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Synthesis of Some New Pyrrole and Pyridine Derivatives and their Antimicrobial, Anticancer Activities

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ABSTRACT

The compounds of 2,2'-[(3,5-dimethyl-1*H*-pyrrole-2,4-diyl) dicarbonyl]dihydrazine carboxamide(2), 2,2'-[(3,5-dimethyl-1*H*-pyrrole-2,4-diyl)dicarbonyl]dihydrazine carbothioamide(3), 2,2'-{[4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl]dicarbonyl}dihydrazine carboxamide(5) and 2,2'-{[4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine -3,5-diyl]dicarbonyl}dihydrazine carbothioamide (6) were synthesized from hydrazinolysis method and synthesized compounds were confirmed by IR, ¹H-NMR, ¹³C-NMR, mass spectral, mass spectral fragmentation and elemental analysis. Synthesized compounds were screened for antimicrobial and anticancer activities. Evaluation of antibacterial, antifungal activity showed that the compounds exhibited better results than reference drugs. The newly synthesized compounds have been screened for preliminary anticancer activity against HepG2(Liver), Hela(Cervical), MCF-7(Breast) cancer cells. Activity has been compared with standard drug. Structure Activity Relationship (SAR) has also been discussed in this study.

Key words: Pyrrole derivative, 1,4-dihydropyridine derivative, antimicrobial activity, anticancer activity, structure activity relationship

INTRODUCTION

Natural as well as synthetic five-member heterocyclic compounds are biological important in particular Pyrrole derivatives are importance in pharmacological activity such as cytotoxicity (Almerico *et al.*, 2000; Baraldi *et al.*, 1996), antiviral (Dannhardt *et al.*, 2000; Khanna *et al.*, 1997) *in vitro* cytotoxic activity against a solid tumor models (Evans *et al.*, 2003), hyperlipidemias (Holub *et al.*, 2004), antibiotic (Whith *et al.*, 1997), anticancer (Sugiyama *et al.*, 1996) and antimicrobial activity (Mohamed *et al.*, 2011). 1,4-dihydropyridine derivatives are importance of biological activity such as anti-inflammatory agent (Evdokimov *et al.*, 2006), antihypoxic and anti-ischemic activities (Khadilkar and Borkar, 1998) and 1,4-dihydropyridine-based calcium channel modulators of the nifedipine type (Schnell *et al.*, 2000), antimicrobial (Vijesh *et al.*, 2011) and Anti-breast cancer activity (Al-Said *et al.*, 2011). These references will serve as the main rationales for the synthesis of new pyrrole and pyridine derivatives and screening their antimicrobial and anticancer activities.

MATERIALS AND METHODS

The entire chemicals used were of AR grade (Sigma-Aldrich). This research article was a part of synthetic work carried out from department of chemistry Jamal Mohamed college, Tamil Nadu, India starting from July 2009 to December 2009 and another part of work conducted at Department of Biotechnology, Presentation College of Applied Sciences, South India; starting from July 2011 to September 2011 and anticancer activity was carried out from Department of Pharmaceutical chemistry, C.L. Baid Metha College of pharmacy, India; starting at April 2010 to November 2010.

Chemistry: The Melting points were recorded in open capillary tubes and were uncorrected. The IR spectra(KBr) were recorded on a Shimadzu 8201pc(4000-400 cm^{-1}). The ^1H -NMR and ^{13}C -NMR were recorded on Bruker DRX-400 MHz. Mass spectra (EI) were recorded on a Jeol JMS D-300 spectrometer operating at 70 eV. The Elemental analysis (C, H, N and S) were recorded using an Elementer analyzer model (Varian EL III). The purity of the compounds was checked by Thin Layer Chromatography (TLC).

Synthesis 2,2'-[(3,5-dimethyl-1H-pyrrole-2,4-diyl)dicarbonyl]dihydrazine carboxamide (2):

A mixture of compound 1 (0.1 mol) and semicarbazide (0.2 mol) in ethanol was refluxed for 7 h. The reaction mixture was poured in a crushed-ice. The precipitate was collected by filtration and recrystallized by absolute ethanol.

IR(KBr, cm^{-1}): ν = 3343(NH), 3224(NH_2), 1739($\text{C}=\text{O}$), 1078(N-C-N); ^1H -NMR(400 MHz, DMSO-d_6 , δ/ppm): δ 11.91 (s, 1H, NH of pyrrole ring), 10.38(d, 2H, 2,4-CONH), 6.34 (s, 4H, 2,4- NH_2), 5.91(d, 2H, 2,4-NHCO), 2.39 (s, 3H, 3 CH_3), 2.06 (s, 3H, 5 CH_3); ^{13}C -NMR (400 MHz, DMSO-d_6 , δ/ppm): δ 168.46(2,4-CONH), 158.99(2,4-CONH $_2$), 144.74(C3- CH_3), 141.69(C5- CH_3), 126.69(C2), 115.41(C4), 28.99(C5- CH_3), 15.04(C3- CH_3); MS(m/z): 297.26[M^+ , 25 %], 254.24(5%), 211.22(100%), 151.16(12%), 96.07 (21%).

2,2'-[(3,5-dimethyl-1H-pyrrole-2,4-diyl)dicarbonyl]dihydrazine carbothioamide (3):

A mixture of compound 1 (0.1 mol) and thiosemicarbazide (0.2 mol) in ethanol and few drop of DMSO was reflux for 7 h. The reaction mixture was poured in a crushed-ice. The predicated was collected by filtration and recrystallized by absolute ethanol.

IR (KBr, cm^{-1}): ν = 3354(NH), 3241(NH_2), 1747($\text{C}=\text{O}$), 1265($\text{C}=\text{S}$), 1084(N-C-N); ^1H -NMR (400 MHz, DMSO-d_6 , δ/ppm): δ = 11.88 (s, 1H, NH of pyrrole ring), 10.41 (d, 2H, 2,4-CONH), 9.51 (s, 4H, 2,4- NH_2), 2.32 (s, 3H, 5 CH_3), 2.10 (s, 3H, CH_3), 1.71 (d, 2H, 2,4-NHCS); ^{13}C -NMR (400 MHz, DMSO-d_6 , δ/ppm): δ = 185.69(2,4-CSNH $_2$), 161.71(2,4-CONH), 144.15(C3- CH_3), 143.2(C5- CH_3), 128.46(C2), 115.50(C4), 18.22 (C5- CH_3), 11.74. MS (m/z): 329.22 [M^+ , 31%], 270.42(70%), 212.46 (100%), 151.16 (34.1%), 96.07(13%).

2,2'-{[4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl]dicarbonyl}dihydrazine carboxamide (5):

A reaction mixture was made up of compound 4 (0.1 mol) and semicarbazide in ethanol (30 mL) was then heated under reflux for 10 h. The solid was obtained, after cool and poured in to crushed ice. The solid was collected by filtration, washed with water and recrystallized using ethanol.

IR(KBr, cm^{-1}): ν 3338(NH), 3220(NH_2), 3190(NH-C = O), 3028 (Ar-H), 2941(C-H str of CH_3), 1717 ($\text{C}=\text{O}$), 1091(N-C-N); ^1H -NMR(400 MHz, DMSO-d_6 , δ/ppm) : δ 6.25(s, 4H, NH_2), 8.63 (s, 1H,

NH in pyridine ring), 8.22 (d, 2H, C₃-CONH and C5-CONH), 7.54(s, 1H, Furyl ring), 6.11-6.21 (d, 2H, Furyl ring), 8.02(s, 2H, 3,5-NHCO), 5.85 (s, 1H, C4-H), 2.32(s, 6H, C2, C6-CH₃); ¹³C-NMR(400 MHz, DMSO-d₆, δ/ppm): δ 184.3(C3-CONH), 164.2 (C5-CONH), 157.86(2 x CONH₂), 147.13(2,6-C-CH₃), 142.86, 110.34, 106.3, 151.3 (Furyl ring), 102.86(3,5-C-CO), 34.03(4-C), 13.94 (2,6-C-CH₃); MS : (EI) m/z 378.25 (M⁺ + 1, 19.10%), 334.33(20.20%), 291.10 (100%), 261.27 (30%).

2,2'-{[4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl]dicarbonyl}dihydrazine carbothioamide (6): A mixture of compound 4 (0.1 mol) and thiosemicarbazide (0.2 mol) in ethanol and few drop of DMSO was reflux for 7 h. The reaction mixture was poured in a crushed-ice. The predicated was collected by filtration and recrystallized by absolute ethanol.

IR(KBr, cm⁻¹): 3370(NH), 3221(NH₂), 3192(NH-C = O), 3037(Ar-H), 1263(C = S), 1095 (N-C-N), 811(Ar-H); ¹H-NMR (400 MHz, DMSO-d₆, δ/ppm): 9.64(s, 2H, NH₂), 8.46 (s, 1H, NH of pyridine ring), 8.12 (d, 2H, C3-CONH and C5-CONH), 7.22 (d, 1H, H-furyl), 6.24-6.32 (d, 2H, furyl ring), 5.15 (s, 1H, C4-H), 2.33 (s, 6H, C2-CH₃ and C6-CH₃), 2.14 (d, 2H, 3,5-NHCS); ¹³C-NMR (400 MHz, DMSO-d₆, δ/ppm): 182.10 (C = S), 168.66 (C = O), 152.79, 142.11, 110.37, 106.79 (C4-furyl ring), 102.79 (C3,5 in pyridine ring), 142.11 (C2,6 in pyridine ring), 38.70(C4 in pyridine ring), 18.72 (C2,6-CH₃ in pyridine ring); MS ((m/z, (relative abundance, %)): 409.45 (M⁺, 30.2%), 350.39, 291.30, 261.27, 175.22, 147.12.

Biological evaluation

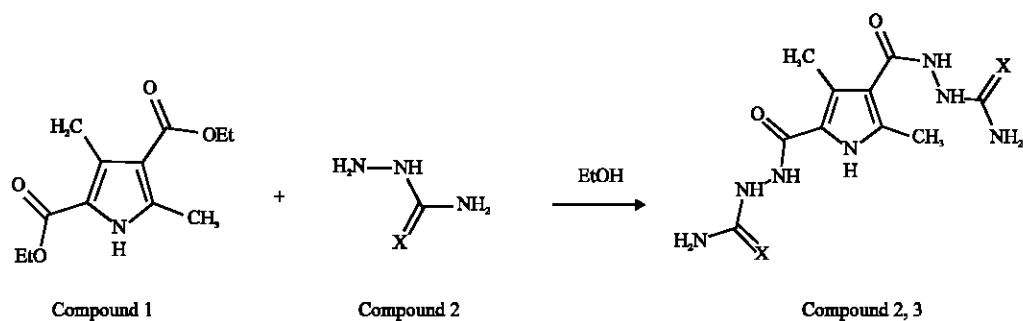
In vitro antibacterial screening: The compounds(1-6) were evaluated for their *in vitro* antibacterial activity against *Escherichia coli* (MTCC-739), *Proteus mirabilis*, non-hemolytic *Streptococcus*, *Pseudomonas aeruginosa* (MTCC-2435), *Micrococcus luteus* (MTCC-106), *Enterococcus faecalis*, *Streptococcus epidermidis*, *Bacillus* sp., *Klebsiella pneumoniae* (recultured), and *Staphylococcus aureus* (MTCC-96), by disc diffusion method (Bauer *et al.*, 1966) was performed using Mueller-Hinton agar (Hi-Media) medium. Ciprofloxacin was used as a standard. Each compound was tested at concentration 100 µg mL⁻¹ in DMSO. The zone of inhibition (mm) was measured after 24 h incubation at 37°C.

In vitro antifungal screening: The compounds (1-6) were evaluated for their *in vitro* antifungal activity such as *Aspergillus niger*, *Candida albicans*, *Microsporum audouinii* and *Cryptococcus neoformans* (recultured) using disc diffusion method with Sabouraud's dextrose agar (Hi-Media). Clotrimazole was used as a standard. Each compound was tested at a concentration of 100 µg mL⁻¹ in DMSO. The zone of inhibition (mm) was measured incubated at 37°C.

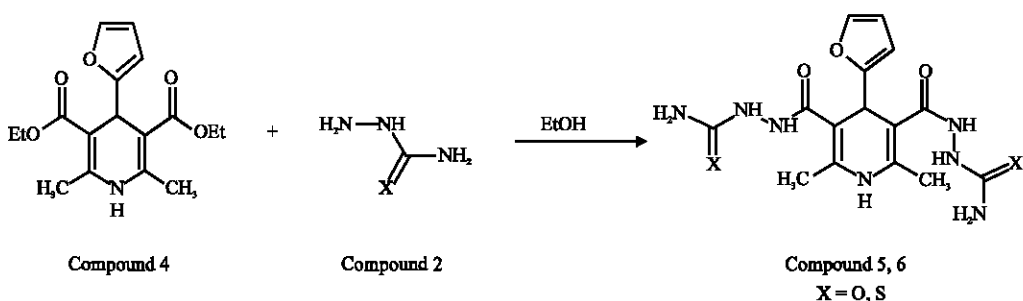
Anticancer activity: The newly synthesized compounds (1-6) were screened for their anticancer activity according to the procedure suggested (Scudiero *et al.*, 1988).

RESULTS AND DISCUSSION

Chemistry: Diethyl 3,5-dimethyl-1*H*-pyrrole-2,4-dicarboxylate(1) was prepared from Fischer condensation method (Fischer, 1935) and (diethyl-4-(furan-2-yl)-2,6-dimethyl-1,4-dihydro pyridine-3,5-dicarboxylate)(4) was synthesized from Hantzsch condensation method Kumar *et al.* (2011a) scheme 1 shows that compounds of 2,2'-[(3,5-dimethyl-1*H*-pyrrole-2,4-diyl)dicarbonyl]dihydrazine



Scheme 1: Synthetic route of the compound (2,3)



Scheme 2: Synthetic route of the compound (5, 6)

carboxamide(2) and 2,2'-[(3,5-dimethyl-1*H*-pyrrole-2,4-diyl)dicarbonyl]dihydrazine carbothioamide (3) were prepared from hydrazinolysis method (Srivastava and Srivastava, 2002). Scheme 2 shows that compounds of 2,2'-{[4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl]dicarbonyl}dihydrazine carboxamide (5) (Ojha *et al.*, 2007) and 2,2'-{[4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl]dicarbonyl}dihydrazine carbothioamide(6) was synthesized from method described in previous our literature (Kumar *et al.*, 2011a, b). The chemical structures of these compounds were determined by the basis of spectral data analysis such as IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, and mass spectral analysis.

The physicochemical data are summarized in Table 1. The compound (2) shows an absorption band for NH, NH_2 , C = O and N-C-N group observed at 3343, 3224, 1739 and 1078 cm^{-1} . The $^1\text{H-NMR}$ spectrum of compound (2) shows signals at δ 6.34, 11.91, 10.38 and 5.91 corresponding to NH_2 , NH, 2,4-CONH and 2,4-NHNHCO protons respectively. $^{13}\text{C-NMR}$ spectra of compound (2) shows the peaks at δ 168.46 and 158.99 corresponding to 2,4-CONH, and 2,4-CONH $_2$ carbons respectively. The mass spectrum of the compound (2) shows (Fig. 1) the molecular ion peak at m/z 297.26, which is confirmed the molecular mass of the compound (2). Figure 2 shows that mass spectral fragmentation of the compound (2).

The IR spectra of compound (3) shows an absorption band 3354, 1747, 1265, 3241 and 1084 cm^{-1} corresponding to NH, C = O, C = S, NH_2 and N-C-N groups, respectively. The $^1\text{H-NMR}$ spectra of compound (3) shows a signals at δ 9.51, 11.88, 10.41 and 1.71 corresponding to NH_2 , NH, 2,4-CONH and 2,4-NHCS protons, respectively. $^{13}\text{C-NMR}$ spectra of compound (3) shows that the peaks at δ 161.71 and 185.69 corresponding to CONH and 2,4-CSNH $_2$ carbons, respectively. The

Table 1: Physicochemical data of compounds (1-6)

Comp. No.	Mp (°C)	MW	Yield (%)	Mf	Elemental analysis calculated (Found) %			
					C	H	N	S
1	127	239.27	71	C ₁₂ H ₁₇ NO ₄	60.24 (60.28)	7.16 (7.13)	5.85 (5.81)	-
2	115	297.12	89	C ₁₀ H ₁₅ N ₇ O ₄	40.40 (40.45)	5.09 (5.09)	32.98 (32.98)	-
3	95	329.40	85	C ₁₀ H ₁₅ N ₇ O ₂ S ₂	36.46 (36.40)	4.59 (4.51)	29.77 (29.72)	19.47 (19.41)
4	158	319.35	91	C ₁₇ H ₂₁ NO ₅	63.94 (63.91)	6.63 (6.69)	4.39 (4.41)	-
5	180	377.35	86	C ₁₅ H ₁₉ N ₇ O ₅	47.74 (47.80)	5.08 (5.12)	25.98 (25.99)	-
6	187	409.48	61	C ₁₅ H ₁₉ N ₇ O ₃ S ₂	44.00 (44.06)	4.68 (4.74)	23.94 (23.98)	15.66 (15.71)

Mf: Molecular formula

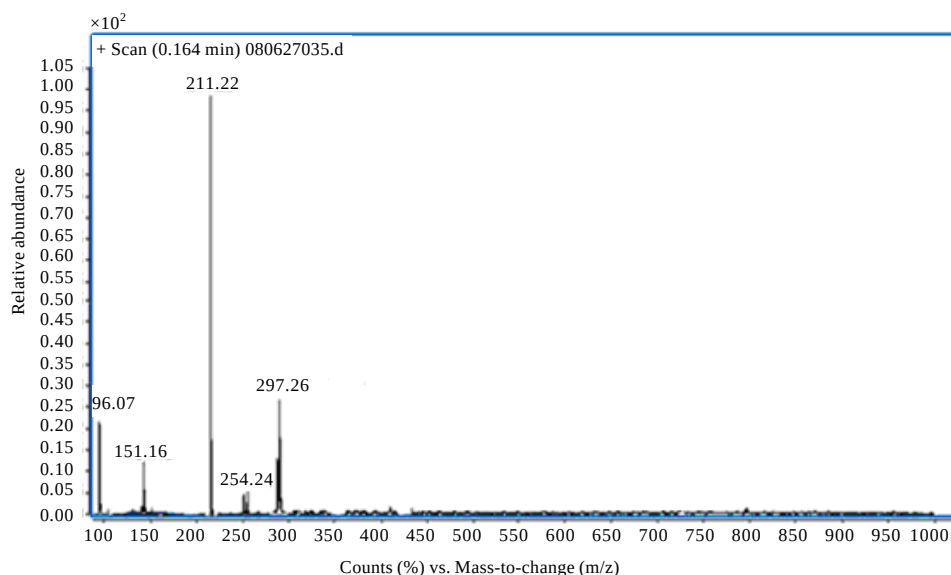


Fig. 1: Mass spectrum of compound (2)

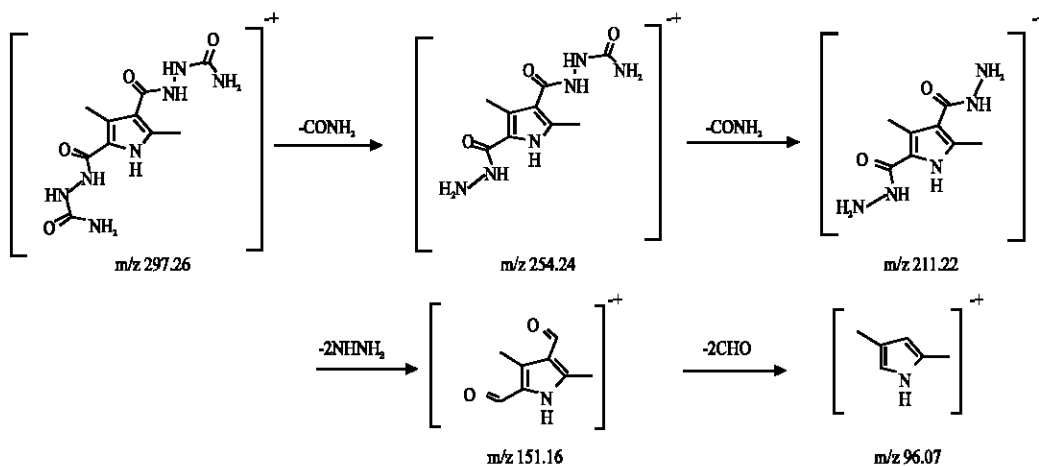


Fig. 2: Fragmentation pattern of compound (2)

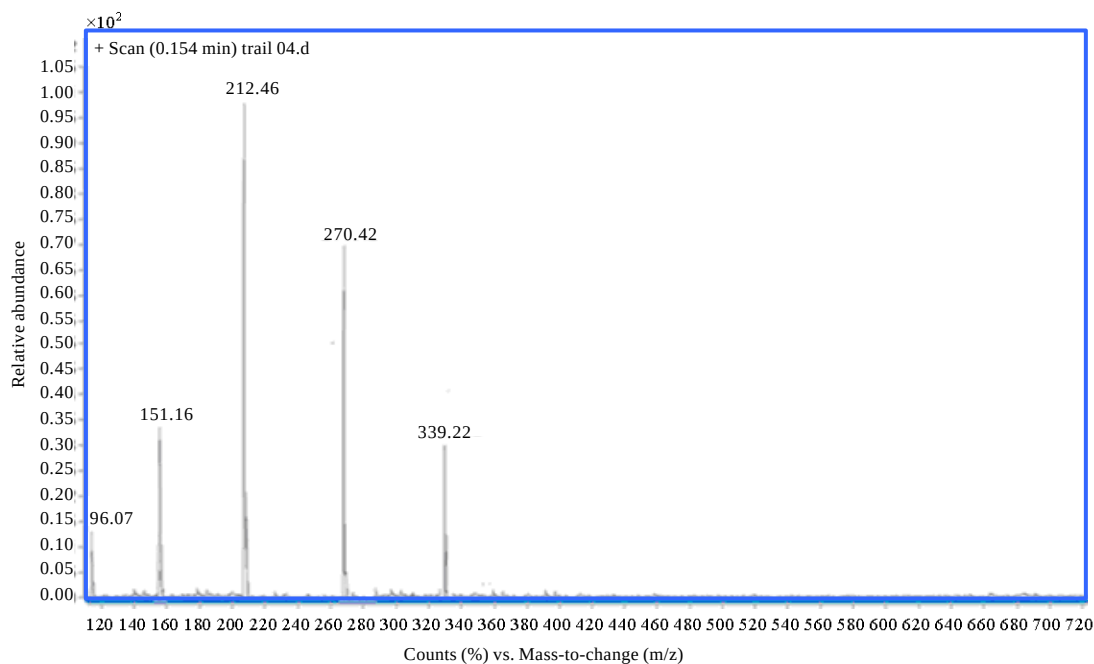


Fig. 3: Mass spectrum of compound (3)

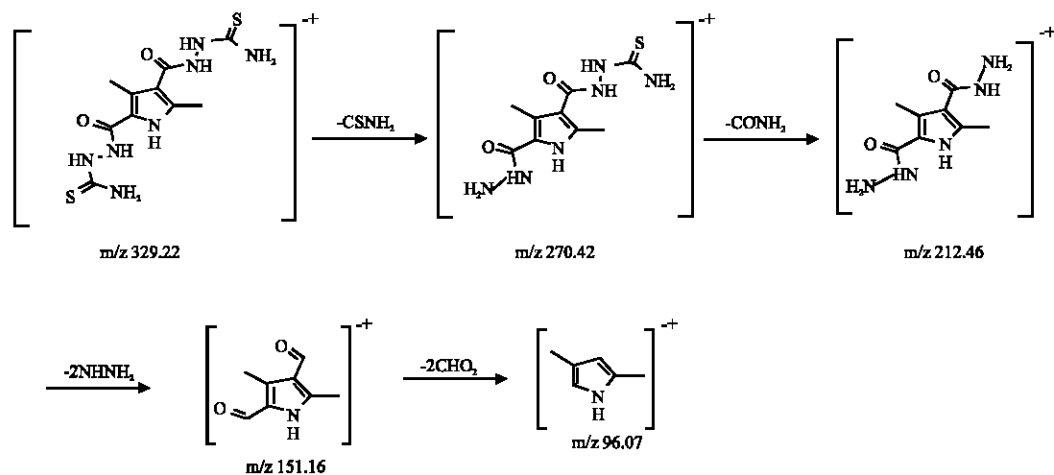


Fig. 4: Fragmentation pattern of compound (3)

mass spectrum of the compound (3) showed (Fig. 3) molecular ion peak at m/z 329.22, which is conformed the molecular mass of compound (3) and fragmentation pattern of compound (3) is represent in Fig. 4.

The IR spectrum of compounds (5) showed an absorption bands at 3338, 3220, 1717 and 1091 cm^{-1} corresponding to the NH, CONH, C = O, C-N-C groups, respectively. The $^1\text{H-NMR}$ spectrum of compound (5) shows signals at δ 8.63, 5.85, 8.22, 8.02 and 9.58 corresponding to 4 CH, CONH, NHCO and NH_2 protons, respectively. The $^{13}\text{C-NMR}$ spectrum of compound (5) shows peaks at δ 164.2, 157.8 and 34.0 corresponding to CONH, CONH_2 and 4-CH. Compound (5) shows (Fig. 5) the Mass spectral molecular ion peak at m/z 378.25, which confirmed the molecular mass of the compound (5) and fragmentation pattern of compound (5) is represent in Fig. 6.

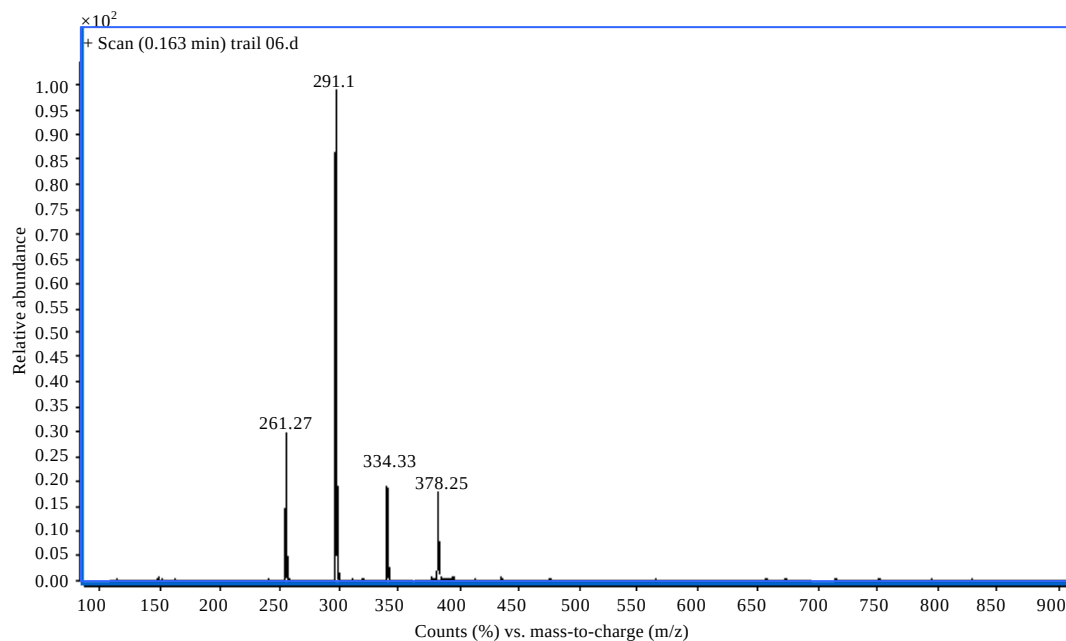


Fig. 5: Mass spectrum of compound (5)

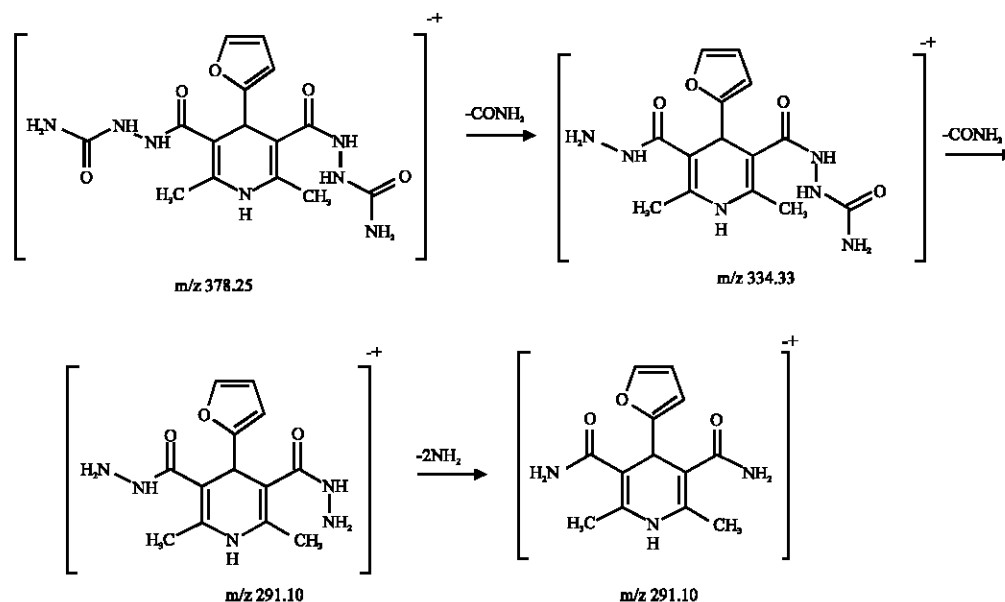


Fig. 6: Mass spectral fragmentation of the compound (5)

The IR spectrum of compound (6) shows an absorption bands at 3370, 3221, 1263 and 1095 cm^{-1} corresponding to the NH_2 , CONH , $\text{C}=\text{S}$ and $\text{N}-\text{C}-\text{N}$ groups, respectively. The ^1H -NMR spectrum of compound (6) shows singlet at d 9.64, 8.46 and 5.15 corresponding to NH_2 , CONH and 4CH protons present in the 1,4-dihydropyridine ring. The ^{13}C -NMR spectrum of analysis compound (6) shows peaks at d 182.10, 168.66 and 38.70 corresponding to CSNH_2 , CONH and 4-CH. Mass spectral analysis of the compound (6) shows the molecular ion peak m/z 409.45, which confirmed the molecular mass of the compound (6).

Table 2: Antibacterial activities for compound (1-6)

Test organisms	Compounds						Standard
	1	2	3	4	5	6	
<i>E. coli</i> (MTCC-739)	10	15	24	10	8	16	18
<i>P. mirabilis</i>	-	-	12	12	10	11	15
Non-hemolytic <i>Streptococcus</i>	8	-	10	14	25	-	16
<i>P. aeruginosa</i> (MTCC-2435)	14	15	11	8	12	30	27
<i>M. luteus</i> (MTCC-106)	7	-	15	10	8	10	20
<i>E. faecalis</i>	-	-	9	8	14	8	29
<i>S. epidermidis</i>	-	24	7	-	-	13	27
<i>K. pneumoniae</i>	-	5	8	-	-	-	21
<i>Bacillus</i> sp.	18	-	-	-	-	-	23
<i>S. aureus</i> (MTCC-2940)	-	16	21	-	8	9	16

Zone of inhibition was measured in mm at concentration 100 $\mu\text{g mL}^{-1}$, Ciprofloxacin is used as a standard

Table 3: Antifungal activities for compound (1-6)

Test organisms	Compounds						Standard
	1	2	3	4	5	6	
<i>A. niger</i>	12	16	20	-	-	-	22
<i>C. albicans</i>	8	12	22	8	12	8	18
<i>C. neoformans</i>	-	8	5	-	10	7	15
<i>M. audouinii</i>	5	16	8	10	8	6	16

Zone of inhibition was measured in mm at concentration of 100 $\mu\text{g mL}^{-1}$, Clotrimazole is used as a standard

Antibacterial activity: The compounds (1-6) were screened for antibacterial activity. The synthesized compound (3) is highly active than standard (ciprofloxacin) against *E. coli* and *P. aeruginosa* at concentration 100 $\mu\text{g mL}^{-1}$. The bacterial zones of inhibition(mm) values are summarized in Table 2.

Compound (1) is higher activity against *Bacillus* sp. compared with other species but low activity compared with standard in all species. Compound (2) is higher activity against *S. epidermidis* in 24 mm of inhibition compared with other species but equipotent activity against *S. aureus* in 16 mm of inhibition. Compound (3) is highly activity compared with standard against *E. coli* in 24 mm of inhibition and *S. aureus* in 21 mm of inhibition. Compound (4) is low activity against in all species. Compound (5) is highly active compared with standard against non hemolytic *Streptococcus* in 25 mm of inhibition. Compound (6) is higher activity compared with standard against *P. aeruginosa* in 30 mm of inhibition.

Antifungal activity: The compounds (1-6) were screened for the antifungal activity. The compound (3) is highly active compared with standard (clotrimazole) against *C. albicans* in 22 mm of inhibition. The compound (3) has equipotent activity compared with standard against *A. niger* at concentration 100 $\mu\text{g mL}^{-1}$. The fungal zones of inhibition (mm) values are summarized in Table 3. Compounds (1, 2, 4, 5 and 6) have low activity compared with standard against in all fungal species.

Anticancer: Compounds (1-6) were found to be active in the preliminary anti-cancer screening studies. The compounds were tested against the three cell lines of liver, cervical, breast cancer

types. Their GI_{50} , TGI and LC_{50} values were determined. The result of the screening was expressed in terms of GI_{50} growth inhibitor concentration.

Table 4 shows that the compound (4) has highly active against HepG2 (liver) cancer cell line for the reason that low Growth of inhibition (GI_{50}) at 16.2 μ m compared to other compounds (1, 2, 3, 5 and 6).

Table 5 shows that the compound (2) has highly active against Hela cancer cell line in 15.2 μ m growth of inhibition (GI_{50}) compared to other compounds (1, 3, 4 and 6).

Table 6 shows that the compound (3) has highly active against MCF7 cancer cell line in 18.3 μ m of growth inhibition (GI_{50}) compared to other compounds (1, 2, 4 and 6).

Structure activity relationship: From the results of antimicrobial and anticancer activities, we are discussed in following structure activity relationships:

Table 4: Anticancer HepG2 (liver), activity of the synthesized compounds (1-6)

Comp. No.	HepG2 (liver)		
	GI_{50} (μ m)	TGI (μ m)	LC_{50} (μ m)
1	18.4	38.2	84.6
2	19.5	42.6	91.4
3	21.2	52.6	>100.0
4	16.2	29.1	88.3
5	22.1	36.8	87.5
6	23.5	47.8	>100.0

GI_{50} : Growth inhibition, TGI: Total growth inhibitory, LC_{50} : Lethal concentration

Table 5: Anticancer Hela (cervical) activity of the synthesized compounds (1-6)

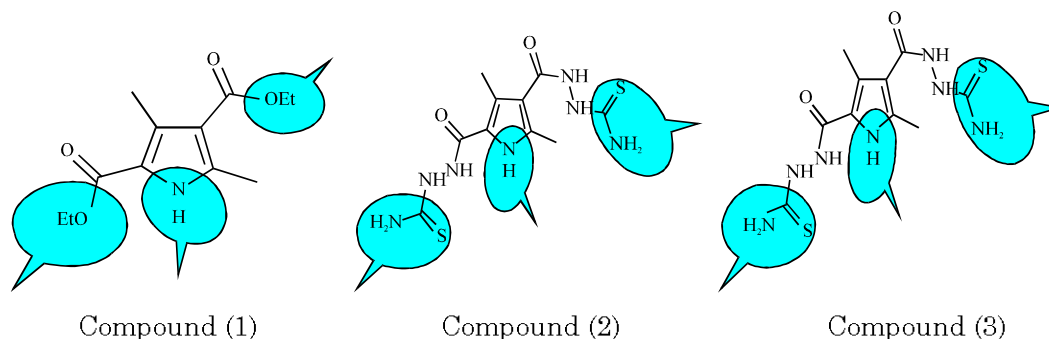
Comp. No.	Hela		
	GI_{50} (μ m)	TGI (μ m)	LC_{50} (μ m)
1	21.5	56.4	>100.0
2	15.2	40.2	88.4
3	19.5	33.1	72.3
4	22.6	48.4	>100.0
5	33.8	57.1	97.8
6	31.1	64.3	71.8

GI_{50} : Growth inhibition, TGI: Total growth inhibitory, LC_{50} : Lethal concentration

Table 6: Anti-cancer MCF-7(Breast) activity of the synthesized compounds (1-6)

Comp. No.	MCF-7		
	GI_{50} (μ m)	TGI (μ m)	LC_{50} (μ m)
1	19.2	41.3	88.5
2	17.5	39.6	85.4
3	18.3	27.9	68.4
4	22.9	46.8	>100.0
5	42.1	67.2	>100.0
6	32.8	58.8	>100.0

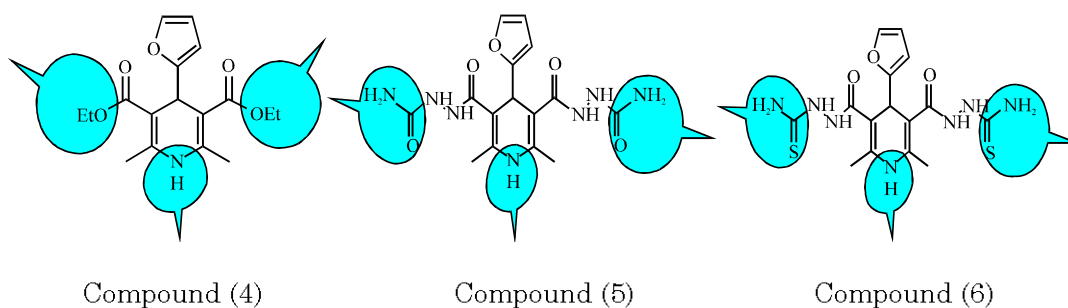
GI_{50} : Growth inhibition, TGI: Total growth inhibitory, LC_{50} : Lethal concentration



The compound (1) is highly active against *Bacillus* sp. (18 mm, inhibition) in antibacterial screening and highly active against *A. niger* in antifungal screening due to presence of -OEt group connecting with pyrrole ring conversely compound (1) responded by Anticancer activity also, activity range measured from Total Growth Inhibition (TGI), which is represented by 38.2, 56.4 and 41.3 μm corresponding to Hep G2 (Liver), Hela(Cervical) and MCF-7 cancer cell lines.

The compound (2) is higher active against *S. epidermidis* in Antifungal screening due to presence of -CONH and -CO-NH₂ connected with pyrrole derivative while the compound (2) is responded by Anticancer activity also, Anticancer activity also, activity range measured from Total Growth Inhibition (TGI) which is represented by 42.6, 40.2 and 39.6 μm corresponding to HepG2 (Liver), Hela(Cervical) and MCF-7 cancer cell lines.

The compound (3) is highly activity against *E. coli* and *C. albicans* due to presence of -CONH and -CS-NH₂ groups in pyrrole ring while responded by Anticancer activity also, activity range measured from Total Growth Inhibition (TGI), which is represented by 52.6, 33.1 and 27.9 μm corresponding to HepG2 (Liver), Hela (Cervical) and MCF-7 cell lines:



The compound (4) is highly active against *P. mirabilis* due to presence of -OEt group in 1,4-dihydropyridine derivative higher antibacterial activity against compared with other organisms and compound (4) was low active in all fungal. Anticancer activity of the compound (4) shows Total Growth Inhibition (TGI) reached at 29.1, 48.4 and 46.8 μm corresponding to HepG2 (Liver), Hela (Cervical) and MCF-7 cancer cell lines.

The compound (5) is containing -CONH and -CO-NH₂ groups exhibit higher antibacterial activity against non-hemolytic *Streptococcus*. Antifungal screening of compound (5) shows highly active against *C. albicans*. Anticancer activity of the compound (5) shows Total Growth Inhibition (TGI) reached at 36.8, 57.1 and 67.2 μm corresponding to HepG2 (Liver), Hela (Cervical) and MCF-7 cancer cell lines.

The compound (6) is containing -CONH and -CS-NH₂ groups exhibit higher antibacterial activity against *P. aeruginosa*. Compared with standard whereas very low active in all antifungal screening. Anticancer activity of the compound (6) shows that Total Growth Inhibition (TGI) reached at 47.8, 64.3 and 58.8 μm corresponding to HepG2 (Liver), Hela (Cervical) and MCF-7 cancer cell lines.

CONCLUSION

Pyrrole and 1,4-dihydropyridine derivatives were synthesized and screened for antimicrobial and anticancer activities. The compound (3) is highly active against *E. coli* and the compound (6) is highly active against *P. aeruginosa* compared with standard Ciprofloxacin at concentration (100 $\mu\text{g mL}^{-1}$) in antibacterial screening. The compound (3) is highly active against *C. albicans* in antifungal screening. The compound (4) has highly active in HepG2(Liver) and compound (2) has highly active in Hela (Cervical) and MCF-7 in anticancer screening. Therefore, we are founded some important detail about biological properties of pyrrole and 1,4-dihydropyridine derivatives (1-6), this compounds could be beneficial for anticancer drug synthesis.

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