



An Overview of the Role of Nanoparticles in Handling the Breast Cancer

Roghayeh Abbasalipourkabir¹, Nasrin Ziamajidi¹

Department of Clinical Biochemistry, School of Medicine, Hamadan University of Medical Sciences, Iran

*Corresponding author: Roghayeh Abbasalipourkabir, Department of Clinical Biochemistry, School of Medicine, Hamadan University of Medical Sciences, 65178, Hamadan, Iran E-mail: Abbasalipourkabir@umsha.ac.ir

Received: 15 May 2019 Accepted: 12 June 2019 ePublished: 25 June 2019

Although the detection and treatment of breast cancer have significantly developed better than in past decades, it is still the most important cause of death in women worldwide. Until today, various methods have been developed to manage breast cancer, including surgery, radiation, and chemotherapy. However, each method has its own limitations. Effective chemotherapy needs to overcome the challenges of treating breast cancer, including drug toxicity, drug resistance, and adverse drug reactions (1,2). Drug resistance is the major complication in cancer chemotherapy for breast cancer (3). Thus, using the proper delivery system as a new route of drug administration may overcome many difficulties. The size of the drug delivery ranging from a few nanometers (colloidal carriers) to micrometers (microparticles) and millimeters (implants) depends on the method of drug administration. One of the most important benefits of a drug delivery system is to target the unhealthy areas of the body. Nanoparticles are promising in the drug delivery system and deliver the drug to the target tissue in a timely manner (4,5). The encapsulation of chemotherapeutic drugs, especially the enzymes, in polymeric nanoparticles enhances their stability against heat, pH, proteases, and the other degradation factors of their structure (6,7). Nanoparticles have been developed for tumors imaging and drug delivery targeting. The other particles such as nanocantilever and nanoprobe, as well as nanoparticles coupled with specific ligands have also been studied in tumor imaging and peripheral metastasis (8,9). Super magnetic nanoparticles that are conjugated with biological antibodies can be useful in imaging and managing breast cancer (10). The nanoparticles used in medicine are classified into two main groups, namely, particles that include carbon-based molecules as the main material and those which usually

contain metals and minerals as the core. In addition, inorganic nanoparticles such as quantum dots that have a central core of magnetic properties can be used for detecting and imaging the tumors while organic nanoparticle systems such as liposomes, solid lipid nanoparticles (SLN), aptamers, dendrimers, and nanobody can be applied for different drug-encapsulations (11-13). Liposomes are used as the drug carriers in the chemotherapy of various human tumors including breast cancer (14). Further, dendrimers are used as contrast agents in MRI which can detect various pathological processes (15,16). Furthermore, aptamers are oligonucleotide (RNA or ssDNA) and peptide molecules that bind to their target molecules (i.e., little biomolecules, proteins, and even the cells) with high affinity and specificity. Moreover, they are used as a tool for the detection and management of diseases including cancer. DNA aptamers are more stable than RNA aptamers, but RNA aptamers are more flexible. Additionally, peptide aptamers are made of a variable peptide loop (with 10-20 amino acids) linked to a protein framework. Furthermore, aptamers can be used in drug-carrier systems. These aptamers bind to cell surface receptors and are pulled into the cell (13). Nowadays, monoclonal nanobodies can be produced in bacteria. In addition, they are more stable than conventional antibodies because of their small size. Further, they are highly soluble and have a high affinity and specificity for their antigen. Thus, monoclonal nanobodies have great potential for cancer detection and management (17). The metastasis of mammary gland cancer cells in the mice was reduced in a study using nanomaterials (18). Meanwhile, quantum dots are fluorescent nanoparticles (2–10 nm) that comprise a center of hundreds to thousands of the atoms of groups II and VI (i.e., Cd, Tc, Zn, and Se) or group III (Ta) and group V (In) (19). However,

the use of quantum particles in imaging and therapeutic applications *in vivo* is imperfect due to the toxic effects of the heavy metal core (20). Ultra-magnetic nanoparticles are suitable for contrast enhancement and MRI. Furthermore, magnetic nanoparticles conjugated with a biomolecule are used to carry the drug in the management of cancer. Moreover, magnetic iron oxide nanoparticles have been used as a magnetic resonance factor for the studies of gene expression, angiogenesis, and cellular traffic (21). Yezhelyev et al developed a quantum dot-based assay to detect and measure estrogen, progesterone, and ERBB2 receptors in cultured breast cancer cells. Quantum dots are available in different sizes and emission spectra which can detect several proteins in a single small tumor sample (22). Similarly, Al-Hajj et al identified simultaneously six proteins in paraffin-embedded breast tumor specimens using antibody-conjugated quantum dots (23). In summary, using quantum dots, it is possible to quantify multiple proteins simultaneously on a tumor fragment or small cancerous specimens and the final treatment strategy is based on these results. Liposomes and lipid peroxidases containing doxorubicin were reported to be useful in the management of metastatic breast cancer (24). SLN, which are with solid lipid background at room temperature, have potentially wide applications (25). SLN are drug-carrier systems that encapsulate hydrophobic or chemically unsettled drugs. Tamoxifen is a non-steroidal and anti-estrogenic drug which is highly hydrophobic. The use of tamoxifen-loaded nanoparticles increases its permeability to the tumor tissue. It has also fewer toxic effects on healthy non-tumor tissue cells (26). The advantages of SLN include its high potential for controlling drug release, drug targeting, stability, and high capacity to encapsulate the drug. Additionally, SLN have a high potential for payload hydrophobic and hydrophilic drugs into the nontoxic delivery system. No organic solvents are required with the SLN and it has a potential for bulky scale production. However, it is expected that nanoparticles are able to reduce drug toxicity. There are still some weaknesses to SLN, including particle growth, particle aggregation, unpredictable gelation tendency, polymorphic transitions, burst drug release, drug ejection, and inherently low incorporation capacities due to the crystalline structure of the solid lipid (27).

Conclusion

In general, SLN can improve the therapeutic application of tamoxifen by reducing its toxicity, particularly in the treatment of breast cancer. Nanoparticles could be potentially used in long-term circulating carrier systems for breast cancer therapy because of their small size. Finally, although there are some challenges and limitations on the use of nanoparticles in medicine, it is hoped that nanoparticles create tremendous revolutionary not only in

oncology but also in medicine in the near future.

Conflict of Interest Disclosures

None.

References

1. Fathy Abd-Ellatef GE, Gazzano E, Chirio D, Hamed AR, Belisario DC, Zuddas C, et al. Curcumin-Loaded Solid Lipid Nanoparticles Bypass P-Glycoprotein Mediated Doxorubicin Resistance in Triple Negative Breast Cancer Cells. *Pharmaceutics*. 2020;12(2). doi: [10.3390/pharmaceutics12020096](https://doi.org/10.3390/pharmaceutics12020096).
2. Tang Y, Wang Y, Kiani MF, Wang B. Classification, treatment strategy, and associated drug resistance in breast cancer. *Clin Breast Cancer*. 2016;16(5):335-43. doi: [10.1016/j.clbc.2016.05.012](https://doi.org/10.1016/j.clbc.2016.05.012).
3. Wong HL, Rauth AM, Bendayan R, Manias JL, Ramaswamy M, Liu Z, et al. A new polymer-lipid hybrid nanoparticle system increases cytotoxicity of doxorubicin against multidrug-resistant human breast cancer cells. *Pharm Res*. 2006;23(7):1574-85. doi: [10.1007/s11095-006-0282-x](https://doi.org/10.1007/s11095-006-0282-x).
4. Mohseni R, ArabSadeghabadi Z, Ziamajidi N, Abbasalipourkabir R, RezaeiFarimani A. Oral administration of resveratrol-loaded solid lipid nanoparticle improves insulin resistance through targeting expression of SNARE proteins in adipose and muscle tissue in rats with type 2 diabetes. *Nanoscale Res Lett*. 2019;14(1):227. doi: [10.1186/s11671-019-3042-7](https://doi.org/10.1186/s11671-019-3042-7).
5. Kalantarian G, Ziamajidi N, Abbasalipourkabir R, Mahjub R, Goodarzi MT, Saidijam M, et al. Effect of insulin-loaded trimethyl chitosan nanoparticles on genes expression in the hippocampus of diabetic rats. *J Basic Clin Physiol Pharmacol*. 2019. doi: [10.1515/jbcpp-2019-0147](https://doi.org/10.1515/jbcpp-2019-0147).
6. Bahreini E, Aghaiypour K, Abbasalipourkabir R, Mokarram AR, Goodarzi MT, Saidijam M. Preparation and nanoencapsulation of l-asparaginase II in chitosan-tripolyphosphate nanoparticles and in vitro release study. *Nanoscale Res Lett*. 2014;9(1):340. doi: [10.1186/1556-276x-9-340](https://doi.org/10.1186/1556-276x-9-340).
7. Zu Y, Zhao Q, Zhao X, Zu S, Meng L. Process optimization for the preparation of oligomycin-loaded folate-conjugated chitosan nanoparticles as a tumor-targeted drug delivery system using a two-level factorial design method. *Int J Nanomedicine*. 2011;6:3429-41. doi: [10.2147/ijn.s27157](https://doi.org/10.2147/ijn.s27157).
8. Fortina P, Kricka LJ, Surrey S, Grodzinski P. Nanobiotechnology: the promise and reality of new approaches to molecular recognition. *Trends Biotechnol*. 2005;23(4):168-73. doi: [10.1016/j.tibtech.2005.02.007](https://doi.org/10.1016/j.tibtech.2005.02.007).
9. Gao X, Chung LW, Nie S. Quantum dots for in vivo molecular and cellular imaging. *Methods Mol Biol*. 2007;374:135-45. doi: [10.1385/1-59745-369-2:135](https://doi.org/10.1385/1-59745-369-2:135).
10. Yang HM, Park CW, Woo MA, Kim MI, Jo YM, Park HG, et al. HER2/neu antibody conjugated poly (amino acid)-coated iron oxide nanoparticles for breast cancer MR imaging. *Biomacromolecules*. 2010;11(11):2866-72. doi: [10.1021/bm100560m](https://doi.org/10.1021/bm100560m).
11. Núñez C, Estévez SV, Del Pilar Chantada M. Inorganic nanoparticles in diagnosis and treatment of breast cancer. *J Biol Inorg Chem*. 2018;23(3):331-45. doi: [10.1007/s00775-018-1542-z](https://doi.org/10.1007/s00775-018-1542-z).
12. Foroughi S, Ziamajidi N, Javid S, Abbasalipourkabir R, Aflatoonian R, Ashrafi M, et al. Study of telomerase reverse transcriptase and uterine-ovarian-specific genes expression in the endometrial tissue of ovariectomized female Sprague-Dawley rats. *Int J Biol Macromol*. 2018;113:1302-7. doi: [10.1016/j.ijbiomac.2018.02.115](https://doi.org/10.1016/j.ijbiomac.2018.02.115).
13. Zhu G, Chen X. Aptamer-based targeted therapy. *Adv Drug Deliv Rev*. 2018;134:65-78. doi: [10.1016/j.addr.2018.08.005](https://doi.org/10.1016/j.addr.2018.08.005).
14. Hofheinz RD, Gnad-Vogt SU, Beyer U, Hochhaus A. Liposomal encapsulated anti-cancer drugs. *Anticancer Drugs*. 2005;16(7):691-707. doi: [10.1097/01](https://doi.org/10.1097/01).

- cad.0000167902.53039.5a.
15. Lee CC, MacKay JA, Fréchet JM, Szoka FC. Designing dendrimers for biological applications. *Nat Biotechnol.* 2005;23(12):1517-26. doi: [10.1038/nbt1171](https://doi.org/10.1038/nbt1171).
 16. Carvalho MR, Reis RL, Oliveira JM. Dendrimer nanoparticles for colorectal cancer applications. *J Mater Chem B.* 2020;8(6):1128-38. doi: [10.1039/c9tb02289a](https://doi.org/10.1039/c9tb02289a).
 17. Romão E, Krasniqi A, Maes L, Vandenbrande C, Sterckx YG, Stijlemans B, et al. Identification of nanobodies against the acute myeloid leukemia marker CD33. *Int J Mol Sci.* 2020;21(1). doi: [10.3390/ijms21010310](https://doi.org/10.3390/ijms21010310).
 18. Van Impe K, Bethuyne J, Cool S, Impens F, Ruano-Gallego D, De Wever O, et al. A nanobody targeting the F-actin capping protein CapG restrains breast cancer metastasis. *Breast Cancer Res.* 2013;15(6):R116. doi: [10.1186/bcr3585](https://doi.org/10.1186/bcr3585).
 19. Medintz IL, Uyeda HT, Goldman ER, Mattoussi H. Quantum dot bioconjugates for imaging, labelling and sensing. *Nat Mater.* 2005;4(6):435-46. doi: [10.1038/nmat1390](https://doi.org/10.1038/nmat1390).
 20. Hardman R. A toxicologic review of quantum dots: toxicity depends on physicochemical and environmental factors. *Environ Health Perspect.* 2006;114(2):165-72. doi: [10.1289/ehp.8284](https://doi.org/10.1289/ehp.8284).
 21. Béalle G, Di Corato R, Kolosnjaj-Tabi J, Dupuis V, Clément O, Gazeau F, et al. Ultra magnetic liposomes for MR imaging, targeting, and hyperthermia. *Langmuir.* 2012;28(32):11834-42. doi: [10.1021/la3024716](https://doi.org/10.1021/la3024716).
 22. Yezhelyev M, Morris C, Gao X, Nie S, Lewis M, Cohen C. Multiple profiling of human breast cancer cell lines with quantum dots–Ab conjugates. *Proc Am Assoc Cancer Res.* 2005;46:510.
 23. Al-Hajj AH, Yezhelyev M, Liu T, Morris C, Gao X, Nie S, et al. Simultaneous, quantitative detection of multiple biomarkers in breast cancers using semiconductor multicolor quantum dots. *Cancer Res.* 2006;66(8 Suppl):841-2.
 24. Abbasalipourkabir R, Fallah M, Sedighi F, Maghsood AH, Javid S. Nanocapsulation of nitazoxanide in solid lipid nanoparticles as a new drug delivery system and in vitro release study. *J Biol Sci.* 2016;16(4):120-7. doi: [10.3923/jbs.2016.120.127](https://doi.org/10.3923/jbs.2016.120.127).
 25. Ding Y, Nielsen KA, Nielsen BP, Bøje NW, Müller RH, Pyo SM. Lipid-drug-conjugate (LDC) solid lipid nanoparticles (SLN) for the delivery of nicotine to the oral cavity—optimization of nicotine loading efficiency. *Eur J Pharm Biopharm.* 2018;128:10-7. doi: [10.1016/j.ejpb.2018.03.004](https://doi.org/10.1016/j.ejpb.2018.03.004).
 26. Zanganeh N, Ziamajidi N, Khodadadi I, Saidijam M, Abbasalipourkabir R. Liver genes expression induced by tamoxifen loaded solid lipid nanoparticles in Wistar female rats. *Cell Biochem Biophys.* 2018;76(1-2):303-10. doi: [10.1007/s12013-017-0833-2](https://doi.org/10.1007/s12013-017-0833-2).
 27. Ghasemiyeh P, Mohammadi-Samani S. Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: applications, advantages and disadvantages. *Res Pharm Sci.* 2018;13(4):288-303. doi: [10.4103/1735-5362.235156](https://doi.org/10.4103/1735-5362.235156).