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# Nanosystems at Nexus: Navigating Nose-to-Brain Delivery for Glioblastoma Treatment

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## Abstract

Glioblastoma multiforme (GBM) is considered to be one of the most devastating brain tumors with a shorter life expectancy. Several factors contribute to the dismal prognosis of GBM patients including the complicated nature of GBM, the ability of tumor cells to resist treatment, and the difficulty of delivering drugs to the brain because of barriers like the blood-brain barrier (BBB) and blood-tumor barrier (BTB). The unique challenges posed by the BBB in delivering therapeutic agents to the brain have led to the development of innovative nanotechnology-based approaches. By exploiting the olfactory/trigeminal pathway, nanosystems offer a promising strategy for targeted drug delivery to the brain, glioblastoma tumors in particular. This review contemplates varied nanocarriers, including polymeric nanoparticles, lipid-based nanosystems, in situ gel formulations, peptide, and stem cell-based nanoformulations, signifying their utility in brain targeting with minimal systemic side effects. Emerging trends in gene therapy and immunotherapy in the context of GBM treatment have also been discussed. Since safety is a paramount aspect for any drug product to get approved, this review also delves into toxicological considerations associated with intranasal delivery of nanosystems. Regulatory aspects and critical factors for the successful development of intranasal products are also explored in this review. Overall, this review underscores the significant advancements in nanotechnology for nose-to-brain delivery and its potential impact on GBM management.

**Keywords:** glioblastoma; immunotherapy; nanoparticles; nose-to-brain delivery; toxicity.

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