ABSTRACT

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Drug delivery in glioblastoma therapy: a review on nanoparticles targeting MGMT-mediated resistance.

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INTRODUCTION: Glioblastoma multiforme (GBM) is the deadliest type of brain cancer with poor response to the available therapies, mainly due to intrinsic resistance mechanisms. Chemotherapy is based on alkylating agents, but DNA-repair mechanisms can revert this cytotoxic effect. O6-methylguanine-DNA methyltransferase (MGMT) protein is the primary mechanism for GBM resistance. Therefore, different strategies to suppress its activity have been explored. However, their clinical use has been hindered due to the high toxicity of MGMT inhibitors verified in clinical trials.

AREAS COVERED: This review article aims to provide the current progress in the development of novel drug delivery systems (DDS) to overcome this resistance. Here, we also review the current knowledge on MGMT-mediated resistance and the clinical outcomes and potential risks of using MGMT inhibitors.

EXPERT OPINION: To overcome therapeutic limitations, nano-based approaches have been proposed as a suitable solution to improve drug accumulation in the brain tumor tissue and decrease systemic toxicity. DDS to overcome MGMT-mediated resistance in GBM have been mostly developed to deliver MGMT inhibitors and for gene therapy to modulate MGMT gene expression.

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