Available online at www.ijpsdr.com

International Journal of Pharmaceutical Sciences and Drug Research
2017; 9(5): 210-213

Research Article

ISSN: 0975-248X
CODEN (USA): IJPSPP

Synthesis and *In-vitro* Anti-Microbial Evaluation of Novel Hydrazones of Substituted Tetrahydropyrimidines

Megha Shukla, Sumeet Kaur Bhatia, Balbir Kaur*

Department of Chemistry, Punjabi University, Patiala-147002, Punjab, India

ABSTRACT

This research article describes the synthesis of phenyl hydrazone derivatives of 5-acetyl-6-methyl-4-substituted phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidines, as no derivatization has been reported at carbonyl functionality at position 5 of corresponding rings till date. The prepared derivatives were characterised using modern spectral techniques and were screened for their *in-vitro* anti-microbial activities by agar diffusion method. Among synthesised derivatives [II(a-g)], compound II(f) was found to be the most potent anti-bacterial agent and rest of the compounds had shown moderate to weak anti-bacterial activity.

Keywords: Anti-microbial activity, phenyl hydrazone derivatives.

DOI: 10.25004/IJPSDR.2017.090501 **Int. J. Pharm. Sci. Drug Res. 2017; 9(5): 210-213**

***Corresponding author**: Prof. Balbir Kaur
Address: Department of Chemistry, Punjabi University, Patiala-147002, Punjab, India
Tel.: +91-9872399168
E-mail ✉: drbalbirkaur@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Received: 22 May, 2017; **Revised:** 02 August, 2017; **Accepted**: 03 August, 2017; **Published:** 15 September, 2017

INTRODUCTION

Pyrimidines are associated with diversified pharmaceutical properties and are counted amongst ones which make the life possible. Wide variety of naturally occurring and synthetic organic compounds having (-C=N-) functionality exhibit broad spectrum of significant pharmacological activities. Hydrazones have emerged as bioactive heterocyclic compounds [1-2] of immense potential. In the field of medicinal chemistry, various synthetic moieties have been designed that possess (-C=N-) group which is responsible for their antimicrobial [3-4], anticonvulsant [5], anti-cancer [6] activities. Micro-organisms such as *Escherichia coli*, *Staphylococcus aureus* are a major threat to human health. [7] Existing drugs, currently in use are losing their killing action on the micro-organisms. Designing of antimicrobial scaffold is an endless project. In the previous years we have synthesised pyrimidine derivatives possessing anti-ulcer [8] activity and biologically significant 5-acetyl-6-methyl-4-substituted phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidines. [9]

Keeping in view the wide range of medicinal importance of hydrazones and to control the menace being created by the troubling micro-organisms, we

herein report the synthesis and evaluation of anti-microbial behaviour of the hydrazone derivatives of above mentioned pyrimidines as our ongoing research programme. And to fulfil this purpose tetrahydropyrimidines have been designed using Microwave irradiations as Green and environmentally friendly procedure.

MATERIALS AND METHODS

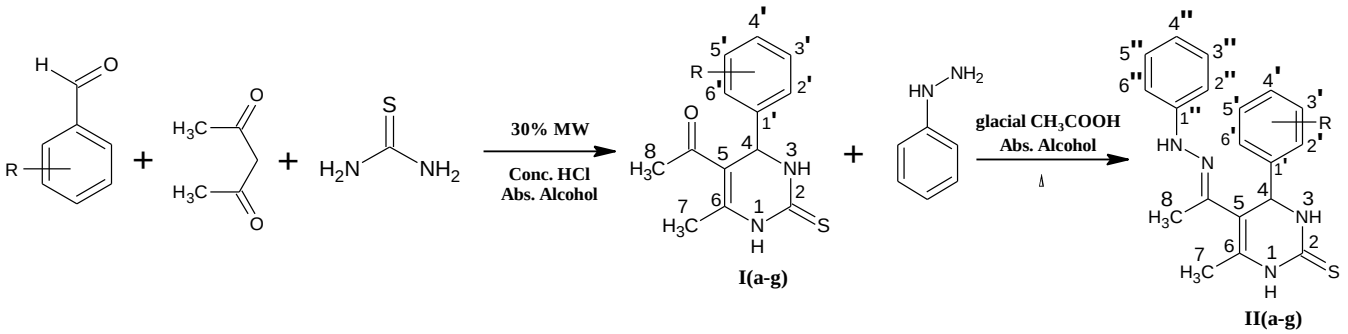
Melting points were determined by open capillary apparatus and were uncorrected. The domestic microwave oven was employed to synthesise precursors required for the present study. The progress of reaction was monitored by TLC (thin layer chromatography), using TLC sheets precoated with silica gel G (Merck) and spots were visualised by iodine vapours. Infrared spectra were determined as KBr discson Perkin Elmer Spectrum RXI FT–IR system and values were represented in cm^{-1}. Proton Magnetic Resonance spectra were recorded on BRUKER AVANCE II 400 NMR Spectrometer at Panjab University, Chandigarh using DMSO-d_6 as solvent, TMS (tetramethylsilane) as internal standard and chemical shifts were recorded in ppm on δ scale. The mass spectra were recorded by GC-MS-QP2010 Plus (Shimadzu Corporation, Kyoto, Japan) at Department of Chemistry, Punjabi University, Patiala. All the compounds gave satisfactory elemental analysis within ±0.4% of the theoretical values. Characterisation data has been given in the methodology employed. All solvents were distilled before use. The biological evaluation of the synthesised compounds was conducted at Biogenic Research and Training Centre in Biotechnology, Hubli, Karnatka.

As per the synthetic method given above (Scheme-(i)), General method for synthesis of (5-acetyl-6-methyl-4-substituted phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine [9] I(a-g)

A mixture of substituted aromatic aldehyde (0.01 mole), acetyl acetone (0.015 mole, 1.54 ml), thiourea (0.01 mole, 0.76 g) was subjected to microwave irradiation using absolute alcohol as energy transfer medium and a few drops of conc. HCl as a catalyst for appropriate time period. The progress of the reaction was monitored by thin layer chromatography. The TLC plates were dried in air and then exposed to iodine vapours to visualise the spots. The reaction mixture was allowed to stand for 24-36 hours. The product thus separated out was filtered under reduced pressure and recrystallised from methanol.

General method for synthesis of phenylhydrazone derivatives of 5-acetyl-6-methyl-4-substituted phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine II(a-g)

A mixture of **I(a-g)** (0.005 mole), phenylhydrazine (0.01 mole, 1 ml) and a few drops of glacial acetic acid using absolute alcohol as reaction medium was gently refluxed on water bath for 3-4 hours. The progress of the reaction was monitored by thin layer chromatography. The reaction mixture was then transferred into a beaker and volume was reduced on water bath. The reaction mixture was kept undisturbed overnight. To this absolute alcohol was added, solid thus obtained was filtered. Crude product was recrystallised from methanol.



R(a-g): a = H, b = 2-OH, c = 3-NO_2, d = 4-NO_2, e = 4-OCH_3, f = (3-OCH_3,4-OH), g = 2,3-(O-CH_2-O)

Scheme-(i)

Physical and spectral data

II(a): 6-methyl-4-phenyl-5-[(1*E*)-1-(2-phenylhydrazinylidene)ethyl]-3,4-dihydropyrimidine-2(1*H*)-thione

Yield 80%; m.p. 132-134°C. IR (KBr) υ (cm^{-1}): 3355, 3160 (N-H str.), 3029 (Ar. C-H str.), 2985, 2872 (methyl C-H str.), 1679 (C=N str.), 1599 (C=C str., Ar. ring), 1450 (C=C skel. vib., Ar. ring), 1246 (C-N vib.), 1208 (C=S ib.). ^{1}H-NMR (400 MHz, DMSO-d_6) δ(ppm): 9.7 (1H, s, N-H), 9.1 (1H, brs, N-H), 8.8 (1H, s, N-H), 7.3-6.6 (10H, m, Ar-H), 5.3 (1H, brs, H-4), 2.08 (3H, s, CH_3), 1.96 (3H, s, CH_3). ^{13}C-NMR (100 MHz, DMSO-d_6) δ(ppm): 173.12 (C-2), 145.70 (C=N), 143.34 (C-6), 139.69 (C-1″), 130.25 (C-1′), 128.41 (C-2″, 6″), 128.02 (C-2′, 6′), 127.01 (C-3″, 5″), 126.73 (C-3′, 5′), 118.45 (C-4″), 112.48 (C-4′), 111.26 (C-5), 56.41 (C-4), 18.25 (C-8), 16.99 (C-7). Mass fragments (m/z): 339 (M+2), 262 (100%), 247, 185, 118, 91, 77, 51. Anal. Calcd. for $C_{19}H_{20}N_4S$: C, 67.83%; H, 5.99%; N, 16.65%; S, 9.53%; Found: C, 67.43%; H, 5.59%; N, 17.05%; S, 9.13%.

II(b): 4-(2-hydroxyphenyl)-6-methyl-5-[(1*E*)-1-(2-phenylhydrazinylidene)ethyl]-3,4-dihydropyrimidine-2(1*H*)-thione

Yield 68%; m.p. 192-194°C. IR (KBr) υ (cm^{-1}): 3396 (O-H str.), 3346, 3175 (N-H str.), 3029 (Ar C-H str.), 2997, 2986 (methyl C-H str.), 1678 (C=N str.), 1598 (C=C str., Ar. ring.), 1442 (C=C skel. vib., Ar. ring), 1208 (C=S), 1028 (C-O str.). ^{1}H-NMR (400 MHz, DMSO-d_6) δ(ppm): 10.87 (1H, s, N-H), 9.65 (1H, brs, N-H), 7.91 (1H, s, N-H), 7.89-6.78 (9H, m, Ar-H), 5.66 (1H, s, O-H), 5.45 (1H, d, H-4), 2.23 (3H, s, CH_3), 1.98 (3H, s, CH_3). ^{13}C-NMR (100 MHz, DMSO-d_6) δ(ppm): 170.2 (C-2), 153.9 (C=N), 152.87 (C-6), 149.2 (C-2′), 142.1 (C-1″), 128.5 (C-3″, 5″), 127.2 (C-6′), 123.21 (C-1′), 122.3 (C-4″), 120.91 (C-5′), 114.7 (C-3′), 112.65 (C-2″, 6″), 104.67 (C-5), 50.4 (C-4), 21.89 (C-8), 19.9 (C-7). Mass fragments (m/z): 353 (M+1), 335, 315, 284, 272, 246, 207, 193, 172 (100%), 154, 130, 103, 77, 51. Anal. Calcd. for $C_{19}H_{20}N_4OS$: C, 64.75%; H, 5.72%; N, 15.90%; O, 4.54%; S, 9.10%. Found: C, 64.35%; H, 5.32%; N, 16.30%; O, 4.94%; S, 9.50%.

II(c): 6-methyl-4-(3-nitrophenyl)-5-[(1*E*)-1-(2-phenylhydrazinylidene)ethyl]-3,4-dihydropyrimidine-2(1*H*)-thione

Yield 64%; m.p. 210-214°C. IR (KBr) υ (cm^{-1}): 3340, 3210 (N-H str.), 3026 (Ar. C-H str.), 2984, 2878 (methyl C-H str.), 1670 (C=N str.), 1598 (C=C str., Ar. ring), 1458 (C=C skel. vib. Ar. ring), 1535 (asymmetric NO_2 str.), 1375 (symmetric NO_2 str.), 1206 (C=S vib.). ^{1}H-NMR (400 MHz, DMSO-d_6) δ(ppm): 11.23 (1H, s, N-H), 9.21 (1H, brs, N-H), 8.15 (1H, s, N-H), 8.12-6.81 (9H, m, Ar-H), 5.12 (1H, d, H-4), 2.23 (1H, s, CH_3), 1.97 (1H, s, CH_3). ^{13}C-NMR (100 MHz, DMSO-d_6) δ (ppm): 172.9 (C-2), 154.7 (C-5), 153.3 (C-6), 142.7 (C-1′), 142.5 (C-1″), 128.4 (C-3″, 5″), 127.4 (C-3′, 5′), 125.4 (C-2′, 6′), 125.1 (C-4′), 121.5 (C-4″), 112.7 (C-2″, 6″), 55.45 (C-4), 22.6 (C-8), 21.3 (C-7). Mass fragments (m/z): 275, 250, 207, 189, 172 (100%), 154, 130, 104, 77, 51. Anal. Calcd. for $C_{19}H_{19}N_5O_2S$: C, 59.82%; H, 5.02%; N, 18.36%; O, 8.39%; S, 8.41%. Found: C, 60.22%; H, 4.62%; N, 18.76%; O, 7.99%; S, 8.81%.

II(d): 6-methyl-4-(4-nitrophenyl)-5-[(1*E*)-1-(2-phenylhydrazinylidene)ethyl]-3,4-dihydropyrimidine-2(1*H*)-thione

Yield 70%; m.p. 212-215°C. IR (KBr) υ (cm^{-1}): 3356, 3145 (N-H str.), 2984 (Ar-C-H str.), 2969, 2879 (methyl C-H str.), 1690 (C=N str.), 1597 (C=C str., Ar. ring), 1462 (C=C skel. vib., Ar. ring), 1527 (asymmetric NO_2 str.), 1360 (symmetric NO_2 str.), 1205 (C=S vib.). ^{1}H-NMR (400 MHz, DMSO-d_6) δ(ppm): 11.98 (1H, s, N-H), 10.12 (1H, brs, N-H), 8.18 (1H, s, N-H), 8.14-6.81 (9H, m, Ar-H), 4.13 (1H, d, H-4), 2.23 (1H, s, CH_3), 2.13 (1H, s, CH_3). ^{13}C-NMR (100 MHz, DMSO-d_6) δ(ppm): 173.8 (C-2), 154.9 (C=N), 153.7 (C-6), 148.5 (C-1′), 144.7 (C-4′), 142.2 (C-1″), 128.6 (C-3″, 5″), 127.5 (C-3′, 5′), 124.7 (C-2′, 6′), 121.4 (C-4″), 112.5 (C-2″, 6″), 104.2 (C-5), 55.1 (C-4), 23.1 (C-8), 18.5 (C-7). Mass fragments (m/z): 381, 350, 322, 281, 265, 234, 218, 192, 180, 134, 133, 91 (100%), 64, 51. Anal. Calcd. for $C_{20}H_{23}N_5O_2$ Calcd.: C, 59.82%; H, 5.02%; N, 18.36%; O, 8.39%; S, 8.41%. Found: C, 59.42%; H, 5.42%; N, 18.76%; O, 8.79%; S, 8.01%.

II(e): 4-(4-methoxyphenyl)-6-methyl-5-[(1*E*)-1-(2-phenylhydrazinylidene)ethyl]-3,4-dihydropyrimidine-2(1*H*)-thione

Yield 61%; m.p. 116-120°C. IR (KBr) υ (cm^{-1}): 3346, 3075 (N-H str.), 3029 (Ar C-H str.), 2983, 2888 (methyl C-H str.), 1674 (C=N str.), 1589 (C=C str. Ar. ring), 1450 (C=C skel. vib., Ar. ring), 1208 (C=S vib.). ^{1}H-NMR (400 MHz, DMSO-d_6) δ(ppm): 13.21 (1H, s, N-H), 9.76 (1H, brs, N-H), 7.39 (1H, s, N-H), 7.29–6.87 (9H, m, Ar-H), 5.12 (1H, d, H-4), 3.65 (3H, s, O-CH_3), 2.28 (3H, s, CH_3), 2.04 (3H, s, CH_3). ^{13}C-NMR (100 MHz, DMSO-d_6) δ(ppm): 175.2 (C-2), 157.9 (C-4′), 154.2 (C=N), 153.9 (C-6), 141.9 (C-1″), 135.8 (C-1′), 128.4 (C-3″, 5″), 124.9 (C-2′, 6′), 121.5 (C-4″), 114.8 (C-3′, 5′), 112.7 (C-2″, 6″), 104.8 (C-5), 56.2 (C-4), 54.9 (0-CH_3), 21.5 (C-8), 18.5 (C-7). Mass fragments (m/z): 366 [M$^+$], 329, 302, 284, 258 (100%), 232, 204, 164, 151, 125, 99, 75, 51. Anal. Calcd. for $C_{20}H_{22}N_4OS$: C, 65.55%; H, 6.05%; N, 15.29%; O, 4.37%; S, 8.75%. Found: C, 65.15%; H, 5.65%; N, 14.89%; O, 4.77%; S, 9.15%.

II(f): 4-(4-hydroxy-3-methoxyphenyl)-6-methyl-5-[(1*E*)-1-(2-phenylhydrazinylidene)ethyl]-3,4-dihydropyrimidine-2(1*H*)-thione

Yield 65%; m.p. 98-102°C. IR (KBr) υ (cm^{-1}): 3396 (O-H str.), 3352, 3200 (N-H str.), 3025 (Ar C-H str.), 2984, 2876 (methyl C-H str.), 1688 (C=N str.), 1597 (C=C str., Ar. ring), 1465 (C=C skel. vib., Ar. ring), 1351 (O-CH_3), 1207 (C=S vib.); ^{1}H-NMR (400 MHz, DMSO-d_6) δ(ppm): 12.24 (1H, s, N-H), 8.21 (1H, brs, N-H), 7.95 (1H, s, N-H), 7.32–6.79 (8H, m, Ar-H), 5.35 (1H, s, OH), 5.23 (1H, d, H-4), 3.79 (3H, s, O-CH_3), 2.21 (3H, s, CH_3), 2.05 (3H, s, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6) δ(ppm): 171.8 (C-2), 154.2 (C=N), 153.9 (C-6), 146.7 (C-4′), 141.9 (C-1″), 135.8 (C-1′), 128.4 (C-3″, 5″), 121.5 (C-4″), 117.9 (C-6′), 114.8 (C-5′), 112.7 (C-2′), 104.8 (C-5), 56.2 (C-4), 54.9 (O-CH_3), 21.5 (C-8), 18.5 (C-7). Mass fragments (m/z): 382 [M·$^+$], 320 (100%), 278, 260, 249, 207, 191, 171, 147, 118, 91, 77, 51. Anal. Calcd. for $C_{20}H_{22}N_4O_2S$: C, 62.80%; H, 5.80%; N, 14.65%; O, 8.37%; S, 8.38%. Found: C, 63.20%; H, 5.40%; N, 15.05%; O, 7.97%; S, 8.78%.

II(g): 4-(2*H*-1,3-benzodioxol-4-yl)-6-methyl-5-[(1*E*)-1-(2-phenylhydrazinylidene)ethyl]-3,4-dihydropyrimidine-2(1*H*)-thione

Yield 67%; m.p. 200-203°C. IR (KBr) υ (cm^{-1}): 3356 (N-H str.), 3159 (Ar C-H str.), 2984, 2888 (methyl C-H str.), 1676 (C=N str.), 1597 (C=C str., Ar ring), 1205 (C=S vib.), 1442 (C=C skel. vib., Ar. ring), 1040 (C-O str.). ^{1}H-NMR (400 MHz, DMSO-d_6) δ(ppm): 13.76 (1H, s, N-H), 9.7 (1H, brs, N-H), 7.8 (1H, s, N-H), 7.35–6.81 (8H, m, Ar–H), 6.1 (2H, s, O-CH_2-O), 4.16 (1H, d, H-4), 2.26 (3H, s, CH_3), 2.07 (3H, s, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6) δ(ppm): 173.9 (C-2), 154.6 (C=N), 153.2 (C-6), 148.9 (C-3′), 147.6 (C-2′), 142.5 (C-1″), 128.5 (C-3″, 5″), 121.5 (C-4″), 122 (C-1′), 120.9 (C-5′), 119.2 (C-6′), 112.5 (C-2″, 6″), 112.1 (C-4′), 104.7 (C-5), 101.3 (O-CH_2-O), 50.8 (C-4), 21.3 (C-8), 18.8 (C-7). Mass fragments (m/z): 381 (M+1), 332, 314, 296, 266, 246, 207, 172, 148 (100%), 121, 92, 63, 58. Anal. Calcd. for $C_{20}H_{20}N_4O_2S$: Calcd.: C,

63.14%; H, 5.30%; N, 14.73%; O, 8.41%; S, 8.43%. Found: C, 62.74%; H, 5.70%; N, 14.33%; O, 8.01%; S, 8.03%.

Table 1: *In-vitro* evaluation of anti-microbial activity of synthesised compounds

Compounds tested	Concentration (µg/mL)	Zone of inhibition (mm)					
		B-1	B-2	B-3	B-4	F-1	F-2
IIa	500	8	-	-	-	-	-
	1000	10	-	8	-	-	-
IIb	500	-	-	-	-	-	-
	1000	9	-	8	10	-	-
IIc	500	-	-	-	-	-	-
	1000	-	-	-	-	-	-
IId	500	-	-	10	-	-	-
	1000	-	-	-	-	-	-
IIe	500	-	6	6	6	-	-
	1000	7	-	7	-	-	-
IIf	500	6	-	9	7	-	-
	1000	11	9	8	11	-	-
IIg	500	-	-	-	-	-	-
	1000	-	-	-	-	-	-
Ciprofloxacin	500	22	27	28	8	-	-
	1000	*	*	*	*	-	-
Amphotericin	500	-	-	-	-	13	5
	1000	-	-	-	-	15	7

(*) denotes Zones could not be measured because of merging.
(-) denotes no activity.
Microbial strains used: for anti-bacterial activity:(B-1 *Bacillus subtilis*, B-2 *Staphylococcus aureus*, B-3 *Escherichia coli*, B-4 *Pseudomonas aeruginosa*); for anti-fungal screening: (F-1 *Candida albicans*, F-2 *Aspergillus flavus*).

In vitro Anti-microbial screening

All the newly synthesised derivatives were screened for their *in vitro* anti-bacterial activity using Gram positive (*Staphylococcus aureus, Bacillus subtilis*) and Gram-negative (*Escherichia coli, Pseudomonas aeruginosa*) bacterial strains. In the similar manner, anti-fungal evaluation was carried out against *Aspergillus flavus* and *Candida albicans*. The average diameter of inhibition zones of bacterial and fungal growth in mm, was determined at 500 & 1000µg/ml. Agar Diffusion Method was used in which bacterial strains were subcultured on nutrient agar medium, whereas fungal strains were incubated at 27°C. In this anti-microbial assay, Ciprofloxacin and Amphotericin were used as standard drugs.

RESULTS AND DISCUSSION

The strategy to synthesise compounds II(a-g) has been shown in **Scheme (i)**. The formation of target organic moieties was confirmed by their structural elucidation using modern spectroscopic techniques such as NMR, IR, GC-Mass and prepared derivatives were obtained in good yields.

The results of *in-vitro* screening of anti-microbial activity thus obtained have been shown in Table 1. Amongst the prepared compounds, **II(f)** was found to be the most potent against *B.subtilis* and *P.aeruginosa* at concentration 1000µg/ml and at concentration 500µg/ml, II(d) was found to be the most active against *E. coli*. However, none of the compounds showed activity against tested fungal strains.

ACKNOWLEDGEMENT

The authors are grateful to U.G.C for financial assistance and Department of Chemistry, Punjabi University, Patiala for providing all the necessary laboratory facilities.

REFERENCES

1. Bala S, Uppal G, Kajal A, Kamboj S, Sharma V. Hydrazones as promising lead with diversity in bioactivity-therapeutic potential in present scenario. Int J Pharm Sci Rev Res. 2013;18(1):65-74.
2. Verma G, Marella A, Shaquiquzzaman M, Akhtar M, Ali MR, Alam MM. A review exploring biological activities of hydrazones. Journal of pharmacy & bioallied sciences. 2014 Apr;6(2):69-80.
3. Harer Sunil L, Rajurkar Vikas G, Patil Pravin HP, Navale Sampat D, Awuti Sandip T, Sonawane Anand A. Synthesis, Characterization and Anti-microbial Evaluation of Some 2-Iodo-N'-[(1E)-Substituted Phenylmethylidene] Benzohydrazide Analogues. Int. J. Pharma. Sci. Drug Res. 2010;2(2):134-136.
4. Singh UK, Pandey SN, Singh A, Srivastava BK, Pandey M. Synthesis and Anti-microbial evaluation of Schiff's and N-Mannich Bases of Isatin and its Derivatives with 4-Amino-N-Carbamimodyl Benzene Sulfonamide. Int. J. Pharma. Sci. Drug Res. 2010; 2(2):151-154.
5. Sameem S, Kumar N, Pathak D. Synthesis and Anti-convulsant of some newer Semicarbazone derivatives. Int. J. Pharma. Sci. Drug Res. 2012; 4(3):195-198.
6. Mahapatra DK, Das D, Shivhare R. Substituted Thiazole Linked Murrayanine-Schiff's Base derivatives as Potential Anti-Breast Cancer Candidates: Future EGFR Kinase Inhibitors. Int. J. Pharma. Sci. Drug Res. 2017; 9(3):139-144.
7. Ajani OO, Obafemi CA, Nwanyi OC, Akinpelu DA. Microwave-Assisted Synthesis and Anti-microbial activity of 2-quinoxaline-3-hydrazone derivatives. Bioorg Med. Chem. 2010; 18:214-221.
8. Rana K, Kaur B, Chaudhary G, Kumar S, Goyal S. Synthesis and Anti-ulcer activity of some dihydropyrimidines. Int. J. Pharma. Sci. Drug Res. 2011; 3(3):226-229.
9. Pathak P. Synthesis and Studies on biologically significant compounds involving some new synthetic methods, Ph.D Thesis, Punjabi University, Patiala, 2006.

HOW TO CITE THIS ARTICLE: Shukla M, Bhatia SK, Kaur B. Synthesis and In-*vitro* Anti-Microbial Evaluation of Novel Hydrazones of Substituted Tetrahydropyrimidine s. Int. J. Pharm. Sci. Drug Res. 2017; 9(5): 210-213. **DOI: 10.25004/IJPSDR.2017.090501**