

Abstract

# Inhibitors of the Inducible Nitric Oxide Synthase as Antiglioma Agents <sup>†</sup>

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Malignant gliomas are highly lethal brain tumors with poor prognosis for patients. The current treatment of glioma consists of maximal surgical resection of the tumor, followed by concurrent chemotherapy (temozolomide, TMZ) and radiation. However, chemotherapy resistance is a major cause of treatment failure.

In general, high levels of reactive oxygen species (ROS) and reactive nitrogen species (RNS) are highly involved in the malignancy of gliomas as well as in chemoresistance, due to the activation of different signaling mediators. In this context, the dysregulated production of the free radical nitric oxide (NO) by inducible nitric oxide synthase (iNOS) plays a recognized role, and NO inhibition can be considered an emerging therapeutic possibility to treat gliomas [1].

From the development of the acetamidine 1400 W, we recently identified a new small potent molecule, able to selectively inhibit iNOS in rat glioma cells without interacting with the constitutive NOS isoforms [2]. This agent compromises the adaptive responses in glioma cells involved in chemoresistance, enhancing the effects of TMZ [3]. As part of this ongoing project, a new set of acetamidines was synthesized, and the biological results of these molecules will be discussed from a medicinal chemistry viewpoint.

## References

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