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MICROWAVE ASSISTED SOLID PHASE SYNTHESIS AND CHARACTERIZATION OF MICROBIALLY POTENT 7H-PYRROLO [2, 3-C: 5, 4-C'] DIISOXAZOLE DERIVATIVES

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ABSTRACT
In this work microwave assisted solid phase synthesis of the new series of 7H-pyrrolo [2, 3-c: 5, 4-c'] diisoxazole derivatives have been carried out by reaction of substituted benzaldehydes with 4-methyl phenyl succinamide **1** and 4-Chloro phenyl succinamide **2** afforded to (3Z 4Z)-3,4- bis (substituted benzylidine)-1-(4-methylphenyl) pyrrolidine- 2,5-dione **3a-e** and (3Z 4Z)-3,4- bis (substituted benzylidine)-1-(4-Chlorophenyl) pyrrolidine- 2,5-dione **4a-e.** These heterocyclic Chalcone derivatives further reacted with hydroxylamine hydrochloride in microwave oven in presence of neutral alumina furnished to diisoxazole derivative **5a-e** and **6a-e.** The structures of all synthesized compounds **5a-e** and **6a-e** have been confirmed by FT IR and ^{1}H NMR spectral analysis. The anti microbial analysis have carried out for compounds **5a-e** and **6a-e** the compound **6a** and **6e** have found to possess potent antibacterial activities and compound **6b** is found to possess potent antifungal activity.

KEYWORDS: Phenyl succinamide, heterocyclic Chalcone, hydroxylamine hydrochloride, diisoxazole.

INTRODUCTION
Isoxazoles are important class of heterocyclic compounds containing oxygen and nitrogen atoms in their structure. It exhibited broad spectrum of pharmaceutical activities such as anticonvulsant, anti cancer.[1] On the other hand isoxazole derivatives has found to have antiviral, insecticidal properties and it is used as corrosion inhibitor and lubricants.[2] The isoxazole ring systems is very stable so it provides opportunity for synthetic chemist to synthesize various derivatives bearing different substituent's. Some derivatives of isoxazole have anti-inflammatory and calcium channel blocker activities[3] it is also found to possess anticancer activity.[4] The recent studies have shown that isoxazole derivatives are used for treatment of neurological disorder like epilepsy it shows good antiepileptic activity,[5] antitubercular activity.[6] The derivatives having isoxazole nuclei exhibited cytotoxic activities,[7] Anti-inflammatory activity.[8] By considering all these diverse pharmaceutical applications of isoxazole derivatives most of research groups continuously engaged in synthesis of such heterocyclic compounds. The substituted imides[9] found to have anticonvulsant activity[10] and bis-succinamide derivatives used for extraction of uranium[11] The heterocyclic chalcones are biologically important[12,13] and versatile synthons for synthesis of diverse heterocyclic compounds[14,15] but by product arising from these chemical processes are toxic and also hazardous to environment so to overcome this problem less expensive solvent free and environmental friendly solid phase synthesis of diisoxazole derivatives have been carried out by using domestic microwave oven. The present synthesis have been furnished in one pot and one step process that gave easy, clean and rapid workup.

MATERIAL AND METHOD
Experimental
All chemicals used in the present work are of synthetic grade. The melting points were taken in to open capillaries and are uncorrected. The I.R spectra were recorded on FTIR shimazdu spectrophotometer using KBr disc method. The ^{1}H NMR spectra were recorded on Bruker mx-500 MHz in DMSO d_6. The chemical shift was recorded in δ unit relative to TMS as internal standard. All the compounds synthesized by using domestic microwave oven in hours. All reactions were executed in solid phase solvent free synthesis. The reaction was monitored by thin layer chromatography by using pre-coated silica gel aluminum plates and mixture of n-hexane: ethyl acetate 7:3 proportion was used as mobile phase. The identification of spots was done by visualizing plate in U.V chamber.

General procedure for synthesis of chalcone
To 10 milimoles 4-methyl phenyl succinamide and 4-Chloro phenyl succinamides in 100 ml glass beakers 2-2.5 grams of neutral alumina is added then 20 milimoles

of substituted benzaldehydes added in to beakers and carefully mixed. It is then irradiated in microwave oven at 450 watt power for 3- 4 min thus resulting fused yellow colored solid of bis-chalcone derivatives obtained and recrystallised it from ethanol.

(3Z, 4Z)-3, 4-bis (2-hydroxybenzylidene)-1-p-tolylpyrrolidine-2, 5-dione (3a):
Yield: 86%; MP:166-168 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 3368 (-OH), 2937(-CH_3), 1611(C=C); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 5.1(s, 1H, -OH), 7.31-7.17(m, 6H, Ar-H and =CH); Elem Anal. Cal for $C_{25}H_{19}NO_4$: C, 75.55; H, 4.82; N, 3.52; O, 16.10; Found C, 75.35; H, 4. 62; N, 3.72; O, 16.12.

(3Z,4Z)-3,4-bis(3-nitrobenzylidene)-1-p-tolylpyrrolidine-2,5-dione (3b):
Yield: 86%; MP: 198-200 ^{0}C; FTIR (KBr, cm^{-1}): 2937(-CH_3), 1705 (C=O), 1611(C=C) 1345 (Ar-NO_2); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3),), 8.47-6.67(m, 6H,Ar-H and =CH); Elem Anal. Cal for $C_{25}H_{17}N_3O_6$: C, 65.93; H, 3.76; N, 9.23; O, 21.08 Found: C, 65.73; H, 3.56; N, 9.43; O, 21.38.

(3Z,4Z)-3,4-bis (2-chlorobenzylidene)-1-p-tolylpyrrolidine-2,5-dione (3c):
Yield:86%; MP:173-175 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 713 (C-Cl), 1611(C=C); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 7.40-7.12 (m, 6H,Ar-H and =CH); Elem Anal. Cal for $C_{25}H_{17}Cl_2NO_2$: C, 69.14; H, 3.95; Cl, 16.33; N, 3.23; O, 7.37 Found: C, 69.34; H, 3.85; Cl, 16.53; N, 3.43; O, 7.47.

(3Z, 4Z)-3, 4-bis (4-methoxybenzylidene)-1-p-tolylpyrrolidine-2,5-dione (3d):
Yield: 86% MP: 162-164 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 1178 (O-CH3) 1611(C=C); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 3.7(s, 3H, -OCH_3), 8.22-6.43(m, 6H,Ar-H and =CH) Elem Anal. Cal for $C_{27}H_{23}NO_4$: C, 76.22; H, 5.45; N, 3.29; O, 15.04; Found C, 76.52; H, 5.65; N, 3.49; O, 15.34.

(3Z, 4Z)-3, 4-bis (4-methyl benzylidene)-1-p-tolylpyrrolidine-2,5-dione (3e):
Yield: 86%; MP: 144-146 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 1611(C=C); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.40 (s, 1H, CH_3), 8.22-6.43(m, 6H,Ar-H and =CH) Elem Anal. Cal for $C_{27}H_{23}NO_2$: C, 82.42; H, 5.89; N, 3.56; O, 8.13 Found: C, 82.62; H, 5.59; N, 3.76; O, 8.33.

(3Z,4Z)-3,4-bis(2-hydroxybenzylidene)-1-(4-chlorophenyl)pyrrolidine-2,5-dione (4a):
Yield: 86%; Yellow solid; MP: 116-118 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 3368 (-OH), 2937(-CH_3), 713 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 5.1(s, 1H, -OH), 7.31-7.17(m, 6H,Ar-H and =CH) Elem Anal. Cal for $C_{24}H_{16}ClNO_4$: C, 68.99; H, 3.86; Cl, 8.48; N, 3.35; O, 15.32; Found: C, 68.79; H, 3.66; Cl, 8.38; N, 3.65; O, 15.52.

(3Z,4Z)-3,4-bis(3-nitrobenzylidene)-1-(4-chlorophenyl)pyrrolidine-2,5-dione (4b):
Yield: 86%; Yellow crystalline solid; MP: 66-68 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 1345 (Ar-NO_2) 713 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.57-7.3(m, 6H,Ar-H and =CH) Elem Anal. Cal for $C_{24}H_{14}ClN_3O_6$: C, 60.58; H, 2.97; Cl, 7.45; N, 8.83; O, 20.17 Found: C, 60.38; H, 2.67; Cl, 7.55; N, 8.73; O, 20.27.

(3Z,4Z)-3,4-bis(2-chlorobenzylidene)-1-(4-chlorophenyl)pyrrolidine-2,5-dione (4c):
Yield: 86%; Yellow solid; MP: 191-193 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 713 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 7.40-7.12 (m, 6H,Ar-H and =CH) Elem Anal. Cal for $C_{24}H_{14}Cl_3NO_2$: C, 63.39; H, 3.10; Cl, 23.39; N, 3.08; O, 7.04; Found: C, 63.59; H, 3.21; Cl, 23.49; N, 3.28; O, 7.34.

(3Z,4Z)-3,4-bis(4-methoxybenzylidene)-1-(4-chlorophenyl)pyrrolidine-2,5-dione (4d):
Yield: 86%; Yellow solid; MP: 156-158 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 1178 (O-CH3), 720 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 3.7(s, 3H, -OCH_3), 7.6-7.2(m, 6H, Ar-H and =CH) Elem Anal. Cal for $C_{26}H_{20}ClNO_4$: C, 70.03; H, 4.52; Cl, 7.95; N, 3.14; O, 14.35; Found: C, 70.23; H, 4.62; Cl, 7.45; N, 3.34; O, 14.65.

(3Z,4Z)-3,4-bis(4-methyl benzylidene)-1-(4-chlorophenyl)pyrrolidine-2,5-dione (4e):
Yield: 86% ; Yellow solid; MP: 134-136 ^{0}C; FTIR (KBr, cm^{-1}): 1705 (C=O), 2937(-CH_3), 713 (C-Cl), ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 2.3 (s, 1H, CH_3), 7.6-7.2(m, 6H,Ar-H and =CH) Elem Anal. Cal for $C_{26}H_{20}ClNO_2$: C, 75.45; H, 4.87; Cl, 8.57; N, 3.38; O, 7.73; Found: C, 75.65; H, 4.47; Cl, 8.67; N, 3.58; O, 7.83.

General procedure for synthesis of 7H-pyrrolo [2, 3-c: 5, 4-c'] diisoxazole derivatives:
To 10 milimoles bis- chalcone derivatives in 100 ml glass beakers 2-2.5 grams of neutral alumina is added then two moles of hydroxylamine hydrochloride added in to beakers and carefully mixed. It is then irradiated in microwave oven at 450 watt power for 4-6 min thus brown colored fused solid derivatives of diisoxazole obtained and recrystallised it from ethanol.

2,2'-(7-(p-tolyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole-3,4-diyl)diphenol (5a):- Yield: 86% ;Brown solid, MP: 130-133 ^{0}C ; FTIR (KBr, cm^{-1}): 1588.48 (C=N), 3630 (-OH), 2916.37 (-CH_3), 925.83 (N-O); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.3-6.9 (m, 6H, Ar-H), 4.5 (d, 1H, CH isoxazole) 2.6 (d, 1H, CH isoxazole), 2.3 (s, 3H, CH_3) 9.3 (s, 1H, -OH) Elem Anal.

Cal for $C_{25}H_{21}N_3O_4$, C, 70.25; H, 4.95; N, 9.83; O, 14.97 Found: C, 70.15; H, 4.45; N, 9.23; O, 14.57.

3,4-bis(3-nitrophenyl)-7-(p-tolyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole (5b):- Yield 76 %, Brown solid, M.P 103-105^{0}C; FTIR (KBr, cm^{-1}): 1537.32 (C=N), 2920.32 (-CH_3), 1350.22 (Ar-NO_2), 925.83(N-O); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.46-7.28 (m ,6H, Ar-H), 4.19 (d , 1H , CH isoxazole) 1.73(d, 1H , CH isoxazole), 2.32 (s, 3H, CH_3). Elem Anal. Cal for $C_{25}H_{19}N_5O_6$, C, 61.85; H, 3.95; N, 14.43; O, 19.77; Found: C, 61.35; H, 3.55; N, 14.73; O, 19.87.

3,4-bis(2-chlorophenyl)-7-(p-tolyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole (5c): Yield 64 %, Brown solid, MP: 112-113 ^{0}C ; FTIR (KBr, cm^{-1}): 1537.88 (C=N), 2937(-CH_3), 713 (C-Cl), 925.83(N-O); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.3-6.9(m, 6H, Ar-H), 4.5 (d, 1H, CH isoxazole) 2.21(d, 1H , CH isoxazole), 2.32 (s, 3H, CH_3) Elem Anal. Cal for $C_{25}H_{19}Cl_2N_3O_2$ C, 64.67; H, 4.12; Cl, 15.27; N, 9.05; O, 6.89; Found: C, 64.77; H, 4.32; Cl, 15.47; N, 9.55; O, 6.29.

3,4-bis(4-methoxyphenyl)-7-(p-tolyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole (5d): Yield: 86% ; Light Brow crystals, MP: 158-160 ^{0}C ; FTIR (KBr, cm^{-1}): 1517.98 (C=N), 1184.29 (O-CH3), 2933.73 (-CH_3), 925.83 (N-O); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.46-7.28 (m, 6H, Ar-H), 4.5 (d , 1H , CH isoxazole) 3.7(s, 3H, -OCH_3) 2.3(d, 1H , CH isoxazole), 2.6 (s, 3H, CH_3) Elem Anal. Cal for $C_{27}H_{25}N_3O_4$ C, 71.19; H, 5.53; N, 9.22; O, 14.05; Found: C, 71.39; H, 5.73; N, 9.52; O, 14.45.

3,4,7-tri-p-tolyl-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole (5e): Yield: 86%; Brown crystals, MP: 136- 138 ^{0}C ; FTIR (KBr, cm^{-1}): 1527.45 (C=N), 1611 (C=C), 2930(-CH_3), 925.83(N-O);^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.4-7.28 (m, 6H, Ar-H), 4.5 (d, 1H, CH isoxazole) 1.73(d, 1H , CH isoxazole), 2.32 (s, 3H, CH_3). Elem Anal. Cal for $C_{27}H_{25}N_3O_2$, C, 76.57; H, 5.95; N, 9.92; O, 7.56; Found: C, 76.77; H, 5.55; N, 9.94; O, 7.66.

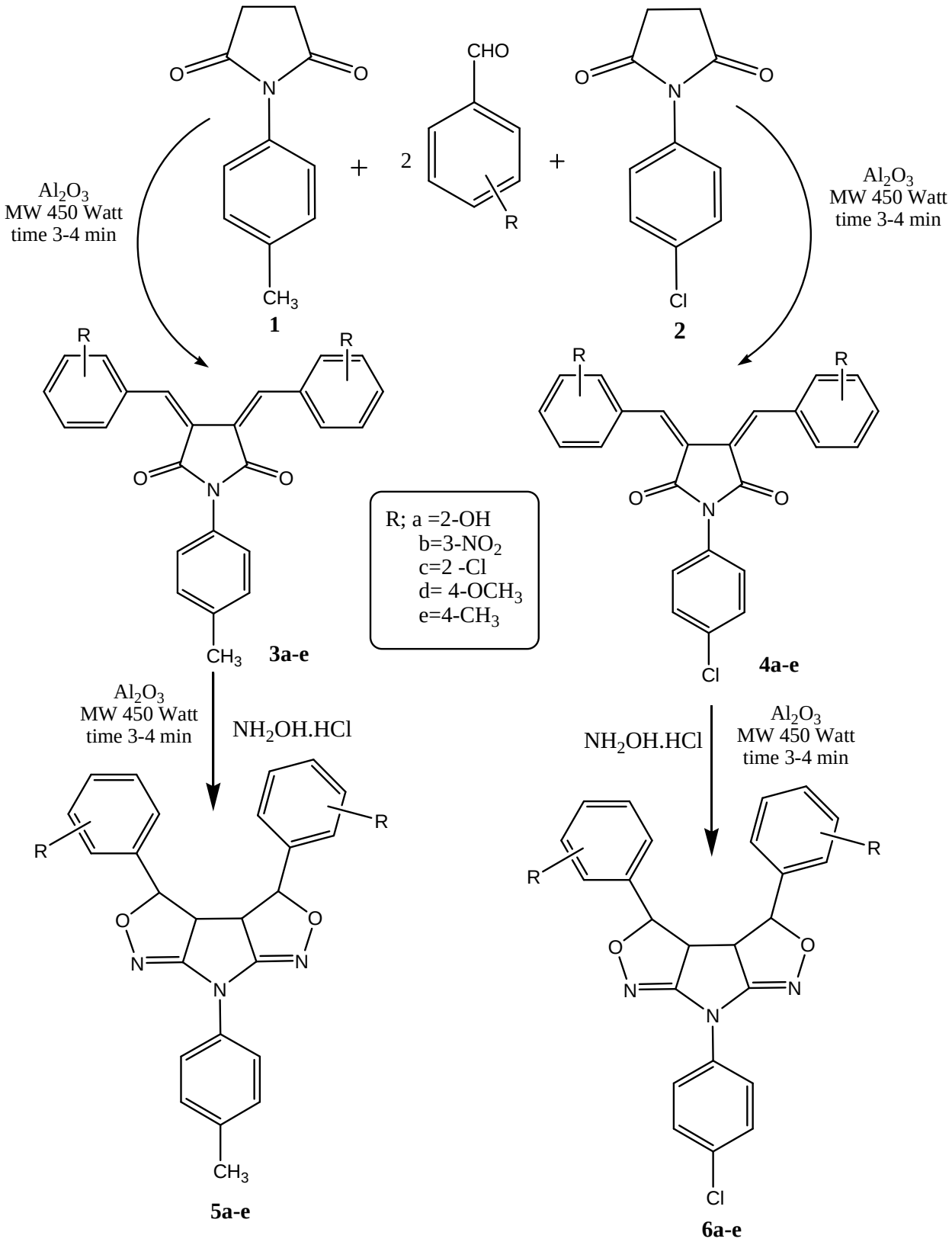
2,2'-(7-(4-chlorophenyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole-3,4-diyl)diphenol (6a): Yield: 86%; Dark brown solid; MP: 140-143 ^{0}C; FTIR (KBr, cm^{-1}): 1567.41 (C=N); 3642.01 (-OH); 925.83(N-O), 725.33 (C-Cl);^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.46-7.28 (m ,6H, Ar-H), 4.6 (d , 1H , CH isoxazole) 2.4 (d, 1H, CH isoxazole), 9.1 (s, 1H, -OH) Elem Anal. Cal for $C_{24}H_{18}ClN_3O_4$, C, 64.36; H, 4.05; Cl, 7.92; N, 9.38; O, 14.29; Found: C, 64.86; H, 4.35; Cl, 7.72; N, 9.78; O, 14.39.

7-(4-chlorophenyl)-3,4-bis(3-nitrophenyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole (6b): Yield: 86%; Dark brown solid; MP:102-104 ^{0}C; FTIR (KBr, cm^{-1}): 1533.41 (C=N); 1352.10 (Ar-NO_2); 713 (C-Cl);^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.7-6.9 (m ,6H, Ar-H), 4.6 (d , 1H , CH isoxazole) 2.4 (d, 1H , CH isoxazole). Elem Anal. Cal for $C_{24}H_{16}ClN_5O_6$, C, 56.98; H, 3.19; Cl, 7.01; N, 13.84; O, 18.98; Found: C, 56.68; H, 3.59; Cl, 7.31; N, 13.64; O, 18.78.

3,4-bis(2-chlorophenyl)-7-(4-chlorophenyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole (6c): Yield: 86%; Dark brown solid; MP: 126-128 ^{0}C; FTIR (KBr, cm^{-1}): 1533.41 (C=N); 780 (C-Cl) ; ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.46-7.28 (m ,6H, Ar-H), 4.6 (d , 1H , CH isoxazole) 2.4 (d, 1H , CH isoxazole) Elem Anal. Cal for $C_{24}H_{16}Cl_3N_3O_2$, C, 59.47; H, 3.33; Cl, 21.94; N, 8.67; O, 6.60; Found: C, 59.67; H, 3.53; Cl, 21.74; N, 8.77; O, 6.80.

7-(4-chlorophenyl)-3,4-bis(4-methoxyphenyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole (6d): Yield: 86%; Dark brown solid; MP: 136-138 ^{0}C; FTIR (KBr, cm^{-1}): 1178 (C-O ether) 1517.98 (C=N); 1184.29 (O-CH_3); 713 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.46-7.28- (m, 6H, Ar-H), 3.4 (d, 1H , CH isoxazole) 2.3(d, 1H , CH isoxazole), 3.7 (s, 1H, -OCH_3). Elem Anal. Cal for $C_{26}H_{22}ClN_3O_4$, C, 65.62; H, 4.66; Cl, 7.45; N, 8.83; O, 13.45; Found: C, 65.72; H, 4.56; Cl, 7.85; N, 8.93; O, 13.75.

7-(4-chlorophenyl)-3,4-di-p-tolyl-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole (6e): Yield: 86% ; Light brown solid; MP:103-105 ^{0}C; FTIR (KBr, cm^{-1}): 1647.21 (C=N); 3145.90 (Ar-CH_3); 823.90 (C-Cl); ^{1}H NMR (500 MHz, DMSO d_6, δ ppm): 8.2-7.1 (m ,6H, Ar-H), 4.5 (d , 1H , CH isoxazole) 2.3(d, 1H , CH isoxazole), 2.5 (s, 3H, CH_3) Elem Anal. Cal for $C_{26}H_{22}ClN_3O_2$, C, 70.35; H, 5.00; Cl, 7.99; N, 9.47; O, 7.21; Found: C, 70.55; H, 5.20; Cl, 7.69; N, 9.77; O, 7.41.


Al2O3
MW 450 Watt
time 3-4 min
CHO
2
R
CH3
1
Cl
2
Al2O3
MW 450 Watt
time 3-4 min
R; a =2-OH
b=3-NO2
c=2 -Cl
d= 4-OCH3
e=4-CH3
3a-e
4a-e
Al2O3
MW 450 Watt
time 3-4 min
NH2OH.HCl
NH2OH.HCl
Al2O3
MW 450 Watt
time 3-4 min
5a-e
6a-e

Scheme 1

RESULT AND DISCUSSION

Chemistry

The FT IR spectra of compounds **3a-e** and **3a-e** shows absorption band at band 1705 cm^{-1} frequency is due to presence of carbonyl group of chalcone when it is irradiated with hydroxyl amine hydrochloride the ring closure is take place and hence carbonyl frequency is diminished and band appear at 1540 due to C=N stretching of isoxazoline. The ^{1}H NMR peak -CH of is obtained at 4.1 δ and 2.5 δ indicates the formation of isoxazole ring.

Microbial assay

The series of 7H-pyrrolo [2, 3-c: 5, 4-c'] diisoxazole derivatives (5a-e) and (6a-e) were screened for antibacterial activity in vitro against Gram positive bacteria Staphylococcus auras (NCIM 2079) , Bacillus subtilies (NCIM 2250) and Gram negative bacteria pseudomonas aeruginosa (NCIM 2036), Escherichia coli (NCIM 2109). The solution of all compounds (5a-e) and (6a-e) were prepared in DMSO solvent .The assay was carried by taking 100 µgm per disc by using disc diffusion method for this purpose nutrient agar media was employed. The results were obtained in the form of zone of inhibition and noted after period of incubation (at $37^{0}C$ for 24-28 hrs).The zone of inhibition was measured in mm and compared with standard antibiotic drug Chloramphenicol. Similarly antifungal evaluation was also carried out in vitro against fungi Aspargillus niger (NCIM 545) and Candida albicans (NCIM 3471) in Hi-Media at conc. of 100 µgm per disc. The zone of inhibition was measured in mm and compared with standard drug Amphotericine-B. The results of anti-bacterial and anti-fungal activites are mentioned in Table.1.

Sr.no	Sample	S.aureus	B.subtilis	E.coli	P.aeruginosa	C.albicans	A.niger
1	**5a**	8.48	-	-	-	-	-
2	**5b**	10.16	-	-	-	-	-
3	**5c**	-	-	-	-	-	-
4	**5d**	-	-	-	-	-	-
5	**5e**	-	-	-	-	6.25	-
6	**6a**	28.66	-	20.66	11.26	7.06	-
7	**6b**	7.70	-	-	-	6.20	31.75
8	**6c**	9.72	-	-	-	7.00	-
9	**6d**	6.71	-	-	-	7.02	-
10	**6e**	33.66		30.58	16.69	8.12	-
Std 1	**Chloramphenicol**	32.13	28.30	27.62	14.18	NA	NA
Std 2	**Amphotericine B**	NA	NA	NA	NA	17.73	10.27

Note:- Means No activity at 100 µg/ml, NA means not applicable.

All synthesized compounds possess antibacterial activities some of them exhibited potent antibacterial activities against bacterial strain of S.aureus and E.Coli shows greater zone of inhibition than antibiotic drug Chloramphenicol shown in fig 1 and 2.

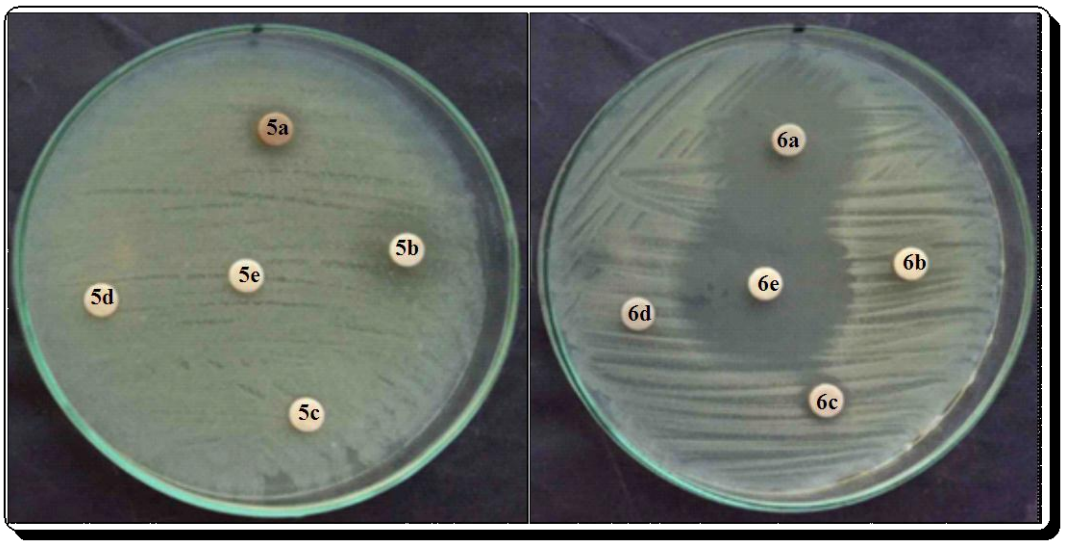


Fig. 1: Agar plate showing zone of inhibition of compounds 6a and 6e against S.aureus.

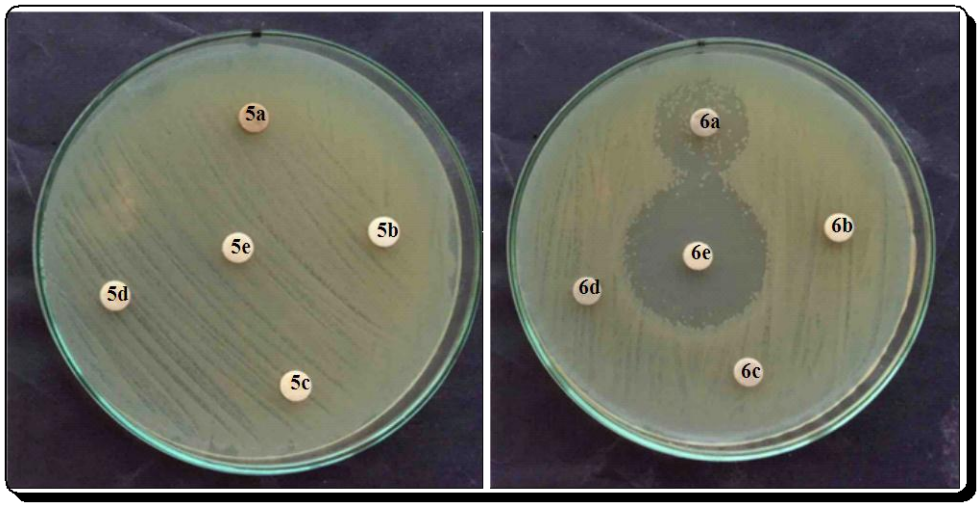
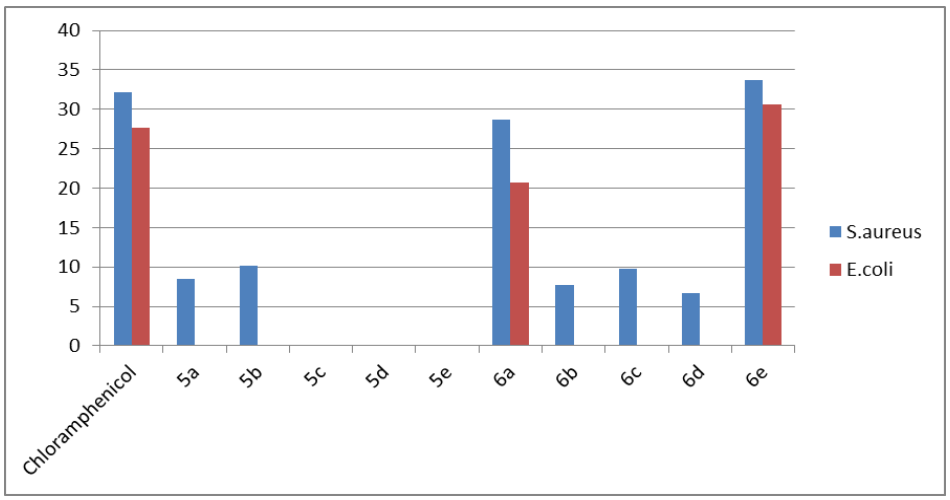


Fig. 2: Agar plate showing zone of inhibition of compounds 6a and 6e against E.Coli.



Graph 1: Shows zone of inhibition in mm by diisoxazole derivatives (5a-e) and (6a-e).

The antifungal screening were also carried out by using pathogenic fungal strain A.niger and C.albicans the antifungal activity of all synthesized derivatives were compared with antibiotic drug Amphotericine B as a standard some of them have antifungal activity aginst fungi C.albicans and exhibited potent antifungal activity aginst fungi A.niger the zone of inhibition is shown in figer 3.

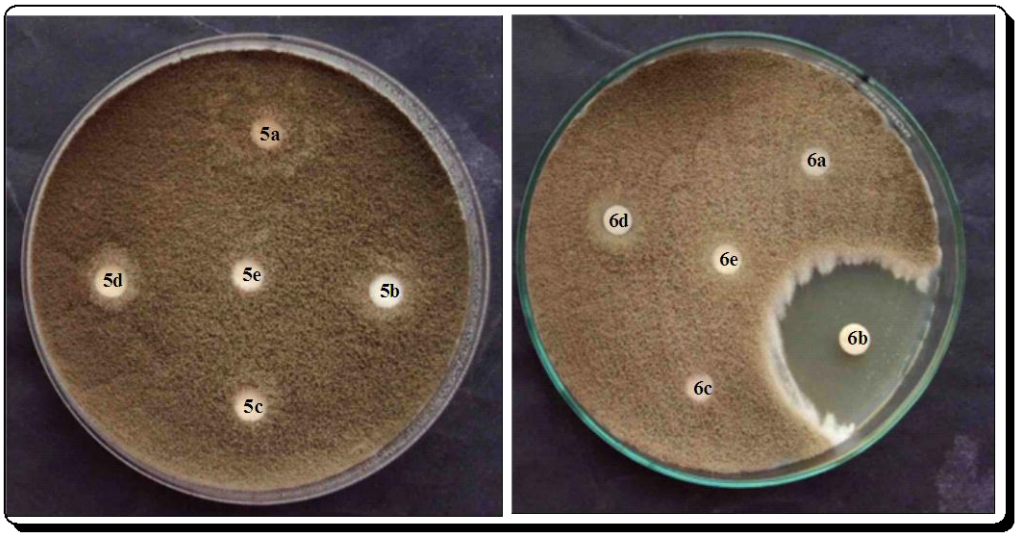
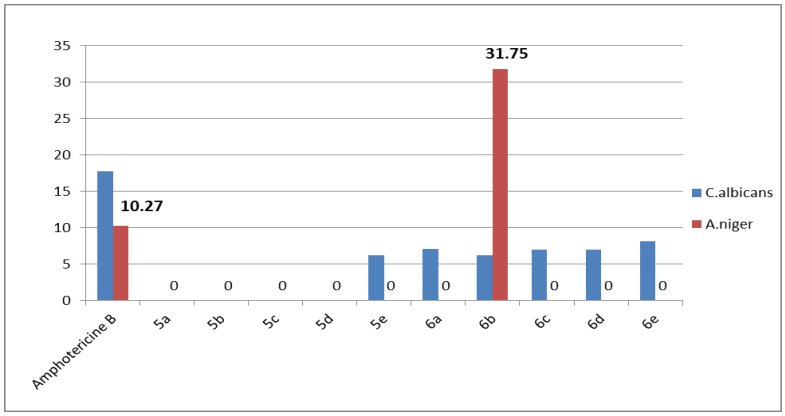


Fig. 3: Agar plate showing zone of inhibition of compounds 6b against A.niger.



Graph 2: Shows zone of inhibition in mm by diisoxazole derivatives (5a-e) and (6a-e).

CONCLUSION

From above research work it is concluded that the solid phase solvent free synthesis of 3z,4z substituted 3,4 benzylidine pyrrolidine dione derivatives (3a-e) and (4a-e) diisoxazole derivatives (5a-e) and (6a-e) by using microwave oven is successfully synthesized in minimum time than conventional methods. The products are obtained in good yield and high purity. From anti-microbial studies it is concluded that the compound 2,2'-(7-(4-chlorophenyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole-3,4-diyl)diphenol **(6a)** promising antibacterial activity and compound 7-(4-chlorophenyl)-3,4-di-p-tolyl-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole **(6e)** exhibited potent antibacterial similarly the compound 7-(4-chlorophenyl)-3,4-bis(3-nitrophenyl)-3,3a,3b,4-tetrahydro-7H-pyrrolo[2,3-c:5,4-c']diisoxazole **(6b)** shows potent antifungal activity. This work has future scope in field of medicinal chemistry.

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