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Synthesis, characterization of novel isoxazoles: Biological evaluation for their Antifungal and radical scavenging potencies

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Abstract: *This study presents the synthesis of thienyl-isoxazoles **5(a-h)** through (3+2) annulation of chalcones **3(a-h)** with hydroxylamine hydrochloride **4** in freshly extracted citrus juice medium under reflux conditions. Structure proofs of synthesized new isoxazoles were provided by spectral and elemental analysis. Preliminary studies on antifungal and DPPH radical scavenging activity shows that compounds **5b** and **5c** with fluro and chloro substitutions have excellent inhibition (12.5-50.0 µg/mL) against the tested fungi species, and better DPPH radical scavenging abilities (20.70-45.26% and 23.91-46.16%) comparable with the standard used.*

Keywords: *Antifungal, annulation, chalcone, cyclocondensation, radical scavenger.*

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I. Introduction

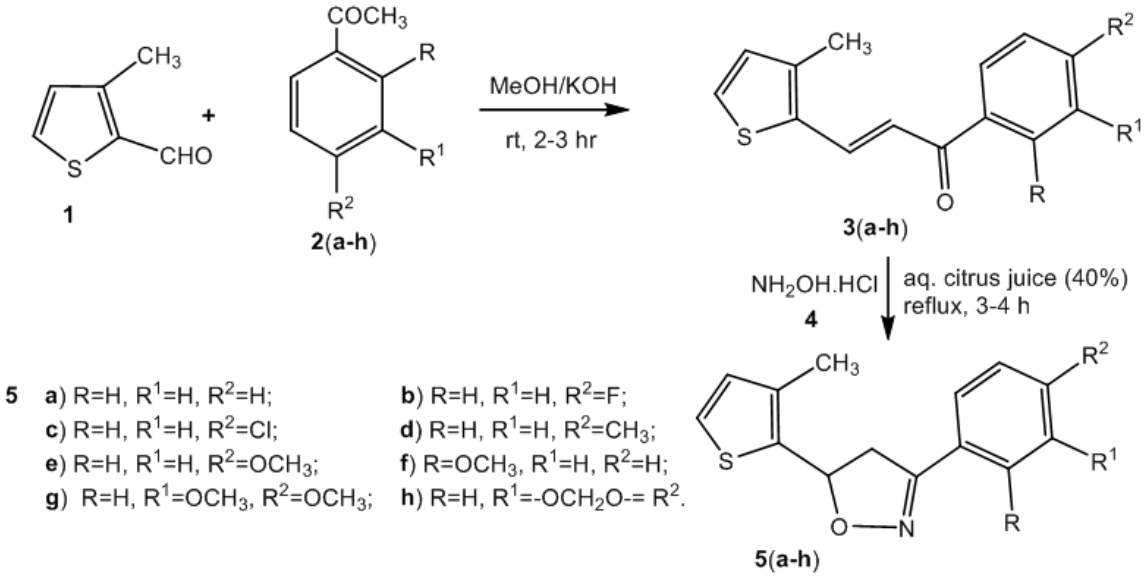
Discovery of small molecules with antimicrobial and antioxidant effects is the pivotal area of research in recent years. In this context, heterocycles, in particular compounds with isoxazole core occupies the prime place in the field of medicinal chemistry for their diverse biological applications. Chalcones are regarded as useful intermediates for the construction of bioactive heterocycles like as pyrazoles [1, 2], benzothiazepines [3], isoxazoles [4,5], pyrrolines [6], thiadiazoles [7] etc. The chalcones themselves possess wide range of biological applications such as anti-diabetic, antiviral, cytotoxic, antimicrobial, and antioxidant activities [8-10].

The compounds with biologically potent isoxazole skeleton are synthesized through various procedures available in the literature. For instance, these class of compounds have prepared by the reaction of 2-alkyn-1-one O-methyl oxime with ICl or I_2 [11], Cu-catalyzed cascade reactions involving amines and alkynes [12], nucleophilic addition of lithiated alkyl nitriles to α-chlorooximes [13], 1,3-dipolar cycloaddition of *in situ* generated nitrile oxide to an alkene [14,15], chalcone [16], to acetyl acetone [17], iron (III) nitrate catalyzed coupling reactions between two alkynes [18], palladium-catalyzed four-component coupling of terminal alkyne, hydroxylamine, carbon monoxide and an aryl iodide [19], Cu(I) catalyzed reaction of nitrile oxide and acetylene [20], and chemoselective synthesis involving the treatment of α-haloketoximes with phosphine, acyl chloride, and a base [21].

Reports on the biological applications of isoxazoles reveals that these derivatives exhibit wide range of pharmaceutical properties, like anti-inflammatory [22,23], anti-tuberculosis [24], antifungal [25], COX-2 inhibitor [26], antioxidant [27], antibacterial [28, 29], and analgesic [30] etc. In this current study, we report the synthesis of series of new thienyl-isoxazoles through (3+2) annulation reactions of chalcones and hydroxylamine hydrochloride in an environmentally benign citrus extract medium, and results of their *in vitro* antifungal and DPPH radical scavenging assays.

II. Materials and Methods

In search of new potent antifungal, and free radical scavenging agents; a series of new isoxazole derivatives, **5**(**a-h**) were synthesized in an environmentally benign reaction conditions. Initially, the intermediate chalcones, **3**(**a-h**) were prepared via Claisen-Schmidt reaction of 3-methylthiophene-2-carbaldehyde, **1** with acetophenones **2**(**a-h**) in methyl alcohol according to our earlier report [31]. The reaction of compounds **3**(**a-h**) with hydroxylamine hydrochloride, **4** in freshly prepared lemon juice in the presence of tetrabutylammonium bromide (TBAB) under reflux conditions yielded isoxazole derivatives **5**(**a-h**) in moderate yields (**Scheme 1**).



Scheme 1: Synthetic route for the synthesis of isoxazoles, **5**(**a-h**)

Antifungal activity: The antifungal activities of compounds **5**(**a**–**h**) were determined as minimum inhibitory concentrations (MIC) by serial dilution method [32,33]. The fungal stains *Aspergillus niger, Aspergillus flavus* and *Candida albicans* (MTCC 227) were used for the study. Nystatin and dimethyl sulfoxide were used as positive and solvent control. The experiments were carried out in triplicate; the results were taken as a mean ± standard deviation.

Antioxidant activity: The DPPH radical scavenging activities of compounds **5**(**a**–**h**) were assessed by *in vitro* DPPH radical scavenging activity by Blois method [34,35]. The experiments were conducted in triplicate; the results were taken as a mean ± standard deviation (SD).

III. Results and Discussion

^{1}H NMR spectra of compounds **5**(**a-h**) recorded on Agilent-NMR (400 *MHz*) spectrometer shows that the methylene carbon of isoxazole rings are diastereotopic. Signals appear as a doublet of doublets at δ 3.502-3.566 (*J=6.1-7.2 Hz* and *J=15.8-17.4 Hz*) ppm for C_4-H_a; at δ 3.728-3.796 (*J=6.6-7.9 Hz* and *J=11.5-12.9 Hz*) ppm for C_4-H_b; and at δ 4.980-5.166 (*J=5.9-6.9 Hz* and *J=12.5-14.0 Hz*) ppm for C_5-H protons, respectively. The methyl protons of thiophene ring show singlets at δ 2.184-2.250 ppm; aromatic protons as multiplet in the region δ 6.954-7.888 ppm and signals due to methyl, methoxy, methylenedioxy protons in the respective regions in their spectra. ^{13}C NMR spectra of compounds recorded on Agilent-NMR (100 *MHz*) spectrometer shows the resonance signals in the region δ 41.7-45.1, 74.3-77.5, and 155.7-159.9 ppm, respectively for C-4, C-5 and C-3 carbons. Aromatic carbons resonate at δ 113.8-158.2 ppm, substitution carbons in the respective regions. Mass spectra of compounds recorded on ESI/APCI-Hybrid Quadrupole, Synapt G2 HDMS ACQUITY UPLC model spectrometer shows the base peaks comparable to their molecular mass; however compound **5c** show M+2 peak with a relative abundance 33%. Further, elemental analysis procured on a Thermo Finnigan Flash EA 1112 CHN analyzer gave comparable data confirming the (3+2) annulation between chalcone and hydroxylamine to isoxazolines.

Antifungal activity: The results of antifungal activity of the synthesized compounds were depicted in **Table 1**.

Table 1: Antifungal activity of synthesized compounds **5**(**a-h**)

Minimum inhibitory concentrations (MIC's) in µg/mL			
Entry	*A. niger*	*A. flavus*	*C. albicans*
5a	37.5 ± 0.75	25.0 ± 0.50	25.0 ± 0.80
5b	50.0 ± 0.75	50.0 ± 0.75	25.0 ± 0.75
5c	37.5 ± 0.42	37.5 ± 0.55	12.5 ± 0.60
5d	75.0 ± 0.44	87.5 ± 0.75	37.5 ± 1.00
5e	75.0 ± 0.88	75.0 ± 0.70	50.0 ± 0.85
5f	>150.0 ± 1.22	>150.0 ± 0.90	>125.0 ± 0.85
5g	>150.0 ± 1.30	>150.0 ± 0.68	>125.0 ± 0.55
5h	50.0 ± 1.02	50.0 ± 0.95	>125.0 ± 0.74
Nystatin	50.0 ± 0.66	50.0 ± 0.72	25.0 ± 0.35
*Values are the mean (n=3) ± SD			

Preliminary screening results shows that synthesized new thienyl-isoxazoles **5**(**a-h**) possess noticeable antifungal activities. Compounds 5-(3-methylthiophen-2-yl)-3-phenyl-4,5-dihydroisoxazole, **5a** and 3-(4-chlorophenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5c** show excellent inhibition against *A. niger* (37.5 µg/mL), *A. flavus* (25.0 and 37.5 µg/mL), and *C. albicans* (25.0 and 12.5 µg/mL) comparable to positive control. Promising activities observed with compounds 3-(4-fluorophenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5b** and 3-(benzo[d][1,3]dioxol-5-yl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5h** against *A. niger* (50.0 µg/mL), *A. flavus* (50.0 µg/mL), and *C. albicans* (25.0 µg/mL), but **5h** found inactive against *C. albicans*.

Compounds, 5-(3-methylthiophen-2-yl)-3-(p-tolyl)-4,5-dihydroisoxazole, **5d** and 3-(4-methoxyphenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5e** have moderate inhibition against *A. niger* (75.0 µg/mL), *A. flavus* (75.0 and 87.5 µg/mL), and *C. albicans* (37.5, 50.0 µg/mL); while the compounds 3-(2-methoxyphenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5f** and 3-(3,4-dimethoxyphenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5g** found almost inactive as they require more than triple the concentrations for inhibition compare to the standard.

DPPH radical scavenging activity: The radical scavenging activity results of synthesized compounds were summarized in **Table 2**.

Table 2: DPPH radical scavenging activity of the compounds **5**(**a–h**)

Entry	% Radical scavenging activity*			
	25 (µg/mL)	50 (µg/mL)	75 (µg/mL)	100 (µg/mL)
5a	17.40 ± 0.75	18.95 ± 0.45	24.33 ± 0.60	28.05 ± 1.10
5b	20.70 ± 0.40	27.40 ± 0.45	35.71 ± 1.50	45.26 ± 0.85
5c	23.91 ± 0.24	26.94 ± 0.44	35.79 ± 0.53	46.16 ± 0.35
5d	13.25 ± 0.55	14.30 ± 0.70	17.22 ± 0.65	21.30 ± 0.62
5e	14.01 ± 1.10	15.55 ± 0.90	16.95 ± 0.85	20.01 ± 0.55
5f	9.20 ± 0.46	11.01 ± 0.85	12.06 ± 0.77	13.16 ± 1.22
5g	7.15 ± 0.80	9.50 ± 0.98	10.18 ± 0.63	11.10 ± 0.56
5h	16.30 ± 1.02	19.90 ± 0.90	23.36 ± 0.86	27.44 ± 0.87
[a]AA	15.08 ± 0.52	16.87 ± 0.89	21.98 ± 0.31	24.25 ± 0.22

*Values are mean ± SD (n = 3); [a]Ascorbic acid was used as standard

The results of *in vitro* DPPH radical scavenging assay shows that, amongst the synthesized series, compounds **5b** and **5c** have excellent antioxidant properties with radical scavenging abilities in the range of (20.70-45.26% and 23.91-46.16%) at the tested concentrations comparable to the standard ascorbic acid. It is emphasized that, the greater activity of these compounds might be attributed to the presence of electronegative halogen substitutions. Promising activities were observed with the compounds **5a** (17.40-28.05%) and **5h** (16.30-27.44%); and compounds **5d** (13.25-21.30%) and **5e** (14.01-20.01%) have moderate radical scavenging abilities. The compounds **5d** and **5e** show poorer activities and found almost inactive. The moderate or poorer activities of the compounds might be due to the presence of electron donating methyl, methoxy substitutions and their positions.

IV. Experimental

General procedure for synthesis of thiophene-isoxazole conjugates, **5**(**a-h**): To a solution of chalcones **3**(**a-h**) (10 mmol) and hydroxylamine hydrochloride **4** (15 mmol) in freshly prepared lemon juice (30 mL), tetrabutylammonium bromide (TBAB) (0.001 mol) was added. Then the mixture was refluxed on a water bath for 3-4 h. The progress of the reaction was monitored by TLC. After the completion, the reaction mixture was poured into crushed ice; the solids separated were filtered and washed successively with dilute $NaHCO_3$ and ice cold water. The crude solids were purified by column chromatography using solvent system hexane:ethylacetate (4:1) to get compounds **5**(**a-h**).

5-(3-Methylthiophen-2-yl)-3-phenyl-4,5-dihydroisoxazole, **5a**: Obtained from 3-(3-methylthiophen-2-yl)-1-phenylprop-2-en-1-one, **3a** (2.28g, 10 mmol) and hydroxylamine hydrochloride, **4** (1.03g, 15 mmol) in 66% yield, m.p. 89-91 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.184 (s, 3H, CH_3), 3.502 (dd, 1H, *J=6.1, 15.8 Hz*, C_4-H_a), 3.740 (dd, 1H, *J=7.0, 11.5 Hz*, C_4-H_b), 4.980 (dd, 1H, *J=5.9, 12.5 Hz*, C_5-H), 6.954-7.089 (m, 2H, Ar-H), 7.456-7.772 (m, 5H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 13.1 (1C, CH_3), 43.6 (1C, C-4), 75.2 (1C, C-5), 122.4 (1C), 125.8 (1C), 128.1 (2C), 128.9 (2C), 129.5 (2C), 130.3 (1C), 132.7 (1C), 141.0 (1C), 158.0 (1C, C-3). MS (ES+) *m/z*: 243.01 (M+, 100); Anal. Calcd. for $C_{14}H_{13}NOS$ (%): C, 69.11; H, 5.39; N, 5.76; Found: C, 69.00; H, 5.36; N, 5.72.

3-(4-Fluorophenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5b**: Obtained from 1-(4-fluorophenyl)-3-(3-methylthiophen-2-yl)prop-2-en-1-one, **3b** (2.46g, 10 mmol) and hydroxylamine hydrochloride, **4** (1.03g,

15 mmol) in 62 % yield, m.p. 100-103 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.190 (s, 3H, CH_3), 3.525 (dd, 1H, *J=7.2, 17.4 Hz*, C_4-H_a), 3.728 (dd, 1H, *J=7.9, 12.8Hz*, C_4-H_b), 5.133 (dd, 1H, *J=6.9, 13.8 Hz*, C_5-H), 7.020-7.176 (m, 2H, Ar-H), 7.320-7.545 (m, 4H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 13.0 (1C, CH_3), 43.9 (1C, C-4), 77.4 (1C, C-5), 116.1 (2C), 121.8 (1C), 126.6 (1C), 127.3 (2C), 129.4 (2C), 131.8 (1C), 137.9 (1C), 159.5 (1C, C-3), 162.1 (1C). MS (ES+) *m/z*: 261.05 (M+, 100); Anal. Calcd. for $C_{14}H_{12}FNOS$ (%): C, 64.35; H, 4.63; N, 5.36; Found: C, 64.22; H, 4.60; N, 5.33.

3-(4-Chlorophenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5c**: Obtained from 1-(4-chlorophenyl)-3-(3-methylthiophen-2-yl)prop-2-en-1-one, **3c** (2.62g, 10 mmol) and hydroxylamine hydrochloride, **4** (1.03g, 15 mmol) in 65% yield, m.p. 140-142 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.244 (s, 3H, CH_3), 3.520 (dd, 1H, *J=6.4, 16.3 Hz*, C_4-H_a), 3.756 (dd, 1H, *J=7.5, 11.7 Hz*, C_4-H_b), 5.166 (dd, 1H, *J=6.0, 12.8 Hz*, C_5-H), 7.030-7.091 (m, 2H, Ar-H), 7.651-7.816 (m, 4H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 14.2 (1C, CH_3), 45.1 (1C, C-4), 77.5 (1C, C-5), 122.0 (1C), 126.1 (1C), 128.4 (2C), 128.8 (2C), 129.0 (1C), 133.0 (1C), 135.5 (1C), 141.7 (1C), 159.3 (1C, C-3). MS (ES+) *m/z*: 277.03 (M+, 100), 279.05 (M+2, 33); Anal. Calcd. for $C_{14}H_{12}ClNOS$ (%): C, 60.54; H, 4.35; N, 5.04; Found: C, 60.40; H, 4.34; N, 5.02.

5-(3-Methylthiophen-2-yl)-3-(p-tolyl)-4,5-dihydroisoxazole, **5d**: Obtained from 3-(3-methylthiophen-2-yl)-1-(p-tolyl)prop-2-en-1-one, **3d** (2.42g, 10 mmol) and hydroxylamine hydrochloride, **4** (1.03g, 15 mmol) in 59% yield, m.p. 119-120 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.113 (s, 3H, CH_3), 2.250 (s, 3H, CH_3), 3.533 (dd, 1H, *J=6.4, 15.9 Hz*, C_4-H_a), 3.752 (dd, 1H, *J=7.3, 11.9 Hz*, C_4-H_b), 5.120 (dd, 1H, *J=6.0, 12.6 Hz*, C_5-H), 7.065-7.138 (m, 4H, Ar-H), 7.541-7.700 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 13.6 (1C, CH_3), 23.1 (1C, CH_3), 43.1 (1C, C-4), 76.6 (1C, C-5), 121.0 (1C), 126.1 (1C), 127.6 (2C), 128.0 (1C), 129.1 (2C), 132.8 (1C), 138.6 (1C), 140.8 (1C), 159.9 (1C, C-3). MS (ES+) *m/z*: 257.06 (M+, 100); Anal. Calcd. for $C_{15}H_{15}NOS$ (%): C, 70.01; H, 5.88; N, 5.44; Found: C, 69.89; H, 5.86; N, 5.41.

3-(4-Methoxyphenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5e**: Obtained from 1-(4-methoxyphenyl)-3-(3-methylthiophen-2-yl)prop-2-en-1-one, **3e** (2.58g, 10 mmol) and hydroxylamine hydrochloride, **4** (1.03g, 15 mmol) in 61% yield, m.p. 126-128 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.219 (s, 3H, CH_3), 3.525 (dd, 1H, *J=6.6, 15.9 Hz*, C_4-H_a), 3.790 (dd, 1H, *J=6.6, 12.2 Hz*, C_4-H_b), 3.844 (s, 3H, OCH_3), 5.055 (dd, 1H, *J=6.7, 13.2 Hz*, C_5-H), 7.020-7.192 (m, 4H, Ar-H), 7.841-7.888 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 13.7 (1C, CH_3), 44.0 (1C, C-4), 56.1 (1C, OCH_3), 76.8 (1C, C-5), 113.8 (2C), 120.8 (1C), 122.4 (1C), 127.3 (1C), 128.6 (2C), 132.7 (1C), 139.6 (1C), 158.2 (1C), 159.4 (1C, C-3). MS (ES+) *m/z*: 273.04 (M+, 100); Anal. Calcd. for $C_{15}H_{15}NO_2S$ (%): C, 65.91; H, 5.53; N, 5.12; Found: C, 65.79; H, 5.51; N, 5.10.

3-(2-Methoxyphenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5f**: Obtained from 1-(2-methoxyphenyl)-3-(3-methylthiophen-2-yl)prop-2-en-1-one, **3f** (2.58g, 10 mmol) and hydroxylamine hydrochloride, **4** (1.03g, 15 mmol) in 68% yield, m.p. 125-126 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.221 (s, 3H, CH_3), 3.531 (dd, 1H, *J=6.8, 16.0 Hz*, C_4-H_a), 3.788 (dd, 1H, *J=6.7, 12.6 Hz*, C_4-H_b), 3.850 (s, 3H, OCH_3), 5.062 (dd, 1H, *J=6.7, 13.3 Hz*, C_5-H), 7.028-7.187 (m, 3H, Ar-H), 7.755-7.840 (m, 3H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 13.1 (1C, CH_3), 44.2 (1C, C-4), 55.8 (1C, OCH_3), 76.3 (1C, C-5), 114.4 (1C), 118.0 (1C), 120.5 (1C), 122.2 (1C), 126.7 (1C), 127.8 (1C), 128.5 (1C), 131.5 (1C), 139.9 (1C), 158.0 (1C), 159.7 (1C, C-3). MS (ES+) *m/z*: 273.09 (M+, 100); Anal. Calcd. for $C_{15}H_{15}NO_2S$ (%): C, 65.91; H, 5.53; N, 5.12; Found: C, 65.82; H, 5.50; N, 5.09.

3-(3,4-Dimethoxyphenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5g**: Obtained from 1-(3,4-dimethoxyphenyl)-3-(3-methylthiophen-2-yl)prop-2-en-1-one, **3g** (2.88g, 10 mmol) and hydroxylamine hydrochloride, **4** (1.03g, 15 mmol) in 70% yield, m.p. 144-145 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.197 (s, 3H, CH_3), 3.513 (dd, 1H, *J=6.2, 15.9 Hz*, C_4-H_a), 3.757 (dd, 1H, *J=6.6, 12.9 Hz*, C_4-H_b), 3.854 (s, 6H, OCH_3), 5.133 (dd, 1H, *J=6.6, 13.4 Hz*, C_5-H), 7.035-7.552 (m, 6H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 14.5 (1C, CH_3), 44.8 (1C, C-4), 55.2 (2C, OCH_3), 76.9 (1C, C-5), 115.6 (1C), 118.2 (1C), 120.5 (1C), 126.0 (1C), 127.3 (1C), 128.6 (1C), 129.0 (1C), 133.9 (1C), 141.8 (1C), 148.0 (1C), 150.5 (1C), 159.6 (1C, C-3). MS (ES+) *m/z*: 303.02 (M+, 100); Anal. Calcd. for $C_{16}H_{17}NO_3S$ (%): C, 63.35; H, 5.65; N, 4.62; Found: C, 63.22; H, 5.61; N, 4.60.

3-(Benzo[d][1,3]dioxol-5-yl)-5-(3-methylthiophen-2-yl)-4,5-dihydroisoxazole, **5h**: Obtained from 1-(benzo[d][1,3]dioxol-5-yl)-3-(3-methylthiophen-2-yl)prop-2-en-1-one, **3h** (2.72g, 10 mmol) and hydroxylamine hydrochloride, **4** (1.03g, 15 mmol) in 71% yield, m.p. 160-161 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.220 (s, 3H, CH_3), 3.566 (dd, 1H, *J=6.7, 16.7 Hz*, C_4-H_a), 3.796 (dd, 1H, *J=7.7, 13.1 Hz*, C_4-H_b), 5.103 (dd, 1H, *J=6.9, 14.0 Hz*, C_5-H), 6.026 (s, 2H, OCH_2O), 7.108-7.567 (m, 5H, Ar-H); ^{13}C NMR ($CDCl_3$, δ ppm): 13.3 (1C, CH_3), 41.7 (1C, C-4), 74.3 (1C, C-5), 103.2 (1C, OCH_2O), 120.7 (1C), 112.5 (1C), 113.9 (1C), 122.0 (1C), 126.3 (1C), 127.6 (1C), 128.5 (1C), 133.2 (1C), 141.8 (1C), 146.1 (1C), 149.7 (1C), 155.7 (1C, C-3). MS (ES+) *m/z*: 287.04 (M+, 100); Anal. Calcd. for $C_{15}H_{13}NO_3S$ (%): C, 62.70; H, 4.56; N, 4.87; Found: C, 62.56; H, 4.53; N, 4.85.

V. Conclusion

This study demonstrates the effective use of greener medium citrus juice, for an efficient synthesis of series of isoxazole derivatives through (3+2) annulations. In vitro screening results of antifungal and DPPH radical scavenging activity shows that some of the synthesized compounds act as potential antifungal and

antioxidant agents. In particular, compounds **5b** with MIC's (12.5-50.0 µg/mL), and **5c** (12.5-37.5 µg/mL) could serve as potent antifungal agents against *A. niger*, *A. flavus* and *C. albicans* organisms. These two molecules might also serve as antioxidants.

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