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Synthesis and biological evaluation of a novel series of methoxylated chalcones as antioxidant and anti-microbial agents

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ABSTRACT

*A series of novel 2, 4, 5-trimethoxy Chalcones derivatives of biological interest were prepared by Claisen–Schmidt Condensation reaction. All the new compounds were evaluated for **(1a-u)** antioxidant (DPPH free radical scavenging activity) and antimicrobial (antifungal and antibacterial) activities against some selected pathogenic bacteria and fungi. Amongst all the 21 compounds screened, compounds **1b** and **1o** exhibited promising antioxidant activity (68 and 71% inhibition, as against standard BHA, 72 % inhibition) while compounds **1c, 1d, 1j** and **1k** exhibited antibacterial and compounds **1c, 1j** and **1k** exhibited promising antifungal activity (MIC of 10-30 µg/ml). The structure–activity relationship (SAR) for all the above stated activities has also been represented.*

Keywords: Methoxylated Chalcones, Anti-oxidant, Anti-bacterial, Anti-fungal.

INTRODUCTION

The treatment of bacterial infections remains a challenging therapeutic problem because of emerging infectious diseases and the increasing number of multidrug-resistant microbial pathogens. Despite the many antibiotic and chemotherapeutic available, the emergence of old and new antibiotic-resistant bacterial strains in the last decades constitutes a substantial need for new classes of anti-bacterial agents.[1]

Chalcones constitute an important group of natural products and serve as precursors for the synthesis of different classes of flavonoids, which are common substances in plants. Chalcones are open-chain flavonoids in which two aromatic rings are joined by a three carbon α, β, -unsaturated carbonyl system (1, 3-diphenyl-2-propen-1-ones). [2] Chalcone derivatives have received a great attention due to their relatively simple structure, and wide verity of pharmacological activities reported for these compounds include anti-inflammatory, [3] anti-tumor, [4-7] anti-ulcerative, [8] analgesic, [9] anti-viral,[10] anti-malarial,[11] and anti-cancer activities.[12] These activities are largely attributed due to the α, β,-unsaturated ketone moiety. Introduction of various substituent's into the two aryl rings is also a subject of interest because it leads to useful structure-activity relationship (SAR) conclusion and thus helps to synthesize pharmacologically active chacones.

In addition, antimicrobial and anti-oxidant activity of methoxylated Chalcones derivatives have been extensively studied and well established in the literature.[13-18]
In present study, in order to further expand the scope of methoxylated Chalcones derivatives as antimicrobial and anti-oxidant agents we report herein the synthesis and biological activity of trimethoxychalcone as antimicrobial and antioxidant agents.

EXPERIMENTAL SECTION

General

All reagent used were of analytical grade (Thomas Baker) ^{1}HNMR spectra were recorded on Cuker Advance spectrometer (300MHz or 500MHz) using tetramethylsilane as internal standard: J values are in Hertz. Chemical shifts are reported in ppm (δ) relative to the solvent peak, Mass spectra were recorded on either GCMS (focus GC with TSQ II mass analyzer and thermoelectro) with autosampler/direct injection (EI/CI) or LCMS (APCI/ESI; Buker daltanoics Micro TOFQ). HPLC purity was checked using Water Alliances or Dionex Ultima 3000 HPLC system. All chromatographic purications were done on silica gel (100-200 mesh). Ethyl acetate and petroleum ether were used for purification of compounds (Merck Kiesel 60 F254, 0.2mm thickness sheet).

General procedure for synthesis of Chalcones (1)

The preparation of the 2, 4, 5-trimethoxychalcone analogues (**1a-u**) were carried out via Claisen–Schmidt condensation (Scheme 1).

Thus, different substituted **(**2-hydroxyacetophenone) (1eqi.) and 2, 4, 5-trimethoxy benzaldehyde (1eqi.) in EtOH (15 mL) was added a 60% of KOH (5 ml) solution drop wise at 0^0C.The in ethanol/KOH at 0–5^0C. The reaction mixture was stirred at room temperature for 6-8 hr. The reaction mixture was cooled and poured into ice water, neutralized using 1NHCl .The light yellow solid thus obtained which was filtered and purified by using silica gel column chromatography (with 1:9 ethyl acetate in hexane) or recrystalized from EtOH, yielded the desired 2, 4, 5-trimethoxychalcone analogues (2–23) with an average yield of 60 –70%.

The physical and spectral data of selective methoxylated chalcones are given below.

(E)-1-(3-chloro-2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one(1a): Yellow solid. Yield 65.32%; ^{1}HNMR (DMSO, 300MHz): δ 13.65 (bs, 1H), 8.27(s, *J* = 6 Hz, 1H), 8.21 (d, *J* = 9 Hz, 1H), 7.89(d, *J* = 9 Hz, 1H), 7.72(d, *J* = 9 Hz, 1H), 7.51(s, *J* = 9 Hz, 1H), 6.67 (m, *J* = 9 Hz, 1H), 6.17 (s, *J* = 6 Hz, 1H), 3.83 (s, 3H), 3.87(s, 3H), 3.89(s, 3H), MS (APCI); *m/z* 349.1[M+1]$^+$; HPLC: 93.34%.

(E)-1-(3-chloro-2-hydroxy-5-methylphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1b): Orange solid. Yield 64%; ^{1}HNMR (DMSO, 300MHz): δ 13.90 (bs, 1H), 8.26 (s, 1H), 8.18 (d, *J* = 15.3 Hz, 1H), 7.81 (d, *J* = 15.3 Hz, 1H), 7.57(s, 1H), 6.98 (s, 1H), 6.72 (s, 1H), 3.87 (s, 3H), 3.95 (s, 3H), 3.81 (s, 3H), MS (APCI); *m/z* 363.1 [M+1]$^+$; HPLC: 95.04%.

(E)-1-(4-chloro-2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1c): Yellow solid. Yield 68 %; ^{1}HNMR (DMSO, 300MHz): δ 13.65 (bs, 1H), 8.27(s, *J* = 6 Hz, 1H), 8.21 (d, *J* = 9 Hz, 1H), 7.89(d, *J* = 9 Hz, 1H), 7.72(d, *J* = 9 Hz, 1H), 7.51(s, *J* = 9 Hz, 1H), 6.67 (m, *J* = 9 Hz, 1H), 6.17 (s, *J* = 6 Hz, 1H), 3.83 (s, 3H), 3.87(s, 3H), 3.89(s, 3H), MS (APCI); *m/z* 349.1[M+1]$^+$; HPLC: 94.34%.

(E)-1-(2,4-dichloro-6-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1d): Yellow solid. Yield 66.66%; ^{1}HNMR (DMSO, 300MHz): δ 13.76 (bs, 1H), 8.29 (s, 1H), 7.82 (d, *J* = 15.3 Hz, 1H), 7.58 (s, 1H), 7.49(d, *J* = 15.3 Hz, 1H), 7.13 (s, 1H), 6.54(s, 1H), 3.99 (s, 3H), 3.97 (s, 3H), 3.95 (s, 3H), MS (APCI); *m/z* 384.1 [M+1]$^+$; HPLC: 93.33%.

(E)-3-chloro-4-hydroxy-5-(3-(2,4,5-trimethoxyphenyl)acryloyl)benzonitrile(1e): Orange solid. Yield 64.66%; ^{1}HNMR (DMSO, 300MHz): δ 12.69 (bs, 1H), 8.20 (s, 1H), 8.15 (d, *J* = 15.3 Hz, 1H), 7.65 (s, 1H), 7.40(d, *J* = 15.3 Hz, 1H), 7.11 (s, 1H), 6.37(s, 1H), 3.99 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), MS (APCI); *m/z* 374.1 [M+1]$^+$; HPLC: 93.45%.

(E)-1-(3-bromo-2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1f): Orange solid. Yield 75%; ^{1}HNMR (DMSO, 300MHz): δ 12.69 (bs, 1H), 8.30(s, 1H), 8.18 (d, *J* = 15.3 Hz, 1H), 7.76(d, *J* = 15.3Hz, 1H), 7.65(d, *J* = 8.6 Hz, 1H), 7.55(s, *J* = 9 Hz, 1H), 6.95(d, *J* = 8.6 Hz, 1H), 6.72 (s, *J* = 6 Hz, 1H), 3.89 (s, 3H), 3.87(s, 3H), 3.81(s, 3H), MS (APCI); *m/z* 394.0 [M+1]$^+$; HPLC: 95.03%.

(E)-1-(4-bromo-2-hydroxy-6-nitrophenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1g): Orange solid. Yield 67.10%; ^{1}HNMR (DMSO, 300MHz): δ 13.90 (bs, 1H), 8.30 (s, 1H), 8.14(d, *J* = 15.3 Hz, 1H), 8.06(s, 1H), 7.47(d, *J* = 15.3 Hz, 1H), 7.10 (s, 1H), 6.49 (s, 1H), 3.98 (s, 3H), 3.95 (s, 3H), 3.93 (s, 3H), MS (APCI); *m/z* 439.0 [M+1]$^+$; HPLC: 97.03%.

(E)-1-(3-fluoro-2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1h): Yellow solid. Yield 69.20%; ^{1}HNMR (DMSO, 300MHz): δ 12.69 (bs, 1H), 8.04(s, 1H), 7.90 (d, *J* = 15.3 Hz, 1H), 7.89(d, *J* = 8.7 Hz, 1H), 7.70(d, *J* = 15.3 Hz, 1H), 7.51(s, 1H), 7.06 (m, *J* = 8.4Hz, 1H), 6.72 (s, 1H), 3.87 (s, 3H), 3.85(s, 3H), 3.80(s, 3H), MS (APCI); *m/z* 333.1[M+1]$^+$; HPLC: 94.04%.

(E)-1-(5-fluoro-2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1i): Orange solid. Yield 80 %; ^{1}HNMR (DMSO, 300MHz): δ 12.61 (bs, 1H), 8.21(d, *J* = 15.3 Hz, 1H), 8.10

(d, *J* = 7.5Hz, 1H), 7.76(d, *J* = 15.3 Hz, 1H), 7.56(s, 1H), 7.45(d, *J* = 7.8Hz, 1H), 6.96(d, *J* = 9 Hz, 1H), 6.73 (s, 1H), 3.90 (s, 3H), 3.87(s, 3H), 3.82(s, 3H), MS (APCI); *m/z* 333.1$[M+1]^+$; HPLC: 94.04%.

(E)-1-(4-fluoro-2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one(1j): Yellow solid. Yield 67.50%; ^{1}HNMR (DMSO, 300MHz): δ 13.48 (bs, 1H), 8.20(s, *J* = 15.3Hz, 1H), 7.93 (m, *J* = 6.8 Hz, 1H), 7.52(d, *J* = 15.3Hz, 1H), 7.10(s, 1H), 6.63(d, *J* = 9 Hz, 1H), 6.63 (dd, 2H), 6.53 (s, 1H), 3.96 (s, 3H), 3.93(s, 3H), 3.91(s, 3H), MS (APCI); *m/z* 333.1$[M+1]^+$; HPLC: 93.40%.

(E)-1-(2,4-difluoro-6-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one(1k): Orange solid. Yield 66.66%; ^{1}HNMR (DMSO, 300MHz): δ 13.87 (bs, 1H), 8.30 (s, 1H), 7.59(d, *J* = 15.3 Hz, 1H), 7.10(s, 1H), 6.51(d, *J* = 15.3 Hz, 1H), 6.49 (s, 1H), 6.63(s, 1H), 3.95 (s, 3H), 3.92 (s, 3H), 3.89 (s, 3H), MS (APCI); *m/z* 351.1.0 $[M+1]^+$; HPLC: 92.04%.

(E)-1-(3,5-difluoro-2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one(1l): Orange solid. Yield 64.5%; ^{1}HNMR (DMSO, 300MHz): δ 12.64 (bs, 1H), 8.23 (s, 1H), 8.00(d, *J* = 15.3 Hz, 1H), 7.70(s, 1H), 7.62(d, *J* = 15.3 Hz, 1H), 7.56 (s, 1H), 6.75 (s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.83 (s, 3H), MS (APCI); *m/z* 351.1.0 $[M+1]^+$; HPLC: 93.54%.

(E)-1-(2-fluoro-6-hydroxy-4-nitrophenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1m) : Orange solid. Yield 69 %; ^{1}HNMR (DMSO, 300MHz): δ 13.76 (bs, 1H), 8.32 (s, 1H), 8.21 (d, *J* = 15.3 Hz, 1H), 8.01 (s, 1H), 7.40(d, *J* = 15.3 Hz, 1H), 7.10 (s, 1H), 6.57(s, 1H), 3.97 (s, 3H), 3.95 (s, 3H), 3.93 (s, 3H), MS (APCI); *m/z* 378.1 $[M+1]^+$; HPLC: 92.04%.

(E)-3-fluoro-5-hydroxy-4-(3-(2,4,5-trimethoxyphenyl)acryloyl)benzonitrile (1n): Orange solid. Yield 61.33%; ^{1}HNMR (DMSO, 300MHz): δ 13.49 (bs, 1H), 8.21 (d, *J* = 15.3 Hz 1H), 7.65 (s, 1H), 7.41 (d, *J* = 15.3 Hz, 1H), 7.33(s, 1H), 6.60 (s, 1H), 6.19(s, 1H), 3.95 (s, 3H), 3.92 (s, 3H), 3.89 (s, 3H), MS (APCI); *m/z* 358.1 $[M+1]^+$; HPLC: 92.04%.

(E)-1-(2-hydroxy-5-methylphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1o): Yellow solid. Yield 65.5%; ^{1}HNMR (DMSO, 300MHz): δ 13.13 (bs, 1H), 8.18(d, *J* =15.3 Hz, 1H), 7.80(d, *J* = 8.09Hz, 1H), 7.57 (d, *J* = 15.3Hz, 1H), 7.12(s, 1H), 6.82 (s, 1H), 6.73 (d, *J* = 8.09 Hz, 1H), 6.53 (s, 1H), 3.95 (s, 3H), 3.93(s, 3H), 3.92(s, 3H), 2.37 (s, 3H), MS (APCI); *m/z* 329.2$[M+1]^+$; HPLC: 93.28%.

(E)-1-(2-hydroxy-4-methyl-6-nitrophenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1p): Orange solid. Yield 69 %; ^{1}HNMR (DMSO, 300MHz): δ 13.69 (bs, 1H), 8.20 (d, , *J* = 15.3 Hz, 1H), 7.99(s, 1H), 7.92(s, 1H), 7.50(d, *J* = 15.3 Hz, 1H), 7.11 (s, 1H), 6.52 (s, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.91 (s, 3H), 2.41 (s, 3H); MS (APCI); *m/z* 374.1 $[M+1]^+$; HPLC: 96.04%.

(E)-1-(2-hydroxy-4-(trifluoromethyl)phenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1q): Yellow solid. Yield 67 %; ^{1}HNMR (DMSO, 300MHz): δ 13.45 (bs, 1H), 8.25(s, *J* = 15.3 Hz, 1H), 8.15(s, 1H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.57(d, *J* = 15.3 Hz, 1H), 7.26 (s, 1H), 7.10 (s,2H), 6.53 (s, 1H), 3.88 (s, 3H), 3.87(s, 3H), 3.79(s, 3H), MS (APCI); *m/z* 383.2$[M+1]^+$; HPLC: 94.64%.

(E)-1-(2-hydroxy-4-nitrophenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1r): Orange solid. Yield 66.00%; ^{1}HNMR (DMSO, 300MHz): δ 13.79 (bs, 1H), 8.74 (s, 1H), 8.33 (d, *J* = 9 Hz, 1H), 8.10(d, *J* = 15.3 Hz, 1H), 7.72(d, *J* = 15.3 Hz, 1H), 7.48 (s, 1H), 7.15(d, *J* = 9 Hz, 1H), 6.73 (s, 1H), 3.89 (s, 3H), 3.87(s, 3H), 3.79(s, 3H), MS (APCI); *m/z* 358.1 $[M-1]^+$; HPLC: 95.32%.

(E)-1-(2-hydroxy-4-(methylsulfonyl)phenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (1s): Orange solid. Yield 67 %; ^{1}HNMR (DMSO, 300MHz): δ 13.83 (bs, 1H), 8.53(d, *J*=15.2 1H), 8.31(dd, *J* = 8.6Hz, 1H), 7.97 (d, *J* = 9 Hz, 1H), 7.60(d, *J* = 15.2 Hz, 1H), 7.16(d, *J* = 8.8Hz, 1H), 7.14(s, 1H), 6.53 (s, 1H), 3.97 (s, 3H), 3.94(s, 3H), 3.92(s, 3H), 3.09(s, 3H), MS (APCI); *m/z* 393.1$[M+1]^+$; HPLC: 93.33%.

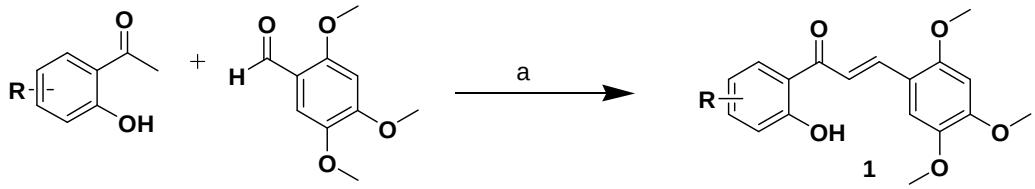
(E)-3-hydroxy-2-(3-(2,4,5-trimethoxyphenyl)acryloyl)benzonitrile (1t): Orange solid. Yield 63 %; ^{1}HNMR (DMSO, 300MHz): δ 14.11 (bs, 1H), 8.31(d, *J* = 15.3Hz, 1H), 8.27(d, *J* = 8.7 Hz, 1H), 8.01(d, *J* = 8.7 Hz, 1H), 7.86(d, *J* = 15.3 Hz, 1H), 7.56(s, 1H), 7.16 (m, 1H), 6.74 (s, 1H), 3.91 (s, 3H), 3.88(s, 3H), 3.81(s, 3H), MS (APCI); *m/z* 340.1$[M+1]^+$; HPLC: 96.06%.

(E)-2-hydroxy-3-(3-(2,4,5-trimethoxyphenyl)acryloyl)benzonitrile (1u): Orange solid. Yield 65 %; ^{1}HNMR (DMSO, 300MHz): δ 14.11 (bs, 1H), 8.33(d, *J* = 15.3Hz, 1H), 8.29(d, *J* = 8.7 Hz, 1H), 8.03(d, *J* = 8.7 Hz, 1H), 7.89(d, *J* = 15.3 Hz, 1H), 7.59(s, 1H), 7.16 (m, 1H), 6.77 (s, 1H), 3.92 (s, 3H), 3.86(s, 3H), 3.83(s, 3H), MS (APCI); *m/z* 340.1$[M+1]^+$; HPLC: 93.66%.

RESULTS AND DISCUSSION

Chemistry

In literature several reports are available for synthesis of 2,4,5-trimethoxychalcone. Our synthetic strategy for (E)-1-(2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one derivatives is illustrated in scheme **1**. The 21 different hydroxychalcone were prepared by Claisen–Schmidt condensation between substituted 2-hydroxy acetophenones and 2,4,5-trimethoxybenzaldehyde in good yields (60-70%). Thus twenty one different chalcone (**1a-u**) were readily obtained using extremely mild conditions and the pure products were obtained by routine aqueous workup followed by column chromatography or recrystalisation. The overall yields of the present procedure are within acceptable range with an average maximum yield of product found to be 65%, as in scheme 1.



R = **1a : 3'-Cl** **1b : 3'-Cl, 5'-CH_3** **1c : 6'-Cl** **1d : 4'-Cl, 6'-Cl** **1e : 3'-CN, 5'-Cl** **1f : 3'-Br** **1g : 4'-Br, 6'-NO_2** **1h : 3'-F** **1i : 5'-F** **1j : 4'-F** **1k : 4'-F, 6'-F** **1l : 3'-F, 5'-F** **1m: 4'-NO_2, 6'-F** **1n : 4-CN, 6'-F** **1o : 5'- CH_3 ,** **1p : 4'-CH_3, 6'- NO_2** **1q : 4'-CF_3** **1r : 4'-NO_2** **1s : 4'-SO_2Me** **1t : 6'-CN** **1u : 3'-CN**

Scheme 1. Reagents and conditions: (a) EtOH,60% KOH, 0-rt 6-8 hr.

Table 1. Anti-oxidant activity of 2,4,5-trimethoxy chalcone derivatives

	Gram-positive		*Gram-negative*	
Compounds	*Staphylococcus aureus*	*Bacillus subtilis*	*Escherichia coli*	*Salmonella typhimurium*
1a	55	65	55	60
1b	75	45	40	60
1c	**15**	**10**	**10**	**20**
1d	**15**	**20**	**10**	**30**
1e	65	65	20	55
1f	75	80	65	70
1g	65	-	65	-
1h	60	75	40	55
1i	80	45	65	45
1j	40	30	15	25
1k	25	35	25	20
1l	30	45	65	60
1m	-	-	90	90
1n	85	-	80	90
1o	-	-	-	-
1p	-	-	85	-
1q	**40**	**65**	**35**	**35**
1r	-	-	90	90
1s	**35**	**50**	**35**	**30**
1t	-	-	-	-
1u	90	-	85	90
Ciprofloxacin	25	20	15	20

[a] *Standard substance.*
[b] *Mean ± SD, n = 3.*

Table 2. Anti-bacterial activity of 2,4,5-trimethoxy chalcone derivatives

Compounds	% DPPH [b]
1a	26.68 ± 0.25
1b	68.00 ± 0.47
1c	30.33 ± 0.20
1d	23.32 ± 0.23
1e	18.23 ± 0.29
1f	17.24 ± 0.22
1g	13.81 ± 0.23
1h	44.91 ± 0.33
1i	**52.00 ± 0.43**
1j	32.33 ± 0.25
1k	34.64 ± 0.18
1l	18.25 ± 0.15
1m	11.28 ± 0.22
1n	16.53 ± 0.32
1o	71.00 ± 0.48
1p	36.53 ± 0.32
1q	**48.29 ± 0.45**
1r	19.21 ± 0.19
1s	23.32 ± 0.23
1t	19.21 ± 0.19
1u	10.12 ± 0.27
BHA [a]	72.00 ± 0.54

Table 3. Anti-fungal activity of 2,4,5-trimethoxy chalcone derivatives.

Compounds	*Candida albicans*	*Aspergillus niger*	*Fusarium solani*	*Aspergillus flavus*
1a	85	55	90	80
1b	90	85	-	90
1c	20	40	15	25
1d	45	35	30	25
1e	75	40	70	85
1f	90	-	90	-
1g	80	-	90	90
1h	45	40	35	30
1i	-	85	90	90
1j	25	40	30	20
1k	25	35	30	15
1l	75	80	90	-
1m	90	-	95	90
1n	85	90	80	85
1o	-	-	-	-
1p	95	-	-	90
1q	30	50	20	30
1r	-	-	90	-
1s	65	75	40	35
1t	-	-	-	95
1u	-	-	-	-
Miconazole	20	20	15	20

Biology

Having secured the structually diverse (E)-1-(2-hydroxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (**1a-u**). Next all the synthesized compounds were evaluated for atioxidant (DPPH assay) and antimicrobial (agar diffusion methode) study. The result of this study are collected in table 1-3. As shown in table-1, the compound **1b** and **1o** were found to be promising antioxidant with 68% and 71% inhibition (against standard BHA 72% inhibition) as determined by DPPH assay.

Thus these two compounds were found to be almost equally effective to the standard BHA for their radical scavenging activity. Compounds **1i** and **1q** from this series were found to be moderately active (52% and 48% inhibition) while remaining compounds of this series exhibited low or poor antioxidant activity with respect to standard BHA.

The antifungal and antibacterial activity data of the novel chalcone is represented in table-2 and 3 respectively. A large number of compounds were found to be the promising antifungal and antibacterial agents against all the tested fungi and bacteria as compared to standard micanazole and ciprofloxacin respectively.Thus as shown in table-2. The compounds **1c, 1d,** and **1k** (tale-2) were found to be potent antibacterial agent at the MIC of (10-30 μg/ml) against all tested bacteria.The compound **1j** shows potent antibacterial activity against gram-negative Escherichia coli and Salmonella typhimurium at the 15-25 μg/ml.,but moderatly active against gram-possitive Staphylococcus aureus and Bacillus subtilis. Compounds **1l, 1q** and **1s** from this series were found to be moderately active at the MIC of (30-65) μg/ml, while remaining compounds exhibited low or poor antibacterial activity with respect to all tested bacteria.

Notably, the compounds **1c,1j** and **1k** (Table- 3), exhibited one to two fold more antifungal activity almost against all the tested fungi as compared to the standard Micanazole at the same level of concentration (MIC of 10 μg/ml). Along with compounds **1d** and **1h** have moderately active at the (MIC of 25-45 μg/ml). The intresting activity of compound **1q** have moderate against candida albicans and aspergillus niger, but shows one to two fold potent against Fusarium solani and Aspergillus flavus tested fungi.

The compounds **1c,1d** and **1k** were found to be promising antibacterial agents with compomd **1k** exhibiting two fold antibacterial activity against all the tested bacterial strain. Remarkably, the compounds **1c,** and **1d** exhibited one and half or two fold antibacterial activity. However, the componds **1o, 1t** and **1u** were found to be completely ineffective as antifungal or antibacterial agents. The remaining compounds of this series were found to have low antifungal or antibacterial activity.

The antioxidant activity of this novel series of compound seems to have no general trend as regard to the structural variation. However, the presence of substituent such as Cl, or CH_3 at 3 or 5 both leading to the compounds **1b** and **1o**, found to be most favorable effect on the antioxidant activity. The compounds **1i** and **1q**, bearing fluoro and CF_3 at 4 and 5 position were found to have moderate antioxidants activity. Thus, in a broader sense, at least the presence of lipophilic group such as fluoro and CH_3 at 3 and 5 positions seems to have favorable effect on the antioxidant activity.

The presence of Cl, F at 3, 4, 5 and 6 position (compounds **1c, 1d, 2j 2k,)** found to have positive effect on the antibacterial activity. The position 6 was found to be the most favorable site as the compounds possessing Cl or F (compound **1c, 1d, 2k,**) at this position found to be the most potent antibacterial agents. Notably, the incorporation of electron withdrawing substituent including the halides, CN, NO_2 at 6' positions found to have dramatic negative effect on the antibacterial activity. For instance, the compound **1e, 1m** and **1n** bearing Cl or F at 6' position with CN or NO_2 at 3' and 4' positions respectively exhibited very low activity as compared to the standard ciprofloxacin. Remarkably, the incorporation of even additional Cl group at 6' position leading to the compound **1d** exhibited almost 50% antibacterial activity that of **1C**. (Table-2, compound **1c** Vs **1d**).

In Conclusion, we have synthesized the novel series of chalcone derivatives under mild conditions and evaluated for their antioxidant, antibacterial and antifungal activity. Few number of newly synthesized compounds were found to be potent antioxidant, antifungal and antibacterial agents. It is to be noted some of these compound found to be much more (two fold potency at same MIC of 10-30 µg/ml) potent than the standard ciprofloxacin or Micanazol We believe that the present work could proved to be of special interest to the drug development sector.

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