Mini Review: Modulating cytotoxicity effects in Cancer Drug Delivery

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ABSTRACT

A review of cytotoxicity associated with cancer treatments as presented in literature was discussed. In all the studies, the research is aware of the cytotoxic effects of the cancer drug and the delivery form such as nanotechnology-based delivery. The scope of the review was limited to showing 1) the need for modulating cytotoxicity and 2) how cytotoxicity has been controlled in actual studies on treatment plans in vivo and in vitro.

Keywords: Cytotoxicity, in vivo, in vitro, nanotechnology, nanoparticles, apoptosis

Introduction

Cytotoxicity is the action of a cytotoxic compound on a cell that the cell will either undergo necrosis by the loss of the integrity of their membrane, followed by its rapid death, or is guided to the pathway of apoptosis or autophagy1-5. Cytotoxic drugs or cytostatics are used for the treatment of cancer where they destroy the cancer-causing cells. By inhibiting cell division, this process of cell destruction is started. While cytotoxic drugs used to reduce metastases help control the spread of cancer and effectively act upon primary and secondary tumors, the drugs also have an effect on surrounding healthy cells6-12. Effect on normal cells is less pronounced compared to cancer cells, and yet in the case of aggressive tumor conditions, the effect on normal cells is also higher, either killing them or necessitating more time for the healthy cells to recover. In this context, research works aim to identify how cancer can be treated by controlling cytotoxicity. This work reviews the effects of modulating cytotoxicity effects in cancer drug delivery by looking up research works on the same13-19.

Cytotoxicity and Treatment Efficacy

The use of nano-technology based medication delivery has been heralded as an optimal solution for cancer treatment. However, cytotoxicity has to be banked against efficacy. The drug that cures should not be the drug that also induces a new issue. All nanomedicines have some amount of cytotoxicity associated with them and hence the therapeutic effect or treatment efficacy to toxicity should always be monitored and modulated20-24. In vitro and in vivo, studies have been conducted to assess this modulation. It was identified that larger surface areas of treatments with nanoparticles could result in heightened and severe cytotoxicity. Nanoparticles used in cancer treatment in rats showed that it caused lung tumors as a side effect—the cytotoxicity. Smaller nanoparticles hence are considered more toxic than an equivalent chemical compound. Hence cytotoxicity has to be managed.

Managing Cytotoxicity

Han et al., analyze combination cancer therapy in the form of multiple anticancer agents delivered via a nanomicelle amphiphilic dendrimer AmD. This combination cancer therapy with nanotechnology form of delivery was observed to offer reduced cytotoxicity in-vitro and synergetic results for the patient. In-vitro cancer activity was checked on MDA-MB-231 cells with 5-FU/DOX-DNM. The cells were treated with an application of the drug mixture in different amounts. The 5-Fu/DOX-DNM, DOX-DNM, 5-Fu-DNM, free dox, and free 5-Fu were used to stain the cells and absorbance was measured in order to understand cytotoxicity. The drug release time curves were mapped for all the drug forms used at different pH levels and it was identified that Dox and 5-Fu in standalone forms were pH dependent, and only around pH 5.0, the drug was rapid release. The cytotoxicity levels of different formulations are presented below.
The micelle becomes positively charged at the same pH levels and electrostatic repulsion is created in the micelles as well, accelerating drug release. 5-Fu release was faster. The particle size of the 5-Fu/Dox was stable under normal pH conditions. In terms of cellular uptake after releasing it was identified that the 5-Fu/Dox-DNM, 5-Fu-DNM, and Dox-DNM showed a more rapid intake with appropriate intracellular concentrations compared to the free 5-Fu and Dox-DNM group. The use of multiple dendrimeter enhanced cell adhesion and disruption. In-vitro cytotoxicity showed that there was a much lower dose of the free Dox and free 5-Fu as compared against non-combination methods of delivery. The use of the drug-loaded micelles resulted in negligible cytotoxicity because the cells in tested concentration were biocompatible. The cationic dendrimeters furthermore were higher than the anionic dendrimeters and they served to shield the positive charges on dendrimeter surface, hence contribution decreased cytotoxicity. Similar results were also observed in the analysis of acute in-vivo toxicity in dendrimers in melanine-based vehicles of drug delivery.

Kang et al., argue the use of nanotechnology for reduction of cytotoxicity. "Cytotoxicity, distribution and the ability to cross the BBB are some of the most significant obstacles involved in chemotherapy for brain tumors. Nanotechnology has been widely exploited in drug delivery, with a tremendous potential for improving drug efficiency and efficacy". However, the researcher notes that the use of nano-technology could, in fact, result in more cytotoxicity, and hence nano-technology use has to be modulated in the following ways.

Firstly, it can be managed by managing its half-life, as this will decrease the amount of time that the nanoparticles spend in circulation or the short drug half-life can be extended in a targeted way to achieve treatment efficacy. Alternatively, cytotoxicity can be maintained by making use of only those compounds that are not cytotoxic. Elements like phospholipids, chitosan and dextran can be made use of in such situations.

Conclusion

Cytotoxicity is a serious concern when it comes to achieving efficient treatment plans. The very treatment plan for a cancer patient should not turn detrimental to their overall health. The issues in cytotoxicity are heightened in the case of aggressive concerns as well. Targeted deliveries and combination drug treatments are useful in controlling cytotoxic, but they carry a danger as well because all nanomedicines carry a certain amount of inherent toxicity. In this case, it is necessary to understanding how to control for cytotoxicity in treatment and this review focused on the different research evidence on modulation.

References

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