

At the Crossroads of Nanotechnology and Biology: Pioneering Applications in Medicine and Biotechnology

By

Aqsa Bashir¹, Shumaila Yasin², Safa Maryam³, Rida Batool⁴, Muhammad Arslan Siddiqi^{5*}, Seemab Hassan⁶, Nimra Ather⁷, Muhammad Haris Baig⁸, Farhan Haider Baryar⁹, Muhammad Zeshan¹⁰

¹Department of Chemistry, Government College University Faisalabad Pakistan

²Government college women university Faisalabad, Punjab Pakistan

³Department of Biochemistry, University of Agriculture Faisalabad, Punjab Pakistan

⁴Department of Biochemistry, University of Agriculture Faisalabad, Punjab Pakistan

^{5*}Department of Chemistry, Government College University Faisalabad, Punjab Pakistan

⁶Department of Microbiology, Quaid e Azam University Islamabad, Pakistan

⁷Department of Zoology, Wildlife and Fisheries, University of Agriculture Faisalabad, Punjab Pakistan

⁸Medical Laboratory Scientist- In Charge - ABWA MEDICAL COLLEGE FAISALABAD

⁹Department of biochemistry Faculty of sciences University of agriculture Faisalabad, Punjab Pakistan

¹⁰Department Environmental Science Government College University Faisalabad



Article History

Received: 05/12/2024

Accepted: 11/12/2024

Published: 13/12/2024

Vol – 3 Issue –12

PP: - 98-108

DOI:10.5281/zenodo.14437123

Abstract

Nanotechnology is revolutionizing biomedicine by providing innovative solutions for diagnostics, therapeutics, and regenerative medicine. At the nano-bio interface, advancements such as quantum dots and magnetic nanoparticles enable early disease detection and precise molecular imaging. Nanoparticle-based drug delivery systems enhance treatment efficacy while minimizing side effects, and Nano scaffolds in regenerative medicine facilitate tissue repair. Despite its transformative potential, challenges like biocompatibility, regulatory hurdles, and scalability remain barriers to clinical translation. This review highlights recent breakthroughs, addresses current limitations, and explores future directions, including multifunctional nanoparticles and AI integration for personalized medicine. Nanotechnology promises a paradigm shift in healthcare, improving diagnosis and treatment outcomes.

Keywords: nanotechnology, drug delivery, diagnostics, regenerative medicine, healthcare innovation

1. Introduction to Nano-Bio Interfaces

The rapid advancement of nanotechnology has fostered a unique convergence with biological sciences, resulting in a novel area known as the Nano-bio interface. This interface explores interactions between nanomaterials and biological systems, leading to innovative applications in areas such as targeted drug delivery, disease diagnostics, and regenerative medicine. Understanding these interactions is essential for developing biocompatible and effective nanomaterials that can perform specific functions within living organisms. The Nano-bio interface refers to the physical interface between the biological system and nanoscale surface topography, functioning as the barrier between two phases where critical reactions occur [1]. Historically, the integration of nanotechnology in biological contexts began with applications

like drug carriers and biosensors, evolving quickly as nanomaterials were found to offer precise control over physical, chemical, and biological properties [2]. By tailoring factors such as nanoparticle size, surface charge, and functionalization, scientists have been able to create materials that interact with biological systems in predictable and beneficial ways [3].

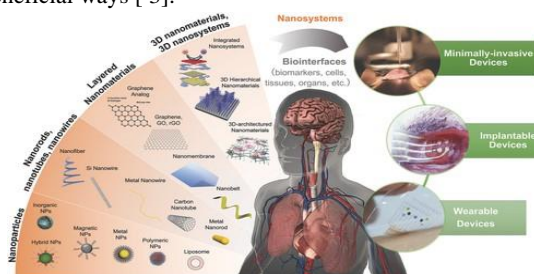


Figure 1: Nanomaterials of multiple dimension scales are shown as the four building blocks for functional bio integrated devices. Representative examples of nanoparticles [4].

Importance and Applications

The potential of Nano-bio interfaces is vast, spanning disciplines from medicine and environmental science to industrial biotechnology. These interfaces allow for enhanced cellular uptake of therapeutics, real-time molecular imaging, and even the development of nanoscale machines that operate within biological systems. Recent studies have shown the potential for nanoparticles to perform as targeted drug carriers, reducing side effects by localizing therapeutic action to specific cell types [5]. Moreover, advances in bio imaging technologies, including quantum dots and magnetic nanoparticles, have revolutionized how biological processes can be visualized with high resolution [6]. Those intelligent materials, therefore, open up possibilities for special medical management to prevent, diagnose, and treat different diseases, including malignancy, bacterial infections, and so forth. With desirable specificity and robust efficacy, these ENMs serve as drug themselves or as drug carriers to deliver one or more drug molecules to the target lesion sites and cure them efficiently. So far, thousands of nanomedicines have received approval for clinical applications, including liposomes, polymeric micelles, and albumin nanoparticles [7].

Nano-Bio-Interfaces

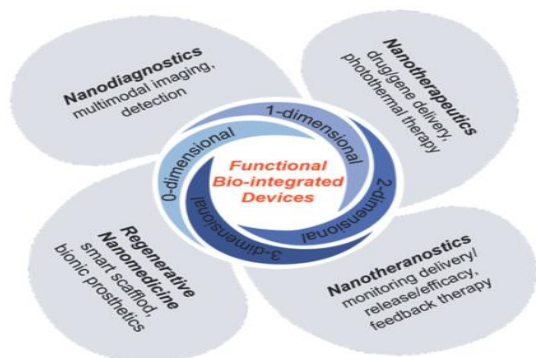


Figure 2: Biomedical applications of functional bio integrated devices at Nano–bio interfaces[8].

With the increasingly extensive application of nanotechnology in biomedical scenarios, the corresponding Nano–bio interfaces are also in the spotlight. At the nano–bio interfaces, nanomaterial interact with biological entities at multiple levels (e.g., proteins, DNA, membranes, organelles, cells, tissues, and organs) through a series of dynamic bio-physicochemical interactions, which can be modulated through the programming of various nanomaterials properties, such as surface chemistry, size, shape, dimension scale and topographic structures. It is therefore crucial in the study of Nano–bio interfaces to control the surface chemical and physical properties, as well as functionalities of nanomaterials, in order to modulate their interfacial interactions with bio entities [9].

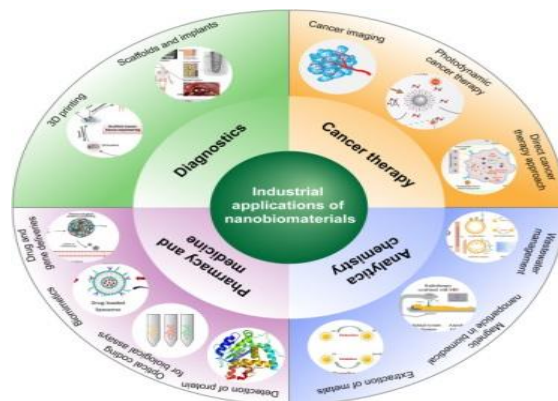


Figure 3: Schematic diagram explaining the interdisciplinary industrial applications of Nano biomaterials [10].

2. Fundamentals of Nano-Bio Interactions

2.1 Surface Chemistry and Properties of Nanomaterials

One of the core aspects of Nano-bio interactions is the surface chemistry of nanomaterials. Nanoparticles can be engineered to exhibit particular surface characteristics, such as charge, hydrophilicity, or specific functional groups, which significantly impact their behavior in biological systems. Surface charge, for example, influences cellular uptake and interactions with cellular membranes. Positively charged nanoparticles generally exhibit higher uptake due to electrostatic attraction with negatively charged cell membranes, though this can also induce toxicity [11].

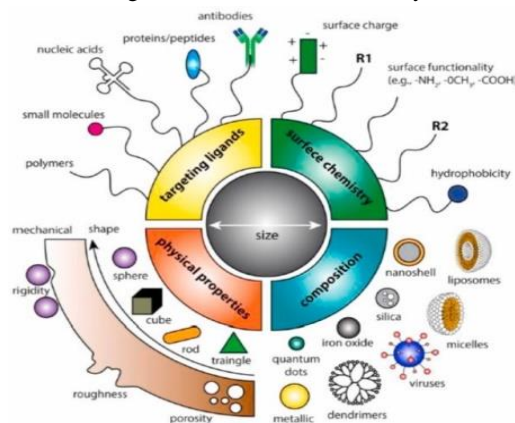


Figure 4: Various types of nanoparticles. Intracellular application of NPs designed using different material composition based on the classes and functionality of NPs, shape, size and targeting ligands [12]

The nanomaterials and nanotechnologies have attracted tremendous attention in researches because of their outstanding physical, chemical, and biological properties. When the size of materials is reduced to Nano range (<100 nm) at least in one dimension, their properties change significantly from those at a larger scale. Exceptionally high surface area to volume ratio and the possible appearance of quantum effects at the nanoscale are the key features of nanomaterials and have a dramatic effect on their properties

[13]. The cells regarded as the basic unit of life, are the building blocks of living organisms with a typical size of 10 μm . Nanoparticles' properties make them appropriate applicants for technical applications in biosensors, humidity sensors, photocatalysis, magnets, drug delivery, magnetic refrigeration, magnetic liquids, photoluminescence, microwave absorbents, ceramic pigments, gas sensing, corrosion protection, water decontamination, antimicrobial agents, biomedicine, and catalysis [13].

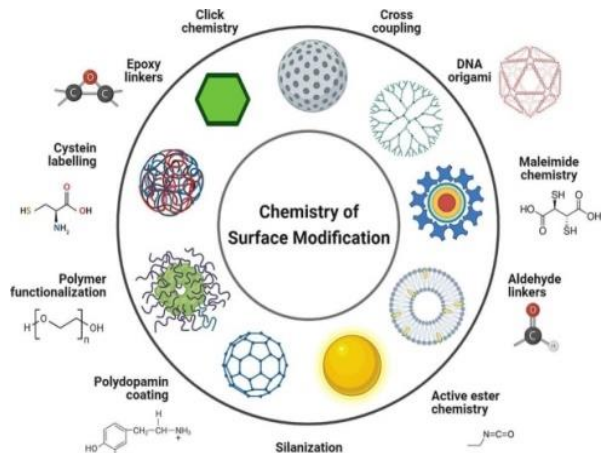


Figure 5: Chemistry of surface modification of nanoparticles [14]

The hydrophilicity or hydrophobicity of nanoparticles also determines their biodistribution and stability. Hydrophobic nanoparticles are more likely to aggregate and become trapped within tissues, while hydrophilic nanoparticles are more readily circulated in biological fluids. Functionalization of nanomaterials with molecules like polyethylene glycol (PEG) enhances biocompatibility by reducing immune recognition, extending circulation time in the bloodstream [15]

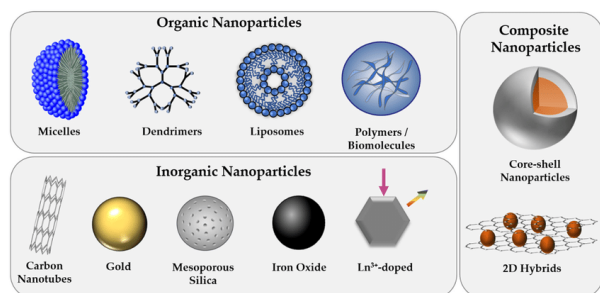


Figure 6: Structure of various nanoparticles [16]

2.2 Biological Response to Nanomaterials: Protein Corona Formation and Immune Response

When nanoparticles enter a biological system, they are immediately coated with a layer of proteins known as the "protein corona." This layer, composed of blood plasma proteins, defines the "biological identity" of the nanoparticle and influences how it is recognized by cells [17]. The formation of a protein corona can impact the particle's cellular uptake, biodistribution, and overall biological function. Studies have shown that the composition of the

protein corona varies depending on nanoparticle size, surface characteristics, and the biological environment [18].

The protein corona has been recognized as a dynamic entity that evolves as proteins continuously adsorb on the NP surface, desorb, and are replaced by other proteins. It is well known that the surface of ENMs is covered by a layer of tightly adsorbed proteins, the so-called hard corona. Strong binding affinity, long residence time, slow exchange time, and high conformational changes are some of the most important characteristics of this layer. Some models suggest that on top of this hard corona, a so-called soft corona may exist, which consists of a more loosely associated and rapidly exchanging layer of biomolecules with a low degree of conformational changes [19].

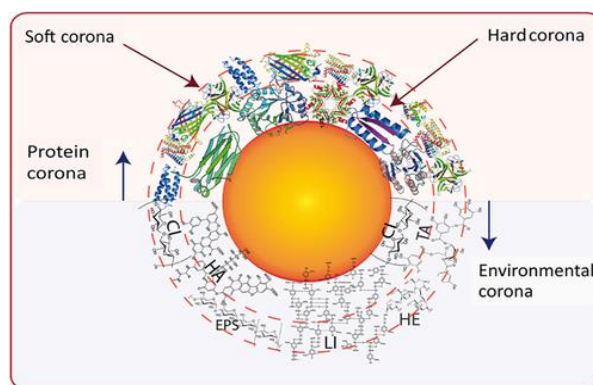


Figure 7: The engineered nanomaterial protein (top) and environmental (bottom) corona. HE = hemicellulose; CI = cellulose; TA = tannic acid; LI = lignin; EPS = exopolymeric substances; HA = humic acid [20]

Nanoparticles (NPs) specifically decorated with targeting moieties such as immune system activating proteins can serve to modulate the immune system and catalyse the design of new therapeutics. Proteomics analyses of protein coronas of various NPs (for example, sensor array) provide a unique opportunity for identification of novel biomolecular patterns with disease detection capacity. The eco-corona forms when NPs enter ecological environments, resulting in spontaneous protein adsorption from ecological sources [21]. Nanoparticles are usually employed as carriers of therapeutic agents (e.g. anticancer drugs) and surface functionalized to promote favorable interactions with target cells. When nanoparticles are administered in vivo, they get covered by a protein corona that activates the immune response and influences the targeted delivery of Nano medicine [22].

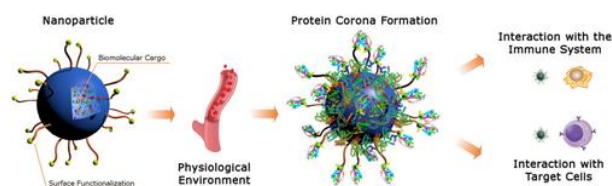


Figure 8: Impact of the protein corona on nanomaterial immune response and targeting ability

The protein corona also plays a role in the immune response. Nanoparticles with a protein corona that resembles "self"

proteins may evade immune detection, while those with "foreign" proteins may trigger immune responses, leading to inflammation or cytotoxicity. Understanding the mechanisms of protein corona formation is essential for designing nanoparticles with optimized biocompatibility and functional properties. The protein corona activates immune response and influences the targeted delivery of nanomaterials. Furthermore, we comment on emerging strategies to manipulate protein binding in order to promote formation of designer artificial coronas and achieve a desired therapeutic outcome. We conclude by debating challenges that must be overcome to obtain widespread clinical adoption of nanomaterials [23].

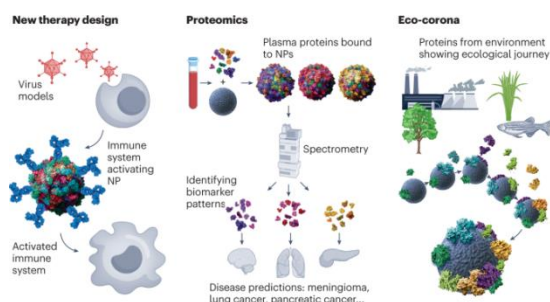


Figure 9: New emerging technologies offered by the protein corona [24].

2.3 Key Parameters Influencing Nano-Bio Interactions

Several key parameters govern how nanomaterials interact with biological systems, including size, shape, surface charge, and functional modifications. Nanoparticle size is particularly critical, as it influences circulation time, cellular uptake, and biodistribution. Smaller nanoparticles generally penetrate cells more readily than larger ones, which may be cleared by the body more quickly through macrophage uptake [25]. The shape of nanoparticles also affects cellular interactions. For example, rod-shaped nanoparticles have shown higher uptake rates in certain cancer cells compared to spherical nanoparticles, potentially due to differences in membrane wrapping dynamics [26]. Surface modifications, such as attaching targeting ligands, further allow nanoparticles to interact selectively with specific cell types or tissues, improving the efficacy of drug delivery systems [27].

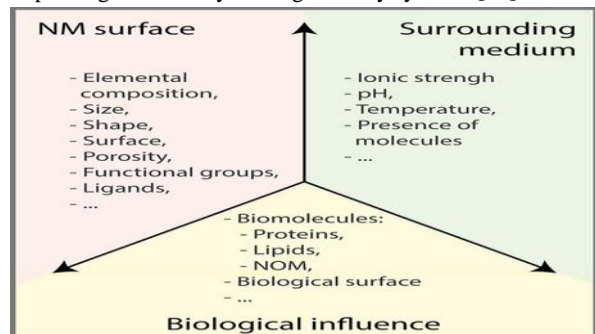


Figure 10: The 3 sides of the bio-nano interface triangle. The main parameters governing the interface are surface, medium characteristics, and biological factors. NM = nanomaterial; NOM = natural organic matter [28].

These 3 general parameters are important in the fate, transport, behavior, and bioavailability of ENMs in the environment, but the last one (adsorption of organic molecules on their surfaces) is critical when ENMs approach biological surfaces. The formation of an external so-called biolayer in the extracellular environment has been shown to alter NP size, shape, and surface properties, creating a biological identity that is distinct from its initial synthetic identity. Therefore, how ENMs interact with different cells and organisms depends on the substances attached to their surface. Recently, the interaction between ENMs and biomolecules has been extensively studied in biomedicine [29].

3. Nanotechnology in Drug Delivery Systems

The integration of nanotechnology into drug delivery has led to significant advancements in the precision and efficacy of treatments across various diseases. Nanoparticles and other nanoscale carriers enable targeted delivery of therapeutic agents, minimizing systemic side effects and enhancing drug bioavailability. This section explores key mechanisms of nanotechnology-based drug delivery, the types of nanocarriers utilized, and the challenges associated with translating these technologies into clinical practice. Nanotechnology has finally and firmly emerged as the realm of drug delivery. Performances of intelligent drug delivery systems are continuously improved with the purpose to maximize therapeutic activity and to minimize undesirable side effects. Recent advances in material design and the emergence of new therapeutics are contributing to the development of more sophisticated systems.

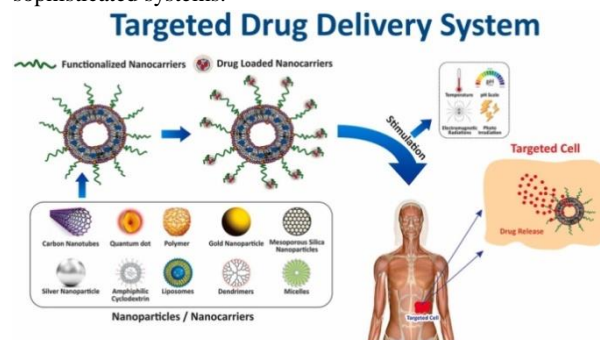


Figure 11: Mechanism of nanocarriers for targeted drug delivery [30].

3.1 Targeted Drug Delivery Using Nanoparticles: Mechanisms and Advances

One of the primary advantages of nanotechnology in drug delivery is the ability to design nanoparticles for targeted delivery. Targeted drug delivery mechanisms can be classified as either passive or active. Passive targeting relies on the enhanced permeability and retention (EPR) effect, a phenomenon where nanoparticles accumulate in tumor tissues due to leaky vasculature and poor lymphatic drainage. This effect has been widely exploited in cancer therapy, where nanoparticle-based formulations preferentially accumulate in tumors, enhancing therapeutic efficacy and reducing side

effects [31]. The selection of nanosized drug delivery systems is very wide, containing pure solid drug nanoparticles and very sophisticated and complex engineered nanomachines. The research in the field of drug Nano carriers is very intensive. The importance of understanding the properties of biological membranes, their impact on permeation, and, most importantly, the need for thorough understanding of the physicochemical properties and the related interactions of the drug nanocarriers with the biological membranes [32].

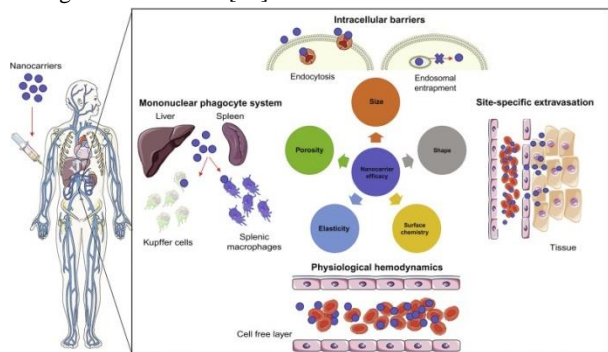


Figure 12: Delivery mechanism of Nano sized drug [33].

Active targeting, on the other hand, involves functionalizing the nanoparticle surface with ligands, such as antibodies, peptides, or small molecules that bind specifically to receptors overexpressed on target cells. This strategy enhances cellular uptake and improves the specificity of drug delivery to diseased tissues, including tumors and inflamed sites [34]. Ligand-mediated targeting has shown promise in improving outcomes in cancer treatment by directing nanoparticles to cancer cells while sparing normal tissues. Nanotechnology has been extensively studied and exploited for cancer treatment as nanoparticles can play a significant role as a drug delivery system. Compared to conventional drugs, nanoparticle-based drug delivery has specific advantages, such as improved stability and biocompatibility, enhanced permeability and retention effect, and precise targeting. The application and development of hybrid nanoparticles, which incorporates the combined properties of different nanoparticles, has led this type of drug-carrier system to the next level. Nanoparticles targeting these mechanisms can lead to an improvement in the reversal of multidrug resistance. Furthermore, as more tumor drug resistance mechanisms are revealed, nanoparticles are increasingly being developed to target these mechanisms. Moreover, scientists have recently started to investigate the role of nanoparticles in immunotherapy, which plays a more important role in cancer treatment [35].

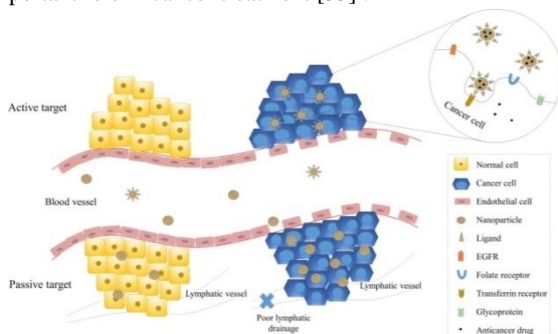


Figure 13. Passive and active targeting of NPs to cancer cells [36].

3.2 Types of Nanocarriers: Liposomes, Dendrimers, and Polymer-Based Nanoparticles

Various types of nanocarriers have been developed to deliver drugs more effectively, each with unique structures and benefits. Liposomes are spherical vesicles with a lipid bilayer that encapsulates drugs, improving their stability and bioavailability. Liposomal formulations, such as Doxil® (doxorubicin-loaded liposomes), have shown considerable success in treating cancer by prolonging circulation time and reducing cardiotoxicity associated with doxorubicin [37]. Dendrimers are another class of nanocarriers, characterized by their branched, tree-like structure that provides numerous sites for drug attachment and functionalization. These highly ordered nanostructures facilitate controlled drug release and enable multivalent interactions with target cells, improving therapeutic efficacy [38]. Polymer-based nanoparticles, including those made from biodegradable polymers like PLGA (poly(lactic-co-glycolic acid)), have gained popularity due to their controlled release profiles and biocompatibility. PLGA nanoparticles have been used in various applications, from anticancer drug delivery to vaccines, due to their ability to degrade into non-toxic byproducts in the body [39].

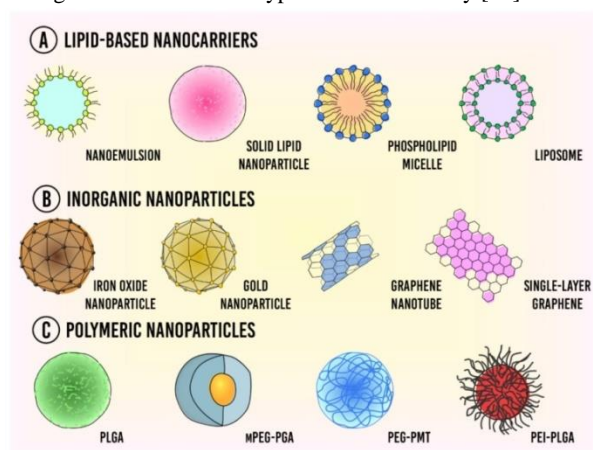


Figure 14: Different types of Nanocarriers [40].

Liposomes

Lipid-based nanocarriers have emerged as a very promising, emerging, and rapidly developing tool for the delivery of various drugs with low solubility, bioavailability, and stability in recent decades. Lipid nanocarriers allow the therapeutic load to be directed to the deep layers of the skin or even reach the blood circulation, making them a promising cutting-edge technology. Lipid nanocarriers refer to a large panel of drug delivery systems. Lipid vesicles are the most conventional, and they are known to be capable of transporting lipophilic and hydrophilic active agents [41]. Others are designed with the objective of achieving a higher encapsulation rate and greater stability, such as solid lipid nanoparticles and nanostructured lipid nanocarriers. The formulation of a liposomal drug improves the biodistribution and pharmacokinetics of a drug. This means that a higher

concentration of the drug can be achieved within the tumors, while reducing the concentration of the drug in normal tissue.

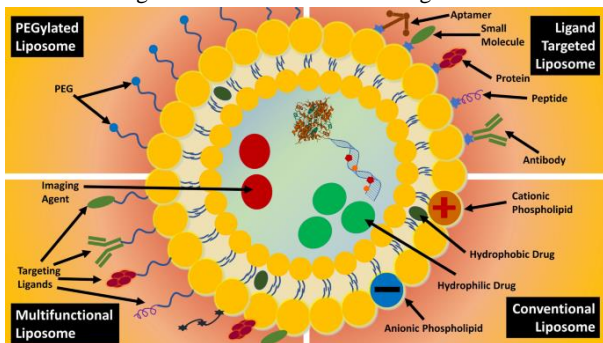


Figure 15: Structure of liposomes and their functionalization with other biomolecules, drugs, or antibodies [42] .

Polymeric nanocarriers

Polymeric nanocarriers are synthesized from different types of natural and synthetic polymers that generally have good biocompatibility and biodegradability. The advantages of these polymer nanomaterials compared to other nanocarriers include stability in various microenvironments, slow release of drugs due to polymer degradation, and their diversity in the types of polymers and types of drugs to be encapsulated. The hydrophobicity and hydrophilicity within the polymer structure can be controlled to suit a variety of drug molecules. Commonly used natural polymers include gelatin, dextran, albumin, chitosan, and alginate, and synthetic biodegradable polymers include polylactic acid (PLA), polyglycolic acid (PGA), copolymer of lactic acid and glycolic acid (PLGA), poly (ε-caprolactone) (PCL), polyalkylcyanoacrylate (PACA), poly (ethylene glycol) (PEG), poly (D,L-lactide-co-glycolide) (PLG), polyethyleneimine (PEI), poly (L-lysine), poly (Tian Particular acid), and others [43] .

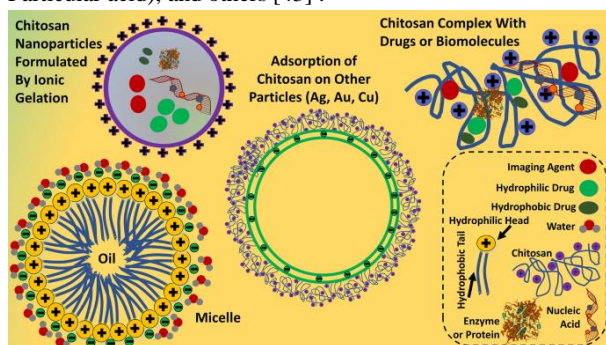


Figure 16: Organic nanoparticles and their complexes [44]

Inorganic Nanoparticles

Among the nanocarriers that are being developed for the diagnosis and treatment of cancer are inorganic nanoparticles, which may consist of iron oxide, silica, gold, and graphene, among other compounds. There is greater difficulty in translating these types of nanomaterials (NMs) to clinical application, due to their lower biocompatibility and the lack of understanding of possible complications caused by their deposition in different organs, such as greater stability, less hydrophobicity, and non-microbial storage. Despite these

difficulties, the physical properties attributed to the constituent materials of inorganic nanoparticles make it possible to apply them in a variety of processes, for example, magnetic nanoparticles can be used for magnetic resonance imaging (MRI) or with magnetic targeting, while gold and silver NM can be used for imaging or heating during targeted treatment [45] .

3.3 Challenges and Regulatory Considerations for Clinical Applications

Despite the promise of nanotechnology-based drug delivery systems, there are significant challenges to their clinical translation. One of the major hurdles is the potential for nanoparticle toxicity, as some nanomaterials can induce immune responses, causing adverse effects. Understanding and mitigating nanotoxicity are essential for the safe development of these technologies, and extensive preclinical studies are required to assess the safety profile of each new nanoparticle formulation [46] .

Regulatory challenges also play a critical role. Nanoparticles often exhibit unique interactions within biological systems, complicating the standardization of safety protocols and quality control measures. Regulatory agencies, including the FDA and EMA, have established guidelines for assessing nanomaterial-based therapeutics, yet inconsistencies in regulatory frameworks across countries can pose additional barriers to commercialization [47] . Additionally, the scalability and reproducibility of nanoparticle synthesis remain technical challenges that need to be addressed to meet industrial and clinical demands.

4. Nanotechnology in Diagnostics and Bioimaging

The application of nanotechnology in diagnostics and bioimaging has transformed how diseases are detected and monitored, allowing for early diagnosis and personalized treatment strategies. Nanoparticles enhance imaging modalities, such as magnetic resonance imaging (MRI), computed tomography (CT), and optical imaging, by improving contrast, resolution, and specificity. This section delves into key nanoparticle-based imaging agents and discusses their role in disease diagnostics, focusing on cancer, cardiovascular diseases, and neurodegenerative disorders.

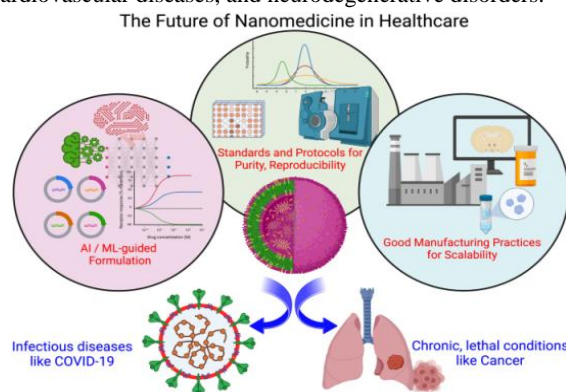


Figure 17; Future of nanoparticles

4.1. Quantum Dots in Fluorescence Imaging

Quantum dots (QDs) are semiconductor nanocrystals that exhibit unique optical properties, including size-tunable fluorescence and exceptional photostability, making them ideal for long-term imaging applications. Their bright, tunable emission wavelengths enable multicolor imaging, allowing simultaneous tracking of multiple biological markers [48]. QDs have been widely utilized in cancer diagnostics, where they can be conjugated with antibodies or peptides to target specific tumor markers, providing high-resolution images that distinguish cancerous cells from healthy tissue [49]. QDs have also shown promise in tracking molecular events within cells, enabling real-time observation of intracellular processes. However, concerns regarding the potential toxicity of cadmium-based QDs have led researchers to explore alternative materials, such as carbon-based and silicon QDs, which offer reduced cytotoxicity and comparable imaging capabilities.

4.2 Magnetic Nanoparticles for MRI

Magnetic nanoparticles (MNPs) have emerged as powerful contrast agents for magnetic resonance imaging (MRI). Superparamagnetic iron oxide nanoparticles (SPIONs) enhance MRI contrast by creating local magnetic field disturbances that improve the visualization of tissues and anatomical structures. SPIONs have been widely used in imaging liver and lymph node metastases, as they selectively accumulate in these tissues, providing enhanced contrast [50]. By functionalizing SPIONs with targeting ligands, researchers have achieved targeted MRI contrast, enabling precise imaging of specific cell types, such as cancer cells or inflamed tissues. Recently, efforts have been made to combine SPIONs with therapeutic agents, creating theranostic (therapy + diagnostic) platforms that enable simultaneous imaging and treatment. This dual functionality is particularly useful for tracking therapeutic responses in real time, paving the way for personalized medicine approaches.

4.3 Gold Nanoparticles in Optical Imaging and Biosensing

Gold nanoparticles (AuNPs) possess unique optical properties, particularly surface plasmon resonance (SPR), which makes them highly sensitive to changes in the local environment. This property enables their use in biosensing and optical imaging, as AuNPs produce a strong optical signal when interacting with specific biomolecules. In cancer diagnostics, AuNPs conjugated with antibodies can detect biomarkers at low concentrations, allowing early detection and precise localization of tumors [51]. In addition to their diagnostic role, AuNPs have shown promise in photothermal therapy, where they absorb light and convert it into heat, selectively destroying cancer cells. This dual diagnostic-therapeutic capability allows for simultaneous imaging and treatment, facilitating a more comprehensive approach to cancer management.

4.4 Challenges and Future Directions in Nano-Bioimaging

Despite the tremendous potential of nanoparticle-based imaging, there are several challenges associated with clinical translation. Biocompatibility remains a primary concern,

particularly with QDs and SPIONs, which may induce cytotoxicity or inflammatory responses over prolonged periods. Additionally, the biodistribution and clearance of imaging agents must be well-understood to prevent accumulation in non-target organs. Regulatory approval processes for nano-imaging agents are also stringent, necessitating rigorous preclinical testing to establish safety and efficacy.

5. Nanotechnology in Therapeutics

Nanotechnology has enabled precise therapeutic approaches by allowing drugs to be delivered directly to specific tissues and cells, enhancing the treatment of conditions such as cancer, infectious diseases, and genetic disorders. In addition to conventional drug delivery, nanotechnology has introduced innovations such as gene therapy and immunotherapy, where nanoparticles play a crucial role in enhancing therapeutic efficacy.

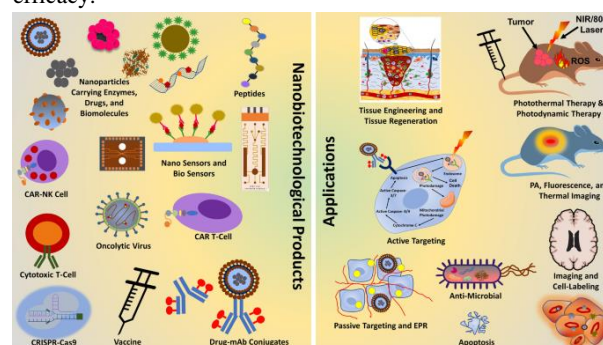


Figure 18: Nanobiotechnology and its applications [52].

5.1 Cancer Therapeutics and Nanomedicine

Cancer remains one of the most prominent applications for nanotechnology-based therapeutics, with nanoscale drug delivery systems designed to improve the therapeutic index and reduce the side effects of chemotherapeutic agents. Polymer nanoparticles, liposomes, and micelles are widely used for encapsulating anticancer drugs, enhancing their solubility, and controlling their release. A notable example is the nanoparticle albumin-bound paclitaxel (Abraxane®), which provides targeted drug delivery and improved efficacy over conventional formulations. Beyond drug delivery, nanoparticles also play a role in cancer immunotherapy. Nanoparticle vaccines can stimulate an immune response against cancer cells by delivering tumor antigens more effectively, improving the activation of dendritic cells, and enhancing T-cell response [53]. Cancer nanotherapeutics have revolutionized treatment by providing targeted delivery of drugs, improving efficacy, and reducing systemic side effects. Recent advances in nanotechnology have extended to immunotherapy, where nanoparticles facilitate tumor antigen presentation, thereby enhancing immune recognition and response."

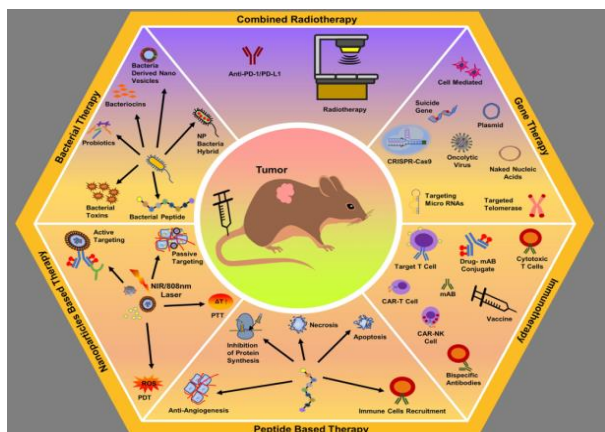


Figure 19: Nanobiotechnology based anti-cancer therapeutic strategies [54].

5.2 Gene Therapy with Nanoparticles

Nanotechnology has also enhanced gene therapy by enabling the efficient and safe delivery of nucleic acids to target cells. Lipid-based nanoparticles are commonly used to deliver small interfering RNA (siRNA) and messenger RNA (mRNA), allowing for gene silencing or protein expression in specific cells. Lipid nanoparticles are critical in the development of mRNA vaccines, such as those for COVID-19, demonstrating their potential in combating viral infections and genetic disorders. Gene therapy has advanced with lipid-based nanoparticles, enabling targeted delivery of genetic material for treating genetic disorders and infectious diseases. These nanoparticles facilitate cellular uptake and protect nucleic acids from degradation, enhancing gene therapy's therapeutic efficacy.

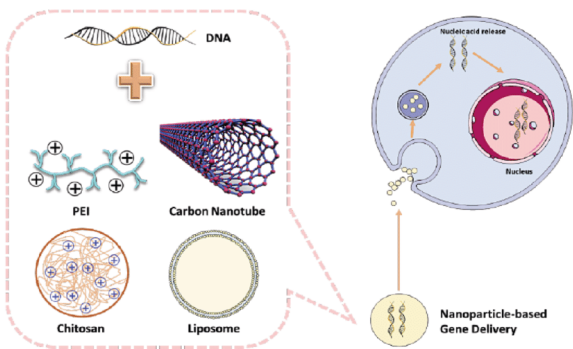


Figure 20: The applications of nanoparticles in gene delivery. Nanoparticle-based gene delivery presents a promising therapeutic method *in vitro* and *in vivo*, and recombinant DNA can be delivered into cells efficiently [55].

6. Nanotechnology in Regenerative Medicine

Nanotechnology is playing a transformative role in regenerative medicine, particularly in tissue engineering and stem cell therapy. Nanomaterials mimic the natural extracellular matrix, creating a supportive scaffold that promotes cell adhesion, proliferation, and differentiation. Nanofibers, hydrogels, and biocompatible nanoparticles serve as scaffolds for regenerating damaged tissues, such as bone,

cartilage, and nerves. Regenerative medicine involves the development of methods to repair and replace diseased or damaged cells, tissues, or organs to restore or establish normal tissue functions. Nanotechnology is a powerful strategy in tissue regeneration for recreating the Nano scale features of tissues that can direct cellular adhesion, migration, and differentiation. Nanomaterials also have unique physical, chemical, optical, electrical, and magnetic properties that are different from their bulk-level counterparts. Based on their size and functional advantages, nanomaterials can be used for effective biomolecule delivery, scaffolds for tissue engineering, *in vivo* cell tracking, and stem cell therapy.

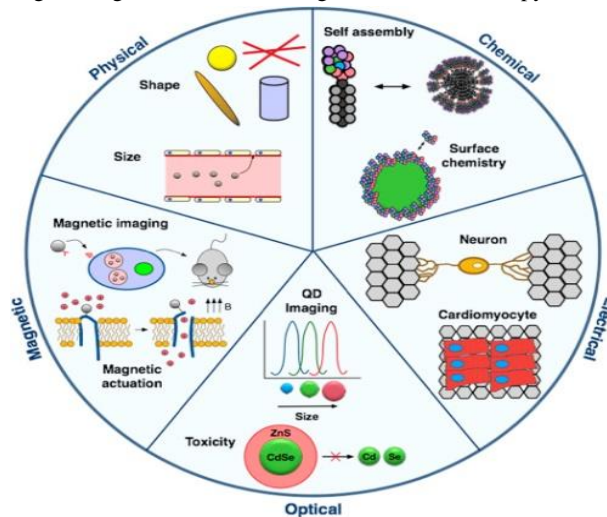


Figure 21: Applications of Nanotechnology for Regenerative Medicine [56].

6.1 Nanoscaffolds in Tissue Engineering

Nanoscaffolds provide structural support and biochemical cues that facilitate tissue regeneration. Electrospun nanofibers, for example, are designed to mimic the fibrous structure of natural tissues, promoting cell attachment and growth. Additionally, nanofibrous scaffolds loaded with growth factors can provide controlled release, further enhancing tissue regeneration.

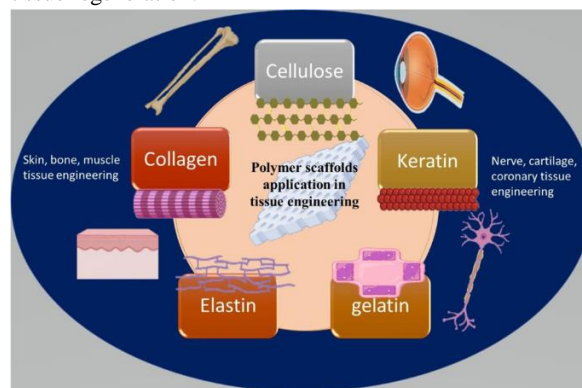


Figure 22: Applications of Nanoscaffolds in Tissue Engineering [57].

The functional scaffolds used in different kinds of tissue engineering such as bone, liver, cartilage, vascular tissue, skin and cardiac tissue, etc., and an overview of various types of materials used in scaffolding for the tissue engineering

applications. Tissue engineering and regenerative medicine are the emerging field of research that encompasses the designing of different types of porous scaffolds using different synthesis techniques and biocompatible ingredients for the homing and growth of stem cells. These stem cells can proliferate and further differentiate into specific cell type that is necessary for replacing the damaged tissue, or they can be grown outside the body and then replaced back to the affected individual. Many progresses have been made in this field by using both natural and artificial scaffolds, but very few have been translated into practical use. Many concomitant studies have indicated that the addition of nanoparticles, such as gold, silver, and other metal and their oxides, has enhanced the stem cell growth and improved the proliferations.

6.2 Stem Cell Therapy and Nanoparticles

Nanoparticles are also used to improve stem cell therapies by enhancing cell tracking and promoting differentiation. Iron oxide nanoparticles, for instance, allow for non-invasive tracking of stem cells via MRI, enabling researchers to monitor stem cell engraftment and migration in real time. Furthermore, nanoparticles can deliver genetic material or growth factors to stem cells, guiding their differentiation into specific cell types for targeted tissue repair. Nanotechnology enhances stem cell therapies by enabling cell tracking and directing cell differentiation. Magnetic nanoparticles offer a means of non-invasively monitoring stem cell migration, while growth-factor-loaded nanoparticles provide cues for differentiation, supporting tissue repair and regeneration.

Conclusion

Nanotechnology has established a new frontier in biomedicine, enabling innovative approaches to drug delivery, diagnostics, and regenerative medicine. Although challenges remain, particularly regarding safety and regulatory approval, continued research and development will pave the way for nanotechnology to become an integral component of modern healthcare. The advancements discussed in this review underscore the potential of nanotechnology to revolutionize disease treatment and diagnosis, ultimately contributing to a future of more personalized, effective, and less invasive healthcare solutions.

References

1. Boisseau, P., & Loubaton, B. (2011). Nanomedicine, nanotechnology in medicine. *Comptes Rendus Physique*, 12(7), 620-636. <https://doi.org/10.1016/j.cryhy.2011.03.003>
2. Bruchez, M., Moronne, M., Gin, P., Weiss, S., & Alivisatos, A. P. (1998). Semiconductor nanocrystals as fluorescent biological labels. *Science*, 281(5385), 2013-2016. <https://doi.org/10.1126/science.281.5385.2013>
3. Bulte, J. W. M., & Kraitchman, D. L. (2004). Iron oxide MR contrast agents for molecular and cellular imaging. *NMR in Biomedicine*, 17(7), 484-499. <https://doi.org/10.1002/nbm.906>
4. Fan, Y., Moon, J. J., & El-Shabrawy, M. (2012). Nanoparticle-based cancer immunotherapy.

5. Gao, X., Cui, Y., Levenson, R. M., Chung, L. W., & Nie, S. (2004). In vivo cancer targeting and imaging with semiconductor quantum dots. *Nature Biotechnology*, 22(8), 969-976. <https://doi.org/10.1038/nbt982>
6. Hsu, S. H., & Huang, G. S. (2013). Applications of carbon nanomaterials in tissue engineering. *Current Opinion in Solid State and Materials Science*, 17(2), 66-71. <https://doi.org/10.1016/j.cossms.2013.02.003>
7. Huang, X., Jain, P. K., El-Sayed, I. H., & El-Sayed, M. A. (2006). Gold nanoparticles: Interesting optical properties and recent applications in cancer diagnostics and therapy. *Nanomedicine*, 2(5), 681-693. <https://doi.org/10.1016/j.nano.2006.09.002>
8. Jain, P. K., Huang, X., El-Sayed, I. H., & El-Sayed, M. A. (2008). Noble metals on the nanoscale: Optical and photothermal properties and some applications in imaging, sensing, biology, and medicine. *Accounts of Chemical Research*, 41(12), 1578-1586. <https://doi.org/10.1021/ar800220m>
9. Jun, Y. W., Lee, J. H., & Cheon, J. (2008). Chemical design of nanoparticle probes for high-performance magnetic resonance imaging. *Angewandte Chemie International Edition*, 47(28), 5122-5135. <https://doi.org/10.1002/anie.200701730>
10. Kabanov, A. V., & Vinogradov, S. V. (2009). Nanogels as pharmaceutical carriers. *Nanomedicine*, 4(2), 149-164. <https://doi.org/10.1016/j.nano.2008.12.003>
11. Kim, B. Y., Rutka, J. T., & Chan, W. C. W. (2010). Nanomedicine. *New England Journal of Medicine*, 363(25), 2434-2443. <https://doi.org/10.1056/NEJMra0912273>
12. Laurencin, C. T., Freeman, J. W., & Katwa, P. (2006). Nanofibers and nanomaterials in regenerative medicine. *Nanomedicine*, 1(1), 1-12. <https://doi.org/10.1016/j.nano.2006.03.001>
13. Liu, Z., Tabakman, S., Chen, Z., & Dai, H. (2009). Preparation, functionalization, and biocompatibility of graphene oxide and its derivatives. *Science China Chemistry*, 53(5), 85-86. <https://doi.org/10.1007/s11426-009-0074-7>
14. Ma, P. X., & Zhang, R. (2005). Synthetic nanoscale fibrous extracellular matrix. *Nature Biotechnology*, 23(12), 1517-1523. <https://doi.org/10.1038/nbt1158>
15. Medintz, I. L., Uyeda, H. T., Goldman, E. R., & Mattoussi, H. (2005). Quantum dot bioconjugates for imaging, labelling and sensing. *Nature Materials*, 4(6), 435-446. <https://doi.org/10.1038/nmat1390>
16. Oberdörster, G., Oberdörster, E., & Oberdörster, J. (2005). Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles. *Environmental Health Perspectives*, 113(7), 823-839. <https://doi.org/10.1289/ehp.7679>

17. Schoenmaker, L., Witzigmann, D., Kulkarni, J. A., Verbeke, R., Kersten, G. F., & Jiskoot, W. (2021). mRNA-lipid nanoparticle COVID-19 vaccines: Structure and stability. *International Journal of Pharmaceutics*, 597, 120-126. <https://doi.org/10.1016/j.ijpharm.2021.120000>
18. Shah, S., Choi, S., & Lee, H. (2015). Nanotechnology-based diagnostic approaches. *Journal of Pharmaceutical and Biomedical Analysis*, 96, 81-92. <https://doi.org/10.1016/j.jpba.2014.10.012>
19. Sun, C., Lee, J. S., & Zhang, M. (2008). Magnetic nanoparticles in MR imaging and drug delivery. *Advanced Drug Delivery Reviews*, 60(11), 1252-1265. <https://doi.org/10.1016/j.addr.2008.03.004>
20. Yardley, D. A. (2013). Nanotechnology in cancer treatment: Focus on albumin-bound paclitaxel (Abraxane®). *Cancer Control*, 20(1), 23-30. <https://doi.org/10.1177/107327481302000106>
21. Yin, H., Kanasty, R. L., and et al. (2014). Non-viral vectors for gene therapy: Delivery and safety. *Human Gene Therapy*, 25(9), 682-687. <https://doi.org/10.1089/hum.2014.155>
22. Cai, P., Leow, W. R., Wang, X., Wu, Y. L., & Chen, X. (2017). Programmable nano-bio interfaces for functional biointegrated devices. *Advanced Materials*, 29(26), 1605529.
23. S. Choi, H. Lee, R. Ghaffari, T. Hyeon, D. H. Kim, *Adv. Mater.* 2016, **28**, 4203
24. U. G. Wegst, H. Bai, E. Saiz, A. P. Tomsia, R. O. Ritchie, *Nat. Mater.* 2015, **14**, 23.
25. Wang, Y., Cai, R., & Chen, C. (2019). The nano-bio interactions of nanomedicines: understanding the biochemical driving forces and redox reactions. *Accounts of chemical research*, 52(6), 1507-1518.
26. Asha, A. B., & Narain, R. (2020). Nanomaterials properties. In *Polymer science and nanotechnology* (pp. 343-359). Elsevier.
27. Nimisha, O.K.; Akshay, M.; Mannya, S.; Reena Mary, A.P. Synthesis and photocatalytic activity of nickel doped zinc ferrite. *Mater. Today Proc.* **2022**, *66*, 2370–2373. [[Google Scholar](#)] [[CrossRef](#)]
28. Dhiman, P.; Rana, G.; Dawi, E.A.; Kumar, A.; Sharma, G.; Kumar, A.; Sharma, J. Tuning the Photocatalytic Performance of Ni-Zn Ferrite Catalyst Using Nd Doping for Solar Light-Driven Catalytic Degradation of Methylene Blue. *Water* **2023**, *15*, 187. [[Google Scholar](#)] [[CrossRef](#)]
29. Jadhav, S.A.; Khedkar, M.V.; Somvanshi, S.B.; Jadhav, K.M. Magnetically retrievable nanoscale nickel ferrites: An active photocatalyst for toxic dye removal applications. *Ceram. Int.* **2021**, *47*, 28623–28633. [[Google Scholar](#)] [[CrossRef](#)]
30. Dippong, T.; Levei, E.A.; Cadar, O. Investigation of structural, morphological and magnetic properties of MFe_2O_4 ($M = Co, Ni, Zn, Cu, Mn$) obtained by thermal decomposition. *Int. J. Mol. Sci.* **2022**, *23*, 8483. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
31. Kalaiselvan, C.R.; Laha, S.S.; Somvanshi, S.B.; Tabish, T.A.; Thorat, N.D.; Sahu, N.K. Manganese ferrite ($MnFe_2O_4$) nanostructures for cancer theranostics. *Coord. Chem. Rev.* **2022**, *473*, 214809. [[Google Scholar](#)] [[CrossRef](#)]
32. Sinha, A., Simnani, F. Z., Singh, D., Nandi, A., Choudhury, A., Patel, P., ... & Verma, S. K. (2022). The translational paradigm of nanobiomaterials: Biological chemistry to modern applications. *Materials today bio*, 17, 100463.
33. Kaymaz, S. V., Nobar, H. M., Sangül, H., Soyulkan, C., Akyüz, L., & Yüce, M. (2023). Nanomaterial surface modification toolkit: Principles, components, recipes, and applications. *Advances in Colloid and Interface Science*, 322, 103035.
34. Gessner, I., & Neundorff, I. (2020). Nanoparticles modified with cell-penetrating peptides: Conjugation mechanisms, physicochemical properties, and application in cancer diagnosis and therapy. *International journal of molecular sciences*, 21(7), 2536.
35. Mahmoudi, M., Landry, M. P., Moore, A., & Coreas, R. (2023). The protein corona from nanomedicine to environmental science. *Nature Reviews Materials*, 8(7), 422-438.
36. Digiacomo, L., Pozzi, D., Palchetti, S., Zingoni, A., & Caracciolo, G. (2020). Impact of the protein corona on nanomaterial immune response and targeting ability. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, 12(4), e1615.
37. Kuruvilla J, Farinha AP, Bayat N, Cristobal S. 2017. Surface proteomics on nanoparticles: A step to simplify the rapid prototyping of nanoparticles. *Nanoscale Horiz* 2: 55–64.
38. Docter D, Strieth S, Westmeier D, Hayden O, Gao M, Knauer SK, Stauber RH. 2015. No king without a crown—Impact of the nanomaterial-protein corona on nanobiomedicine. *Nanomed Nanotech Biol Med* 10: 503–519.
39. Yang ST, Liu Y, Wang YW, Cao A. 2013. Biosafety and bioapplication of nanomaterials by designing protein-nanoparticle interactions. *Small* 9: 1635–1653.
40. Pulido-Reyes, Gerardo, Francisco Leganes, Francisca Fernández-Piñas, and Roberto Rosal. "Bio-nano interface and environment: A critical review." *Environmental toxicology and chemistry* 36, no. 12 (2017): 3181-3193.
41. Rana, V., & Sharma, R. (2019). Recent advances in development of nano drug delivery. *Applications of targeted nano drugs and delivery systems*, 93-131.
42. Shah, A., Aftab, S., Nisar, J., Ashiq, M. N., & Iftikhar, F. J. (2021). Nanocarriers for targeted drug

- delivery. *Journal of Drug Delivery Science and Technology*, 62, 102426.
43. B. Wu, Y. Liang, Y. Tan, C. Xie, J. Shen, M. Zhang, X. Liu, L. Yang, F. Zhang, L. Liu. Genistein-loaded nanoparticles of star-shaped diblock copolymer mannitol-core PLGA-TPGS for the treatment of liver cancer. *Mater. Sci. Eng. C*, 59 (2016), pp. 792-800
 44. R.P. Das, V.V. Gandhi, B.G. Singh, A. Kunwar, N.N. Kumar, K. Priyadarsini. Preparation of albumin nanoparticles: optimum size for cellular uptake of entrapped drug (Curcumin) Colloid. *Surface. Physicochem. Eng. Aspect.*, 567 (2019), pp. 86-95
 45. Peltonen, L., Singhal, M., & Hirvonen, J. (2020). Principles of nanosized drug delivery systems. In *Nanoengineered Biomaterials for Advanced Drug Delivery* (pp. 3-25). Elsevier.
 46. Yao, Yihan, Yunxiang Zhou, Lihong Liu, Yanyan Xu, Qiang Chen, Yali Wang, Shijie Wu, Yongchuan Deng, Jianmin Zhang, and Anwen Shao. "Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance." *Frontiers in molecular biosciences* 7 (2020): 193.
 47. Akbarzadeh, A.; Rezaei-Sadabady, R.; Davaran, S.; Joo, S.W.; Zarghami, N.; Hanifehpour, Y.; Samiei, M.; Kouhi, M.; Nejati-Koshki, K. Liposome: Classification, preparation, and applications. *Nanoscale Res. Lett.* 2013, 8, 102.
 48. Kulkarni, J.; Cullis, P.R.; van der Meel, R. Lipid Nanoparticles Enabling Gene Therapies: From Concepts to Clinical Utility. *Nucleic Acid Ther.* 2018, 28, 146–157.
 49. Shamant, B.S.; Moin, A.; Gowda, D.V.; Rashmi, R.; Hiremath, R. Lipid based drug delivery systems in arthritis and allied conditions. *World J. Pharm. Sci.* 2016, 4, 61–68.
 50. Ansari, M.T.; Ramlan, T.A.; Jamaluddin, N.N.; Zamri, N.; Salfi, R.; Khan, A.; Sami, F.; Majeed, S.; Hasnain, M.S. Lipid-based Nanocarriers for Cancer and Tumor Treatment. *Curr. Pharm. Des.* 2020, 26, 4272–4276.
 51. Ahuja, R.; Panwar, N.; Meena, J.; Singh, M.; Sarkar, D.P.; Panda, A.K. Natural products and polymeric nanocarriers for cancer treatment: A review. *Environ. Chem. Lett.* 2020, 18, 2021–2030.
 52. Sun, Q.; Zhu, Y.; Du, J. Recent progress on charge-reversal polymeric nanocarriers for cancer treatments. *Biomed. Mater.* 2021, 16, 042010.
 53. Avramović, N.; Mandić, B.; Savić-Radojević, A.; Simić, T. Polymeric Nanocarriers of Drug Delivery Systems in Cancer Therapy. *Pharmaceutics* 2020, 12, 298.
 54. Alsehli, M. Polymeric nanocarriers as stimuli-responsive systems for targeted tumor (cancer) therapy: Recent advances in drug delivery. *Saudi Pharm. J.* 2020, 28, 255–265.
 55. Paul, W.; Sharma, C.P. Inorganic nanoparticles for targeted drug delivery. *Biointegration Med. Implant. Mater.* 2020, 334–373.
 56. Torchilin, V.P. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. *Nat. Rev. Drug Discov.* 2014, 13, 813–827.
 55. Oh, N.; Park, J.-H. Endocytosis and exocytosis of nanoparticles in mammalian cells. *Int. J. Nanomed.* 2014, 9, 51.
 56. Bardhan, N. (2022). Nanomaterials in diagnostics, imaging and delivery: applications from COVID-19 to cancer. *Mrs Communications*, 12(6), 1119-1139.
 57. Dutt Y, Pandey RP, Dutt M, Gupta A, Arpana V, Raj VS, Chang C-M, Priyadarshini A. Silver nanoparticles phyto-fabricated through *Azadirachta Indica*: anti-cancer, apoptotic, and wound healing properties. *Antibiotics*. 2022.