ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol.3, Issue, 4, pp.057-058, April, 2011

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

EVALUATION OF *IN VITRO* ANTIMICROBIAL ACTIVITIES OF 2*r*,6*c*-DIARYLPIPERIDIN-4-ONE (3′-HYDROXY-2′-NAPHTHOYL) HYDRAZONES

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ARTICLE INFO

Article History:
Received 10th January, 2011
Received in revised form
14th February, 2011
Accepted 11th March, 2011
Published online 17th April 2011

Key words:
Staphylococcus aureus
Streptococcus pyogenes
Salmonella typhi,
Klebsiella pneumoniae
Escherichia coli

ABSTRACT

2r,6c-Diarylpiperidin-4-one(3[1]-hydroxy-2[1]-aphthoyl)hydrazones 1-8 were screened for their in vitro antimicrobial activity against a panel of pathogenic bacteria (*Staphylococcus aureus*, *Streptococcus pyogenes*, *Salmonella typhi, Klebsiella pneumoniae* and *Escherichia coli*) and a panel of pathogenic fungai (Candida albicans, Aspergillus flavus, Aspergillus niger and Cryptococcus neoformans) by two fold serial dilution method. DMSO was used as control while drugs Cefotaxime and Miconazole were used as standard drugs for antibacterial and antifungal studies, respectively. Compounds 3, 6 and 7 are more active than the standard drug against all the tested bacterials strains. Compounds 2 and 7 are more active than the standard against all the tested fungal stains.

INTRODUCTION

The studies of heterocyclic compounds are of much interest due to their biological importance. The high pharmacological concern about piperidin-4-ones is due to their important role as intermediates in the synthesis of many drugs. Piperidine-4-ones and their derivatives have been reported to possess antimicrobial activity (Mobio et al., 1989). The earlier reports indicate that the biological activities of piperidin-4-ones are associated with substitutions at 2, 3 and 6 positions (Perumal et al., 2001; Bochringer and Shochne, 1961). Hydrazides and hydrazones have interesting ligation properties due to presence of several coordination sites. Furthermore, a number of hydrazide–hydrazone derivatives have been claimed to possess interesting antibacterial and antifungal (Loncle et al., 2004; Garoufalias et al., 2002; Vicini et al., 2002) activities. The derivatives of 3-hydroxy-2-naphthoic acid hydrazide (3-NAH) have been found to exhibit antimicrobial (Dogan et al., 1998, 2002, 2005) and anticancer activities (Duran et al., 2002). In an earlier study (Sylvestre and Pandiarajan, 2010) we have reported the synthesis and NMR spectral study of some 2*r*,6*c*-diarylpiperidin-4-one (3′-hydroxy-2′-naphthoyl)hydrazones 1-8 with special reference to *γ-syn* effect. In the present study, we have evaluated the *in vitro* antimicrobial activity against a panel of pathogenic bacteria and a panel of pathogenic fungai by two fold serial dilution method.

MATERIALS AND METHODS

Chemicals

3-Hydroxy-2-naphthoic acid hydrazide were purchased from Sigma-Aldrich and were used as such. All other reagents and solvents were of laboratory grade. Preparation of 2r,6c-diarylpiperidin-4-one (3'-hydroxy-2'-naphthoyl)hydrazones 1-8 Hydrazones 1-8 were synthesized following literature procedure (Sylvestre and Pandiarajan, 2010) using the reactions shown in Scheme 1.

Evaluation of antibacterial activity

The in vitro antibacterial activity of the compounds was tested in nutrient broth (NB, Hi-media, Mumbai) for bacteria by twofold serial dilution method (Dhar et al., 1968).

Evaluation of antifungal activity

The in vitro antifungal activity of the compounds was tested in Sabouraud's dextrose broth (SDB, Hi-media, Mumbai) for fungi by twofold serial dilution method (Dhar et al., 1968).

RESULTS AND DISCUSSION

The preliminary antimicrobial activities of compounds 1-8 were examined using two fold serial dilution method. The MIC values for antimicrobial activities were obtained in µg/mL. However, these values are quoted in µM in order to compare the activities of compounds with different molecular weights. The experimental values obtained in µg/mL were converted to µM using the following formula where M is the molecular weight of the compound.

$$1\ \mu M = \frac{1\mu g}{mL} \times \frac{1000}{M}$$

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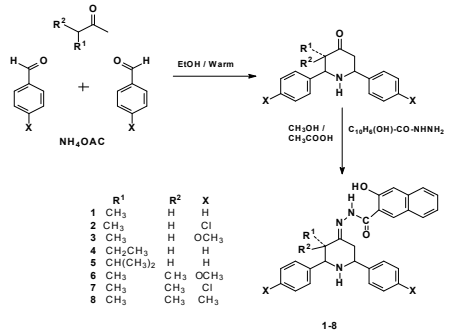
Table 1. *In vitro* antibacterial activity of compounds 1-8

Compounds	Minimum inhibitory concentration (MIC) in µM				
	Staphylococcus aureus	*Streptococcus pyogenes*	*Salmonella typhi*	*Klebsiella pneumoniae*	*Escherichia coli*
1	222.72	222.72	222.72	a	a
2	12.06	12.06	48.27	24.10	193.0
3	49.11	49.11	49.11	49.11	12.27
4	216.0	216.0	216.0	216.0	216.0
5	104.8	104.8	104.8	209.6	104.8
6	23.90	23.90	47.80	47.80	11.95
7	11.75	11.75	23.5	11.75	18.8
8	101.8	50.91	101.8	101.8	50.91
Cefotaxime	54.89	54.89	109.78	109.78	54.89

'a' no inhibition even at 200 µg/mL

Antibacterial study

The bacterial strains *viz., Staphylococcus aureus, Streptococcus Pyogenes, Salmonella typhi, Klebsiella pneumoniae and Escherichia coli* were used for this study. DMSO was used as control while Cefotaxime is used as standard. The MIC values for antibacterial activities are given in Table 1. It is seen that compounds 3, 6 and 7 are more active than the standard drug against all the tested bacterials strains. Compound 2 is more active than the standard against bacterial strains except *Escherichia coli*. It is also seen that compounds with a halogen atom in the aromatic ring are more active than compounds without an aromatic substituent and compounds with a methoxy group in the aromatic ring.



Scheme 1 Synthesis of compound s 1-8

Antifungal activity

The fungal strains *viz*., *Candida albicans, Aspergillus flavus, Aspergillus niger and Cryptococcus neoformans* were used for this study. DMSO was used as control while Miconazole is used as standard. The MIC values for antibacterial activities are given in Table 2. It is seen that 2 and 7 are more active than the standard against all the tested fungal stains. Compounds 5 and 8 are more active than the reference drug against fungal stains except *Cryptococcus neoformans*. Compound 3 is more active against two fungal stains. Presence of a halogen atom in the aromatic ring is found to increase the antifungal activity.

Table 2. *In vitro* antifungal activity of compounds 1-8

Compounds	Minimum inhibitory concentration (MIC) in µM			
	Candida albicans	*Aspergillus flavus*	*Aspergillus niger*	*Cryptococcus neoformans*
1	111.40	55.70	111.40	111.40
2	48.30	24.1	24.1	48.3
3	98.23	a	49.11	24.55
4	107.9	107.9	107.9	107.9
5	52.41	52.41	52.41	104.82
6	47.80	a	23.90	23.90
7	23.50	11.75	23.5	23.5
8	50.91	25.45	50.91	101.83
Miconazole	60.01	120.15	120.15	60.01

'a' no inhibition even at 200 µg/mL

Conclusion

This study clearly shows that compounds 1-8 have reasonably good antimicrobial activity. Compounds 3, 6 and 7 are more active than the standard drug against all the tested bacterials strains. Compounds 2 and 7 are more active than the standard against all the tested fungal stains. Presence of halogen atom in the aromatic ring is found to be increase the antimicrobial activity.

Acknowledgements

The authors are thankful to SIF, Indian Institute of Science, Bangalore and to SAIF IIT Chennai for recording NMR spectra. Thanks are due to CECRI, Karaikudi for elemental analysis. Thanks are due to D. Jeyarajan, Head, Department of Microbiology, Divine Mother College, Puducherry, India, for antimicrobial work. One of the authors (S. Sylvestre) is thankful to UGC for the award of a fellowship.

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