






# Nose-to-brain delivery of teriflunomide-loaded lipid-based carbopol-gellan gum nanogel for glioma: Pharmacological and *in vitro* cytotoxicity studies

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## Abstract

The research work was intended to formulate teriflunomide (TFM) loaded nano lipid-based (TNLC) carbopol-gellan gum *in situ* gel (TNLCGHG) and to investigate its therapeutic efficacy against glioma, a brain and spine tumor. Nanoformulation was developed using gellan gum and carbopol 974P as gelling and mucoadhesive agents, respectively, Glyceryl di-behenate and Glyceryl mono-linoleate blend as lipids, and Gelucire 44/14: water blend as surfactant system. Globule size, PDI, zeta potential, encapsulation efficiency, mucoadhesive strength, and nasal permeation were found to be 117.80 nm, 0.56, -21.86 mV, 81.16%, 4.80 g, and 904  $\mu\text{g}/\text{cm}^2$ , respectively. Anticancer efficacy of TFM-loaded nano lipid-based carbopol-gellan gum *in situ* gel (TNLCGHG) was determined in human U-87MG glioma cell line.  $\text{IC}_{50}$  was found 7.0  $\mu\text{g}/\text{mL}$  for TNLCGHG, 4.8  $\mu\text{g}/\text{mL}$  for pure TFM, and 78.5  $\mu\text{g}/\text{mL}$  for TNLC, which approve the superiority of surfactant along with gellan gum as permeation enhancer. Brain  $C_{\text{max}}$  for technetium ( $^{99\text{m}}\text{TC}$ ) labeled intranasal (*i.n.*)  $^{99\text{m}}\text{TC}$ -TNLCGHG was found 2-folds higher than  $^{99\text{m}}\text{TC}$ -TNLC (*i.n.*) and  $^{99\text{m}}\text{TC}$ -TNLC intravenous (*i.v.*) because the TNLCGHG formulation contains surfactant with natural gelling polymers, which promisingly improved drug permeability. Finally, this research revealed encouraging outcomes and successfully developed intranasal TNLCGHG nanoformulation as a novel tool for safe delivery of TFM in glioma patients.