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Mini Review

Mini-review: Combination and Co-delivery in Cancer Treatment Efficacy

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ABSTRACT

The mini-review focuses on the cancer therapy treatment efficacy as enhanced through combination and co-delivery methods. The focus is on nano-delivery methods and how in spite of the challenges in developing co-delivery, their potential is analyzed across different clinical fields.

Keywords: Cancer therapy, combination, co-delivery, nano-delivery, nano micelles, nanoscale, nanoparticles



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INTRODUCTION

Cancer therapy treatments are often questioned and verified with clinical efficiency trials. It has been identified that combination therapy often has a considerable improvement on the response rate in cancer patients¹⁻⁸. It improves the drug resistance effects that reduce response rates argue, the combination of chemotherapy and related anticancer drugs are more effective and feasible. In fact, co-delivery of anticancer drugs with nanotechnology is considered as one of the foremost desired forms of drug delivery⁹⁻¹⁷. This article presents a review of the co-delivery of drugs and some of the positive response rates reported in such co-delivery. The scope of the paper is restricted to reviewing the actions of cancer treatment

with combination and co-delivery. Only secondary research evidence is used in the review.

COMBINATION AND CO-DELIVERY

Combination chemotherapy drugs that make use of two and more anti-cancer drugs are more effective and feasible in clinical practice. Combination therapy is a therapeutic intervention so constructed that the therapy or medication administered to the cancer patient is more than one¹⁸⁻²⁵. It could be the administration of different medicines or administration of different treatment plans involving more than one medicine. Researchers like Qi et al.^{26,27} and Han et al.² in their research work have identified that combinatory forms with co-delivery are better for cancer treatment.

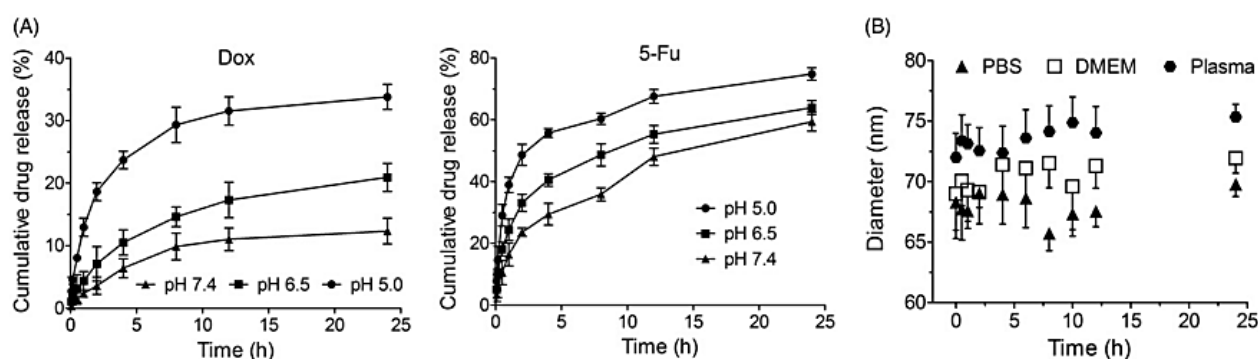


Figure 1: In-vitro drug release profile and stability, (Han et al., 2017)

Combination chemotherapy drugs would not be significant on their own when it comes to enhancing treatment efficacy. In the chemotherapeutic treatments on malignant cancer, it has been identified that drug resistance is a significant issue. MDR results in the state where the treatment dosages have to be significantly increased^{26,28-31}. The toxicity of the drugs used to fight cancer cells attacks normal cells. Very high dosages of the drug as necessitated by the multidrug resistance (MDR) hence result in significant health issues, toxicity issues and sometimes

even the death of the patient. In this context, combination drugs were considered as a solution, but then the co-administration of different therapeutic drugs in themselves cannot bring much of a clinical advantage. The combined drugs had different pharmacokinetic properties. Only the use of nanomedicine and nanotechnology-based co-delivery are helpful in this situation^{27,32-35}. Co-delivery is therefore necessary for achieving said benefits. Co-delivery has the capacity of reversing the effects of MDR.

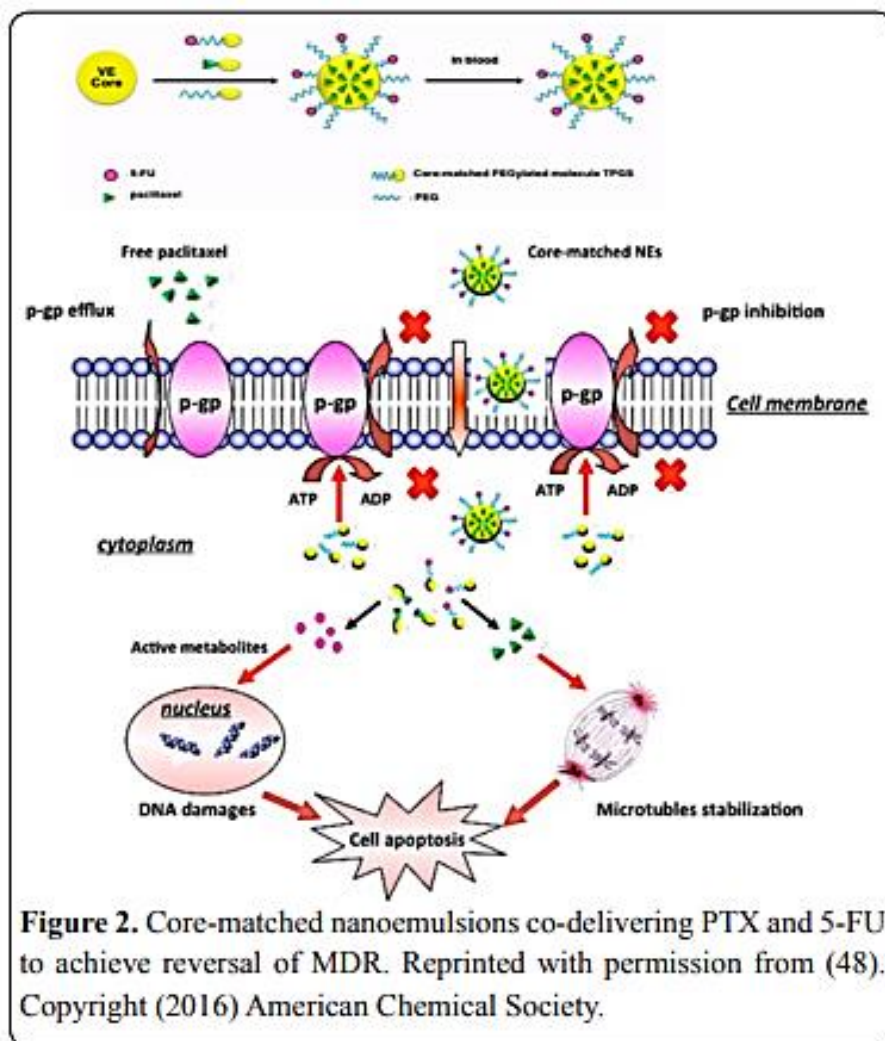


Figure 2: MDR reversal, (Sun et al., 2016)

Co-delivery systems help deliver these combination treatment plans. Nanodrug based co-delivery systems NDCDS have been assessed as a strategy of choice by researchers Qi et al.²⁷ where two different drugs which are different in physicochemical and pharmacological properties were used as part of a combination delivery system. The use of such drugs resulted in synergistic inhibition of growth of tumors as compared to other drugs. This shows the possibility of nanoparticle co-delivery and combination drug therapy in the prospective future. Han et al. argue about the efficacy of combination drugs in tumor reduction. Their work is focused on usage of multiple anticancer agents delivered as a drug encapsulated dendritic nano micelles³⁶⁻³⁹. The parallel activity of 5-fluorouracil (5-Fu) and doxorubicin (Dox) results in synergistic anticancer efficacy. In specific, Han et al. noted that the combined cytotoxicity of the treatment drugs on

human breast cancer cells of the MDA-MB-231 type increased by 11.2 and 6.1. In other forms of cancer cells, like brain tumors, Kang et al. place the argument that nano-delivery forms have better chances of crossing the blood-brain barrier. The increased cytotoxicity inhibits tumor cells from growing, and the progression of the growth is controlled. These forms of combination trials pave the way for multiple co-encapsulation of chemotherapy drugs which would be useful for treating cancer. In the case of gene delivery to cancer cells, researchers like Yang et al. (2016) even support the significance of nanoscaled EMs. Thus, Co-delivery systems as shown in the work of Han et al.² and Qi et al.²⁷ play a significant role in the delivery of combination drugs.

Design of co-delivery systems is of many types such as nano micelles, nanoparticles, and liposomes. Drug loading

capacity is high in these co-delivery systems. They are able to reach and deliver chemotherapeutic agents to the tumor regions because of their permeability and retention aspects. While there are many advantages in using the combination and co-delivery systems, there are some challenges to using them. The nano-delivery systems have limited stability. The diameter distribution is very dispersed, and they can be used only with certain drugs. Adaption to many drugs with these nano-delivery systems is still investigated and until then the co-delivery systems cannot be used in a large scale in clinics. However, as the research work of Han et al. highlights, there is potential for development. Co-delivery systems are studied across different medical fields like anti-cancer treatment and anti-psychosis. Han et al.² designed AmD with hydrophilic polyamidoamine dendrons and hydrophobic poly. Once they are self-assembled into nano-delivery micelles, they work to co-encapsulate the medications and deliver them to the designated regions. Preferential drug release aspects

make them work on targeted tumor lesions instead of attacking normal cells. Cytotoxicity is enhanced in the tumor lesions more and the overall drug efficacy is enhanced because of targeted action that is promoted by the co-delivery technique. Therefore, in spite of the main challenges that are present in combination and co-delivery, researchers work on finding optimal solutions that can support multiple drugs.

CONCLUSION

The review conducted on combination therapy with co-delivery shows that the combination methods in themselves are not that effective given that they are different in their pharmacokinetic properties. It is the use of co-delivery systems that enhance their efficacy. Research works have been conducted on the nano-delivery system and their effects on brain tumors and breast cancers are documented. Future research hence has to focus on extending the form of co-delivery systems.

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