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Novel approach to the synthesis of new isoxazole analogues as potent antioxidant agents

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ABSTRACT

*A series of new 3-aryl-4-phenyl-4,5-dihydroisoxazol-5-yl)ethanones (**10-17**) were synthesized by the 1,3-dipolar cycloaddition of benzalacetone and nitrile oxides generated in situ by the catalytic dehydrogenation of aromatic aldoximes using chloramine-T. The synthesised new compounds were tested for their antimicrobial susceptibility '*

Key words: Isoxazole, Dipolar, Cycloaddition, Antioxidant, DPPH.

INTRODUCTION

The exploitation of a simple molecule with different functionalities for the synthesis of heterocycles is a worthwhile contribution in the chemistry. Heterocycles containing nitrogen and oxygen atom are considered as useful scaffolds for the synthesis of biologically active molecules. Among such classes of compounds isoxazolines occupies a prime position in medicinal chemistry for their diverse biological applications [1]. The larger intensity of biological potency exhibited by isoxazoline moiety stimulated the researchers work in this area to develop new novel synthetic approaches for their synthesis and study their activity. Of the methods developed, 1,3-dipolar cycloaddition of nitrile oxides to alkenes was most commonly employed for its easy and accessible procedure. The recent reviews reported on Huisgen cycloaddition reactions and nitrile oxides completely describes the method of synthesizing isoxazolines, stereochemistry, mechanistic considerations of 1,3-dipolar cycloaddition reactions [2-3].

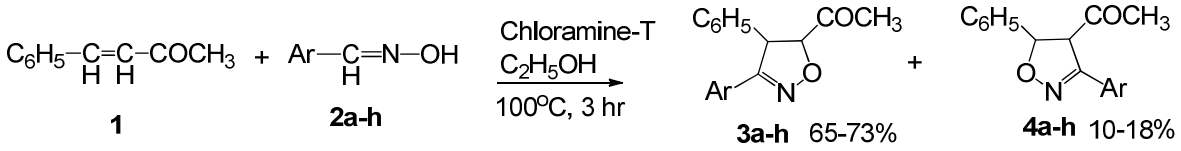
Isoxazolines were synthesized by the sequential reaction of ketones with arylacetylenes and hydroxylamine in the presence of $KOBu^t$/DMSO followed by the treatment of the reaction mixture with H_2O and KOH leads to Δ^2-isoxazolines in good yields [4], by 1,3-dipolar cycloaddition of in situ generated nitrile oxide with alkenes [5], and by the reaction of unprotected *O*-propargylic hydroxylamines on cyclisations by exposing briefly to silver nitrate adsorbed onto silica gel [6]. The isoxazoles acts as selective cyclooxygenase-2 (COX-2) inhibitory antiinflammatory (AI) agents [7], antimicrobials [8], anti-arthritic and anti-inflammatory [9], and anti-tuberculosis [10] agents.

In search of potential antioxidants agents; herein we report the present study of synthesis and *in vitro* screening for antioxidant activities of series of new isoxazolines. The synthesis of series of mixture of isoxazolines (**3**) major and (**4**) minor products involve 1,3-dipoar cycloaddition of benzalacetone (**2**) and nitrile imines generated *in situ* from aldoximes (**2**) using chloramine-T (CAT) as catalytic dehydrogenating agent. The synthesized new compounds have been evaluated *in vitro* for their DPPH radical scavenging ability.

EXPERIMENTAL SECTION

The chemicals/reagents used were purchased from Sigma-Aldrich Chemicals (India) and Merck Chemicals (India). IR spectra were recorded on a Nujol mull on a Shimadzu 8300 spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Supercon 400 MHz spectrophotometer using $CDCl_3$ as solvent and TMS as an internal standard. The chemical shifts are expressed in δ ppm. Mass spectra were obtained on a Shimadzu LCMS-2010A spectrophotometer (chemical ionization) and the important fragments are given with the relative intensities in the bracket. Elemental analysis was obtained on a Thermo Finnigan Flash EA 1112 CHN analyzer. Thin layer chromatography (TLC) was performed on precoated silica gel sheets (HF 254, sd-fine) using benzene:ethyl acetate (7:2) eluent, and visualization of the spots was done in iodine vapor and UV light. Chromatographic separations were carried out on a silica gel column (70-230 mesh, Merck) using hexane:ethyl acetate (8:1) as the eluent.

In a typical 1,3-dipolar cycloaddition reaction, the nitrile oxides generated by the catalytic dehydrogenation of aromatic aldoximes (**2a-h**) with chloramine-T in ethyl alcohol were trapped *in situ* with benzalacetone (**1**), the reaction yielded an isomeric mixture of 3-aryl-4-phenyl-4,5-dihydroisoxazol-5-yl)ethanones (**3a-h**) as major and 3-aryl-5-phenyl-4,5-dihydroisoxazol-4-yl)ethanones (**4a-h**) as minor products (Scheme-1).



3 or 4 a) Ar = C_6H_5, b) Ar = 4-$OCH_3C_6H_4$, c) Ar = 3,4-$(OCH_3)_2C_6H_3$, d). Ar = 4-$CH_3C_6H_4$,
e) Ar = 4-FC_6H_4, f) Ar = 4-ClC_6H_4, g) Ar = 4-BrC_6H_4, h) Ar = 4-$NO_2C_6H_4$.

Scheme-1: Synthesis of isoxazolines by 1,3-dipolar cycloaddition reaction

General procedure for dipolar cycloaddition:
A mixture of aromatic aldehoximes **2a-h** (4.0 mmol), benzalacetone **1** (4.0 mmol) and chloramine-T trihydrate (5.0 mmol) in ethanol was refluxed in a water bath for 3 hours. The progress of the reaction was monitored by TLC. After the completion of the reaction, the sodium chloride formed was filtered off, and the filtrate was evaporated in vacuo. The residual mass was extracted into ether (25 mL) and washed successively with water (2 x 15 mL), 10% sodium hydroxide (2 x 15 mL) and saturated brine solution (1 x 10 mL). The organic layer was dried over anhydrous sodium sulfate. The organic layer was dried over anhydrous sodium sulphate and the solvent was evaporated to dryness. The reaction produced light to brown oily mass, which showed two spot corresponding to the cycloadducts (**3** and **4**) in TLC. The products were separated by column chromatography using benzene: ethyl acetate (8:3 v/v) as eluent.

Antioxidant activity
The capacity to scavenge the stable free radical 2,2-diphenyl-1-picrylhydrazyl (DPPH) was monitored according to the Blois method [11] using ascorbic acid as standard antioxidant. Samples dissolved in methanol (0-50 µg/mL; 0-5 µg/mL ascorbic acid) in 200 µL aliquot was mixed with 100 mM tris-HCl buffer (800 µL, pH 7.4) and then added 1 mL of 500 µM DPPH in ethanol (final concentration of 250 µM). The mixture was shaken vigorously and left to stand for 20 min at room temperature in the dark. The absorbance of the resulting solution was measured spectrophotometrically at 517 nm. The experiments were performed in triplicates; the results are expressed as mean ± standard deviation (SD).

RESULTS AND DISCUSSION

***3,4-Diphenyl-4,5-dihydroisoxazol-5-yl)ethanone*, 3a**: Obtained as pale yellow oil in 72% yield. IR (Nujol): 1634 (C=N str.), 1682 (C=O str.) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.276 (s, 3H, CH_3), 4.452 (d, 1H, C_4-H), 4.823 (d, 1H, C_5-H), 7.269-7.705 (m, 10H, Ph-, Ar-H). ^{13}C NMR ($CDCl_3$): δ 26.54 (1C, <u>C</u>H_3), 27.52 (1C, 4-<u>C</u>), 85.98 (1C, 5-<u>C</u>), 125.24 (1C, Ph-<u>C</u>), 127.53 (1C, Ph-<u>C</u>), 127.54 (1C, Ph-<u>C</u>), 128.02 (1C, Ar-<u>C</u>), 128.18 (1C, Ar-<u>C</u>), 128.68 (1C, Ph-<u>C</u>), 128.71 (1C, Ph-<u>C</u>), 128.95 (1C, Ar-<u>C</u>), 128.99 (1C, Ar-<u>C</u>), 130.69 (1C, Ar-<u>C</u>), 134.44 (1C, Ar-<u>C</u>), 139.62 (1C, Ph-<u>C</u>), 158.81 (1C, 3-<u>C</u>), 207.35 (1C, <u>C</u>=O). MS (relative abundance) m/z: 266 (MH^+, 100), 265 (M^+, 20), 250 (10), 236

(16), 222 (12), 220 (26). Anal. Calcd. for $C_{17}H_{15}NO_2$: C, 76.96, H, 5.70, N, 5.28%; Found: C, 76.91, H, 5.71, N, 5.22%.

***3-(4-Methoxyphenyl)-4-phenyl-4,5-dihydroisoxazol-5-yl)ethanone,* 3b**: Obtained as pale yellow oil in 79% yield. IR (Nujol): 1630 (C=N str.), 1690 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.202 (s, 3H, CH_3), 3.832 (s, 3H, OCH_3), 4.322 (d, 1H, C_4-H), 4.720 (d, 1H, C_5-H), 7.106 (dd, 2H, Ar-H), 7.269-7.405 (m, 5H, Ph-H), 7.901 (dd, 2H, Ar-H). ^{13}C NMR ($CDCl_3$): δ 26.20 (1C, $\underline{C}H_3$), 28.02 (1C, 4-$\underline{C}$), 55.72 (1C, O$\underline{C}H_3$), 88.70 (1C, 5-$\underline{C}$), 114.28 (2C, Ar-$\underline{C}$), 125.30 (1C, Ph-$\underline{C}$), 126.90 (1C, Ar-$\underline{C}$), 127.62 (2C, Ph-$\underline{C}$), 128.38 (2C, Ar-$\underline{C}$), 128.64 (2C, Ph-$\underline{C}$), 140.12 (1C, Ph-$\underline{C}$), 159.96 (1C, 3-$\underline{C}$), 161.25 (1C, Ar-$\underline{C}$), 207.20 (1C, $\underline{C}$=O). MS (relative abundance) m/z: 296 (MH^+, 100), 295 (M^+, 18), 280 (14), 266 (20), 252 (10), 250 (32). Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.20, H, 5.80, N, 4.74%; Found: C, 73.12, H, 5.71, N, 4.70%.

***3-(3,4-Dimethoxyphenyl)-4-phenyl-4,5-dihydroisoxazol-5-yl)ethanone,* 3c**: Obtained as pale yellow oil in 71% yield. IR (Nujol): 1640 (C=N str.), 1693 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.130 (s, 3H, CH_3), 3.840 (s, 6H, OCH_3), 4.380 (d, 1H, C_4-H), 4.708 (d, 1H, C_5-H), 7.010-7.415 (m, 8H, Ph-, Ar-H). ^{13}C NMR ($CDCl_3$): δ 26.00 (1C, $\underline{C}H_3$), 28.30 (1C, 4-$\underline{C}$), 55.92 (2C, O$\underline{C}H_3$), 88.82 (1C, 5-$\underline{C}$), 112.18 (1C, Ar-$\underline{C}$), 114.70 (1C, Ar-$\underline{C}$), 120.55 (1C, Ar-$\underline{C}$), 125.36 (1C, Ph-$\underline{C}$), 127.40 (1C, Ar-$\underline{C}$), 127.72 (2C, Ph-$\underline{C}$), 128.88 (2C, Ph-$\underline{C}$), 140.06 (1C, Ph-$\underline{C}$), 148.20 (1C, Ar-$\underline{C}$), 151.36 (1C, Ar-$\underline{C}$), 160.10 (1C, 3-$\underline{C}$), 207.18 (1C, $\underline{C}$=O). MS (relative abundance) m/z: 326 (MH^+, 100), 325 (M^+, 12), 310 (8), 296 (10), 282 (8), 280 (24), 206 (8). Anal. Calcd. for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31%; Found: C, 70.20; H, 5.84; N, 4.30%.

***3-(4-Methylphenyl)-4-phenyl--4,5-dihydroisoxazol-5-yl)ethanone,* 3d**: Obtained as pale yellow oil in 86% yield. IR (Nujol): 1635 (C=N str.), 1684 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.214 (s, 3H, CH_3), 2.480 (s, 3H, CH_3), 4.316 (d, 1H, C_4-H), 4.698 (d, 1H, C_5-H), 7.202 (dd, 2H, Ar-H), 7.280-7.422 (m, 5H, Ph-H), 7.706 (dd, 2H, Ar-H). ^{13}C NMR ($CDCl_3$): δ 21.72 (1C, $\underline{C}H_3$), 26.02 (1C, $\underline{C}H_3$), 28.36 (1C, 4-$\underline{C}$), 88.66 (1C, 5-$\underline{C}$), 125.44 (1C, Ph-$\underline{C}$), 127.10 (2C, Ar-$\underline{C}$), 127.58 (2C, Ph-$\underline{C}$), 128.50 (2C, Ph-$\underline{C}$), 129.34 (2C, Ar-$\underline{C}$), 131.80 (1C, Ar-$\underline{C}$), 139.90 (1C, Ar-$\underline{C}$), 140.04 (1C, Ph-$\underline{C}$), 160.82 (1C, 3-$\underline{C}$), 207.04 (1C, $\underline{C}$=O). Anal. Cacld. for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01%; Found: C, 77.46; H, 6.12; N, 5.06%.

***3-(4-Fluorophenyl)-4-phenyl-4,5-dihydroisoxazol-5-yl)ethanone,* 3e**: Obtained as pale yellow oil in 86% yield. IR (Nujol): 1638 (C=N str.), 1678 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.218 (s, 3H, CH_3), 4.292 (d, 1H, C_4-H), 4.580 (d, 1H, C_5-H), 7.366 (dd, 2H, Ar-H), 7.259-7.380 (m, 5H, Ph-H), 7.821 (dd, 2H, Ar-H). ^{13}C NMR ($CDCl_3$): δ 25.88 (1C, $\underline{C}H_3$), 28.10 (1C, 4-$\underline{C}$), 89.15 (1C, 5-$\underline{C}$), 115.32 (2C, Ar-$\underline{C}$), 126.06 (1C, Ph-$\underline{C}$), 127.51 (2C, Ph-$\underline{C}$), 128.48 (2C, Ph-$\underline{C}$), 128.94 (2C, Ar-$\underline{C}$), 129.40 (1C, Ar-$\underline{C}$), 140.10 (1C, Ph-$\underline{C}$), 159.86 (1C, 3-$\underline{C}$), 163.20 (1C, Ar-$\underline{C}$), 207.38 (1C, $\underline{C}$=O). MS (relative abundance) m/z: 284 (MH^+, 100), 283 (M^+, 10), 368 (12), 354 (14), 340 (13), 338 (22). Anal. Calcd. for $C_{17}H_{14}FNO_2$: C, 72.07; H, 4.98; N, 4.94%; Found: C, 72.07; H, 4.93; N, 4.90%.

***3-(4-Chlorophenyl)-4-phenyl-4,5-dihydroisoxazol-5-yl)ethanone,* 3f**: Obtained as pale yellow oil in 78% yield. IR (Nujol): 1640 (C=N str.), 1695 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.230 (s, 3H, CH_3), 4.301 (d, 1H, C_4-H), 4.670 (d, 1H, C_5-H), 7.240-7.385 (m, 5H, Ph-H), 7.506 (dd, 2H, Ar-H), 7.980 (dd, 2H, Ar-H). ^{13}C NMR ($CDCl_3$): δ 26.14 (1C, $\underline{C}H_3$), 28.16 (1C, 4-$\underline{C}$), 88.86 (1C, 5-$\underline{C}$), 125.88 (1C, Ph-$\underline{C}$), 127.22 (2C, Ph-$\underline{C}$), 128.02 (2C, Ar-$\underline{C}$), 128.52 (2C, Ph-$\underline{C}$), 128.80 (2C, Ar-$\underline{C}$), 132.74 (1C, Ar-$\underline{C}$), 135.92 (1C, Ar-$\underline{C}$), 141.00 (1C, Ph-$\underline{C}$), 160.36 (1C, 3-$\underline{C}$), 207.02 (1C, $\underline{C}$=O). MS (relative abundance) m/z: 301 (M^+, ^{37}Cl, 33), 299 (M^+, ^{35}Cl, 100), 284 (08), 270 (18), 256 (16), 254 (06). Anal. Calcd. for $C_{17}H_{14}ClNO_2$: C, 68.12; H, 4.71; N, 4.67%; Found: C, 68.18; H, 4.79; N, 4.64%.

***3-(4-Bromophenyl)-4-phenyl-4,5-dihydroisoxazol-5-yl)ethanone,* 3g**: Obtained as white solid in 78% yield, m.p 105-106ºC. IR (Nujol): 1641 (C=N str.), 1688 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.230 (s, 3H, CH_3), 4.398 (d, 1H, C_4-H), 4.744 (d, 1H, C_5-H), 7.436 (dd, 2H, Ar-H), 7.230-7.442 (m, 5H, Ph-H), 7.790 (dd, 2H, Ar-H). Anal. Calcd. for $C_{17}H_{14}BrNO_2$: C, 59.32; H, 4.10; N, 4.07%; Found: C, 59.30; H, 4.14; N, 4.03%.

***3-(4-Nitrophenyl)-4-phenyl-4,5-dihydroisoxazol-5-yl)ethanone,* 3h**: Obtained as pale yellow oil in 70% yield. IR (Nujol): 1645 (C=N str.), 1683 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.248 (s, 3H, CH_3), 4.375 (d, 1H, C_4-H), 4.688 (d, 1H, C_5-H), 7.310-7.486 (m, 5H, Ph-H), 8.010 (dd, 2H, Ar-H), 8.341 (dd, 2H, Ar-H). ^{13}C NMR ($CDCl_3$): δ 26.14 (1C, $\underline{C}H_3$), 29.16 (1C, 4-$\underline{C}$), 89.08 (1C, 5-$\underline{C}$), 125.14 (1C, Ph-$\underline{C}$), 127.12 (2C, Ar-$\underline{C}$), 127.34 (2C, Ph-$\underline{C}$), 127.82 (2C, Ar-$\underline{C}$), 128.56 (2C, Ph-$\underline{C}$), 139.20 (1C, Ar-$\underline{C}$), 140.05 (1C, Ph-$\underline{C}$), 152.10 (1C, Ar-$\underline{C}$), 159.72 (1C, 3-$\underline{C}$), 207.28

(1C, C=O). MS (relative abundance) m/z: 311 (MH^+, 100), 310 (M^+, 12), 295 (16), 281 (22), 267 (10), 265 (09). Anal. Calcd. for $C_{17}H_{14}N_2O_4$: C, 65.80, H, 4.55, N, 9.03%; Found: C, 65.86, H, 4.50, N, 9.07%.

The physical and analytical data of the two isomeric minor products 4d and 4e were given below.

***3-(4-Methylphenyl)-5-phenyl--4,5-dihydroisoxazol-4-yl)ethanone*, 4d**: Obtained as pale yellow oil in 12% yield. IR (Nujol): 1630 (C=N str.), 1680 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.222 (s, 3H, CH_3), 2.412 (s, 3H, CH_3), 4.304 (d, 1H, C_4-H), 4.660 (d, 1H, C_5-H), 7.112 (dd, 2H, Ar-H), 7.240-7.332 (m, 5H, Ph-H), 7.754 (dd, 2H, Ar-H). ^{13}C NMR ($CDCl_3$): δ 21.34 (1C, CH_3), 26.32 (1C, CH_3), 28.44 (1C, 4-C), 88.56 (1C, 5-C), 125.50 (1C, Ph-C), 127.00 (2C, Ar-C), 127.60 (2C, Ph-C), 128.80 (2C, Ph-C), 129.56 (2C, Ar-C), 131.79 (1C, Ar-C), 138.10 (1C, Ar-C), 140.66 (1C, Ph-C), 161.12 (1C, 3-C), 203.14 (1C, C=O). Anal. Cacld. for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01%; Found: C, 77.52; H, 6.04; N, 5.03%.

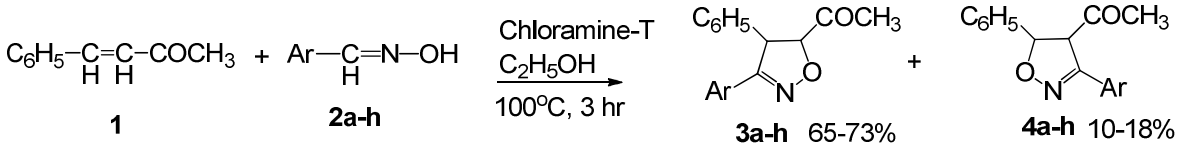
***3-(4-Fluorophenyl)-5-phenyl-4,5-dihydroisoxazol-4-yl)ethanone*, 4e**: Obtained as pale yellow oil in 16% yield. IR (Nujol): 1645 (C=N str.), 1680 (C=O str.) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.328 (s, 3H, CH_3), 4.442 (d, 1H, C_4-H), 4.590 (d, 1H, C_5-H), 7.426 (dd, 2H, Ar-H), 7.280-7.460 (m, 5H, Ph-H), 7.846 (dd, 2H, Ar-H). ^{13}C NMR ($CDCl_3$): δ 24.80 (1C, CH_3), 28.16 (1C, 4-C), 89.30 (1C, 5-C), 115.40 (2C, Ar-C), 126.22 (1C, Ph-C), 127.66 (2C, Ph-C), 128.67 (2C, Ph-C), 128.90 (2C, Ar-C), 129.20 (1C, Ar-C), 140.45 (1C, Ph-C), 159.96 (1C, 3-C), 163.00 (1C, Ar-C), 204.30 (1C, C=O). MS (relative abundance) m/z: 284 (MH^+, 100), 283 (M^+, 14), 368 (20), 354 (22), 340 (18), 338 (22). Anal. Calcd. for $C_{17}H_{14}FNO_2$: C, 72.07; H, 4.98; N, 4.94%; Found: C, 72.17; H, 4.90; N, 4.86%.

The structures of the cycloadducts were provided by IR, ^1H NMR, ^{13}C NMR, MS spectral studies and elemental analysis. In IR spectrum of the cycloadducts (**3a-h**), a strong absorption bands in the region 1630-1645 cm^{-1} and in the region 1678-1695 cm^{-1}, these absorptions bands were assigned to C=N (str) and C=O (str) frequencies respectively.

In ^1H NMR spectra, all the new products (**3a-h**) showed the peaks due to aromatic and substituent protons at the expected region. The consistent pattern signals due to C_4-H and C_5-H appeared as doublet in the region δ 4.122-4.240 ppm. and δ 4.390-4.491 ppm. The coupling constant (*J*) values obtained were in range 6.8-9.4 *Hz;* indicating that both C_4-H and C_5-H are in *cis* fashion.

In ^{13}C NMR, all products gave the signals due to aromatic and substituent carbons at the expected region. The signals due to newly formed C_4-carbon appeared in the region δ_c 41.56-41.88 ppm, while, C_5-carbon showed the signals in the region δ_c 51.24-51.92 ppm. The signals due to CN group carbon appear in the region δ_c 116.2-118.0 ppm which shows that the CN triple bond is unaffected during cycloaddition and is retained in the product. The new compounds (3a-h) gave significantly stable molecular ion peaks with a relative abundance ranging up to 40% and base peak at (MH^+). Further, all showed satisfactorily CHN analysis with a deviation of ±0.02% from the theoretically calculated values. All these observations strongly favor the formation of the cycloadducts.

The results of antioxidant activity of the synthesized compounds against different bacterium were tabulated in Table-1.



3 or 4 a) Ar = C_6H_5, b) Ar = 4-$OCH_3C_6H_4$, c) Ar = 3,4-$(OCH_3)_2C_6H_3$, d). Ar = 4-$CH_3C_6H_4$,
e) Ar = 4-FC_6H_4, f) Ar = 4-ClC_6H_4, g) Ar = 4-BrC_6H_4, h) Ar = 4-$NO_2C_6H_4$.

Scheme-1: Synthesis of isoxazolines by 1,3-dipolar cycloaddition reaction

The compounds **3a-g** showed promising free radical scavenging ability but of lesser activity compared with the standard antioxidant. No much significant variations in the free radical scavenging ability were observed at the initial concentrations of (10-20 µg/mL). However, at the higher concentrations (30-50 µg/mL) all showed a promising activity. Among the series of synthesized compounds **3f** having chloro substitution in the aromatic ring

howed radical scavenging ability up to 58%, while the compounds **3a** and **3e** having no and fluro substitution in the aromatic ring showed radical scavenging ability of 44% and 46% respectively.

Table-1: DPPH Radical Scavenging activity of the compounds 3a-g relative to the standard ascorbic acid

Samples	% Radical Scavenging activity				
	Concentration (µg/mL)				
	10	20	30	40	50
3a	12.76 ± 0.94	15.23 ± 0.88	29.20 ± 0.71	39.66 ± 0.98	44.17 ± 0.82
3b	13.16 ± 0.80	17.25 ± 0.90	26.92 ± 0.96	31.60 ± 0.95	36.00 ± 0.88
3c	17.30 ± 0.89	24.28 ± 0.79	29.36 ± 0.97	32.22 ± 0.78	35.16 ± 0.82
3d	12.22 ± 0.85	14.92 ± 0.89	22.61 ± 0.68	29.96 ± 0.91	33.61 ± 0.75
3e	13.46 ± 0.82	23.30 ± 0.89	29.88 ± 0.81	37.52 ± 0.98	46.73 ± 0.83
3f	15.16 ± 0.78	28.36 ± 0.92	37.42 ± 0.83	46.23 ± 0.78	58.42 ± 0.99
3g	09.32 ± 0.86	14.36 ± 0.98	17.23 ± 0.91	20.70 ± 0.79	22.40 ± 0.91
3h	08.12 ± 0.88	11.36 ± 0.98	14.80 ± 0.81	18.50 ± 0.70	20.20 ± 0.76
Control at Concentration 0 µg/mL 0.00 ± 0.00					
**Values are expressed as mean ± standard deviation (n=3)*					

The compounds **3g** and **3h** having bromo substitution in the aromatic ring and furan ring in place of aromatic ring exhibited least activity (up to 22%) of the synthesized compounds with reference to the standard antioxidant. While the compounds **3b**, **3c**, **3d** containing a strong electron donating groups such as methyl and methoxy substitution in the aromatic ring showed moderate scavenging ability 33-36%.

CONCLUSION

The easy and accessible procedure for the synthesis of new isoxazolines and their antioxidant activity results validates the significance of this study. The study revealed that the most of the compounds tested showed moderate to good antioxidant activities. However, the SAR studies of the synthesized compounds for their antioxidant activity remains to be studied.

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