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ORIGINAL RESEARCH

Novel 2-pyrazoline derivatives as potential anticonvulsant agents

Shradha Bhandari · Avinash C. Tripathi · Shailendra K. Saraf

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Abstract A series of new 2-pyrazoline derivatives has been synthesized by reacting 3-(substituted-phenyl)-1-pyridin-2-yl-propenones using two routes one using thiosemicarbazide and the other by hydrazine hydrate. The chemical structures were established by IR, Mass, ^{1}H-NMR, ^{13}C-NMR spectroscopic data, and elemental analysis. The anticonvulsant activity of the synthesized compounds was evaluated by the "maximal electroshock seizure" (MES) test and pentylenetetrazole (PTZ) test using male albino mice. Compounds **2e,** 5-(naphthalene-1-yl)-3-(pyridine-2-yl)-4,5-dihydro-1*H*-pyrazole-1-carbothioic acid amide, and **3c,** *N*-ethyl-5-(naphthalene-1-yl)-3-(pyridine-2-yl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide showed appreciable activity in the MES as well as PTZ test at all the evaluated doses.

Keywords 2- Pyrazolines · Anticonvulsant activity · Claisen-Schmidt condensation · MES test · PTZ test

Introduction

Epilepsy is the most frequent neurologic affection, characterized by excessive temporary neuronal discharge, which may be due to a number of different causes leading to epileptic seizures (Jones, 2002). The overall prevalence of the disease is 0.5–1.0 % of the population and up to 50 million people worldwide (Lowenstein *et al.,* 2005). The anti-seizure drugs act mainly by three mechanisms: calcium channel blocking, sodium channel blocking, and GABA mediated potassium channel opening (Kwan *et al.,* 2001).

The interest in pyrazoles stemmed from their applications in drugs, dyes, and as anesthetics. Pyrazolines are less stable than the corresponding pyrazoles but can be converted into the latter using mild oxidizing agents, such as bromine or lead tetra-acetate (Vardanyan and Hruby, 2006). Increasing evidence suggests that pyrazoline derivatives possess a broad spectrum of biological activities such as antimicrobial, anticancer, tranquilizing, muscle relaxant, antidepressant, monoamine oxidase inhibitory (MAOI), anticonvulsant, anti-hypertensive, anti-inflammatory, and anti-amebic (Agrawal *et al.,* Online First, 16 November 2011; Rahman and Siddiqui, 2010; Bhatia *et al.,* 2010; Stirrett *et al.,* 2008; Revanasiddappa *et al.,* 2010; Dawane *et al.* 2010; Ghorab *et al.,* 2010; Palaska *et al.,* 2001; Rajendra Prasad *et al.,* 2005; Ozdemir *et al.,* 2007, 2008; Jayaprakash *et al.,* 2008; Ruhoglu *et al.,* 2005; Parmar *et al.,* 1974; Guniz Kucukguzel *et al.,* 2000; Turan-Zitouni *et al.,* 2000; Amir *et al.,* 2008; Rani *et al.,* 2004; Budakoti *et al.,* 2007; Budakoti *et al.,* 2008). Nowadays, the therapeutic interest of MAOIs falls into two major categories. MAO-A inhibitors have been used mostly in the treatment of mental disorders, in particular depression, anxiety, and convulsion; and MAO-B inhibitors which could be used in the treatment of Parkinson's disease and Alzheimer's disease (Bortolato *et al.,* 2008; Youdim *et al.,* 2006). The classical period of the MAO-inhibitors started with hydrazine derivatives and 2-pyrazolines can be considered as cyclic hydrazine moieties, reported to have MAO inhibitory, anti-depressant, and anticonvulsant activity (Ozdemir *et al.,* 2007, 2008; Manna *et al.,* 1998, 2002; Chimenti *et al.,* 2004,

S. Bhandari · A. C. Tripathi · S. K. Saraf (✉)
Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology, BBD City, Faizabad Road, Chinhut, Lucknow 227105, U.P., India
e-mail: dirpharmniec@gmail.com

S. Bhandari
e-mail: shradhapharma@gmail.com

A. C. Tripathi
e-mail: aviniec31@gmail.com

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