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REVIEW ARTICLE

Recent Updates on Pyrazoline Derivatives as Promising Candidates for Neuropsychiatric and Neurodegenerative Disorders

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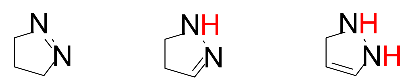
Abstract: Pyrazolines are five-membered heterocyclic compounds containing two nitrogen atoms that represent a privileged scaffold for various bioactive compounds with diverse pharmacological activities. Chalcones and hydrazine derivatives are excellent precursors for pyrazolines, which provide easy access for fabricating the pyrazoline ring at *N*1, C3 and C5 positions that give rise to a wide range of pyrazoline designs. In addition, this method institutes a new asymmetric center at C5 position and extent of the conjugation between phenyl group at C3 position to *N*1 that could greatly enhance the physicochemical and pharmacological properties towards the target enzymes and hence they are reported to have a wide spectrum of biological activities such as anti-cancer, anti-inflammatory, *etc*. Most importantly, they have remarkable effects on the central nervous system (CNS). Several reports show that the pyrazoline derivatives have a significant inhibitory effect towards the monoamine oxidase enzymes (MAOs), which are known to be responsible for neurodegenerative disorders. These enzymes have two isoforms, namely MAO-A and MAO-B which are, in particular, responsible for psychiatric and neurological disorders, respectively. Chalcones are generally potential and more selective inhibitors towards MAO-B isoform whereas pyrazolines derived from chalcones mostly turned into selective inhibitors of MAO-A isoform may be due to the presence of two nitrogen heteroatoms. Therefore, these two derivatives have received much attention from medicinal chemists as they could solve entire CNS-related issues; however pyrazolines have not been studied as much as chalcones. Our group already documented the importance of pyrazolines towards MAO-A inhibition in 2013. With their growing importance, several studies on pyrazolines have constantly been reported for their MAO inhibitions. Therefore, in this review, we report up-to-date developments (after 2014) on pyrazolines as potential MAO inhibitors.

Keywords: Pyrazolines, MAO-A, Chalcones, MAO-B, SAR, Hydrazines.

1. INTRODUCTION

Pyrazolines are partially hydrogenated analogues of pyrazoles with the three tautomeric forms such as 1-pyrazoline, 2-pyrazoline and 3-pyrazoline as shown in Fig. (**1**). Amongst, 2-pyrazolines are being paid much importance due to their stability and ease of synthesis [1]. The semi-saturated nature of the pyrazoline core obtained from chalcones and hydrazines provides a room for diverse substitution patterns with a stereocenter at 5-position as shown in Fig. (**2**) [2]. Usually the substitution portrayed on pyrazoline framework on N1, C3, and C5 positions with a variety of aliphatic or substituted aromatic/heteroaromatic pharmacophores would allow accessing a wide variety of derivatives [3]. Numerous reports suggested that 2-pyrazolines can be obtained chemically by the cyclization reaction of α,β-unsaturated ketones (chalcones) with hydrazine derivatives or cycloaddition reactions of azomethine imines [4, 5].



(I) (II) (III)

Fig. (1). Three tautomeric forms of pyrazoline: 1-pyrazoline (**I**), 2-pyrazoline (**II**), and 3-pyrazoline (**III**).

The 3,5-diaryl-4,5-dihydro-1*H*-pyrazole and its derivatives are representative of the 2-pyrazoline class and many researchers largely focused on the extensive structural manipulations on C3 and C5 positions by designing the starting chalcones structure and *N*1 position the pyrazoline core preferably by late stage functionalization of NH group (Fig. **2**) [6].

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