TMZ-BioShuttle – a reformulated Temozolomide

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ABSTRACT

There is a large number of effective cytotoxic drugs whose side effect profile, efficacy, and long-term use in man are well understood and documented over decades of use in clinical routine e.g. in the treatment of recurrent glioblastoma multiforme (GBM) and the hormone-refractory prostate cancer (HRPC). Both cancers are insensitive against most chemotherapeutic interventions; they have low response rates and poor prognoses. Some cytotoxic agents can be significantly improved by using modern technology of drug delivery or formulation. We succeeded to enhance the pharmacologic potency with simultaneous reduction of unwanted adverse reactions of the highly efficient chemotherapeutic temozolomide (TMZ) as an example. The TMZ connection to transporter molecules (TMZ-BioShuttle) resulted in a much higher pharmacological effect in glioma cell lines while using reduced doses. This permits the conclusion that a suitable chemistry could realize the ligation of pharmacologically active, but sensitive and highly unstable pharmaceutical ingredients without functional deprivation. The re-formulation of TMZ to TMZ-BioShuttle achieved a nearly 10-fold potential of the established pharmacaceutic TMZ far beyond the treatment of brain tumors cells and results in an attractive reformulated drug with enhanced therapeutic index.

Keywords: BioShuttle, Carrier Molecules, Drug Delivery, facilitated Transport, Glioblastoma multiforme (GBM), Reformulation, Temozolomide (TMZ)