WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 8, 1131-1143. Research Article ISSN 2277– 7105

ANTIBACTERIAL AND ANTIFUNGAL STUDIES OF 5-ACETYL-4-ARYL-6-METHYL-3, 4-DIHYROPYRIMIDIN-2(1*H*)-ONES

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Article Received on
12 May 2015,

Revised on 07 June 2015,
Accepted on 04 July 2015

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ABSTRACT

Eight 5-acetyl-4-aryl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-ones 4a-h are prepared and screened for their antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella typhi* and antifungal activity against *Candida albicans*, *Aspergillus flavus*, *Rhizopus* and *Mucor*. Compounds 4d-h exhibited excellent *in vitro* antibacterial activity against *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*. Whereas the same set of compounds exerted potent *in vitro* antifungal activity against *Candida albicans* and *Aspergillus flavus*.

KEY WORDS: Dihydropyrimidinones, antibacterial activity, antifungal activity, Synthesis.

INTRODUCTION

Dihydropyrimidinones are an important class of compounds due to their therapeutic and pharmacological properties.[1] Their derivatives exhibit a wide range of biological effects including antifungal, antiviral, anticancer, antibacterial, anti-inflammatory and antihypertensive effects.[2] It also exhibit a biological activity of antitumour property.[3] In addition, these compounds have emerged as the integral backbones of several calcium channel blockers,[4] antagonists.[5] and antihypertensive agents.[6] Recently, some marine alkaloids possessing dihydropyrimidine-5-carboxylate core have been shown to exhibit interesting biological activities such as potent HIV-gp-120-CD4 inhibitors as well as anti-HIV agents.[7]

Parlato *et al.*[8] synthesized various dihydropyrimidinone derivatives by modification of the substituents in virtually all the six positions of the pyrimidine nucleus which provided with interesting activity against HIV, ASFV, Sendai Virus and Rubella Virus. Importantly, all the dihydropyrimidin-2(1H)-ones are pharmacologically active as antioxidant agents.[9] Thus, synthesis of this heterocyclic nucleus is of much current importance. The aim of this study was to evaluate the biological activities of dihydropyrimidin-2(1H)-ones. The results of the antibacterial and antifungal activities are discussed in this paper.

MATERIALS AND METHODS

Experimental

Melting points were determined in open capillaries and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 400 spectrometer operating at 400.13 MHz for ^{1}H and 100.62 MHz for ^{13}C in DMSO-d_6. For recording ^{1}H NMR spectra, solutions were prepared by dissolving about 10 mg of the compound in 0.5 ml of the solvent. For recording ^{13}C NMR spectra, solutions were prepared by dissolving about 50 mg of the compound in 0.5 ml of the solvent. IR spectra were recorded in KBr discs on a Avatar (300 FT-IR) Thermo Nicolet spectrometer. CHN analyses were performed on a Elementar Vario EL III analyzer. The mass spectrum was obtained on a JEOL SX-102 mass spectrometer.

Chemistry

Preparation and characterization of DHPMS (4a-h)

A mixture of acetylacetone (10 mmol), aldehyde (10 mmol), urea (15 mmol), CaF_2 (1 mmol, 10 mol %) and EtOH (20 ml), was heated at 40°C [10]. All the products were characterized by elemental analyses, IR, ^{1}H NMR and ^{13}C NMR spectra.

4a) IR (KBr) cm^{-1}: 3261 and 3115 (N–H str.), 3000 (aromatic C–H str.), 2923 (aliphatic C–H str.), 1705 and 1676 (C=O str.). ^{1}H NMR (DMSO-d_6), δ: 9.19 (s, 1H, H–1), 7.83 (s, 1H, H–3), 7.24–7.35 (m, 5H, aromatic CH), 5.25 (d, 1H, J = 4 Hz, H–4), 2.29 (s, 3H, methyl protons at C–6), 2.11 (s, 3H, methyl protons of the acetyl group). ^{13}C NMR (DMSO-d_6) δ: 194.3 (carbonyl carbon), 152.1 (C–6), 148.1 (carbonyl carbon of the urea), 144.2 (*ipso* carbon of the aryl group), 128.5, 127.3, 126.4 (other aromatic carbons), 109.6 (C–5), 53.8 (benzylic carbon at C–4), 30.3 (methyl carbon of the acetyl group), 18.9 (methyl carbon at C–6). MS *m/z*: 231 (M+1), 157, 202, 154. Anal. calcd for $C_{13}H_{14}N_2O_2$: C, 67.82; H, 6.09; N, 12.17. Found: C, 67.71; H, 6.11; N, 12.14.

4b) IR (KBr) cm^{-1}: 3230 and 3123 (N–H str.), 3022 (aromatic C–H str.), 2952 (aliphatic C–H str.), 1701 and 1635 (C=O str.). ^1H NMR (DMSO-d_6) δ: 9.14 (s, 1H, H–1), 7.75 (s, 1H, H–3), 7.14 (d, 2H, J = 8 Hz, aromatic CH), 6.86 (d, 2H, J = 8 Hz, aromatic CH), 5.18 (s, 1H, H–4), 3.70 (s, 3H, methoxy proton at the aryl ring), 2.26 (s, 3H, methyl protons at C–6), 2.05 (s, 3H, methyl protons of the acetyl group). ^{13}C NMR (DMSO-d_6) δ: 194.3 (carbonyl carbon), 158.4 (methoxy bearing aromatic carbon), 152.0 (C–6), 147.7 (carbonyl carbon of the urea), 136.3 (*ipso* carbon of the aryl group), 127.6 and 113.8 (other aromatic carbons), 109.5 (C–5), 55.0 (methoxy carbon at the aryl ring), 53.3 (benzylic carbon at C–4), 30.1 (methyl carbon of the acetyl group), 18.7 (methyl carbon at C–6). Anal. calcd for $C_{14}H_{16}N_2O_3$: C, 64.61; H, 6.15; N, 10.76. Found: C, 64.58; H, 6.16; N, 10.75.

4c) IR (KBr) cm^{-1}: 3229 and 3120 (N–H str.), 3016 (aromatic C–H str.), 2920 (aliphatic C–H str.), 1701 and 1619 (C=O str.). ^1H NMR (DMSO-d_6) δ: 9.14 (s, 1H, H–1), 7.77 (s, 1H, H–3), 7.11 (s, 4H, aromatic CH), 5.19 (d, 1H, J = 4 Hz, H–4), 2.26 (s, 3H, methyl protons at C–6), 2.24 (s, 3H, methyl protons at the aryl group), 2.06 (s, 3H, methyl protons of the acetyl group). ^{13}C NMR (DMSO-d_6) δ: 194.3 (carbonyl carbon), 152.1 (C–6), 147.8 (carbonyl carbon of the urea), 141.3 (*ipso* carbon of the aryl group), 136.4 (methyl bearing aromatic carbon), 129.0 and 126.3 (other aromatic carbons), 109.5 (C–5), 53.5 (benzylic carbon at C–4), 30.1 (methyl carbon of the acetyl group), 20.6 (methyl carbon at the aryl ring), 18.8 (methyl carbon at C–6). Anal. calcd for $C_{14}H_{16}N_2O_2$: C, 68.85; H, 6.55; N, 11.47. Found: C, 69.00; H, 6.53; N, 11.43.

4d) IR (KBr) cm^{-1}: 3288 and 3121 (N–H str.), 2989 (aromatic C–H str.), 2922 (aliphatic C–H str.), 1701 and 1619 (C=O str.). ^1H NMR (DMSO-d_6) δ: 9.23 (s, 1H, H–1), 7.86 (s, 1H, H–3), 7.38 (d, 2H, J = 8Hz, aromatic CH), 7.24 (d, 2H, J = 8Hz, aromatic CH), 5.23 (d, 1H, J = 4Hz, H–4), 2.27 (s, 3H, methyl protons at C–6), 2.11 (s, 3H, methyl protons of the acetyl group). ^{13}C NMR (DMSO-d_6) δ: 194.0 (carbonyl carbon), 152.0 (C–6), 148.4 (carbonyl carbon of the urea), 143.1 (*ipso* carbon of the aryl group), 131.8 (chlorine bearing aromatic carbon), 128.4 and 128.2 (other aromatic carbons), 109.4 (C–5), 53.0 (benzylic carbon at C–4), 30.0 (methyl carbons of the acetyl group), 18.9 (methyl carbon at C–6). Anal. calcd for $C_{13}H_{13}N_2O_2Cl$: C, 58.99; H, 4.91; N, 10.58. Found: C, 58.92; H, 4.90; N, 10.56.

4e) IR (KBr) cm^{-1}: 3246 and 3120 (N–H str.), 2945 (aromatic C–H str.), 2924 (aliphatic C–H str.), 1704 and 1622 (C=O str.). ^{1}H NMR (DMSO-d_6) δ: 9.26 (s, 1H, H–1), 7.73 (s, 1H, H–3), 7.42 (d, 1H, J = 8Hz, aromatic CH), 7.32–7.23 (m, 3H, aromatic CH), 5.64 (d, 1H, J = 4Hz, H–4), 2.32 (s, 3H, methyl protons at C–6), 2.04 (s, 3H, methyl protons of the acetyl group). ^{13}C NMR (DMSO-d_6) δ: 194.1 (carbonyl carbon), 151.6 (C–6), 148.9 (carbonyl carbon of the urea), 140.8 (*ipso* carbon of the aryl group), 132.0 (chlorine bearing aromatic carbon), 129.7, 129.4, 128.5 and 127.9 (other aromatic carbons), 108.5 (C–5), 51.6 (benzylic carbon at C–4), 30.1 (methyl carbons of the acetyl group), 18.9 (methyl carbon at C–6). Anal. calcd for $C_{13}H_{13}N_2O_2Cl$: C, 58.99; H, 4.91; N, 10.58. Found: C, 58.92; H, 4.93; N, 10.55.

4f) IR (KBr) cm^{-1}: 3257 and 3153 (N–H str.), 3044 (aromatic C–H str.), 2940 (aliphatic C–H str.), 1708 and 1675 (C=O str.). ^{1}H NMR (DMSO-d_6) δ: 9.11 (s, 1H, H–1), 7.64 (s, 1H, H–3), 7.28–7.33 (m, 4H, aromatic CH), 5.35 (d, 1H, J = 4Hz, H–4), 2.23 (s, 3H, methyl protons at C–6), 2.11 (s, 3H, methyl protons of the acetyl group). ^{13}C NMR (DMSO-d_6) δ: 194.7 (carbonyl carbon), 161.5 (fluorine bearing aromatic carbon), 152.5 (C–6), 147.8 (carbonyl carbon of the urea), 139.6 (*ipso* carbon of the aryl group), 128.2 and 115 (other aromatic carbons), 109.5 (C–5), 53.5 (benzylic carbon at C–4), 30.0 (methyl carbons of the acetyl group), 19.0 (methyl carbon at C–6). Anal. calcd for $C_{13}H_{13}N_2O_2F$: C, 62.90; H, 5.24; N, 11.29. Found: C, 62.85; H, 5.23; N, 11.26.

4g) IR (KBr) cm^{-1}: 3251 and 3120 (N–H str.), 2994 (aromatic C–H str.), 2929 (aliphatic C–H str.), 1727 and 1623 (C=O str.). ^{1}H NMR (DMSO-d_6) δ: 9.38 (s, 1H, H–1), 8.00 (s, 1H, H–3), 8.15 (d, 2H, J = 8 Hz, aromatic CH), 7.54 (d, 2H, J = 8 Hz, aromatic CH), 5.45 (d, 1H, J = 4Hz, H–4), 2.35 (s, 3H, methyl protons at C–6), 2.20 (s, 3H, methyl protons of the acetyl group). ^{13}C NMR (DMSO-d_6) δ: 194.2 (carbonyl carbon), 152.6 (nitrogen bearing aromatic carbon), 151.7 (C–6), 149.3 (carbonyl carbon of the urea), 147 (*ipso* carbon of the aryl group), 128.0 and 123.9 (other aromatic carbons), 109.8 (C–5), 53.7 (benzylic carbon at C–4), 30.9 (methyl carbon of the acetyl group), 19.5 (methyl carbon at C–6). Anal. calcd for $C_{13}H_{13}N_3O_4$: C, 56.72; H, 4.72; N, 15.27. Found: C, 56.80; H, 4.73; N, 15.31.

4h) IR (KBr) cm^{-1}: 3267 and 3108 (N–H str.), 3000 (aromatic C–H str.), 2959 (aliphatic C–H str.), 1699 and 1648 (C=O str.). ^{1}H NMR (DMSO-d_6) δ: 9.18 (s, 1H, H–1), 8.95 (s, 1H, H–3), 7.41 (d, 2H, J = 8 Hz, aromatic CH), 7.01 (d, 2H, J = 8 Hz, aromatic CH), 5.14 (d,

1H, *J* = 4Hz, H–4), 2.24 (s, 3H, methyl protons at C–6), 1.98 (s, 3H, methyl protons of the acetyl group). ^{13}C NMR (DMSO-d_6) δ: 195.8 (carbonyl carbon), 157.4 (hydroxy bearing aromatic carbon), 153.2 (C–6), 148.1 (carbonyl carbon of the urea), 135.1 (*ipso* carbon of the aryl group), 128.4, 116.0 (other aromatic carbons), 110.2 (C–5), 55.0 (benzylic carbon at C–4), 30.6 (methyl carbon of the acetyl group), 19.7 (methyl carbon at C–6). Anal. calcd for $C_{13}H_{14}N_2O_3$: C, 63.41; H, 5.69; N, 11.38. Found: C, 63.50; H, 5.68; N, 11.35.

Pharmacology

The bacterial strains *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Salmonella typhi* and fungal strains *Candida albicans, Aspergillus flavus, Rhizopus, Mucor* are obtained from the department of medical microbiology, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalainagar, Tamil Nadu, India.

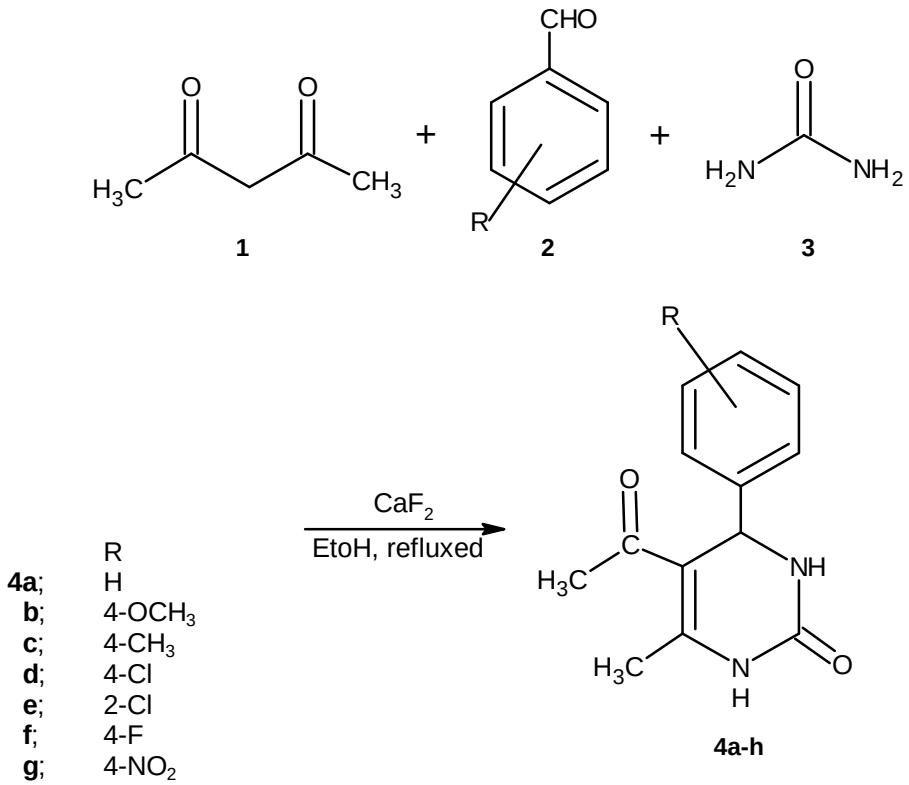
***In vitro* antibacterial and antifungal activity**

The *in vitro* antimicrobial activities of the compounds were tested in Sabouraud's dextrose broth (SDB, Hi-media, Mumbai) for fungi and nutrient broth (NB, Hi-media, Mumbai) for bacteria by the twofold serial dilution method[11]. The test compounds were dissolved in dimethyl sulfoxide (DMSO) to obtain 1 mg/ml stock solutions. Seeded broth (broth containing microbial spores) was prepared in NB from 24 hour old bacterial cultures on nutrient agar (Hi-media, Mumbai) at 37 ± 1°C while fungal spores from 24 hour to 7-day-old Sabouraud's agar slant cultures were suspended in SDB. The colony-forming units (cfu) of the seeded broth were determined by the plating technique and adjusted in the range of 10^4 – 10^5 cfu/ml. The final inoculum size was 10^5 cfu/ml for the antibacterial assay and 1.1-1.5 × 10^2 cfu/ml for the antifungal assay. Testing was performed at 7.4 ± 0.2. Exactly 0.2 ml of the solution of test compound was added to 1.8 ml of seeded broth to form the first dilution. One ml of this was diluted with a further 1 ml of the seeded broth to give the second dilution and so on until six such dilutions were obtained. A set of assay tubes containing only seeded broth was kept as control and likewise solvent controls were also run simultaneously. The tubes were incubated in Biochemical oxygen demand (BOD) incubators at 37 ± 1°C for bacteria and 28 ± 1°C for fungi. The minimum inhibitory concentrations (MICs) were recorded by visual observations after 24 hours (for bacteria) and 72-96 hours (for fungi) of incubation. Ciprofloxacin was used as a standard for the bacterial study while Amphotericin B was used as a standard for the fungal study.

RESULTS AND DISCUSSION

Chemistry

The Biginelli reaction involving acetylacetone (**1**), benzaldehyde (**2**) and urea (**3**) were carried out using calcium fluoride as catalyst **(Scheme 1)**.



Scheme 1

To comprehend structure activity relationship well, numberings of the target compound is shown in Fig. 1.

Scheme 1. Synthetic route for the formation of 3,4-dihydropyrimidinones 4a-h

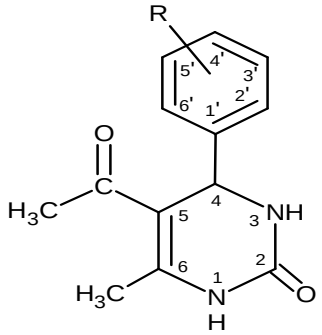


Fig. 1

Fig. 1. Target compound numbering

A broad range of structurally diverse aromatic aldehydes are subjected under this procedure to produce the corresponding dihydropyrimidinones. The results are reported in Table I.

Table I. Physical data of different 3,4-dihydropyrimidinones 4a-h

Compound	R	Time (h)	Yield (%)	m.p. (°C)
4a	H	2	96	264-265
4b	4-OCH_3	2	98	201-202
4c	4-CH_3	2	90	256-257
4d	4-Cl	3	96	258-260
4e	2-Cl	2	92	282-283
4f	4-F	2	90	260-261
4g	4-NO_2	3	90	Above 400
4h	OH	2	92	236-238

It seen that many of the pharmacologically relevant substitution patterns on the aromatic ring could be introduced with high efficiency. It is also clear that, aromatic aldehydes carrying either electron-donating or electron –withdrawing substituents in the *ortho* and *para* positions afford high yields of products with high purity and another important feature of this procedure is that of the survival of a variety of functional groups such as halides, nitro, methyl, methoxy, hydroxy etc.

In compounds **4a, 4c, 4d, 4e, 4f, 4g** and **4h** the benzylic proton appeared as a doublet around 5.39 ppm. This is due to the coupling with adjacent NH (H-3) proton. In compound **4b** the benzylic proton appeared as a broad singlet at 5.18 ppm due to poor resolution of the coupling with NH proton.

Pharmacology

Antibacterial activity

The synthesized 5-acetyl-4-aryl-6-methyl-3,4-dihydropyrimidinones **4a-h** were tested for their antibacterial activity against *Staphylococcus aureus Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Salmonella typhi*. Ciprofloxacin was used as standard drug whose minimum inhibitory concentration (MIC) values were provided in **Table II**. In general the dihydropyrimidinones **4a-h** exerted a wide range of modest antibacterial activity *in vitro* against the tested organisms.

Table II. *In vitro* antibacterial activity of compounds 4a-h

Compound	Minimum inhibitory concentration (MIC) in µg/ml				
	Staphylococcus aureus	***Escherichia coli***	***Klebsiella pneumoniae***	***Pseudomonas aeruginosa***	***Salmonella typhi***
4a	100	100	200	200	200
4b	50	50	100	100	100
4c	50	50	200	100	200
4d	25	12.5	25	25	50
4e	25	25	50	25	50
4f	6.25	12.5	25	6.25	25
4g	6.25	6.25	6.25	6.25	6.25
4h	6.25	6.25	12.5	6.25	12.5
Ciprofloxacin	12.5	12.5	50	25	50

Compound **4a** without any substituent at the *para* position of the aryl moiety at **C-4** position of the six membered heterocyclic ring exhibited antibacterial activity *in vitro* at 200 µg/ml against all the tested organisms except *S. aureus* and *E. coli.* They inhibit *S. aureus* and *E. coli* at a MIC of 100 µg/ml.

Replacement of hydrogen present at the *para* position of the aryl moiety at **C-4** position of the six membered heterocyclic ring by a methoxy function in **4a** (*i.e.*, in **4b**) results two fold increase in activity against all the tested organisms.

Instead of methoxy functionality, substitution of methyl group in **4b** (*i.e.*, in **4c**) the activity was suppressed against *K. pneumoniae* and *S. typhi.* There is no change in the activity against *S. aureus, E. coli* and *P. aeruginosa*.

Due to the introduction of chloro group at the *para* position of the aryl moiety at **C-4** position of the six membered heterocyclic ring in the place of methyl function in **4c** (*i.e.,* in **4d**) showed activity in the range of 12.5 to 50 µg/ml against all the tested organisms.

Replacement of hydrogen present at the *ortho* position of the aryl moiety at **C-4** position of the six membered heterocyclic ring by a chloro function in **4a** (*i.e.*, in **4c**) the activity was highly increased against all the tested organisms.

Instead of chloro functionality, substitution of fluoro group in **4d** (*i.e.*, in **4f**) showed good antibacterial activity against all the tested organisms.

Due to the introduction of nitro group at the *para* position of the aryl group at **C-4** position of the six membered heterocyclic moiety in the place of fluoro function in **4f** (*i.e.,* in **4g**) results amazing antibacterial activity against all the tested organisms.

Replacement of nitro group present at the *para* position of the aryl moiety at **C-4** position of the six membered heterocyclic ring by a hydroxy function in **4g** (*i.e.,* in **4h**) showed excellent antibacterial activity against all the tested organisms.

A comparative studies of minimum inhibitory concentration for the compounds **4a-h** using standard ciprofloxacin versus bacterial strains given in **Fig. 2**.

Y-axis – MIC in µg/ml and

X-axis- Compound

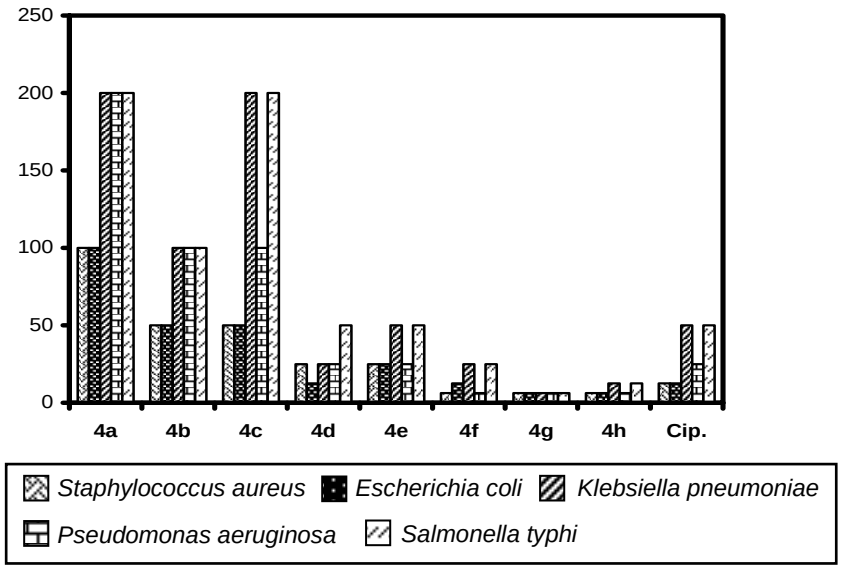


Fig. 2 Cip. – Ciprofloxacin

Fig. 2. Comparison of minimum inhibitory concentration of compounds 4a-h with Ciprofloxacin (as standard) against bacterial strains from serial dilution method

Antifungal activity

The *in vitro* antifungal activity of the 5-acetyl-4-aryl-6-methyl-3,4-dihydropyrimidinones **4a-h** was studied against the fungal strains *viz., Candida albicans, Aspergillus flavus, Rhizopus* and *Mucor*. Amphotericin B was used as a standard drug whose minimum inhibitory concentration (MIC) values were furnished in **Table III.**

Table III. *In vitro* antifungal activity of compounds 4a-h

Compound	Minimum inhibitory concentration (MIC) in µg/ml			
	Candida albicans	***Aspergillus flavus***	***Rhizopus***	***Mucor***
4a	200	200	-	-
4b	100	50	100	100
4c	100	100	100	200
4d	25	25	25	50
4e	25	25	50	50
4f	12.5	12.5	25	25
4g	6.25	3.13	12.5	12.5
4h	6.25	6.25	12.5	25
Amphotericin B	25	50	50	12.5

'—' No inhibition even at a higher concentration of 200 µg*/ml.*

The antifungal profile of compound **4a** without any substituent at the *para* position of the aryl group at C-4 position of the six membered heterocyclic moiety exhibited antifungal activity in vitro at 200 µg/ml against all the tested organisms except *Rhizopus* and *Mucor* even at the high concentration of 200 µg/ml.

Due to the introduction of methoxy function at the *para* position of the aryl group at C-4 position of the six membered heterocyclic moiety in the place of hydrogen function in **4a** (*i.e.*, in **4b**) results increase in antifungal activity against all the tested organisms.

Replacement of methoxy function present at the *para* position of the aryl moiety at C-4 position of the six membered heterocyclic ring by a methyl function in **4b** (*i.e.,* in **4c**) showed two fold decrease in activity against all the tested organisms except *C. albicans* and *Rhizopus.*

Instead of methyl functionality substitution of chloro group in **4c** (*i.e.*, in **4d**) the activity was increased against all the tested organisms.

Replacement of hydrogen present at the *ortho* position of the aryl moiety at C-4 position of the six membered heterocyclic ring by a chloro function in **4a** (*i.e.,* in **4e**) showed good antifungal activity against all the tested organisms.

Due to the introduction of fluoro function at the *para* position of the aryl group at C-4 position of the six membered heterocyclic moiety in the place of chlorofunction in **4d** (*i.e.*, in **4f**) showed activity in the range of 12.5 to 25 µg/ml against all the tested organisms.

Instead of fluoro functionality, substitution of nitro group in **4f** (*i.e.*, in **4g**) results amazing antifungal activity against all the tested organisms.

Due to the introduction of hydroxy function at the *para* position of the aryl moiety at **C-4** position of the six membered heterocyclic moiety in the place of nitro function in **4g** (*i.e.*, in **4h**) exhibited excellent antifungal activity against all the tested organisms.

Minimum inhibitory concentration of compounds **4a-h** was compared with standard Amphotericin B against fungal strains shown in **Fig. 3**.

Y-axis – MIC in µg/ml and

X-axis- Compound

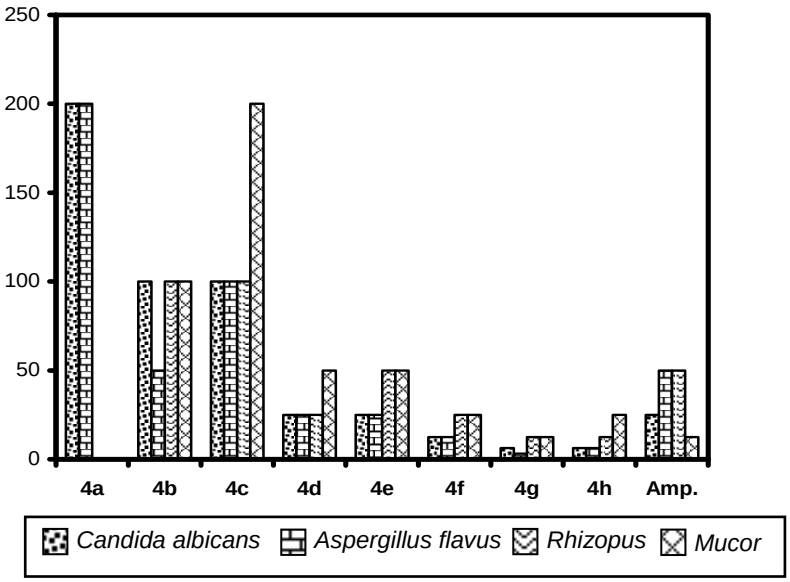


Fig. 3 Amp.- Amphotericin B

Fig. 3. Comparison of minimum inhibitory concentration of compounds 4a-h with Amphotericin B (as standard) against fungal strains from serial dilution method

CONCLUSION

A close examination of the *in vitro* antibacterial and antifungal activity profile in differently substituted some 5-Acetyl-4-aryl-6-methyl-3,4-dihydropyrimidinones **4a-h** against the tested bacterial strains *viz., S. aureus, E. coli, K. pneumoniae, P. aeruginosa* and *S. typhi* and the fungal strains *viz., C. albicans, A. flavus, Rhizopus* and *Mucor*, respectively, provides a better structure activity relationship correlation. This may be summarized as follows: the results of this study show that the presence of both electron-donating substituent (methyl, methoxy) and

electron-withdrawing substituent (chloro, fluoro, hydroxy, nitro) at the *ortho, para* positions on the phenyl ring in compounds **4a-h** are responsible for the activity against all the tested organisms.

Specifically of the some 5-Acetyl-4-aryl-6-methyl-3,4-dihydropyrimidinones tested, the compounds with nitro function at the *para* position of the aryl moiety at C-4 position of the six membered heterocyclic moiety exhibited amazing antibacterial activity against all the tested organisms and the 5-Acetyl-4-aryl-6-methyl-3,4-dihydropyrimidinones with fluoro and hydroxy moiety at the *para* position of the aryl group at C-4 position of the six membered heterocyclic ring showed excellent antibacterial activity against all the organisms.

5-Acetyl-4-aryl-6-methyl-3,4-dihydropyrimidinones with nitro moiety at the *para* position of the aryl group at C-4 position of the six membered heterocyclic ring exerted amazing antifungal activity against all the tested organisms and the 5-acetyl-4-aryl-6-methyl-3,4-dihydropyrimidinones with hydroxy at the *para* position of the aryl moiety at **C-4** position of the six membered heterocyclic ring exhibited excellent antifungal activity against all the tested organisms.

These observations may promote a further development of our research in this field. Further development of this group of compounds may lead to compounds with better pharmacological profile than standard drugs and serve as templates for the construction of better drugs to combat bacterial and fungal infection.

ACKNOWLEDGEMENTS

The authors are thankful to SIF, Indian Institute of Science, Bangalore for recording all the NMR spectra. The authors place sincere thanks to Department of Microbiology, Annamalai University, India for his kind help in conducting antimicrobial studies.

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