

## Synthesis and antimycobacterial activity of novel heterocycles

M. SHAHAR YAR\*, A. AHMAD SIDDIQUI and M. ASHRAF ALI

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard (Hamdard University), New Delhi-110062, India (e-mail: yarmsy@yahoo.co.in)

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**Abstract:** In the present investigation 4-hydroxy-3-methylacetophenone on condensation with various aromatic aldehydes in methanolic KOH solution yielded the corresponding chalcones (**C<sub>I</sub>–C<sub>XI</sub>**). These chalcones were further reacted with hydrazine hydrate in ethanol which led to the formation of pyrazoline derivatives (**H<sub>I</sub>–H<sub>XI</sub>**). The newly synthesized heterocycles were characterized on the basis of their chemical properties and spectroscopic data. All newly synthesized compounds were evaluated for their antimycobacterial activities against *Mycobacterium tuberculosis* H37<sub>Rv</sub>.

**Keywords:** pyrazoline, antimycobacterial, *Mycobacterium tuberculosis*.

### INTRODUCTION

Tuberculosis (TB) is by far the most frequently encountered mycobacterial disease in the world. Although its incidence has diminished significantly in the industrially more developed countries, it remains a major public health problem in most developing nations. Tuberculosis is still the single largest infection having a high mortality rate and 0.1 to 0.3 percent of the population become infected each year in the developed countries. This year, 2 million people may develop the disease and 30 million may die worldwide (as per a WHO report). It is commonly known that *Mycobacterium tuberculosis* has developed resistance to the majority of the existing drugs. However, powerful new anti-TB drugs with new mechanisms of action have not been developed in the last forty years. In the developing countries, the annual infection rate is 20–50 times greater than in the developed countries and its high level shows little or no downward trend. It is expected that development of new effective anti-TB drugs will bring various outcomes *viz*: shortening the total duration of therapy, reducing the total expenditure and treatment of multiple drug resistant tuberculosis (MDR-TB) by single dosage regiment.<sup>1,2</sup> In pursuit of achieving this goal, our research efforts are focused on the development of novel structural moieties having antimycobacterial properties.<sup>2,3</sup> Chalcones have vari-

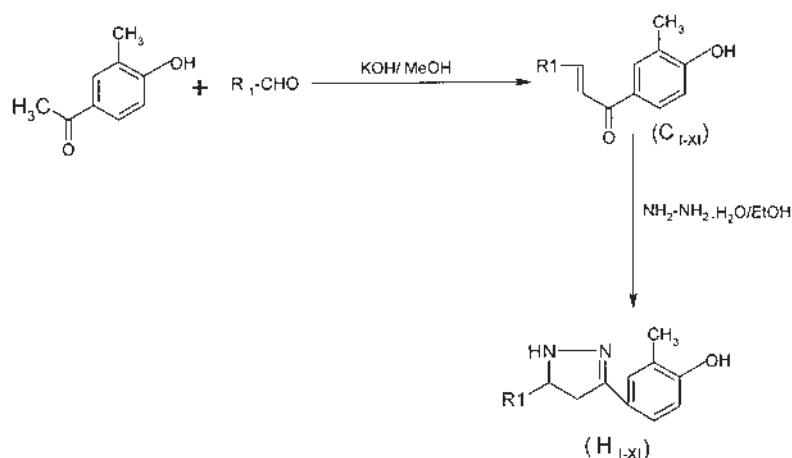
\* Author for correspondence.

ous biological activities such as cytotoxic,<sup>4</sup> antimalarial,<sup>5</sup> antioxidant,<sup>6</sup> tyrosinase inhibitory,<sup>7</sup> anti-inflammatory,<sup>8</sup> cancer chemopreventive<sup>8</sup> and antibacterial.<sup>9</sup> Several pyrazolines are also known to have various biological activities, *e.g.*, anti-bacterial,<sup>10,11</sup> anti-inflammatory,<sup>12</sup> hypoglycemic,<sup>13</sup> anti-HIV<sup>14</sup> and anti-tumor.<sup>14</sup> Herein the synthesis and *in vitro* antimycobacterial activity of novel chalcone and pyrazoline derivatives are reported.

## RESULTS AND DISCUSSION

### Chemistry

The synthesis of chalcone and pyrazoline derivatives was performed following the steps shown in Scheme 1. In the initial step, chalcones (**C<sub>I</sub>–C<sub>XI</sub>**) were synthesized by condensing 4-hydroxy-3-methylacetophenone with appropriate aromatic aldehydes in dilute methanolic potassium hydroxide solution at room temperature. The compounds (**H<sub>I</sub>–H<sub>XI</sub>**) were synthesized by reacting the appropriate chalcone with hydrazine hydrate in ethanol. The purity of the compounds was controlled by TLC. Spectral data (IR and <sup>1</sup>H-NMR) of all the newly synthesized compounds were in full agreement with the proposed structures.



Scheme 1.

### Biological screening

#### Microbiology

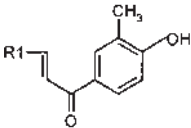
The *in vitro* activities of the synthesized compounds for tuberculosis inhibition against the *Mycobacterium tuberculosis* H37<sub>RV</sub> (ATCC27294) strain were performed using the micro plate almar blue assay (MABA) method. Compounds exhibiting fluorescence are tested in a BACTEC-460 radiometric system<sup>15,16</sup> and/or broth micro dilution assay and the activities expressed as minimum inhibitory concentration (MIC, µg/ml) are summarized in Tables I and II. Compounds dem-

onstrating at least 90 % inhibition were re-tested at lower concentrations by the broth micro dilution assay to determine the actual MIC, a value defined as the lowest concentration inhibiting  $\approx 90$  % of the inoculums relative to the control.

#### Antimycobacterial activity

Twenty two compounds were screened for their antimycobacterial activity against *Mycobacterium tuberculosis* H37<sub>RV</sub> using a BACTEC-460 radiometric system. Among the chalcones (**C<sub>I</sub>**–**C<sub>XI</sub>**) and pyrazolines (**H<sub>I</sub>**–**H<sub>XI</sub>**), compounds **C<sub>III</sub>**, **C<sub>X</sub>** and **H<sub>III</sub>** produced the highest efficacy and exhibited  $> 90$  % inhibition at  $\approx 6.25$   $\mu\text{g/ml}$  in the primary screen (Tables I and II). Compounds **C<sub>II</sub>**, **C<sub>V</sub>**, **C<sub>VIII</sub>**, **C<sub>IX</sub>**, **H<sub>VII</sub>** and **H<sub>XI</sub>** exhibited  $\approx 90$  % inhibition against *Mycobacterium tuberculosis* at MIC  $> 6.25\mu\text{g/ml}$  (Tables I and II). These antimycobacterial data clearly show that the presence of dimethylaminophenyl substituted chalcone and pyrazoline causes remarkable improvements in antitubercular activity.

TABLE I. Physicochemical data and *in vitro* anti-mycobacterial screening of novel chalcones against *Mycobacterium tuberculosis* H37<sub>RV</sub> strain



Compound	R1	M.p./°C	Yield/%	Mol. formula	% Inhibition	MIC $\mu\text{g/ml}$
<b>C<sub>I</sub></b>	4-Methoxyphenyl-	190–192	75	C <sub>17</sub> H <sub>16</sub> O <sub>3</sub>	72	$>6.25$
<b>C<sub>II</sub></b>	4-Chlorophenyl-	156–158	77	C <sub>16</sub> H <sub>13</sub> O <sub>2</sub> Cl	90	$>6.25$
<b>C<sub>III</sub></b>	4-Dimethylaminophenyl-	126–128	67	C <sub>18</sub> H <sub>19</sub> O <sub>2</sub> N	91	6.25
<b>C<sub>IV</sub></b>	Phenyl-	113–115	90	C <sub>16</sub> H <sub>14</sub> O <sub>2</sub>	ND	ND
<b>C<sub>V</sub></b>	3,4-Dimethoxyphenyl-	156–158	85	C <sub>18</sub> H <sub>18</sub> O <sub>4</sub>	92	$>6.25$
<b>C<sub>VI</sub></b>	3,4,5-Trimethoxyphenyl-	144–146	65	C <sub>19</sub> H <sub>20</sub> O <sub>5</sub>	77	$>6.25$
<b>C<sub>VII</sub></b>	2-Furyl-	97–99	76	C <sub>14</sub> H <sub>12</sub> O <sub>3</sub>	73	$>6.25$
<b>C<sub>VIII</sub></b>	4-Fluorophenyl-	161–163	80	C <sub>18</sub> H <sub>13</sub> O <sub>4</sub> F	94	$>6.25$
<b>C<sub>IX</sub></b>	2-Chlorophenyl-	189–191	90	C <sub>16</sub> H <sub>13</sub> O <sub>2</sub> Cl	88	$>6.25$
<b>C<sub>X</sub></b>	2,6-Dichlorophenyl-	111–113	76	C <sub>16</sub> H <sub>12</sub> O <sub>2</sub> Cl <sub>2</sub>	90	6.25
<b>C<sub>XI</sub></b>	3-Nitrophenyl-	141–143	70	C <sub>16</sub> H <sub>13</sub> O <sub>4</sub> N	65	$>6.25$

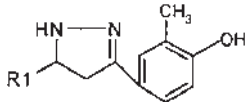
Recrystallization: ethanol, acetic acid; ND = not done

#### CONCLUSION

To summarize, a new class of chalcone and pyrazoline derivatives, as a novel class of antitubercular agents, was synthesized. The newly synthesized novel heterocycles exhibited promising antitubercular activities against both drug-sensitive and drug-resistant strains of *Mycobacterium tuberculosis*. These results make

novel chalcone and pyrazoline derivatives interesting lead molecules for further synthetic and biological evaluation. It can be concluded that this class of compounds certainly holds great promise towards the pursuit to discover novel classes of antimycobacterial agents. Further studies to acquire more information concerning structure–activity relationships are in progress.

TABLE II. Physicochemical data and *in vitro* antimycobacterial screening of novel pyrazoline derivatives against *Mycobacterium tuberculosis* H37<sub>RV</sub> strain



Compound	R1	M.p./°C	Yield/%	Mol. formula	% Inhibition	MIC μg/ml
<b>H<sub>I</sub></b>	4-Methoxyphenyl-	147–149	75	C <sub>17</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	76	>6.25
<b>H<sub>II</sub></b>	4-Chlorophenyl-	139–141	77	C <sub>16</sub> H <sub>15</sub> N <sub>2</sub> OCl	90	>6.25
<b>H<sub>III</sub></b>	4-Dimethylaminophenyl-	160–162	67	C <sub>18</sub> H <sub>21</sub> N <sub>3</sub> O	92	6.25
<b>H<sub>IV</sub></b>	Phenyl-	180–182	90	C <sub>16</sub> H <sub>16</sub> N <sub>2</sub> O	88	ND
<b>H<sub>V</sub></b>	3,4-Dimethoxyphenyl-	119–121	85	C <sub>18</sub> H <sub>20</sub> N <sub>2</sub> O <sub>3</sub>	78	>6.25
<b>H<sub>VI</sub></b>	3,4,5-Trimethoxyphenyl-	101–103	65	C <sub>19</sub> H <sub>22</sub> N <sub>2</sub> O <sub>4</sub>	86	>6.25
<b>H<sub>VII</sub></b>	2-Furyl-	161–163	76	C <sub>14</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	90	>6.25
<b>H<sub>VIII</sub></b>	4-Fluorophenyl-	142–144	80	C <sub>16</sub> H <sub>15</sub> N <sub>2</sub> OF	85	>6.25
<b>H<sub>IX</sub></b>	2-Chlorophenyl-	140–142	90	C <sub>16</sub> H <sub>15</sub> N <sub>2</sub> OCl	83	>6.25
<b>H<sub>X</sub></b>	2,6-Dichlorophenyl-	139–141	76	C <sub>16</sub> H <sub>14</sub> N <sub>2</sub> OCl	83	>6.25
<b>H<sub>XI</sub></b>	3-Nitrophenyl-	149–151	70	C <sub>16</sub> H <sub>15</sub> N <sub>3</sub> O <sub>3</sub>	88	>6.25

Recrystallization: ethanol, acetic acid; ND = not done

## EXPERIMENTAL

### Chemistry

Chemicals were supplied by E. Merck (Germany) and S. D. Fine Chemicals (India). Melting points were determined by the open tube capillary method and are uncorrected. The purity of the compounds was controlled by thin layer chromatography (TLC) plates (silica gel G) in the solvent system toluene–ethyl formate–formic acid (5:4:1) and benzene–methanol (8:2). The spots were located under iodine vapor or UV light. The spectra were obtained on a Perkin-Elmer 1720 FT-IR spectrometer (KBr pellets). The <sup>1</sup>H-NMR spectra were recorded on a Bruker AC 300 MHz spectrometer using TMS as the internal standard in DMSO-*d*<sub>6</sub>/CDCl<sub>3</sub>.

*General method for the synthesis of 1-(4-hydroxy-3-methylphenyl)-3-[(substituted)phenyl]-2-propen-1-ones (C<sub>I–XI</sub>)*. To a mixture of 4-hydroxy-3-methylacetophenone (0.005 mol) and the appropriate aromatic aldehyde (0.005 mol) in oxygen-free ethanol was added a solution of potassium hydroxide in oxygen-free distilled water with constant shaking of the reaction flask. The reaction mixture was stirred for a specified period on a magnetic stirrer and poured onto crushed ice. The solid mass which separated out was filtered, washed with water and crystallized from a suitable solvent to give the desired product.

*1-(4-Hydroxy-3-methylphenyl)-3-(4-methoxyphenyl)-2-propen-1-one (C<sub>I</sub>)*. IR (KBr, cm<sup>−1</sup>) 3180–3210 (OH), 1675–1686 (C=O), 3035–3042 (CH); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>, ppm): 9.4 (1H, s, OH), 2.2 (3H,

*s*, CH<sub>3</sub>), 7.7–8.2 (7H, *m*, aromatic), 3.9 (3H, *s*, OCH<sub>3</sub>), 6.9–7.5 (1H×2, *dd*, –CH=CH).

3-(4-Chlorophenyl)-1-(4-hydroxy-3-methylphenyl)-2-propen-1-one (**C<sub>II</sub>**). IR: (KBr) cm<sup>-1</sup> 3210 (OH), 1682, C=O, 3042 (CH); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 7.7–8.2 (7H, *m*, aromatic), 6.9–7.5 (1H×2, *dd*, –CH=CH), 2.2 (3H, *s*, CH<sub>3</sub>).

3-(4-Dimethylaminophenyl)-1-(4-hydroxy-3-methylphenyl)-2-propen-1-one (**C<sub>III</sub>**). IR: (KBr) cm<sup>-1</sup> 3212 (OH), 1680 (C=O); 3032 (CH). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 7.7–8.2 (7H, *m*, aromatic), 6.9–7.5 (1H×2, *dd*, –CH=CH), 2.9 (2H×2, *s*, –N(CH<sub>3</sub>)<sub>2</sub>), 2.2 (3H, *s*, CH<sub>3</sub>).

1-(4-Hydroxy-3-methylphenyl)-3-phenyl-2-propen-1-one (**C<sub>IV</sub>**). IR: (KBr) cm<sup>-1</sup> 3180 (OH), 1687 (C=O), 3040 (CH). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.4 (1H, *s*, OH), 2.2 (3H, *s*, CH<sub>3</sub>), 7.7–8.2 (8H, *m*, aromatic), 6.9–7.5 (1H×2, *dd*, –CH=CH).

3-(3,4-Dimethoxyphenyl)-1-(4-hydroxy-3-methylphenyl)-2-propen-1-one (**C<sub>V</sub>**). IR: (KBr) cm<sup>-1</sup> 3200 (OH), 1680 (C=O), 3030 (CH). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 2.2 (3H, *s*, CH<sub>3</sub>), 7.7–8.2 (6H, *m*, aromatic), 6.9–7.5 (1H×2, *dd*, –CH=CH), 3.3 (6H, *s*, 2×OCH<sub>3</sub>).

1-(4-Hydroxy-3-methylphenyl)-3-(3,4,5-trimethoxyphenyl)-2-propen-1-one (**C<sub>VI</sub>**). IR: (KBr) cm<sup>-1</sup> 3196 (OH), 1680 (C=O), 3040 (CH); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 2.2 (3H, *s*, CH<sub>3</sub>), 7.7–8.2 (5H, *m*, aromatic), 3.9 (9H, *s*, 3×OCH<sub>3</sub>), 6.9–7.5 (1H×2, *dd*, –CH=CH).

3-(2-Furyl)-1-(4-hydroxy-3-methylphenyl)-2-propen-1-one (**C<sub>VII</sub>**). IR: (KBr) cm<sup>-1</sup> 3200 (OH), 1688 (C=O), 3030 (CH). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 2.2 (3H, *s*, CH<sub>3</sub>), 7.7–8.2 (3H, *m*, aromatic), 7.43–7.48 (3H, *m*, furan), 6.9–7.5 (1H×2, *dd*, –CH=CH).

3-(4-Fluorophenyl)-1-(4-hydroxy-3-methylphenyl)-2-propen-1-one (**C<sub>VIII</sub>**). IR: (KBr) cm<sup>-1</sup> 3200 (OH), 1680 (C=O), 3040 (CH); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 2.2 (3H, *s*, CH<sub>3</sub>), 7.7–8.2 (7H, *m*, aromatic), 6.9–7.5 (1H×2, *dd*, –CH=CH).

3-(2-Chlorophenyl)-1-(4-hydroxy-3-methylphenyl)-2-propen-1-one (**C<sub>IX</sub>**). IR: (KBr) cm<sup>-1</sup> 3200 (OH), 1680 (C=O), 3030 (CH). <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 2.2 (3H, *s*, CH<sub>3</sub>), 7.7–8.2 (7H, *m*, aromatic), 6.9–7.5 (1H×2, *dd*, –CH=CH).

3-(2,6-Dichlorophenyl)-1-(4-hydroxy-3-methylphenyl)-2-propen-1-one (**C<sub>X</sub>**). IR: (KBr) cm<sup>-1</sup> 3200 (OH), 1680 (C=O), 3040 (CH); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 2.2 (3H, *s*, CH<sub>3</sub>), 7.7–8.2 (6H, *m*, aromatic), 6.9–7.5 (1H×2, *dd*, –CH=CH).

1-(4-Hydroxy-3-methylphenyl)-3-(3-nitrophenyl)-2-propen-1-one (**C<sub>XI</sub>**). IR: (KBr) cm<sup>-1</sup> 3200 (OH), 1680 (C=O), 3040 (CH); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 2.2 (3H, *s*, CH<sub>3</sub>), 7.7–8.2 (7H, *m*, aromatic), 6.9–7.5 (1H×2, *dd*, –CH=CH).

*General method for the synthesis of 3-(4-hydroxy-3-methylphenyl)-5-[(substituted)phenyl]-2-pyrazolines.* To a solution of 0.01 mol of the required chalcone (**C<sub>I</sub>**–**X<sub>I</sub>**), in 10 mL of ethanol, 0.02 mol hydrazine hydrate (99 %) was added dropwise. The reaction mixture was heated under reflux for 7 h, then cooled and poured onto crushed ice. The so-obtained solid product was filtered and recrystallized from ethanol (**H<sub>I</sub>**–**X<sub>I</sub>**).

3-(4-Hydroxy-3-methylphenyl)-5-(4-methoxyphenyl)-2-pyrazoline (**H<sub>I</sub>**). IR: (KBr, cm<sup>-1</sup>) 3307 (OH), 1590 (C=N), 1320 (C–N); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.5 (1H, *s*, OH), 7.3–8.7 (7H, *m*, aromatic), 5.52 (1H, *s*, NH), 4.24 (1H, *s*, CH), 3.9 (3H, *s*, OCH<sub>3</sub>), 3.4 (3H, *s*, CH<sub>3</sub>), 2.3 (2H, *s*, CH<sub>2</sub>).

5-(4-Chlorophenyl)-3-(4-hydroxy-3-methylphenyl)-5-(4-chlorophenyl)-2-pyrazoline (**H<sub>II</sub>**). IR: (KBr, cm<sup>-1</sup>): 3307 (OH), 1590 (C=N), 1320 (C–N), 770 (C–Cl); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.5 (1H, *s*, OH), 3.4 (3H, *s*, CH<sub>3</sub>), 7.0–7.6 (7H, *m*, aromatic), 5.50 (1H, *s*, NH), 4.24 (1H, *s*, CH), 2.3 (2H, *s*, CH<sub>2</sub>).

5-(4-Dimethylaminophenyl)-3-(4-hydroxy-3-methylphenyl)-2-pyrazoline (**H<sub>III</sub>**). IR: (KBr, cm<sup>-1</sup>) 3307 (OH), 1580 (C=N), 1324 (C–N); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.5 (1H, *s*, OH), 7.4–8.0 (7H, *m*, aromatic), 5.52 (1H, *s*, NH), 4.24 (1H, *s*, CH), 3.4 (3H, *s*, CH<sub>3</sub>), 2.9 (3H×2, *s*, –N(CH<sub>3</sub>)<sub>2</sub>), 2.3 (2H, *s*, CH<sub>2</sub>).

3-(4-Hydroxy-3-methylphenyl)-5-phenyl-2-pyrazoline (**H<sub>IV</sub>**). IR (KBr, cm<sup>-1</sup>) 3307 (OH), 1590 (C=N), 1320 (C–N); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.5 (1H, *s*, OH), 7.3–7.8 (8H, *m*, aromatic), 5.54 (1H, *s*, NH), 4.24 (1H, *s*, CH), 3.4 (3H, *s*, CH<sub>3</sub>), 2.3 (2H, *s*, CH<sub>2</sub>).

5-(3,4-Dimethoxyphenyl)-3-(4-hydroxy-3-methylphenyl)-2-pyrazoline (**H<sub>V</sub>**). IR: (KBr, cm<sup>-1</sup>) 3310 (OH), 1590 (C=N), 1320 (C–N); <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub> ppm): 9.2 (1H, *s*, OH), 7.0–7.8 (6H, *m*, aromatic), 5.50 (1H, *s*, NH), 4.24 (1H, *s*, CH), 3.7 (6H, *s*, 2×OCH<sub>3</sub>), 3.4 (3H, *s*, CH<sub>3</sub>), 2.3 (2H, *s*, CH<sub>2</sub>).

3-(4-Hydroxy-3-methylphenyl)-5-(3,4,5-trimethoxyphenyl)-2-pyrazoline (**H<sub>VI</sub>**). IR: (KBr  $\text{cm}^{-1}$ ) 3307 (OH), 1596 (C=N), 1320 (C-N);  $^1\text{H-NMR}$  (DMSO- $d_6$  ppm): 9.5 (1H, s, OH), 7.3–7.8 (5H, m, aromatic), 5.48 (1H, s, NH), 4.24 (1H, s, CH), 3.6 (9H, s,  $3\times\text{OCH}_3$ ), 3.4 (3H, s,  $\text{CH}_3$ ), 2.3 (2H, s,  $\text{CH}_2$ ).

5-(2-Furyl)-3-(4-hydroxy-3-methylphenyl)-2-pyrazoline (**H<sub>VII</sub>**). IR: (KBr  $\text{cm}^{-1}$ ) 3317 (OH), 1590 (C=N), 1320 (C-N);  $^1\text{H-NMR}$  (DMSO- $d_6$  ppm): 9.2 (1H, s, OH), 7.3–7.8 (3H, m, aromatic), 7.8–8.2 (3H, m, furan), 5.52 (1H, s, NH), 4.20 (1H, s, CH), 3.42 (3H, s,  $\text{CH}_3$ ), 2.3 (2H, s,  $\text{CH}_2$ ).

5-(4-Fluorophenyl)-3-(4-hydroxy-3-methylphenyl)-2-pyrazoline (**H<sub>VIII</sub>**). IR: (KBr  $\text{cm}^{-1}$ ) 3312 (OH), 1590 (C=N), 1320 (C-N), 700 (C-F);  $^1\text{H-NMR}$  (DMSO- $d_6$  ppm): 9.4 (1H, s, OH), 7.3–7.8 (7H, m, aromatic), 5.42 (1H, s, NH), 4.24 (1H, s, CH), 3.4 (3H, s,  $\text{CH}_3$ ), 2.3 (2H, s,  $\text{CH}_2$ ).

5-(2-Chlorophenyl)-3-(4-hydroxy-3-methylphenyl)-2-pyrazoline (**H<sub>IX</sub>**). IR: (KBr  $\text{cm}^{-1}$ ) 3306 (OH), 1586 (C=N), 1320 (C-N), 774 (C-Cl);  $^1\text{H-NMR}$  (DMSO- $d_6$  ppm): 9.5 (1H, s, OH), 7.6–8.2 (7H, m, aromatic), 5.50 (1H, s, NH), 4.24 (1H, s, CH), 3.4 (3H, s,  $\text{CH}_3$ ), 2.3 (2H, s,  $\text{CH}_2$ ).

5-(2,6-Dichlorophenyl)-3-(4-hydroxy-3-methylphenyl)-2-pyrazoline (**H<sub>X</sub>**). IR: (KBr  $\text{cm}^{-1}$ ) 3317 (OH), 1594 (C=N), 1320 (C-N), 770 (C-Cl);  $^1\text{H-NMR}$  (DMSO- $d_6$  ppm): 9.5 (1H, s, OH), 7.3–7.8 (6H, m, aromatic), 5.54 (1H, s, NH), 4.24 (1H, s, CH), 3.4 (3H, s,  $\text{CH}_3$ ), 2.3 (2H, s,  $\text{CH}_2$ ).

3-(4-Hydroxy-3-methylphenyl)-5-(3-nitrophenyl)-2-pyrazoline (**H<sub>XI</sub>**). IR: (KBr  $\text{cm}^{-1}$ ) 3307 (OH), 1590 (C=N), 1320 (C-N);  $^1\text{H-NMR}$  (DMSO- $d_6$  ppm): 9.4 (1H, s, OH), 7.8–8.4 (7H, m, aromatic), 5.56 (1H, s, NH), 4.20 (1H, s, CH), 3.2 (3H, s,  $\text{CH}_3$ ), 2.7 (2H, s,  $\text{CH}_2$ ).

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## ИЗВОД

### СИНТЕЗА И АНТИМИКОБАКТЕРИЈСКА АКТИВНОСТ НОВИХ ХЕТЕРОЦИКЛА

M. SHAHAR YAR, A. AHMAD SIDDIQUI и ASHRAF ALI

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard (Hamdard University), New-Delhi-110062, India

Кондензацијом 4-хидрокси-3-метил-ацетофенона са различитим ароматичним алдехидима у метанолном раствору КОН добијени су одговарајући халкони (**C<sub>I</sub>**–**C<sub>XI</sub>**). Реакцијом ових халкона са хидразин-хидратом у етанолу добијени су деривати пиразолина (**H<sub>I</sub>**–**H<sub>XI</sub>**). Нови синтетизовани хетероцикли окарактерисани су према својим хемијским својствима и спектроскопским подацима. Испитивана је антимикобактеријска активност нових синтетизованих једињења према *Mycobacterium tuberculosis* H37<sub>Rv</sub>.

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