Central Nervous System Agents in Medicinal Chemistry, 2016, *16*, 240-248

Schiff Bases of Benzothiazol-2-ylamine and Thiazolo[5,4-*b*] pyridin-2-ylamine as Anticonvulsants: Synthesis, Characterization and Toxicity Profiling

Rashmi Shukla[1], Ajeet P. Singh[2], Pankaj K. Sonar[1], Mudita Mishra[2] and Shailendra K. Saraf[1*]

[1]*Division of Pharmaceutical Chemistry, Faculty of Pharmacy, Babu Banarasi Das Northern India, Institute of Technology, Lucknow-227105, Uttar Pradesh, India;* [2]*Division of Pharmacology, Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology, Lucknow-227105, Uttar Pradesh, India*

S.K. Saraf

Abstract: ***Background***: Schiff bases have a broad spectrum of biological activities like anti-inflammatory, analgesic, antimicrobial, anticonvulsant, antitubercular, anticancer, antioxidant, anthelmintic and so forth. Thus, after a thorough perusal of literature, it was decided to conjugate benzothiazol-2-ylamine/thiazolo [5, 4-*b*] pyridin-2-ylamine with aromatic and heteroaromatic aldehydes to get a series of Schiff bases.

Objective: Synthesis, characterization, in-silico toxicity profiling and anticonvulsant activity of the Schiff bases of Benzothiazol-2-ylamine and Thiazolo [5, 4-*b*] pyridin-2-ylamine.

Method: Aniline/4-aminopyridine was converted to the corresponding thiourea derivatives, which were cyclized to obtain benzothiazol-2-ylamine/thiazolo [5, 4-*b*] pyridin-2-ylamine. Finally, these were condensed with various aromatic and heteroaromatic aldehydes to obtain Schiff bases of benzothiazol-2-ylamine and thiazolo [5, 4-*b*] pyridin-2-ylamine. The synthesized compounds were characterized and screened for their anticonvulsant activity using maximal electroshock (MES) test and isoniazid (INH) induced convulsions test. In-silico toxicity profiling of all the synthesized compounds was done through "Lazar" and "Osiris" properties explorer.

Results: Majority of the compounds were more potent against MES induced convulsions than INH induced convulsions. Schiff bases of benzothiazol-2-ylamine were more effective than thiazolo [5, 4-*b*] pyridin-2-ylamine against MES induced convulsions. The compound benzothiazol-2-yl-(1*H*-indol-2-ylmethylene)-amine (*VI*) was the most potent member of the series against both types of convulsions.

Conclusion: Compound *VI* exhibited the most significant activity profile in both the models. The compounds did not exhibit any carcinogenicity or acute toxicity in the in-silico studies. Thus, it may be concluded that the Schiff bases of benzothiazol-2-ylamine exhibit the potential to be promising and non-toxic anticonvulsant agents.

Keywords: Anticonvulsant, benzothiazol-2-ylamine, INH, Lazar, MES, osiris, schiff base, thiazolo [5,4-*b*] pyridin-2-ylamine.

Received: April 01, 2016 **Revised: April 22, 2016** **Accepted: April 22, 2016**

1. INTRODUCTION

Epilepsy is a common neurological condition, affecting 0.5-1% of the population worldwide [1]. It refers to a clinical phenomenon rather than a single disease entity, since there are many forms and causes of epilepsy [2]. It is often a chronic and progressive disorder characterized by periodic and unpredictable occurrence of epileptic seizures, which are caused by abnormal discharge from cerebral neurons [3]. Antiepileptic drugs appear to act primarily by blocking the initiation or spread of seizures. This occurs through a variety of mechanisms that modify the activity of ion-channels or neurotransmitters, and in most cases drugs have pleiotropic effects. The anti-seizure drugs act mainly by three mechanisms: calcium channel blocking, sodium channel blocking, and GABA mediated chloride channel opening. Other mechanisms that may operate with some drugs are inhibition of glutamate release and block of glutamate receptors [4, 5]. The search for antiepileptic compounds with better activity continues to be an area of investigation. A rational drug design process to a new anticonvulsant can be achieved in several ways. The first strategy is the identification of new targets through better understanding of molecular mechanisms of epilepsy. Another way is to modify already existing drugs and formulations [1].

*Address correspondence to this author at the Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology, Sector-2, Dr. Akhilesh Das Nagar, Faizabad Road, Lucknow, 227105, U.P., India; Tel: +91-522-3911052; +919839228022; Fax: +91-522-3911111;
E-mail: dirpharmniec@gmail.com

1875-6166/16 $58.00+.00