JPR INFO.com
Journal of Pharma Research

Journal of Pharma Research
Available online through
www.jprinfo.com

Research Article
ISSN: 2319-5622

Antioxidant and Metal Chelating Activities of some Novel Imidazoquinolie Incorporated [1,2,4]-Triazolo Heterocycles

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Received on: 16-02-2014; Revised and Accepted on: 25-02-2014

ABSTRACT

The [1,2,4]triazoloimidazoquinoline found to own high antioxidant activity. A series of imdazoquinoline fused substituted [1,2,4]triazoles have been evaluated for antioxidant and metal chelating activity. Antioxidant activity data obtained from DPPH free radical scavenging assay. To probe [1,2,4]triazoloimidazoquinoline derivatives may exert their antioxidant effect through transition metal ion chelation, the ferrous chelating abilities of these derivatives were investigated. The [1,2,4]-triazoloimidazoquinoline derivatives ***2a, 2d, 2e, 2g, 2h*** *showed excellent antioxidant and metal chelating activity.*

Keywords: *Hydrazone, [1,2,4]-Triazole, Antioxidant activity, Metal chelation activity.*

INTRODUCTION

The antioxidants are extensively studied for their capacity to protect organisms and cells from damage induced by oxidative stress. Scientists in various disciplines have become more interested in new compounds, either synthesized or obtained from natural sources, which could provide active components to prevent or reduce the impact of oxidative stress on cells [1]. Exogenous chemicals and endogenous metabolic processes in the human body or in food system might produce highly reactive free radicals, especially oxygen derived radicals, which are capable of oxidizing biomolecules, resulting in cell death and issue damage. Oxidative damages play a significant pathological role in human diseases. For example, cancer, emphysema, cirrhosis, atherosclerosis and arthritis anticancer, anticardiovascular, anti-inflammatory and many other activities are correlated with oxidative damage. Also, the excessive generation of ROS (reactive oxygen species) induced by various stimuli and, which exceeds the antioxidant capacity of the organism leads to a variety of pathophysiological processes such as inflammation, diabetes, genotoxicity etc. The free metals become more harmful in the pathogenesis of many diseases, accounting for continuing interest in the identification and development of novel antioxidants that prevent metal-induced damages.

Further, [1,2,4]triazole derivatives have shown significant biological activities, such as antibacterial [2], anti-inflammatory [3] and, anticancer [4], anticonvulsant [5]. This gave a great impetus to the search for potential pharmacologically active drugs carrying imidazoquinoline substituents. Keeping in view of this and in continuation of our search for biologically potent molecules, we hereby report the evaluation of antioxidant and metal chelating properties some new [1,2,4]triazole derivatives containing imidazoquinoline nucleus.

MATERIALS AND METHODS

Antioxidant activitiy:

Free radical scavenging activity of the synthesized compounds **2a-f** and **3a-f** were carried based on Brand-Williams et al [6]. The scavenging activity of stable DPPH 100 mg/mL of each test sample and the standard BHT was taken in different test tubes and the volume was adjusted to 1 mL using MeOH. Freshly prepared 3 mL of 0.1 mM DPPH solution was mixed and vortexed thoroughly and left in dark for 30 min. The absorbance of stable DPPH was measured at 517 nm. The DPPH control (containing no sample) was prepared using the same procedure. Radical scavenging activity was expressed as the inhibition percentage and was calculated using the equation of DPPH radical.

DPPH radical scavenging activity (%) = [(Abs Control - Abs Sample) /Abs Control] x 100:

Where Abs Control is the absorbance of DPPH radical + methanol; Abs Sample is the absorbance of DPPH radical + test sample/standard BHT

Iron-chelating ability:

The chelating effect was determined according to the literature method [7]. The test solution 100 mg/mL of each test sample in methanol was added to a solution of 2 mM $FeCl_2$ (0.05 mL) and the reaction was initiated by adding 5 mM ferrozine (0.2 mL) and total volume was adjusted to 5 mL with methanol. Then, the mixture was shaken vigorously and left at room temperature for 10 min. The absorbance of the solution was measured spectrophotometrically at 562 nm. The inhibition percentage of ferrozine–Fe+2 complex formations was calculated by the formula:
Metal chelating effect (%) = $[(A_{control} - A_{sample}) / A_{control}] \times 100$
where $A_{control}$ is the absorbance of control (control contains $FeCl_2$ ferrozine complex) and

A_{sample} is the absorbance of test compounds. Ascorbic acid is used as control.

RESULTS AND DISCUSSIONS

All the synthesized compounds **1a-h** and **2a-h** were evaluated for their antioxidant and metal chelating activities are represented in (**Fig. 1**).

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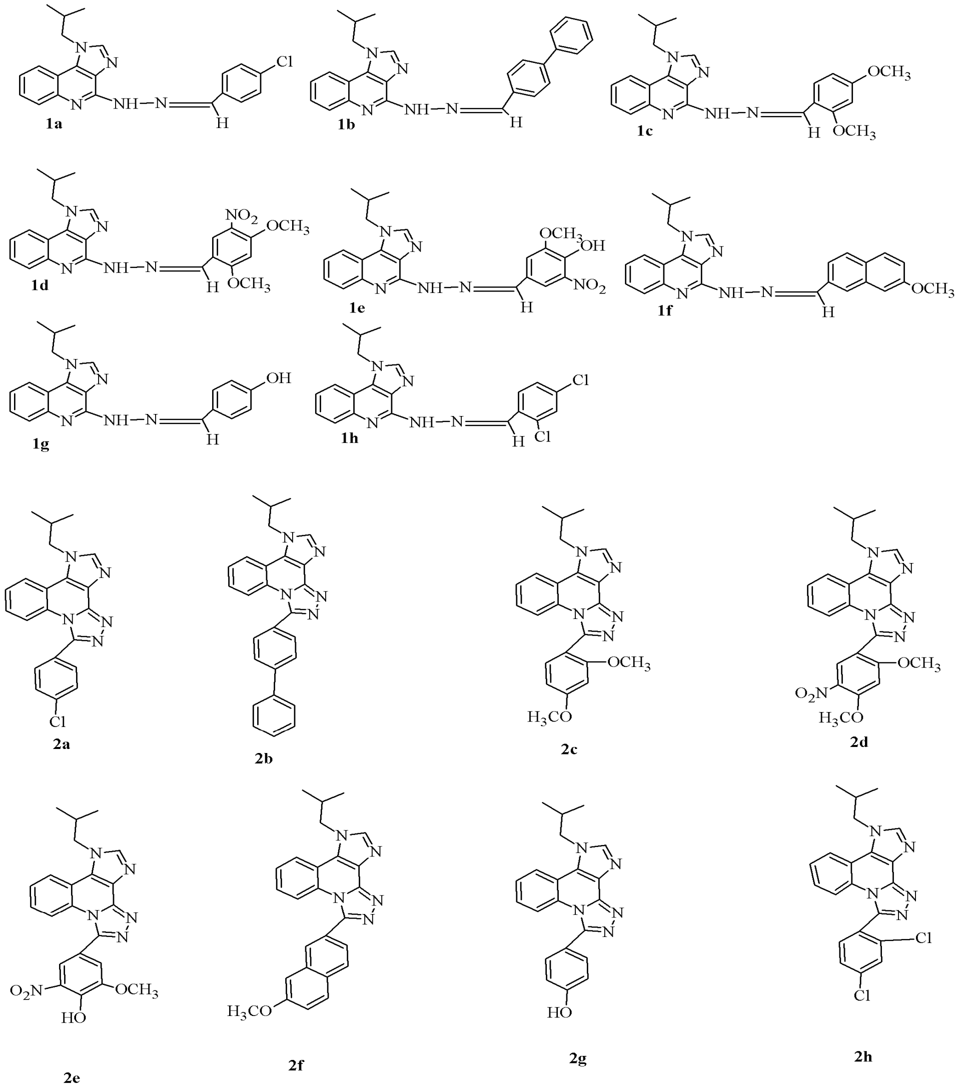

Fig. 1: Structure of the [1,2,4]triazoloimidazoquinoline derivatives

All compounds have exhibited free radical scavenging capacity less significant than the standard Butylated Hydroxytoulene (BHT). DPPH assay was carried out for compounds **1a-h** and **2a-h** at 100 μM concentration. Among the tested compounds **2a-h** showed significant antioxidant activity < (33.8%). The [1,2,4]triazoloimidazoquinolines **(2a-h)** exhibited higher antioxidant activity than their hydrazone derivatives **(1a-h).** The prominent antioxidant activity of [1,2,4]triazoloimidazoquinolines may be owning to azole-based derivatives easily bind with the enzymes and receptors in organisms through non-covalent interactions such as hydrogen bonds, coordination bonds, ion-dipole, cation-π,π-π stacking and hydrophobic effect as well as van der Waals force. Among the [1,2,4]triazoloimidazoquinolines **2a, 2d, 2e, 2g, 2h** showed antioxidant activity > (45.1%) compared to **2b, 2c, 2f** reasons may be the presence of eletron withdrawing groups and electron withdrawing groups along with donating groups.

Table No. 1: DPPH radical scavenging activity of compounds 1a-h and 2a-h

Compound No.	DPPH assay in %
1a	45.1
1b	23.1
1c	22.1
1d	35.5
1e	40.8
1f	27.1
1g	58.1
1h	50.1
2a	57.3
2b	33.8
2c	32.7
2d	45.1
2e	50.8
2f	37.1
2g	78.1
2h	65.2
BHT	92.13

Metal-chelating Activity:

Iron chelating activity is a capacity to measure the antioxidant activity Iron binding capacity of the synthesized compounds and the reference compound EDTA were examined (**Table 2**). The range and mean of Fe^{+2} chelating capacities varied significantly among the different compounds on the basis of substitution at Imdazoquinoline fused substituted [1,2,4]triazoles. The compounds **2a, 2d, 2e, 2g, 2h** showed high metal chelating activity > (70.1%) than its un-cyclised derivatives < (70.1%), but less than standard EDTA. Among the hydrazone derivatives **(1a-h) 1a, 1d, 1e, 1g, 1h** showed metal chelating activity **> (45.5%).**

Table NO. 1: DPPH radical scavenging activity of compounds 1a-h and 2a-h

Compound No.	DPPH assay in %
1a	55.1
1b	33.1
1c	32.1
1d	45.5
1e	50.8
1f	37.1
1g	68.1
1h	70.1
2a	77.3
2b	43.8
2c	42.7
2d	75.1
2e	70.8
2f	47.1
2g	78.1
2h	75.2
EDTA	83.6

CONCLUSION

In conclusion, we have shown that the [1,2,4]-triazoloimidazoquinoline derivatives **(2a-h)** have shown greater free radical scavenging activity and chelation with transition metal ions than its hydrazone derivatives **(1a-h).** The results indicated that the [1,2,4]-triazoloimidazoquinoline derivatives may exert their antioxidant effect through transition metal ion chelation and the transition metal ion chelation play an important role in their antioxidant activity.

ACKNOWLEDGEMENTS

The Authors are grateful to the management, SeQuent Scientific LTD, New Mangalore, India for their encouragement and invaluable support for research work.

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Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil