

Original Article

ANTIOXIDANT AND PHARMACOLOGICAL ACTIVE MICROWAVE MEDIATED SYNTHESIS OF 2-(4/-PHENOTHIAZINYL PYRAZOLYL) PYRROLES

MEGHASHAM N. NARULE\*<sup>1</sup>, MAHESH K. GAIDHANE<sup>2</sup>, PRAVIN K. GAIDHANE<sup>3</sup>

<sup>1</sup>Department of Chemistry, Vidya Vikas Arts, Commerce & Science College, Samudrapur, 442305, India, <sup>2</sup>Department of Chemistry, Shri Lendeo Patil Mahavidyalaya, Mandhal, Kuhi, India, <sup>3</sup>Department of Chemistry, Govindrao Wanjari Engineering and Technology, Hudkshwar Road Nagpur 441204, India.  
Email: meghasham\_n@rediffmail.com

Received: 17 Nov 2014, Revised and Accepted: 20 Dec 2014

ABSTRACT

Phenothiazine derivatives substituted in the 2 and 10 positions belong to a big group of tricyclic aromatic compounds. They are in extensive use in psychiatry as tranquilizers and neuroleptics. Phenothiazines belong to an important class of heterocyclic compounds known for their pharmaceutical properties. Phenothiazine core is the active component in sedatives, tranquilizers, antituberculotics or bactericides. Phenothiazines are electron donor compounds with a low oxidation potential and they can form easily radical-cations. Lately phenothiazine has become very popular in material science or in biochemistry as marker for proteins and DNA.

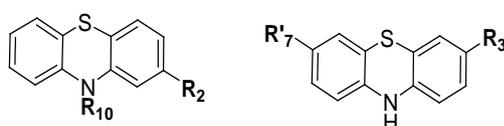
2-[4/-hydroxyl benz-1/-(propene-1//one)] Pyrrole (**2**) on treatment with primary amine gives 2-[biphenyl amine-1/-(propane-1//one)] pyrrole (**3**) which react with sulphur and iodine affording substituted 2-[phenothiazinyl-8/-(propane-1//one)] pyrrole (**4a-j**) which undergoes cyclization with NH<sub>2</sub>. NH<sub>2</sub>H<sub>2</sub>O and Substituted 2-(4/-phenothiazinyl pyrazolyl) pyrrole (**5a-j**) is obtained. The structure products were characterized by elemental analysis and spectral data.

**Keywords:** Pyrrole, Phenothiazinyl pyrazolyl, Antioxidant activity, Pharmacological activities Microwave method.

INTRODUCTION

Phenothiazine (FEE-noe-THYE-a-zeen)- derivative antihistamines are used to relived or prevent the symptoms of hay fever and other types of allergy. They work by preventing the effects of a substance called histamine, which is produced by the body. Histamine cause itching, sneezing, runny nose and watery eyes. Also in some person's histamine can close up the bronchial tubes (air passages of the lungs) make breathing difficult [1].

A group of compounds called phenothiazine derivatives includes compounds characterized by a tricyclic aromatic ring with sulfur and nitrogen atoms and substituents in the 2 and 10 or 3 and 7 positions:



Phenothiazine positions are anticholinergic derivatives substituted in the 2 and 10 commonly known as antipsychotropic and antihistaminic drugs. They have been intensely studied in a number of fields of chemical, biological and medical research owing to their pharmacological activity. Many derivatives of the phenothiazine are also used in analytical chemistry, especially those substituted in the 3 and 7 positions (dyes of Methylene Blue group), as well as those substituted at position 10 alone and positions 2 and 10[2].

Phenothiazine derivatives possess diverse biological activities like antiparkinsonian[3,4], anticonvulsant[5], antihistaminic[6], antihelminthic[7], antiviral[8], antiparasitic[9] and CNS deprement[10]. Pyrazole derivatives possess wide range of pharmacological activities like antioxidant[11], antiinvasive[12], antiviral[13], antipyretic[14], anti-inflammatory[15], antidepressant[16], blood pressure lowering[17]etc. Pyrazoles are also used as agrochemicals[18], dyestuffs in sunscreen materials[19] etc. Pyrroles and their derivatives exhibit different important biological activities like antibacterial, antioxidant, cytotoxic, insecticidal, anti-inflammatory, anticoagulant, antiallergic, antiarhythmic, hypotensive and anticonvulsant [20-21] etc.

Microwave-induced organic reaction is used for carrying out chemical transformations [22]. The microwave assisted organic reactions are more safe and an environmentally friendly with enhanced purity and yields[23] of products. Shorter reaction time periods and higher yields render the microwave method superior to the classical method. Heterocycles are the largest class of organic compounds. Among them, pyrroles have a distinguished position in the chemistry of living organisms due to their close biogenetic connection to the porphyrins, the chlorins, and the corrins. Furthermore, they are regarded as privileged structures by synthetic chemists because of wide spread applications in medicinal chemistry and materials science [24].

In view of the above mention pharmacological activities of Phenothiazine, pyrazole and pyrrole a number of the 2-substitued, 2-(4/-phenothiazinyl pyrazolyl) pyrrole derivatives have been synthesized which containing above moieties.

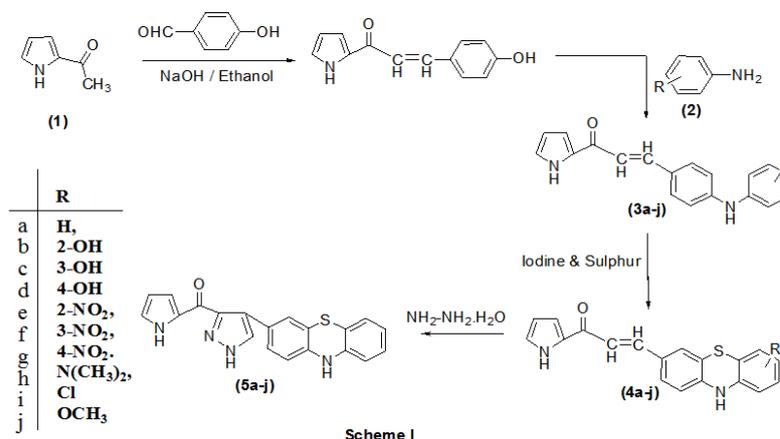
RESULT AND DISCURSION

The reaction sequence leading to the formation of desired heterocyclic compounds are outlined in **Scheme-I**. The starting material 2-[4/-hydroxy benz-1/-(propene-1//one)]Pyrrole **2** was prepared by the reaction of 2-acetyl pyrrole with 4-hydroxy benzaldehyde in presence of 40 % NaOHwhich on treatment with different aryl amine gives 2-[diphenyl amine-1/-(propane-1//one)]pyrrole **3** reacts with sulphur in the presence of iodine catalyst gives substituted 2-[phenothiazinyl-8/-(propane-1//one)]pyrrole (**4a-j**) which under goes cyclization with NH<sub>2</sub>NH<sub>2</sub>. H<sub>2</sub>O gives substituted 2-(4/-phenothiazinyl pyrazolyl) pyrrole (**5a-j**). The structural assignment of synthesized compounds is based on the spectral data. IR spectral bands of all the compounds indicates peak at 690-840 cm<sup>-1</sup> (substituted phenyl) and number of peaks at 1020-1340, 1400-1500, 3050 and 3300-3400 for C-N stretching C=C, aromatic Ar-H stretching and N-H stretching respectively.

A characteristic peak at 1600-1660 cm<sup>-1</sup> indicates the presence of C=N band. The PMR spectrum indicates singlet for N-H, pyrrole, Phenothiazine and pyrazole. The benzenoid protons appeared in the range of 6.40-7.60. The m/z molecular ion peak for **3**, **4**, **5** appeared at 333, 363.06 and 375.0 respectively. A reaction should be

conducted under solvent-free conditions with minimal or no side product formation and with utmost atom economy. In classical method the yield is lower as compared to microwave irradiation. Microwave irradiation facilitates the polarization of the molecule under irradiation causing rapid reaction. A comparative study in

terms of yield and reaction period is shown in **Table-III**. All the synthesized compounds were first purified by successive recrystallisation using appropriate solvents. The synthesized compounds were characterized, subjected to spectral analysis such as IR, <sup>1</sup>H-NMR and were screened for antimicrobial activities.



## MATERIALS AND METHODS

The synthesized compounds are first purified by re-crystallisation using appropriate solvents. Melting points were determined in an open capillary tube and are uncorrected. The IR spectra were recorded on ABB BOMEM FTIR Spectrometer using KBr disc technique. The NMR spectra were recorded as Bruker 400MHz NMR Spectrometer in DMSO using TMS as an internal standard. Chemical shift is given in  $\delta$  ppm. Mass spectra were recorded on GCMS QP 5000 Shimadzu. Thin layer chromatography was performed using pre-coated aluminium plates, coated with silica gel GF254 [E. Merck]. The spots were visualized in the iodine chamber. Characterization data of compounds are given in **table II**.

### Synthesis of Compounds (5a-j) from Compounds (4a-j) By microwave irradiation method

#### A) Solid phase MWI

A solution of (4a-j) (0.01 mol) and NH<sub>2</sub>NH<sub>2</sub>. H<sub>2</sub>O (0.01 mol) in ethanol (2 ml) was taken in a 100 ml borosil flask and to this KOH (1g) and basic alumina (3g) was added. The reaction mixture was thoroughly mixed, dried in air and irradiated inside a microwave oven for 2-3 min. at power level (700W), the reaction mixture was cooled and extracted with ethanol (3x10 ml). The resultant solid (5a-j) was recrystallized using aqueous ethanol.

#### B) Solution phase MWI

Equimolar quantities of compounds (4a-j), NH<sub>2</sub>NH<sub>2</sub>. H<sub>2</sub>O (0.01 mol) and KOH (1g) in ethanol (30 ml) were taken in a 100 ml borosil flask

fitted with a funnel as a loose top. The reaction mixture was irradiated in a microwave oven for 5-6 min. at 20% power level (300W) with short interruption of 20 sec, to avoid the excessive evaporation of the solvent.

This protocol was repeated in overall heating time. On completion of the reaction (TLC) the reaction mixture was cooled and acidified with dil. HCl. The product (5a-j) separated by filtered and washed with cold water, dried and recrystallized from ethanol.

### Synthesis of 2-[4/-hydroxy benz-1/(propene-1/-one)]Pyrrole (2)

2-acetyl pyrrole (1) (0.01 mol) and 4-hydroxy benzaldehyde (0.01 mol) was dissolved in 100 ml ethanol. To this solution, NaOH (40%, 10 ml) was added drop wise with constant stirring at room temp. till a dark yellow mass was obtained. The reaction mixture was kept 7-8 hr and acidified with dil. HCl. The solid obtained was washed with cold water. It was filtered and dried. It was crystallized from ethanol. Yield 85%, M. P 153°.

### Synthesis of substituted 2-[diphenyl amine-1/(propane-1/-one)]pyrrole (3a-j)

A mixture of 2 (0.05 mole) and add substituted aromatic primary amine (0.05 mole) in absolute ethanol (50 ml) was heated under reflux in the presence of anhydrous. ZnCl<sub>2</sub> (0.5g) for 6 hr. on a water bath. On cooling, a solid mass separated out which was wash with acidified water to remove inorganic materials, then it was filtered off to obtain (3a-j) and crystallized from ethanol.

**Table I: comparative study data of compounds 5a-j**

Compounds	Microwave Classical	M. P. (°C)	Microwave		Reaction time Classical (hr)	Microwave Yield (%)	
			Solid phase (min)	Solvent Phase (min)		Solid phase	Solvent phase
5a		216 <sup>o</sup>	5	6	8	77	72
5b		207 <sup>o</sup>	6	6	8	82	80
5c		121 <sup>o</sup>	5.5	6.5	7	78	73
5d		210 <sup>o</sup>	6	6	8	85	83
5e		194 <sup>o</sup>	5	7	7	79	78
5f		215 <sup>o</sup>	6	6	8	80	78
5g		199 <sup>o</sup>	5	7	7	85	76
5h		220 <sup>o</sup>	5.5	6	8	83	84
5i		123 <sup>o</sup>	6	7	7	68	62
5j		227 <sup>o</sup>	5	7	7	69	64

**Synthesis of substituted 2-[phenothiazinyl-8'-(propane-1'-one)]pyrrole (4a-j)**

A mixture of substituted derivative of (3a-j) (0.01 mole) sulphur (0.1 mole) and Iodine (0.5 g) was rapidly heated at 120°C in an oil bath for 2 hr. The hot melt was rapidly poured in to a mortar and crushed to a fine powder, to give Substituted solid compounds (4a-j). It was washed with water dried and crystallized from ethanol.

**Synthesis of substituted 2-(4'-phenothiazinyl pyrazolyl) pyrrole (5a-j)**

A mixture of compound 4 and NH<sub>2</sub>NH<sub>2</sub>. H<sub>2</sub>O (0.01 mol) in ethanol (30 ml) was refluxed for 5 hours. The reaction mixture was poured on ice cold water and acidified with dil. HCl. A pale brown solid (5a-j) slowly separated out. It was filtered, washed with water and dried.

**Synthesis of 2-(4'-phenothiazinyl pyrazolyl) pyrrole (5a)**

Yield 71%, M. P.216°C: IR (KBr, cm<sup>-1</sup>): 3570 (NH-pyrrole), 3422 (NH-Phenothiazine), 3324 (NH-pyrazole), 1635 (ArH), 1445 (C=N), 817 (C-N), 740 (C-S); <sup>1</sup>H-NMR (DMSO, δ in ppm): 8.28 (s, 1H, NH-pyrrole), 7.8 (s, 1H, N-H-phenothiazine), 7.28 (s, 1H, NH-pyrazole) 6.8 (m, 5H, ArH), [13]C NMR(300 MHz, DMSO-d<sub>6</sub>) 38.9, 39.2, 39.5, 39.7, 40.0, 40.3, 58.5, 76.8, 77.2, 77.6, 111.8, 119.1, 126.2, 137.3, 162.2.

**Synthesis of 2-(4'-hydroxyl phenothiazinyl pyrazolyl) pyrrole (5b)**

Yield 67%, M. P.207°C: IR (KBr, cm<sup>-1</sup>): 3532 (NH-pyrrole), 3426.9 (NH-Phenothiazine), 3344 (NH-pyrazole), 1630 (ArH), 1443 (C=N), 814 (C-N), 730 (C-S); <sup>1</sup>H-NMR (DMSO, δ in ppm): 8.20 (s, 1H, NH-pyrrole), 7.7 (s, 1H, N-H-phenothiazine), 7.18 (s, 1H, NH-pyrazole) 6.8 (m, 5H, ArH), [13]C NMR (300MHz, DMSO-d<sub>6</sub>) 40.9, 39.2, 39.5, 39.9, 40.0, 42.3, 59.5, 76.9, 77.7, 77.6, 110.8, 118.1.

**Synthesis of 2-(4'-hydroxyl phenothiazinyl pyrazolyl) pyrrole (5c)**

Yield 65%, M. P.121°C: IR (KBr, cm<sup>-1</sup>): 3574 (NH), 3426 (NH-Phenothiazine), 3334 (NH-pyrazole), 1635 (ArH), 1445 (C=N), 817 (C-N), 742 (C-S); <sup>1</sup>H-NMR (DMSO, δ in ppm): 8.25 (s, 1H, NH-pyrrole), 7.87 (s, 1H, N-H-phenothiazine), 7.28 (s, 1H, NH-pyrazole) 6.4 (m, 5H, ArH); [13]C NMR(300MHz, DMSO-d<sub>6</sub>) 38.4, 39.6, 39.3, 39.8, 40.6, 40.2, 58.8, 76.1, 77.5, 77.9, 111.2, 119.6, 126.6, 137.8, 162.7.

**Synthesis of 2-(4'-hydroxy phenothiazinyl pyrazolyl) pyrrole (5d)**

Yield 58%, M. P.210°C: IR (KBr, cm<sup>-1</sup>): 3568 (NH-pyrrole), 3426 (NH-phenothiazine), 3332 (NH-pyrazole), 1631 (ArH), 1443 (C=N), 817 (C-N), 735 (C-S); <sup>1</sup>H-NMR (DMSO, δ in ppm): 8.22 (s, 1H, NH-pyrrole), 7.3 (s, 1H, N-H-phenothiazine), 7.26 (s, 1H, NH-pyrazole) 6.9 (m, 5H, ArH); [13]C NMR (300 MHz, DMSO-d<sub>6</sub>) 38.9, 39.9, 39.1, 39.4, 40.2, 126.9, 137.2.

**Synthesis of 2-(4'-nitro phenothiazinyl pyrazolyl) pyrrole (5e)**

Yield 78%, M. P.194°C: IR (KBr, cm<sup>-1</sup>): 3575 (NH), 3428 (NH-phenothiazine), 3314 (NH-pyrazole), 1625 (ArH), 1440 (C=N), 820 (C-N), 745 (C-S); <sup>1</sup>H-NMR (DMSO, δ in ppm): 8.22 (s, 1H, NH-pyrrole), 7.1 (s, 1H, N-H-phenothiazine), 7.28 (s, 1H, NH-pyrazole), 6.3 (m, 5H, ArH), [13]C NMR(300MHz, DMSO-d<sub>6</sub>) 39.1, 39.8, 39.1, 39.4, 40.9, 40.6, 58.1, 76.3, 77.3, 111.5, 119.2, 126.4, 137.7, 162.3.

**Synthesis of 2-(4'-nitro phenothiazinyl pyrazolyl) pyrrole (5f)**

Yield 68%, M. P. 215°C: IR (KBr, cm<sup>-1</sup>): 3685 (OH), 3320 (NH-pyrrole), 1620 (ArH), 1422 (C=N), 1320(CH<sub>3</sub>), 1545 (C-NO<sub>2</sub>), 842 (C-N); <sup>1</sup>H-NMR (DMSO, δ in ppm): 2.98 (s, 6H, 2xCH<sub>3</sub>), 6.7 (m, 5H, ArH) 8.51 (s, 1H, NH), [13]C NMR (300 MHz, DMSO-d<sub>6</sub>) 40.9, 49.2, 50.5, 50.7, 50.9, 52.3, 53.5, 77.2, 77.2, 111.4, 119.5, 126.6, 137.4, 162.0.

**2-(4'-nitro phenothiazinyl pyrazolyl) pyrrole (5g)**

Yield 64%, M. P.199°C: IR (KBr, cm<sup>-1</sup>): 3560 (OH), 3570 (NH), 1632 (ArH), 1447 (C=N), 1323 (CH<sub>3</sub>), 818 (C-N), 738 (C-Cl); <sup>1</sup>H-NMR (DMSO, δ in ppm): 3.21 (s, 6H, 2xCH<sub>3</sub>), 6.8 (m, 5H, ArH), 8.22 (s, 1H, NH), [13]C NMR (300 MHz, DMSO-d<sub>6</sub>) 38.4, 39.8, 39.1, 39.4, 40.2, 40.7, 58.1, 76.6, 77.9, 77.1, 111.3, 119.1, 126.2, 137.3, 162.9.

**Synthesis of 2-(4'-dimethyl amine phenothiazinyl pyrazolyl) pyrrole (5h)**

Yield 81%, M. P.220°C: IR (KBr, cm<sup>-1</sup>): 3520 (NH-pyrrole), 3422. 4 (NH-Phenothiazine), 3321 (NH-pyrazole), 1635 (ArH), 1445 (C=N), 817 (C-N), 740(C-S); <sup>1</sup>H-NMR (DMSO, δ in ppm): 8.28 (s, 1H, NH-pyrrole), 7.8 (s, 1H, N-H-phenothiazine), 7.28 (s, 1H, NH-pyrazole) 6.8 (m, 5H, ArH), [13]C NMR(300MHz, DMSO-d<sub>6</sub>) 37.9, 38.2, 38.9, 37.7, 39.9, 40.8, 58.2, 76.8, 77.7, 77.9, 111.8, 119.7, 126.2, 137.3, 163.1.

**Synthesis of 2-(4'-chloro phenothiazinyl pyrazolyl) pyrrole (5i)**

IR (KBr, cm<sup>-1</sup>): Yield 65%, M. P.123°C: IR (KBr, cm<sup>-1</sup>): 3577 (NH-pyrrole), 3427 (NH-Phenothiazine), 3348 (NH-pyrazole), 1637(ArH), 1445 (C=N), 813 (C-N), 745 (C-S); <sup>1</sup>H-NMR (DMSO, δ in ppm): 8.26 (s, 1H, NH-pyrrole), 7.45 (s, 1H, N-H-phenothiazine), 7.30 (s, 1H, NH-pyrazole) 6.82 (m, 5H, ArH); [13]C NMR (300 MHz DMSO-d<sub>6</sub>) 38.2, 39.7, 39.1, 39.4, 40.5, 40.9, 58.4, 76.2, 77.8, 77.9, 111.2, 119.5, 126.7, 137.2, 162.8.

**Synthesis of 2-(4'-methoxy phenothiazinyl pyrazolyl) pyrrole (5j)**

Yield 77%, M. P.227°C: IR (KBr, cm<sup>-1</sup>): 3540(NH-pyrrole), 3469 (NH-Phenothiazine), 3354 (NH-pyrazole) 1635 (ArH), 1465 (C=N), 811 (C-N), 740 (C-S); <sup>1</sup>H-NMR (DMSO, δ in ppm): 8.24 (s, 1H, NH-pyrrole), 7.8 (s, 1H, N-H-phenothiazine), 7.25 (s, 1H, NH-pyrazole) 6.2 (m, 5H, ArH); <sup>13</sup>C NMR (300 MHz, DMSO-d<sub>6</sub>) 48.9, 49.2, 49.5, 49.7, 50.0, 50.3, 58.5, 76.8, 77.2, 77.6, 111.8, 119.1, 120.2, 130.3, 160.2.

**Table III: Characterization data of newly synthesized compounds (5a-j)**

Comp	R	Mol Formula	M. P. (°C)	Yield (%)	Analysis formula (calcd)% (obs)			
					C	H	N	S
5a	-H	C <sub>19</sub> H <sub>14</sub> N <sub>4</sub> S	216	71	69.0 (69.1)	4.2 (4.3)	16.9 (16.7)	9.7 (9.4)
5b	2-OH	C <sub>19</sub> H <sub>14</sub> ON <sub>4</sub> S	207	67	65.76 (65.74)	4.0 (4.0)	16.1 (16.2)	9.2 (9.1)
5c	3-OH	C <sub>19</sub> H <sub>14</sub> ON <sub>4</sub> S	121	65	65.76 (65.74)	4.0 (4.0)	16.1 (16.2)	9.2 (9.1)
5d	4-OH	C <sub>19</sub> H <sub>14</sub> ON <sub>4</sub> S	210	58	65.76 (65.74)	4.0 (4.0)	16.1 (16.2)	9.2 (9.1)
5e	2-NO <sub>2</sub>	C <sub>19</sub> H <sub>13</sub> O <sub>2</sub> N <sub>5</sub> S	194	78	60.7 (60.6)	3.4 (3.6)	18.1 (18.2)	8.5 (8.4)
5f	3-NO <sub>2</sub>	C <sub>19</sub> H <sub>13</sub> O <sub>2</sub> N <sub>5</sub> S	215	68	60.7 (60.6)	3.4 (3.6)	18.1 (18.2)	8.5 (8.4)
5g	4-NO <sub>2</sub>	C <sub>19</sub> H <sub>13</sub> O <sub>2</sub> N <sub>5</sub> S	199	64	60.7 (60.6)	3.4 (3.6)	18.1 (18.2)	8.5 (8.4)
5h	N(CH <sub>3</sub> ) <sub>2</sub>	C <sub>21</sub> H <sub>19</sub> N <sub>5</sub> S	220	81	67.5 (67.6)	5.3 (5.1)	18.7 (18.5)	8.5 (8.3)
5i	-Cl	C <sub>19</sub> H <sub>13</sub> N <sub>4</sub> ClS	123	66	62.5 (62.6)	5.3 (5.3)	15.3 (15.2)	8.7 (8.8)
5j	-OCH <sub>3</sub>	C <sub>20</sub> H <sub>16</sub> ON <sub>4</sub> S	227	77	66.5 (66.6)	4.3 (4.3)	15.5 (15.4)	8.9 (8.6)

**Pharmacological activities**

The synthesized compounds were tested for their antimicrobial activity in vitro against gram positive bacterium *S. aureus* and gram negative bacterium *E. Coli*. using ciprofloxacin as standard, Nutrient Agar was prepared separately and divided into two equal parts in two 250 ml of conical flasks and sterilized by autoclaving. To a sterilized petriplates first basal layer of nutrient agar was seeded with bacterial cultures (*E. coli* & *S. aureus*) & allowed to set.

After solidifications, a hole in the center of plate was bored with sterile bases and filled with heterocyclic compounds under studies and observed for zone of inhibition. Synthesized compounds, 5a, 5e, 5f, 5h, show good antibacterial activity against *S. aureus* and 5b, 5g, 5h show moderate to good activity against *E. coli*. The synthesized compounds were tested at 100g/ml table IV.

**Antioxidant activity**

Free radical scavenging activity of the test compounds 3a-g, 4a-g, 5a-g and 6a-g were determined by the 1, 1- diphenyl picryl hydrazyl (DPPH) assay method [18]. Drug stock solution (1 mg mL<sup>-1</sup>) was diluted to final concentrations of 2, 4, 6, 8 and 10 mg mL<sup>-1</sup> in methanol. DPPH methanol solution (1 mL, 0.3 mmol) was added to 2.5 mL of drug solutions of different concentrations and allowed to react at room temperature.

After 30 min the absorbance values were measured at 518 nm and converted into the percentage antioxidant activity. Methanol was used as the solvent and ascorbic acid as the standard. The percentage of inhibition extrapolated against concentration is depicted in fig. 1. Results are presented in table 4. The standard drug used was ascorbic acid.

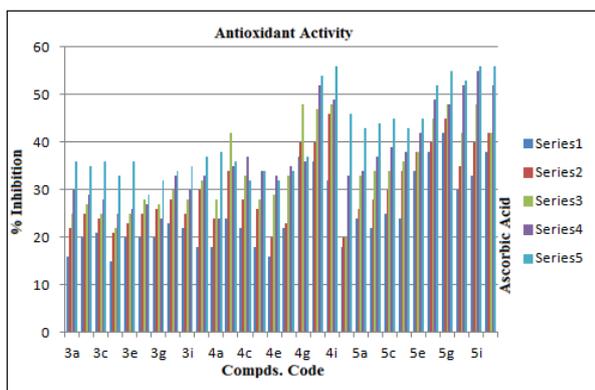
**Table IV: Antibacterial and antifungal activities of compounds 5 a-j**

Compounds	<i>A. niger</i>	<i>S. aureus</i>	<i>E. Coli</i>	<i>S. aureus</i>	<i>B. subtilis</i>
5a	14	12	15	13	11
5b	13	11	12	15	16
5c	15	12	17	18	13
5d	11	9	11	10	14
5e	16	12	9	11	14
5f	12	14	19	16	13
5g	16	18	15	10	11
5h	14	14	13	8	15
5i	16	19	18	10	13
5j	17	15	14	14	12
SM	24	23	24	17	13
GF					

Minimum inhibitory concentration's 100g/ml, SM (Streptomycin) and GF (Griesofulvin)

**Table V: Antioxidant activity of the compounds 3a-j, 4a-j, 5a-j and 6a-j**

Comp. Code	% Inhibition				
	20 µg	40 µg	60 µg/	80 µg	100 µg/ml
3a	16	22	25	30	36
3b	20	25	27	29	35
3c	21	24	25	28	36
3d	15	21	22	25	33
3e	20	23	25	26	36
3f	20	25	28	27	29
3g	20	26	27	24	32
3h	23	28	30	33	34
3i	22	25	28	30	35
3j	18	30	32	33	37
4a	18	24	28	24	38
4b	24	34	42	35	36
4c	22	28	33	37	32
4d	18	26	28	34	34
4e	16	20	29	33	32
4f	22	23	33	35	34
4g	37	40	48	36	37
4h	36	40	47	52	54
4i	32	46	48	49	56
4j	18	20	20	33	46
5a	24	26	33	34	43
5b	22	28	34	37	44
5c	25	30	34	39	45
5d	24	34	36	38	43
5e	34	38	38	42	45
5f	38	40	45	49	52
5g	42	45	48	48	55
5h	30	35	42	52	53
5i	33	40	48	55	56
5j	38	42	42	52	56
	<b>2 µg/ml</b>	<b>4 µg/ml</b>	<b>6 µg/ml</b>	<b>8 µg/ml</b>	<b>10 µg/ml</b>
Ascorbic acid	10	15	20	35	58



**Fig. 1: Antioxidant Activity of the compounds 3a-j, 4a-j, 5a-j and 6a-j**

## CONCLUSION

2-[4'-hydroxyl benz-1'-(propene-1'//one)] Pyrrole (**2**) on treatment with primary amine gives 2-[biphenyl amine-1'-(propane-1'//one)] pyrrole (**3**) which react with sulphur and iodine affording substituted 2-[phenothiazinyl-8'-(propane-1'//one)] pyrrole (**4a-j**) which undergoes cyclization with  $\text{NH}_2\text{NH}_2 \cdot \text{H}_2\text{O}$  and Substituted 2-(4'-phenothiazinyl pyrazolyl) pyrrole (**5a-j**) is obtained. The structure products were characterized by elemental analysis and spectral data. These compounds show antibacterial and antifungal activities within the series of compounds synthesized. Hence these compounds shall be exploited further for antibacterial activity and anti-oxidant Activity to attain a potential pharmacophore.

## ACKNOWLEDGEMENT

I highly thankful to Dr. R. S. Bobhote, principal, VVACSC, Samudrapur for providing necessary facility for the complexation of this research work. The authors are also thankful to the Head, Department of Pharmaceutical Science Nagpur University for screening antimicrobial and Anti-oxidant activities, Head RSIC, CDRI, Lucknow for providing the spectral data of the compounds.

## REFERENCES

1. Chemical search engine. 'Histamine cause itching, sneezing, runny nose and watery eyes'. 9/5/2014.
2. J Karpinskat, B Starczewska, H Puzanowska-Tarasiewicz. 'Analytical Properties of 2-Phenothiazine Derivatives' Analytical Sci 1996;12(2):161-70.
3. Harwood PD, Jestad AC. 'Diverse biological activities like antiparkinsonian'. J Parasitol 1938;24:16-8.
4. Halpern BN. 'Diverse biological activities like antiparkinsonian'. J Am Med Assoc 1945;129:1219-22.
5. Kalinowsky LB, Hoch PH. Somatic treatment in psychiatry: Academic press. New York; 1961. p. 122-32.
6. Clane NT, Witten LK, Eilmer DS. 'Biological activities like antihistaminic. Aust Ver J 1947;23:344-6.
7. Douglass JR, Baker NF. Biological activity like antihelminthic'. J Am Vet 1956;17:318-20.
8. Ddhbom R, Ekstramd T. 'Biological activity like antiviral'. Arch Intern Pharmacodyn 1966;159:70-8.
9. Craig JC, Tate HF. Progr 'Biological activity'. Drug Res 1901;3:75-8.
10. Janssen PAJ, Niemegeers CJE. 'Biological activity like CNS depressant'. Arzneimittel Forsch 1965;15:1196-9.
11. Parmar VS, Kumar A. 'Antioxidant'. Bioory Med Chem 1999;7:1425-7.
12. Breacke ME, Philippe J, Wengel J. ' Pharmacological activity'. Bioorg Med Chem 1997;5:1609-11.
13. Buchanan JG, Stobie A. Biological activity like antiviral'. J Perkin Trans 1981;14:2374-7.
14. Behr LC, Fusco R. 'The chemistry of heterocyclic compounds (antipyretic)'. A weissberger interscience: New York; 1967. p. 1-30.
15. Bailey DM, Hansen PE. Anti-inflammatory Activity'. J Med Chem 1985;28:256-8.
16. Kidwai M, Shashi B. 'Antidepressant activity'. Chem Rev 2000;15:34-8.
17. Srivastava KP. 'Blood pressure lowering'. J Chem Environ 2001;59:77-81.
18. Tahiliani NJ, Ojha KG. 'Pyrazoles are also used as agrochemicals'. J Chem An Indian 2003;1:1171-5.
19. Suzuki H, Hanane M. 'Dyestuff's in sunscreen materials'. J Tokkyo 2003;236-368.
20. Hondershausen M. 'Pyrroles and their derivatives exhibit different important biological activities'. Pestic Sci 1996;48:269-78.
21. Fahmy BSM, Elnagdi MH. 'Pyrroles and their derivatives exhibit different important biological activities'. J Chem Tech 1980;15:30-7.
22. Garcia H, Miranda MA. 'Microwave-induced organic reaction is used for carrying out chemical transformations'. J Heterocycl 1991;32:1745-8.
23. Sundberg RJ. 'The chemistry of indole'. Academic press: New York; 1970. p. 134-67.
1. Murat K, Dorota F, Marcel H, Christine W, Till Opatz Beilstein. 'Applications in medicinal chemistry and materials science'. J Org Chem 2014;10:466-70.