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NANOBIOTECHNOLOGY IN DRUG DELIVERY: EXPLORING INNOVATIONS AND APPLICATIONS

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ABSTRACT

Background: Nanobiotechnology, an interdisciplinary field that merges nanotechnology with biotechnology, is revolutionizing drug delivery systems. By applying principles from biology, chemistry, physics, and engineering, researchers have developed nanoscale molecules and devices with significant potential in biomedical applications, particularly in drug delivery, gene therapy, and diagnostics. **Aim:** This article explores the innovations and applications of nanobiotechnology in drug delivery, emphasizing the role of nanoparticles (NPs) in enhancing the precision, bioavailability, and targeted distribution of therapeutic agents. **Methods:** The review examines various nanomaterials, including metallic, organic, and composite nanoparticles, and their engineering for specific therapeutic and diagnostic applications. It also discusses advancements in nanomedicine, the use of nanomaterials in drug delivery systems, and the application of nanotechnology in medical diagnosis and treatment. **Results:** The transition to nanoscale drug delivery systems has introduced several promising approaches, such as polymeric nanoparticles, liposomes, and polymeric micelles. These systems provide controlled release, targeted delivery, and improved bioavailability. Metal nanoparticles, polymer nanoparticles, and chitosan-based systems are highlighted for their unique properties and potential in addressing challenges in drug delivery and medical treatment. **Conclusion:** Nanobiotechnology is poised to play a pivotal role in advancing healthcare by offering innovative solutions for drug delivery, diagnostics, and therapeutic targeting. As research progresses, the integration of nanotechnology with traditional medical approaches promises to enhance the effectiveness and specificity of treatments, thereby shaping the future of medical science.

KEYWORDS:- Nanobiotechnology, drug delivery, nanoparticles, nanomedicine, polymeric nanoparticles, liposomes, chitosan, biomedical applications.

INTRODUCTION

Scientists often find inspiration in nature when conducting their scientific inquiries, as the majority of biological processes on Earth occur at the nanoscale. Researchers can use the principles of biology to reproduce laboratory results by applying the fields of chemistry, physics, nanotechnology, and engineering. This allows them to create, study, and design nanoscale biological molecules and devices using biological systems. The integration of multiple disciplines resulted in the development of a novel technology called nanobiotechnology.[1] Nanobiotechnology is the merger of biotechnology with nanotechnology, combining molecular biological processes with classical microtechnology. Biotechnology utilizes biological knowledge and methods to modify genetic, molecular, and cellular processes, resulting in the creation of products and services that are used in a wide range of industries, including agriculture and medical. The potential gains resulting from this interdisciplinary approach are extraordinary, as the convergence of nanotechnology, biotechnology, and information technology presents various substantial applications in the field of life sciences.[2,3]

Nanobiotechnology is anticipated to stimulate innovation and have a crucial impact on several biomedical applications, such as gene therapy, drug delivery, biomarkers, molecular imaging, and biosensors. The research in this subject is centered around the development of precise medicinal treatments and advanced diagnostic techniques for diseases. The potential impact of this technology is expected to be significant.[4] Pharmaceutical development is expected to be the most important application of clinical nanotechnology in the near future. Research on drug delivery is advancing from the level of microscopic particles to the level of nanoscale particles. Nanoparticles (NPs) have emerged as a promising approach for drug administration, offering precise control over release, targeted distribution, and improved bioavailability.[5,6] Nanoscale polymer capsules provide benefits such as biodegradability, regulated drug delivery, efficient absorption, and accurate targeting.[7]

Scientists globally are currently focused on the development of novel polymers and the evaluation of certain polymer-drug pairings. One way to make nanocapsules is by using monomers or by depositing premade polymers by nanodeposition.[8] Currently, researchers are investigating nanocapsules that are made from liposomes and albumin. Nanospores can be utilized in implantable medication delivery devices to regulate the release of drugs. In addition, nanomaterials are widely used in medical science, namely in the field of nanomedicine, where they modify the physical properties and features of materials to assist in molecular-level treatment and diagnostics. Nanomaterials are specifically designed to engage with molecules, identify alterations at the molecular scale, and convey diagnostic and therapeutic substances. As a result, nanomaterials can be accurately designed to attain the intended dimensions, configuration, surface characteristics, composition, and arrangement for particular uses.[9,10]

Nanomaterials are typically categorized into three groups: metallic particles, organic particles, and composites consisting of both metals and nanometals, often known as semiconducting particles. In order to improve the absorption and specificity, the exteriors of nanoparticles (NPs) are frequently altered with natural, pseudo-natural, or biorecognition compounds. Comprehending the processes of combining and distributing substances, as well as their use as tools for diagnosis, is crucial for creating and developing systems for delivering medication. When formulating nanoparticles (NPs), important factors to consider are their surface area-to-volume ratios, shape, and size. These features allow NPs to pass through biological barriers.[11] Frequently employed nanoparticles (NPs) consist of iron oxide crystals, colloidal gold, and quantum dot semiconductor NPs. Gold nanoparticles (NPs) have been used as quenchers in fluorescence resonance energy transfer (FRET) studies.[12] Iron oxide nanoparticles (NPs) are extensively utilized in diagnostics, primarily because of their superparamagnetic characteristics. These properties are employed in magnetic resonance imaging (MRI), gene expression monitoring, and the identification of various pathologies, including brain inflammation, cancer, atherosclerotic plaques, and arthritis.[13-15] Quantum dots improve the performance of biological systems for detecting and analyzing samples in laboratory settings (in vitro) and living organisms (in vivo) using electrical or optical techniques.[16] A recent study emphasized the utilization of quantum dots for monitoring the movement of metastatic tumor cells. The higher surface area-to-volume ratio of quantum dots offers possibilities for the development of multifunctional nanosystems.[17-19]

In 2002, the National Institutes of Health (NIH) coined the term 'nanomedicine' to describe the use of nanotechnology in the diagnosis, monitoring, control, and therapy of biological systems.[20] Nanomedicine comprises various disciplines such as nanomachines, biomimetic materials, nanofibers, polymeric nanobiomaterials, diagnostic laboratories, and sensors.[21] Nanomedicine is mostly used for rational drug delivery, pharmaceutical targeting, diagnostic agents, and therapeutic approaches. These applications entail the identification of target cells and receptors in specific circumstances, as well as the selection of suitable nanoparticles to accomplish the desired therapeutic results while minimizing any adverse consequences. The cells targeted in these systems encompass dendritic cells, mononuclear phagocytes, cancer cells, and endothelial cells. The integration of nanotechnology and nanoscience is propelling the development and composition of particles, thereby broadening the market for diverse pharmaceuticals and creating a lucrative niche in the sector. Nevertheless, certain products have been excessively exaggerated for their expected advantages.[20]

Nanobiotechnology, an interdisciplinary field merging biotechnology with nanotechnology, has revolutionized the approach to biomedical applications. By leveraging the principles of biology, chemistry, physics, and engineering, researchers have developed nanoscale biological molecules and devices that hold immense potential for advancements in drug delivery, gene therapy, molecular imaging, and biosensors. The transition from microscopic to nanoscale drug delivery systems has introduced nanoparticles (NPs) as promising tools for achieving controlled release, targeted distribution, and enhanced bioavailability. Nanomaterials, categorized into metallic, organic, and composite particles, are meticulously engineered to interact with biological systems at the molecular level, facilitating precise therapeutic and diagnostic applications. The emergence of nanomedicine, defined by the National Institutes of Health (NIH) in 2002, underscores the transformative impact of nanotechnology in the medical field, offering novel solutions for rational drug delivery, diagnostics, and targeted therapies. As research progresses, nanobiotechnology is set to play a pivotal role in shaping the future of healthcare.

The application of nanotechnology in medical diagnosis

Traditional medicine specifically targets biological cells by identifying and focusing on illness recognition areas. During the initial phases of technological advancement, the cell theory of the 19th century heavily depended on the use of light microscopy and staining techniques for the purpose of histological analysis.[22] Over the course of time, this hypothesis underwent development in the

20th century to encompass investigations conducted at the atomic and molecular scales. Cells were extracted, and their organelles were refined and examined using many physical and chemical techniques, resulting in notable progress, such as the investigation of the human genome. Significantly, the atomic structures of several proteins were also ascertained during this period.[23] Now, advancements in nanotechnology have allowed us to examine cells at the nanometer scale. This has enabled the application of techniques originally designed for analyzing molecules and atoms, including as nuclear magnetic resonance, X-ray diffraction, mass spectrometry, and spectroscopy, to be extended to nanoscale structures and other large molecules. In addition, electron microscopy has made significant progress through the use of tomography and cryo-fixation techniques. Furthermore, a novel form of scanning microscope now offers the ability to observe cell surfaces at the atomic level.

The application of nanomedicine in medical treatment

Nanomedicine seeks to efficiently distribute and target medications, diagnostics, and therapeutic agents. This process include the identification of precise clinical targets, such as specific cells and receptors, and the careful selection of suitable nanocarriers to deliver the intended therapeutic results while minimizing any potential adverse effects. Typical targets consist of macrophages, dendritic cells, cancer cells, and endothelial cells.[20]

Parasitic diseases including leishmaniasis, malaria, and trypanosomiasis pose enormous worldwide issues since they behave inside cells and are found in various areas. These issues have raised concerns regarding the limited rate of identification of anti-parasitic medicines, pushing researchers to concentrate on enhancing medication delivery techniques.[24]

Biopharmaceuticals and the biological barriers that hinder the successful delivery of drugs for parasite disorders have received considerable focus in recent years. Scientists have thoroughly investigated colloidal carriers, polymeric nanoparticles (NPs), lipid nanocarriers (such as lipid-drug conjugate NPs), and liposomes for their ability to improve the targeted administration of anti-leishmanial, anti-trypanosomal, and anti-malarial agents.[25] The macrophages of the reticuloendothelial system, renowned for their swift identification and elimination of nanoparticles (NPs), present a favorable objective for medication administration, given the pivotal role macrophages play in the development of diseases. Regulating the process of macrophage clearance could be beneficial in the treatment of illnesses such as autoimmune, atherosclerosis, and severe infections. Macrophages typically eliminate germs, but certain pathogens such as Mycobacterium TB, Leishmania species, and Listeria monocytogenes, have developed strategies to avoid being destroyed. A strategic strategy is to target these pathogens within macrophages utilizing nanoparticles (NPs) that are coated with antibacterial agents.[25] The endocytic pathway guides nanocarriers to lysosomes, which are the dwelling place of parasites. This enables the enzymes present in lysosomes to break down the nanocarriers and release the drug in the surrounding area. Approved medication delivery systems now utilize lipid-based nanocarriers that contain amphotericin B (Amp B) to treat visceral leishmaniasis and fungal infections. These systems reduce the necessary amount of Amp B, resulting in a potent concentration within macrophages.[25]

Drug delivery systems utilizing nanoparticles (NPs)

Metal nanoparticles

Current developments in nanotechnology have specifically emphasized the antibacterial characteristics of metal nanoparticles (NPs).[28] The smaller size of metal nanoparticles (NPs) facilitates their interaction with the cellular membranes of microorganisms.[29,30] Metal nanoparticles (NPs) that are fixed or adorned with antimicrobial substances find utility in medical devices, the food sector, and water treatment. In addition, metallic nanoparticles have the ability to chemically bond with polymers, which presents opportunities for their use in the development of treatments for cancer, tumors, and microbial infections. Metal nanoparticles are extensively utilized in sensors, catalytic devices, and the healthcare industry.[30]

Polymer nanoparticles

Polymer nanoparticles, usually with a size below 100 nm, are created using both artificial and natural polymers. These nanoparticles have attracted considerable interest in pharmaceutical research because of their capacity to transport various medications to particular regions of the body for extended durations. The diminutive dimensions of NPs are vital for their effective distribution throughout the body. Nevertheless, the use of natural polymers such as carbohydrates and proteins for drug administration has been limited due to their inconsistent purity and the requirement for cross-linking, which could potentially alter the structure of the enclosed pharmaceuticals. As a result, there has been an increased focus on synthetic polymer nanoparticles. The polymer nanoparticles that are most frequently utilized include poly-α-caprolactone, poly(glycolic acid), poly(lactic acid), and their copolymers, such as poly(lactide-co-glycolide).[32,33] Furthermore, the combination of poly(ethylene glycol) (PEG) with poly(lactic acid) and poly(amino acids) is utilized to create nanoparticles (NPs) and structures resembling micelles.[34,35] These polymers possess notable biocompatibility and can undergo degradation through natural processes.

Utilizing polymers as nanoparticle delivery systems

Liposomes are small spherical vesicles composed of lipid bilayers

Lipid bilayers have undergone thorough investigation in both natural and scientific settings. Within live cells, these bilayers govern and manage the transportation of chemicals into and out of cells. Liposomes, designed to replicate the composition of natural cell membranes, have been created as a sophisticated method for delivering drugs.[36] Liposomes' capacity to mimic natural cellular processes, specifically in the transportation of diverse substances, has resulted in its utilization for drug delivery.[37,38] Liposomes are highly biocompatible, which makes them a central area of interest in drug delivery research. Medically authorized liposomal formulations, such as doxorubicin (Caelyx®/Doxil® and Myocet®) and daunorubicin (Daunosome®), are utilized as anticancer medications.[39] Liposomes have the ability to transport a diverse array of medicines, including lipophilic, amphiphilic, and hydrophilic molecules. Phospholipids have the ability to self-assemble in water due to their amphiphilic nature. This results in the formation of a bilayer structure with a watery center that surrounds hydrophilic pharmaceuticals, while hydrophobic medications are lodged within the layers of lipids.[40] Nevertheless, a disadvantage of liposomal drug administration is the fast elimination of the medication from the bloodstream by the reticuloendothelial or mononuclear phagocyte systems. To overcome this constraint, researchers have developed liposomes called 'PEGylated Stealth®' that decrease protein absorption and improve drug transport by modifying the liposome surface with PEG.[41,42] PEG incorporation extends the liposome's duration of activity from a few minutes to many hours.[43] PEGylation additionally increases the liposome's vulnerability to ultrasound-induced permeability, potentially revolutionizing localized and targeted drug administration by utilizing ultrasound as a remote mechanical stimulus for precise drug discharge. In addition, liposomes have the ability to bind with sugar chains and glycoproteins in order to specifically target certain cells.[45]

Polymeric micelles are structures formed by the self-assembly of polymers

Polymeric micelles are created by combining block copolymers that consist of hydrophobic and hydrophilic segments. The hydrophobic portion constitutes the inner core of the micelle, whereas the hydrophilic portion forms the outside shell.[46] Polymeric micelles provide a new method for delivering medications by either enclosing hydrophobic drugs in the core or chemically attaching drugs to the hydrophobic block prior to micelle formation.[47] This encapsulation provides a protective barrier for the medicine, preventing chemical degradation and minimizing the occurrence of negative effects.[48] Polymeric micelles provide numerous benefits as a drug delivery mechanism, such as their diminutive size (<100 nm) and hydrophilic outer layer. These characteristics render them almost undetectable by the reticuloendothelial system, enabling prolonged circulation in the bloodstream. In addition, micelles have strong stability as a result of thermodynamic equilibrium, which is comparable to that of vesicles. Micelles are formed spontaneously when the concentration of amphiphiles, such as surfactants, lipids, or block copolymers, surpasses the critical micelle concentration (CMC). It is worth mentioning that amphiphiles with larger molecular weight have a considerably lower critical micelle concentration (CMC) in comparison to lipids or surfactants.[49]

Micelles with a Worm-like Structure

Worm-like micelles are a new type of cylindrical supramolecular carriers for medicines and dyes.[50] These spontaneously formed structures are highly efficient in transporting drugs because they can easily pass through narrow openings, improve blood flow for long durations (weeks), and selectively bind to specific places or cells with a strong receptor attraction.[51] When worm-like micelles attach to a specific location, they are capable of delivering a greater amount of the medication simultaneously. The efficiency of the polymer depends on its molecular weight in relation to the diameter of the worm, as well as the stability and flexibility of the micelle.[52] Nanoparticles generated from worm-like micelles exhibit exceptional stability and bear a striking resemblance to filamentous phages. These phages have proven to be effective in vivo for targeting tumor ligands using phage display technology.[53] Like phages that transport nucleic acids, these micelles are capable of delivering lipophilic medicines.

Polymersomes are structures composed of polymers that form vesicles or hollow spheres

Current studies have concentrated on polymeric vesicles, namely polymersomes, that consist of hydrophilic-hydrophobic diblock copolymers. These polymersomes are utilized as drug delivery systems.[54] Polymersomes provide improved durability and versatility, enabling the adjustment of bilayer properties like as chemical composition and thickness.[55] The interaction between proteins and polymeric bilayers diverges markedly from that with lipid bilayers, resulting in a major influence on drug delivery properties, such as the duration of in vivo blood circulation. A 2003 study showed that increasing the thickness of polymeric lipid bilayers was associated with a longer duration of blood circulation in vivo.[56] Subsequent research has revealed significant differences in the characteristics of polymeric lipid bilayers compared to ordinary lipid bilayers. This presents an opportunity to enhance the properties of carriers and enhance medication delivery.[57]

Utilizing chitosan nanoparticles for drug delivery

Pharmaceutical nanotechnology has made significant progress in developing therapeutically active chemicals using biocompatible nanoscale frameworks, including micellar systems, nanocapsules, and conjugates. The size of nanoparticles is crucial for the benefits provided by these drug delivery systems.[57] A wide range of nanoparticulate systems are used for drug delivery, such as polymeric micelles, biodegradable polymeric nanoparticles, lipid-based nanoparticles, solid nanoparticles like lipid drug conjugates (LDCs), nanostructured lipid carriers, solid lipid nanoparticles, inorganic nanoparticles, nanoliposomes, magnetic nanoparticles, ferrofluids, dendrimers, and quantum dots. Chitosan, chemically referred to as α(1-4)-2-amino-2-deoxy β-D-glucan, is obtained by removing the acetyl groups from chitin, a polysaccharide that is widely present in the shells of crustaceans. Chitosan, which was first identified in the 19th century, started to get substantial interest in biomedical and drug delivery research approximately twenty years ago.[58]

Chitosan is easily soluble in water and has a positive charge, which enables it to interact with large molecules, polymers, and negatively charged polyanions. These interactions result in a sol-gel transition phase, which has been successfully employed for nanoscale encapsulation purposes.[59] Chitosan's capacity to stick to mucosal surfaces makes it highly advantageous for delivering drugs to mucosal areas.[60] Chitosan polymers possess excellent biocompatibility and minimal toxicity, making them a highly promising platform for the biopharmaceutical industry.[61]

Scientists are presently prioritizing the development of more affordable, better-tolerated, thermally stable, non-toxic, sustained-release formulations that enhance effectiveness by suppressing drug resistance. These formulations are being explored as substitutes for lipid-based formulations. A variety of thiolated polymers, referred to as "thiomers," have been developed. These agents usually consist of polymeric backbones with SH-group-bearing attachments. Thiomers have exhibited several advantageous characteristics for drug administration, such as mucoadhesion, in situ gelling, permeability augmentation, efflux pump inhibition, and enzyme inhibition.[62-70]

CONCLUSION

Nanobiotechnology, by merging biotechnology with nanotechnology, has emerged as a transformative force in the field of drug delivery and biomedical applications. This interdisciplinary approach has enabled the development of nanoscale biological molecules and devices that offer unprecedented control over drug release, targeted distribution, and bioavailability. Nanoparticles (NPs), whether metallic, organic, or composite, have shown great potential in overcoming traditional limitations in drug delivery systems. Innovations such as polymeric nanoparticles, liposomes, and polymeric micelles have paved the way for more efficient and precise delivery of therapeutic agents, with applications extending to gene therapy, molecular imaging, and biosensors. The emergence of nanomedicine, as defined by the National Institutes of Health (NIH) in 2002, underscores the significant impact of nanotechnology in the medical field. It offers novel solutions for rational drug delivery, diagnostics, and targeted therapies, revolutionizing the treatment of diseases at the molecular level. The ability of nanomaterials to interact with biological systems, identify molecular changes, and deliver therapeutic substances with precision makes them invaluable in modern medicine. As research in nanobiotechnology advances, it is set to play a crucial role in shaping the future of healthcare. The integration of nanotechnology with traditional medical practices promises to enhance the specificity and effectiveness of treatments, leading to better patient outcomes. The potential of nanobiotechnology in drug delivery and other biomedical applications is vast, and its continued exploration is likely to yield groundbreaking innovations that will redefine the landscape of medical science.

REFERENCES

1. Roco M.C.: ‘Nanotechnology: convergence with modern biology and medicine’, *Curr. Opin. Biotechnol*, 2003; 14(3): 337 – 346. (doi: https://doi.org/10.1016/S0958-1669(03)00068-5)
2. Ernest H. Shetty R.: ‘Impact of nanotechnology on biomedical sciences: review of current concepts on convergence of nanotechnology with biology’, *J. Nanotechnol. Online*, 2005; 1: 1 –14.
3. Sahoo S. Parveen S. Panda J.: ‘The present and future of nanotechnology in human health care’, *Nanomed. Nanotechnol. Biol. Med*, 2007; 3(1): 20 – 31. (doi: https://doi.org/10.1016/j.nano.2006.11.008)
4. Sahoo S.K. Labhasetwar V.: ‘Nanotech approaches to drug delivery and imaging’, *Drug Discov. Today*, 2003; 8(24): 1112 – 1120. (doi: https://doi.org/10.1016/S1359-6446(03)02903-9)
5. Brigger I. Dubernet C. Couvreur P.: ‘Nanoparticles in cancer therapy and diagnosis’, *Adv. Drug Deliv. Rev*, 2002; 54(5): 631 – 651. (doi: https://doi.org/10.1016/S0169-409X(02)00044-3)
6. Crommelin D.J. Storm G. Jiskoot W. Stenekes R. Mastrobattista E. Hennink W.E.: ‘Nanotechnological approaches for the delivery of macromolecules’, *J. Control. Release*, 2003; 87(1): 81 –88. (doi: https://doi.org/10.1016/S0168-3659(03)00014-2)
7. Na K. Bae Y.: ‘Self-assembled hydrogel nanoparticles responsive to tumor extracellular pH from pullulan derivative/sulfonamide conjugate: characterization, aggregation, and adriamycin release in vitro’, *Pharm. Res*, 2002; 19(5): 681 – 688. (doi: https://doi.org/10.1023/A:1015370532543)
8. Couvreur P. Barratt G. Fattal E. Legrand P. Vauthier C.: ‘Nanocapsule technology: a review’, *Crit. Rev. Ther. Drug Carrier Syst*, 2002; 19(2): 99 –

134. (doi: https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v19.i2.10)

9. Xia Y. Xiong Y. Lim B. Skrabalak S.E.: 'Shape-controlled synthesis of metal nanocrystals: simple chemistry meets complex physics?', *Angew. Chem. Int. Ed*, 2009; 48(1): 60 – 103. (doi: https://doi.org/10.1002/anie.200802248)
10. Peer D. Karp J.M. Hong S. Farokhzad O.C. Margalit R. Langer R.: 'Nanocarriers as an emerging platform for cancer therapy', *Nat. Nanotechnol*, 2007; 2(12): 751 –760. (doi: https://doi.org/10.1038/nnano.2007.387)
11. Kim B.Y. Rutka J.T. Chan W.C.: 'Nanomedicine', *N. Engl. J. Med*, 2010; 363(25): 2434 –2443. (doi: https://doi.org/10.1056/NEJMra0912273)
12. Tyagi S. Kramer F.R.: 'Molecular beacons: probes that fluoresce upon hybridization', *Nat. Biotechnol*, 1996; 14(3): 303 – 308. (doi: https://doi.org/10.1038/nbt0396-303)
13. Jaffer F.A. Weissleder R.: 'Seeing within molecular imaging of the cardiovascular system', *Circ. Res*, 2004; 94(4): 433 – 445. (doi: https://doi.org/10.1161/01.RES.0000119321.18573.5A)
14. Perez J.M. Josephson L. Weissleder R.: 'Use of magnetic nanoparticles as nanosensors to probe for molecular interactions', *Chem. Biol. Chem*, 2004; 5(3): 261 – 264. (doi: https://doi.org/10.1002/cbic.200300730)
15. Saleh A. Schroeter M. Jonkmanns C. Hartung H.P. Mödder U. Jander S.: 'In vivo MRI of brain inflammation in human ischaemic stroke', *Brain*, 2004; 127(7): 1670 – 1677. (doi: https://doi.org/10.1093/brain/awh191)
16. Watson A. Wu X. Bruchez M.: 'Lighting up cells with quantum dots', *Biotechniques*, 2003; 34(2): 296.
17. Chan W.C. Maxwell D.J. Gao X. Bailey R.E. Han M. Nie S.: 'Luminescent quantum dots for multiplexed biological detection and imaging', *Curr. Opin. Biotechnol*, 2002; 13(1): 40 – 46. (doi: https://doi.org/10.1016/S0958-1669(02)00282-3)
18. Jaiswal J.K. Mattoussi H. Mauro J.M. Simon S.M.: 'Long-term multiple color imaging of live cells using quantum dot bioconjugates', *Nat. Biotechnol*, 2003; 21(1): 47 – 51. (doi: https://doi.org/10.1038/nbt767)
19. Larson D.R. Zipfel W.R. Williams R.M. *et al*.: 'Water-soluble quantum dots for multiphoton fluorescence imaging in vivo', *Science*, 2003; 300(5624): 1434 – 1436. (doi: https://doi.org/10.1126/science.1083780)
20. Moghimi S.M. Hunter A.C. Murray J.C.: 'Nanomedicine: current status and future prospects', *FASEB J*, 2005; 19(3): 311 – 330. (doi: https://doi.org/10.1096/fj.04-2747rev)
21. Rolland J.P. Maynor B.W. Euliss L.E. Exner A.E. Denison G.M. DeSimone J.M.: 'Direct fabrication and harvesting of monodisperse, shape-specific nanobiomaterials', *J. Am. Chem. Soc*, 2005; 127(28): 10096 –10100. (doi: https://doi.org/10.1021/ja051977c)
22. O'Brien T.P. Bult C.J. Cremer C. *et al*.: 'Genome function and nuclear architecture: from gene expression to nanoscience', *Genome Res*, 2003; 13(6a): 1029 –1041. (doi: https://doi.org/10.1101/gr.946403)
23. Buzea C. Pacheco I.I. Robbie K.: 'Nanomaterials and nanoparticles: sources and toxicity', *Biointerphases*, 2007; 2(4): MR17 – MR71. (doi: https://doi.org/10.1116/1.2815690)
24. Trouiller P. Olliaro P. Torreele E. Orbinski J. Laing R. Ford N.: 'Drug development for neglected diseases: a deficient market and a public-health policy failure', *Lancet*, 2002; 359(9324): 2188 – 2194 (doi: https://doi.org/10.1016/S0140-6736(02)09096-7)
25. Allen T.M. Cullis P.R.: 'Drug delivery systems: entering the mainstream', *Science*, 2004; 303(5665): 1818 – 1822. (doi: https://doi.org/10.1126/science.1095833)
26. Miller C. Waller E. Klingemann H. *et al*.: 'Lipid formulations of amphotericin B preserve and stabilize renal function in HSCT recipients', *Bone Marrow Transplant*, 2004; 33(5): 543 – 548. (doi: https://doi.org/10.1038/sj.bmt.1704408)
27. Varshney R. Bhadauria S. Gaur M.S.: 'A review: biological synthesis of silver and copper nanoparticles', *Nano Biomed. Eng*, 2012; 4(2): 99 – 106 (doi: https://doi.org/10.5101/nbe.v4i2.p99-106)
28. Morones J.R. Elechiguerra J.L. Camacho A. *et al*.: 'The bactericidal effect of silver nanoparticles', *Nanotechnology*, 2005; 16(10): 2346. (doi: https://doi.org/10.1088/0957-4484/16/10/059)
29. Raveh A. Zukerman I. Shneck R. Avni R. Fried I.: 'Thermal stability of nanostructured superhard coatings: a review', *Surf. Coat. Technol*, 2007; 201(13): 6136 – 6142. (doi: https://doi.org/10.1016/j.surfcoat.2006.08.131)
30. Parveen S. Misra R. Sahoo S.K.: 'Nanoparticles: a boon to drug delivery, therapeutics, diagnostics and imaging', *Nanomed. Nanotechnol. Biol. Med*, 2012; 8(2): 147 – 166. (doi: https://doi.org/10.1016/j.nano.2011.05.016)
31. Govender T. Stolnik S. Garnett M.C. Illum L. Davis S.S.: 'PLGA nanoparticles prepared by nanoprecipitation: drug loading and release studies of a water soluble drug', *J. Control. Release*, 1999; 57(2): 171 – 185. (doi: https://doi.org/10.1016/S0168-3659(98)00116-3)
32. Fonseca C. Simoes S. Gaspar R.: 'Paclitaxel-loaded PLGA nanoparticles: preparation, physicochemical characterization and in vitro anti-tumoral activity', *J. Control. Release*, 2002; 83(2): 273 –

286. (doi: https://doi.org/10.1016/S0168-3659(02)00212-2)

33. Dong Y. Feng S.-S.: 'Methoxy poly (ethylene glycol)-poly (lactide)(MPEG-PLA) nanoparticles for controlled delivery of anticancer drugs', *Biomaterials*, 2004; 25(14): 2843 – 2849 (doi: https://doi.org/10.1016/j.biomaterials.2003.09.055)
34. Zhang X. Li Y. Chen X. *et al.*: 'Synthesis and characterization of the paclitaxel/MPEG-PLA block copolymer conjugate', *Biomaterials*, 2005; 26(14): 2121 – 2128. (doi: https://doi.org/10.1016/j.biomaterials.2004.06.024)
35. Torché A.-M. Jouan H. Le Corre P. *et al.*: 'Ex vivo and in situ PLGA microspheres uptake by pig ileal Peyer's patch segment', *Int. J. Pharm*, 2000; 201(1): 15 –27. (doi: https://doi.org/10.1016/S0378-5173(00)00364-1)
36. Fielding R.M.: 'Liposomal drug delivery', *Clin. Pharmacokinet*, 1991; 21(3): 155 –164.
37. Lasic D.D. Papahadjopoulos D.: ' *Medical applications of liposomes*' (Elsevier, 1998).
38. Sapra P. Allen T.: 'Ligand-targeted liposomal anticancer drugs', *Prog. Lipid Res*, 2003; 42(5): 439 –462. (doi: https://doi.org/10.1016/S0163-7827(03)00032-8)
39. Allen T. Chonn A.: 'Large unilamellar liposomes with low uptake into the reticuloendothelial system', *FEBS Lett*, 1987; 223(1): 42 – 46. (doi: https://doi.org/10.1016/0014-5793(87)80506-9)
40. Gabizon A. Papahadjopoulos D.: 'Liposome formulations with prolonged circulation time in blood and enhanced uptake by tumors', *Proc. Natl. Acad. Sci*, 1988; 85(18): 6949 – 6953. (doi: https://doi.org/10.1073/pnas.85.18.6949)
41. Papahadjopoulos D. Gabizon A.: 'Liposomes designed to avoid the reticuloendothelial system', *Prog. Clin. Biol. Res*, 1989; 343: 85 –93.
42. Lin H.-Y. Thomas J.L.: 'PEG-lipids and oligo (ethylene glycol) surfactants enhance the ultrasonic permeabilizability of liposomes', *Langmuir*, 2003; 19(4): 1098 – 1105. (doi: https://doi.org/10.1021/la026604t)
43. Allen T. Hansen C.: 'Pharmacokinetics of stealth versus conventional liposomes: effect of dose', *Biochim. Biophys. Acta (BBA)-Biomembr*, 1991; 1068(2): 133 – 141. (doi: https://doi.org/10.1016/0005-2736(91)90201-I)
44. Yamazaki N. Kojima S. Yokoyama H.: 'Biomedical nanotechnology for active drug delivery systems by applying sugar-chain molecular functions', *Curr. Appl. Phys*, 2005; 5(2): 112 – 117. (doi: https://doi.org/10.1016/j.cap.2004.06.017)
45. Kwon G.S. Kataoka K.: 'Block copolymer micelles as long-circulating drug vehicles', *Adv. Drug Deliv. Rev*, 1995; 16(2): 295 – 309. (doi: https://doi.org/10.1016/0169-409X(95)00031-2)
46. Cammas-Marion S. Okano T. Kataoka K.: 'Functional and site-specific macromolecular micelles as high potential drug carriers', *Colloids Surf. B Biointerfaces*, 1999; 16(1): 207 – 215. (doi: https://doi.org/10.1016/S0927-7765(99)00071-5)
47. Lavasanifar A. Samuel J. Kwon G.S.: 'Poly (ethylene oxide)-*block* -poly (l-amino acid) micelles for drug delivery', *Adv. Drug Deliv. Rev*, 2002; 54(2): 169 – 190. (doi: https://doi.org/10.1016/S0169-409X(02)00015-7)
48. Kabanov A.V. Batrakova E.V. Melik-Nubarov N.S. *et al.*: 'A new class of drug carriers: micelles of poly (oxyethylene)-poly (oxypropylene) block copolymers as microcontainers for drug targeting from blood in brain', *J. Control. Release*, 1992; 22(2): 141 –157. (doi: https://doi.org/10.1016/0168-3659(92)90199-2)
49. Dalhaimer P. Bates F.S. Aranda-Espinoza H. Discher D.: 'Synthetic cell elements from block copolymers – hydrodynamic aspects', *Comptes Rendus Phys*, 2003; 4(2): 251 – 258. (doi: https://doi.org/10.1016/S1631-0705(03)00028-8)
50. Dalhaimer P. Engler A.J. Parthasarathy R. Discher D.E.: 'Targeted worm micelles', *Biomacromolecules*, 2004; 5(5): 1714 – 1719. (doi: https://doi.org/10.1021/bm049884v)
51. Bermudez H. Brannan A.K. Hammer D.A. Bates F.S. Discher D.E.: 'Molecular weight dependence of polymersome membrane structure, elasticity, and stability', *Macromolecules*, 2002; 35(21): 8203 – 8208. (doi: https://doi.org/10.1021/ma020669l)
52. Arap W. Pasqualini R. Ruoslahti E.: 'Chemotherapy targeted to tumor vasculature', *Curr. Opin. Oncol*, 1998; 10(6): 560 – 565. (doi: https://doi.org/10.1097/00001622-199811000-00014)
53. Gao Z. Oh K. Kim C.-K.: 'Preparation and characterization of sustained-release microspheres of chlorpromazine', *J. Microencapsul*, 1998; 15(1): 75 –83. (doi: https://doi.org/10.3109/02652049809006837)
54. Discher B.M. Won Y.-Y. Ege D.S. *et al.*: 'Polymersomes: tough vesicles made from diblock copolymers', *Science*, 1999; 284(5417): 1143 – 1146. (doi: https://doi.org/10.1126/science.284.5417.1143)
55. Cai S. Vijayan K. Cheng D. Lima E.M. Discher D.E.: 'Micelles of different morphologies – advantages of worm-like filomicelles of PEO-PCL in paclitaxel delivery', *Pharm. Res*, 2007; 24(11): 2099 –2109.
56. Pata V. Dan N.: 'The effect of chain length on protein solubilization in polymer-based vesicles (polymersomes)', *Biophys. J*, 2003; 85(4): 2111 –

2118. (doi: https://doi.org/10.1016/S0006-3495(03)74639-6)
57. Vinogradov S.V. Bronich T.K. Kabanov A.V.: 'Nanosized cationic hydrogels for drug delivery: preparation, properties and interactions with cells', *Adv. Drug Deliv. Rev*, 2002; 54(1): 135 –147. (doi: https://doi.org/10.1016/S0169-409X(01)00245-9)
58. Patel M. Shah T. Amin A.: 'Therapeutic opportunities in colon-specific drug-delivery systems', *Crit. Rev. Ther. Drug Carrier Syst*, 2007; 24(2): 147 –202. (doi: https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v24.i2.20)
59. Min K.H. Park K. Kim Y.-S. *et al.*: 'Hydrophobically modified glycol chitosan nanoparticles-encapsulated camptothecin enhance the drug stability and tumor targeting in cancer therapy', *J. Control. Release*, 2008; 127(3): 208 –218. (doi: https://doi.org/10.1016/j.jconrel.2008.01.013)
60. Sharma S. Kulkarni J. Pawar A.: 'Permeation enhancers in the transmucosal delivery of macromolecules', *Pharmazie, Int. J. Pharm. Sci*, 2006; 61(6): 495 –504.
61. Rodrigues S. Dionísio M. López C.R. Grenha A.: 'Biocompatibility of chitosan carriers with application in drug delivery', *J. Funct. Biomater*, 2012; 3(3): 615 –641. (doi: https://doi.org/10.3390/jfb3030615)
62. Hornof M.D. Kast C.E. Bernkop-Schnürch A.: 'In vitro evaluation of the viscoelastic properties of chitosan–thioglycolic acid conjugates', *Eur. J. Pharm. Biopharm*, 2003; 55(2): 185 –190. (doi: https://doi.org/10.1016/S0939-6411(02)00162-5)
63. Moghaddam F.A. Atyabi F. Dinarvand R.: 'Preparation and in vitro evaluation of mucoadhesion and permeation enhancement of thiolated chitosan-pHEMA core-shell nanoparticles', *Nanomed. Nanotechnol. Biol. Med*, 2009; 5(2): 208 –215. (doi: https://doi.org/10.1016/j.nano.2008.09.006)
64. Kast C.E. Valenta C. Leopold M. Bernkop-Schnürch A.: 'Design and in vitro evaluation of a novel bioadhesive vaginal drug delivery system for clotrimazole', *J. Control. Release*, 2002; 81(3): 347 –354. (doi: https://doi.org/10.1016/S0168-3659(02)00077-9)
65. Martien R. Loretz B. Thaler M. Majzoob S. Bernkop-Schnürch A.: 'Chitosan–thioglycolic acid conjugate: an alternative carrier for oral nonviral gene delivery?', *J. Biomed. Mater. Res. A*, 2007; 82(1): 1 –9. (doi: https://doi.org/10.1002/jbm.a.31135)
66. Roldo M. Hornof M. Caliceti P. Bernkop-Schnürch A.: 'Mucoadhesive thiolated chitosans as platforms for oral controlled drug delivery: synthesis and in vitro evaluation', *Eur. J. Pharm. Biopharm*, 2004; 57(1): 115 –121. (doi: https://doi.org/10.1016/S0939-6411(03)00157-7)
67. Luo Y. Zhang B. Cheng W.-H. Wang Q.: 'Preparation, characterization and evaluation of selenite-loaded chitosan/TPP nanoparticles with or without zein coating' *Carbohydrate Polymers*, 2010; 82(3): 942 –951. (doi: https://doi.org/10.1016/j.carbpol.2010.06.029)
68. Schneider T. Sachse A. Leike J. *et al.*: 'Surface modification of continuously extruded contrast-carrying liposomes: effect on their physical properties', *Int. J. Pharm*, 1996; 132(1): 9 –21. (doi: https://doi.org/10.1016/0378-5173(95)04247-4)
69. Hayward R.C. Utada A.S. Dan N. Weitz D.A.: 'Dewetting instability during the formation of polymersomes from block-copolymer-stabilized double emulsions', *Langmuir*, 2006; 22(10): 4457 –4461 (doi: https://doi.org/10.1021/la060094b)
70. Khan, I., Khan, M., Umar, M. N., & Oh, D. H. Nanobiotechnology and its applications in drug delivery system: a review. *IET nanobiotechnology*, 2015; *9*(6): 396-400.

تقنية النانو الحيوية في توصيل الأدوية: استكشاف الابتكارات والتطبيقات.

الملخص:

الخلفية: تقنية النانو الحيوية، وهي مجال متعدد التخصصات يجمع بين تقنية النانو والتكنولوجيا الحيوية، تُحدث ثورة في أنظمة توصيل الأدوية. من خلال تطبيق مبادئ من علم الأحياء والكيمياء والفيزياء والهندسة، قام الباحثون بتطوير جزيئات وأجهزة نانوية الحجم لها إمكانيات كبيرة في التطبيقات الطبية الحيوية، خاصة في توصيل الأدوية، والعلاج الجيني، والتشخيص.

الهدف: يستكشف هذا المقال الابتكارات والتطبيقات الخاصة بتقنية النانو الحيوية في توصيل الأدوية، مع التركيز على دور الجسيمات النانوية (NPs)في تعزيز الدقة، والتوافر البيولوجي، والتوزيع المستهدف للعوامل العلاجية.

الطرق: تستعرض المراجعة المواد النانوية المختلفة، بما في ذلك الجسيمات النانوية المعدنية، والعضوية، والمركبة، وهندستها لتطبيقات علاجية وتشخيصية محددة. كما يناقش التقدمات في الطب النانوي، واستخدام المواد النانوية في أنظمة توصيل الأدوية، وتطبيق تقنية النانو في تشخيص وعلاج الأمراض.

النتائج: أدى الانتقال إلى أنظمة توصيل الأدوية النانوية الحجم إلى إدخال عدة أساليب واعدة، مثل الجسيمات النانوية البوليمرية، والليبوسومات، والميكلات البوليمرية. توفر هذه الأنظمة إطلاقًا محكومًا، وتوصيلًا مستهدفًا، وتحسين التوافر البيولوجي. تُبرز الجسيمات النانوية المعدنية، والجسيمات النانوية البوليمرية، والأنظمة المستندة إلى الكيتوسان لخصائصها الفريدة وإمكانياتها في مواجهة التحديات في توصيل الأدوية والعلاج الطبي.

الخلاصة: من المتوقع أن تلعب تقنية النانو الحيوية دورًا محوريًا في تحسين الرعاية الصحية من خلال تقديم حلول مبتكرة لتوصيل الأدوية، والتشخيص، والاستهداف العلاجي. مع تقدم البحث، يعد تكامل تقنية النانو مع الأساليب الطبية التقليدية بتحسين فعالية العلاجات وخصوصيتها، مما سيشكل مستقبل العلوم الطبية.

الكلمات الرئيسية: تقنية النانو الحيوية، توصيل الأدوية، الجسيمات النانوية، الطب النانوي، الجسيمات النانوية البوليمرية، الليبوسومات، الكيتوسان، التطبيقات الطبية الحيوية.