

Open  Access

Mini Review

Nanoparticle drug delivery for reducing cytotoxicity and MDR risks to cancer patients

Zhenggang Wu

Shenzhen Zijian Biotech Co., Ltd., Nanshan, Shenzhen, 518057, China

Article Info: Received 24 March 2019; Review Completed 24 April 2019; Accepted 30 April 2019; Available online 15 May 2019



Cite this article as:

Wu Z, Nanoparticle drug delivery for reducing cytotoxicity and MDR risks to cancer patients, Journal of Drug Delivery and Therapeutics. 2019; 9(3):502-504 <http://dx.doi.org/10.22270/jddt.v9i3.2626>

*Address for Correspondence:

Zhenggang Wu, Division of Life Science and Applied Genomics Center, Hong Kong University of Science and Technology, Clear Water Bay, Hong Kong, China

Introduction

Fast growing cancers such as malignant brain tumors, for instance, can attack the brain and the spinal cord in rapidly¹⁻⁴. They attack the central nervous system and leave patients with inferior prognosis. A patient with glioblastoma, for instance, will have a six-percentage chance for a five-year survival rate. The options for most patients with a brain tumor or a localized tumor is debulking surgery, followed by radiation or chemotherapy. In this context, the use of chemotherapy is inevitable for most patients, and as research literature note, issues of multidrug resistance and cytotoxicity go hand in hand with the treatment. Cytotoxic drugs also called as cytostatic are drugs that target cancer cells. These drugs aim to inhibit cell division, and in this way, they lead to the death of cancer cells⁵⁻¹⁰. Their capability to destroy tumors results in better outcomes for patients after their debulking surgeries. The drugs are not only useful for a primary tumor but also can be rendered for destroying smaller tumors. The problem with the drugs is that they affect all other healthy cells as well, although they are particularly sensitive to cancer cells. Medications are often delivered as either high dosage drugs for some aggressive cancers or as a combinatorial therapy¹¹⁻¹⁵.

Sun et al.¹⁶ discuss how the co-delivery of dual-drugs with nanoparticle can help prevent multidrug resistance MDR in cancer patients. Chemotherapy plays a very vital role when it comes to treating different types of cancer. However, many of the existing treatments are problematic in themselves because they are either cytotoxic and hence cause ill-health of the patient or in some situations could provoke multi-drug resistance¹⁷⁻²⁰. The drugs that target the tumor cells will also affect the healthy tissues. In the case of MDR, the tolerance barrier has to be crossed by introducing more amount of the drug to treat the cancer patient, and this, in turn, contributes to increased cytotoxicity²¹⁻²⁴.

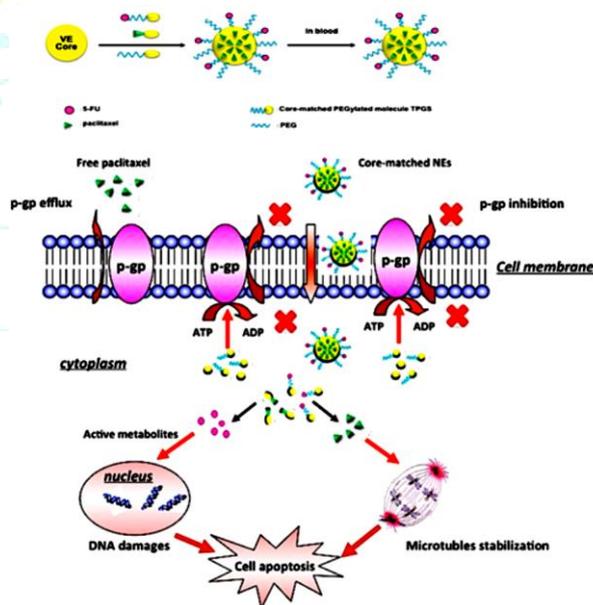


Figure 1: Co-delivery for achieving reversal of MDR, the core matched nano-emulsions are co-delivering PTX and 5-FU for achieving reversal of multidrug-resistance^{16,25}.

Kang et al.¹⁵ presented a conjugate drug, and the camptothecin CPT loaded on a nanoparticle as the answer to selectively deliver the drug to the tumor cell. This way the healthy cells are not affected. Sun et al. on the other hand, present a targeted drug delivery system with dual drugs used to combat MDR. In some cases, it is even possible to reverse MDR through nano drug co-delivery mechanism as presented in the above diagram that highlights how Nano-

emulsions are co-delivering PTX and 5FU to achieve the reversal of MDR^{16,26,27}.

Sun et al.^{16,25} in their review identified that the use of multiple drugs as chemotherapeutic agents did provide some efficacy in the context of treating cancer. It did reduce multidrug resistance as well because various medications have different pharmacokinetic properties. However, the efficacy observed was very nominal. It was identified that the use of different drugs, with nanotechnology, gene engineering, and associated significant data insights, shows much more promise. Improving the anticancer index is possible. Nanoparticle drug delivery system has the capability of selectivity in targeting tumor regions. An important adverse effect in radiation and chemotherapy was the loss of healthy cells^{25,28-30}. Healthy cells also absorb the drug and are led to apoptosis. In the case of selective targeting, as is observed in the case of a nanoparticle drug delivery system, the healthy cells are spared, and hence the cytotoxicity effect is reduced. MDR problems are overcome as the nanotechnology carefully protects the payload³¹⁻³³. The payload is usually a combination of chemotherapeutic drugs and an MDR sensitizer that reduces MDR effects. The nanotechnology capability is what helps encapsulate the drug and the inhibitor and helps deliver them in one shot³⁴⁻³⁶.

The work aim was to review Nanoparticle drug delivery for reducing cytotoxicity and MDR risks to cancer patients. The work identified how in the context of cancer treatment, especially in the case of fast-growing cancer, and other malignant brain tumors, the use of chemotherapeutic agents are inevitable. Even with debulking surgeries, the patient has to undergo a regime of radiation or delivery of drugs. It is in this context that secondary health issues arise for the patient, such as cytotoxicity of drugs which harms their health or multidrug resistance that they develop which will stop the efficacy of their treatment drug action. Nanotechnology-based drug delivery systems were identified to hold much promise for preventing cytotoxicity and for MDR.

References

- Chen, Y., et al. Identification of 4-aminoquinoline core for the design of new cholinesterase inhibitors. *PeerJ* **4**, e2140 (2016).
- Cheng, X. & Lee, R.J. The role of helper lipids in lipid nanoparticles (LNPs) designed for oligonucleotide delivery. *Adv Drug Deliv Rev* **99**, 129-137 (2016).
- Cheng, X., et al. Lipid Nanoparticles Loaded with an Antisense Oligonucleotide Gapmer Against Bcl-2 for Treatment of Lung Cancer. *Pharmaceutical research* **34**, 310-320 (2017).
- Cheng, X., et al. T7 Peptide-Conjugated Lipid Nanoparticles for Dual Modulation of Bcl-2 and Akt-1 in Lung and Cervical Carcinomas. *Molecular pharmaceutics* **15**, 4722-4732 (2018).
- Davis, M.E., Chen, Z.G. & Shin, D.M. Nanoparticle therapeutics: an emerging treatment modality for cancer. *Nat Rev Drug Discov* **7**, 771-782 (2008).
- Han, R., Sun, Y., Kang, C., Sun, H. & Wei, W. Amphiphilic dendritic nanomicelle-mediated co-delivery of 5-fluorouracil and doxorubicin for enhanced therapeutic efficacy. *Journal of Drug Targeting* **25**, 140-148 (2017).
- Kang, C. *Ion channels, protein kinase C and caveolae in cardioprotection*, (The Ohio State University, 2015).
- Kang, C., Hernandez, V.A. & Hu, K. Functional interaction of the two-pore domain potassium channel TASK-1 and caveolin-3. *Biochimica et Biophysica Acta (BBA)-Molecular Cell Research* **1864**, 1537-1544 (2017).
- Kang, C. & Hu, K. Role of caveolin-3 in adenosine-induced increase in mitochondrial PKC ϵ . *The FASEB Journal* **27**, 1191.1197-1191.1197 (2013).
- Kang, C. & Hu, K. Modulation of the two-pore domain potassium channel TASK-1 by caveolin-3. *The FASEB Journal* **29**, 845.814 (2015).
- Kang, C. & Hu, K. Impact of hypoxia in the expression and regulation of the TASK-1 potassium channel in cardiac myocytes. *The FASEB Journal* **30**, lb598-lb598 (2016).
- Kang, C., Qin, J., Osei, W. & Hu, K. Regulation of protein kinase C-epsilon and its age-dependence. *Biochemical and Biophysical Research Communications* **482**, 1201-1206 (2017).
- Kang, C., Qin, J., Osei, W. & Hu, K. Age-dependent Mitochondrial Targeting Of Protein Kinase C Epsilon In Cardioprotection. *The FASEB Journal* (2017).
- Kang, C., Sun, Y., Wang, M. & Cheng, X. Nanosized camptothecin conjugates for single and combined drug delivery. *European Journal of BioMedical Research* **2**, 8-14 (2016).
- Kang, C., et al. Delivery of nanoparticles for treatment of brain tumor. *Current Drug Metabolism* **17**, 745-754 (2016).
- Sun, Y., Kang, C., Liu, F. & Song, L. Delivery of antipsychotics with nanoparticles. *Drug Development Research* **77**, 393-399 (2016).
- Li, Q., et al. Identification by shape-based virtual screening and evaluation of new tyrosinase inhibitors. *PeerJ* **6**, e4206 (2018).
- Liu, F., Sun, Y. & Kang, C. Controlling Amphiphilic Functional Block Copolymers' Self-Assembly: From Structure to Size. (2016).
- Liu, F., Sun, Y., Kang, C. & Zhu, H. Pegylated Drug Delivery Systems: From Design to Biomedical Applications. *Nano LIFE* **6**, 1642002 (2016).
- Peng, J., et al. Enhanced Liver Regeneration After Partial Hepatectomy in Sterol Regulatory Element-Binding Protein (SREBP)-1c-Null Mice is Associated with Increased Hepatocellular Cholesterol Availability. *Cellular Physiology and Biochemistry* **47**, 784-799 (2018).
- Qiao, H., et al. Orally delivered polycurcumin responsive to bacterial reduction for targeted therapy of inflammatory bowel disease. *Drug Delivery* **24**, 233-242 (2017).
- Qiao, H., et al. Redox-triggered mitoxantrone prodrug micelles for overcoming multidrug-resistant breast cancer. *Journal of drug targeting* **26**, 75-85 (2018).
- Shuhong, X., et al. Dynamic expression of AQP4 in early stage of ischemia/reperfusion rats and cerebral edema. *Chinese Pharmacological Bulletin* **32**, 1433-1441 (2016).
- Song, L., et al. Crocetin inhibits lipopolysaccharide-induced inflammatory response in human umbilical vein endothelial cells. *Cellular Physiology and Biochemistry* **40**, 443-452 (2016).
- Sun, Y., et al. Co-delivery of dual-drugs with nanoparticle to overcome multidrug resistance. *European Journal of BioMedical Research* **2**, 12-18 (2016).
- Sun, Y. & Kang, C. Self-Assembly of Peptides into Hydrogel. *Journal of Organic & Inorganic Chemistry* **2**, 5 (2016).
- Sun, Y., et al. RGD Peptide-Based Target Drug Delivery of Doxorubicin Nanomedicine. *Drug development research* **78**, 283-291 (2017).
- Sun, Y., Kang, C., Yao, Z., Liu, F. & Zhou, Y. Peptide-Based Ligand for Active Delivery of Liposomal Doxorubicin. *Nano Life* **6**, 1642004 (2016).
- Waller, A.P., et al. GLUT12 functions as a basal and insulin-independent glucose transporter in the heart. *Biochimica et*

- Biophysica Acta (BBA)-Molecular Basis of Disease* **1832**, 121-127 (2013).
30. Xue, X., *et al.* Discovery of novel inhibitors disrupting HIF-1 α /von Hippel-Lindau interaction through shape-based screening and cascade docking. *PeerJ* **4**, e2757 (2016).
 31. Yan, G., *et al.* Application of Real-Time Cell Electronic Analysis System in Modern Pharmaceutical Evaluation and Analysis. *Molecules* **23**, 3280 (2018).
 32. Yang, Z., *et al.* Functional exosome-mimic for delivery of siRNA to cancer: in vitro and in vivo evaluation. *Journal of Controlled Release* **243**, 160-171 (2016).
 33. Yao, Z., Sun, Y. & Kang, C. Structure and self-assembly of multicolored Naphthalene Diimides Semiconductor. *Nano LIFE* **6**, 1642007 (2016).
 34. Yeh, C.Y., Hsiao, J.K., Wang, Y.P., Lan, C.H. & Wu, H.C. Peptide-conjugated nanoparticles for targeted imaging and therapy of prostate cancer. *Biomaterials* **99**, 1-15 (2016).
 35. Yung, B.C., *et al.* Lipid nanoparticles composed of quaternary amine-tertiary amine cationic lipid combination (QTsome) for therapeutic delivery of AntimiR-21 for lung cancer. *Molecular pharmaceutics* **13**, 653-662 (2016).
 36. Zhong, X., Sun, Y., Kang, C. & Wan, G. The theory of dielectrophoresis and its applications on medical and materials research. *European Journal of BioMedical Research* **2**, 7-11 (2017).

Journal of Drug Delivery & Therapeutics



JDDT