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Research Article

SYNTHESIS, CHARACTERIZATION AND MICROBIAL SCREENING OF PYRAZOLINE DERIVATIVES OF 2, 6-DICHLORO-1-(N-SUBSTITUTED PHENYL)-1, 4-DIHYDROPYRIDINE-3, 5-DICARBALDEHYDE

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ABSTRACT

A series of pyrazolines Va-f have been synthesized by the action of hydrazine hydrate on compound IV while the compounds IVa-f were prepared by the condensation of 2,6-dichloro-1-(N-substituted phenyl)-1,4-dihydropyridine-3,5-dicarbaldehyde III with different aromatic ketones. The structures of the newly synthesized compounds have been confirmed on the basis of elemental analysis and spectral studies. The newly synthesized title compounds have been screened for their in *vitro* antimicrobial activities against *B. subtilis, E. coli, S. aureus, P.aeroginosa, A. niger* and *C. albicans*. All the compounds showed moderate to good antimicrobial activity. Some compounds were found more potent than standard drug.

Keywords: Dihydropyridines, Propenones, 2-Pyrazolines, Antimicrobial activity.

INTRODUCTION

Chlorodihydropyridine represents one of the most active classes of heterocyclic compounds possessing a wide spectrum of biological activities. Dihydropyridines are reported as calcium and sodium channel blockers[1,2]. Literature survey reveals that pyrazolines have been found to be associated with diverse biological activities which highlighted their chemistry and uses. Among various pyrazoline derivatives, 2-pyrazolines are most frequently studied.Pyrazolines are well known important nitrogen containing five membered heterocyclic compounds. Pyrazolines are also used as useful synthones in the field of organic chemistry[3] and drug designing. They posses a broad spectrum of biological activities such as antibacterial[4-7], antifungal[8-9], inflammatory[10-12], antidepressant[13], antitumor[14], antidiabetic[15], antiarthritics, muscle relaxant[16], analgesic[17] and anti convulsant[18,19]. Pyrazolines also find wide applications in agrochemical industries. In view of the above and in a continuation of earlier work, new series of propenones[20] IVa-f, pyrazolines Va-f are reported (**Scheme I**).

MATERIALS AND METHODS

Experimental

All melting points were determined in open capillary and are uncorrected. The IR spectra were recorded on FT-IR spectrophotometer. ^{1}HNMR spectra were recorded on Varian USA Mercury plus 300 MHz NMR spectrometer with DMSO-d_6 as a solvent using TMS as internal reference (chemical shift in δ ppm). The starting compounds were synthesized according to scheme-I. Glutaric acid I was converted into N-substituted phenyl glutarimides IIa-f which were then diformylated using Vilsmeier-Haack reaction to form IIIa-f.

General procedure for preparation of propenones IVa-f (i), (ii):- Different aromatic methyl ketones (2.0 mmole) in ethanol (95%, 20 ml) were added to the mixture of III (1.0 mmole), ethanol (95%, 30ml) and aq. Sodium hydroxide (40% just to alkaline) and stirred for 24 hr. The contents were poured on to crushed ice and isolated by acidification and recrystalised from ethanol to give IV(Scheme-I). Physical data of IVa-f(i),(ii) are given (Table-1). Characterization data of these compounds are given in (Table-2).

General procedure for preparation of pyrazolines Va-f (i), (ii):- A mixture of propenones (1mmole), 25 ml ethanol, hydrazine hydrate (2 mmole) was refluxed for 5-6 hr. The reaction mass was then poured into ice cold water. The solid obtained was filtered, washed with water, dried and purified by crystallization from ethanol to give Va-f (i),(ii)(Scheme-I). Physical and elemental analysis data of Va-f (i), (ii) are listed in (Table-3).

2,6-dichloro-3,5-bis [3-(phenyl)-pyrazoline]-1-(phenyl)-1,4-dihydropyridine Va (i):- IR (KBr): 3198 (NH of pyrazoline), 3297 (N-N, pyrazoline moiety), 1598 (C=N), 1442 (ArC=C), 1247 (C-N), 755 (C-Cl) cm^{-1}., ^{1}HNMR (DMSO-d_6): δ 2.32-2.50 (d, 2H, CH_2, pyraz.), 7.04-7.57 (m, ArH), 6.55 (s,1H, NH), 3.60-3.78 (m,1H, CH_2, pyraz.), 2.17 (s, 2H, CH_2).

2,6-dichloro-3,5-bis[3-(phenyl)-pyrazoline]-1-(4-methylphenyl)-1,4-dihydropyridine Vb (i):- IR(KBr): 3200 (NH of pyrazoline), 3312 (N-N, pyrazoline moiety), 1602(C=N), 1405 (ArC=C), 1248 (C-N), 2921 (CH_3), 815 (C-Cl) cm^{-1}., ^{1}HNMR(DMSO-d_6): δ 2.37-2.49 (d, 2H, CH_2, pyraz.), 7.06-7.50 (m, ArH), 6.58(s, 1H, NH), 3.59-3.78 (m,1H, CH_2, pyraz.), 2.67 (s, 2H, CH_2), 2.23 (s, 3H, CH_3).

2,6-dichloro-3,5-bis[3-(phenyl)-pyrazoline]-1-(2-chlorophenyl)-1,4-dihydropyridine Vc (i):- IR(KBr): 3178 (NH of pyrazoline), 3308 (N-N, pyrazoline moiety),1598 (C=N), 1460 (ArC=C), 1250 (C-N), 756 (C-Cl) cm^{-1}., ^{1}HNMR(DMSO-d_6): δ 2.32-2.49 (d, 2H, CH_2, pyraz.), 7.05-7.63 (m, ArH), 6.60 (s,1H, NH), 3.70-3.80 (m,1H, CH_2, pyraz.), 2.25 (s, 2H, CH_2).

2,6-dichloro-3,5-bis[3-(phenyl)-pyrazoline]-1-(4-chlorophenyl)-1,4-dihydropyridine Vd (i):- IR(KBr): 3198 (NH of pyrazoline), 3245 (N-N, pyrazoline moiety), 1596 (C=N), 1491 (ArC=C), 1246 (C-N), 771 (C-Cl) cm^{-1}., ^{1}HNMR(DMSO-d_6): δ 2.50 (d, 2H, CH_2, pyraz.), 7.06-7.70 (m, ArH), 6.87 (s,1H, NH), 3.72-3.82 (m,1H, CH_2, pyraz.), 2.62 (s, 2H, CH_2).

2,6-dichloro-3,5-bis[3-(phenyl)-pyrazoline]-1-(3-chlorophenyl)-1,4-dihydropyridine Ve (i):- IR(KBr): 3178 (NH of pyrazoline), 3308 (N-N, pyrazoline moiety), 1594 (C=N), 1430 (ArC=C), 1250 (C-N), 780 (C-Cl) cm^{-1}., ^{1}HNMR(DMSO-d_6): δ 2.49 (d, 2H, CH_2, pyraz.), 7.08-7.93 (m, ArH), 6.55 (s,1H, NH), 3.70-3.80 (m,1H, CH_2, pyraz.),2.26 (s, 2H, CH_2).

2,6-dichloro-3,5-bis[3-(phenyl)-pyrazoline]-1-(4-methoxyphenyl)-1,4-dihydro-pyridine Vf (i):- IR(KBr): 3178 (NH of pyrazoline), 3308 (N-N, pyrazoline moiety), 1598 (C=N), 1509 (ArC=C), 1247 (C-N), 830 (C-Cl),1297 (OCH_3) cm^{-1}., ^{1}HNMR (DMSO-d_6): δ 2.33-2.52 (d, 2H, CH_2, pyraz.), 7.04-7.59 (m, ArH), 6.67 (s,1H, NH), 3.65-3.74 (m,1H, CH_2, pyraz.), 2.17 (s, 2H, CH_2), 3.70 (s, 3H, OCH_3).

2,6-dichloro-3,5-bis[3-(4-hydroxyphenyl)-pyrazoline]-1-(phenyl)-1,4-dihydro-pyridine Va (ii):- IR(KBr): 3178 (NH of pyrazoline), 3303 (N-N, pyrazoline moiety, OH), 1598 (C=N), 1442 (ArC=C), 1249 (C-N), 756 (C-Cl) cm^{-1}., ^{1}HNMR(DMSO-d_6): δ 2.49 (d, 2H, CH_2, pyraz.), 7.04-7.56 (m, ArH), 6.56 (s,1H, NH), 3.56-3.70 (m,1H, CH_2,pyraz.), 2.19 (s, 2H, CH2).

2,6-dichloro-3,5-bis[3-(4-hydroxyphenyl)-pyrazoline]-1-(4-methylphenyl)-1,4-dihy-dropyridine Vb (ii):- IR(KBr): 3178 (NH of pyrazoline), 3297 (N-N, pyrazoline moiety, OH), 1603 (C=N), 1405 (ArC=C), 1249 (C-N), 2923 (CH_3), 815 (C-Cl) cm^{-1}., ^{1}HNMR(DMSO-d_6): δ 2.51 (d, 2H, CH_2, pyraz.), 7.05-7.50 (m, ArH), 6.80 (s,1H, NH), 3.58-3.69 (m,1H, CH_2, pyraz.), 2.66 (s, 2H, CH_2), 2.25 (s, 3H, CH_3).

2,6-dichloro-3,5-bis[3-(4-hydroxyphenyl)-pyrazoline]-1-(2-chlorophenyl)-1,4-dihy-dropyridine Vc (ii):- IR(KBr): 3198 (NH of pyrazoline), 3356 (N-N, pyrazoline moiety, OH),1600 (C=N), 1450 (ArC=C), 1247 (C-N), 751 (C-Cl) cm^{-1}., ^{1}HNMR (DMSO-d_6): δ 2.49 (d, 2H, CH_2, pyraz.), 7.05-7.66 (m, ArH), 6.62 (s,1H, NH), 3.86-3.78 (m,1H, CH_2, pyraz.), 2.27 (s, 2H, CH_2).

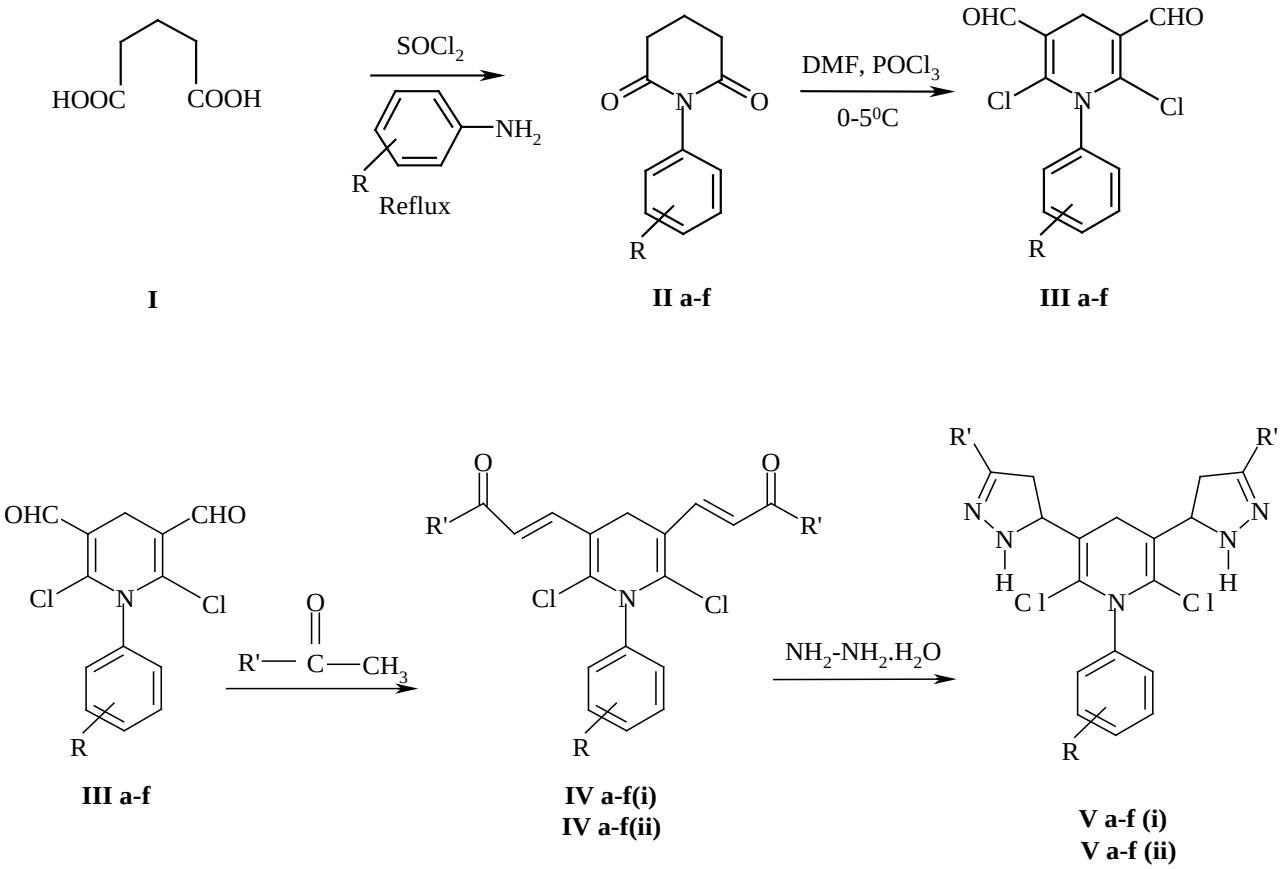
2,6-dichloro-3,5-bis[3-(4-hydroxyphenyl)-pyrazoline]-1-(4-chlorophenyl)-1,4-dihy-dropyridine Vd (ii):- IR(KBr): 3178 (NH of pyrazoline), 3308 (N-N, pyrazoline moiety, OH), 1597 (C=N), 1491 (ArC=C), 1245 (C-N), 780 (C-Cl) cm^{-1}., ^{1}HNMR (DMSO-d_6): δ 2.50 (d, 2H, CH_2, pyraz.), 7.04-7.57 (m, ArH), 6.67 (s,1H, NH), 3.65-3.77 (m,1H, CH_2, pyraz.), 2.67 (s, 2H, CH_2).

2,6-dichloro-3,5-bis[3-(4-hydroxyphenyl)-pyrazoline]-1-(3-chlorophenyl)-1,4-dihy-dropyridine Ve (ii):- IR(KBr): 3178 (NH of pyrazoline), 3308 (N-N, pyrazoline moiety, OH), 1594 (C=N), 1490 (ArC=C), 1298 (C-N), 779 (C-Cl) cm^{-1},. ^{1}HNMR(DMSO-d_6): δ 2.48 (d, 2H, CH_2, pyraz.), 7.07-7.94 (m, ArH), 6.59 (s,1H, NH), 3.56-3.68 (m,1H, CH_2, pyraz.), 2.26 (s, 2H, CH_2).

2,6-dichloro-3,5-bis[3-(4-hydroxyphenyl)-pyrazoline]-1-(4-methoxyphenyl)-1,4-dihy-dropyridine Vf (ii):- IR(KBr): 3178 (NH of pyrazoline), 3308 (N-N, pyrazoline moiety, OH),1603 (C=N), 1445 (ArC=C), 1247 (C-N), 829 (C-Cl), 1298 (OCH_3) cm^{-1}., ^{1}HNMR (DMSO-d_6): δ 2.50 (d, 2H, CH_2, pyraz.), 7.05-7.48 (m, ArH), 6.85 (s,1H, NH), 3.71-3.81 (m,1H, CH_2, pyraz.), 2.67 (s, 2H, CH_2), 3.70 (s, 3H, OCH_3).

Antimicrobial activity

The compounds Va-f (i),(ii) were screened for their in vitro antimicrobial activities against *B. subtilis, E. coli, S. aureus, P.aeroginosa, A. niger* and *C. albicans*. The agar diffusion assay (Well method, Disc size 6mm, Hi media) was used. The compounds were tested at the concentration of 100µg/ml in DMF. The results were compared with respective standards Chloramphenicol and Nystatin. All the compounds showed moderate to good antimicrobial activity(Table-4). The compounds Vc(ii), Vd(ii) and Ve(ii) were found more potent than standard against *A. niger*. Also the compounds Va(i), Vc(ii), Vd(i), Vd(ii) and Vf(i) were found more potent than standard against *C. albicans*.(Figure-1). These can be used as very good antifungal drugs.



R
a = - H
b = - 4 CH_3
c = - 2 Cl
d = - 4 Cl
e = - 3 Cl
f = - 4 OCH_3

R', (i) = -Ph
(ii) = -4OH-Ph

Scheme-I: Synthesis of propenones and pyrazolines

RESULTS AND DISCUSSION

The ^{1}HNMR spectra of compounds Va-f show multiplate of $-CH_2$ near about δ 3.7 confirmed the cyclization in pyrazoline moiety. The appearance of multiplate at δ 7.93-7.04 was due to aromatic protons. The reaction sequences for the synthesis of title compounds are shown in Scheme-I.

The formation of pyrazolines was confirmed by FTIR, ^{1}HNMR, Mass spectral data and elemental analysis. The IR spectra of compounds IVa-f show the characteristic band in the region of 1660-1650 cm^{-1} which indicated the presence of C=O group. The IR spectrum of compound Vb(i) exhibited peaks due to groups NH, N-N, C=N and C=C at 3200, 3312, 1602 and 1405 cm^{-1} respectively.

Table 1: It shows physical data of compounds IVa-f (i) and IVa-f (ii)

Compd No.	R	R^1	M.F.	M.P. (^{o}C)	Yield (%)
IVa(i)	-H	-Ph	$C_{29}H_{21}O_2NCl_2$	160	51
IVb(i)	-4CH_3	-Ph	$C_{30}H_{23}O_2NCl_2$	172	56
IVc(i)	-2Cl	-Ph	$C_{29}H_{20}O_2NCl_3$	180	49
IVd(i)	-4Cl	-Ph	$C_{29}H_{20}O_2NCl_3$	152	48
IVe(i)	-3Cl	-Ph	$C_{29}H_{20}O_2NCl_3$	174	50
IVf(i)	-4OCH_3	-Ph	$C_{30}H_{23}O_3NCl_2$	150	51
IVa(ii)	-H	-4OH-Ph	$C_{29}H_{21}O_4NCl_2$	165	50
IVb(ii)	-4CH_3	-4OH-Ph	$C_{30}H_{23}O_4NCl_2$	155	45
IVc(ii)	-2Cl	-4OH-Ph	$C_{29}H_{20}O_4NCl_3$	158	50
IVd(ii)	-4Cl	-4OH-Ph	$C_{29}H_{20}O_4NCl_3$	168	60
IVe(ii)	-3Cl	-4OH-Ph	$C_{29}H_{20}O_4NCl_3$	163	55
IVf(ii)	-4OCH_3	-4OH-Ph	$C_{30}H_{23}O_5NCl_2$	177	58

Table 2: It shows IR spectral data of compounds IVa-f (i) and IV a-f (ii)

Compound	IR (KBr) cm^{-1}
IVa(i)	1660 (C=O), 1598 (C=C), 2919 (aliphatic C-H str.), 1440 (Ar C=C), 1249 (C-N), 757 (C-Cl)
IVb(i)	1656 (C=O), 1600 (C=C), 2920 (aliphatic C-H str.), 1407 (Ar C=C), 1247 (C-N), 816 (C-Cl)
IVc(i)	1658 (C=O), 1609 (C=C), 2919 (aliphatic C-H str.), 1440 (Ar C=C), 1247 (C-N), 753 (C-Cl)
IVd(i)	1660 (C=O), 1595 (C=C), 2925 (aliphatic C-H str.), 1491 (Ar C=C), 1247 (C-N), 827 (C-Cl)
IVe(i)	1657 (C=O), 1594 (C=C), 2923 (aliphatic C-H str.), 1481 (Ar C=C), 1260 (C-N), 780 (C-Cl)
IVf(i)	1658 (C=O), 1609 (C=C), 2930 (aliphatic C-H str.), 1510 (Ar C=C), 1248 (C-N), 830 (C-Cl), 1298 (OCH_3)
IVa(ii)	3407 (OH), 2918 (aliphatic C-H str.), 1660 (C=O), 1598 (C=C), 1442 (ArC=C), 1250 (C-N), 756 (C-Cl)
IVb(ii)	3312 (OH), 2920 (aliphatic C-H str.), 1656 (C=O), 1602 (C=C), 1406 (ArC=C), 1249 (C-N), 814 (C-Cl)
IVc(ii)	3374 (OH), 2921 (aliphatic C-H str.), 1659 (C=O), 1592 (C=C), 1439 (ArC=C), 1254 (C-N), 754 (C-Cl)
IVd(ii)	3327 (OH), 2921 (aliphatic C-H str.), 1660 (C=O), 1594 (C=C), 1434 (ArC=C), 1246 (C-N), 828 (C-Cl)
IVe(ii)	3316 (OH), 2920 (aliphatic C-H str.), 1650 (C=O), 1594 (C=C), 1481 (ArC=C), 1240 (C-N), 780 (C-Cl)
IVf(ii)	3396 (OH), 2918 (aliphatic C-H str.), 1660 (C=O), 1600 (C=C), 1450 (ArC=C), 1247 (C-N), 830 (C-Cl), 1299 (OCH_3)

Table 3: Shows physical and elemental analysis data of compounds Va-f (i), and Va-f(ii)

Compd No.	R	R^1	M.F.	M.P. (^{o}C)	Yield (%)	% Found (Calcd.)		
						C	H	N
Va(i)	-H	-Ph	$C_{29}H_{25}N_5Cl_2$	166	86	67.60 (67.70)	4.79 (4.89)	13.58 (13.61)
Vb(i)	-4CH_3	-Ph	$C_{30}H_{27}N_5Cl_2$	120	95	68.11 (68.18)	5.10 (5.14)	13.19 (13.25)
Vc(i)	-2Cl	-Ph	$C_{29}H_{24}N_5Cl_3$	171	44	63.41 (63.45)	4.34 (4.40)	12.70 (12.75)
Vd(i)	-4Cl	-Ph	$C_{29}H_{24}N_5Cl_3$	148	92	63.39 (63.45)	4.31 (4.40)	12.69 (12.75)
Ve(i)	-3Cl	-Ph	$C_{29}H_{24}N_5Cl_3$	168	81	63.42 (63.45)	4.33 (4.40)	12.71 (12.75)
Vf(i)	-4OCH_3	-Ph	$C_{30}H_{27}ON_5Cl_2$	215	91	66.15 (66.17)	4.90 (4.99)	12.81 (12.86)
Va(ii)	-H	-4OH-Ph	$C_{29}H_{25}O_2N_5Cl_2$	178	93	63.72 (63.74)	4.60 (4.61)	12.79 (12.81)
Vb(ii)	-4CH_3	-4OH-Ph	$C_{30}H_{27}O_2N_5Cl_2$	160	86	64.22 (64.28)	4.78 (4.85)	12.40 (12.49)
Vc(ii)	-2Cl	-4OH-Ph	$C_{29}H_{24}O_2N_5Cl_3$	130	92	59.88 (59.96)	4.12 (4.16)	11.96 (12.05)
Vd(ii)	-4Cl	-4OH-Ph	$C_{29}H_{24}O_2N_5Cl_3$	110	88	59.89 (59.96)	4.10 (4.16)	12.01 (12.05)
Ve(ii)	-3Cl	-4OH-Ph	$C_{29}H_{24}O_2N_5Cl_3$	122	93	59.87 (59.96)	3.99 (4.16)	11.99 (12.05)
Vf(ii)	-4OCH_3	-4OH-Ph	$C_{30}H_{27}O_3N_5Cl_2$	250	96	62.45 (62.50)	4.68 (4.72)	12.10 (12.14)

Table 4: Shows results of antimicrobial activity of the compounds Va-f (i) and Va-f (ii)

Compound	*B. subtilis*	*E. coli*	*S. aureus*	*P. aeroginosa*	*A. niger*	*C. albicans*
V ai	-	9.06	-	8.06	9.12	10.44
V aii	-	9.85	-	7.50	7.56	8.81
V bi	-	8.32	-	9.12	6.45	9.21
V bii	-	7.59	-	6.59	8.23	9.20
V ci	-	11.61	-	10.61	7.12	9.06
V cii	-	10.42	8.12	11.42	10.56	14.57
V di	9.97	9.67	9.00	8.67	-	13.97
V dii	11.84	9.05	10.84	7.05	14.23	22.06
V ei	10.66	7.87	9.66	8.87	8	9.07
V eii	15.95	7.90	13.50	5.90	12	8.76
V fi	9.93	-	7.93	-	-	12.18
V fii	12.44	11.72	11.10	12.50	-	7.95
Chloramphenicol (10 mcg/disc)	30.94	20.52	30.94	20.52	NA	NA
Nyastatin (100 U/ml)	NA	NA	NA	NA	9.53	9.53

Diameter in mm calculated by digital Vernier Caliper; "-" means no zone of inhibition,NA "Not Applicable"

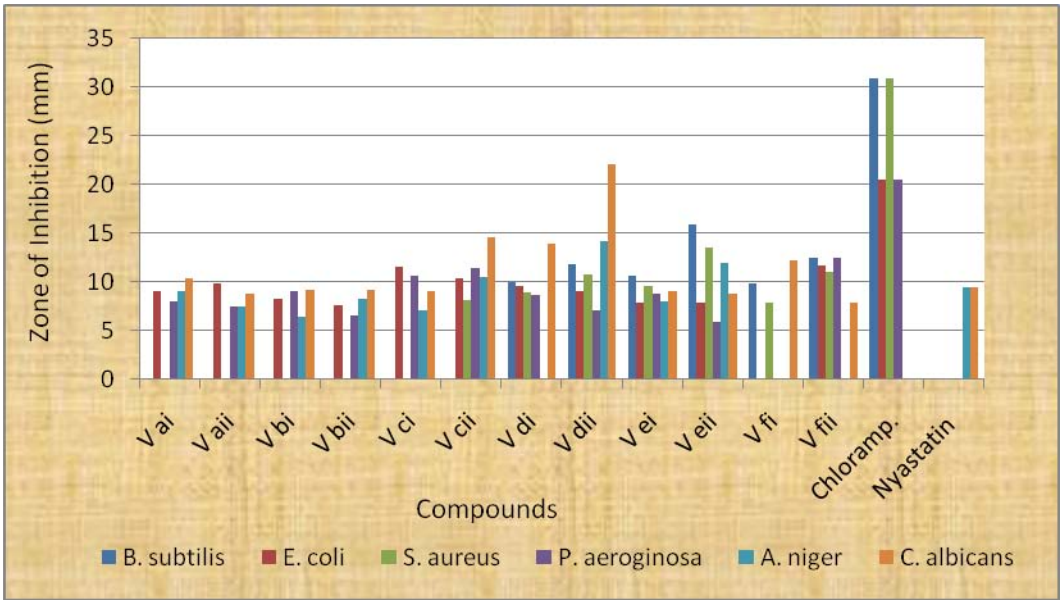


Fig. 1: Shows Zone of inhibition of compounds Va-f (i) and Va-f (ii)

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REFERENCES

1. Atwal KS, Swanson BN, Unger SE, Floyd DM, Moreland S, Hedberg A and O' Reilly BC. Dihydropyrimidine Calcium Channel Blockers. 3-Carbamoyl-4-aryl-1,2,3,4-tetrahydro-6-methyl-5-pyrimidinecarboxylic acid esters as orally effective antihypertensive agents. J. Med. Chem. 1991; 34: 806.
2. Winter J, Bevan S and Campbell EA. Capsaicin and pain mechanisms. Br. J. Anesth. 1995; 75: 157.
3. Padmavathi V, Sumarthi RP, Chandrasekhar BN and Bhaskarreddy D. J. Chem. Research. 1999; 610.
4. Nauduri D and Reddy GB. Antibacterials and Antimycotics: Part 1: Synthesis and activity of 2- pyrazoline derivatives. Chem. Pharm. Bull. (Tokyo) 1998; 46:1254.
5. Jamode VS, Chandak HS and Bhagat PR. Asian J. Chem. 2004; 16, 233: Chem. Abstr. 2004; 141: 243402 s.
6. Azarifar D and Shaebanzadeh M. Synthesis and Characterization of New 3,5-Dinaphthyl Substituted 2-Pyrazolines and Study of Their Antimicrobial Activity. Molecules. 2002; 7: 885.
7. Abunada NM, Hassaneen HM, Kandile NG and Miqdad OA. Synthesis and Biological Activity of Some New Pyrazoline and Pyrrolo[3,4-c] pyrazole-4,6- dione Derivatives: Reaction of Nitrilimines with Some Dipolarophiles. Molecules 2008; 13: 1011.
8. Gautam N and Chourasia OP. Synthesis, antimicrobial and insecticidal activity of some new cinnoline based chalcones and cinnoline based pyrazoline derivatives. Indian J. Chem. 2010; 49B: 830.
9. Korgaokar SS, Patil PH, Shah MT and Parekh HH. Studies on Pyrazolines: Preparation and antimicrobial activity of 3-(3'(*P*-Chlorophenyesulphonamidophenyl) -5-aryl- 1H/acetyl pyrazolines. Indian J. Pharm. Sci. 1996; 58: 222.
10. Malhotra P, Pattan S. and Nikalje AP. Microwave assisted synthesis and anti-inflammatory activity of 3,5-diaryl substituted-2-pyrazolines. Int J Pharmcy Pharm Sci. 2010; 2(2): 21.
11. 11 Udupi RH, Kushnoor AS, Bhat AR. Synthesis and Biological Evaluation of Certain Pyrazoline Derivatives of 2-[6-

methoxynaphthyl]-propionic Acid . Indian J. Heterocyclic Chem. 1998; 8: 63.

12. Azarifar D, Ghasemnejad H. Microwave-Assisted Synthesis of Some 3,5- Arylated 2- pyrazolines. Molecules. 2003; 8: 642.
13. 13 Palaska E, Aytemir M, Uzbay IT, Erol D. Synthesis and Antidepressant activities of Some 3,5-diphenyl-2-pyrazolines. Eur. J. Med. Chem. 2001; 36: 539.
14. Taylor EC, Patel HH. Synthesis of Pyrazol[3,4-d]pyrimidine Analogues of The Potent Agent N-{4-[2-(2-amino-4(3H)-oxo-7H-pyrrolo[2,3-d]pyrimidin-5-yl)ethyl]benzoyl}-L-glutamic acid. Tetrahedron. 1992; 48: 8089.
15. Soliman R, Faid-Allah HM and el-sadany SK. J. Pharm. Sci. 1987**;** 76: 626.
16. Rangari V, Gupta VN and Atal CK., Indian J. Pharm. Soc. 1990**;** 52:158.
17. Manna F, Chimenti F, Bolasco A, Cenicola ML, Amico M, Parrilo C, Rossi F and Marmo E. Eur. J. Med. Chem. 1992**;** 27: 633.
18. Ozdemir Z, Kandilici HB, Gumusel B, Calis U, Bilgin AA. Synthesis and studies on antidepressant and anticonvulsant activities of some 3-(2-furyl)-pyrazoline derivatives. Eur. J. Med. Chem. 2007; 42: 373.
19. Ruhogluo O, Ozdemir Z, Calis U, Gumusel B, Bilgin AA. Synthesis and pharmacological studies on the antidepressant and anticonvulsant activities of some 1,3,5-trisubstituted pyrazolines. Arzneimittelforschung. 2005; 55: 431.
20. Choudhary AN and Juyal V. Synthesis of chalcone and their derivatives as antimicrobial agents. Int J Pharmcy Pharm Sci. 2011; 3(3): 125.