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Some Bioactivities of Heterocyclic Compounds Containing Pyrazoline Moiety – A Short Review

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Abstract: Current research on chemistry of heterocyclic compounds is particularly focused on the development of diversity-oriented molecules containing nitrogen atom in the form of pyrazoline. Although less familiar than pyrazoles, they have shown to exhibit appreciable biological activities. This review highlights some pyrazoline compounds as promising agents for antioxidant, antitrypanosomal, antitubercular, antitumor and MAO inhibitor.
Keywords : heterocyclic compound, biological activities, pyrazoline.

1. Introduction

Among the nitrogen heterocycles, 4,5-dihydro-1*H*-pyrazole (pyrazoline)derivative compounds possessed a wide spectrum of bioactivities[1]. They have known as potent anticancer[2,3], antioxidant[4] and antitumor[5]agents. In short, the pyrazoline skeleton plays an important role as building block for the construction of a variety of biologically active compounds. This paper summarizes the activity of pyrazoline derivatives as potent antioxidant, antitrypanosomal, antitubercular, antitumor and MAO inhibitor.

2. Bioactivities

2.1 Antioxidant

To develop future applicable antioxidative agents, a novel series of trisubstituted thiophenyl-1-thiazolyl-2-pyrazoline derivatives were synthesized and investigated for their xanthine oxidase inhibitory activity and free radical scavenging performance against DPPH radical[6]. The result highlighted that compound **(1)** showed comparable inhibitory activity to allopurinol with IC_{50} value of 6.2 μM. Moreover, it was denoted as the best free radical scavenger with IC_{50} of 15.6 μM, close to positive control, ascorbic acid (IC_{50} = 11.5 μM). Pharmacological evaluation as antioxidant of some synthesized fluorine containing hydroxypyrazoline derivatives was done by Dinesha *et al.*[7]. Analogues of 1,3,5-trisubstituted aryl-5-hydroxypyrazoline bearing 3-fluoro-4-methoxyphenyl moiety were tested for DPPH radical scavenging activity. The maximum scavenging performance has been shown by compound **(2)** with IC_{50} value of 16.08 μg/mL. Structure-activity relationship revealed that the presence of electron-donating and halo functionalities increased antioxidant activity. A novel class of antioxidant based 3-(benzofuran-2-yl)-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole structure was

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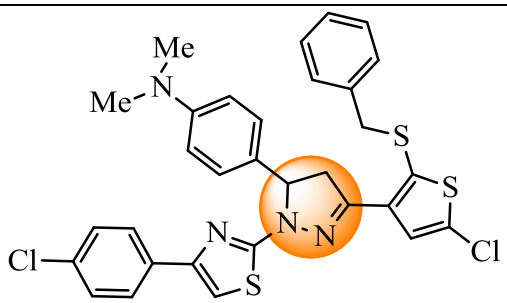
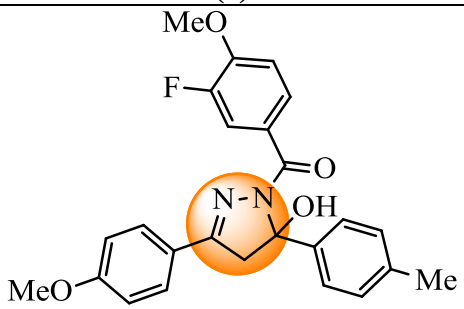
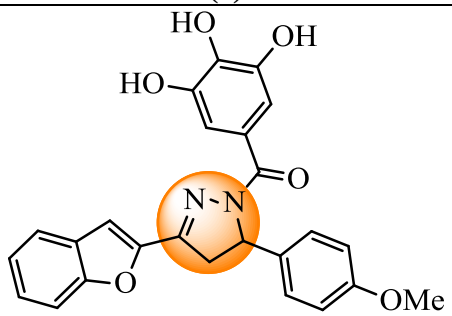
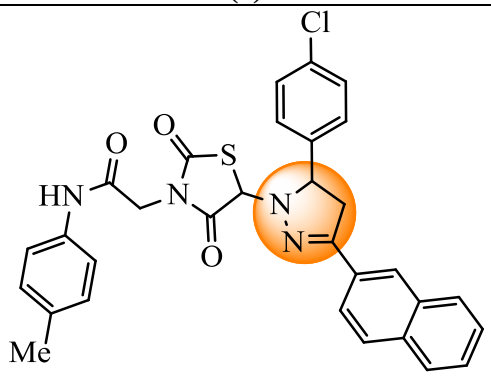
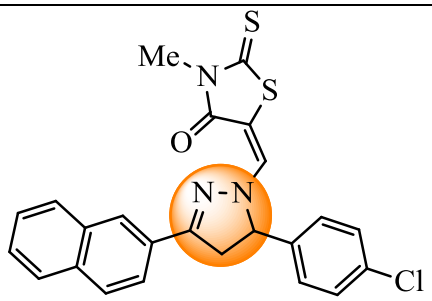
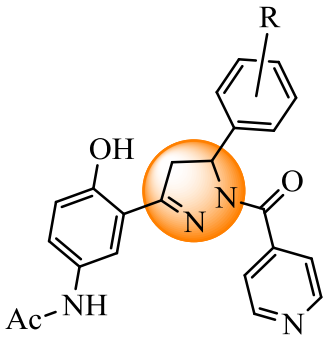
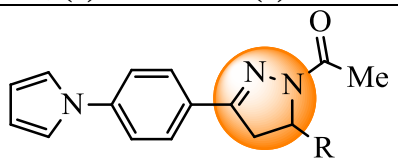
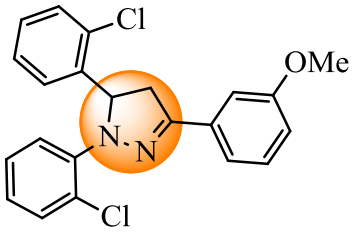
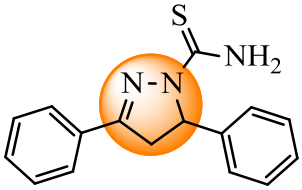
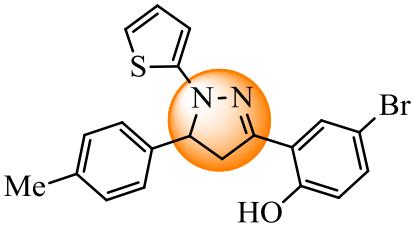
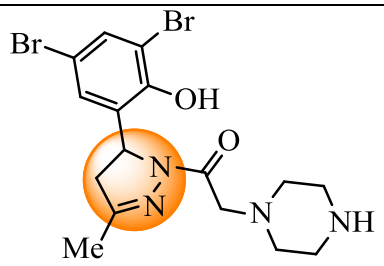
studied by Rangaswamy and co-workers[8]. Compound **(3)** displayed a dominant scavenging performance against three radicals: DPPH, LPO and ABTS with IC_{50} values of 9, 4.3 and 18.9 µM, respectively. It was more active than standard butylated hydroxy anisole (IC_{50} of 12.5, 6.4 and 20.9 µM, respectively).

Table 1. Some Pyrazoline Derivatives and Their Bioactivities

Compound	Bioactivity	[References]
 **(1)**	Antioxidant	[6]
 **(2)**	Antioxidant	[7]
 **(3)**	Antioxidant	[8]
 **(4)**	Antitrypanosomal	[2]

 (**5**)	Antitrypanosomal	[9]
 (**6**): R = 4-Cl; (**7**): R = 2,4-Cl; (**8**): R = 4-NO_2	Antitubercular	[10]
 (**9**): R = 4-Me; (**10**): R = 4-OMe; (**11**): R = 4-$CH(Me)_2$; (**12**): R = 3-OMe; (**13**): R = 2,4-OMe	Antitubercular	[11]
 (**14**)	Antitumor	[12]
 (**15**)	Antitumor	[13]
 (**16**)	MAO inhibitor	[14]

 (**17**)	MAO inhibitor	[15]

2.2 Antitrypanosomal

A new series of 5-pyrazoline substituted 4-thiazolidinone compounds have been prepared by Havrylyuk *et al*[2]. The in vitro assessment against *Trypanosoma brucei brucei* (Tbb) and *Trypanosoma brucei gambiemse* (Tbg) was used to check the efficacy of synthesized compounds. It was denoted that compound **(4)** displayed a moderate activity against both parasites with IC_{50} of 5.43 and 2.53 µM against Tbb and Tbg, respectively. Havrylyuk *et al.* also developed other novel pyrazoline-thiazolidinone hybrids with trypanocidal effects[9]. Compound **(5)** (IC_{50} values of 0.6µM)exhibited 6-times more active in comparison with commercial drug nifurtimox. It was noted that trypanocidal activity is crucially affected by methyl or aryl substituent at the thiazolidinone N-3 position.

2.3 Antitubercular

Two novel series of pyrazoline derivatives were prepared by Ahmad *et al*[10]. Through activity against *Mycobacterium tuberculosis*, compounds **(6)** – **(8)** showed a remarkable activity. They were found superior with MIC values of 3.12 µg/mL, two-fold more effective than reference drug Streptomycin (MIC 6.25 µg/mL). Out of the prepared compounds, isoniazid-pyrazoline derivatives having 2,4-dichloro and 4-nitro moieties displayed prominent activity. New pyrrole derivatives integrated with pyrazoline, isoxazole and phenyl thiourea skeleton were synthesized and antimycobacterial screened by Joshi and co-workers[11]. The preliminary anti-TB assay showed that most of the developed compounds exhibited medium to good activity. In pyrazoline series, it was noted that there were five derivatives (**9-13)** with MIC value of 6.25 µg/mL.

2.4 Antitumor

A novel class of antitumor agents in the form of trisubstituted and tetrasubstituted pyrazolines synthesized and investigated for their cell-growth inhibitory activity against wild type p53 [12]. Some compounds were active against the tested cell lines having low IC_{50} values with compound **(14)** as the best candidate in this series. Potential antitumor performance of 1-thiocarbamoyl-3,5-diaryl-4,5-dihydro-1*H*-pyrazole derivatives were studied by Tessmann *et al*[13]. Two human bladder cancer cell lines 5647 and T24 were used to investigate antitumor efficacy, and the result revealed that compound **(15)** was denoted as the most promising antitumor agent by decreasing cell viability and inducing apoptosis.

2.5 MAO Inhibitor

Monoamine oxidase (MAO) plays a fundamental role in oxidative catabolism of dietary amines and neurotransmitters[14]. In the MAO type A, development of inhibitors for this type are used to antidepressants. Evranos-Aksoz *et al.* synthesized some new 2-pyrazoline derivatives and screened their activity against human monoamine oxidase (hMAO). Compound **(16)**, that bear bromine atom denoted to be the most selective MAO-A inhibitor with selectivity index of 12615.38. A new series of 2-pyrazoline-1-ethanone derivatives were synthesized and developed as selective MAO inhibitors by Tong and co-workers[15]. Among the obtained compounds, **(17)** possessed the best selectivity and inhibitory activity against hMAO-A with IC_{50} value of 2.00 µM, more effective than reference drug Clorgyline (IC_{50} = 2.76 µM).

3. Conclusion

This short review paper presents biological performance of pyrazoline derivatives. Based on assays, several pyrazolines displayed more effective than reference drugs. It was considered as promising bioactive

molecules for the development of novel antioxidant, antitrypanosomal, antitubercular, antitumor and MAO inhibitors.

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