

Nanotechnology in Drug Delivery

Mohamed J. Saadh^{1*}, Roaa K. Jadullah¹

¹Middle East University, Amman, Jordan

*roaa.jad@gmail.com

Abstract

Nanotechnology is currently playing a critical role in electronics, biology, and medicine. Its utility can be assessed since it includes materials that must be developed at the atomic and molecular level. Nanospheres have been found to be reliable drug delivery systems due to their small size, and they may be beneficial for encapsulating pharmaceuticals and permitting more accurate targeting with controlled release. In this study, we focus on current advances in this technology for drugs and drug delivery systems.

Keywords: *Drug delivery Nanotechnology Inorganic nanoparticles Organic nanoparticles*

Introduction

Nanoparticles, like antibodies and DNA plasmids, are organic or inorganic structures with sizes ranging from 1 to 100 nanometers (1). Nanotechnology has advanced significantly in recent decades, and it is now feasible to produce, analyze, and manipulate the functional features of nanoparticles (2, 3). Nanobiotechnology connects the physical and biological sciences, with nanophase and nanostructure applications in a variety of fields, particularly healthcare, where these objects are of tremendous interest. Nanoparticles are affecting medicine in a variety of ways, including nanobiotechnology, microfluidics, biosensors, medication delivery, and microarrays (4). Metal, organic, and polymeric nanoparticles, as well as liposomes, are often explored and can be created for site-specific drug administration, particularly for medicines with low solubility and absorption (5, 6).

Nanoparticles for drug delivery

Nanomaterials are one of the most important materials used in promising applications for drug delivery at a specific site. Nanoparticles have a great ability to eliminate tumor growth without causing any collateral damage by delivering them to the tumor site with high specificity. Therefore, nanoparticles contributed greatly to building drug delivery systems (7, 8). Originally, they were created as vaccination and anticancer medication carriers (9). Then, by altering drug biodistribution and toxicodynamics, nanoscale size ranges may greatly improve medication delivery (10, 11) This can make in vivo distribution of a variety of medications with significant delivery of products a comparatively simple process. A remarkable consequence of this technology is the modification or functionalization of nanoparticles to carry medications past the blood brain barrier for the treatment of brain cancers (12, 13). Doxorubicin, for example, does not penetrate the blood-brain barrier. However, combining it with polysorbate 80 modified polybutylcyano acrylate nanoparticles can significantly improve its transport to the brain.

Nanoparticle systems are important in the development of DNA delivery vectors because of their size, shape, and functionality (14, 15). They have the ability to penetrate deep into tissues and

are quickly absorbed by the cells. Nano-sized colloidal drug carriers can be considered a breakthrough in pharmacotherapy. They can carry a variety of medications, including anti-cancer, anti-hypertensive, and hormones, among others (16). Submicron colloidal particles have been employed as nanoparticles in the administration of drugs and in the detection of illnesses (17, 18). Pharmacokinetics for insoluble medicines has been expanded thanks to nanoparticles. For example, a novel medication delivery method was created using trans-retinoic acid nanoparticles coated with CaCO₃, which produced aggregates after spray drying. The resulting aggregates were discovered to re-disperse in water, stimulating insulin release from the islets (19).

Nanoparticles made of polymers

Biocompatible and biodegradable materials, as well as a range of natural (gelatin, albumin) and synthetic polymers, are used to create polymeric nanoparticle (polylactides, polyalkylcyanoacrylates) (20). Metals and semiconductor nanoparticles rely heavily on polymers as a host material. These nanoparticles are intended to serve as drug carriers, delivering active compounds to their designated targets (21, 22). In nano-composites, polymers are filled with distributed nano-fillers (less than 100 nm) The drug's adsorption capability is affected by polymer hydrophobicity, nanoparticle area, and monomer concentration (23).

Drugs can be introduced to the polymerization process and entrapped inside the nanoparticle polymer network. Nanotechnology can help with medication bioavailability issues. Nano-scale cavities containing liposomes or encapsulated polymers can be constructed to promote medication absorption and bioavailability of hydrophobic pharmaceuticals (paclitaxel or 5-fluorouracil), metabolizing drugs at optimum rates for intended therapeutic impact in target tissues (24). Polymers, albumin, and liposomes can all be used to make nano capsules (25). There are numerous polymers that can be used to make nanoparticles. Synthetic polymers include polylactide-polyglycolide copolymers, polyacrylates, and polycaprolactones, among others, whereas natural polymers include albumin, gelatin, alginate,

collagen, and chitosan (26). Polylactides and poly (DL-lactide-co-glycolide) polymers are largely researched for drug delivery because they undergo hydrolysis upon implantation and create biologically suitable fragments (27).

It is obvious that chemical conjugation of medicines with different polymers affords potential to boost their activity. The created amphiphilic N-(2-hydroxy)-propyl-3-trimethylammonium-chitosan-cholic acid polymers by covalently attaching cholic acid and glycidyl trimethyl ammonium chloride to chitosan, which then self-assembled into nanoparticles in phosphate-buffered saline. Doxorubicin might be encased in these nanoparticles, which would then be easily up taken and released into the cytoplasm by breast cancer (MCF-7) cells (28, 29). The construct a drug carrier with active paclitaxel targeting using folic acid-conjugated chitosan-polylactide copolymers. MCF-7 breast cancer cells that express the folic acid receptor were used to confirm the targeting property (30). The manufacture of a quaternized poly (propylene imine) dendrimer of generation-3, QPPI (G3) as a drug carrier for the weakly soluble anti-inflammatory medication nimesulide was documented in one study, and the drug's solubility was improved Ibuprofen-containing encapsulated nanoscaled emulsion with viscosity modifiers carbopol 934, 940, and ultrez 10 (31, 32). The researches studied influence of silica nanoparticles on α -amylase activity. Park and his colleagues. Also, adriamycin nanoparticles based on glycol chitosan are useful for prolonged and selective adriamycin administration, with lower cytotoxicity than adriamycin alone (33). To develop successful formulations of nanoparticles, diffusion characteristics, biodegradation and drug release must be considered to achieve effective therapeutic capabilities (Figure 1) (34).

Inorganic nanoparticles

In biomedical applications, nanoparticles provided essential multifunctional platforms. Nanoparticles with unique features, such as silica nanoparticles, quantum dots metal nanoparticles, and lanthanide nanoparticles, can be used for a variety of bio-analysis applications (35). Metal nanoparticles such as quantum dots and lanthanide

nanoparticles have distinct features that may be used in a variety of bio-analysis applications (36). A nanoparticle is vital not only for indicating medication distribution, but also for confirming target delivery. Nanomedicine must be tracked from the systemic to the subcellular level. There are many fluorescent markers available; however, nanoparticles offer the benefit of improving fluorescent markers not only for medical imaging and diagnostic applications, but also for in vivo imaging of cancers and other disorders [37].

As example, generated Fe₃O₄ nanocrystals on uniform dye doped mesoporous silica nanoparticles to be employed as a contrast agent in magnetic resonance imaging with doxorubicin loaded in the pores. This device has a lot of potential as magnetic resonance and fluorescence imaging probes, and doxorubicin was successfully administered to tumor locations while maintaining its anticancer effectiveness. Histidine is found in magnetic silica nanoparticles coated with cyan protein which are used in drug delivery systems and fluorescence imaging or as drug carriers and are also widely used in biological research (38). Iron oxide and gold nanoparticles are the most widely used among the nanoparticles (39).

Gold, copper, and silver nanoparticles are characterized by the presence of surface plasmons, so they absorb light in the visible region, allowing the analysis of size-dependent light absorption using surface plasmon resonance (SPR). Many unique features of gold nanoparticles and nanorods have been investigated for possible applications in biomolecular detection (40). Gold nanoparticles, as approved by the FDA, offer specific benefits over other metallic particles in terms of biocompatibility and non-cytotoxicity, and might potentially be used as a preferred carrier for drug administration. Amino acids and proteins can be coupled using these nanoparticles (41). More significant is the fabrication of gold nanoparticles and their functionalization with organic molecules in order to interact with any physiological system. These functionalized nanoparticles are a viable drug delivery option as well as indicators for treatment resistance in cancer cells (42).

Insulin administration by nasal route, increased antibacterial effect against *E. coli* strains, and ciprofloxacin conjugated with gold

nanoparticles for increase activity and for better drug release. Also, the gold nanoparticles out of natural gellan gum used for the delivery of doxorubicin hydrochloride and proved that doxorubicin could be loaded onto gold nanoparticles successfully. On the other hand, developed a very precise assessment of biological activity using a well-specified gold drug nanoparticle method (43). The Fe₃O₄ and gold as the core was used, three paclitaxel-conjugated nanoparticles were created. These conjugated nanomaterials provide a new class of anticancer therapeutic prospects. The production and functionalization of gold nanoparticles have been studied by our group (44).

Gold nanoparticles have been functionalized with several anticancer medications for target drug delivery as well as as reducing and capping agents for gold nanoparticle production. As a result, the applications are quite diverse and suitable for releasing a variety of physiologically active compounds. According to our recent research, Au NPs-Au NRs complexes can also be employed to further bind medicines and biomolecules for possible targeted drug delivery (45). According to our findings, surface modification can improve the stability of Au NRs, and Au NRs can be used as multiplex biosensors. The creation of nanoparticles for bio-sensing and tailored drug delivery for cancer therapies was our main emphasis. We used a unique chemical linking process to create folic acid and doxorubicin-tagged nanoparticles, and we tagged folic acid and doxorubicin on distinct planes of the nanorods. The nanorods in this arrangement have the ability to target cancer cells extremely specifically and deliver a cancer treatment with great efficiency. This system's biological activity is being investigated and will be reported on Particle size, surface charge, surface functionality, as well as optical and magnetic characteristics, may all be measured during nanoparticle characterization. the formation of nanoparticles indicated using the UV-Vis-NIR absorption spectra to detect surface plasmon resonance. the nanoparticles size was determined using transmission electron microscopy (TEM) and scanning electron microscopy (SEM). The zeta potential of a particle is used to determine nanoparticle colloidal stability and also provides a full picture of total charges. Furthermore, it can aid

in the formulation of more stable nanoparticles by providing information on the impact of different parameters such as pH, additive concentration, and medium ionic strength on it (46). Recently, silver nanoparticles used as antiviral therapeutic agent by inhibit virus entry in to the host cell and inhibit RNA synthesis against influenza H₅N₁, H₉N₂, H₅N₁, H₉N₂, Peste des petits ruminant's virus and SARS-Cov-2. This combination makes it difficult to adapt to the virus, which helps reduce resistance to infection as shown in figure 2 (45-50). Moreover, silver nanoparticles become very active against both gram positive and gram-negative bacteria (figure 2) (51).

References

1. Li, C., Samulski, R.J., Engineering adeno-associated virus vectors for gene therapy. *Nat Rev Genet* 2020; 21:255–272.
2. Albota, M.A., Xu, C., Webb, W.W., Two-photon fluorescence excitation cross sections of biomolecular probes from 690 to 960 nm. *Appl Opt* 1998; 37:7352–7356.
3. Arafa, M.G., El-Kased, R.F., Elmazar, M.M., Thermoresponsive gels containing gold nanoparticles as smart antibacterial and wound healing agents. *Sci Rep* 2018; 8:13674.
4. Bora, N.S., Mazumder, B., Pathak, M.P., Joshi, K., Pronobesh Chattopadhyay *Nanotechnology*, 1st Edition First Published. 2019.
5. Swamy, M.K., Sinniah, U.R. Patchouli (*Pogostemon cablin* Benth.): botany, agrotechnology and biotechnological aspects. *Ind Crops Prod* 2016; 87:161–176.
6. Mohanty, S.K., Swamy, M.K., Sinniah., *Leptadenia reticulata* (Retz.) Wight & Arn. (*Jivanti*): botanical, agronomical, phytochemical, pharmacological, and biotechnological aspects. *Molecules* 2019;1019:22.
7. Zhou, C., Zhang, H., Li, Z., *Lab Chip* 2016; 16:1797
8. Varshney, R., Alam, M., Chinmayee Agashe, Roymon Joseph and Debabrata Patra *Chem. Commun* 2020; 56:9284
9. Couvreur, P., Kante, B., Grislain, L., et al., Toxicity of polyalkylcyanoacrylate

- nanoparticles II: doxorubicinloaded nanoparticles. *J. Pharm. Sci* 1982; 71:790-792.
10. Dan, N., Setua, S., Kashyap, V., et al. Antibody-drug conjugates for cancer therapy: chemistry to clinical implications. *Pharmaceuticals* 2018; 11:32.
 11. Polakis, P., Antibody drug conjugates for cancer therapy. *Pharmacol Rev* 2016; 68:3-19.
 12. Kumar R., Cristiam, F., Chalarca, S., et al., Polymeric Delivery of Therapeutic Nucleic Acids. *Chemical Reviews* 2021; 121:11527-11652.
 13. Chen, G., Katrekar, D., Mali, P., RNA-Guided Adenosine Deaminases: Advances and Challenges for Therapeutic RNA Editing. *Biochemistry* 2019; 58:1947-1957.
 14. Brightman, M.W., Morphology of blood-brain interfaces. *Exp Eye Res* 1977; 25 Suppl.: 1-25.
 15. Misra, A., Ganesh, S., Aliasgar, S., et al., Drug delivery to the central nervous system: a review. *J Pharm Pharmaceut Sci* 2003; 6:252-273.
 16. Amić A., Marković, Z., Klein, E., et al., Theoretical study of the thermodynamics of the mechanisms underlying antiradical activity of cinnamic acid derivatives *Food Chemistry* 2018; 246:481-489.
 17. Vauthier, C., Labarre, D., Ponchel, G., Design aspects of poly(alkylcyanoacrylate) nanoparticles for drug delivery. *J Drug Target* 2007; 15:641.
 18. Abd-Elsalam, K., Mohamed, A.A., Prasad, R., Magnetic nanostructures: environmental and agricultural applications. Springer, New York. ISBN 978-3-030-16438-6. 2019.
 19. Vilasrao Deshmukh Foundation School of Pharmacy, Vilasrao Deshmukh Foundation Group of Institutions, New MIDC, Airport Road, Latur, Maharashtra 413531, India. Appeared or available online. 2021.
 20. Yamada, S., Shanbhag, S., Mustafa, K., Scaffolds in Periodontal Regenerative Treatment. *Dent Clin N Am* 2022; 66:111-130
 21. Zhang, C., Luo, J., Yu Y., et al., Building carbazole-decorated styrene-acrylic copolymer latexes and films for iron (III) ion detection *Colloids and Surfaces A: Physicochemical and Engineering Aspects*. 2021; 629.
 22. Reis, D.R., Zin, G., Lemos-Senna, E., et al., A modified premix method for the emulsification of spearmint essential oil (*Mentha spicata*) by ceramic membranes *Surfaces and Interfaces* 2021; 26.
 23. Bustamante-Torres, M., Pino-Ramos, V.H., Romero-Fierro, D., et al., Synthesis and Antimicrobial Properties of Highly Cross-Linked pH-Sensitive Hydrogels through Gamma Radiation. *Polymers* 2021; 13: 2223.
 24. Alaei, S., Ghasemian, E., Vatanara, A., Spray drying of cefixime nanosuspension to form stabilized and fast dissolving powder. *Powder Technol* 2016; 288:241248.
 25. Anand, P., Nair, H.B., Sung, B., et al., Design of curcumin loaded PLGA nanoparticles formulation with enhanced cellular uptake, and increased bioactivity in vitro and superior bioavailability in vivo. *Biochem Pharmacol* 2020; 79:330-338.
 26. Sharma, S., Sudhakara, P., Singh, J., et al., Critical Review of Biodegradable and Bioactive Polymer Composites for Bone Tissue Engineering and Drug Delivery Applications. *Polymers* 2021; 13:2623.
 27. Rizwan, k., Rasheed, T., Bilal, M., Nano-biodegradation of polymers *Biodegradation and Biodeterioration At the Nanoscale*. 2022; 213-238.
 28. Murugaiah, A.M., Subbaiah, N.A. Meanwell. Bioisosteres of the Phenyl Ring: Recent Strategic Applications in Lead Optimization and Drug Design. *Journal of Medicinal Chemistry* 2021; 64:14046-14128.
 29. Lin, B., Weiwei, Lu., Chen, Z., et al., Enhancing the Potential of Miniature-Scale DNA-Compatible Radical Reactions via an Electron Donor-Acceptor Complex and a Reversible Adsorption to Solid Support Strategy. *Organic Letters* 2021; 23:7381-7385.
 30. Al-Jamal, K.T., Nunes, A., Methven, L., et al., Degree of Chemical Functionalization of Carbon Nanotubes Determines Tissue Distribution and Excretion Profile. *Angew Chem Int Ed*. 2012; 51:6389-6393.
 31. Rebecca, M. Law, H.I., Maibach Lateral spread and percutaneous penetration: An

- overview International Journal of Pharmaceutics 2020; 588:119765.
32. Emami, S., Siah-Shadbad, M., Barzegar-Jalali, M., Characterizing eutectic mixtures of gliclazide with succinic acid prepared by electrospray deposition and liquid assisted grinding methods Journal of Drug Delivery Science and Technology. 2018; 45:101-109.
 33. Kawano, Y., Chen, S., Hanawa, T., Adsorption of a poorly water-soluble drug onto porous calcium silicate by the sealed heating method. International Journal of Pharmaceutics 2020; 587:119637.
 34. Zhang, Y., Wang, C., Jian, Z., A comprehensive study on highly active pentiptyceny-substituted bis(imino)pyridyl iron (II) mediated ethylene polymerization. European Polymer Journal. 2020; 128:109605.
 35. Zhao, Y., Bai, C., Brinker, C.J., et al., Nano as a rosetta stone: the global roles and opportunities for nanoscience and nanotechnology. ACS Nano 2019; 13:10853-10855
 36. Algar W.R., Massey, M., Rees, K., et al., Chemical Reviews American Chemical Society. 2021.
 37. Gul-Uludağ, H., Valencia-Sema J., Kucharski, C., et al., Polymeric nanoparticle-mediated silencing of CD44 receptor in CD34+ acute myeloid leukemia cells Leukemia Research. 2014; 38:1299-1308.
 38. Academic Editor: Jianjun Wei Molecules 2021; 26:3437.
 39. Aldana, J., Wang, Y.A., Peng, X., Photochemical instability of CdSe nanocrystals coated by hydrophilic thiols. J Am Chem Soc 2001; 123:8844-8850.
 40. Viktor M. Gololobov, V.V. Kononenko, V.I. Laser nanoablation of a diamond surface in air and vacuum Optics & Laser Technology 2020; 131:106396.
 41. Gurushankar, K., Rimac, H., Potemkin, V., Investigation of the newly characterized baimantuoloamide a and baimantuoloamide b alkaloids as potential cyclin-dependent kinase 4 (CDK4) inhibitors using molecular docking and molecular dynamics simulations. Journal of Molecular Structure 2021; 1230:129925.
 42. Jhaveri, J.; Raichura, Z.; Khan, T.; et al., Chitosan Nanoparticles-Insight into Properties, Functionalization and Applications in Drug Delivery and Theranostics. Molecules 2021; 26:272.
 43. Akamatsu, K., Takei, S., Mizuhata, M., et al., Preparation and characterization of polymer thin films containing silver and silver sulfide nanoparticles. Thin Solid Films 2000; 359:55-60.
 44. Abrahamse, H., Hamblin, MR., New photosensitizers for photodynamic therapy. Biochem J 2016; 473:347-364.
 45. Saadh, M.J., Synthesis, Role In Antibacterial, Antiviral, And Hazardous Effects Of Silver Nanoparticles. Pharmacologyonline 2021; 2: 1331-1336.
 46. Saadh, M.J., Aldalaen, S.M., Inhibitory effects of epigallocatechin gallate (EGCG) combined with zinc sulfate and silver nanoparticles on avian influenza A virus subtype H5N1. Eur Rev Med Pharmacol Sci 2021; 25:2630-2636
 47. Saadh, M.J., Mostafa M. Aggag, M.M., et al., Silver nanoparticles with epigallocatechingallate and zinc sulphate significantly inhibits avian influenza A virus H9N2. Microbial Pathogenesis 2021; 158: 105071.
 48. Saadh, M.J., Epigallocatechin gallate (EGCG) combined with zinc sulfate inhibits Peste des petits ruminants virus entry and replication. Saudi J. Biol. Sci 2021; 28:6674-6678.
 49. Saadh, M.J., Sauchinone With Zinc Sulphate Significantly Inhibits The Activity Of Sars-Cov-2 3cl-Protease. Pharmacologyonline 2021; 2:242-248.
 50. Saadh, M.J., Almaaytah, A.M., Alaraj, M., Punicalagin and zinc (II) ions inhibit the activity of SARS-CoV-2 3CL-protease in vitro. Eur Rev Med Pharmacol Sci 2021; 25:3908-3913.
 51. Saadh, M.J., Effect of silver nanoparticles on the antibacterial activity of Levofloxacin against methicillin-resistant Staphylococcus aureus Eur Rev Med Pharmacol Sci 2021; 25:5507-5510.

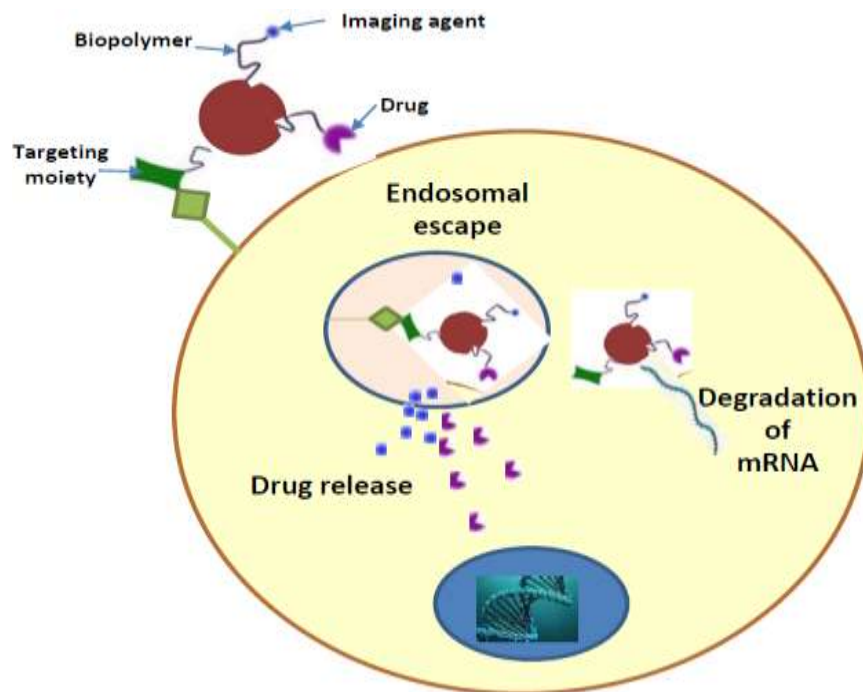


FIGURE 1. Nanotechnology in Drug Delivery

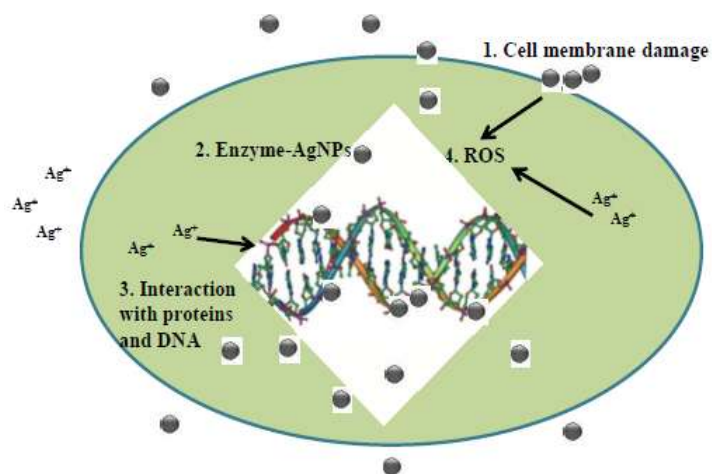


FIGURE 2. Antimicrobial mechanism of silver nanoparticles.