bioavailability of poorly water-soluble drugs, Asian J. Pharm. Sci. 10 (2015) 13–23.
[10] J. Sun, F. Wang, Y. Sui, Z. She, W. Zhai, C. Wang, Y. Deng, Effect of particle size on solubility, dissolution rate, and oral bioavailability: evaluation using coenzyme Q (1)(0) as naked nanocrystals, Int. J. Nanomedicine 7 (2012) 5733–5744.
[11] V.B. Junyapraserta, B. Morakula, Nanocrystals for enhancement of oral bioavail- ability of poorly water-soluble drugs, Asian J. Pharm. Sci. (Amsterdam, Neth.) 10 (2015) 13–23.
[12] T. Niwa, S. Miura, K. Danjo, Universal wet- milling technique to prepare oral na- nosuspension focused on discovery and preclinical animal studies - development of particle design method, Int. J. Pharm. (Amsterdam, Neth.) 405 (2011) 218–227.
[13] A.J. Paredes, J.M. Llabot, S. Sanchez Bruni, D. Allemandi, S.D. Palma, Self-dis-persible nanocrystals of albendazole produced by high pressure homogenization and spray-drying, Drug Dev. Ind. Pharm. 42 (2016) 1564–1570.

[14] V. Nekkanti, V. Vabalaboina, R. Pillai, Drug nanoparticles – an overview, in: A.A. Hashim (Ed.), The Delivery of Nanoparticles, InTech, Rijeka, Croatia, 2012, pp. 111–118.
[15] R.H. Müller, C. Jacobs, O. Kayser, Nanosuspensions as particulate drug formulations in therapy, Adv. Drug Deliv. Rev. 47 (2001) 3–19.
[16] R.H. Muller, C. Jacobs, Buparvaquone mucoadhesive nanosuspension: preparation, optimisation and long-term stability, Int. J. Pharm. (Amsterdam, Neth.) 237 (2002) 151–161.
[17] A. Foster, C. Young, ContrasolTM: Novel Nanotechnology for the Enhanced Development of Intravenous Formulations, IOTA NanoSolutions (2010).
[18] R. Shegokar, R.H. Muller, Nanocrystals: industrially feasible multifunctional formulation technology for poorly soluble actives, Int. J. Pharm. (Amsterdam, Neth.) 399 (2010) 129–139.
[19] M. Caldorera-Moore, N. Guimard, L. Shi, K. Roy, Designer nanoparticles: incorporating size, shape and triggered release into nanoscale drug carriers, Expert Opin. Drug Deliv. 7 (2010) 479–495.
[20] C.F. Thorn, C. Oshiro, S. Marsh, T. Hernandez-Boussard, H. McLeod, T.E. Klein, R.B. Altman, Doxorubicin pathways: pharmacodynamics and adverse effects, Pharmacogenet. Genomics 21 (2011) 440–446.
[21] N. Desai, V. Trieu, Z. Yao, L. Louie, S. Ci, A. Yang, C. Tao, T. De, B. Beals, D. Dykes, P. Noker, R. Yao, E. Labao, M. Hawkins, P. Soon-Shiong, Increased antitumor activity, intratumor paclitaxel concentrations, and endothelial cell transport of cremophor-free, albumin-bound paclitaxel, ABI-007, compared with cremophor-based paclitaxel, Clin. Cancer Res. 12 (2006) 1317–1324.
[22] W.B. Liechty, N.A. Peppas, Expert opinion: responsive polymer nanoparticles in cancer therapy, Eur. J. Pharm. Biopharm. 80 (2012) 241–246.
[23] J.I. Hare, T. Lammers, M.B. Ashford, S. Puri, G. Storm, S.T. Barry, Challenges and strategies in anti-cancer nanomedicine development: an industry perspective, Adv. Drug Deliv. Rev. 108 (2017) 25–38.
[24] J.C. Kraft, J.P. Freeling, Z. Wang, R.J. Ho, Emerging research and clinical development trends of liposome and lipid nanoparticle drug delivery systems, J. Pharm. Sci. 103 (2014) 29–52.
[25] J.M. Caster, A.N. Patel, T. Zhang, A. Wang, Investigational nanomedicines in 2016: a review of nanotherapeutics currently undergoing clinical trials, Wiley Interdisc. Rev. Nanomed. Nanobiotechnol. 9 (2017).
[26] R. Trivedi, U.B. Kompella, Nanomicellar formulations for sustained drug delivery: strategies and underlying principles, Nanomedicine (London, U. K.) 5 (2010). 485–505.
[27] S. Ashton, Y.H. Song, J. Nolan, E. Cadogan, J. Murray, R. Odedra, J. Foster, P.A. Hall, S. Low, P. Taylor, R. Ellston, U.M. Polanska, J. Wilson, C. Howes, A. Smith, R.J. Goodwin, J.G. Swales, N. Strittmatter, Z. Takats, A. Nilsson, P. Andren, D. Trueman, M. Walker, C.L. Reimer, G. Troiano, D. Parsons, D. De Witt, M. Ashford, J. Hrkach, S. Zale, P.J. Jewsbury, S.T. Barry, Aurora kinase inhibitor nanoparticles target tumors with favorable therapeutic index in vivo, Sci. Transl. Med. 8 (2016) (325ra317).

[28] K.S. Soppimath, T.M. Aminabhavi, A.R. Kulkarni, W.E. Rudzinski, Biodegradable polymeric nanoparticles as drug delivery devices, J. Control. Release 70 (2001) 1–20.
[29] H. Maeda, H. Nakamura, J. Fang, The EPR effect for macromolecular drug delivery to solid tumors: improvement of tumor uptake, lowering of systemic toxicity, and distinct tumor imaging in vivo, Adv. Drug Deliv. Rev. 65 (2013) 71–79.
[30] Y. Matsumura, H. Maeda, A new concept for macromolecular therapeutics in cancer chemotherapy: mechanism of tumoritropic accumulation of proteins and the anti- tumor agent smancs, Cancer Res. 46 (1986) 6387–6392.
[31] Y.H. Bae, K. Park, Targeted drug delivery to tumors: myths, reality and possibility, J. Control. Release 153 (2011) 198–205.
[32] H. Chen, S. Kim, L. Li, S. Wang, K. Park, J.X. Cheng, Release of hydrophobic molecules from polymer micelles into cell membranes revealed by Forster resonance energy transfer imaging, Proc. Natl. Acad. Sci. U. S. A. 105 (2008) 6596–6601.