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Morpholinylbenzothiazine consider as bioactive compound

[*1]Praveen Kumar Sharma, [2]Gulshan Kumar, [1]Prem Singh and [3]Leena Parihar

[1]Department of Chemistry, Lovely Professional University, Phagwara, Punjab, India-144411
[2]Department of Chemistry, Seth G.L. Bihani , S.D.P.G. College, Sri Ganganagar, Rajasthan, India-335001
[3]Department of Botany, Seth G.L. Bihani, S.D.P.G. College, Sri Ganganagar, Rajasthan, India-335001

ABSTRACT

In the present work, antioxidant activity and antimicrobial activity of Morpholinyl-4H-1,4-benzothiazines was investigated. Free radical scavenging activity was evaluated using 1,1-diphenyl-2-picrylhydrazyl(DPPH).For antimicrobial activity, Morpholinyl-4H-1,4-benzothiazines were tested for its potent antimicrobial activity against bacteria, Bacillus alkalophilus (MTCC NO=7913), Bacillus subtilis (MTCC NO=411), Bacillus flexus (MTCC NO=7024), Bacillus subtilis (MTCC NO=121), Bacillus subtilis (MTCC NO=1305) as well as their antifungal activity against Aspergillus Nigrum, Aspergillus Flexus. Thus from the results, it has been found that morpholinyl-4H-1,4-benzothiazines consider as bioactive compounds.

Keywords: Antioxidants, Antibacterial activity, Antifungal activity, Antimicrobial activity, Morpholinyl-4H-1,4-benzothiazines, 4H-1,4-benzothiazine, DPPH , Morpholine.

INTRODUCTION

In existing years, there has been a growing interest in the synthesis of heterocycles because most of the compounds with biological activity are derived from heterocyclic structures. The heterocyclic compounds are rich in nature and involved in the synthesis of pharmaceutical and biological important molecules. The morpholine and their derivatives are played important role in heterocyclic chemistry. Large number morpholine derivatives also exhibited various biological activities such as anti microbial, anti inflammatory, analgesic, local anaesthetic, anti malaria, anti depressant, anti proliferative, hypocholestrolemic and anti-leukemic etc [1-9].

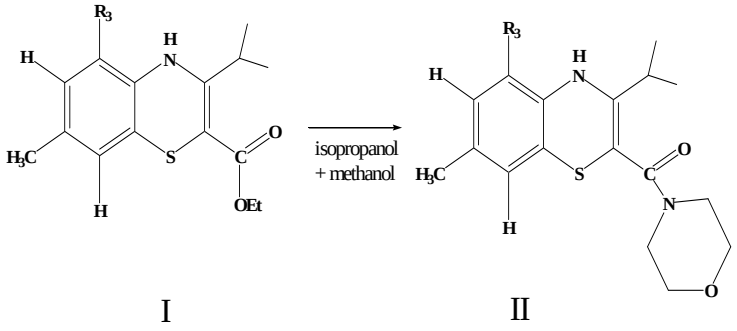
4H-1,4-benzothiazene create an important class of heterocyclic compounds, include both Nitrogen and Sulphur heteroatoms. 1,4 benzothiazene derivatives are important because of their remarkable biological properties such as antibacterial, anti-viral, anti-hyperpedimic, anti HIV, antitumour, anti-fungal[10-16].

Morpholine, and 4H-1,4-benzothiazine heterosystems have been observe as important pharmacophores for integration of design, and synthesize biologically active molecules. The heterocycles incorporating the biodynamic heterosystem; 1,4-benzothiazine-morpholine.The presence of morpholine heterosystem in above combination will make them to interact more effectively with biological receptors to make the synthesized compounds therapeutically attractive. In recent years benzothiazoles, benzothiazines and its derivatives fused/attached with other biodynamic heterosystems, especially morpholine, piperazine etc have gained unique importance due to broad spectrum of biological/pharmacological activities which are reflected by their uses as anti-covulsant, anesthetic, anticancer, anti-tuberculosis, anti-hypertensive, anti-malarial, hypoglycemic, anti-biotic, etc [17-19].

MATERIALS AND METHODS

Preparation of morpholine substituted 4H-1,4-benzothiazines II

Morpholine substituted 4H-1,4-benzothiazines II **(Scheme-1)** were synthesized by the use of method present in literature[20] Spectral data of synthesized compounds match with literature [20-31].



I II

(Scheme-1)

Scheme-1:- Schematic presentation for the Synthesis of Morpjolinybenzothiazine from thiazine ring system

Synthesized morpholinylcarbonyl-4H-1,4-benzothiazines (II) is given as :

(II) 3-isoprpyl-7-methyl-2-(4-morpholinylcarbonyl)-4H-1,4-benzothiazine

Antimicrobial Activities

Synthesized compound were screened for their antimicrobial activity against bacteria, *Bacillus alkalophilus* (MTCC NO=7913), *Bacillus subtilis* (MTCC NO=411), *Bacillus flexus* (MTCC NO=7024), *Bacillus subtilis* (MTCC NO=121), *Bacillus subtilis* (MTCC NO=1305*)* as well as their antifungal activity against *Aspergillus Nigrum*, *Aspergillus Flexus* by Agar disc diffusion method [32]. The results obtained were given in **Table:1-2**

Methodology

In this method, the bacterial inoculums fix to certain concentration was inoculated on to the entire surface of a plate with a sterile cotton-tipped swab to form an even lawn. The above components were dissolved and sterilized in an autoclave at 15 lbs and 121^{o}C for 15 minutes. The sterilized medium was discharge into different sterilized Petra-plates in laminar, and was allowed to solidify. The paper disks (6 mm in diameter) permeated with diluted compound II solution was placed on the surface of each NA plate using a sterile pair of forceps.

Then the plates were incubated aerobically and the diameter of zone inhibition was observed by a calliper. Based on the diameter of the inhibition zone and the results were then assigned to three categories, susceptible, intermediate, or resistant. The bigger the diameter of the inhibition zone, the more susceptible is the microorganism to the antimicrobial compound**.**

Table1:- Antibacterial activities of the compound (II) at different concentration in ethanol as control

Name of Bacteria	Zone of inhibition in different concentration in (mm)			
	250ppm	200ppm	150ppm	100ppm
Bacillus Alkalophillus (MTCC NO. 7913)	11mm	11.5mm	6mm	6mm
Bacillus Subtilus (MTCC NO. 411)	8mm	7mm	6mm	8mm
Bacillus Flexus (MTCC NO. 7024)	8mm	7mm	6mm	6mm
Bacillus Subtilis (MTCC NO. 121).	12mm	9mm	8mm	6mm
Bacillus Subtilis (MTCC NO. 1305).	6.2mm	6.2mm	5.9mm	5.7mm

Table-2 Antifungal activity of the compounds (IIA) at different concentrations in ethanol as control

Name of Fungal	Zone of inhibition in different concentration (in mm)		
	200ppm	150ppm	100ppm
Aspergillus Nigrum	18mm	10mm	19mm
Aspergillus Flexus	10mm	21mm	25mm

Antioxidant activities
Synthesized compound II were screened for antioxidant activity by DPPH method

Sample preparation for the antioxidant activity of compound (II)
Add 0.0197 mg of DPPH to the 100 ml of methanol and centrifuged for some time to prepare 0.5 milimolar of DPPH solution [33].

Mother solution prepared by addition of 2.5 mg of compound (IIA) to 100 ml of methanol solution. Dilution was prepared by addition of 2, 4, 6, 8, 10 microgram/ml solution from mother solution.

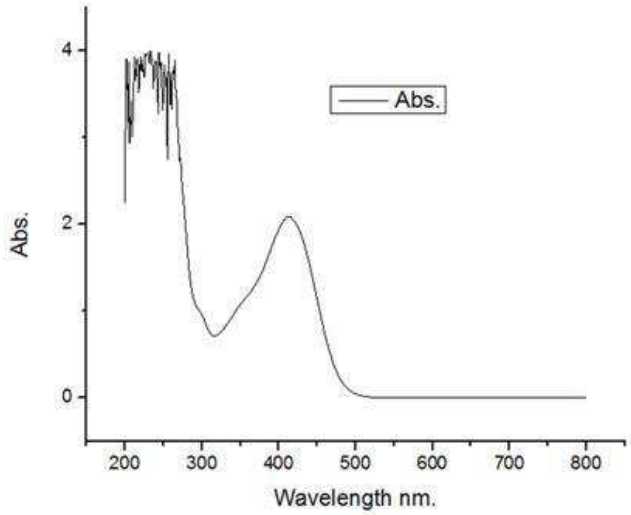


Fig-1- Graphical representation of anti oxidant activities compound (II)

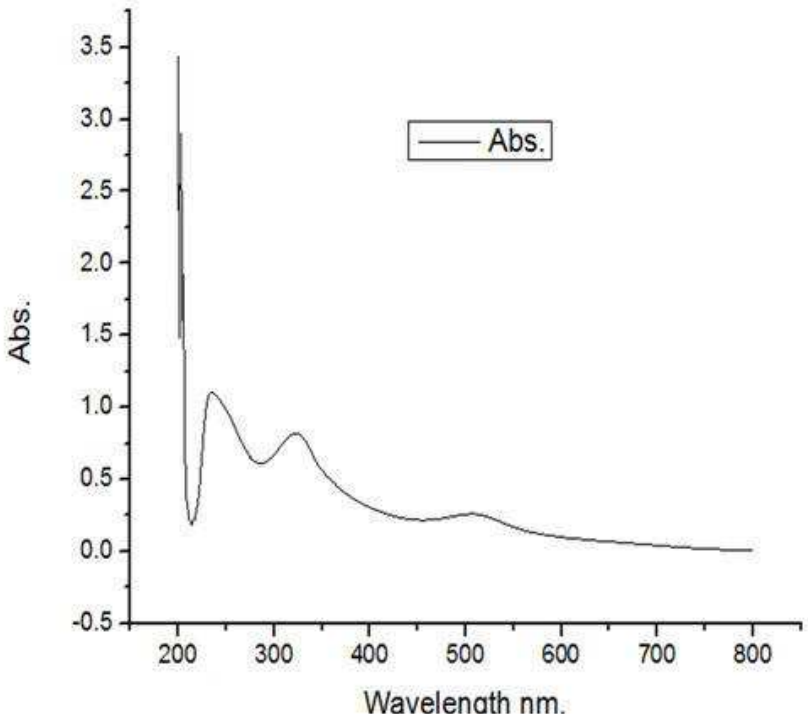


Fig-2- Graphical representation ant oxidant activities of DPPH solution

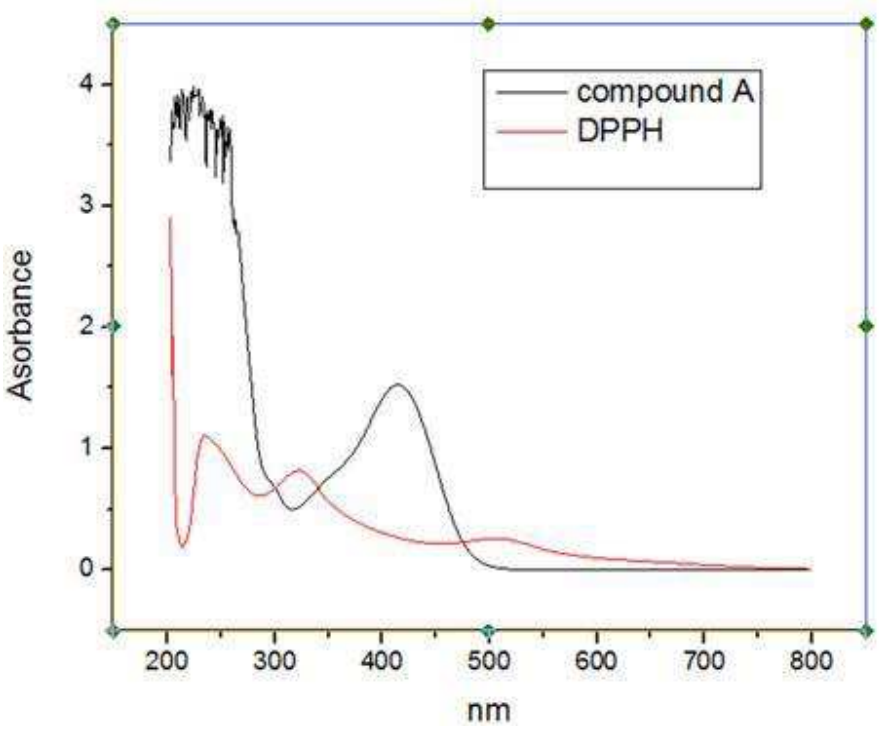


Fig-3-Comparative studies of antoxidant activities of compound (II) and DPPH

A spectrum of DPPH solution and sample solution was taken separately. Then from each of the sample solution 4.5 ml of solution is to be taken and to that of the above diluted sample solutions, 0.5 ml of DPPH solution is to be added. Measure the wave length of each of the sample solution separately by UV **(Fig-1-3).**

Analysis of Antioxidant activities:-
Percentage inhibition is carried out by given method.
Calculation of anti oxidant properties

% of inhibition = $(control - sample) \div control.$

Control=absorbance of DPPH solution
Sample=DPPH +sample
Calculation for compound (II)
Absorption of control at 517nm= 0.1435
Absorption of sample at same wavelength= 0.003
% of inhibition= 97.90%

RESULTS AND DISCUSSION

It has been observed that the synthesized compound (II) show antimicrobial activity against microbes. Except this compound II show antioxidant activity by 1,1-diphenyl-2-picrylhydrazyl (DPPH) method. Thus from the results, it has been found that morpholinyl-4H-1, 4-benzothiazines shows ample variety of antimicrobial and antioxidant activities in comparison to morpholine or 4H-1,4-benzothizines separately thus consider as bioactive compounds.

CONCLUSION

On the basis of present work, synthesized compound show activity against microbes and show antioxidant activities, Thus Substituted benzothiazine will be consider as Bioactive heterocyclic compounds and may be treated as medicinal material.

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