Chapter-16

BIOMEDICAL NANOTECHNOLOGY: THE PROMISING IMPACTS OF NANOBIOTECHNOLOGY ON HUMAN HEALTH AND DISEASE MANAGEMENT

Navin Kumar*
Assistant Professor, School of Biotechnology, Gautam Buddha University, Greater Noida, Uttar Pradesh, India.

Komal Choudhary
Student, School of Biotechnology, Gautam Buddha University, Greater Noida, Uttar Pradesh, India.

Sanjay Kumar
Professor, Glocal College of Paramedical Science and Research Centre, Glocal University, Saharanpur, U.P., India.

***Correspondence to:** navinkumar@gbu.ac.in*

DOI: https://doi.org/10.52458/9789388996846.nsp2023.eb.ch-16
Ch.Id:-GU/NSP/EB/CMDT/2023/Ch-16

ABSTRACT

Nanotechnology has become a game changer, with substantial implications for human health and illness treatment. Nanoparticles, with their distinctive physiochemical properties have opened up interesting new possibilities in the domains of therapeutics, drug delivery, bio-imaging, and diagnostics. In the field of diagnostics, nanoparticles enable the expansion of exceptionally sensitive and targeted biosensors for early detection of disease. They serve as therapeutic agent carriers, allowing for targeted drug administration and reducing systemic side effects. Furthermore, nanoparticles have revolutionized diagnostic approaches, improving the resolution and accuracy of tests such as magnetic resonance imaging (MRI) and computed tomography (CT) scans. Nanobiotechnology has potential uses in oncology, infectious diseases, neurological disorders, and regenerative medicine. Nanoparticles can be designed to target specific tissue, allowing chemotherapeutic drugs to be delivered directly to tumors. However, understanding nanoparticle toxicity and long-term effects is crucial for safe clinical translation. This chapter presents an overview of nanobiotechnology critical role in addressing multiple facets of human health and disease management.

Keywords: *Nanobiotechnology, nanomedicine, cancer therapy, virus detection, Bioimaging*.

16.1 INTRODUCTION

The expansion of nanomaterials and the enhancement of their formulations have indeed propelled nanobiotechnology into among the most promising and exciting research areas in recent years. Nanomaterials are materials with unique nanoscale characteristics and structures, typically ranging from 1 to 100 nanometers (nm) in size. These materials exhibit distinctive physical, chemical, and biological because of their compact size and high surface area-to-volume ratio, they have advantages over bulk counterparts. Nanomaterials have a wide range of applications across various fields, including biomedical sciences. There are different form of nanomaterial including solid nanoparticles, nanofibers, quantum dots, nanowires, nanoplates or nanosheets etc. solid nanoparticles are composed of various materials such as metals (e.g., gold, silver), metal oxides (e.g., titanium dioxide, iron oxide), and polymers. Nanofibers are ultrafine fibers with diameters in the nanometer range. They have applications in tissue engineering, filtration, and textiles. Electrospinning is a common method to produce nanofibers. Quantum dots are semiconductor nanocrystals that exhibit size-dependent electronic properties. They are used as fluorescent probes in biological imaging and display quantum confinement effects.

Nanobiotechnology allows for the precise targeting of specific cells, tissues, or pathogens at the nanoscale. Nanomaterials, such as liposomes, nanoparticles, and dendrimers, can carry drugs or therapeutic agents to their intended destinations more effectively than traditional drug delivery methods. This targeted drug delivery minimizes side effects and maximizes the therapeutic effect of medications. Nanoscale biosensors and imaging agents allow for the early identification and precise diagnosis of diseases such as cancer, infectious diseases, and neurological disorders. This can lead to earlier intervention and improved patient outcomes. Nanotechnology plays a crucial role in tissue engineering and regenerative medicine. It facilitates the development of biomaterials and scaffolds that can encourage tissue regeneration and repair, potentially revolutionizing the treatment of injuries and degenerative diseases. Vaccine Development: Nanobiotechnology has the potential to enhance vaccine efficacy by improving antigen delivery and immune response modulation. This is particularly relevant for making vaccines against emerging infectious diseases.

Nanomaterials have revolutionized drug delivery by enhancing the bioavailability, targeting, and controlled release of therapeutic agents. Lipid-based nanocarriers, such as liposomes and lipid nanoparticles, offer biocompatible and versatile drug delivery platforms [1]. Polymeric nanoparticles enable the encapsulation and controlled release of drugs, facilitating targeted drug delivery. Nanoparticles have transformed cancer treatment by improving drug delivery to tumors and reducing systemic toxicity [2]. Gold nanoparticles have been used for drug delivery and imaging applications, owing to their unique properties [3]. Nanoparticle-based carriers are being explored for the delivery of RNA-based therapeutics, such as siRNA and mRNA [4]. Nanoparticles are being designed to overcome the blood-brain barrier and deliver drugs to the central nervous system [5]. Nanomaterials in drug delivery continue to advance, offering innovative solutions for enhancing therapeutic outcomes while minimizing side effects. Functionalized nanoparticles serve as diagnostic probes, allowing for the detection and visualization of specific molecular targets. This is invaluable in the initial diagnosis and monitoring of diseases. Researchers and clinicians are continually exploring new applications and optimizing existing systems to improve patient care.

16.2 APPLICATIONS OF NANOBIOTECHNOLOGY IN HUMAN HEALTH AND DISEASES

Nanoparticles, whether simple or complex, have an extensive range of physical and chemical properties that play a dynamic role in physical, biological, medicinal, and pharmacological applications [6-8]. The capacity of nanoparticles to administer medications within the ideal dosage range has attracted rising interest from many areas

of medicine. This frequently results in better therapeutic effectiveness of the medications, less side effects, and improved patient compliance [9]. ***Figure-16.1 shows the applications of nanoparticles in human health and diseases.*** Different applications of nanoparticle are briefly described below.

i. **Nanotechnology in medicine:** According to the National Institutes of Health (NIH), nanomedicine is "highly specific therapeutic action at the molecular scale for disease diagnosis, prevention, and treatment." One a few ways are now being employed in the application of nanotechnology in medicine, while others are being considered [10]. The majority of the techniques are still in the research phase. Biosensors, antimicrobial methods, diagnostic and monitoring tools, treatments for DD, cell repair, and biological system management are nearly of the medical applications of nanotechnology. Using fiberoptic technology, diseases are monitored. Physical characteristics like blood flow rate, radiation exposure, blood oxygen levels, and pH are measured using optical biosensors. With the aid of nanofiber technology, endoscopy will become more capable in the future, and its applications will advance from imaging to diagnosis and therapy [11]. Nanomaterials are used to diagnose many ophthalmic applications, such as retinitis pigmentosa, diabetic retinopathy, and retinoblastoma for the back of the eyes. Drug and gene delivery to the specific target tissue, for example the retina and choroid, improves retinal prosthesis and diagnosis methods [12&13]. Bone regeneration has been efficiently carried out using magnetic and silica NPs. Calcium phosphate-based NPs are used in bone disorders without harming the bone tissues. NPs coupled to bisphosphonates have been used to treat osteoarthritis, osteosarcoma, metabolic bone cancer, and arthritis [14]. Moreover, nanoparticles are able to cross the blood-brain barrier and release medications that target infected cells. Many disorders of the central nervous system, including Alzheimer's disease, brain tumors, storage diseases, inborn metabolic (lysosomal infectious) diseases, and aging, can be identified with this drug delivery technology. The majority of medicinal substances are unable to cross either the blood-brain or blood-cerebrospinal fluid barriers. One of a few numbers of medications may penetrate the blood–brain barrier because of their high lipid solubility and low molecular weight. Drugs are conveniently transported by nanoparticles through the blood–brain barrier [15&16].

ii. **Nanotechnology in Drug delivery and design:** The Drug Delivery System (DDS) is a term coined by the National Institutes of Health (NIH) and defined as "Formulation of a device that enables the overview of therapeutic substances into the body and improves efficiency and safety by control of the rate, time, and place

of drug release in the body." The three main components of the drug delivery (DD) process are as follows:

- Drug administration procedures can be categorized as either invasive or noninvasive. The invasive type of drug delivery includes the use of nanoneedles and injections, whereas the noninvasive type of drug administration includes oral, nasal, and topical inhalation.
- Finally, the administrative drugs enter the active component.
- Lastly, transport of the drug's active components through the membrane.

The formulation of the drug and followed by its delivery to the target site may have an impact on drug-delivery system interfaces between the drug and patient [17]. The overall DDS is not functioning at a satisfactory level due to various limitations, including a limited ability to control the size range, a very low drug loading tendency, poor bioavailability, no control over time, side effects, low solubility, poor therapeutic effectiveness, location, and a lack of target delivery. Lower dosages reduced the therapeutic impact, whereas higher quantities can make them poisonous to health. Due to these restrictions, researchers are concentrating to develop a novel but safe DDS that can regulate and manage the rate and target of drug release [18]. Proteins and DNA have been conjugated with NPs by researchers that are less than 2 nm in diameter, or the size of double-stranded DNA. The Mycoplasma bacterium, which is about 200 nm in size, is the tiniest known biological form in the world, although the largest NP is just 100 nm. The new DDS includes the use of NPs for the delivery and targeting of medications and diagnostic chemicals. The ultimate objective of NPs DD is to promote precise and accurate disease prevention and treatment diagnostics [19,20].

Several nanocomposites of DNA, antibody and drugs have been studies to target the severe diseases, including cancer, diabetes, hypertension, and asthma. To rise the effectiveness of medication delivery systems, hundreds of researchers are working on a variety of topics [21]. Nanobiotechnology enables the development of biocompatible, precisely targeted, biodegradable, and stimulation-responsive carriers of various sizes and shapes [22]. Liposomes, nanocrystals, polymeric nanoparticles, polymeric micelles, dendrimers, CNTs, Magnetic nanoparticles, and polymeric drug conjugates are some of the nanomers used in drug delivery applications for disease therapy (Table-16.1). Because of their distinguishing characteristics, notably the extremely high stability of the drug in the bloodstream, nanomaterials, especially nanoparticles, are well-known DDS. nanoparticles have a high drug loading capacity, easy bloodstream transport, easy incorporation of both hydrophobic and hydrophilic medicines, and easy control over .

Table-16.1: Several nanomaterials in Drug Delivery applications and treatments

Nanomaterials	Conjugated Drug	Therapeutic/drug delivery	Reference
Polymeric NPs	Clotrimazole Carboplatin	Antifungal drug Ovarian cancer	24
Dendrimers	Doxorubicin hydrochloride	Breast cancer	24
Liposomes	Camptothecin Cytarabine Amphotericin B	Anticancer Lymphomatous meningitis Kaposi's sarcoma	24
Liposomes	Doxorubicin	Clinical Pharmacokinetics	25
Nanocrystals	Rapamycin Fenofibrate Vancomycin	Immunosuppressive Hypercholesterolemia Antibiotic drug	24
Albumin-bound paclitaxel in a nanometer particle	Paclitaxel	patients with metastatic breast cancer (MBC)	26
Chitosan nanoparticles	cisplatin-loaded chitosan nanoparticles with and without linked to rituximab (mAbCCNP)	targeted delivery to MCF-7 ATCC human breast cancer	27
Gold nanoparticles	skin drugs	treatment of skin disease	28
Mesoporous Silica Nanoparticle	Ovotransferrin Antibacterial Peptide	Effective Antibiotic Delivery System Treating Bacterial Infection In Vivo	29
Gold nanoparticles	Antimicrobial peptides	Peptide drug delivery to mesenchymal stem cells	30
Gold nanoparticles	Herceptin	Acute apoptosis of breast cancer cells	31

Drug release to the target from the nanoparticle matrix. They can also quickly penetrate tissues (including malignant cells). Both invasive and noninvasive approaches can be used to administer nanoparticle-conjugated medications; the cells naturally take

up the nanoparticles through endocytosis. The medication's bioavailability, control over drug release, and time of circulation have all been improved by these unique features of nanoparticles with a drug-delivery system [23]. ***Several nanomaterials usesd in drug delivery applications and treatments are tabulated in Table-16.1.***

iii. **Nanoparticles for Cancer Therapy:** D. K. Chatterjee and Y. Zhang created biodegradable chitosan nanoparticles that include quantum dots and have an appropriate surface modification to immobilize both a chemokine and a tumor targeting drug. Optical microscopy was used to see how immune cells and tumor cells interacted. A significant development in this field is the usage of quantum dots in the treatment of cancer. When UV light is shone upon, quantum dots shine. They infiltrate into cancerous tumors when injected, and the surgeon may see the luminous tumor as a result. The wounded nerves could be repaired with the use of nanotechnology. However, during the past ten years, advances in surface microscopy, silicon fabrication, biology, physical chemistry, and computational engineering have come together to offer astonishing capabilities for comprehending, creating, and modifying atomic-scale structures. Nanotechnology will likely become most of the dominating technologies of the twenty-first century, as evidenced by the quick development of this new science and the prospects for its application [32]. In a recent work, doxorubicin (DOX) and antibody-conjugated magnetic poly-(D, L-lactide-co-glycolide) nanoparticles were created for breast cancer treatment and simultaneous targeted detection. Fe_2O_3 nanoparticles were utilized as an imaging agent, and DOX, an anticancer medication, was combined through magnetic nanoparticles into PLGA nanoparticles (Figure 1). Herceptin 1 antibody was also utilized to specifically target breast cancer [33].

iv. **Nanoparticles in combating bacterial infection:** Nanoparticles with antibacterial properties have been studied widely for their potential applications in combating bacterial infections. Nanoparticles exhibit antibacterial activity through various mechanisms, making them promising agents for combating bacterial infections. Some nanoparticles, particularly silver nanoparticles, can interact with bacterial cell membranes, leading to structural damage and increased permeability. This disruption can cause leakage of essential cellular components, ultimately leading to cell death. Certain nanoparticles, such as titanium dioxide (TiO2) and zinc oxide (ZnO) nanoparticles, have photocatalytic properties. When exposed to light, they can produce reactive oxygen species like superoxide radicals and hydrogen peroxide, which are toxic to bacteria. Cadmium-based quantum dots, can interact with bacterial DNA, leading to DNA damage and inhibition of DNA replication

and transcription. They can disrupt the formation and stability of bacterial biofilms, which are protective matrices that bacteria use to evade antibiotics and the immune system. Importantly, nanoparticles can enhance the efficacy of antibiotics when used in combination. This synergy can help combat antibiotic-resistant bacteria.

Silver Nanoparticles (AgNPs) is known to be a metallic antibiotic that is highly effective against a wide range of bacteria, including both Gram-positive and Gram-negative strains. Copper Nanoparticles (CuNPs) also known for their antibacterial properties, they can interrupt bacterial cell membranes and inhibit bacterial growth. Iron Oxide Nanoparticles (Fe3O4 NPs) and Zinc Oxide Nanoparticles (ZnO NPs) exhibit antibacterial activity by generating reactive oxygen species (ROS) when exposed to UV light or visible light. Titanium Dioxide Nanoparticles (TiO2 NPs) have been used popularly in the cosmetics that have photocatalytic properties that produce ROS, leading to bacterial cell damage and death under light exposure. Chitosan Nanoparticles are natural polymeric nanoparticles that are derived from chitin, these nanoparticles have intrinsic antibacterial properties and are biocompatible. Likewise, various types of polymeric nanoparticles, such as poly (lactic-co-glycolic acid) (PLGA) NPs, have been loaded with antibacterial agents for drug delivery applications.

v. **Nanotechnology in Bioimaging:** Nanoparticles such as quantum dots, gold nanoparticles, and superparamagnetic iron oxide nanoparticles (SPIONs) have revolutionized bioimaging research. Their optical and magnetic properties are tunable, which has improved diagnostic imaging approaches. Quantum dots, for example, provide remarkable brightness and stability for fluorescence imaging, whereas SPIONs improve MRI sensitivity. These developments have resulted in more accurate and early disease diagnosis, monitoring, and personalized therapy planning. Numerous molecular imaging methods, including positron-emission tomography (PET), optical imaging (OI), magnetic resonance imaging (MRI), ultrasound imaging (USI), and others, have been reported for the imaging of in vitro and in vivo biological specimens [34, 35]. Gold nanoparticles (AuNPs) have emerged as highly effective contrast agents across a spectrum of medical imaging modalities. X-ray based computed tomography (CT) is not regarded as a molecular imaging modality, in contrast to magnetic resonance imaging (MRI) and different nuclear medicine imaging modalities, because targeted and molecularly specific contrast agents have not yet been developed. However, more recent advances in nanoscience have made CT more sensitive and target-specific. As an example, gold nanoprobes can specifically and sensitively target tumor-

specific antigens while creating unique contrast in CT imaging [36]. To address the issue of excreting AuNPs bigger than 5.5 nm from kideny, a unique platform was developed that involves the incorporation of sub-5.5 nm AuNPs into the biodegradable polymer PCPP, resulting in the production of Au-PCPP nanoparticles. This unique technique takes advantage of bigger AuNPs' specific benefits, for example, their near-infrared absorption properties. Furthermore, it was observed that the bigger nanoparticles showed outstanding biocompatibility with a range of cell types when enclosed within the PCPP matrix. Furthermore, our in vitro investigations have demonstrated Au-PCPP nanoparticles' capacity to disintegrate over time, underscoring their promise as a suitable option for safe and efficient medical imaging applications. Bioimaging technologies are being advanced by the present development of luminous and magnetic nanoparticles [37,38]. Luminescent nanoprobes for OI and magnetic nanoparticles for MRI are two separate types of nanoparticles that have been extensively employed for imaging. Additionally, dual-mode nanoparticles are available for simultaneous OI and MRI imaging [39,40].

vi. **In Vitro Diagnostics:** Diagnostic devices and sensors are used to implement novel sensor concepts based on nanotubes, nanowires, cantilevers, or atomic force microscopy. These sensors are designed to increase sensitivity, lower production costs, or assess novel analytes (such Alzheimer plaques), which have only recently been discovered. For instance, Bioforce's Virichip (Ames, Iowa) employs atomic force microscopy to find entire viruses for the early identification of viral infections, and Nanomix (Emeryville, California) has created carbon nanotube-based sensors for monitoring respiratory processes [41]. Applications for known core materials and corresponding potential ligands utilized for surface functionalization.

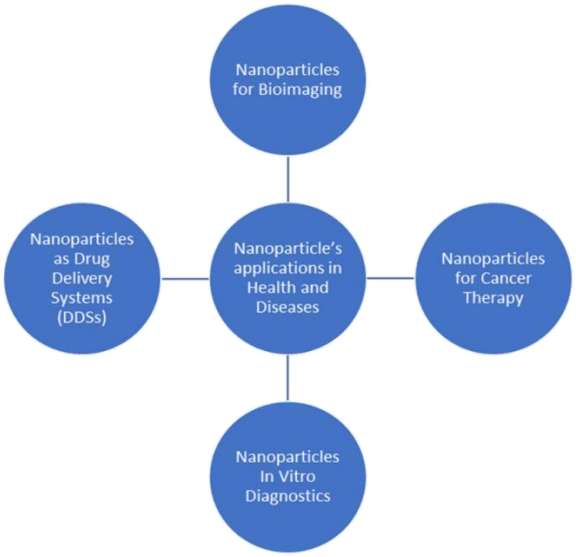

Figure-16.1: Applications of nanoparticles in human health and diseases

16.3 CONCLUSION

Nanobiotechnology has emerged as a transformative field with profound implications for improving human health and addressing various diseases. This multidisciplinary approach harnesses the unique properties of nanoparticles and nanomaterials to revolutionize diagnostics, therapeutics, and disease management. In this conclusion report, we summarize the key advancements in nanobiotechnology and its applications in bioimaging, drug delivery, cancer therapy, antibacterial activity, and more. Nanoparticles are flexible drug carriers that overcome the constraints of traditional drug delivery techniques. Liposomes, polymeric nanoparticles, and dendrimers have allowed for precise drug release control, enhanced bioavailability, and targeted drug delivery to specific cells or tissues. This has transformed the treatment of many diseases, including cancer, by reducing side effects and increasing therapeutic efficacy. Liposomal doxorubicin (Doxil) for cancer treatment and polymeric nanoparticles for controlled drug release are two notable examples. Nanobiotechnology has ushered in groundbreaking advances in cancer therapy. Gold nanoparticles in particular have been functionalized for photothermal treatment (PTT) and drug administration, allowing both noninvasive tumor ablation and targeted chemotherapy. Furthermore, nanoparticles such as albumin-bound paclitaxel (Abraxane) have improved therapy outcomes for individuals with breast cancer. The combination of nanoparticles and standard chemotherapy or immunotherapy has opened up novel possibilities for cancer treatment and drug resistance. The emergence of antibiotic-

resistant microorganisms needs the development of innovative antibacterial techniques. Metal nanoparticles, such as silver and copper nanoparticles, have powerful antibacterial action via a number of mechanisms, including cell membrane disruption and the generation of reactive oxygen species (ROS). These nanoparticles have showed potential in terms of bacterial infection prevention. Furthermore, novel materials such as chitosan nanoparticles and graphene oxide nanoparticles have showed antibacterial characteristics while causing little harm to human cells. Nanobiotechnology's impact on human health and illness management continues to evolve and expand. The interaction of nanomaterials, biology, and medicine holds great promise for the creation of precise and patient-centered therapeutics. Continuous research and cross-disciplinary collaboration are essential for realizing the full potential of nanobiotechnology in solving the intricate challenges of human health and disease.

REFERENCES

1. *Alexis, F., Pridgen, E., Molnar, L. K., & Farokhzad, O. C. (2008). Factors affecting the clearance and biodistribution of polymeric nanoparticles. Mol. Pharmaceutics. 5: 505-515.*
2. *Allen, T. M., & Cullis, P. R. (2013). Liposomal drug delivery systems: from concept to clinical applications. Advanced drug delivery reviews, 65(1), 36-48.*
3. *Bamrungsap, S., Zhao, Z., Chen, T., Wang, L., Li, C., Fu, T., & Tan, W. (2012). Nanotechnology in therapeutics: a focus on nanoparticles as a drug delivery system. Nanomedicine, 7(8), 1253-1271.*
4. *Bhaskar, S., Tian, F., Stoeger, T., Kreyling, W., de la Fuente, J. M., Grazú, V., ... & Razansky, D. (2010). Multifunctional Nanocarriers for diagnostics, drug delivery and targeted treatment across blood-brain barrier: perspectives on tracking and neuroimaging. Particle and fibre toxicology, 7(1), 1-25.*
5. *Chen, Y., & Feng, X. (2022). Gold nanoparticles for skin drug delivery. International Journal of Pharmaceutics, 122122.*
6. *De, M., Ghosh, P. S., & Rotello, V. M. (2008). Applications of nanoparticles in biology. Advanced Materials, 20(22), 4225-4241.*
7. *Dreaden, E. C., Alkilany, A. M., Huang, X., Murphy, C. J., & El-Sayed, M. A. (2012). The golden age: gold nanoparticles for biomedicine. Chemical Society Reviews, 41(7), 2740-2779.*
8. *Gabizon, A., Shmeeda, H., & Barenholz, Y. (2003). Pharmacokinetics of pegylated liposomal Doxorubicin: review of animal and human studies. Clinical pharmacokinetics, 42, 419-436.*

9. *Gelperina, S., Kisich, K., Iseman, M. D., & Heifets, L. (2005). The potential advantages of nanoparticle drug delivery systems in chemotherapy of tuberculosis. American journal of respiratory and critical care medicine, 172(12), 1487-1490.*

10. *Gradishar, W. J., Tjulandin, S., Davidson, N., Shaw, H., Desai, N., Bhar, P., ... & O'Shaughnessy, J. (2005). Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil–based paclitaxel in women with breast cancer. Journal of clinical oncology, 23(31), 7794-7803.*

11. *Gu, W., Wu, C., Chen, J., & Xiao, Y. (2013). Nanotechnology in the targeted drug delivery for bone diseases and bone regeneration. International journal of nanomedicine, 2305-2317.*

12. *Jabbari, A., & Sadeghian, H. (2012). Amphiphilic cyclodextrins, synthesis, utilities and application of molecular modeling in their design. Recent Advances in Novel Drug Carrier Systems, 331-354.*

13. *Jain, K. K. (2008). Drug delivery systems-an overview. Drug delivery systems, 1-50.*

14. *Kanasty, R., Dorkin, J. R., Vegas, A., & Anderson, D. (2013). Delivery materials for siRNA therapeutics. Nature materials, 12(11), 967-977.*

15. *Kaparissides, C., Alexandridou, S., Kotti, K., & Chaitidou, S. (2006). Recent advances in novel drug delivery systems. Journal of Nanotechnology online, 2, 1-11.*

16. *Kircher, M. F., Mahmood, U., King, R. S., Weissleder, R., & Josephson, L. (2003). A multimodal nanoparticle for preoperative magnetic resonance imaging and intraoperative optical brain tumor delineation. Cancer research, 63(23), 8122-8125.*

17. *Kompella, U. B., Amrite, A. C., Ravi, R. P., & Durazo, S. A. (2013). Nanomedicines for back of the eye drug delivery, gene delivery, and imaging. Progress in retinal and eye research, 36, 172-198.*

18. *Loureiro, A., G Azoia, N., C Gomes, A., & Cavaco-Paulo, A. (2016). Albumin-based nanodevices as drug carriers. Current pharmaceutical design, 22(10), 1371-1390.*

19. *Ma, B., Chen, Y., Hu, G., Zeng, Q., Lv, X., Oh, D. H., ... & Jin, Y. (2021). Ovotransferrin antibacterial peptide coupling mesoporous silica nanoparticle as an effective antibiotic delivery system for treating bacterial infection in vivo. ACS Biomaterials Science & Engineering, 8(1), 109-118.*

20. *Maeda, H., Nakamura, H., & Fang, J. (2013). The EPR effect for macromolecular drug delivery to solid tumors: Improvement of tumor uptake, lowering of systemic toxicity, and distinct tumor imaging in vivo. Advanced drug delivery reviews, 65(1), 71-79.*

21. *Margolis, D. J., Hoffman, J. M., Herfkens, R. J., Jeffrey, R. B., Quon, A., & Gambhir, S. S. (2007). Molecular imaging techniques in body imaging. Radiology, 245(2), 333-356.*

22. *Martis, E., Badve, R., & Degwekar, M. (2012). Nanotechnology based devices and applications in medicine: An overview. Chronicles of young Scientists, 3(1), 68-68.*

23. *Meng, E., & Hoang, T. (2012). Micro-and nano-fabricated implantable drug-delivery systems. Therapeutic delivery, 3(12), 1457-1467.*

24. *Mukherjee, B., Dey, N. S., Maji, R., Bhowmik, P., Das, P. J., & Paul, P. (2014). Current status and future scope for nanomaterials in drug delivery. In Application of nanotechnology in drug delivery. IntechOpen.*

25. *Nikalje, A. P. (2015). Nanotechnology and its applications in medicine. Med chem, 5(2), 081-089.*

26. *Ochekpe, N. A., Olorunfemi, P. O., & Ngwuluka, N. C. (2009). Nanotechnology and drug delivery part 1: background and applications. Tropical journal of pharmaceutical research, 8(3).*

27. *Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. D. P., Acosta-Torres, L. S., ... & Shin, H. S. (2018). Nano based drug delivery systems: recent developments and future prospects. Journal of nanobiotechnology, 16(1), 1-33.*

28. *Peng, L. H., Huang, Y. F., Zhang, C. Z., Niu, J., Chen, Y., Chu, Y., ... & Mao, Z. W. (2016). Integration of antimicrobial peptides with gold nanoparticles as unique non-viral vectors for gene delivery to mesenchymal stem cells with antibacterial activity. Biomaterials, 103, 137-149.*

29. *Popovtzer, R., Agrawal, A., Kotov, N. A., Popovtzer, A., Balter, J., Carey, T. E., & Kopelman, R. (2008). Targeted gold nanoparticles enable molecular CT imaging of cancer. Nano letters, 8(12), 4593-4596.*

30. *Quan, Q., & Zhang, Y. (2015). Lab-on-a-Tip (LOT): Where nanotechnology can revolutionize fibre optics. Nanobiomedicine, 2, 3.*

31. *Rathinaraj, P., Al-Jumaily, A. M., & Huh, D. S. (2015). Internalization: acute apoptosis of breast cancer cells using herceptin-immobilized gold nanoparticles. Breast Cancer: Targets and Therapy, 51-58.*

32. *Sakamoto, J. H., van de Ven, A. L., Godin, B., Blanco, E., Serda, R. E., Grattoni, A., ... & Ferrari, M. (2010). Enabling individualized therapy through nanotechnology. Pharmacological research, 62(2), 57-89.*

33. *Saraiva, C., Praça, C., Ferreira, R., Santos, T., Ferreira, L., & Bernardino, L. (2016). Nanoparticle-mediated brain drug delivery: Overcoming blood–brain barrier to treat neurodegenerative diseases. Journal of controlled release, 235, 34-47.*

34. *Schellenberger, E. A.; Sosnovik, D.; Weissleder, R.; Josephson, L. Magneto/Optical Annexin V, A Multimodal Protein. Bioconjug. Chem. 2004, 15, 1062–1067.*

35. *Sharma, P., Brown, S., Walter, G., Santra, S., & Moudgil, B. (2006). Nanoparticles for bioimaging. Advances in colloid and interface science, 123, 471-485.*

36. *Singh, M., Singh, S., Prasad, S., & Gambhir, I. S. (2008). Nanotechnology in medicine and antibacterial effect of silver nanoparticles. Digest Journal of Nanomaterials and Biostructures, 3(3), 115-122.*

37. *Sultan, M. H., Moni, S. S., Madkhali, O. A., Bakkari, M. A., Alshahrani, S., Alqahtani, S. S.,... & Alshamrani, M. (2022). Characterization of cisplatin-loaded chitosan nanoparticles and rituximab-linked surfaces as target-specific injectable nano-formulations for combating cancer. Scientific reports, 12(1), 468.*

38. *Tan, W., Wang, K., He, X., Zhao, X. J., Drake, T., Wang, L., & Bagwe, R. P. (2004). Bionanotechnology based on silica nanoparticles. Medicinal research reviews, 24(5), 621-638.*

39. *Wagner, V., & Dullaart, A. (2006). Bock, AK & Zweck, A. The emerging nanomedicine landscape. Nat Biotechnol, 24, 1211-1217.*

40. *Weissleder, R. (2002). Scaling down imaging: molecular mapping of cancer in mice. Nature Reviews Cancer, 2(1), 11-18.*

41. *Xu, Q., Kambhampati, S. P., & Kannan, R. M. (2013). Nanotechnology approaches for ocular drug delivery. Middle East African journal of ophthalmology, 20(1), 26.*