ABSTRACT

Pharmacol Rep. 2022 Jan 20. doi: 10.1007/s43440-021-00349-6. Online ahead of print.

How do phosphodiesterase-5 inhibitors affect cancer? A focus on glioblastoma multiforme.

Sanati M(1), Aminyavari S(2), Mollazadeh H(3), Bibak B(3), Mohtashami E(4), Afshari AR(5).

Author information:

(1)Department of Pharmacology and Toxicology, Faculty of Pharmacy, Birjand University of Medical Sciences, Birjand, Iran.

(2)Department of Neuroscience and Addiction Studies, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran.
(3)Department of Physiology and Pharmacology, Faculty of Medicine, North Khorasan University of Medical Sciences, Bojnurd, Iran.

(4)Pharmacological Research Center of Medicinal Plants, Mashhad University of Medical Sciences, Mashhad, Iran.

(5)Department of Physiology and Pharmacology, Faculty of Medicine, North Khorasan University of Medical Sciences, Bojnurd, Iran. AR.afshari@nkums.ac.ir.

Since the discovery of phosphodiesterase-5 (PDE5) enzyme overexpression in the central nervous system (CNS) malignancies, investigations have explored the potential capacity of current PDE5 inhibitor drugs for repositioning in the treatment of brain tumors, notably glioblastoma multiforme (GBM). It has now been recognized that these drugs increase brain tumors permeability and enhance standard chemotherapeutics effectiveness. More importantly, studies have highlighted the promising antitumor functions of PDE5 inhibitors, e.g., triggering apoptosis, suppressing tumor cell growth and invasion, and reversing tumor microenvironment (TME) immunosuppression in the brain. However, contradictory reports have suggested a pro-oncogenic role for neuronal cyclic guanosine monophosphate (cGMP), indicating the beneficial function of PDE5 in the brain of GBM patients. Unfortunately, due to the inconsistent preclinical findings, only a few clinical trials are evaluating the therapeutic value of PDE5 inhibitors in GBM treatment. Accordingly, additional studies should be conducted to shed light on the precise effect of PDE5 inhibitors in GBM biology regarding the existing molecular heterogeneities among individuals. Here, we highlighted and discussed the previously investigated mechanisms underlying the impacts of PDE5 inhibitors in cancers, focusing on GBM to provide an overview of current knowledge necessary for future studies.

 $\ensuremath{\mathbb{O}}$ 2022. The Author(s) under exclusive licence to Maj Institute of Pharmacology Polish Academy of Sciences.

DOI: 10.1007/s43440-021-00349-6 PMID: 35050491