Journal of Chemical Health Risks

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JCHR (2025) 15(3), 374-383 | ISSN:2251-6727

Nanoparticle Drug Delivery System for Bioavailability Enchancement

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(Received: 16 March 2025 Revised: 20 April 2025 Accepted: 01 May2025)

KEYWORDS

Bioavailability Enhancement, Novel Drug Delivery Systems, Nanoparticle, Targeted delivery, Nanotechnology

ABSTRACT:

Nanoparticle-based drug delivery systems have revolutionized the field of pharmaceutical sciences by providing a promising approach to enhance the bioavailability of poorly soluble drugs. By formulating drugs into nanoparticles, their solubility, stability, and permeability can be improved, leading to increased bioavailability and therapeutic efficacy. This review aims to provide a comprehensive overview of nanoparticle-based drug delivery systems, including lipid nanoparticles, polymeric nanoparticles, and inorganic nanoparticles, and their applications in enhancing the bioavailability of various drugs. The use of nanoparticles as drug delivery systems offers several advantages, including increased surface area, improved permeability, and targeted delivery. Nanoparticles can be designed to interact with biological membranes, enhancing the permeability of drugs across epithelial barriers. Additionally, nanoparticles can be engineered to target specific tissues or cells, reducing the distribution of drugs to non-target sites and increasing their bioavailability. Nanotechnology is the concept used in NDDS that enables a weight reduction of drug particles accompanied by an increase in stability and improved functionality. Various approaches such as nanosuspensions, liposomes, niosomes, nanoemulsions, cubosomes, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), cyclodextrins, phytosome etc., are used for the enhancement of bioavailability. The present review focuses on the different approaches used for bioavailability enhancement along with their advantages and disadvantages.

Introduction: Bioavailability of the drugs can be enhanced using novel drug delivery systems by transport the drug to the place of action, hence, its influence on vital tissues and undesirable side effects can be minimized so the accumulation of therapeutic compounds in the target site increases and consequently, the required doses of drugs become lower at a predestined rate i.e., offers controlled rate, slow and target delivery. Recent developments in nanotechnology have shown that nanoparticles (structures smaller than 100 nm) have a great potential as drug carriers. These nanostructures exhibit unique physicochemical and biological properties (e.g., an enhanced reactive area as well as an ability to cross cell and tissue barriers) due to their small sizes, which make them a favorable material for biomedical applications. Nanoparticles have greater surface area to volume ratio, means more surface is exposed which results in faster dissolution of nanoparticles in solution, resulted in greater bioavailability, smaller drug doses and less toxicity. In traditional drug delivery systems such as oral or intravascular delivery, the drug or therapeutic molecules are distributed throughout the body through the systemic blood circulation, so the majority of molecules does not reach their targets and subsequently, stay in the body causing side effects. The drug and therapeutic molecules have a short plasma half-life, poor stability in serum and potential immunogenicity, and insolubility in water, which results in their rapid clearance of the mononuclear phagocytic system (MPS) and limits their efficiency. Bioavailability refers to the extent and rate at which the active moiety (drug or metabolite) enters systemic circulation, thereby accessing the site of action.[1]. Bioactivity is concerned with the drug's ability to produce the intended biological response. There are some common attributes that create challenges for DDS related to bioavailability.

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JCHR (2025) 15(3), 374-383 | ISSN:2251-6727

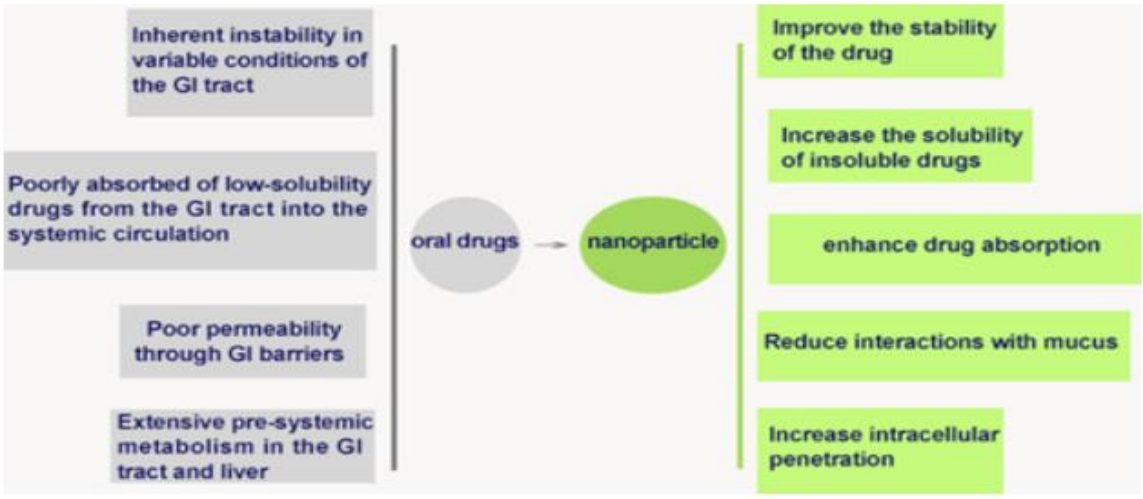

Figure: 1 The benefits of using nanoparticle

Poorly Soluble Drugs: Drugs with low water solubility may have limited dissolution in the gastrointestinal tract, leading to poor absorption and reduced bioavailability. DDS must address strategies to enhance drug solubility or employ alternative routes of administration.

First-Pass Metabolism: Drugs administered orally are subject to first-pass metabolism in the liver before reaching the systemic circulation. This can significantly reduce bioavailability. DDS can aim to bypass first–pass metabolism through alternative routes or develop prodrugs that undergo less metabolism.

Gastric Degradation: Some drugs are susceptible to degradation in the acidic environment of the stomach, reducing their bioavailability. DDS must protect drugs from gastric degradation or use alternative routes of administration.

Fast Excretion: The fast excretion process refers to the rapid removal of waste products and toxins from the body. This is facilitated by organs like the kidneys, which filter blood to remove waste and excess substances, producing urine that is then excreted from the body. The body's efficiency in eliminating waste is crucial for maintaining overall health and preventing the buildup of harmful substances.

Fraction of Drug Required Zone: Some specific tumor cells require more amount of drug accumulation in our body, which is high as compared to normal cells for effective cancer treatment. Bioactivity is an approach that refers to the ability of a drug to exert its intended pharmacological or therapeutic effect on the target site of action. In other words, it is the drug's ability to bind to its receptor or target and initiate the desired physiological response.

The bioactivity associated with drug delivery symptoms refers to the issue of maintaining the therapeutic efficacy of the drug throughout the delivery process.

Targeting Specificity: The drug should be delivered specifically to the target site to maximize bioactivity and minimize off target effects. Achieving precise targeting is challenging especially when dealing with complex biological barriers and heterogeneous diseases.

Drug Stability: Many drugs are sensitive to environmental conditions, such as temperature, light, and humidity, which can cause degradation and loss of bioactivity. Ensuring the stability of the drug within the DDS during storage and transportation is crucial.

Drug Release Kinetics: Controlling the rate and duration of drug release from the DDS is essential to achieve the desired therapeutic effect. If the drug is released too quickly, it may lead to adverse effects or inadequate treatment, whereas slow release may result in suboptimal bioactivity.[2]

Impact of Nanodrug Delivery Systems on Bioavailability and Bioactivity

Drug Delivery: Nanotechnology offers precise control over the design and fabrication of drug delivery systems. By

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encapsulating drugs within nanoparticles or nanocarriers, their stability, solubility, and targeted delivery can be improved. Nanoparticles can protect drugs from degradation, enhance their absorption, and enable controlled release, thus improving bioavailability.

Increased Surface Area: Nanostructured materials possess a high surface-to-volume ratio, which enhances their interaction with biological systems. This increased surface area facilitates better absorption of nutrients, drugs, or therapeutic agents, thereby improving bioavailability [3]

Targeted Therapy: Nanoparticles can be engineered to specifically target diseased cells or tissues while sparing healthy ones. Functionalized nanoparticles can be designed to attach to specific molecules or receptors found on cancer cells, for instance. This targeted approach reduces systemic side effects and enhances the bioactivity of therapeutic agents.

Improved Solubility: Many bioactive compounds have poor solubility, limiting their absorption and effectiveness. Nanotechnology can improve solubility by formulating these compounds into nanoscale structures, such as nanoparticles or nanosuspensions, which increase their surface area and improve their dissolution properties. This, in turn, enhances bioavailability [4].

Enhanced Cellular Uptake: Nanoparticles can facilitate the cellular uptake of bioactive substances by overcoming barriers such as cell membranes. Surface modifications of nanoparticles can improve their interaction with cells, promoting efficient internalization and subsequent bioactivity.

Diagnostic Tools: Nanotechnology-based sensors and imaging agents allow for highly sensitive and specific detection of biological molecules or markers associated with diseases. This enables early diagnosis and monitoring of treatment response, leading to improved bioactivity and better patient outcomes.[3]

Literature search: It was conducted a comprehensive and methodical search of recent literature that was relevant to the aforementioned questions over the last few years (1990–2022), resulting in a meta-analysis of recent literature which reported nanotechnology as a potential method for improving oral bioavailability. In light of the findings of this study, we anticipate from the metadata that it contains will be of great help to those researchers planning on implementing nanotechnology to improve poor oral bioavailability using nanotechnology.[4]

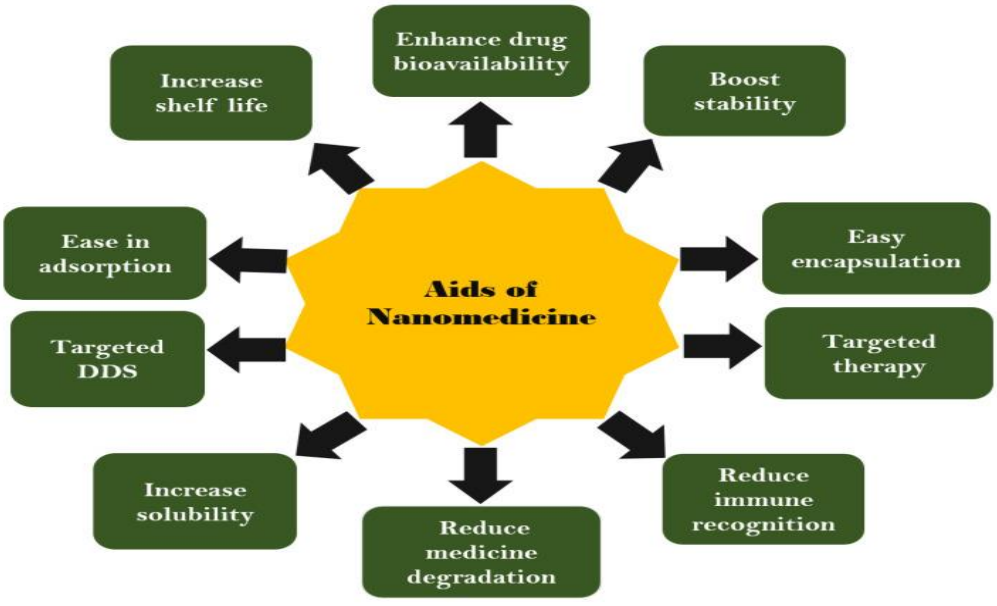

Figure 2: Aids of using nanomedicine platform for delivering drugs to the tumor complex.

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Working Principles of Nanomedicine Drug Delivery Systems: Nanoparticle drug delivery systems utilize nanomaterials as carriers, leveraging their ultra-small size, high-energy catalytic activity of surface atoms, and protective capabilities for the encapsulated drugs [6-7] These systems enable drugs to bypass physiological barriers, reduce or avoid immune clearance and the effects of bodily fluids on the drug, and target drugs for cellular or subcellular-level slow release. The overarching goals of these strategies are to enhance drug utilization [5] and minimize drug toxicity and side effects. These systems offer a promising avenue in drug delivery by addressing some of the key limitations of conventional drug delivery methods, particularly for drugs that face challenges in solubility, stability, and targeted delivery.

Mechanisms of Enhanced Bioavailability in Nano Drug Delivery Systems: The formidable efficacy of many drugs contrasts starkly with their low bioavailability upon entering the body, a disparity influenced by cellular physiological absorption barriers and drug stability, thus constraining their application.[8] Nano drug delivery systems can enhance drug bioavailability by capitalizing on the material's favorable properties such as pH-responsiveness, bioadhesion, biocompatibility, biodegradability, modifiability, and processability.

- Enhancing Cellular Uptake
- Promoting Intracellular Release
- Avoiding Early Metabolism of Drug

Table: 1 Examples of drugs loaded into different nano-delivery systems for improvement of oral bioavailability and permeability

Drug	Nano-delivery systems	Major outcomes	Reference
Quercetin (QT)	Zein nanoparticles (ZNP) with an outer shell of caseinate	*In vivo* bioavailability study in rats: the AUC of SC-ZNP was increased by 2.34 folds compared to QT suspensions Caco-2 cells: QT- sSEDDS showed significantly (p<0.05) higher uptake than free QT.	[24]
	Supersaturable self-emulsifying drug delivery system (s-SEDDS)	*In vivo* pharmacokinetics (PK) studies in rats: QT-sSEDDS revealed 2.2 and 2-fold increases in Cmax and AUC, respectively, in comparison to conventional QT-SEDDS	[25]
	Polymeric micelles	*In vivo* PK in rats: The Cmax values of QT are much higher than that obtained for free QT, and the AUC0–24h value for micellar QT was increased 1.19 times than the free drug.	[26]
Insulin	CS-PLGA	*in vivo* PK studies in rats: showed significant and relatively longer hypoglycemic activity after oral administration of insulin/CS-PLGA NPs produced.	[27]

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	Chitosan coating zein-carboxymethylated short-chain amylose (IN-Z-CSA) nanocomposites	Caco-2 cells: The transepithelial permeability of the nanocomposites was 12-fold higher than that of insulin.	[28]
	Trimethyl chitosan (TMC)and fucoidan self-assembled nanoparticles	*In vivo* pharmacological and PK studies: orally administered nanocomposites had a significantly higher hypoglycemic effect with a relative bioavailability of 15.19%.	[29]
	Folate-chitosan nanoparticles (FA-CS-NPs)	Caco-2 cells: insulin loaded-CS/FD NPs Increased the Papp value compared with the native insulin.	[30]
	Chitosan-modified SLNs (THQ-CS-SLNs)	*In vivo* PK in rats: the rats that received insulin-loaded FA-CS NPs had increased AUC0-∞ compared with the injected insulin.	[31]
		The everted gut sac of a goat: increase in permeability coefficient (Papp) of THQ-CS-SLNs 4 times compared to THQ suspension. chitosan nanovesicles (CS-nanovesicles)	[32]
Thymoquinone (THQ)	Chitosan (CS) modified polycaprolactone (PL) nanoparticles chitosan nanovesicles (CS-nanovesicles)	*In vivo* PK studies in rats: CS nanovesicles revealed a significantly higher flux (1.9 times) thanTHQsolution. *In vivo* PK studies in rats: increase in the AUC0-12h	[33]

Advantages and Challenges of Nano Drug Delivery Systems

Enhancing Drug Stability: The hydrophobic nature of many pharmaceutical compounds significantly impedes their bioavailability. Encapsulation of these drugs within nanoparticles is a strategy to augment their solubility. [9-10] For instance, nanocrystals of varying sizes exhibit different affinities and functionalities, with 660 nm crystals favoring follicular accumulation and 250 nm crystals optimizing rapid dissolution. Further, exposure to light, oxygen, moisture, and the enzymatic degradation within the body, as well as adverse physiological conditions, can lead to premature drug decomposition or alteration before reaching the intended target site. This premature degradation severely hampers the therapeutic efficacy of drugs. Therefore, enhancing drug stability constitutes a critical approach to ensure the therapeutic performance of pharmaceuticals. Nanocarriers, characterized by their diminutive size, extensive surface area, and ease of modification, provide a more stable and secluded environment for the drugs. This sequestration significantly mitigates pre-target degradation or inactivation issues,

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thereby improving the stability of the drug during its delivery. [11-12]

Prolonging Circulation Time: The journey of drug molecules to their site of action entails traversing through several physiological barriers, including blood, tissue, cellular, and intracellular transport barriers,[13] In the context of drug delivery, nanocarriers navigate these obstacles, particularly within the gastrointestinal tract. This process involves a complex interplay of mechanisms such as the endocytosis by epithelial cells, phagocytosis in the m-cell rich regions of Peyer's Patches, absorption across intestinal interstitial spaces, and paracellular uptake under pathological conditions. [14-15]

Increased Therapeutic Efficacy: Enhanced bioavailability ensures that a larger fraction of the administered drug reaches the bloodstream, leading to higher drug concentrations at the target site [19]. This increased exposure improves the drug's ability to interact with its molecular targets, resulting in more robust therapeutic effects. For drugs with narrow therapeutic windows or low potency, improving bioavailability becomes especially critical in achieving the desired clinical outcomes.

Reduced Dosage Requirements: Higher bioavailability allows for reduced dosage requirements to achieve the same therapeutic effect. Lower dosing not only reduces the overall drug burden on the body but also minimizes the potential for adverse effects [20]. Consequently, patient compliance may improve as a result of reduced pill burden, making treatment more manageable and effective.

Rapid Onset of Action: Drugs with enhanced bioavailability often exhibit faster onset of action due to higher and quicker peak concentrations in the bloodstream. This attribute is particularly advantageous for treating acute conditions where rapid symptom relief is essential [21].

Bioavailability And Bioactivity: Role of Nanocarriers in Bioavailability: The field of nanotechnology has opened up new possibilities for enhancing the bioavailability of various therapeutic agents, revolutionizing drug delivery and improving patient outcomes. Nanocarriers are nanoscale drug delivery systems designed to encapsulate and protect therapeutic agents, enabling controlled release, targeted delivery, and increased solubility of poorly water-soluble drugs. This chapter explores the critical role of nanocarriers in improving the bioavailability of therapeutic agents, shedding light on their potential applications in medicine and pharmaceuticals [16].

Overcoming Bioavailability Challenges: Bioavailability refers to the fraction of an administered drug that reaches systemic circulation and is available to exert its pharmacological effect. Several drugs, especially those with low water solubility, face significant bioavailability challenges. Poorly water-soluble drugs often suffer from reduced absorption and limited therapeutic efficacy. Nanocarriers, such as liposomes, micelles, nanoparticles, and nanosuspensions, have been developed to address these issues [17].

Enhanced Solubility: One of the key roles of nanocarriers is to enhance the solubility of poorly water-soluble drugs. Nanoparticles, for example, can effectively solubilize lipophilic drugs and enhance their bioavailability by increasing their surface area and improving dispersion properties. By encapsulating hydrophobic drugs within their hydrophilic cores, nanocarriers facilitate their transport through the biological barriers, leading to improved absorption and bioavailability [17].

Controlled Release and Targeted Delivery: Nanocarriers offer the advantage of controlled drug release, allowing sustained and prolonged drug activity, reducing dosing frequency, and minimizing side effects. Furthermore, these carriers can be functionalized with ligands that target specific tissues or cells, enabling site-specific drug delivery. This targeted approach enhances drug accumulation at the desired site, reducing systemic exposure and potential toxicity [18].

Overcoming Biological Barriers: Biological barriers, such as the blood-brain barrier (BBB) and mucosal barriers, pose significant challenges to drug delivery. Nanocarriers can be engineered to traverse these barriers efficiently. For example, surface modification with specific ligands can facilitate receptor-mediated transcytosis, enabling drugs to cross the BBB and reach the central nervous system [17].

Comparative analysis of the usage of nanotechnology in enhancing bioavailability: Regarding the advantages and disadvantages, the emergence of nanotechnology also has pros and cons that should be considered prior to use in terms of their production methods and applications. Green synthesis of NPs using different natural plant-based BACs may have exceptional functional surfaces by exposing

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certain organic ligands, peptides, oligo- or poly-saccharides, and alcohols, which are not found on NPS prepared through chemical or physical methods.The preparation of NPs through chemical or physical methods may pose certain level of toxicity in the environment and human body along with higher costs incurred. Green synthesis of NPs is quite advantageous over the physical or chemical methods that involve the use of natural BACs that are potent in binding and reducing metal ions into NPs. Moreover, green synthesis of NPs is cheaper, quick, no toxicity to human body, and requires little energies. Additionally, encapsulation of BACs onto NPs may enhance bioavailability, surface area, and targeted release.This technique of NPs-based BACs target release is highly viable under hydrophobic and hydrophilic environments. BACs delivered via oral routes may encounter numerous physiological barriers such as gut variable pH conditions, mucus and epithelium layers, and hence in this regard smart delivery systems such as NPs are a promising strategy to protect BACs from degradation having improved bioavailability. [22]

Application of Nanotechnology

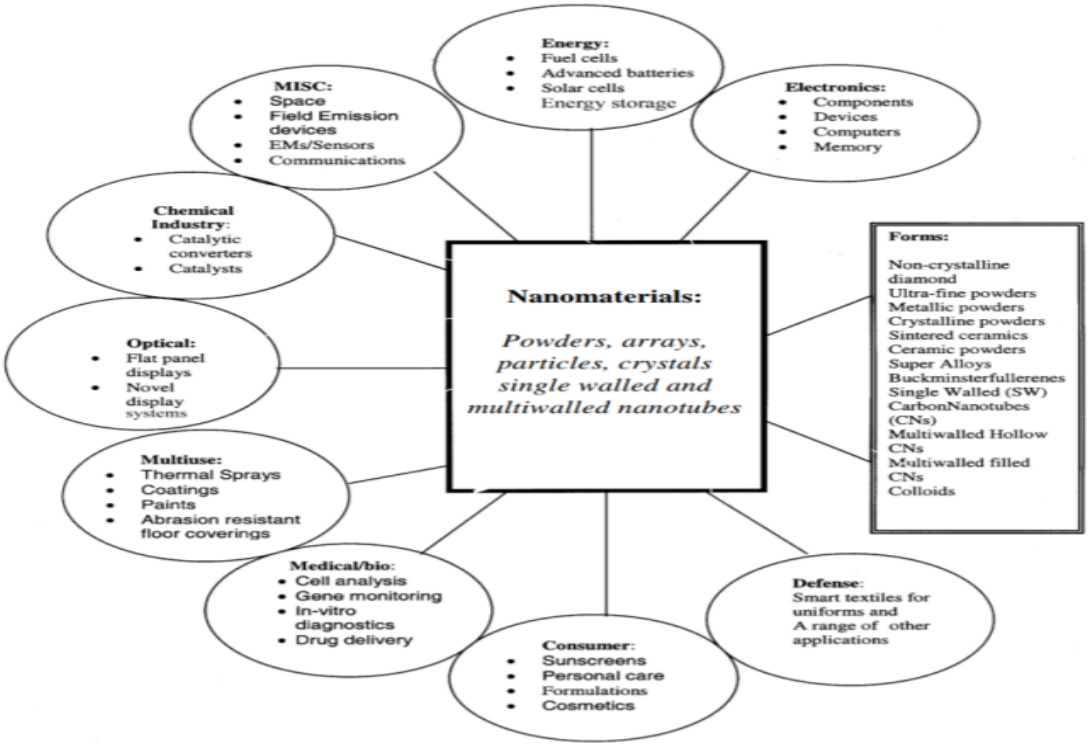

Figure: 3 Application of Nanotechnology

Challenges and Future Directions [23]: The integration of nanotechnology and MNPs into drug design presents significant opportunities for enhancing drug delivery, improving therapeutic outcomes, and reducing biological variability in drug response. However, this promising field also faces several critical challenges that must be addressed to fully realize its potential in clinical applications. This section explores these challenges, the impact of nanotechnology on biological variability, and the future research directions necessary for advancing this technology.

- Overcoming Hurdles in Integrating Nanotechnology and MNPs into Drug Design
- Synthesis and Functionalization Challenges
- Biocompatibility and Safety Concerns
- Regulatory and Manufacturing Challenges
- Overcoming Biological Barriers

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Reducing Biological Variability in Drug Response through Advanced Nanotechnologies

Biological variability in drug response is a significant challenge in drug design and therapeutic interventions, often leading to varied efficacy and safety outcomes across different patient populations. This variability can arise from numerous factors, including genetic differences, environmental influences, and individual health conditions. Advanced nanotechnologies offer promising solutions to reduce this variability, thereby enhancing the precision and effectiveness of therapeutic interventions. This section explores how these technologies are being leveraged to minimize biological variability in drug response and the potential implications for personalized medicine.

- Precision Drug Delivery Systems
- Genetic Influence on Drug Response
- Computational Models and Nanotechnology Integration
- Personalized Nanomedicine

Charting the Future: Interdisciplinary Research and Innovation in Nanotechnology for Therapeutics: The integration of nanotechnology into therapeutics represents one of the most promising frontiers in modern medicine. This convergence of disciplines—ranging from materials science and molecular biology to data science and engineering—has opened new avenues for treating diseases with unprecedented precision and efficacy. As we chart the future of nanotechnology in therapeutics, interdisciplinary research and innovation will play a pivotal role in overcoming existing challenges and pushing the boundaries of what is possible in healthcare.

- The Role of Interdisciplinary Collaboration
- Innovation in Nanotechnology for Cancer Therapeutics
- Expanding the Scope of Nanotechnology in Therapeutics
- The Economic and Societal Impact of Nanotechnology
- Future Directions in Interdisciplinary Research

Conclusion: Nanoparticle-based drug delivery systems offer a promising approach to enhancing drug bioavailability, particularly for poorly soluble medications. By reducing particle size to the nanoscale, these systems increase surface area, improve dissolution rates, and facilitate drug absorption, ultimately leading to faster onset of action and reduced adverse effects. Nano-drug delivery systems have emerged as a transformative approach to significantly enhance the bioavailability and bioactivity of various therapeutic agents. This chapter has provided a comprehensive overview of the diverse nano-based technologies utilized for targeted drug delivery, controlled release, and improved therapeutic efficacy. Through the ingenious use of nanoparticles, such as liposomes, polymeric nanoparticles, dendrimers, carbon nanotubes, metallic nanoparticles, solid lipid nanoparticles, and protein-based nanoparticles, researchers have unlocked new avenues to address the limitations of conventional drug delivery methods.

As research in the field continues to advance, challenges related to large-scale production, regulatory considerations, and long-term safety profiles must be addressed to accelerate the translation of these technologies from the laboratory to clinical practice. Nevertheless, the progress achieved thus far in nano-drug delivery systems offers a glimpse into the future of pharmaceutical sciences, with the potential to revolutionize the treatment landscape and improve patient outcomes across a wide range of medical conditions. Embracing the promise of nano-based drug delivery represents a promising pathway toward the realization of safer, more efficient, and patient-tailored therapies in modern medicine.

Refeerence

[1] Mehta Abhinav, Jain Neha , Grobler Anne, Vandana Bharti Role of Novel Drug Delivery Systems in Bioavailability Enhancement: At A Glance International Journal of Drug Delivery Technology IJDDT, January 2016 - March 2016, Volume 6, Issue 1

[2] Dr. Ratna Jyoti Das Ms. Purabi Das Dr. Kalyani Pathak Mrs. Parimita Kalita nano-drug delivery systems for the enhancement of bioavailability and bioactivity nano-drug delivery systems for the enhancement of bioavailability and bioactivity Futuristic Trends in Pharmacy & Nursing Volume 3 Book 3

[3] P. Venkatesan, R. Manavalan, and K. Valliappan. Microencapsulation: A vital technique in novel drug delivery system. Journal of pharmaceutical sciences and research. Journal of pharmaceutical sciences and research. Vol-002 Issue-003 August 2011, 159-162

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 374-383 | ISSN:2251-6727

[4] Gurunathan S, Wu C, Freidag B. DNA vaccines: a key for inducing long-term cellular immunity. Curr. Opin. Immunol, 2000; 12: 442-447.

[5] Sridhar V, Gaud R, Bajaj A, et al. Pharmacokinetics and pharmacodynamics of intranasally administered selegiline nanoparticles with improved brain delivery in Parkinson's disease. *Nanomedicine*. 2018;14(8):2609–2618.

[6] Mistry A, Stolnik S, Illum L, et al. Nanoparticles for direct nose-to-brain delivery of drugs. *Int J Pharm*. 2009;379(1):146–157.

[7] Hegewald AB, Breitwieser K, Ottinger SM, et al. Extracellular miR-574-5p Induces Osteoclast Differentiation via TLR 7/8 in Rheumatoid Arthritis. *Front Immunol*. 2020; 11:585282.

[8] Costa CP, Moreira JN, Sousa Lobo JM, et al. Intranasal delivery of nanostructured lipid carriers, solid lipid nanoparticles and nanoemulsions: a current overview of in vivo studies. *Acta Pharmaceutica Sinica B*. 2021;11(4):925–940.

[9] Miyata K, Christie RJ, Kataoka K. Polymeric micelles for nano-scale drug delivery. *React Funct Polym*. 2011;3(71).

[10] Wei X, Ling P, Zhang T, et al. Polymeric micelles, a promising drug delivery system to enhance bioavailability of poorly water-soluble drugs. *J Drug Delivery*. 2013; 2013:340315.

[11] .Jahangirian H, Ghasemian Lemraski E, Webster TJ, et al. A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine. *Int j Nanomed*. 2017; 12:2957–2978.

[12] Lam P-L, Wong W-Y, Bian Z, Chui C-H, Gambari R. Gambari R. Recent advances in green nanoparticulate systems for drug delivery: efficient delivery and safety concern. *Nanomedicine*. 2017; 12:357–385.

[13] Lam P-L, Wong W-Y, Bian Z, Chui C-H, Gambari R. Gambari R.Recent advances in green nanoparticulate systems for drug delivery: efficient delivery and safety concern. *Nanomedicine*. 2017; 12:357–385.

[14] Powell JJ, Faria N, Thomas-McKay E, et al. Origin and fate of dietary nanoparticles and microparticles in the gastrointestinal tract. *J Autoimmun*. 2010;34(3):J226–33.

[15] Turner JR. Intestinal mucosal barrier function in health and disease. *Nat Rev Immunol*. 2009;9(11):799–809.

[16] Torchilin V. P. (2006). Multifunctional nanocarriers. Advanced drug delivery reviews, 58(14), 1532–1555.

[17 Puri, A., Loomis, K., Smith, B., Lee, J. H., & Pavlovich, A. (2009). Lipid-Based Nanoparticles as Pharmaceutical Drug Carriers: From Concepts to Clinic. Critical Reviews™ in Therapeutic Drug Carrier Systems, 26(6), 523-580.

[18] Etheridge, M. L., Campbell, S. A., Erdman, A. G., Haynes, C. L., Wolf, S. M., & McCullough, J. (2013). The Big Picture on Nanomedicine: The State of Investigational and Approved Nanomedicine Products. Nanomedicine, 9(1), 1-14.

[19] Sharma, A., Arora, K., Mohapatra, H., Sindhu, R. K., Bulzan, M., Cavalu, S., Paneshar, G., Elansary, H. O., El-Sabrout, A. M., Mahmoud, E. A., & Alaklabi, A. (2022). Supersaturation-Based Drug Delivery Systems: Strategy for Bioavailability Enhancement of Poorly Water-Soluble Drugs. Molecules (Basel, Switzerland), 27(9), 2969.

[20] Yang, M., Gong, W., Wang, Y., Shan, L., Li, Y., & Gao, C. (2016). Bioavailability Improvement Strategies for Poorly Water-Soluble Drugs Based on the Supersaturation Mechanism: An Update. Journal of pharmacy & pharmaceutical sciences: a publication of the Canadian Society for Pharmaceutical Sciences, Societe canadienne des sciences pharmaceutiques, 19(2), 208–225.

[21] Dole R, Kothapally D, Chuckwalla S, Thatipelli RC, Approaches to Improve Oral Bioavailability of Antihypertensive Drugs: A Mini-Review, Journal of Drug Delivery and Therapeutics. 2023; 13(5):73-77.

[22] Muhammad Farrukh Nisar, Chunpeng Wan, Nanotechnology-based Delivery Systems for Enhanced Bioavailability of Antioxidant Compounds in Fruits and Vegetables Current Research in Nutrition and Science ISSN: 2347-467X,

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 374-383 | ISSN:2251-6727

[23] Yue Zhuo, Yong-Gang Zhao, Yun Zhang, Enhancing Drug Solubility, Bioavailability, and Targeted Therapeutic Applications through Magnetic Nanoparticles Molecules 2024 Oct 13;29(20):4854.

[24] Zhou JF, Zheng GD, Wang WJ, Yin ZP, Chen JG, Li JE. Physicochemical properties and bioavailability comparison of two quercetin loading zein nanoparticles with outer shell of caseinate and chitosan. Food Hydrocoll. 2021; 120:106959.

[25] Sirvi A, Kuche K, Chaudhari D, Ghadi R, Date T, Katiyar SS. Supersaturable self-emulsifying drug delivery system: a strategy for improving the loading and oral bioavailability of quercetin. J Drug Deliv Sci Technol. 2022; 71:103289.

[26] Sheth U, Nagane R, Bahadur P, Bahadur A. Salt effect on solubilization of hydrophobic drugs in block copolymeric micelles and investigation of their *in vitro* and *in vivo* oral efficiency. J Drug Deliv Sci Technol. 2017; 39:531-41.

[27] Wu J, Chen L, Zhang X, Xu C, Liu J, Gu J. A core-shell insulin/CS-PLGA nanoparticle for enhancement of oral insulin bioavailability: *in vitro* and *in vivo* study. Int J Polym Mater Polym Biomater. 2022:1-9.

[28] Ji N, Hong Y, Gu Z, Cheng L, Li Z, Li C. Chitosan coating of zein-carboxymethylated short-chain amylose nanocomposites improves oral bioavailability of insulin *in vitro* and *in vivo*. J Control Release. 2019; 313:1-13.

[29] Tsai LC, Chen CH, Lin CW, Ho YC, Mi FL. Development of mutlifunctional nanoparticles self-assembled from trimethyl chitosan and fucoidan for enhanced oral delivery of insulin. Int J Biol Macromol. 2019; 126:141-50.

[30] El Leithy ES, Abdel-Bar HM, Ali RAM. Folate-chitosan nanoparticles triggered insulin cellular uptake and improved *in vivo* hypoglycemic activity. Int J Pharm. 2019; 571:118708.

[31] Rahat I, Rizwanullah M, Gilani SJ, Bin-Jummah MN, Imam SS, Kala C. Thymoquinone loaded chitosan–solid lipid nanoparticles: formulation optimization to oral bioavailability study. J Drug Deliv Sci Technol. 2021; 64:102565.

[32] Rahat I, Imam SS, Rizwanullah M, Alshehri S, Asif M, Kala C. Thymoquinone-entrapped chitosan-modified nanoparticles: formulation optimization to preclinical bioavailability assessments. Drug Deliv. 2021;28(1):973-84.

[33] Fakhria A, Gilani SJ, Imam SS, Chandrakala. Formulation of thymoquinone loaded chitosan nano vesicles: *in vitro* evaluation and *in vivo* anti-hyperlipidemic assessment. J Drug Deliv Sci Technol. 2019; 50:339-46.