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Design, synthesis, molecular docking and pharmacological evaluation of novel triazine-based triazole derivatives as potential anticonvulsant agents

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ABSTRACT

Triazine-linked triazole compounds (**4a-j**) were designed, synthesized, and then examined for their anticonvulsant abilities. Compounds **4e**, **4f**, **4g**, **4i**, and **4j** displayed significant anticonvulsant activity in both maximum electroshock seizure (MES) and pentylenetetrazole (PTZ) induced seizure during the preliminary screening. The phase II anticonvulsant activity statistics revealed that compounds **4e**, **4f**, **4g**, **4i**, and **4j** demonstrated excellent activity as compared to the conventional drugs methaqualone and valproate, supporting the potential of these triazine-linked triazole analogues as novel anticonvulsant agents. To take use of the findings, computational parameters including docking analysis and drug-likeness prediction were carried out. Molecular modelling studies supported the essential pharmacophoric information that the structure activity relationship offered. The triazine-linked triazole analogues that were investigated might be viewed as helpful models for future research and derivatization.

The ailment known as epilepsy is a diverse set of conditions defined by episodes of sensory, motor, or autonomic phenomena with or without loss of consciousness [1]. Epilepsy is also characterized by neuronal hyperexcitability and hypersynchronous neuronal activity. A significant section of the world's population is afflicted by this disease, which is chronic and progressive and is characterized by recurrent seizures in many different forms. The quality of life of epilepsy sufferers is negatively impacted by severe psychological effects as well as financial consequences [2]. The main factor in reducing the emotional and financial implications of this condition is effective seizure management. Convulsions are still insufficiently managed by current medication therapy in 30 % of epileptics, despite substantial advancements in epilepsy research [3]. Refractory epilepsy still has important clinical demands, and currently available medicines are ineffective enough to treat it. The traditional AEDs as well as a number of more modern medications have both been used to treat epilepsy recently. Despite the fact that these medications have been demonstrated to reduce partial and generalized seizures in a number of individuals with epileptic syndromes [4]. Despite the availability of sophisticated anti-epileptic drugs (AEDs), a number of challenges remain for researchers, including dose-related toxicity, adverse medication responses that can be fatal, as well as patient resistance to well-established AEDs [5,6]. The ongoing quest for safer and more potent antiepileptic medications is both necessary and challenging in medicinal chemistry in light of the aforementioned considerations.

Numerous authors tried to pinpoint the structural elements essential for anticonvulsant action while taking the aforementioned restrictions into account. Several pharmacophoric models have been described as a result of these studies, allowing for a more logical design of novel anticonvulsants. As a result, the nitrogen heterocyclic system [7,8], which is often connected to the heterocyclic system with phenyl or alkyl groups, is one of the key core pieces of anticonvulsants. The architecture of both older and more modern AEDs has this common framework [9]. There are several synthesized *N*-heterocyclic compounds that have been

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