EuroSciCon

17th Edition of International Conference and Exhibition on

Pharmaceutics and Novel Drug Delivery Systems

October 04-06, 2018
Moscow, Russia

Tamara Zwain et al., Int J Drug Dev & Res 2018, Volume 10
DOI: 10.21767/0975-9344-C1-002

Selective targeted therapy of glioblastoma by aptamer functionalised nanostructure lipid carrier: *In-vitro* evaluation in immortalised, primary glioma cell lines and 3D BBB model

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Approximately 54% of all malignant brain tumor patients are diagnosed with glioblastoma (GB). The major clinical challenge in the treatment of GB is the permeation of the blood-brain barrier (BBB). Docetaxel (DTX) is a hydrophobic anticancer drug that is used alone and in combination with other drugs to treat tumors, however, it suffers from the drawback of non-specific cytotoxicity. To address these clinical challenges and improve the therapeutic potential of DTX this project aimed to develop a nanostructure lipid carrier (NLC) loaded with DTX and functionalized with a selective aptamer (SA43) for specific targeting of GBs that can pass the blood-brain barrier (BBB). In this study, the developed DTX-NLC and SA43-DTX-NLC were demonstrating a low particle size and uniform distribution. DTX-NLCs were characterised with high drug content and encapsulation efficiency and stability for up to six months in a freeze-dried form. The functionalized NLCs with the SA43 aptamer (SA43-DTX-NLC) exhibited more toxicity than DTX-NLC when a patient-derived short-term culture (BTNW911) cells line were treated, and similar activity when a grade IV glioblastoma cell lines (U87MG) where treated, interestingly the SA43-DTX-NLC found to be significantly less toxic towards the non-cancerous brain cell lines (SVG P12) when compared with DTX and DTX-NLC. The uptake and internalization results demonstrated the selectivity of SA43-DTX-NLC towards glioblastoma U87MG cells with the highly significant difference in fluorescent intensity when compared to non-cancerous cell line SVG P12. The *in-vitro* BBB model was characterized by high TEER measurements and a significant increase with time (regularly over 260 Ohm/cm^2), indicating that the model was suitable for testing the interaction between the BBB and potential drug candidates. This study displayed the ability of DTX-NLC and SA43-DTX-NLC to permeate through the *in-vitro* BBB model and uptake by glioblastoma U87MG monolayer cells. This study will contribute to solving some of chemotherapeutic drug delivery drawbacks in passing the BBB and targeting brain cancer glioblastoma.

Biography

Tamara Zwain has completed her PhD in the School of Pharmacy and *Biomedical Science*s University of Central Lancashire in the UK. She has worked alongside Professor Kamalinder Singh and Dr Jane Alder in developing nanoparticles and functionalized nanoparticles for novel drug delivery to treat brain cancer and developing a selective treatment for glioblastoma. Also, she has worked in screening nanoparticles and aptamers through 2D cell lines, 3D spheroids and 3D *in-vitro* BBB models and her research interest are developing *in-vitro* 3D models and nanoparticles for novel drug delivery.

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