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RESEARCH ARTICLE

Synthesis and Study of Antibacterial and Antifungal Activities of Novel 3-Alkyl-2,6-diarylpiperidin-4-one-2-thienoyl Hydrazone

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Abstract: In the present work a new series of 3-alkyl-2,6-diarylpiperidin-4-one-2-thienoyl hydrazones have synthesized by the reaction of 3-alkyl-2, 6-diarylpiperidin-4-one with 2-thiophenecarboxylic acid hydrazide and characterized by spectral (IR, ^{1}H NMR, ^{13}C NMR, HSQC, HMBC, NOESY and COSY) techniques. The hydrazones were screened for their *in vitro* antibacterial and antifungal activities against some selected micro organism. The results show that, compounds with halo-substituents at para position of the phenyl showed good antibacterial profile and antifungal against all tested organism.

Keywords: Hydrazones, Antibacterial, Antifungal

Introduction

Heterocyclic ring systems having piperidin-4-one nucleus have aroused great interest in the past and recent years due to their wide variety of biological properties such as antitumor[1,2] anti-inflammatory[3] central nervous system[4-9] local anaesthetic[10] anticancer[11] and antimicrobial activities[12] and their derivative piperidines are also biologically important and act as neurokinin receptor antogonists[13], analgesic and antihypertensive agents[14]. The importance of piperidin-4-one as intermediate in the synthesis of a variety of compounds of physiologically active has been reviewed by Prostakov Gaivoronskaya[15].

Thiophenecarboxylic acid hydrazide have attracted considerable attention due to the biological activity of the 2-thiophene moiety which has been widely recognized and practically applied in several drugs[16-18], herbicides[19] and fungicides[20,21]. Thiophene-carboxylic hydrazide were tested for antituberculous activity[22] and found to show β-adrenergic blocking activities[23].

Synthesis of molecules, which are novel still resembling known biologically active molecules by virtue of the presence of some critical structural features, is an essential

component of the search for new leads in drug designing programme. Certain small heterocyclic molecules act as highly functionalized scaffolds and are known pharmacophores of a number of biologically active and medicinally useful molecules. In the interest of above, we planned to synthesize a system, which combines both bio active piperidine and 2-thiophenecarboxylic acid hydrazide components together to give a title compounds.

Experimental

All the reagents were commercially available and used without further purification. Solvents were distilled from appropriate drying agents immediately prior to use.

Physical measurements

The course of reaction and the purity were ascertained by performing TLC, melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in Perkin-Elmer 297 spectrophotometer with KBr pellets. ^{1}H NMR spectra were recorded at 400MHz on Bruker AMX-400MHz spectrophotometer in $CDCl_3$ using tetramethyl silane (TMS) as internal standard and ^{13}C NMR spectra were recorded at 100MHz on Bruker AMX-400MHz spectrophotometer in $CDCl_3$. Elemental analyses (C, H and N) were carried out on a Carlo Erba model 1106 and Perkin Elmer models 240 CHN analyzer. The results are within ±0.4% of the theoretical values.

Table 1. Elemental analysis data

Compounds	R_1	X	Carbon % (found /calculated)	Hydrogen % (found /calculated)	Nitrogen % (found /calculated)
14	CH_3	H	70.27/70.24	5.67/5.71	14.91/14.94
15	CH_3	Cl	72.34/72.32	6.15/6.14	13.47/13.43
16	CH_3	Br	71.25/71.24	5.43/5.41	12.36/12.35
17	CH_3	CH_3	70.71/70.73	6.10/6.07	13.56/13.57
18	CH_3	F	74.21/74.19	4.87/4.91	14.56/14.51
19	CH_3	NO_2	71.91/71.94	6.21/6.19	13.54/13.51
20	C_2H_5	H	73.50/73.49	5.92/5.94	12.82/12.83
21	C_2H_5	Cl	70.95/70.94	6.84/6.82	13.12/13.11
22	C_2H_5	Br	74.51/74.49	5.81/5.82	14.12/14.14
23	C_2H_5	CH_3	72.71/72.73	4.87/4.84	12.54/12.53
24	C_2H_5	F	74.31/74.32	6.47/6.43	13.01/13.02
25	C_2H_5	NO_2	70.61/70.62	4.32/4.31	14.64/14.65

Synthesis

From the literature precedent[24] 3-alkyl 2,6-diarylpiperidin-4-one (**1-14**) were prepared (Scheme 1) by the condensation of appropriate ketones, aldehydes and ammonium acetate in 1:2:1 ratio.

*General procedure for the synthesis of 3-alkyl-2,6-diarylpiperidin-4- one-2-thienoyl hydrazone (**14-25**)*

A mixture of 3-alkyl-2,6-diarylpiperidin-4-one (**1-14**) (1mmol), 2-thiophene-carboxylic acid hydrazide (1.5 mmol) in methanol and chloroform (1:1v/v) and a few drops of acetic acid was added and refluxed for 2-4 hours. On completion of the reaction time, a solid mass was formed, which was then cooled to room temperature. The precipitate was filtered off and washed with ice-cooled water-ethanol mixture. The crude product was recrystallized from ethanol.

Spectral Data

*3-Methyl-2,6-diphenylpiperidin-4-one-2-thienoyl hydrazone **(14)***

IR (KBr) (cm^{-1}): 3074, 2880(C-H stretching), 1650(N─C═O stretching). ^{1}H NMR (δppm): 1.09(d, 3H, CH_3 at C-3), 2.07(s, 1H, N─H at piperidine ring), 2.68(t, 1H, H_{3e}), 2.25(t, 1H, H_{5e}), 3.36(d, 1H, H_{5e}), 3.59(d, 1H, H_{2a}), 3.93(d, 1H, H_{6a}), 9.90(s, 1H, HN─C═O), 7.06-7.96(m, 14H, aryl and thienoyl ring protons). ^{13}C NMR (δppm): 13.52(CH_3), 35.79(C-5), 46.04(C-3), 60.91(C-6), 69.44(C-2), 163.17(HN─C═O), 142.59 and 143.14(ipso carbons), 126.39–135.54 and 156.46(aryl and thienoyl ring carbons).

*3-Methyl-2,6-bis(p-chlorophenyl)piperidin-4-one-2-thienoyl hydrazone **(15)***

IR (KBr) (cm^{-1}): 3070, 2878(C-H stretching), 1648(N─C═O stretching). ^{1}H NMR (δppm): 0.94(d, 3H, CH_3 at C-3), 2.02(s, 1H, N─H at piperidine ring), 2.56(t, 1H, H_{3e}), 2.08(d, 1H, H_{5e}), 2.95(s, 1H, H_{5e}), 3.51(d, 1H, H_{2a}), 3.83(d,1H, H_{6a}), 10.93(s, 1H, HN─C═O), 7.17-8.03(m, 12H, aryl and thienoyl ring protons), ^{13}C NMR (δppm): 13.43(CH_3), 30.66(C-5), 45.02 (C-3), 59.01(C-6), 67.73(C-2), 162.02(HN─C═O), 142.03, 142.87(ipso carbons), 127.99–134.35 and 153.84(aryl and thienoyl ring carbons).

*3-Methyl-2,6-bis(p-bromophenyl)piperidin-4-one-2-thienoyl hydrazone **(16)***

IR (KBr) (cm^{-1}): 3072, 2884(C-H stretching), 1644(N─C═O stretching). ^{1}H NMR(δppm): 0.93(s, 3H, CH_3 at C-3), 2.08(m, 2H, N─H at piperidine ring, H_{5e}), 2.53(t, 1H, H_{3e}), 2.93 (s, 1H, H_{5a}), 3.44(s, 1H, H_{2a}), 3.81(d, 1H, H_{6a}), 10.91(s, 1H, HN─C═O), 7.16–8.02(m, 12H, aryl and thienoyl ring protons), ^{13}C NMR (δppm): 13.40(CH_3), 35.92 (C-5), 44.96 (C-3), 59.06 (C-6), 67.76(C-2), 162.05(HN─C═O), 142.42 and 143.27(ipso carbons), 119.98–134.42 and 156.88(aryl and thienoyl ring carbons).

*3-Methyl-2,6-bis(p-methylphenyl)piperidin-4-one-2-thienoyl hydrazone **(17)***

IR (KBr) (cm^{-1}): 3080, 2880(C-H stretching), 1640(N─C═O stretching). ^{1}H NMR (δppm): 1.08(s, 3H, CH_3 at C-3), 2.02(s, 1H, N─H at piperidine ring), 2.07(t, 1H, H_{5e}), 2.34(s, 6H, CH_3 at aryl ring), 2.62(d, 1H, H_{3e}), 3.03 (d, 1H, H_{5a}), 3.54(s, 1H, H_{2a}), 3.86(d, 1H, H_{6a}), 9.07(s, 1H, HN─C═O), 7.09–8.09(m, 12H, aryl and thienoyl ring protons), ^{13}C NMR (δppm): 13.41(CH_3 at C-3), 21.16(CH_3 at aryl ring), 35.67(C-5), 45.96(C-3), 60.64(C-6), 69.11 (C-2), 162.72(HN─C═O), 140.10 and 139.60(ipso carbons), 126.52–137.59 and 156.23(aryl and thienoyl ring carbons).

*3-Methyl-2,6-bis(p-fluorophenyl)piperidin-4-one-2-thienoyl hydrazone **(18)***

IR (KBr) (cm^{-1}): 3080, 2920(C-H stretching), 1640(N─C═O stretching). ^{1}H NMR (δppm): 1.07(d, 3H, CH_3 at piperidine ring), 2.02(s,1H, N─H at piperidin ring), 2.19(t, 1H, H_{5e}), 2.61 (s, 1H , H_{3e}), 3.23(d, 1H, H_{5a}), 3.58(d, 1H, H_{2a}), 3.91(d, 1H, H_{6a}), 9.71(s, 1H, HN─C═O), 7.04–7.95(m, 12H, aryl and thienoyl ring protons), ^{13}C NMR (δppm): 13.36(CH_3 at piperidine ring), 35.87(C-5), 46.12(C-3), 60.19(C-6), 68.59(C-2), 163.64(HN─C═O), 138.82 and 138.24(ipso carbons), 115.26–135.49 and 155.65(aryl and thienoyl ring carbons).

*3-Methyl-2,6-bis(p-nitrophenyl)piperidin-4-one-2-thienoyl hydrazone **(19)***

IR (KBr) (cm^{-1}): 3072, 2913(C-H stretching), 1632(N─C═O stretching). ^{1}H NMR(δppm): 1.12(d, 3H, CH_3 at piperidine ring), 2.12(s, 1H, N─H at piperidine ring), 2.20(t, 1H, H_{5e}), 2.72 (s, 1H, H_{3a}), 3.32(d, 1H, H_{5a}), 3.61(d, 1H, H_{2a}), 3.94(d, 1H, H_{6a}), 9.84(s,1H, HN─C═O), 7.11–7.84(m, 10H, aryl and thienoyl ring protons), ^{13}C NMR (δppm): 13.20(CH_3 at piperidine ring), 34.24(C-5), 45.72(C-3), 61.21(C-6), 67.84(C-2),162.24(HN─C═O), 140.20 and 139.82 (ipso carbons), 118.92–135.21 and 154.46 (aryl and thienoyl ring carbons).

*3-Ethyl-2,6-diphenylpipseridin-4-one-2-thienoyl hydrazone (**20**)*

IR (KBr) (cm^{-1}): 3070, 2888(C-H stretching), 1646(N─C═O stretching). ^{1}H NMR (δppm): 0.08(t, 3H, CH_2-$\underline{C}H_3$ at C-3), 1.41(t, 2H, $\underline{C}H_2$-CH_3), 2.01(s, 1H, N─H at piperidine ring), 2.24(t, 1H, H_{5e}), 2.54(t, 1H, H_{3e}), 3.22(d, 1H, H_{5a}), 3.73(d, 1H, H_{2a}), 3.93(d, 1H, H_{6a}), 9.57(s, 1H, HN─C═O), 7.06–7.99 (m, 12H, aryl and thienoyl ring protons),^{13}C NMR (δ ppm): 12.48(CH_2-$\underline{C}H_3$), 19.18($\underline{C}H_2$-CH_3), 36.17(C-5), 52.58(C-3), 60.96(C-6), 67.78(C-2), 162.97 (HN─$\underline{C}$═O), 142.54 and 143.10(ipso carbons), 126.45–135.45 and 154.85 (aryl and thienoyl ring carbons).

*3-Ethyl-2,6-bis(p-chlorophenyl)piperidin-4-one-2-thienoyl hydrazone (**21**)*

IR (KBr) (cm^{-1}): 3074, 2920(C-H stretching), 1640(N─C═O stretching). ^{1}H NMR (δppm): 1.37(t, 3H, CH_2-$\underline{C}H_3$ at piperidine ring), 1.09 and 1.84(m, 2H, $\underline{C}H_2$-CH_3), 1.96(s, 1H, N─H at piperidine ring), 2.46(t, 1H, H_{3e}), 3.21 (d, 1H, H_{5a}), 3.70(d, 1H, H_{2a}), 3.90(d, 1H, H_{6a}), 9.63(s, 1H, HN─C═O), 7.08–7.93(m, 10H, aryl and thienoyl ring protons), ^{13}C NMR (δppm): 12.45(CH_2-$\underline{C}H_3$),19.08($\underline{C}H_2$-CH_3), 30.97(C-5), 52.56(C-3), 60.25(C-6), 66.96(C-2), 161.54(HN─$\underline{C}$═O), 141.45 and 140.86(ipso carbons), 126.51–134.22 and 153.79(aryl and thienoyl ring carbons).

*3-Ethyl-2,6 –bis(p-bromophenyl)piperidin-4-one-2-thienoyl hydrazone (**22**)*

IR (KBr) (cm^{-1}): 3071, 2886(C-H stretching), 1642(N─C═O stretching). ^{1}H NMR (δppm): 0.78(t, 3H, CH_2-$\underline{C}H_3$ at C-3), 1.21(s, 2H, $\underline{C}H_2$-CH_3), 1.79 (s,1H, $\underline{C}H_2$-CH_3), 2.03(s, 1H, N─H at piperidine ring), 2.50 (t, 1H, H_{3e}), 2.88 (s, 1H, H_{5e}), 3.63(d, 1H, H_{2e}), 3.84(d, 1H, H_{6a}), 10.88(s, 1H, HN─C═O), 7.16–8.03(m,10H, aryl and thienoyl ring protons), ^{13}C NMR(δppm): 12.25(CH_2-$\underline{C}H_3$), 18.82($\underline{C}H_2$-CH_3), 30.66(C-5), 51.57(C-3), 59.09(C-6), 66.22(C-2), 167.44(HN─$\underline{C}$═O), 143.26 and 142.38(ipso carbons), 119.98–134.30 and 155.59(aryl and thienoyl ring carbons).

*3-Ethyl-2,6-bis(p-methylphenyl)piperidin-4-one-2-thienoyl hydrazone (**23**)*

IR (KBr) (cm^{-1}): 3074, 2924(C-H stretching), 1640(N─C═O stretching). ^{1}H NMR(δppm): 0.88(t, 3H, CH_2-$\underline{C}H_3$ at piperidine ring), 1.38 and 1.85 (m, 2H, $\underline{C}H_2$-CH_3), 1.95(s, 1H, N─H at piperidine ring), 2.20(t, 1H, H_{5e}), 2.51(t, 1H, H_{3e}), 3.0(d, 1H, H_{5a}), 3.68(d, 1H, H_{2a}), 3.86(d, 1H, H_{6a}), 9.17(s, 1H, HN─C═O), 7.08–8.07(m, 10H, aryl and thienoyl ring protons), 2.34(s, 6H, CH_3 at phenyl ring), ^{13}C NMR(δppm): 12.47(CH_2-$\underline{C}H_3$), 19.17($\underline{C}H_2$-CH_3), 21.17(CH_3 at phenyl ring), 36.12(C-5), 52.53(C-3), 60.67(C-6), 67.46(C-2), 164.08 (HN─$\underline{C}$═O), 140.12, 139.57, 137.56 and 137.53(ipso carbons), 126.53–135.44 and 154.76(aryl and thienoyl ring carbons).

*3-Ethyl-2,6-bis(p-fluorophenyl)piperidin-4-one-2-thienoyl hydrazone (**24**)*

IR (KBr) (cm^{-1}): 3068, 2918(C-H stretching), 1634(N─C═O stretching). ^{1}H NMR (δppm): 0.87(t, 3H, CH_2-$\underline{C}H_3$), 1.35 and 1.86(m, 2H, $\underline{C}H_2$-CH_3), 1.96(s, 1H, N─H at piperidine ring), 2.18(t, 1H, H_{3e}), 2.46(t, 1H, H_{5e}), 3.05 (d, 1H, H_{5a}), 3.70(d, 1H, H_{2a}), 3.89(d, 1H, H_{6a}), 9.09(s,1H, HN─C═O), 7.02–8.08(m, 10H, aryl and thienoyl ring protons), ^{13}C NMR (δppm): 12.45(CH_2-$\underline{C}H_3$), 19.09($\underline{C}H_2$-CH_3), 36.36(C-5), 52.73(C-3), 60.21(C-6), 66.96(C-2), 163.11(HN─$\underline{C}$═O), 138.88 and 138.25(ipso carbons), 115.30–135.43(aryl and thienoyl ring carbons).

*3-Ethyl-2,6-bis(p-nitrophenyl)piperidin-4-one-2-thienoyl hydrazone (**25**)*

IR (KBr) (cm^{-1}): 3072, 2920(C-H stretching), 1632(N─C═O stretching). ^{1}H NMR (δppm): 1.10(t, 3H, CH_2-$\underline{C}H_3$ at piperidine ring), 1.34 and 1.80(m, 2H, $\underline{C}H_2$-CH_3), 1.92(s, 1H, N─H at piperidine ring), 2.14(t, 1H, H_{5e}), 2.47(t, 1H, H_{3e}), 3.12(d, 1H, H_{5a}), 3.64(d, 1H, H_{2a}),

3.92(d, 1H, H_{6a}), 9.82(s, 1H, HN─C═O), 7.11–8.12(m, 10H, aryl and thienoyl ring protons), ^{13}C NMR (δppm): 12.14(CH_2-$\underline{C}H_3$), 20.11($\underline{C}H_2$-CH_3), 35.82(C-5), 53.19(C-3), 61.24(C-6), 68.11(C-2), 163.21(HN─$\underline{C}$═O), 141.23, 140.24, 139.24 and 139.12 (ipso carbons), 125.87–135.42 and 151.24(aryl and thienoyl ring carbons).

Antimicrobial activity (Structure-activity relationship)

The new class of compounds in this paper have been preliminarily evaluated for their antibacterial and antifungal activities against a band of certain selected bacterial (*Escherichia coli, Salmonella typhi, Staphylococcus aureus, Klebsiella pneumonia and Pseudomonas aeruginosa)* and fungal (*Aspergillus niger, Aspergillus flavus, Candida albicans and Rhizopus sp*.,) pathogens *in vitro* by conventional twofold serial dilution method[25]. The obtained results were compared to ciprofloxacin and Amphotericin B which were used as the standard drugs for bacterial and fungal strains respectively. The antibacterial and antifungal potencies of the synthesized compounds are reproduced in Table 2 and 3 respectively.

Table 2. *In vitro* antibacterial activities of compounds (**14-25**) against selected bacterial strain in µg/mL

Compds	R_1	X	*E.Coli*	*Salmonella typhi*	*Staphylococcus aureus*	*Klebsiella pneumonia*	*Pseudomona aeruginosa*
14	CH_3	H	200	100	-	200	100
15	CH_3	Cl	25	25	12.5	25	25
16	CH_3	Br	12.5	25	50	25	25
17	CH_3	CH_3	100	200	100	50	100
18	CH_3	F	12.5	12.5	25	12.5	25
19	CH_3	NO_2	50	100	50	25	100
20	C_2H_5	H	200	100	100	200	100
21	C_2H_5	Cl	25	25	12.5	25	25
22	C_2H_5	Br	25	12.5	12.5	25	25
23	C_2H_5	CH_3	100	100	200	100	100
24	C_2H_5	F	12.5	25	12.5	25	12.5
25	C_2H_5	NO_2	50	50	100	50	50
Ciprofloacin			25	50	12.5	12.5	25

Table 3. *In vitro* antifungal activities of compounds (**14-25**)

Compounds	R_1	X	*A.niger*	*A. flavus*	*Candida albicans*	*Rhizopus*
14	CH_3	H	-	200	-	200
15	CH_3	Cl	25	12.5	25	25
16	CH_3	Br	12.5	25	25	25
17	CH_3	CH_3	100	50	100	100
18	CH_3	F	12.5	12.5	12.5	25
19	CH_3	NO_2	50	100	100	50
20	C_2H_5	H	200	100	-	200
21	C_2H_5	Cl	25	12.5	25	12.5
22	C_2H_5	Br	25	12.5	25	25
23	C_2H_5	CH_3	100	50	50	50
24	C_2H_5	F	12.5	12.5	25	12.5
25	C_2H_5	NO_2	100	50	50	100
Amphotericin B			25	25	25	25

Compounds **14** and **20** without any substituent at para position of the aryl moieties at C-2 and C-6 position of the piperidine exhibited antibacterial activity *in vitro* at 200 µg/mL against all the tested organism except *Salmonella typhi* and *P.aeruginosa*. They inhibit both the organism at MIC of 100µg /mL.

Introduction of chloro, bromo and fluoro groups at the para position of the aryl moieties at C-2 and C-6 in piperidine in compound **15, 16** and **18** produced twice the activity against all the organisms. Replacement of halo groups present at the para position of the aryl moieties at C-2 and C-6 of **14** by nitro group yielded moderate activity against all the tested organism except *Salmonella typhi* and *P.aeruginosa*.

Introduction of an ethyl groups in place of methyl function in **14** (compound **20**) exhibited appreciable inhibition potency towards the tested bacteria strains in the range of 100-200 µg/mL. Introduction of chloro, bromo and fluoro groups at the para position of the aryl moieties at C-2 and C-6 in piperidine in compound **21, 22** and **24** produced antibacterial activity in the range of 12.5-25 µg/mL.

Replacement of halo moieties present at the para position of aryl groups by nitro group (compound **25**) produced antibacterial activity in the range of 50-100 µg/mL. Compound **23**, which have methyl group at the para position C-2 and C-6 in piperidine ring exhibited antibacterial activity in the region of 100-200 µg/mL.

Antifungal activities

The *in vitro* antifungal activity of the novel compounds **14-25** were examined against the four fungal strains *Aspergillus niger*, *Aspergillus flavus, Candida albicans and Rhizopus sp.,* Here, Amphotericin B was used as standard drug.

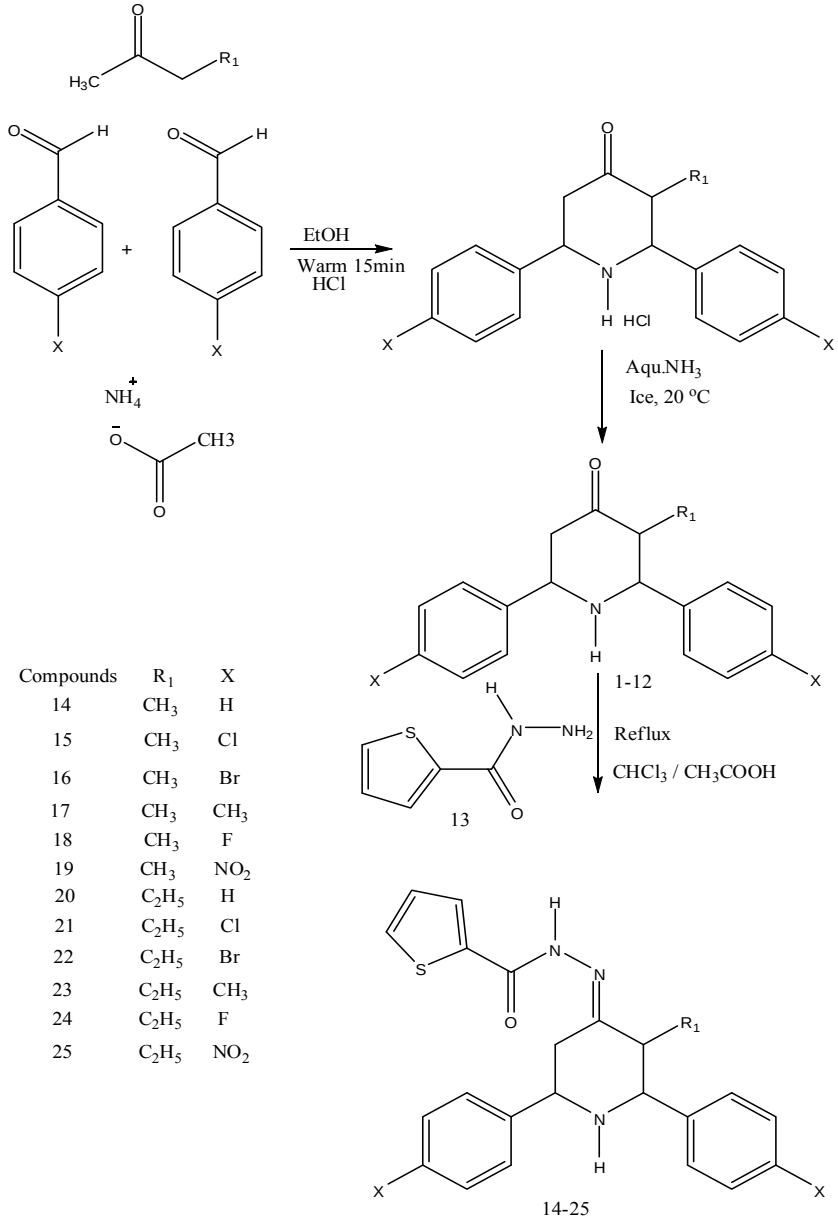
The compound **14** and **20** without any substituents at the para position of phenyl groups present at the carbon atom adjacent to the heterocyclic nitrogen exhibited antifungal activity in the region 100-200 µg/mL. However, compound **14** against *A.niger* and **20** against *Candida albicans* did not show antifungal activity even at a maximum concentration of 200 µg/mL. Compounds **15, 16, 18, 21, 22** and **24**, which have electron withdrawing chloro, bromo and fluoro substitution at the para position of phenyl rings attached to C-2 and C-6 carbons of piperdine moiety exerted activity in the region of 12.5-25µg/mL.

Due to introduction of a methyl group in place of the halo function present at the para position of the phenyl groups (compound **17** and **23**), the activity was suppressed against all the tested organisms. Introductions of nitro group at the para position of phenyl rings attached to C-2 and C-6 carbons of piperidine moiety shows antifungal activities in the range of 50-100 µg/mL.

Results and Discussion

The obvious synthetic pathway that leads to the title compounds is represented in Scheme 1 structures of all the synthesized compounds were established on the basis of ^{1}H NMR and ^{13}C NMR spectral data. The purities of the compounds were checked by elemental analysis. The analytic data agreed well with their proposed molecular formulas.^{1}H NMR assignment of compounds **14-25** is made based on their one- and two- dimensional NMR spectral studies. In the ^{1}H NMR spectra of the target hydrazones, a broad and more downfield D_2O exchangeable singlet at 9.73 ppm was characteristic of the N-H amide group. The two doublet signal appeared at 3.94 and 3.59 ppm, corresponding to one proton integrals. These two signals are attributed to benzylic protons H_{6a} and H_{2a} respectively. However, signals that appeared at 3.31 and 2.25 ppm should be due to the H_{5a} and H_{5e}. The methyl proton appeared at 1.09 ppm corresponding to three proton integrals. A triplet appeared at 2.66 ppm due to the

H_{3a}, corresponding to one proton integral. Aromatic protons appeared as a multiplet in the region of 7.06-7.96 ppm. In the ^{13}C NMR spectrum of compound **15**, an absorptions at 13.52 ppm is assigned to methyl carbon at C-3. The benzylic carbon C-2 and C-6 are observed at 69.44 and 60.91 ppm. The ^{13}C resonance at 46.04 and 35.79 ppm is due to C-3 and C-5.The chemical shift value at 163.17 ppm is assigned to C=O carbon. The ^{13}C resonance at 143.14 and 142.59 ppm is assigned to ipso carbons of two phenyl substituents at C-2 and C-4. The aromatic carbons and thiophene carbons appeared in the region of 126.37-156.46 ppm.



Compounds	R_1	X
14	CH_3	H
15	CH_3	Cl
16	CH_3	Br
17	CH_3	CH_3
18	CH_3	F
19	CH_3	NO_2
20	C_2H_5	H
21	C_2H_5	Cl
22	C_2H_5	Br
23	C_2H_5	CH_3
24	C_2H_5	F
25	C_2H_5	NO_2

Scheme 1

Conclusion

A close examination of the *in vitro* antibacterial and antifungal activity profile of the new 2, 6-diaryl piperidin-4-one-2-thienoyl hydrazone against all tested bacterial and fungal organism gives a clear picture about the structure-activity correlations among the compound **14-25** under study. Compounds **14-25** with chloro, bromo and fluoro functions at the para position of the aryl groups present at the C-2 and C-6 position of the piperidine moiety along with methyl and ethyl substituent at the C- 3 position exerted a strong activity, while the activity was not significant for compounds **14** and **20** without any substituent at the para position of phenyl groups.

Similarly, against the tested fungal strains, compounds **15, 16, 18, 21, 22** and **24** with fluoro, bromo and chloro functions at the para position of phenyl rings attached at C-2 and C- 6 carbons of piperidine moiety along with methyl and ethyl substituent at the position C-3 of the piperdine ring exerted a good range of biological activities, while the activity was not significant for compounds **14** and **20** without any substituents at the para position of the phenyl groups.

Furthermore, the observed marked antifungal and antibacterial activities may be considered as key step for the building of novel chemical entities with comparable pharmacological profile to that of the standard drugs.

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