SYNTHESIS AND PHARMACOLOGICAL SCREENING OF SOME BIODYNAMIC THIOSEMICARBAZONES AND ITS DERIVATIVES

A.K. Halve* Vasudha Sharma and Bhuwan Bhashkar

School of Studies in Chemistry, Jiwaji University, Gwalior (INDIA)

Received May 19, 2006            Accepted October 17, 2006

ABSTRACT

Thiosemicarbazones are found to be the new clinical candidates in the class of organic compounds. These compounds possess a wide range of biological activity depending on the parent aldehyde or ketone. It has also aroused considerable interest in chemistry and biology due to their wide spectrum of pharmacological activity. Besides the antimicrobial activity thiosemicarbazones have also been assessed for antitubercular, anticancer, anticonvulsants and anti-inflammatory activity hence find wide application in medicinal era. In light of these findings, some new thiosemicarbazones have been synthesized and screened for their in-vitro antimicrobial activity against various bacterial and fungal pathogens. Present communication reports the synthesis of a new series of thiosemicarbazones from thiosemicarbazide derivatives bearing potentially active pharmacophores. All the synthesized compounds have been screened in-vitro and have shown promising antimicrobial activity.

Key Words: Thiosemicarbazone, Antimicrobial activity, Biodynamic compounds, Thiosemicarbazide, In-vitro screening.

INTRODUCTION

Paul Ehrlich (1913), articulate the concept of chemotherapy which has revolutionized the discovery of new and potent class of antimicrobials. Since bacteria develops resistant to penicillin and other antibiotics, stimulation for further research in the synthesis of newer antimicrobials have been started.

Thiosemicarbazones have proved to be a potent drug and played a central role in the vigil against bacterial and fungal pathogens over past few decades. The derivatives of thiosemicarbazone containing -N-C=S and -CH=N- pharmacophores have evoked keen interest owing to their analytical and biological applications viz. antifungal, antibacterial, antitubercular, antiviral etc. against variety of micro organisms. The present paper highlight the synthesis of some thiosemicarbazones by the condensation of substituted phenyl thio-semicarbazide with substituted azo-salicyladehydes and their antimicrobial activity on different microbes.

* Author for correspondence
MATERIAL AND METHODS

All the chemicals used were of A.R. grade. Aniline and Lead nitrate were purchased from Merck. Carbon disulfide and DMSO from Qualigens. Aniline was distilled before use and DMSO is dehydrated on molecular sieves.

Compounds 4-(4’ methoxy phenyl) thiosemicarbazide (I) (0.01M) and 2-hydroxy 5-(2” chlorophenylazo) benzaldehyde (0.01 M) were dissolved separately in dimethyl sulfoxide and mixed with continuous shaking. The contents were refluxed for 8 hours and the reaction mixture was cooled at 0°C. Finally the light brown solid separated out, on addition of requisite amount of water, which was repeatedly washed with water followed by ethanol. The product was soluble in DMSO and DMF.

Purity of the compounds were ascertained by thin layer and column chromatography; (1:3, acetone : hexane).
Elemental analysis (viz. C and H) was performed on Carlo Erba 1108 analyzer for C_{21}H_{18}N_{2}O_{2}S_{2}Cl.

The IR spectrum of compounds were taken on Perkin Elmer 337 spectrophotometer with KBr pellets which shows the bands at 3430 (-OH), 3245 (NH), 1620. (C=N), 1590 (N=N), 1350 (C-N) and 1225 (C=S) cm^{-1} and the ^1HNMR spectra on a Bruker WM 400 FT MHz NMR instrument using DMSO – d_6 as solvent with TMS as an internal references. Signals were observed at 6.5 (S, 1H, – OH), 7.3-7.9 (m, 12H, H), 9.2 (S, 1H, –CH=), 10.02 (S, 1H, NH), 8.22 (S, 1H, NH).

RESULTS AND DISCUSSION

Some of the newly synthesized compounds were screened in-vitro for their antimicrobial activity against a variety of bacterial strains such as E. Coli, S. aureus, S. typhi, B. anthrasis and P. aeruginosa and fungi such as A niger, C. albicans, C. neoformans, A. fumigatus and A. flavus.

The activity was determined using disc diffusion techniques, by measuring the inhibition zones in mm. All the bacterial cultures were grown in nutrient agar at 37°C for 24 hrs whereas yeast and moulds were grown in sabourauds agar at 30°C for 4-8 hours. Chloramphenicol and fluconazole were used as standard drugs. Compounds having chloro substituents and methoxy group at para position (2g) showed significant activity against bacterial strain in the following order:

E.Coli. > S. aureus > S. typhi > B. anthrasis > P. aeruginosa and the antifungal activity of compounds having methoxy and fluoro substituents at para position (2f) shows significant activity in following order:

A. niger> C. albicans > C. neoformans > A. fumigatus > A. flavus.

CONCLUSION

In view of exploding microbial infections, the present research work will definitely have a significant role, which may add a handful of drugs out of the multitude available and will contribute in the field of new antimicrobials.

ACKNOWLEDGEMENT

Our sincere thanks to the Dean, BIMR and college of life sciences, Gwalior (India) for antimicrobial screening. Sincere thanks are also to DRDE, Gwalior for spectral analysis and to the U.G.C., New Delhi for providing financial assistance.

REFERENCES