

## ABSTRACT

Curr Pharm Des. 2022 Jun 3. doi: 10.2174/1381612828666220603152918. Online ahead of print.

Temozolomide: an Overview of Biological Properties, Drug Delivery Nanosystems, and Analytical Methods.

Dutra JAP(1), Luiz MT(2), Tavares Junior AG(1), Di Filippo LD(1), Carvalho SG(1), Chorilli M(1).

Author information:

(1)School of Pharmaceutical Science of Sao Paulo State University (UNESP), Araraquara, Sao Paulo, Brazil.

(2)School of Pharmaceutical Science of Ribeirao Preto, University of Sao Paulo (USP), Ribeirao Preto, São Paulo, Bra-zil.

Temozolomide (TMZ) is an imidazotetrazine prodrug used to treat glioblastoma multiforme. Its physicochemical properties and small size confer the ability to cross the blood-brain barrier. The antitumor activity depends on pH-dependent hydrolysis of the methylidiazonium cation, which is capable of methylating purine bases (O6-guanine; N7-guanine, and N3-adenine) and causing DNA damage and cell death. TMZ is more stable in acidic media ( $\text{pH} \leq 5.0$ ) than in basic media ( $\text{pH} \geq 7.0$ ) due to the protonated form that minimizes the catalytic process. Because of this, TMZ has high oral bioavailability, but it has a half-life of 1.8 h and low brain distribution (17.8%), requiring a repeated dosing regimen that limits its efficacy and increases adverse events. Drug delivery Nanosystems (DDNs) improve the physicochemical properties of TMZ and may provide controlled and targeted delivery. Therefore, DDNs can increase the efficacy and safety of TMZ. In this context, to ensure the efficiency of DDNs, analytical methods are used to evaluate TMZ pharmacokinetic parameters, encapsulation efficiency, and the release profile of DDNs. Among the methods, high-performance liquid chromatography is the most used due to its detection sensitivity in complex matrices such as tissues and plasma. Micellar electrokinetic chromatography features fast analysis and no sample pretreatment. Spectrophotometric methods are still used to determine encapsulation efficiency due to their low cost, despite their low sensitivity. This review summarizes the physicochemical and pharmacological properties of free TMZ and TMZ-loaded DDNs. In addition, this review addresses the main analytical methods employed to characterize TMZ in different matrices.

Copyright© Bentham Science Publishers; For any queries, please email at [epub@benthamscience.net](mailto:epub@benthamscience.net).

DOI: 10.2174/1381612828666220603152918

PMID: 35658888