D-PENICILLAMINE LOADED NANO LIPID CARRIERS FOR TARGETING GLIOBLASTOMA

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Abstract

Glioblastoma is a lethal cancer with a median survival of about 15 months. It is a well-known fact that most Glioblastoma's are rich in collagens. Specifically, the mesenchymal subtype of Glioblastoma, which has the worst prognosis, is enriched with numerous extracellular matrix proteins such as collagens. While collagen accumulation can be viewed as a downstream effect of mesenchymal differentiation, it was found that the feed forward increases in collagen, extracellular matrix stiffness and biomechanical influences cause enhanced self-renewal and mesenchymal transition in glioma stem cells with a consequent increase in treatment resistance of these cells. Further, recent studies have also shown that mechanical stress plays an overarching role in the regulation of TAZ signalling. TAZ is a mediator of mesenchymal differentiation in glioma, which relates with collagen stiffness, promotes mesenchymal transition and gliomagenesis via TAZ signalling. D-penicillamine is a known inhibitor of collagen maturation, which acts by increasing the conversion of insoluble to soluble collagen and disrupting the formation of intermolecular bonds. The therapeutic benefit of D-penicillamine has not been extensively evaluated in Glioblastoma especially in the context of glioma stem cells, which represent faithful models of this disease. Directing therapeutic agents such as D-penicillamine towards deeply embedded brain tumours with biophysical barriers such as blood brain barrier and collagen remains a challenge. Hence, in the present study it is proposed to load D-penicillamine into Nano lipid carriers, which can accumulate passively in tumours via leaky tumour vasculature, caused by focused ultrasound. These triggered release strategies disrupt the blood brain barrier, confirming deep penetration in tumours, and overcome the biophysical constraints, which tackle both the challenges (drug delivery and collagen disruption) simultaneously.

Keywords: Collagen, D-penicillamine, Glioblastoma, Mesenchymal

Professional Biography

Mr. B. Mahendran is currently pursuing his PhD in Pharmaceutical Sciences in the interdisciplinary area of Molecular Oncology at JSS University, Mysuru, India. He completed his M. Pharmacy from JSS University, Mysuru with University gold medal and he is the recipient of Indian Pharmaceutical Association Gold medal for two consecutive years for his excellence in academics. He also received best outgoing student award in his B. Pharmacy. He has received best poster award for his presentation in a national level seminar. He has published 06 papers in reputed journals and has been serving as a reviewer of Journal of Drug Research and Development.



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Any Comments: