Temozolomide is the first line alkylating agent used for the treatment of glioblastoma multiforme and refractory anaplastic astrocytoma. High dose of temozolomide is required to achieve therapeutic level of drug in brain due to its short half-life. Blood-brain barrier (BBB) and brain-tumor barrier (BTB) check the entry of drug to the tumor, resulting in low concentration at the site. To overcome this higher doses are to be administered. This leads to toxicity, high cost burden and other disadvantages. Literature review suggested that colloidal carrier is one of the best approaches to achieve overcome the barrier in brain targeting. Nanosupension, being simple in its nature and preparation, offers an option to achieve brain concentrations. The modulation of tight junction proteins expressed on the BBB and BTB suggested one more approach. Claudin-5 is a tight junction protein, which predominantly expresses on BBB. The protein can be targeted to modulate BBB and improve the drug delivery through paracellular pathway.

The present study was aimed to adopt a simple and affordable approach to increase the drug penetration to glioma. The nanosuspensions of temozolomide were prepared using combination technology and using claudin (BBB) modulator. The prepared nanosuspensions were evaluated for in vitro permeability and cytotoxicity assays. The optimized nanosuspensions were further evaluated for improved brain permeability, toxicity and therapeutic activities in animals. The prepared nanosuspensions showed increased cellular uptake and increased brain concentration in animal pharmacokinetics study. The optimized nanosuspensions also showed tumor regression in C6 glioma model.