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Review Article

# **Emerging Frontiers and Future Directions in Nanomedicine: A Comprehensive Review**

Ramdas Bhat\* Assistant Professor, Department of Pharmacology,

Srinivas College of Pharmacy, Valachil, Post

Farangipete, Mangalore, Karnataka, India-574143.

Himasvi M M UG scholar, Department of pharmacy practice, Srinivas

College of Pharmacy, Valachil, Post Farangipete,

Mangalore, Karnataka, India-574143

Varshini N UG scholar, Department of pharmacy practice, Srinivas

College of Pharmacy, Valachil, Post Farangipete,

Mangalore, Karnataka, India-574143

AR Shabaraya Principle and Director, Srinivas College of Pharmacy,

Valachil, Post Farangipete, Mangalore, Karnataka,

India-574143.

\*Corresponding author

Nanomedicine stands at the forefront of healthcare advancements, leveraging nanotechnology to enhance diagnosis, treatment, and disease prevention. Within this rapidly growing field, nanoparticles exhibit unique traits, such as a notable surface area-to-volume ratio and precise targeting abilities, making them valuable in medical applications. The article delves into diverse types of nanomedicines utilized in the pharmaceutical sector, exploring their potential advantages and examining targeted drug delivery mechanisms. Key breakthroughs, like globally recognized therapies such as Doxil and Abraxane, have emerged from nanomedicine. However, it emphasizes the necessity to address regulatory and ethical considerations to ensure both safety and efficacy. The article sheds light on limitations in targeted drug delivery, including issues like limited drug payload capacity and a lack of specificity, emphasizing the importance of addressing these challenges. Despite hurdles, the future of nanomedicine appears promising, poised to revolutionize personalized medicine, elevate disease detection and treatment, and support tissue regeneration and repair. Integration with artificial intelligence is highlighted as a potential avenue for achieving more precise and efficient drug delivery and disease diagnosis. The article underscores the significance of ongoing investments and collaborations among researchers, healthcare providers, and industry partners to surmount obstacles and unlock the full potential of nanomedicine. In conclusion, nanomedicine stands as a dynamic and promising field with the potential to bring about significant improvements in healthcare outcomes.

**Keywords:** Nanomedicine, Targeted drug delivery system, Treatment, Healthcare, FDA (food and drug administration).

#### Introduction

Nanomedicine applies nanotechnology principles to transform approaches to disease diagnosis, treatment, and prevention. It focuses on utilizing nanoparticles, typically sized between 1-100 nanometers, to devise innovative therapies with the potential to enhance patient outcomes [1]. These nanoparticles possess distinct characteristics, including a high surface area-to-volume ratio, unique optical and magnetic properties, and the ability to target specific cells The primary goal of

nanomedicine is to pioneer more effective and personalized treatments across a spectrum of diseases, ranging from cancer and infectious diseases to neurological disorders [3]. Researchers are actively working on engineering nanoparticles to selectively accumulate in diseased tissues, enable controlled drug release, and improve the efficacy and safety of existing therapies, overcoming limitations associated with traditional drugs. The potential of nanomedicine to revolutionize healthcare by advancing disease diagnosis and treatment is considerable [4,5].

However, the journey of nanomedicine is not without challenges, underscoring the importance of addressing regulatory and ethical considerations to ensure the safety and efficacy of these pioneering therapies. As nanomedicine continues to evolve, navigating these challenges becomes crucial for unlocking its full potential and ushering in a new era of healthcare innovation.

# **Types Of Nanomedicines Used in The Pharmaceutical Industry**

Nanomedicines constitute a category of medical interventions employing nanoparticles or materials at the nanoscale to diagnose, treat, or prevent diseases. Their notable advantages stem from their diminutive size, expansive surface area, and potential for precise drug delivery [6]. Within the realm of pharmaceuticals, various forms of nanomedicines have undergone development and examination.

- Nano-emulsions: Nano-emulsions represent thermodynamically stable systems comprising oil, water, and surfactants. These versatile formulations serve to encapsulate both hydrophobic and hydrophilic drugs, enhancing solubility and bioavailability. Nano-emulsions find application across multiple administration routes, encompassing oral, topical, and parenteral routes. [7].
- **Polymeric Nanoparticles:** Polymeric nanoparticles, crafted from biodegradable polymers, possess the ability to encapsulate drugs within their matrix. These versatile nanoparticles can be customized for targeted drug delivery, sustained release, and improved stability [8].
- Solid-Lipid Nanoparticles (SLNs): Solid lipid nanoparticles (SLNs) represent lipid-based nanoparticles providing heightened drug stability, controlled release, and enhanced bioavailability. These nanoparticles comprise a solid lipid core capable of encapsulating both hydrophobic and hydrophilic drugs [9].
- **Quantum Dots:** Quantum dots are semiconductor crystals at the nanoscale that emit distinct wavelengths of light determined by their size. Their tunable optical properties and high brightness make them valuable for applications in imaging and diagnostics [10].
- **Colloidal Gold:** Colloidal gold nanoparticles have unique optical properties and are used in diagnostic assays, imaging, and targeted drug delivery. They can be conjugated with ligands for specific cell targeting [11].
- **Dendrimers:** Dendrimers are highly branched polymers with a well-defined structure. They can be used to encapsulate drugs within their interior and can be functionalized for targeted drug delivery, gene delivery, and imaging [12].
- **Nanocrystals:** Nanocrystals are crystalline particles with nanometer-scale dimensions. They improve drug solubility and dissolution rate, enhancing the bioavailability of poorly water-soluble drugs [13].
- **Liposomes:** Liposomes, as described earlier, are vesicles composed of lipid bilayers that can encapsulate drugs. They are widely used for drug delivery, particularly for improving the pharmacokinetics and targeting of drugs [14].
- **Carbon Nanotubes:** Carbon nanotubes have been explored for drug delivery, imaging, and even as carriers for gene therapy due to their unique structural and surface properties [15].

# **Targeted Drug Delivery by Nanomedicines**

Targeted drug delivery using nanomedicines is a strategy that aims to deliver therapeutic agents

specifically to the site of action within the body while minimizing their exposure to healthy tissues. This approach enhances the therapeutic efficacy of drugs and reduces potential side effects [16]. Here's how targeted drug delivery by nanomedicines works:

- Design and Functionalization: Nanoparticles are designed and engineered to have specific properties that enable them to target certain cells, tissues, or organs. Surface modifications, such as attaching targeting ligands (antibodies, peptides, aptamers) or coatings, allow nanoparticles to interact selectively with receptors on the target cells [17].
- Active Targeting: Active targeting involves nanoparticles binding to specific molecules or receptors on the surface of target cells. This binding can be facilitated by the functionalized nanoparticle ligands or antibodies, ensuring a higher concentration of the therapeutic agent at the desired site [18].
- Passive Targeting (Enhanced Permeability and Retention, EPR): Tumors and inflamed tissues often have leaky blood vessels and compromised lymphatic drainage. Nanoparticles can exploit this phenomenon by accumulating at these sites due to their size and charge. This passive accumulation is known as the enhanced permeability and retention (EPR) effect [19].
- Responsive Targeting: Some nanoparticles are designed to respond to specific environmental cues at the target site, such as changes in pH, temperature, or enzymatic activity. This responsiveness can trigger drug release only when the nanoparticles are in close proximity to the target, further enhancing the selectivity of drug delivery [20].
- Internalization and Drug Release: Once the nanoparticles reach the target site and bind to the target cells, they are often internalized by the cells. The nanoparticles then release the therapeutic agent in a controlled manner, either due to the local environment or through an external trigger (e.g., light, magnetic field) [21].
- Avoiding the Immune System: Nanoparticles can be designed to evade recognition and clearance by the immune system, allowing them to circulate in the bloodstream and reach their target more effectively [22].
- Reduced Systemic Toxicity: Targeted drug delivery reduces the exposure of healthy tissues to the drug, minimizing off-target effects and toxicity [23].

This targeted approach is particularly advantageous in the treatment of diseases like cancer, where conventional chemotherapy can damage healthy tissues and cause severe side effects. By concentrating the therapeutic effect at the tumour site, targeted nanomedicines enhance the effectiveness of treatment while mitigating harm to healthy tissues [24]. However, it's important to note that achieving successful targeted drug delivery involves complex factors, including nanoparticle design, choice of targeting ligands, understanding the target's molecular characteristics, and ensuring safety and regulatory approval. The field of nanomedicine continues to advance, refining these techniques and pushing the boundaries of targeted drug delivery for a wide range of medical applications.

# **Applications Of Nanoparticles in Medicine: Targeted Therapies And Beyond**

Nanoparticles have found diverse applications in medicine, extending beyond targeted therapies to encompass a wide range of innovative approaches. These versatile nanoscale materials are being harnessed for various purposes that have the potential to revolutionize diagnostics, treatment, and disease management [25]. Nanoparticles revolutionize medicine with applications like targeted therapies (oncology), improved diagnostics (MRI, CT, PET), regenerative medicine (tissue repair), enhanced vaccines (antigen delivery), gene therapy (genetic disorders), antimicrobial agents (infections), personalized medicine (individualized treatment), blood-brain barrier penetration (neurological transplantation disorders), wound healing (growth factors), organ (immunosuppression), drug combinations (synergy), theranostics (visualization and treatment), neurological disorders (Alzheimer's, Parkinson's), cardiovascular health (atherosclerosis), and organ imaging (precision surgeries) [26-40].

## **Globally Marketed Nanomedicines**

Pharmaceutical nanomedicine products have achieved remarkable prominence within the global healthcare landscape. With over 70 nanomedicine products securing approval from the FDA and EMA since 1995, and an even larger number progressing through clinical trials, nanomedicine's trajectory is one of robust growth. This surge is driven by the pursuit of elevated drug effectiveness coupled with diminished toxicity, effectively showcasing nanotechnology's prowess in revolutionizing drug delivery [41].

Since 1989, the global market has welcomed 78 nanomedicines, with the FDA granting 66 approvals and the EMA endorsing 31. Among these, 20 have earned the coveted joint approval of both agencies, while others have secured the backing of either the FDA (43) or the EMA (12) individually. The dynamic focus on nanomedicine development, fortified by its transformative healthcare advantages, has precipitated a substantial upswing in market presence post-2010. This diverse array of nanomedicines encompasses an assortment of nanocrystals, lipid-based and polymer-based nanoparticles, dendrimer-based nanoparticles, protein-based nanoparticles, and inorganic nanoparticles [5]. Inorganic nanoparticles constitute a particularly intriguing facet, offering a dual role encompassing diagnostics and therapy. Ranging from metal and carbon nanotubes to calcium phosphate, iron oxide, silica, and quantum dot nanoparticles, these agents adeptly serve as stable and biocompatible carriers for therapeutic agents [42]. However, the journey is not without challenges, as their gradual dissolution and lack of biodegradation present obstacles to sustained, long-term utilization [43]. Conversely, organic carriers encompassing lipidbased vectors, polymer-based vectors, and dendrimers act as protective envoys for therapeutic agents, boosting drug-loading capacity and fine-tuning pharmacokinetic profiles. As nanomedicine's transformative journey unfolds, it continues to redefine the boundaries of pharmaceutical methodologies [44].

In tandem with this, numerous exemplars of globally marketed nanomedicines accentuate the substantial potential of this field. Noteworthy instances include Doxil (liposomal doxorubicin), Abraxane (nanoparticle-bound paclitaxel), Onivyde (liposomal irinotecan), and other innovations spanning nanocrystal-based formulations, iron replenishment therapies, and precision-targeting antibody-drug conjugates. Collectively, these pioneering nanomedicines underscore the diversified applications of nanotechnology in amplifying therapeutic outcomes and elevating overall patient well-being [45-48].

#### **Regulatory And Ethical Considerations in Nanomedicine**

Nanomedicine has the potential to transform healthcare, but with this potential comes a need for responsible and ethical development, as well as stringent regulation to ensure safety and efficacy [1]. The unique properties of nanoparticles raise concerns about their potential toxicity and long-term effects on human health and the environment. Thus, it is crucial to evaluate and minimize potential risks associated with nanomedicine development and application [49]. Regulatory bodies such as the FDA have developed guidelines for the evaluation and approval of nanomedicine products. These guidelines include recommendations for testing and evaluation of the safety and efficacy of nanomedicine products. Furthermore, ethical considerations are crucial, including issues related to patient consent, privacy, and informed decision-making. Ensuring the safety and efficacy of nanomedicine requires collaboration between regulatory agencies, researchers, healthcare providers, and patients. Additionally, clear communication and education about nanomedicine development and its potential risks and benefits are necessary to establish public trust and facilitate responsible and ethical development [50].

#### Limitations of Nanomedicines in t argeted d rug d elivery

While nanomedicines hold great promise for targeted drug delivery, they are not without limitations.

One significant challenge is their limited drug payload capacity, which can restrict the number of therapeutic agents that can be loaded onto nanoparticles [6]. Moreover, the lack of absolute specificity in targeting can lead to off-target effects, potentially affecting healthy tissues and diminishing the desired precision [23]. The efficiency of targeting is another concern, as successful delivery to specific cells or tissues may not always be achieved, reducing the therapeutic impact [51]. The variability in biological responses among individuals can also influence the effectiveness of nanomedicines, making it challenging to predict uniform outcomes [51,52]. Navigating regulatory challenges poses another hurdle, as the approval process for novel nanomedicines involves demonstrating their safety, efficacy, and manufacturing consistency [52]. Additionally, the cost considerations associated with developing and producing nanomedicines can be substantial, potentially limiting their accessibility to a wider population [5,52]. These limitations underscore the need for ongoing research and development efforts to overcome these challenges, optimize nanomedicine designs, and unlock their full potential for revolutionizing targeted drug delivery in healthcare.

## **Future Prospects of Nanomedicine in Targeted Drug Delivery**

The prospects for nanomedicine are exciting, with the potential to revolutionize personalized medicine, improve disease detection and treatment, and support tissue regeneration and repair. One important direction in nanomedicine is the development of nanorobots and nanosensors that can perform complex tasks within the body, such as drug delivery, disease detection, and tissue repair. Nanoparticles can also deliver multiple drugs or therapies simultaneously, leading to more effective treatments for complex diseases. Additionally, nanoparticles can be used as non-invasive diagnostic tools to detect diseases in their early stages. Integrating artificial intelligence and nanomedicine can also lead to more precise and efficient drug delivery and more accurate disease detection and diagnosis. However, there are still challenges, such as safety and toxicity concerns, regulatory issues, and cost-effectiveness. Continued investment and collaboration between researchers, healthcare providers, and industry partners can help to overcome these challenges and unlock the full potential of nanomedicine.

#### **Conclusion**

Nanomedicine is a rapidly growing field with promising applications in drug delivery, disease detection, and tissue regeneration. Targeted therapies with nanoparticles have shown potential in improving patient outcomes and quality of life. However, there are also limitations and challenges, including safety and toxicity concerns, regulatory issues, and cost-effectiveness. Despite these challenges, the future of nanomedicine is promising, and continued investment and collaboration between researchers, healthcare providers, and industry partners can help to overcome these obstacles and realize the full potential of this exciting field.

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#### Reference

- 1. Astruc D. Introduction to nanomedicine. Molecules. 2015;21(1):E4. doi: 10.3390/molecules21010004, PMID 26791291.
- 2. Khan I, Saeed K, Khan I. Nanoparticles: properties, applications and toxicities. ArabJChem. 2019;12(7):908-31. doi: 10.1016/i.arabic.2017.05.011.
- 3. Ventola CL. The nanomedicine revolution. PharmTher.2012;40:525.

- 4. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. NatRev Drug Discov. 2021;20(2):101-24. doi: 10.1038/s41573-020-0090-8, PMID 33277608.
- 5. Farjadian F, Ghasemi A, Gohari O, Roointan A, Karimi M, Hamblin MR. Nanopharmaceuticals and nanomedicines currently on the market: challenges and opportunities. Nanomedicine (Lond). 2019;14(1):93-126. doi: 10.2217/nnm-2018-0120, PMID 30451076.
- 6. Patra JK, Das G, Fraceto LF, Campos EVR, Rodriguez-Torres MDP, Acosta-Torres LS, et al. 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.
- 7. Singh TG, Dhiman S, Jindal M, Sandhu IS, Chitkara M. Nanobiomaterials. Singapore: Springer Nature Singapore Pte Ltd; 2016. p. 401-29.
- 8. Mehanna MM, Mohyeldin SM, Elgindy NA. Respirable nanocarriers as a promising strategy for antitubercular drug delivery. J Control Release. 2014;187:183-97. doi: 10.1016/j.iconrel.2014.05.038, PMID 24878180.
- 9. Dichello GA, Sarker DK. Encapsulation of lethal, functional, and therapeutic medicinal nanoparticles and quantum dots for the improved diagnosis and treatment of infection. In: Nanostructures for Antimicrobial Therapy. 1st ed. Publisher: Elsevier; 2017. p. 597-622.
- 10. Domínguez-Álvarez E, Rácz B, Marć MA, Nasim MJ, Szemerédi N, Viktorová J, et al. Selenium and tellurium in the development of novel small molecules and nanoparticles as cancer multidrug resistance reversal agents. Drug Resist Updat. 2022;63:100844. doi: 10.1016/j.drup.2022.100844, PMID 35533630.
- 11. Ebara M, Uto K. Gold nanomaterials for gene therapy. In: Narain R, editor. Polymers and Nanomaterials for Gene Therapy. Woodhead Publishing; 2016. p. 189-214.
- 12. Chabre YM, Roy R. Design and creativity in synthesis of multi valentneogly co-conjugates. Adv Carbohydr Chem Biochem. 2010;63:165-393. doi: <a href="https://doi.org/10.1016/S0065-2318(10)63006-5">10.1016/S0065-2318(10)63006-5</a>, PMID 20381707.
- 13. Brijpuriya DS, Peshwe DR, Kumar A. Crystalline nanomaterials for antimicrobial applications. In: Mallakpour S, Hussain CM, editors. Industrial Applications of Nanocrystals. 1st ed. Elsevier; 2022. p. 353-364.
- 14. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. Heliyon. 2022;8(5):e09394. doi: 10.1016/j.heliyon.2022.e09394, PMID 35600452.
- 15. Bates K, Kostarelos K. Carbon nanotubes as vectors for gene therapy: past achievements, present challenges and future goals. Adv Drug Deliv Rev. 2013;65(15):2023-33. doi: 10.1016/j.addr.2013.10.003, PMID 24184373.
- 16. Tewabe A, Abate A, Tamrie M, Seyfu A, Abdela Siraj E. Targeted drug delivery from magic bullet to nanomedicine: principles, challenges, and future perspectives. J Multi discip Healthc. 2021;14:1711-24. doi: 10.2147/JMDH.S313968, PMID 34267523.
- 17. Yetisgin AA, Cetinel S, Zuvin M, Kosar A, Kutlu O. Therapeutic nanoparticles and their targeted delivery applications. Molecules. 2020;25(9):2193. doi: 10.3390/molecules25092193, PMID 32397080.
- 18. Friedman AD, Claypool SE, Liu R. The smart targeting of nanoparticles. Curr Pharm Des. 2013;19(35):6315-29. doi: 10.2174/13816128113199990375, PMID 23470005.
- 19. Subhan MA, Yalamarty SSK, Filipczak N, Parveen F, Torchilin VP. Recent advances in tumor targeting via EPR effect for cancer treatment. J PersMed. 2021;11(6):571. doi: 10.3390/jpm11060571, PMID 34207137.
- 20. Pawar V, Maske P, Khan A, Ghosh A, Keshari R, Bhatt M, et al. Responsive nanostructure for targeted drug delivery. J Nanotheranostics. 2023;4(1):55-85. doi: 10.3390/jnt4010004.
- 21. de Jong WH, Borm PJ. Drug delivery and nanoparticles: applications and hazards. 'Int J Nanomedicine. 2008;3(2):133-49. doi: 10.2147/ijn.s596, PMID 18686775.
- 22. Liu Y, Hardie J, Zhang X, Rotello VM. Effects of engineered nanoparticles on the innate immune system. Semin Immunol. 2017;34:25-32. doi: 10.1016/j.smim.2017.09.011, PMID 28985993.
- 23. Manzari MT, Shamay Y, Kiguchi H, Rosen N, Scaltriti M, Heller DA. Targeted drug delivery

- strategies for precision medicines. Nat Rev Mater. 2021;6(4):351-70. doi: 10.1038/s41578-020-00269-6, PMID 34950512.
- 24. Debela DT, Muzazu SG, Heraro KD, Ndalama MT, Mesele BW, Haile DC, et al. New approaches and procedures for cancer treatment: current perspectives. SAGE Open Med. 2021;9:20503121211034366. doi: 10.1177/20503121211034366, PMID 34408877.
- Murthy SK. Nanoparticles in modern medicine: state of the art and future challenges. Int J Nanomedicine. 2007;2(2):129-41. PMID <u>17722542</u>.
- 26. Yao Y, Zhou Y, Liu L, Xu Y, Chen Q, Wang Y, et al. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance. Front Mol Biosci. 2020;7:193. doi: 10.3389/fmolb.2020.00193, PMID 32974385.
- 27. Han X, Xu K, Taratula O, Farsad K. Applications of nanoparticles in biomedical imaging. Nanoscale. 2019;11(3):799-819. doi: 10.1039/c8nr07769j, PMID 30603750.
- 28. Fathi-Achachelouei M, Knopf-Marques H, Ribeiro da Silva CE, Barthès J, Bat E, Tezcaner A, et al. Use of nanoparticles in tissue engineering and regenerative medicine. Front Bioeng Biotechnol. 2019;7:113. doi: 10.3389/fbioe.2019.00113, PMID 31179276.
- 29. Diaz-Arévalo D, Zeng M. Nanoparticle-based vaccines: opportunities and limitations. In: Kulkarni V, Soppimath K, editors. Nanopharmaceuticals. Amsterdam, The Netherlands: Elsevier; 2020. p. 135-150.
- 30. Luo M, Lee LKC, Peng B, Choi CHJ, Tong WY, Voelcker NH. Delivering the promise of gene therapy with nanomedicines in treating central nervous system diseases. Adv Sci (Weinh). 2022;9(26):e2201740. doi: 10.1002/advs.202201740, PMID 35851766.
- 31. Lee NY, Ko WC, Hsueh PR. Nanoparticles in the treatment of infections caused by multidrug-resistant organisms. Front Pharmacol. 2019;10:1153. doi: 10.3389/fphar.2019.01153, PMID 31636564.
- 32. Alghamdi MA, Fallica AN, Virzì N, Kesharwani P, Pittalà V, Greish K. The promise of nanotechnology in personalized medicine. J Pers Med. 2022;12(5):673. doi: 10.3390/jpm12050673, PMID 35629095.
- 33. Teleanu DM, Chircov C, Grumezescu AM, Volceanov A, Teleanu RI. Blood-brain delivery methods using nanotechnology. Pharmaceutics. 2018;10(4):269. doi: 10.3390/pharmaceutics10040269, PMID 30544966.
- 34. Kushwaha A, Goswami L, Kim BS. Nanomaterial-based therapy for wound healing. Nanomaterials (Basel). 2022;12(4):618. doi: 10.3390/nano12040618, PMID 35214947.
- 35. Ochando J, Braza MS. Nanoparticle-based modulation and monitoring of antigenpresenting cells in organ transplantation. Front Immunol. 2017;8:1888. doi: 10.3389/fimmu.2017.01888, PMID 29312352.
- 36. Chen D, Liu X, Lu X, Tian J. Nanoparticle drug delivery systems for synergistic delivery of tumor therapy. Front Pharmacol. 2023;14:1111991. doi: 10.3389/fphar.2023.1111991, PMID 36874010.
- 37. Mittal KR, Pharasi N, Sarna B, Singh M, Rachana HS, Haider S, et al. Nanotechnology-based drug delivery for the treatment of CNS disorders. Transl Neurosci. 2022;13(1):527-46. doi: 10.1515/tnsci-2022-0258, PMID 36741545.
- 38. Hossaini Nasr S, Huang X. Nanotechnology for targeted therapy of atherosclerosis. Front Pharmacol. 2021;12:755569. doi: 10.3389/fphar.2021.755569, PMID 34867370.
- 39. Singhal S, Nie S, Wang MD. Nanotechnology applications in surgical oncology. Annu Rev Med. 2010;61:359-73. doi: 10.1146/annurev.med.60.052907.094936, PMID 20059343.
- 40. Halwani AA. Development of pharmaceutical nanomedicines: from the bench to the market. Pharmaceutics. 2022;14(1):106. doi: 10.3390/pharmaceutics14010106, PMID 35057002.
- 41. Huang HC, Barua S, Sharma G, Dey SK, Rege K. Inorganic nanoparticles for cancer imaging and therapy. JControl Release. 2011;155(3):344-57. doi: 10.1016/i.jconrel.2011.06.004, PMID 21723891.
- 42. Remya RR, Julius A, Suman TY, Mohanavel V, Karthick A, Pazhanimuthu C, et al. Role of nanoparticles in biodegradation and their importance in environmental and biomedical applications. J Nanomater. 2022;2022:1-15. doi: 10.1155/2022/6090846.
- 43. Wahane A, Waghmode A, Kapphahn A, Dhuri K, Gupta A, Bahal R. Role of lipid-based and

- polymer-based on-viral vectors in nucleic acid delivery for next-generation gene therapy. Molecules, 2020;25(12):2866. doi: 10.3390/molecules25122866, PMID 32580326.
- 44. Zhao M, Ding XF, Shen JY, Zhang XP, Ding XW, Xu B. Use of liposomal doxorubicin for adjuvant chemotherapy of breast cancer in clinical practice. J Zhejiang Univ Sci B. 2017;18(1):15-26. doi: 10.1631/jzus.B1600303, PMID 28070993.
- 45. Milano G, Innocenti F, Minami H. Liposomal irinotecan (Onivyde): exemplifying the benefits of nanotherapeutic drugs. Cancer Sci. 2022;113(7):2224-31. doi: 10.1111/cas.15377, PMID 35445479.
- 46. Pillai G, Ceballos-Coronel ML. Science and technology of the emerging nanomedicines in cancer therapy: A primer for physicians and pharmacists. SAGE Open Med. 2013;1: 2050312113513759. doi: 10.1177/2050312113513759, PMID 26770691.
- 47. Wang R, Billone PS, Mullett WM. Nanomedicine in action: an overview of cancer nanomedicine on the market and in clinical trials. J Nanomater. 2013;2013:1-12. doi: 10.1155/2013/629681.
- 48. RAY PC, YU H, FU PP. Toxicity and environmental risks of nanomaterials: challenges and future needs. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2009;27(1):1-35. doi: 10.1080/10590500802708267, PMID 19204862.
- 49. Paradise J. Regulating nanomedicine at the Food and Drug Administration. AMA J Ethics. 2019 1;21(4): E347-355. doi: 10.1001/amajethics.2019.347, PMID 31012422.
- 50. Rosenblum D, Joshi N, Tao W, Karp JM, Peer D. Progress and challenges towards targeted delivery of cancer therapeutics. NatCommun. 2018;9(1):1410. doi: 10.1038/s41467-018-03705-v, PMID 29650952.
- 51. Đorđević S, Gonzalez MM, Conejos-Sánchez I, Carreira B, Pozzi S, Acúrcio RC, et al. Current hurdles to the translation of nanomedicines from the bench to the clinic. Drug Deliv Transl Res. 2022;12(3):500-25. doi: 10.1007/s13346-021-01024-2, PMID 34302274.
- 52. Patil M, Mehta DS, Guvva S. Future impact of nanotechnology on medicine and dentistry. J Indian Soc Periodontol. 2008;12(2):34-40. doi: 10.4103/0972-124X.44088, PMID 20142942.