Molecular Pharmaceutics & Organic Process Research

ISSN: 2329-9053

Extended Abstracts Vol 8, Iss2

Synthesis and screening of new indole derivatives as anticonvulsant agents

Konda Swathi, Manasa Cidda and Manda Sarangapani, Kakatiya University, India
Email: kswathi84@yahoo.co.in

ABSTRACT

Isatin is an endogeneous compound isolated in 1998 and reported to possess a good range of central systema nervosum activities. Surendranath pandya et al. reported the synthesis and anticonvulsant activity of some novel n-methyl/acetyl, 5-(un)-substituted isatin-3-semicarbazones. In the previous couple of years, Isatin derivatives are discovered which show potential hypnotic, antibacterial and MAO inhibitory activity. It is evident from the literature survey that Isatin derivatives dialkylamino alkyl derivatives showing brighter central systema nervosum and anticonvulsant activities. In the present work, some new 5-[2(3)-dialkylamino alkoxy] Indole 2, 3-diones were prepared from 5-hydroxy isatin. The structures of the products were characterized by IR, NMR and MASS Spectral studies. All the compounds were evaluated for anticonvulsant effect by MTT assay method. Some of these compounds showed good anticonvulsant activity compared with standard compounds. The compounds were mostly synthesized by conventional methods and described in experimental selection and also by the methods established in our laboratory. A new series of 5 5-[2(3)-dialkyl amino alkoxy] Indole 2,3 dione derivatives were synthesized by reacting 5-hydroxyindole 2,3 dione with 2-N,N di alkylamino alkyl halides. Evaluation of those compounds as anticonvulsants, activity revealed that the compounds (IIIa,IIIb) with a dimethyl and diethyl amino ethyl chain derivatives was found to be relatively superior in anticonvulsant activity and other compounds (IIIc, IIId, IIIe) are next in the order of activity. All the compounds showed less neurotoxicity compared to Diazepam.

The discovery of new effective drugs for the treatment of depression still remains a top priority as it affects approximately 21% of the world population. The World Health Organization (WHO) forecasts that; it will be the second leading cause of death by the year 2020 owing to complications arising from stress and the cardiovascular system Depression is a chronic,

recurring and potentially life-threatening serious illness characterized by persistent feelings of sadness, hopelessness, pessimism, guilt, loss of interest in activities and decreased energy. Conventionally, decreased levels of brain monoamines like norepinephrine, serotonin and dopamine are considered responsible for depression. Recent antidepressant agent increases the synaptic concentration of either two (5-HT and NE) or all three (5-HT, NE and dopamine (DA) neurotransmitters .Convulsions or epilepsy is a chronic neurological disorder characterized by the periodic and unpredictable occurrence of seizures that affects the people of all ages with the incidence of 3% in the population At present, available antiepileptic drugs (AEDs) provide ample seizure controls in many patients, still about 28–30% of patients are estimated to be poorly treated These drugs have proven to be effective in reducing convulsions as well as depression, at the same time their therapeutic efficacy is conquered by some undesirable side effects These observations of existing drugs, along with the sharp rise of depressive and convulsion cases in today's scenario, prompted research in the field of antidepressant and anticonvulsant as a major thrust area. Antidepressants and anticonvulsants are amongst the most widely utilized drugs for the treatment of CNS disorders .Indole, the most useful heterocyclic nucleus has gained prominence in medicinal chemistry due to its diverse biological activities Several studies have demonstrated the antidepressant potential of indole derivatives Similarly numerous indole derivatives are reported to exhibit potent The 2-pyrazolines can be considered as a cyclic hydrazine moiety and are considered as an important heterocyclic scaffold for the development of potential antidepressant and anticonvulsant agents. Pyrazoline derivatives were achieved via treatment of chalcones (α,β-unsaturated ketones) with hydrazine derivatives. Pyrazoline nucleus has been reported to possess various pharmacological activities. So far, various substituted pyrazoline derivatives have been synthesized and investigated for their antidepressant and anticonvulsant activities and found high activity. Prasad et al. and Parmar et al., had reported the

This work is partly presented at 16th International Conference and Exhibition on Pharmaceutical Formulations July 26-27,2018

synthesis and antidepressant and anticonvulsant activity of 1,3,5 triphenyl 2-pyrazoline derivatives. Promising antidepressant or anticonvulsant activity of some pyrazoline derivatives prompted us to research them further. However, a pyrazoline ring has not appeared to be linked with indole so far. It was hypothesized that the combination of both chemical systems in one compound with a cyclic hydrazine moiety, which is prerequisite for antidepressant and anticonvulsant activity, may prove to be a breakthrough for the development of the lead molecule for future antidepressant and anticonvulsant research. These findings motivated us to link various heterocyclic moieties to synthesize a new series of pyrazoline derivatives by combining the indole moiety at the 5th position in order to evaluate the effect of this substitution on antidepressant and anticonvulsant activity. Based on the above mentioned facts, and in continuation with our research on new heterocyclic scaffold as an antidepressant .in the proposed study we aim to investigate whether indolyl pyrazoline derivatives show antidepressant and anticonvulsant activity using the forced swimming and scPTZ test, respectively.

n summary, we have reported a simple, eco-friendly, high yielding microwave assisted method for the synthesis of indolyl pyrazoline derivatives, as a novel candidate for antidepressant as well as anticonvulsant. Compounds 2b, 2e and 2k induced amazing antidepressant activity compared to standard drugs at the dose of 20 mg/kg. Other compounds 2f, 2i and 2j furnished good antidepressant activity. Generally, derivatives with an electron donating group on the phenyl ring of indolyl pyrazoline possess remarkable antidepressant activity. Moreover, compounds 2c and 2d revealed the most protective class of the tested compounds against clonic seizures induced by scPTZ. It is worth aphorism that the compounds having electron withdrawing substituent at the phenyl ring of indolyl pyrazoline exhibited a remarkable anticonvulsant activity. Consequently, such compounds would signify a fruitful matrix for the development of a new class of anticonvulsant and antidepressant agent and would warrant further investigation and derivatization as a promising scaffold.

Keywords: Pyrazoline, Microwave assisted synthesis, Anticonvulsan, tIndole, Antidepressant