CHAPTER - 3

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SOME NEW 1, 3, 5 - TRISUBSTITUTED - 2 - PYRAZOLINES
3.1 LITERATURE REVIEW

Pyrazole is a π-excessive aromatic monocyclic heterocycle containing two nitrogen atoms in a five membered 1,2-diazole ring. It was in the late nineteenth century that Fischer and Knovenagel described the reaction of acrolein with phenylhydrazine\(^1\) to provide a 2-pyrazoline type compound (117). Their experiment seems to be the first example of pyrazoline formation by the reaction of an \(\alpha, \beta\)-enone with a hydrazine derivative. Later, Auwers \textit{et al.}\(^2,3\) corroborated that the product of this reaction was 1-phenyl 2-pyrazoline. During the last century, after these pioneering studies, numerous 2-pyrazolines were synthesized by the reaction of \(\alpha, \beta\)-enones with hydrazines. This simple and convenient procedure has remained one of the most popular method for the preparation of 2-pyrazolines.

Pyrazoles exhibit aromatic character with properties resembling those of both pyrrole and pyridine. 1-pyrazoline, 2-pyrazoline and 3-pyrazoline are the three partially reduced forms of the pyrazole structure with different positions of the double bonds and exists in equilibrium one with the other (Scheme 19). 2-pyrazoline exhibits the
monoimino character and hence more stable than the rest even though all the three types have been synthesized.\(^4\)

![Scheme 19](image1.png)

**Scheme 19.** All the three partially reduced forms of pyrazoline

Pyrazole is feebly basic and forms salts with inorganic acids. The imino hydrogen may be replaced by an acyl group. Pyrazole is very resistant to oxidation and reduction, but may be hydrogenated catalytically, first to pyrazoline and then to pyrazolidine (Scheme 20). Both of these compounds are stronger bases than pyrazole.

![Scheme 20](image2.png)

**Scheme 20**

Pyrazoline derivatives differ considerably in their properties from those of pyrazole, owing to their much lower stability. The pyrazolines give the reactions of aliphatic derivatives, resembling unsaturated compounds in their behavior towards permanganate and nascent hydrogen. They resemble hydrazones in the manner in which they are hydrolyzed by mineral acids, and aldazines in their decomposition into gaseous nitrogen and nitrogen-free substances. Pyrazoline and its homologues are weak bases. In general they only dissolve in
concentrated acids, forming unstable salts which dissociate on the addition of water. The parent substance, pyrazoline, an oil of boiling point 114°C, is the most stable of all these compounds. The pyrazolidines possess strong reducing properties and readily give up hydrogen to form pyrazolines.

**GENERAL METHODS OF SYNTHESIS OF PYRAZOLINES:**

1. α, β-unsaturated carboxylic acid esters reacts with diazomethane to give 2-pyrazolines. The mechanism of this reaction was correctly anticipated by Pechmann in which the primary product of this reaction is a 1-pyrazoline, formed by 1,3-dipolar cycloaddition, which spontaneously isomerizes into its thermodynamically more stable 2-pyrazoline isomer by a 1,3-H shift (Scheme 21).

\[ \text{Scheme 21} \]

2. Benzylideneacetone on reaction with diazomethane by 1,3-dipolar cycloaddition yield 2-pyrazolines (Scheme 22). This is probably the first example of the synthesis of a pyrazoline from the reaction of an α,β-unsaturated ketone and diazomethane and was published by Azzarello in 1906. Later, this reaction was reinvestigated by Smith and Howard and by Raju and Rao and the assumption made by Azzarello were corroborated.
3. 1,3-Dipolar cycloaddition of chalcones and diazomethane was first investigated by Smith and Pings and 3-benzoyl-4-phenyl-1-pyrazoline was prepared as a primary product which was then isomerized into the 3-benzoyl-4-phenyl-2-pyrazoline on gentle heating (Scheme 23).

4. The reaction of 2-arylidene-3-phenyl-1-indanones with diazomethane performed by Mustafa and Hilmy can be considered as the first example of pyrazoline formation by the cycloaddition of an exocyclic α,β-unsaturated ketone and diazomethane (Scheme 24).
5. α,β-unsaturated aldehydes or ketones do react with phenylhydrazine to form hydrazones as intermediates. These hydrazone intermediates on treatment with acetic acid or hydrochloric acid in ethanol isomerizes to Δ²-pyrazolines. The reaction scheme is given below (Scheme 25).
6. Pijewska et al.\textsuperscript{11,12} studied the reaction of 3-arylideneflavanones and diazomethane to yield pyrazolines. The structure and stereochemistry of the pyrazolines formed have been elucidated by various NMR techniques. This detailed spectroscopic investigation\textsuperscript{13-16} unambiguously proved that the (E) isomers of flavanones provided trans-spiro-1-pyrazolines, which were then isomerized to trans-spiro-2-pyrazolines (Scheme 26).
7. Mannich bases on reaction with phenylhydrazine and aqueous ethanolic NaOH at reflux temperature yield substituted 2-pyrazolines\(^{17}\) (Scheme 27).

\[ \text{Ph}_1\text{COCH}_2\text{CH}_2\text{NR}^1\text{R}^2 + \text{Ph}_2\text{NHNH}_2 \xrightarrow{\text{NaOH}} \]

**Scheme 27**

8. The synthesis of tricyclic 2-pyrazolines by an intramolecular 1,3-dipolar cycloaddition of nitrile imines is well documented in the literature.\(^{18-20}\) 2, 3, 3\(^a\), 4-tetrahydro- 2-aryl [1] benzopyrano [4,3-c] pyrazolines have been prepared by the intramolecular 1,3-dipolar cycloaddition of nitrile imines generated either from 1-(o-allyloxyphenyl)- N-(arylhydrazidoyl) chloride on treatment with triethyl amine or by the irradiation of 2-aryl-5-(o-allyloxyphenyl) tetrazole (Scheme 28).
9. The reaction of chalcones with hydrazines is probably the most popular procedure for the synthesis of 2-pyrazolines. The most commonly used method is the reaction of hydrazine and the chalcones in acetic acid solution to prepare 2-pyrazolines in high yield\textsuperscript{21-23} (Scheme 29). This method is used with or without the isolation of the hydrazone intermediate. Synthesis of 2-pyrazolines can also be achieved under alkaline conditions by using pyridine as catalyst in ethanolic solution\textsuperscript{24}. In some cases the two reactants were refluxed in alcoholic solution without a catalyst to provide 2-pyrazolines\textsuperscript{25,26}. 

**Scheme 28**
10.2-aryl carbonyl ethylthiosulfates when heated with two equivalents of phenyl hydrazine in water for 0.5-3 hours under reflux yield 1-phenyl-3-aryl-2-pyrazolines27 (Scheme 30).

Scheme 30

11.1,2-disubstituted hydrazine react with formalin and a carbonyl compound (Hinmann synthesis) to yield pyrazolines28 (Scheme 31).
12. Cycloaddition reaction of substituted styrenes with \( p \)-anisyldiazo methane at low temperature yield \textit{trans}-3, 5-bis-(\( p \)-anisyl)-1-pyrazoline\(^{29}\) (Scheme 32).
SPECTRAL FEATURES OF PYRAZOLINES:

NMR SPECTRA OF PYRAZOLINES:

A pyrazoline ring is identified by characteristic spectral features\(^{30}\) in its \(^1\)H NMR spectrum. The three protons in the pyrazoline ring (118) will show AMX splitting pattern, \(H_A\) proton appearing at \(\delta 2.98\) (dd), \(J_{AM} = 7.6\) Hz and \(J_{AX} = 12\) Hz, \(H_M\) proton resonating at \(\delta 3.64\) (dd), \(J_{AM} = 12\) Hz and \(J_{MX} = 12\) Hz and \(H_X\) proton appearing at \(\delta 5.2\) (dd), \(J_{AX} = 7.6\) Hz and \(J_{MX} = 12\) Hz.

![Pyrazoline Ring](image)

(118)

MASS SPECTRA OF PYRAZOLINES:

Sržić \textit{et al.}\(^{31}\) studied the fragmentation pathway of 1,3-diphenyl-2-pyrazoline employing ion kinetic energy spectrometry (IKES) and mass analyzed ion kinetic energy spectrometry (MIKES) of the native compound and specifically of isotope (\(^2\)H, \(^{13}\)C, \(^{15}\)N) labelled compounds, combined with high resolution mass determinations. The results clearly demonstrated that the large majority of cleavages had the molecular ion as their precursor.

Sayed \textit{et al.}\(^{32}\) studied the mass spectrometric fragmentations of the 3, 5-bisaryl-2-pyrazoline derivatives by high resolution mass spectrometry. The observed ions may be arranged in three main
groups according to their assumed mechanistic formation, \textit{viz.} (a) by 1,2-elimination processes (\textbf{Scheme 33}), (b) by $\alpha$-cleavage (\textbf{Scheme 34}) and (c) by assumed cyclo-reversion (\textbf{Scheme 35}).

In 1, 2-elimination, as given below, molecular hydrogen and one aryl substituent as anisole were lost from the molecular ion.

\textbf{Scheme 33.} Mass fragmentation of 3, 5- disubstituted 2-pyrazoline involving 1, 2-elimination process
The α-cleavage involves the radical loss of the N-1 substituent and this cleavage may be rationalized as one electron transfer with and without hydrogen transfer in either direction initiated by cation radical locations somewhere in the Ar-C=N-N-π orbital system.

**Scheme 34.** Mass fragmentation of 3,5- disubstituted 2-pyrazoline involving α-cleavage
A cyclo-reversion process involves the cleavage of the pyrazoline ring structure and gives rise to a majority of the middle to low mass range fragments.

Scheme 35. Mass spectral fragmentation of substituted 2-pyrazolines involving cyclo-reversion
BIOLOGICAL ACTIVITIES OF 2-PYRAZOLINES:

The pyrazoline nucleus is a ubiquitous feature of various compounds possessing many pharmacological and physiological activities and therefore they are useful materials in drug research. It was reported in the literature that different substituted 2-pyrazolines possess antimicrobial, anti-inflammatory, analgesic, antipyretic, antidepressant, antitubercular, antiamoebic, anthelmintic, anticonvulsant, antihypertensive, antidiabetic, antitumor, anti-HIV, local anaesthetic, antioxidant, insecticidal and tranquilizing activities. Given below is a brief account of various modifications reported on 2-pyrazoline nucleus, which showed a variety of biological and pharmacological activities.

Antimicrobial activity:

Deshmukh et al.\textsuperscript{33} synthesized chloro substituted $\Delta^2$-pyrazolines (119) that showed antibacterial activity when assayed against some human pathogens.
Sim et al.\textsuperscript{34} synthesized 1-acyl-3-naphthyl-5-substitutedphenyl-2- pyrazolines (120); the antimicrobial activity of these compounds was determined by using ampicillin and clotrimazole as standards.

\begin{center}
\includegraphics[width=0.5\textwidth]{120}
\end{center}

(120)

Desai et al.\textsuperscript{35} synthesized 1H-3-(2-hydroxy-3-nitro-5-methylphenyl)-5-aryl-2-pyrazolines (121) that exhibited antimicrobial activity against \textit{S. aureus} and \textit{E. coli}.

\begin{center}
\includegraphics[width=0.5\textwidth]{121}
\end{center}

(121)

Roda et al.\textsuperscript{36} synthesized 5-aryl-1-phenyl-3-(3-isopropyl-4-hydroxy-6-methyl phenyl)-2-pyrazolines (122); these were tested for antimicrobial activity.
Davood et al.\textsuperscript{37} synthesized 3,5-dinaphthalene-1-yl-substituted \textsuperscript{-2}-pyrazolines (123) that showed antibacterial activity.

Saundane et al.\textsuperscript{38} synthesized a novel substituted 2-pyrazoline (124), which was screened for antimicrobial activity against \textit{S. aureus}, \textit{E. coli} and \textit{A. niger}.
Naik et al.\textsuperscript{39} synthesized 3-(2-hydroxy-5-methyl-4,6-dibromophenyl)-5-(substituted phenyl)-2-pyrazolines (125) possessing antibacterial activity.

\[
\begin{align*}
\text{R} = \text{Ph, C}_6\text{H}_4X & \\
\text{R}_1 = \text{Me, Ph}
\end{align*}
\]

(125)

Karthikeyan et al.\textsuperscript{40} synthesized 1-aryloxy-3-aryl-5-hydroxy-5-arylpyrazolines (126) which showed very good antimicrobial activity.

\[
\begin{align*}
\text{R} = \text{H, OCH}_3, \text{CN} & \\
\text{R}_1 = \text{Cl, CH}_3
\end{align*}
\]

(126)

Thakare et al.\textsuperscript{41} synthesized 3-coumaryl-4-aroyl-5-aryl-2-pyrazolines (127) that showed antimicrobial activity against pathogenic bacteria.
Balakrishna, et al. synthesized 1-nicotinoyl-3,5-diaryl-5-hydroxy-2-pyrazolines (128) that showed significant antimicrobial activity.

Akbas et al. reported the synthesis of some new 1H-pyrazole-3-carboxylic acids (129) and evaluated for their antibacterial activities against Bacillus cereus 7064, Staphylococcus aureus ATCC 6538, Escherichia coli ATCC 4230 and Pseudomonas putida using tube dilution method. The minimal inhibitory concentration (MIC)
experiments revealed that all the compounds showed inhibitory effects on the growth of the test microorganisms.

\[
\begin{align*}
\text{O} & \quad \text{COOH} \\
\text{Ph} & \quad \downarrow \\
\text{Ph} & \quad \downarrow \\
\text{R} & \quad \downarrow
\end{align*}
\]

(129)

**Anti-inflammatory, Analgesic and Antipyretic activities:**

Gurar *et al.*\(^{44}\) synthesized 1-aryl -2-pyrazolines (130) exhibiting anti-inflammatory and analgesic activity.

\[
\begin{align*}
\text{N} & \quad \text{H} \quad \text{Y} \\
\text{N} & \quad \downarrow \\
\text{R} & \quad \downarrow
\end{align*}
\]

(130)

R = CF\(_3\), H, Me, CH\(_2\)Ph, Ph
Y = CSNH\(_R\), CSNH\(_2\), =CHR\(_1\)

Manna *et al.*\(^{45}\) synthesized N-acetyl-\(\Delta^2\)-pyrazolines (131) that showed anti-inflammatory, analgesic and antipyretic activities.

\[
\begin{align*}
\text{OH} & \quad \text{R} & \quad \text{R'} \\
\text{N} & \quad \text{NAc} & \quad \downarrow \\
\end{align*}
\]

(131)
Huang et al. synthesized 1-arylalkoxy and 1-arylalkyl thioaryl-2-pyrazolines (132) that showed anti-inflammatory and antiallergic activity.

\[
\text{PhCH}_2\text{O} \quad \text{N} \\text{N} \\text{NH}_2
\]

(132)

Fredrick et al. synthesized 3-N-substituted amino-1-[3-(trifluoromethyl) phenyl]-2-pyrazolines (133) which showed anti-inflammatory activity.

\[
\text{RHN} \quad \text{N} \quad \text{N} \quad \text{CF}_3
\]

R = H, Me, Pro, Bu, PhMe, 2-butenyl

(133)

Bansal et al. synthesized 1-acetyl-5 (substitutedaryl)-3-(β-aminonaphthyl)-2-pyrazolines (134) exhibiting anti-inflammatory activity against standard drugs phenyl butazone and indomethacin.
Amir et al.\textsuperscript{49} synthesized 3,5-disubstituted pyrazolines (135), which showed analgesic activity.

![Chemical structure](image1)

(135)

Gursoy et al.\textsuperscript{50} reported the synthesis of some novel pyrazolines (136) possessing analgesic activity on acetic acid induced writhing. The analgesic activity was superior to that of antipyrine and aminopyrine.

![Chemical structure](image2)

(136)

**Antidepressant activity:**

Palaska et al.\textsuperscript{51,52} synthesized 1,3,5-triphenyl-2-pyrazolines (137) and these compounds showed significant antidepressant activity when compared to the standard antidepressant drugs clomipramine and tranylcypromine.
Prasad et al.\textsuperscript{53} synthesized 1, 3, 5-triphenyl-2-pyrazolines (138) and 3-(2′-hydroxynaphthalene-1″-yl)-1,5-diphenyl-2-pyrazolines (139) which showed significant antidepressant activity.
Nesrin et al. synthesized 1-N-substituted thiocarbamoyl-3-phenyl-5-thienyl-2-pyrazolines (140); these compounds showed antidepressant activity.

![Chemical Structure 140](image)

Palaska et al. prepared 3,5-diphenyl-2-pyrazolines (141) possessing antidepressant activity.

![Chemical Structure 141](image)

Prasad et al. synthesized 3-(3''-coumarinyl)-1, 5-diphenyl-2-pyrazolines (142) and 3-(2''-hydroxynaphthalen-1''-yl)-1, 5-diphenyl-2-pyrazolines (143) that showed significant antidepressant activity.
**Antitubercular activity:**

Kumar *et al.*\(^{57}\) synthesized substituted 2-pyrazolines (144) which showed antitubercular activity.

Babu *et al.*\(^{58}\) prepared 1, 3, 5-trisubstituted pyrazolines (145) having antitubercular activity.
Shaharyar et al. synthesized 1-N-nicotinyl-3-(4’-hydroxy-3’-methylphenyl)-5 [(sub) phenyl]-2-pyrazolines (146) showing antimycobacterial activity against *Mycobacterium tuberculosis*.

![Chemical structure](image)

R = phenyl, 4-methoxyphenyl, 4-chlorophenyl

(146)

**Antiamoebic activity:**

Budakoti et al. synthesized 1-N-substituted thiocarbamoyl-3, 5-diphenyl-2-pyrazolines (147) which exhibited better antiamoebic activity than the standard drug metronidazole.

![Chemical structure](image)

R = 2- adamantylamino, 4- methylpiperidino

(147)

Abid et al. synthesized 1-N-substituted thiocarbamoyl-3-phenyl-2-pyrazolines (148) having antiamoebic activity when tested against standard drug metronidazole.
Abid et al. synthesized 1-(thiazolo [4,5-b] quinoxaline-2-yl)-3-phenyl-2-pyrazolines (149) and thiocarboxamide-3-phenyl-2-pyrazolines (150), which showed antiamoebic activity.
**Insecticidal and Herbicidal activities:**

Grosscurt *et al.* synthesized 3,4-diphenyl-1-phenylcarbamoyl-2-pyrazolines (151) possessing insecticidal activity.

![Chemical structure](151)

Sirrenberg *et al.* synthesized phenylcarbamoyl-2-pyrazolines (152) having insecticidal activity.

![Chemical structure](152)

Rolf *et al.* synthesized 1-phenylcarbamoyl-2-pyrazolines (153) and 3, 5-diphenyl-1-phenylcarbamoyl-2-pyrazolines (154) which showed insecticidal properties.

![Chemical structure](153)
Kobus et al.\textsuperscript{66} synthesized 1-phenylcarbamoyl-2-pyrazolines (155) and 3-phenyl-1-phenylcarbamoyl-2-pyrazolines (156) having insecticidal activity.

Kiyomi et al.\textsuperscript{67} synthesized 3-difluoromethoxyphenyl-1-phenylcarbamoyl-2-pyrazolines (157) that showed insecticidal activity.
Jac \textit{et al.}\textsuperscript{68} synthesized 2-pyrazolines (158) and screened for their herbicidal activity. All the compounds showed good to moderate activity.

\[ \begin{array}{c}
\text{R}^1 \text{R}^2 \\
\text{N} \begin{array}{c}
\text{N} \\
\text{CONHSO}_2
\end{array} \\
\text{Ph}
\end{array} \]

(158)

Vergiya \textit{et al.}\textsuperscript{69} synthesized 3,5-diaryl-1-phenyl/isonicotinoyl-2-pyrazolines (159) exhibiting herbicidal activities.

\[ \begin{array}{c}
\text{HO} \\
\text{Br} \\
\text{Br} \\
\text{Br} \\
\text{N}
\end{array} \\
\begin{array}{c}
\text{Ph} \\
\text{CONHSO}_2 \\
\text{Ph}
\end{array} \\
\text{OMe}
\]

(159)
Miscellaneous activities:

Nawal et al.\textsuperscript{70,71} synthesized some new 2-pyrazolines \((160-162)\) exhibiting mollucidal activity.

\begin{align*}
\text{N} & \quad \text{N} \\
\text{R} & \quad \text{R}^1 \\
\text{X} & = \quad \text{NHR}^2 \\
\end{align*}

\((160)\)

\begin{align*}
\text{N} & \quad \text{N} \\
\text{R} & \quad \text{R}^1 \\
\text{R}^2 & / \\
\end{align*}

\((161)\)

\begin{align*}
\text{N} & \quad \text{N} \\
\text{R} & \quad \text{R}^1 \\
\text{Ac} & / \\
\end{align*}

\((162)\)

Soliman et al.\textsuperscript{72} prepared 3,5-diarylpyrazoline sulfonylurea derivatives \((163)\) having antidiabetic activity.

\begin{align*}
\text{N} & \quad \text{N} \\
\text{R} & \quad \text{R}^1 \\
\text{Z} & = \quad \text{Y} \\
\text{SO}_2\text{NHCXNHR} & = \quad \text{Me}, \text{cyclohexyl}, \text{Ph} \\
\text{X} & = \quad \text{O}, \text{S} \\
\text{Y} & = \quad \text{H}, \text{Cl}, \text{Br}, \text{Me} \\
\text{z} & = \quad \text{H}, \text{Me} \\
\end{align*}

\((163)\)

Tripathi et al.\textsuperscript{73} synthesized substituted 2-pyrazoline derivatives \((164)\) that showed hypoglycemic activity.
Archana et al.\textsuperscript{74} prepared 1-acetyl-5-aryldenyl-3-(2’-oxo/thiobarbituinyl)-2-pyrazolines \textbf{(165)} that showed anticonvulsant activity.

\begin{center}
\includegraphics[width=0.5\textwidth]{165.png}
\end{center}

\textbf{(165)}

Pandey et al.\textsuperscript{75} synthesized 1, 3-disubstituted-5-(2-arylindol-3-yl-)\(\Delta^2\)-pyrazolines \textbf{(166)} which exhibited CNS depressant activity.

\begin{center}
\includegraphics[width=0.5\textwidth]{166.png}
\end{center}

\textbf{(166)}

Malhotra et al.\textsuperscript{76} synthesized substituted pyrazolines \textbf{(167)} possessing cardiovascular activity.

\begin{center}
\includegraphics[width=0.5\textwidth]{167.png}
\end{center}

\textbf{(167)}
Alleheiligen et al.\textsuperscript{77} synthesized 3-phenyl-2-pyrazolines (168) which are used in the treatment of cardiovascular and thromboembolic diseases.

![Chemical Structure of 168](image1)

Marayam et al.\textsuperscript{78} synthesized 1-(2-thiazolyl)-3,5-disubstituted-2-pyrazolines (169) exhibiting antihypertensive activity when compared with clonidine as standard.

![Chemical Structure of 169](image2)
Shivarama et al.\textsuperscript{79} synthesized aryl-furyl $\Delta^2$-pyrazolines (170) that showed anthelmintic activity.

\begin{center}
\includegraphics[width=0.8\textwidth]{170.png}
\end{center}

(170)

Suthakaran et al.\textsuperscript{80} synthesized 7-methoxybenzofuran-2-pyrazolines (171) which showed antioxidant activity.

\begin{center}
\includegraphics[width=0.8\textwidth]{171.png}
\end{center}

(171)

Sook et al.\textsuperscript{81} synthesized 3, 5-diarylpyrazolines (172) which showed antioxidant activity and was found as an inhibitor of LDL oxidation.

\begin{center}
\includegraphics[width=0.8\textwidth]{172.png}
\end{center}

(172)
Therapeutically important drugs \(^{82-85}\) containing pyrazole or pyrazoline moiety along with their structures are given below:

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ACTIVITY</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Celecoxib" /></td>
<td>NSAID</td>
</tr>
<tr>
<td>Celecoxib (173)</td>
<td></td>
</tr>
<tr>
<td><img src="image" alt="Phenylbutazone" /></td>
<td>NSAID</td>
</tr>
<tr>
<td>Phenylbutazone (174)</td>
<td></td>
</tr>
<tr>
<td><img src="image" alt="Oxyphenbutazone" /></td>
<td>NSAID</td>
</tr>
<tr>
<td>Oxyphenbutazone (175)</td>
<td></td>
</tr>
<tr>
<td><img src="image" alt="Antipyrine" /></td>
<td>Analgesic</td>
</tr>
<tr>
<td>Antipyrine (176)</td>
<td></td>
</tr>
<tr>
<td>DRUG</td>
<td>ACTIVITY</td>
</tr>
<tr>
<td>-----------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Aminopyrine (177)</td>
<td>Analgesic, Antipyretic</td>
</tr>
<tr>
<td>Dipyrone (178)</td>
<td>Analgesic, Antipyretic, Antirheumatic</td>
</tr>
<tr>
<td>Allopurinol (179)</td>
<td>Treatment of gout</td>
</tr>
<tr>
<td>Muzolimine (180)</td>
<td>Diuretic</td>
</tr>
<tr>
<td><strong>DRUG</strong></td>
<td><strong>ACTIVITY</strong></td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Stanozolol (181)</td>
<td>Anabolic and Androgenic activity</td>
</tr>
<tr>
<td>Amaranth (182)</td>
<td>Used in ulcerative colitis</td>
</tr>
<tr>
<td>7-Amino-5-nitroindazole (183)</td>
<td>Antibacterial</td>
</tr>
<tr>
<td>5,7-Dinitroindazole (184)</td>
<td>Antibacterial</td>
</tr>
<tr>
<td>DRUG</td>
<td>ACTIVITY</td>
</tr>
<tr>
<td>------</td>
<td>----------</td>
</tr>
<tr>
<td><img src="image" alt="Chemical Structure" /> Zaleplon (185)</td>
<td>Hypnotic and Sedative</td>
</tr>
</tbody>
</table>
3.2 EXPERIMENTAL WORK

**Aims and objectives:**

It is evident from the literature that 2-pyrazolines and their derivatives possess important biological activities. A number of 1, 3, 5-trisubstituted-2-pyrazolines earlier synthesized in our laboratory possessed significant anti-inflammatory, analgesic and antimicrobial activities and in continuation of that work it is aimed to synthesize some more new substituted 1, 3, 5-trisubstituted-2-pyrazolines.

1. To condense the chalcones described in Chapter-1 with Phenylhydrazine hydrochloride in absolute ethanol to obtain 2-pyrazolines and to purify these 2-pyrazolines by chromatographic and crystallization methods.

2. To characterize the compounds using spectral (IR, ¹H NMR and Mass) methods and Elemental analysis. The data related to structural characterization are given in the form of tables.

3. To screen the synthesized 2-pyrazolines for their toxicity and possible biological activities like anti-inflammatory, analgesic, antibacterial and antifungal activities.

4. To identify the active compounds for further exploitation.
**Materials and Methods:**

The same chemicals, solvents, procedures and instruments that were mentioned in chapter-1 were also used here. Phenylhydrazine hydrochloride used in the synthesis was purchased from Merck, Mumbai. The chalcones that were used in the reaction with phenylhydrazine hydrochloride were prepared from 3'-methyl- 4'-hydroxyacetophenone as described in chapter-1.

**General Procedure for the synthesis of 1, 3, 5- trisubstituted- 2-pyrazolines**

The chalcones were condensed with phenylhydrazine in absolute ethanol in the presence of pyridine at reflux temperature (2 to 6 hours). The solvent was completely evaporated and the residue was poured into ice cold water, which resulted in the formation of the corresponding 2-pyrazolines (Scheme 36). Reaction completion was identified by TLC using silica gel - G. After completion of the reaction, the reaction mixture was poured into crushed ice with constant stirring. The separated solid was filtered and dried. It was purified by column chromatography on silica gel, using ethyl acetate and hexane mixture as the mobile phase. After purification, the 2-pyrazolines were obtained as light or bright coloured powders.
The chalcones that were used in the synthesis of 2-pyrazolines:

1. 1-(3’-methyl -4’-hydroxyphenyl)-3-(2”-pyridinyl)-2-propen-1-one (B₁)
2. 1-(3’-methyl -4’-hydroxyphenyl)-3-(3”-pyridinyl)-2-propen-1-one (B₂)
3. 1-(3’-methyl -4’-hydroxyphenyl)-3-(4”-pyridinyl)-2-propen-1-one (B₃)
4. 1-(3’-methyl -4’-hydroxyphenyl)-3-(2”-furyl)-2-propen-1-one (B₄)
5. 1-(3’-methyl -4’-hydroxyphenyl)-3-(2”-pyrrolyl)-2-propen-1-one (B₅)
6. 1-(3’-methyl -4’-hydroxyphenyl)-3-(2”-thienyl)-2-propen-1-one (B₆)
7. 1-(3’-methyl -4’-hydroxyphenyl)-3-(2”-indolyl)-2-propen-1-one (B₇)
8. 1-(3’-methyl -4’-hydroxyphenyl)-3-(2”-quinolinyl)-2-propen-1-one (B₈)
9. 1-(3’-methyl -4’-hydroxyphenyl)-3-(9”-anthracenyl)-2-propen-1-one (B₉)
10. 1-(3’-methyl -4’-hydroxyphenyl)-3-(4”-fluorophenyl)-2-propen-1-one (B₁₀)
11. 1-(3’-methyl -4’-hydroxyphenyl)-3-(4”-chlorophenyl)-2-propen-1-one (B₁₁)
12. 1-(3’-methyl -4’-hydroxyphenyl)-3-(4”-bromophenyl)-2-propen-1-one (B₁₂)
13. 1-(3’-methyl -4’-hydroxyphenyl)-3-(4”-methylphenyl)-2-propen-1-one (B₁₃)
14. 1-(3’-methyl -4’-hydroxyphenyl)-3-(4”-methoxyphenyl)-2-propen-1-one (B₁₄)
15. 1-(3’-methyl -4’-hydroxyphenyl)-3-(3”, 4”, 5”-trimethoxyphenyl)-2-propen-1-one (B₁₅)

![Scheme 36](image)
Where Ar =

B₁
B₂
B₃
B₄
B₅
B₆
B₇
B₈
B₉
B₁₀
B₁₁
B₁₂
B₁₃
B₁₄
B₁₅
Procedure:

**Synthesis of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-pyridinyl)-2-pyrazoline (B$_1$PY$_1$):**

1-(3’-methyl -4’-hydroxyphenyl)-3-(2''-pyridinyl)-2-propen-1-one (B$_1$) (0.001 mol) was condensed with phenylhydrazine hydrochloride (0.001 mol) in the presence of pyridine (0.002 mol) in absolute ethanol (5 ml) at reflux temperature on a water bath for 2 to 6 hours. The solvent was evaporated *in vacuo* and crushed ice was added to the residue while mixing thoroughly, whereupon a bright yellow solid separated out. This solid was filtered under vacuum, dried and purified by column chromatography to give a pure pale yellow solid.

The **compound** B$_1$PY$_1$ was analyzed for molecular formula as C$_{21}$H$_{19}$N$_3$O, m.p. 208°C, supported by a [M+H]$^+$ ion at m/z 330 (Fig. 38).

The IR (KBr disc, cm$^{-1}$) spectrum (Fig. 36) showed the characteristic bands at 3406 (O–H), 1594 (C = N) and 1437 (CH=CH).

The $^1$H NMR spectrum (400 MHz, CDCl$_3$, Fig. 37) of compound B$_1$PY$_1$ showed the characteristic H$_A$, H$_M$ and H$_X$ protons at $\delta$ 3.05, 3.60 and 5.36 respectively as doublet of doublets (dd) with $J_{AM}$=16.5 Hz, $J_{AX}$=7.30 Hz and $J_{MX}$ = 9.5 Hz. The spectrum also accounted for all the 12 aromatic protons which appeared in between 6.79 – 8.15. A singlet at $\delta$ 2.31 integrating for 3 protons is due to the methyl group present on the aromatic ring.

The results of Elemental analysis were also in close agreement with those of the calculated values.
Based on the above spectral data and elemental analysis, the structure of the compound \( \text{B}_1\text{PY}_1 \) was confirmed as 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-pyridyl)-2-pyrazoline.

By adopting the above synthetic procedure, pyrazolines of 3'-methyl-4'-hydroxyacetophenone chalcones (Chapter–1) were synthesized and the physical and spectral characteristics of these new pyrazolines (\( \text{B}_1\text{PY}_1-\text{B}_{15}\text{PY}_{15} \)) were presented separately in detail.
The new 1, 3, 5-trisubstituted 2-pyrazolines synthesized:

1. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-pyridinyl)-2-pyrazoline (B₁PY₁)
2. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(3''-pyridinyl)-2-pyrazoline (B₂PY₂)
3. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-pyridinyl)-2-pyrazoline (B₃PY₃)
4. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-furyl)-2-pyrazoline (B₄PY₄)
5. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-pyrrolyl)-2-pyrazoline (B₅PY₅)
6. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-thienyl)-2-pyrazoline (B₆PY₆)
7. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-indolyl)-2-pyrazoline (B₇PY₇)
8. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-quinolinyl)-2-pyrazoline (B₈PY₈)
9. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(9''-anthracenyl)-2-pyrazoline (B₉PY₉)
10. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-fluorophenyl)-2-pyrazoline (B₁₀PY₁₀)
11. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-chlorophenyl)-2-pyrazoline (B₁₁PY₁₁)
12. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-bromophenyl)-2-pyrazoline (B₁₂PY₁₂)
13. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-methylphenyl)-2-pyrazoline (B₁₃PY₁₃)
14. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-methoxyphenyl)-2-pyrazoline (B₁₄PY₁₄)
15. 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(3'',4'',5''-trimethoxyphenyl)-2-pyrazoline (B₁₅PY₁₅)
Characterization of the new 1, 3, 5- trisubstituted-2-pyrazolines

Table 16. Physical characterization data of 1, 3, 5- trisubstituted-2-pyrazolines

![Chemical structure of 1, 3, 5-trisubstituted-2-pyrazolines]

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>Molecular Formula</th>
<th>Relative Molecular Mass (RMM)</th>
<th>Melting Point (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B₁PY₁</td>
<td>![Pyridine]</td>
<td>C₂₁H₁₉N₃O</td>
<td>329</td>
<td>208</td>
<td>78</td>
</tr>
<tr>
<td>B₂PY₂</td>
<td>![Pyrazine]</td>
<td>C₂₁H₁₉N₃O</td>
<td>329</td>
<td>213</td>
<td>75</td>
</tr>
<tr>
<td>B₃PY₃</td>
<td>![Pyridazine]</td>
<td>C₂₁H₁₉N₃O</td>
<td>329</td>
<td>202</td>
<td>77</td>
</tr>
<tr>
<td>B₄PY₄</td>
<td>![Oxazole]</td>
<td>C₂₀H₁₈N₂O₂</td>
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<td>187</td>
<td>72</td>
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<tr>
<td></td>
<td>Chemical Structure</td>
<td>Formula</td>
<td>MW 1</td>
<td>MW 2</td>
<td>MW 3</td>
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<td>-------</td>
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<tr>
<td>B₅PY₅</td>
<td><img src="image1.png" alt="Image" /></td>
<td>C₂₀H₁₉N₃O</td>
<td>317</td>
<td>243</td>
<td>70</td>
</tr>
<tr>
<td>B₆PY₆</td>
<td><img src="image2.png" alt="Image" /></td>
<td>C₂₀H₁₈N₂SO</td>
<td>334</td>
<td>205</td>
<td>76</td>
</tr>
<tr>
<td>B₇PY₇</td>
<td><img src="image3.png" alt="Image" /></td>
<td>C₂₄H₂₁N₃O</td>
<td>367</td>
<td>226</td>
<td>65</td>
</tr>
<tr>
<td>B₈PY₈</td>
<td><img src="image4.png" alt="Image" /></td>
<td>C₂₅H₂₁N₃O</td>
<td>379</td>
<td>216</td>
<td>68</td>
</tr>
<tr>
<td>B₉PY₉</td>
<td><img src="image5.png" alt="Image" /></td>
<td>C₃₀H₂₄N₂O</td>
<td>428</td>
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<tr>
<td>B₁₀PY₁₀</td>
<td><img src="image6.png" alt="Image" /></td>
<td>C₂₂H₁₉N₂FO</td>
<td>346</td>
<td>235</td>
<td>70</td>
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<tr>
<td>B₁₁PY₁₁</td>
<td><img src="image7.png" alt="Image" /></td>
<td>C₂₂H₁₉N₂ClO</td>
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<td>242</td>
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<tr>
<td>Chemical</td>
<td>Structure</td>
<td>Formula</td>
<td>Molar Mass</td>
<td>Crystal</td>
<td>Thermo</td>
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<td>------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>B_{12}PY_{12}</td>
<td>![Br]</td>
<td>C_{22}H_{19}N_{2}BrO</td>
<td>407</td>
<td>249</td>
<td>69</td>
</tr>
<tr>
<td>B_{13}PY_{13}</td>
<td>![CH3]</td>
<td>C_{23}H_{22}N_{2}O</td>
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<td>204</td>
<td>67</td>
</tr>
<tr>
<td>B_{14}PY_{14}</td>
<td>![OCH3]</td>
<td>C_{23}H_{22}N_{2}O_{2}</td>
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<td>220</td>
<td>66</td>
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<tr>
<td>B_{15}PY_{15}</td>
<td>![OCH3]</td>
<td>C_{25}H_{26}N_{2}O_{4}</td>
<td>418</td>
<td>255</td>
<td>72</td>
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Table 17. Elemental analysis data of 1, 3, 5-trisubstituted-2-Pyrazolines

<table>
<thead>
<tr>
<th>Compound</th>
<th>(% Calculated)</th>
<th>(% Found)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>C</td>
<td>H</td>
</tr>
<tr>
<td>B₁PY₁</td>
<td>76.57</td>
<td>5.81</td>
</tr>
<tr>
<td>B₂PY₂</td>
<td>76.57</td>
<td>5.81</td>
</tr>
<tr>
<td>B₃PY₃</td>
<td>76.57</td>
<td>5.81</td>
</tr>
<tr>
<td>B₄PY₄</td>
<td>75.40</td>
<td>5.67</td>
</tr>
<tr>
<td>B₅PY₅</td>
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<tr>
<td>B₆PY₆</td>
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<td>B₇PY₇</td>
<td>78.45</td>
<td>5.76</td>
</tr>
<tr>
<td>B₈PY₈</td>
<td>79.15</td>
<td>5.54</td>
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<tr>
<td>B₉PY₉</td>
<td>84.05</td>
<td>5.65</td>
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<tr>
<td>B₁₀PY₁₀</td>
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<td>B₁₁PY₁₁</td>
<td>72.80</td>
<td>5.20</td>
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<tr>
<td>B₁₂PY₁₂</td>
<td>64.86</td>
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</tr>
<tr>
<td>B₁₃PY₁₃</td>
<td>80.57</td>
<td>6.48</td>
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<tr>
<td>B₁₄PY₁₄</td>
<td>77.07</td>
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<tr>
<td>B₁₅PY₁₅</td>
<td>71.75</td>
<td>6.26</td>
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</table>
Table 18. IR spectral data of 1, 3, 5-trisubstituted-2-pyrazolines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Position of absorption band (cm(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>B(_1)PY(_1)</td>
<td>3406 (O-H), 1594 (C=N), 1494 (C=C Quadrant of Ar), 1437 (CH=CH)</td>
</tr>
<tr>
<td>B(_2)PY(_2)</td>
<td>3404 (O-H), 1595 (C=N), 1495 (C=C Quadrant of Ar), 1436 (CH=CH)</td>
</tr>
<tr>
<td>B(_3)PY(_3)</td>
<td>3405 (O-H), 1593 (C=N), 1496 (C=C Quadrant of Ar), 1435 (CH=CH)</td>
</tr>
<tr>
<td>B(_4)PY(_4)</td>
<td>3403 (O-H), 1596 (C=N), 1493 (C=C Quadrant of Ar), 1437 (CH=CH), 1205 (-C-O-)</td>
</tr>
<tr>
<td>B(_5)PY(_5)</td>
<td>3401 (O-H), 1594 (C=N), 1492 (C=C Quadrant of Ar), 1436 (CH=CH)</td>
</tr>
<tr>
<td>B(_6)PY(_6)</td>
<td>3406 (O-H), 1597 (C=N), 1495 (C=C Quadrant of Ar), 1435 (CH=CH), 690 (C-S)</td>
</tr>
<tr>
<td>B(_7)PY(_7)</td>
<td>3403 (O-H), 1596 (C=N), 1494 (C=C Quadrant of Ar), 1438 (CH=CH)</td>
</tr>
<tr>
<td>B(_8)PY(_8)</td>
<td>3407 (O-H), 1595 (C=N), 1492 (C=C Quadrant of Ar), 1437 (CH=CH)</td>
</tr>
<tr>
<td>B(_9)PY(_9)</td>
<td>3401 (O-H), 1597 (C=N), 1495 (C=C Quadrant of Ar), 1439 (CH=CH)</td>
</tr>
<tr>
<td>B(<em>{10})PY(</em>{10})</td>
<td>3405 (O-H), 1593 (C=N), 1491 (C=C Quadrant of Ar), 1439 (CH=CH), 1122 (C-F)</td>
</tr>
<tr>
<td>B_{11}PY_{11}</td>
<td>3403 (O-H), 1596 (C=N), 1496 (C=C Quadrant of Ar), 1438 (CH=CH), 853 (C-Cl)</td>
</tr>
<tr>
<td>B_{12}PY_{12}</td>
<td>3402 (O-H), 1594 (C=N), 1493 (C=C Quadrant of Ar), 1436 (CH=CH), 1024 (C-Br)</td>
</tr>
<tr>
<td>B_{13}PY_{13}</td>
<td>3409 (O-H), 1591 (C=N), 1492 (C=C Quadrant of Ar), 1433 (CH=CH)</td>
</tr>
<tr>
<td>B_{14}PY_{14}</td>
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</tr>
<tr>
<td>B_{15}PY_{15}</td>
<td>3401 (O-H), 1598 (C=N), 1495 (C=C Quadrant of Ar), 1438 (CH=CH), 1070 (-O-CH_{3})</td>
</tr>
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</table>
Table 19. $^1$H NMR spectral data of 1, 3, 5-trisubstituted-2-pyrazolines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical shift (δ) in ppm</th>
</tr>
</thead>
</table>
| B$_1$PY$_1$ | 3.05 (1H, dd, H$_A$)  
             | 3.60 (1H, dd, H$_M$)  
             | 5.36 (1H, dd, H$_X$)  
             | 2.31 (3H, s, C-3'-CH$_3$)  
             | 5.50 (1H, s, Ar-OH)  
             | 6.79 – 8.15 (12H, Ar-H) |
| B$_2$PY$_2$ | 3.15 (1H, dd, H$_A$)  
             | 3.90 (1H, dd, H$_M$)  
             | 5.40 (1H, dd, H$_X$)  
             | 2.31 (3H, s, C-3'-CH$_3$)  
             | 5.50 (1H, s, Ar-OH)  
             | 6.79 – 7.68 (12H, Ar-H) |
| B$_3$PY$_3$ | 3.25 (1H, dd, H$_A$)  
             | 3.75 (1H, dd, H$_M$)  
             | 5.40 (1H, dd, H$_X$)  
             | 2.31 (3H, s, C-3'-CH$_3$)  
             | 5.50 (1H, s, Ar-OH)  
             | 6.79 – 7.75 (12H, Ar-H) |
| B$_4$PY$_4$ | 3.15 (1H, dd, H$_A$)  
             | 3.85 (1H, dd, H$_M$)  
             | 5.30 (1H, dd, H$_X$)  
             | 2.31 (3H, s, C-3'-CH$_3$)  
             | 5.50 (1H, s, Ar-OH)  
             | 6.21 – 7.65 (11H, Ar-H) |
| B$_5$PY$_5$ | 3.20 (1H, dd, H$_A$)  
             | 3.79 (1H, dd, H$_M$)  
             | 5.30 (1H, dd, H$_X$)  
             | 2.31 (3H, s, C-3'-CH$_3$)  
             | 5.50 (1H, s, Ar-OH)  
<pre><code>         | 6.70 – 7.62 (12H, Ar-H) |
</code></pre>
<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical Shifts</th>
</tr>
</thead>
<tbody>
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<td>B&lt;sub&gt;6&lt;/sub&gt;PY&lt;sub&gt;6&lt;/sub&gt;</td>
<td>3.25 (1H, dd, H&lt;sub&gt;A&lt;/sub&gt;)</td>
</tr>
<tr>
<td></td>
<td>3.77 (1H, dd, H&lt;sub&gt;M&lt;/sub&gt;)</td>
</tr>
<tr>
<td></td>
<td>5.50 (1H, dd, H&lt;sub&gt;X&lt;/sub&gt;)</td>
</tr>
<tr>
<td></td>
<td>2.31 (3H, s, C-3'-CH&lt;sub&gt;3&lt;/sub&gt;)</td>
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<tr>
<td></td>
<td>5.50 (1H, s, Ar-OH)</td>
</tr>
<tr>
<td></td>
<td>6.89 – 7.67 (11H, Ar-H)</td>
</tr>
<tr>
<td>B&lt;sub&gt;7&lt;/sub&gt;PY&lt;sub&gt;7&lt;/sub&gt;</td>
<td>3.15 (1H, dd, H&lt;sub&gt;A&lt;/sub&gt;)</td>
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<tr>
<td></td>
<td>3.85 (1H, dd, H&lt;sub&gt;M&lt;/sub&gt;)</td>
</tr>
<tr>
<td></td>
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<td>5.50 (1H, s, Ar-OH)</td>
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<td>6.79 – 7.68 (14H, Ar-H)</td>
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<tr>
<td>B&lt;sub&gt;8&lt;/sub&gt;PY&lt;sub&gt;8&lt;/sub&gt;</td>
<td>3.15 (1H, dd, H&lt;sub&gt;A&lt;/sub&gt;)</td>
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<tr>
<td></td>
<td>3.85 (1H, dd, H&lt;sub&gt;M&lt;/sub&gt;)</td>
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<tr>
<td></td>
<td>5.38 (1H, dd, H&lt;sub&gt;X&lt;/sub&gt;)</td>
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<td>2.31 (3H, s, C-3'-CH&lt;sub&gt;3&lt;/sub&gt;)</td>
</tr>
<tr>
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<td>5.50 (1H, s, Ar-OH)</td>
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<td>6.45 – 7.95 (14H, Ar-H)</td>
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<tr>
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<td></td>
<td>3.92 (1H, dd, H&lt;sub&gt;M&lt;/sub&gt;)</td>
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<td>5.60 (1H, dd, H&lt;sub&gt;X&lt;/sub&gt;)</td>
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<tr>
<td></td>
<td>2.31 (3H, s, C-3'-CH&lt;sub&gt;3&lt;/sub&gt;)</td>
</tr>
<tr>
<td></td>
<td>5.50 (1H, s, Ar-OH)</td>
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<tr>
<td></td>
<td>6.79 – 7.69 (17H, Ar-H)</td>
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<tr>
<td>B&lt;sub&gt;10&lt;/sub&gt;PY&lt;sub&gt;10&lt;/sub&gt;</td>
<td>3.15 (1H, dd, H&lt;sub&gt;A&lt;/sub&gt;)</td>
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<td>3.85 (1H, dd, H&lt;sub&gt;M&lt;/sub&gt;)</td>
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<td></td>
<td>5.40 (1H, dd, H&lt;sub&gt;X&lt;/sub&gt;)</td>
</tr>
<tr>
<td></td>
<td>2.31 (3H, s, C-3'-CH&lt;sub&gt;3&lt;/sub&gt;)</td>
</tr>
<tr>
<td></td>
<td>5.50 (1H, s, Ar-OH)</td>
</tr>
<tr>
<td></td>
<td>6.79 – 7.67 (12H, Ar-H)</td>
</tr>
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</table>
| B<sub>11</sub>PY<sub>11</sub> | 3.14 (1H, dd, H<sub>A</sub>)  
3.85 (1H, dd, H<sub>M</sub>)  
5.30 (1H, dd, H<sub>X</sub>)  
2.31 (3H, s, C-3'-CH<sub>3</sub>)  
5.50 (1H, s, Ar-OH)  
6.79 – 7.44 (12H, Ar-H) |
| B<sub>12</sub>PY<sub>12</sub> | 3.40 (1H, dd, H<sub>A</sub>)  
3.90 (1H, dd, H<sub>M</sub>)  
5.40 (1H, dd, H<sub>X</sub>)  
2.31 (3H, s, C-3'-CH<sub>3</sub>)  
5.50 (1H, s, Ar-OH)  
6.79 – 7.48 (12H, Ar-H) |
| B<sub>13</sub>PY<sub>13</sub> | 3.15 (1H, dd, H<sub>A</sub>)  
3.75 (1H, dd, H<sub>M</sub>)  
5.30 (1H, dd, H<sub>X</sub>)  
2.31 (3H, s, C-3'-CH<sub>3</sub>)  
2.15 (3H, s, C-4''-CH<sub>3</sub>)  
5.50 (1H, s, Ar-OH)  
6.79 – 7.44 (12H, Ar-H) |
| B<sub>14</sub>PY<sub>14</sub> | 3.15 (1H, dd, H<sub>A</sub>)  
3.50 (1H, dd, H<sub>M</sub>)  
5.40 (1H, dd, H<sub>X</sub>)  
2.31 (3H, s, C-3'-CH<sub>3</sub>)  
3.74 (3H, s, C-4''-OCH<sub>3</sub>)  
5.50 (1H, s, Ar-OH)  
6.79 – 7.67 (12H, Ar-H) |
| B<sub>15</sub>PY<sub>15</sub> | 3.20 (1H, dd, H<sub>A</sub>)  
3.65 (1H, dd, H<sub>M</sub>)  
5.20 (1H, dd, H<sub>X</sub>)  
2.31 (3H, s, C-3'-CH<sub>3</sub>)  
3.85 (9H, s, 3 x-OCH<sub>3</sub>)  
5.50 (1H, s, Ar-OH)  
6.51 – 7.67 (10H, Ar-H) |
Fig. 36. IR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-pyridinyl)-2-pyrazoline (B₁PY₁)
Fig. 37. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-pyridinyl)-2-pyrazoline (B$_1$PY$_1$)
Fig. 38. Mass spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-pyridinyl)-2-pyrazoline (B₁PY₁)
Fig. 39. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(3'-pyridinyl)-2-pyrazoline (B$_2$PY$_2$)
Fig. 40. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-pyridinyl)-2-pyrazoline (B$_3$PY$_3$)
Fig. 41. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2"-furyl)-2-pyrazoline (B$_4$PY$_4$)
Fig. 42. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2'-pyrrolyl)-2-pyrazoline (B$_5$PY$_5$)
Fig. 43. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-thienyl)-2-pyrazoline (B$_6$PY$_6$)
Fig. 44. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-indolyl)-2-pyrazoline (B$_7$PY$_7$)
Fig. 45. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(2''-quinolinyl)-2-pyrazoline (B$_8$PY$_8$)
Fig. 46. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(9''-anthracenyl)-2-pyrazoline (B$_9$PY$_9$)
Fig. 47. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-fluorophenyl)-2-pyrazoline (B$_{10}$PY$_{10}$)
Fig. 48. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-chlorophenyl)-2-pyrazoline (B$_{11}$PY$_{11}$)
Fig. 49. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-bromophenyl)-2-pyrazoline (B$_{12}$PY$_{12}$)
Fig. 50. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-methylphenyl)-2-pyrazoline (B$_{13}$PY$_{13}$)
Fig. 51. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(4''-methoxyphenyl)-2-pyrazoline (B$_{14}$PY$_{14}$)
Fig. 52. $^1$H NMR spectrum of 1-phenyl-3-(3'-methyl-4'-hydroxyacetophenone)-5-(3'', 4'', 5''-trimethoxyphenyl)-2-pyrazoline (B$_{15}$PY$_{15}$)
3.3 BIOLOGICAL EVALUATION

PRESENT WORK

A number of 2-pyrazolines were reported to possess diverse biological activities like antimicrobial, antidepressant, analgesic, anti-inflammatory, antiviral, antileishmanial, antitubercular, anti-HIV and antimalarial activities. In view of the varied biological and pharmacological importance of different series of 2-pyrazoline derivatives, it is felt worthwhile to evaluate them for possible activities. These compounds therefore were screened for anti-inflammatory, analgesic, antibacterial and antifungal activities.

EXPERIMENTAL METHODS

ACUTE TOXICITY

The same protocols and procedures that were followed in Chapter-1 were used to study the acute toxicity of 2-pyrazolines.

All the 2-pyrazolines employed in the pharmacological screening have been found to be free form toxicity as well as toxic symptoms even at a high dose of 1000 mg/kg body weight and hence they were considered safe.
3.3.1 ANTI-INFLAMMATORY ACTIVITY

The same protocols and procedures that have been followed in Chapter-1 are used to study anti-inflammatory activity of 2-pyrazolines (B1PY1-B15PY15). The results are presented in Table 20.
Table 20. Anti-inflammatory activity of 1, 3, 5-trisubstituted-2-pyrazolines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>% inhibition ± SEM at various time intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.5h</td>
</tr>
<tr>
<td>B₁PY₁</td>
<td>2''-pyridinyl</td>
<td>5±1</td>
</tr>
<tr>
<td>B₂PY₂</td>
<td>3''-pyridinyl</td>
<td>5±1</td>
</tr>
<tr>
<td>B₃PY₃</td>
<td>4''-pyridinyl</td>
<td>6±1</td>
</tr>
<tr>
<td>B₄PY₄</td>
<td>2''-furyl</td>
<td>5±1</td>
</tr>
<tr>
<td>B₅PY₅</td>
<td>2''-pyrrolyl</td>
<td>12±1</td>
</tr>
<tr>
<td>B₆PY₆</td>
<td>2''-thienyl</td>
<td>6±1</td>
</tr>
<tr>
<td>B₇PY₇</td>
<td>2''-indolyl</td>
<td>13±1</td>
</tr>
<tr>
<td>B₈PY₈</td>
<td>2''-quinolinyl</td>
<td>6±1</td>
</tr>
<tr>
<td>B₉PY₉</td>
<td>9''-anthracenyl</td>
<td>9±1</td>
</tr>
<tr>
<td>B₁₀PY₁₀</td>
<td>4''-fluorophenyl</td>
<td>8±1</td>
</tr>
<tr>
<td>B₁₁PY₁₁</td>
<td>4''-chlorophenyl</td>
<td>7±1</td>
</tr>
<tr>
<td>B₁₂PY₁₂</td>
<td>4''-bromophenyl</td>
<td>6±1</td>
</tr>
<tr>
<td>B₁₃PY₁₃</td>
<td>4''-methylphenyl</td>
<td>10±1</td>
</tr>
<tr>
<td>B₁₄PY₁₄</td>
<td>4''-methoxyphenyl</td>
<td>11±1</td>
</tr>
<tr>
<td>B₁₅PY₁₅</td>
<td>3'',4'',5''-trimethoxyphenyl</td>
<td>13±1</td>
</tr>
<tr>
<td>Aceclofenac (standard)</td>
<td>22±1</td>
<td>23±1</td>
</tr>
</tbody>
</table>

All values are represented as mean±SEM (n=6). *P<0.01 compared to reference standard Aceclofenac. Student’s t-test. **Dosage:** Aceclofenac-2 mg/kg and test compounds-10 mg/kg body weight of rat.
DISCUSSION ON THE RESULTS:

The anti-inflammatory activities of all the 2-pyrazolines synthesized have been evaluated by using carrageenan-induced rat paw oedema method.

The results clearly revealed the potential anti-inflammatory activity of all these 2-pyrazolines when compared with the standard drug aceclofenac, but not at an identical dose level. Of all the compounds tested, compound B₇PY₇ having the indolyl substitution at the 5-position of the 2-pyrazoline ring showed maximum activity and this is followed by compounds having a pyrrolyl ring (compound B₅PY₅) on the pyrazoline nucleus. These results of anti-inflammatory activity for the 2-pyrazolines is consistent with the literature reports. However, the contributing physico-chemical properties of these substituents need to be established by a proper QSAR study. Such a study also may provide useful information in the design and synthesis of 2-pyrazolines with promising anti-inflammatory activity.
3.3.2 ANALGESIC ACTIVITY

A number of pyrazolines were reported to possess significant analgesic activity and in fact some of the drugs currently used in therapy possessed pyrazoline structure and hence it was felt worthwhile to screen these compounds synthesized in the present study for analgesic activity by tail flick method. The working procedure is described separately and the results are given in Table 21.

Experimental:

Tail immersion test method / tail flick method\textsuperscript{88,89} was adopted for evaluation of analgesic activity of the test compounds. The tail of the control, standard and test group animals (rats) was dipped in a beaker of water maintained $55 \pm 1^\circ C$ and the time taken to withdraw the tail clearly out of water is taken as the reaction time.

Requirements:

Animals: Albino rats of either sex

Standard drug: Ibuprofen suspension in 2% v/v Tween 80 solution administered orally at the dose of 100 mg/kg body weight.

Samples: Test compounds were suspended in 2% v/v Tween 80 solution and administered orally at the dose of 100 mg/kg body weight. Water was heated in a beaker and the temperature was maintained at $55 \pm 1^\circ C$. 
Working procedure:

85 albino rats of either sex weighing between 150-200 grams were divided into 17 groups of 5 animals each and they were numbered individually. The animals were fasted for 24 hours before administering the drug with water ad libitum.

Group I was administered with only 2% v/v Tween 80 solution, which served as control. Group II was administered with 100 mg/kg body weight of ibuprofen suspension orally, which served as a standard. Group III to group XVII were administered with test compounds respectively, the dose being 100 mg/kg body weight selected on the basis of the standard drug used. All the animal tails were dipped into a beaker containing water maintained at 55 ± 1 °C and the time taken for the animals to flick the tail from the hot water completely is recorded at 15 minutes, 30 minutes, 1 hour, 2 hours and 3 hours respectively.

The percentage of protection in the control, standard and drug treated animals were recorded and calculated by using the formula.

\[
\text{% Analgesic activity (PAA) = \left[ \frac{R_t}{R_c} - 1 \right] \times 100}
\]

Where Rt and Rc are the reaction time in test and control respectively.

The results of analgesic activity of ibuprofen and the compounds tested are shown in Table 21.
Table 21. Analgesic activity of 1, 3, 5-trisubstituted-2-pyrazolines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>% Analgesic activity (PAA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>15 min</td>
</tr>
<tr>
<td>B₁PY₁</td>
<td>2''-pyridinyl</td>
<td>75±1</td>
</tr>
<tr>
<td>B₂PY₂</td>
<td>3''-pyridinyl</td>
<td>74±1</td>
</tr>
<tr>
<td>B₃PY₃</td>
<td>4''-pyridinyl</td>
<td>74±1</td>
</tr>
<tr>
<td>B₄PY₄</td>
<td>2''-furyl</td>
<td>80±1</td>
</tr>
<tr>
<td>B₅PY₅</td>
<td>2''-pyrrolyl</td>
<td>81±1</td>
</tr>
<tr>
<td>B₆PY₆</td>
<td>2''-thienyl</td>
<td>78±1</td>
</tr>
<tr>
<td>B₇PY₇</td>
<td>2''-indolyl</td>
<td>82±1</td>
</tr>
<tr>
<td>B₈PY₈</td>
<td>2''-quinoliny</td>
<td>70±1</td>
</tr>
<tr>
<td>B₉PY₉</td>
<td>9''-anthracenyl</td>
<td>63±1</td>
</tr>
<tr>
<td>B₁₀PY₁₀</td>
<td>4''-fluorophenyl</td>
<td>92±1</td>
</tr>
<tr>
<td>B₁₁PY₁₁</td>
<td>4''-chlorophenyl</td>
<td>89±1</td>
</tr>
<tr>
<td>B₁₂PY₁₂</td>
<td>4''-bromophenyl</td>
<td>85±1</td>
</tr>
<tr>
<td>B₁₃PY₁₃</td>
<td>4''-methylphenyl</td>
<td>94±1</td>
</tr>
<tr>
<td>B₁₄PY₁₄</td>
<td>4''-methoxyphenyl</td>
<td>96±1</td>
</tr>
<tr>
<td>B₁₅PY₁₅</td>
<td>3''',4''',5'''-trimethoxyphenyl</td>
<td>99±1</td>
</tr>
<tr>
<td>Ibuprofen (standard)</td>
<td></td>
<td>103±1</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SEM (n=5). *p<0.05; **p<0.01; ***p<0.001 compared to controls. Students’s t-test
DISCUSSION ON THE RESULTS:

All the 2-pyrazolines tested for analgesic activity showed considerable activity when compared to the standard drug ibuprofen. It is interesting to note that compound $B_{15}PY_{15}$ having 3, 4, 5-trimethoxyphenyl, compound $B_{14}PY_{14}$ having 4-methoxyphenyl, compound $B_{13}PY_{13}$ having 4-methylphenyl ring at the 5-position of the 2-pyrazoline ring possessed the maximum activity. It clearly indicates the favorable effect of electron releasing substituents on the analgesic activity of the 2-pyrazolines. 2-Pyrazolines having these substituents both on the aromatic and the heteroaromatic rings, if synthesized and tested, may possess significant analgesic activity. Literature reports also indicated the necessity of electron releasing groups in enhancing the analgesic activity. 2-Pyrazolines with a fluorine substituent (compound $B_{10}PY_{10}$) on the aromatic ring also enhanced the activity. Hence, compounds having fluorine and other halogens at one or more positions of the aromatic rings can be synthesized to have compounds with much better activity.
3.3.3 ANTIBACTERIAL ACTIVITY

The same protocols and procedures that have been followed in Chapter-1 are used to study antibacterial activity of newly synthesized 2- pyrazolines (B₁PY₁-B₁⁵PY₁⁵). The results are presented in Table 22.
Table 22. Antibacterial activity of 1, 3, 5-trisubstituted-2-pyrazolines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>Zone of inhibition in mm</th>
<th>Quantity in µg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>B. subtilis</td>
</tr>
<tr>
<td>B1PY1</td>
<td>2''-pyridinyl</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>B2PY2</td>
<td>3''-pyridinyl</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>B3PY3</td>
<td>4''-pyridinyl</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>B4PY4</td>
<td>2''-furyl</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>B5PY5</td>
<td>2''-pyrrolyl</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>B6PY6</td>
<td>2''-thienyl</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>B7PY7</td>
<td>2''-indolyl</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>B8PY8</td>
<td>2''-quinolinyl</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>B9PY9</td>
<td>9''-anthracenyl</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>B10PY10</td>
<td>4''-fluorophenyl</td>
<td></td>
<td>23</td>
</tr>
<tr>
<td>B11PY11</td>
<td>4''-chlorophenyl</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>B12PY12</td>
<td>4''-bromophenyl</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>B13PY13</td>
<td>4''-methylphenyl</td>
<td></td>
<td>09</td>
</tr>
<tr>
<td>B14PY14</td>
<td>4''-methoxyphenyl</td>
<td></td>
<td>08</td>
</tr>
<tr>
<td>B15PY15</td>
<td>3'',4'',5''-trimethoxyphenyl</td>
<td></td>
<td>06</td>
</tr>
<tr>
<td>Benzyl penicillin (standard)</td>
<td></td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>Control (DMSO)</td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
DISCUSSION ON THE RESULTS:

All the 2-pyrazolines \( B_1PY_1-B_{15}PY_{15} \) have been evaluated for their antibacterial activity against *Bacillus subtilis*, *Bacillus pumilis*, *Staphylococcus aureus* (Gram-positive) and *Escherichia coli*, *Proteus vulgaris* (Gram-negative), using cup-plate method. The results of this evaluation have been compared by taking benzyl penicillin as standard. The antibacterial activity data of 2-pyrazolines \( B_1PY_1-B_{15}PY_{15}, \textbf{Table 22} \) indicated that the compounds have significant inhibitory activity on all the bacteria at both 50 \( \mu g \) (0.05 ml) and 100 \( \mu g \) (0.1 ml) dose levels when compared with benzyl penicillin.

Among all the compounds tested, compounds \( B_{10}PY_{10}, B_{11}PY_{11} \) and \( B_8PY_8 \) possessed maximum activity. The first two compounds possessed the halogens on the aromatic ring and thus reveal the positive contribution of electron withdrawing groups to the antibacterial activity, while the third compound possessed quinoline nucleus responsible for antibacterial activity. The results are consistent with the literature reports. Compounds having these substituents on the hetero aryl ring can also be synthesized and screened for antibacterial activity, with a hope to get better compounds in this series. A QSAR study on a large data bank of 2-pyrazolines may further provide insights into the structural requirements and the contributing physico-chemical properties in enhancing the antibacterial activity.
3.3.4 ANTIFUNGAL ACTIVITY

The same protocols and procedures that have been followed in Chapter-1 are used to study antifungal activity of 2-pyrazolines (B₁PY₁-B₁₅PY₁₅). The results are presented in Table 23.
### Table 23. Antifungal activity of 1, 3, 5-trisubstituted-2-pyrazolines

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>Zone of inhibition (in mm)</th>
<th>Quantity in µg/ml</th>
<th>A. niger</th>
<th>C. albicans</th>
<th>R. oryzae</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>50</td>
<td>100</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>B₁PY₁</td>
<td>2''-pyridinyl</td>
<td>13</td>
<td>15</td>
<td>10</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>B₂PY₂</td>
<td>3''-pyridinyl</td>
<td>12</td>
<td>14</td>
<td>10</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>B₃PY₃</td>
<td>4''-pyridinyl</td>
<td>11</td>
<td>13</td>
<td>09</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>B₄PY₄</td>
<td>2''-furyl</td>
<td>17</td>
<td>19</td>
<td>16</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>B₅PY₅</td>
<td>2''-pyrrolyl</td>
<td>15</td>
<td>17</td>
<td>12</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>B₆PY₆</td>
<td>2''-thienyl</td>
<td>14</td>
<td>16</td>
<td>11</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>B₇PY₇</td>
<td>2''-indolyl</td>
<td>16</td>
<td>18</td>
<td>14</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>B₈PY₈</td>
<td>2''-quinolinyl</td>
<td>18</td>
<td>20</td>
<td>17</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>B₉PY₉</td>
<td>9''-anthracenyl</td>
<td>10</td>
<td>12</td>
<td>08</td>
<td>10</td>
<td>08</td>
</tr>
<tr>
<td>B₁₀PY₁₀</td>
<td>4''-fluorophenyl</td>
<td>22</td>
<td>24</td>
<td>20</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td>B₁₁PY₁₁</td>
<td>4''-chlorophenyl</td>
<td>20</td>
<td>22</td>
<td>19</td>
<td>21</td>
<td>19</td>
</tr>
<tr>
<td>B₁₂PY₁₂</td>
<td>4''-bromophenyl</td>
<td>19</td>
<td>22</td>
<td>18</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>B₁₃PY₁₃</td>
<td>4''-methylphenyl</td>
<td>08</td>
<td>11</td>
<td>07</td>
<td>09</td>
<td>07</td>
</tr>
<tr>
<td>B₁₄PY₁₄</td>
<td>4''-methoxyphenyl</td>
<td>07</td>
<td>10</td>
<td>06</td>
<td>07</td>
<td>06</td>
</tr>
<tr>
<td>B₁₅PY₁₅</td>
<td>3'',4'',5''-trimethoxyphenyl</td>
<td>06</td>
<td>08</td>
<td>05</td>
<td>06</td>
<td>06</td>
</tr>
<tr>
<td>Fluconazole (standard)</td>
<td></td>
<td>26</td>
<td>29</td>
<td>25</td>
<td>30</td>
<td>24</td>
</tr>
<tr>
<td>Control (DMSO)</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
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DISCUSSION ON THE RESULTS:

The antifungal activity of the substituted 2-pyrazolines was evaluated against *A.niger*, *C.albicans* and *R. oryzae*, employing fluconazole as the standard drug and using the cup- plate method.

A close examination of the Table 23 pertaining to the antifungal activity data of 2-pyrazolines revealed that all the compounds in this series have been found to be effective against all the fungi at both the dose levels tested, when compared with the reference standard. Like in the case of antibacterial activity, here also compounds with electron withdrawing groups enhanced the activity and it is much more than what is observed in the case of antifungal activity of pyrimidines. Compounds having electron releasing groups also contributed favorably to the antifungal activity. The contributing physico-chemical properties of these compounds, however, need to be established by QSAR studies. 2-Pyrazolines having electron withdrawing and releasing substituents on the hetero aryl ring can also be synthesized and screened for antifungal activity in order to get compounds with promising activity.
3.4 REFERENCES


