CHAPTER-VII

NOVEL PYRAZOLINES – DESIGN, SYNTHESIS, CHARACTERIZATION AND THEIR BIOLOGICAL EVALUATION
**Introduction**

**Pyrazoles:**

The simple five membered ring double unsaturated having 2 N-atoms adjacent to each other and three carbon atoms are called as Pyrazoles. In 1883 this class of compounds were named by Ludwig Knorr. On reduction pyrazloes give pyrzanline and pyrazolidine. Numerous Pyrazolines substituted compounds are found to possess medicinal properties. Some of these substituted compounds are called pyrazolone and pyrazolidinedione.

![Pyrazole and Derivatives](image)

\[ \text{Pyrazole} \quad \text{Pyrazoline} \quad \text{Pyrazolidine} \quad \text{5-Pyrazolone} \quad \text{3,5-Pyrazolidinedione} \]

\[ \beta-(1\text{-pyrazolyl}) \text{ alanine} \text{ was found in the seeds of watermelons} \quad \text{(Citrullus lanatus)} \text{ and was isolated in 1959.} \]
**Chemistry:** Pyrazole is a colorless solid. M.P. 70°C with high boiling point of 187-188°C. The intermolecular H2 bond makes it a dimer. Tautomerism can be demonstrated by pyrazole derivatives and cannot be shown in pyrazole itself.

Pyrazoles show aromatic nature, pyrazoles are easily reacted with sulphuric acid, nitric acid and HCl. The group enters at fourth position.

Possible resonating structures for pyrazole are shown below:

with inorganic acids; pyrazole forms salts showing its basic nature.

**General Synthesis:** Pyrazoles and their derivatives can be synthesized by following classical methods for practical methods two very important methods are followed:

(1) Reaction of β-bifunctional compounds and hydrazines

(2) Reaction of hydrazines and 1,3-bipolr cycloadditions.
Sucrow et al \(^1\) reported preparation of Pyrazolines and different methods of preparation including the cyclization of monomethylhydrazones of dialkyl oxalacetates to 5-pyrazolones via an enehydrazine.

\[
\begin{align*}
\text{COOR} & \quad \text{COOR} \\
\text{H} & \quad \text{NMe} \\
\text{H}_2\text{N} & \\
\text{COOR} & \quad \text{COOR} \\
\text{HN} & \quad \text{Me} \\
\text{NMe} & \\
\text{HN} & \\
\text{Me} & \\
\text{COOR} &
\end{align*}
\]

Brewbaker et al\(^2\) have synthesized the certain pyrazole derivative by a concerted, intramolecular 1,3-dipolar cycloaddition.

\[
\begin{align*}
\text{N}_2\text{CHCH}_2\text{CHN}_2 & \quad \text{CH}_2\text{CH:} \\
\text{HC-} & \quad \text{N}^+\text{N:} \\
\text{N} & \quad \text{H} \\
\text{N} & \\
\text{H} & \\
\text{N} &
\end{align*}
\]

Pyrazoles have been prepared by the action of hydrazines on heterocyclic derivatives, which react as marked functional groups of a 1,3-bifunctional derivative. A carbonyl group can be replaced by a three membered ring, usually an oxirane or an aziridine or by a \(\beta\)-substituted pyrrole or indole derivative.
The addition of aliphatic diazo compounds to acetylenes gives pyrazoles. The same reactions as applied to olefins leads to dihydropyrazoles which are termed pyrazolines (Pechmann).

**Pharmacological interest:** Pyrazoles form important class of organic derivatives possessing wide range of chemical and biological property in modern times Pyrazolines have become important and attracted the interested of many researchers in the field of medicinal chemistry because of their broad spectrum biological activities. Several
Pyrazolines derivatives are found in the pharmaceutical industry and medicine for treating many diseases.

**Phenylbutazone:** It is a pyrazoline derivative known for its analgesic and anti-inflammatory and anti-pyretic properties. Because of its high toxicity good phenyl butazone is normally not used as analgesic and anti-pyretic.

**Muzolimine:** Muzolimine is a pyrazoline derivative used as a diuretic and differs from the structures of other diuretic compounds.
**Forbisen:** It is a byproduct separated the during synthesis of antipyrine. This pyrazoline is used in bovine analplasmosis.

![Forbisen](image1)

**Oxyphenbutazone:** It is a pyrazoline derivative similar to phenyl butazone. It is an active metabolite of phenyl butazone. The difference with phenyl butazone is the presence of p-hydroxypheny group instead of phenyl at position 1 of phenylbutazone.

![Oxyphenbutazone](image2)
**Sulphinpyrazone:** A derivative of phenyl butazone is sulphinpyrazone, it is used as uricosuric drug. It contains 2-phenyl sulphinyl ethyl group instead of n-butyl group at fourth position. It improves elimination of uric acid and urate by preventing their tubular reabsorption.

![Sulphinpyrazone](image)

**Feprazone:** It is used for treating rheumatic disorders and is structurally same as that of phenyl butazone.

![Feprazone](image)
**Phenazone:** Phenazone is used as local anesthetic in ear drops. It is also well known for its analgesic and anti-pyretic properties. It is a white crystalline powder and chemically a derivative of pyrazoline.

**Propylphenazone:** It is a analgesic and derivative of phenazone with an isopropyl group at fourth position.

***Phenazone***

\[
\begin{align*}
\text{Phenazone} & : \quad \begin{array}{c}
\text{C}_6\text{H}_5 \\
\text{O} \\
\text{N} \quad \text{N} \\
\text{N} \quad \text{C}_3\text{H}_7 \\
\text{CH}_3
\end{array} \\
\begin{array}{c}
\text{N} \quad \text{C}_3\text{H}_7 \\
\text{C}_6\text{H}_5 \\
\text{O}
\end{array}
\end{align*}
\]

***Propyl Phenazone***

\[
\begin{align*}
\text{Propyl Phenazone} & : \quad \begin{array}{c}
\text{C}_6\text{H}_5 \\
\text{O} \\
\text{N} \quad \text{N} \\
\text{H}_3\text{C} \quad \text{C}_3\text{H}_7 \\
\text{CH}_3
\end{array} \\
\begin{array}{c}
\text{N} \quad \text{C}_3\text{H}_7 \\
\text{C}_6\text{H}_5 \\
\text{O}
\end{array}
\end{align*}
\]

**Analgin:** Analgin is a white crystalline powder and may be slightly yellowish and easily soluble in water. It taste bitter and normally this drug is kept in airtight containers. It is a popular analgesic and antipyretic and it is also a derivative of phenazone containing \(\text{N-}(\text{CH}_3)\text{CH}_2\text{SO}_3\text{Na}\) substituent at position 4.

***Analgin***

\[
\begin{align*}
\text{Analgin} & : \quad \begin{array}{c}
\text{C}_6\text{H}_5 \\
\text{O} \\
\text{N} \quad \text{N} \\
\text{H}_3\text{C} \quad \text{C}_3\text{H}_7 \\
\text{CH}_3 \\
\text{N} \quad \text{C}_3\text{H}_7 \\
\text{H}_3\text{C} \quad \text{C}_3\text{H}_7 \\
\text{CH}_3 \\
\text{CH}_2\text{SO}_3\text{Na}
\end{array}
\end{align*}
\]
Review Of Literature

Pyrazoles and Pyrazolines:

Dadiboyena et al\textsuperscript{3} prepared certain derivatives of pyrazoles (14) and evaluated their anti microbial and anti inflammatory properties.

Porter et al\textsuperscript{4} prepared certain Pyrazolines (15) and showed the functions of inhibitors of Bcl-2.
Wahab et al. synthesized and evaluated antimicrobial activity of following Pyrazolines (16), (17) and (18).

Prakash et al. prepared and carried out evaluation of antibacterial property of some new Pyrazolines (19).

Gupta et al. prepared certain cyanopyrazole and reported their xanthine oxidase inhibition activity. (20).
Kralj et al\textsuperscript{8} reported a simple synthesis of 4-(2-aminoethyl)-5-hydroxy-1H-pyrazole (21).

![Chemical Structure of 4-(2-aminoethyl)-5-hydroxy-1H-pyrazole (21)]

Pyrazoline as antimicrobial and anti bacterial:

Sachchar et al\textsuperscript{9} prepared good number of hetero aryl pyrazoline derivatives (22) and evaluated their antibacterial property.

![Chemical Structure of Hetero Aryl Pyrazoline (22)]

R = furyl, thieryl, pyridyl
R\textsuperscript{1} = F, Cl, OH, CH\textsubscript{3}

Many other authors also showed the preparation and antibacterial property of certain new Pyrazolines compounds.\textsuperscript{10-14}

Stirrewiberg et al\textsuperscript{15} reported the antimicrobial as well as insecticidal property of few pyrazolines (23).

![Chemical Structure of Few Pyrazolines (23)]
Desai et al\textsuperscript{16} synthesized several pyrazoline derivatives of phenothiazines and reported their antibacterial activity and tuberculostatic activity of some compounds.

Ead et al\textsuperscript{17} carried out the preparation of novel Pyrazolines and reported their anti-microbial property.

Sachchar et al\textsuperscript{18} prepared certain Pyrazolines and showed that these derivatives possess anti-fungal property.

Ritcha et al\textsuperscript{19} prepared nitro and nitroso pyrazole derivatives and reported their fungicidal property.

Mitra et al\textsuperscript{20} prepared pyrazoline derivatives and reported their fungicidal activity. \textsuperscript{(24)}

\begin{center}
\begin{tikzpicture}
\node[draw] at (0,0) {\includegraphics[width=0.5\textwidth]{pyrazoline.png}};
\end{tikzpicture}
\end{center}

Mitra et al\textsuperscript{24} have synthesized pyrazolinone derivatives by Mannich condensation and reported their fungicidal activity.
Sadasiva et al\textsuperscript{25} prepared certain Pyrazolines (25) and screened their antimicrobial and fungicidal activity.

\[
\begin{align*}
\text{R} &= \text{alkyl or aryl} \\
\text{R}^1 &= \text{H or phenyl}
\end{align*}
\]

Nayak et al\textsuperscript{26} prepared certain bis-pyrazolines and reported their fungicidal property.

Tiwari et al\textsuperscript{27} prepared certain pyrazoles and pyrazolines and reported their antimicrobial properties.

Mohanthy et al\textsuperscript{28} prepared certain pyrazoline derivatives and evaluated their antifungal activity.

Sachachar et al\textsuperscript{29-32} reported synthesis of Pyrazolines bearing hetero aryl moiety and screened their antiviral property.

They also reported pyrazoline derivatives which exhibited activity against serotoninin and anti-inflammatory properties. But were not useful clinically for treating rheumatic arthritis and also synthesized Nicotinyl amino bearing derivatives which were effective clinically useful anti-inflammatory agent.
Frangnly et al\textsuperscript{33} synthesized new Pyrazolines and reported their anti-oedema property.

Modification of the above to sulphinpyrazole\textsuperscript{34} enhanced activity of uricosuric property and is potent against gout.

\[
\begin{array}{c}
R^1 & R^2 \\
\text{Phenyl butazone} & -\text{C}_6\text{H}_5 & -\text{C}_4\text{H}_9 \\
\text{Oxyphen butazone} & -\text{C}_6\text{H}_4\text{-OH (P)} & -\text{C}_4\text{H}_9 \\
\text{Sulfin pyrazone} & -\text{C}_6\text{H}_5 & -\text{CH}_2\text{-CH}_2\text{-S-}\text{C}_6\text{H}_5 \\
\end{array}
\]

Coli et al\textsuperscript{35} reported that pyrazoles itself has anti-inflammatory activity (27) e.x. Benzylame.

\[
\begin{array}{c}
\text{R} = -\text{CH}_2\text{-CH}_2\text{-N (CH}_3)_2\text{-COCH}_3 \\
\end{array}
\]
Sarangam et al\textsuperscript{36} have prepared series of pyrazole-pyrimidine diones (28) and evaluated their CNS depressant property and anti-inflammatory property on par with aspirin.\textsuperscript{37}

\[
\begin{align*}
\text{R}_1 &= \text{Phenyl, o-Tolyl} \\
\text{R}_2 &= \text{Phenyl, o-Tolyl, o-Anisyl}
\end{align*}
\]

Froesch et al\textsuperscript{38} has reported antidiabetic activity in the 5-methyl pyrazole-3-carboxylic acid (29).

\[
\begin{align*}
\text{N} & \quad \text{H} \\
\text{C} & \quad \text{O} \\
\text{H}_3\text{C} & \quad \text{COOH}
\end{align*}
\]

Brunner et al\textsuperscript{39} prepared certain Pyrazolines derivatives and evaluated their vasodilator property (30).

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{C} & \quad \text{H}_3\text{C} \\
\text{N} & \quad \text{CH}_3
\end{align*}
\]
Smith et al\textsuperscript{40} carried out synthesis of pyrazoles processing hypoglycemic activity (31).

Arya et al\textsuperscript{41} prepared certain pyrazolidines and carried out screening of their hypotensive property. (32)

\[
\text{\begin{center}
\includegraphics[width=\textwidth]{image1}
\end{center}}
\]

Sweeny et al\textsuperscript{42} prepared pyrazofurin and reported its antibiotic property.

Chasin et al\textsuperscript{43} synthesized pyridine bearing Pyrazoline derivatives (33) and reported its use as brain PDE in rat.

\[
\text{\begin{center}
\includegraphics[width=\textwidth]{image2}
\end{center}}
\]
Novinson et al\textsuperscript{44} synthesis certain pyrimidine containing pyrazoles (34,35) and reported their inhibition activity in rabbit lung and beef heart.

Several pyrazoles are known to exhibit different biological activities\textsuperscript{45-48}.
PYRAZOLINES

Scheme

\[
\text{HOOC-(CH}_2\text{)}_4\text{COOH} \quad \overset{\text{C}_2\text{H}_5\text{OH, H}_2\text{SO}_4}{\underset{1}{\longrightarrow}} \text{C}_2\text{H}_5\text{OOC-(CH}_2\text{)}_4\text{COOC}_2\text{H}_5
\]

\[
\text{C}_2\text{H}_5\text{OOC-(CH}_2\text{)}_4\text{COOC}_2\text{H}_5 \quad \overset{\text{NH}_2\text{NH}_2\text{H}_2\text{O (99%)}}{\underset{2}{\longrightarrow}} \text{H}_2\text{HNOC-(CH}_2\text{)}_4\text{CONHNH}_2
\]

1) Ar\textsuperscript{1}-C-CH=CH-Ar

2) CH\textsubscript{3}COOH

\[
\text{H}_2\text{HNOC-(CH}_2\text{)}_4\text{CONHNH}_2 \quad \overset{\text{I) Ar}\textsuperscript{1}-C-CH=CH-Ar \quad \text{II) CH}_3\text{COOH}}{\underset{3}{\longrightarrow}} \text{Ar}\textsuperscript{1}\text{Ar} \quad \text{Ar}\textsuperscript{1} \quad \text{Ar}\textsuperscript{1}
\]

{\text{P1 - P18}}
Experimental

Synthesis of adipic acid hydrazide

A mixture of adipic acid (0.01 mol) and ethyl alcohol (50 ml) was heated for 6hrs using 0.5 ml of H2SO4. Excess of solvent was distilled off. Add anhydrous ethyl alcohol (50 ml) and NH2NH2.H2O (99%, 0.03 mol) and heated for 12-16 hrs. Cooled and allowed the solid to settle down. The product was removed by filtration and purified by crystallization using ethyl alcohol (yield 85%,).

Chalcone synthesis

Each of acetophenone (0.1mol) and benzaldehyde (0.1mol) dissolved in 100ml of ethyl alcohol separately and were mixed by stirring. KOH 10% is then added dropwise. The intermediate solution is shaked in a mechanical shaker for 12 hrs. The product separated was filtered and purified by crystallization technique using ethyl alcohol. Other Chalcone were also synthesized using same technique.

Preparation of Pyrazolines: (P1-P18).

Chalcone, adipic acid hydrazide in equi molar proportion was dissolved in ethyl alcohol (50 ml) and CH3COOH (1 ml) was heated for seven hours. Cooled and product obtained by filtration was purify by crystallization using ethyl alcohol. Rest of the compounds were obtained using same technique. Purity of the derivative was established by TLC using mobile phase, ethyl acetate ad n-hexane (2:8 v/v). Characterization data of the derivatives is presented in the table No. 49.
Table No. 49: Characterization details of Pyrazoline derivatives

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<th>Sr. No</th>
<th>Code</th>
<th>Ar&lt;sup&gt;1&lt;/sup&gt;</th>
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<th>mol. formula</th>
<th>m.p. (°C)</th>
<th>yield (%)</th>
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<td>104</td>
<td>68</td>
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</table>
Spectral Data Of Chalcone CA4

IR (KBr) cm⁻¹:
IR spectrum of Chalcone (CA4) showed its characteristic absorption bands in the following region. 3052.82 (Ar, C-H-Str), 1669.68 (C=O), 1604 (C=C), 1578, 1569, 1512, (C=C ring Str) 1569 and 1341 (NO₂) 1215.8 (C-O), 791.57 (1,2- disubstituted phenyl ring)

¹H NMR : (δ ppm)
The ¹H NMR data of Chalcone (CA4) showed the signals in the following region. δ 7.262 – 8.18 (11H,m, 9H of Ar-H and 2H of CH=CH)
**Spectral data for PYR4**

![Chemical structure of PYR4]

**IR (KBr) CM⁻¹:**
The IR spectrum of PYR4 showed its characteristic absorption bands in the following region.

3054 (Ar-C-H Str), 2926-52 and 2830 (C-H Str of CH₂ groups asymmetric and symmetric) 1667.78 (C=O), 1604(C=N), 1569, 1513, 1446 (C=C ring Str) 1446 and 1341 (C-H bending of CH₂ asymmetric and symmetric) 1569 and 1341 (NO₂), 1290 (C-O), 791 (1.2-disubstituted phenyl ring) 741 (mono substituted phenyl ring)

**¹H NMR : (δ ppm)**
The ¹HNMR Spectrum of PYR4 showed the signals in the following region. δ 2.2 (2H,s,CH₂) 2.4 (2H,s,CH₂) 2.9 and 3.0 (4H,s, 2XCH₂ of Pyrazoline rings) 4.0 (2H,s,2XCH of Pyrazoline rings) 4.9 (2H,s,CH₂ of -C=O-OCH₃) 5.2 (2H,s,CH₂ of -C=O-CH₂) 6.89 to 8.17 (18H,m,Ar-H)
Spectral data for PYR4

13CNMR:

13CNMR Spectrum of PYR4 gave the signals for its 36 magnetically different environmental carbon atoms as indicated below.

- C16 and C21 (2 C=O groups) 190.786
- C11 and C26 (2 C-NO2) 148.967
- C1 and C24 (2 C=N) 133.99
- C3 and C22 (2 C-N) 140.49
- C4, C5, C6, C7, C8, C9,
- C10, C12, C13, C14, C15,
- C25, C27, C28, C29, C30, 124.98-133.55
- C31, C32, C33, C34, C35 & C36 (22 carbon atoms of aromatic rings)
- C2 and C23 57.45 and 48.96
- C17 and C20 42.94 and 41.30
- C18 and C19 24.28

Mass Spectrum of PYR4

The pyrazoline derivative PYR4 (mol.wt 644) showed a parent ion peak at m/e 645 which is (M+1) peak. The base peak is observed at m/e 219 other important peaks are m/e 499, 378, 310, 254, 219, 180, 130, 124, 105, 77.

Seven membered most stable ring
Spectral Data for PYR-13

**IR (KBr) CM⁻¹:**
IR spectrum of PYR-13 showed its characteristic absorption bands in the following region.
3060 (Ar-C-H Str), 2970.68 and 2870 (C-H str of CH₂ groups asymmetric and symmetric). 1670 (C=O), 1609 (C=N), 1569, 1512, (C=C ring Str) 1436 and 1342 (C-H bending of CH₂ groups asymmetric and symmetric) 1569 and 1342 (NO₂), 1399 (C-N) 1290 (C-O) 827.72 (p-disubstitution benzene rings) 790 (1.2-disubstitution benzene ring) 530.5 (C-Cl)

**¹H NMR : (δ ppm)**
The ¹H NMR spectrum of PYR-13 showed the signals in the following region. δ 1.86 (2H,s,CH₂) 2.03 (2H,s,CH₂) 3.07-3.18 (4H,d,2XCH₂ of pyrazolin ring) 3.95-4.10 (6H,m,4H of 2CH₂ groups of C=O-CH₂ + 2H of 2XCH of pyrazoline rings) 7.04-8.85 (16H,m,Ar-H)

**Mass Spectrum of PYR-13**
The pyrazoline derivative PYR-13 (mol wt 711) showed a parent ion peak at m/e 711. The base peak is observed at m/e 254.
TIC of O1: from Sample 46 (PYR13 M/Z-618) of Directmass06012010.wiff (Turbo Spray)

Max. 3.1e7 cps.

O1: 0.323 to 0.323 min from Sample 46 (PYR13 M/Z-618) of Directmass06012010.wiff (Turbo Spray), subtracted (0.010 to 0.212 min)

Max. 1.9e5 cps.
Spectral Data for HAA (Adipic acid hydrazide)

\[
\begin{align*}
H_2N\text{HN} & \quad \text{C} \quad (\text{CH}_2)_4\text{C} \quad \text{NH.NH}_2 \\
\end{align*}
\]

IR (KBr) cm\(^{-1}\):
IR spectrum of Adipic acid hydrazide (HAA) showed its characteristic absorption bands in the following region.
3311 (NH\(_2\)), 3181 (NH), 2960, 2863, (C-H Str of CH\(_2\) groups), The broad peak at 1635 (C=O of CONH) and N-H bending of CH\(_2\) group, 1275 (C-O), 1460 and 1379 C-H bending of CH2 groups symm and symm)
Spectral Data for CA-9

\[
\text{Cl-C} = \text{CH-CH-CH} \quad \text{CM}^{-1}
\]

**IR (KBr) CM^{-1}**:  
IR spectrum of chalcone CA-9 showed its characteristic absorption bands in the following region.  
3057 (Ar. C-H Str), 1661 (C=O), 1605, 1485, 1448 (C=C ring Str), 1288 (C-O) 829 (1.4–disubstituted phenyl ring), 872 (substituted phenyl ring), 574 (C-Cl)
**Spectral Data for PYR-9**

The bispyrazoline PYR-9 is obtained on heating the hydrazide of a dicarboxylic acid like adipic acid with a chalcone like CA-9. The characteristic absorption bands appeared in the IR Spectrum of hydrazide have been disappeared in the IR Spectrum of bispyrazoline PYR-9, further the C=O groups of CONH of hydrazide which appeared at 1635 have also been shifted to the higher range of 1662 in the IR Spectrum of bispyrazoline PYR9. These observations confirm the formation of series of bispyrazolines prepared by this method.

**IR (KBr) CM⁻¹:**
The bispyrazoline PYR-9 showed its characteristic absorption bands in the following region. 3053 (Ar, C-H Str), 2970, 2865, (C-H Str of CH₂ groups), 1662 (C=O), 1605, 1522, 1494, 1448 (C=C ring Str), 1217 (C-O), 829 (1.4 disubstituted phenyl ring), 729 (mono substituted phenyl ring), 574 (C-Cl)
Spectral Data for PYR-10

IR (KBr) CM⁻¹:
IR spectrum of PYR10 showed its characteristic absorption bands in the following region.

3444 (NH₂), 3059 (Ar, C-H Str), 2924,2853 (C-H Str of CH₂ asymm and symm), 1656 (C=O), 1595 (C=N), 1594,1537,1510 (C=C ring Str), 1474,1314, (C-H bending of CH₂ asymm & symm), 1280 (C-O bending), 846 (1.4-disubstituted phenyl ring), 875 (substituted phenyl ring) 700 (C-Br), 560 (C-Cl)
**Spectral Data for PYR-11**

IR (KBr) cm⁻¹:

IR spectrum for PYR18 showed its characteristic absorption bands in the following region.

3080 (Ar, C-H Str), 2937, 2842 (C-H Str of OCH₃ & CH₂), 1655 (C=O), 1594 (C=N), 1594, 1510, 1486 (C=C ring Str), 1463, 1331 (C-H bending of OCH₃ & CH₂), 1255 (C-O), 1171 (C-O-C), 839 (1.4-disubstituted phenyl ring), 872 (mono substituted phenyl ring), 548 (C-Cl)
Spectral Data for PYR-18

IR (KBr) cm⁻¹:
IR spectrum of PYR-18 showed its characteristic absorption bands in the following region.
3073 (Ar C-H Str), 2940, 2810 (C-H Str of CH₂ groups asymmetric and symmetric), 1660 (C=O), 1598 (C=N), 1598, 1505 (C=C ring Str), 1416,1335 (C-H bending of CH₂ group asymmetric and symmetric), 1284 (C-O), 871 (substituted phenyl ring), 823 (1.4-disubstituted phenyl ring), 984 (C-F)
Antibacterial Activity of bis-Pyrazolines

The invitro antibacterial screening was carried out at the microbiology department, Navodaya Medical College and Research Centre, Raichur. Diffusion method as described in Chapter-III was used. The result is presented in Table No. 50.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Sample No.</th>
<th>Zone of Inhibition (mm)</th>
<th>Staphylococcus aureus</th>
<th>E.Coli</th>
<th>Pseudomonas aeruginosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P1</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2</td>
<td>P2</td>
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<td>00</td>
<td>00</td>
<td>00</td>
</tr>
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</tr>
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<td>00</td>
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</tr>
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<tr>
<td>7</td>
<td>P7</td>
<td>28</td>
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<td>00</td>
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</tr>
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<td>00</td>
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<tr>
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<td>P9</td>
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<td>00</td>
<td>32</td>
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<tr>
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<td>00</td>
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<td>26</td>
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</tr>
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<td>24</td>
<td>24</td>
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</tr>
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<td>28</td>
<td>00</td>
<td>00</td>
<td>28</td>
</tr>
<tr>
<td>13</td>
<td>P13</td>
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<td>00</td>
<td>00</td>
<td>24</td>
</tr>
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<td>14</td>
<td>P14</td>
<td>26</td>
<td>00</td>
<td>00</td>
<td>30</td>
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<tr>
<td>15</td>
<td>P15</td>
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<td>00</td>
<td>00</td>
</tr>
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<td>24</td>
<td>22</td>
<td>00</td>
<td>00</td>
</tr>
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<td>18</td>
<td>P18</td>
<td>20</td>
<td>00</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>19</td>
<td>Ciprofloxacin</td>
<td>30</td>
<td>28</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Gentamycin</td>
<td>34</td>
<td>30</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Tobramycin</td>
<td>30</td>
<td>32</td>
<td>34</td>
<td></td>
</tr>
</tbody>
</table>
**Pyrazoline - results and discussion**

Derivatives of the Pyrazoline series (P1-P18) were evaluated for antimicrobial studies against the organisms *Staphylococcus aureus*, *E.coli* and *Pseudomonas aeruginosa* at the Conc 10 µg/ml. Reference drugs employed are Ciprofloxacin, Gentamycin and Tobramycin of Conc. 10 µg/ml. These derivatives were found to be active against *Staphylococcus aureus*. The compound P13 showed significance activity against *Staphylococcus aureus*, when compared with all the standard drugs used for the study. Some of the compounds showed moderate to significance activity. Only three compounds P10, P11 and P17 showed moderate activity against *E.coli* and remaining derivatives were inactive. The Pyrazoline derivatives P9, P12 and P14 showed almost equipotent activity with one or the other standard drug where as P10, P11, P13 and P15 showed moderate activity against remaining derivatives are inactive against *Pseudomonas aeruginosa*. 
Antifungal Activity of Pyrazolines

The invitro antifungal property of the Pyrazoline derivatives is done at Maratha Madals Nathaji Rao Dental College and Research Centre, Belgaum recognized by Rajiv Gandhi University of Health Sciences, Bangalore as nodal centre for carrying out biological evaluation.

Table 51: Antifungal Activity of Pyrazolines

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Compounds</th>
<th>Concentration (µg/ml)</th>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
<td>75</td>
</tr>
<tr>
<td>1</td>
<td>P-1</td>
<td>16mm</td>
</tr>
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<td>2</td>
<td>P-2</td>
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<td>P-6</td>
<td>12mm</td>
</tr>
<tr>
<td>7</td>
<td>P-7</td>
<td>20mm</td>
</tr>
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<td>P-8</td>
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</tr>
<tr>
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<td>P-9</td>
<td>20mm</td>
</tr>
<tr>
<td>10</td>
<td>P-10</td>
<td>R</td>
</tr>
<tr>
<td>11</td>
<td>P-11</td>
<td>R</td>
</tr>
<tr>
<td>12</td>
<td>P-12</td>
<td>26mm</td>
</tr>
<tr>
<td>13</td>
<td>P-13</td>
<td>33mm</td>
</tr>
<tr>
<td>14</td>
<td>P-14</td>
<td>16mm</td>
</tr>
<tr>
<td>15</td>
<td>P-15</td>
<td>14mm</td>
</tr>
<tr>
<td>16</td>
<td>P-16</td>
<td>18mm</td>
</tr>
<tr>
<td>17</td>
<td>P-17</td>
<td>22mm</td>
</tr>
<tr>
<td>18</td>
<td>P-18</td>
<td>16mm</td>
</tr>
</tbody>
</table>

Table 52: Antifungal Activity by MIC Method

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Compounds</th>
<th>Concentration (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>500</td>
</tr>
<tr>
<td>1</td>
<td>P-13</td>
<td>S</td>
</tr>
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</table>
**Results and Discussions**

Survey on literature showed that chalcones and pyrazoline analogues, exhibit wide range of antibacterial property. The pyrazoline derivatives P1 to P18 were screened for antifungal activity against the organism. The results indicated that most of the derivatives belonging to this group exhibit weak to medium antibacterial property. The compounds P6, P8, P10, P11 and P15 exhibited no activity. Perhaps the bulkiness of the molecule of bis pyrazoline derivatives having several crowded groups might have caused stearic hinderance thereby reducing the activity of the compounds.
Analgesic and Anti Odema (Anti-inflammatory)

Property of Pyrazolines

The Analgesic and Antiodema property was carried out at Navodaya Medical College & Research Centre, Raichur, Karnataka similar method as explained in the above mentioned in Chapter-IIIB was used for evaluation of analgesic and antiodema propert.

Table 53: Anti-inflammatory Activity of Pyrozolines (PYR series)

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Treatment</th>
<th>Percentage inhibition of rat’s hind paws Oedema at different time intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>30min</td>
</tr>
<tr>
<td>01</td>
<td>Control</td>
<td>0.00</td>
</tr>
<tr>
<td>02</td>
<td>Diclofenac Sodium</td>
<td>18.47</td>
</tr>
<tr>
<td>03</td>
<td>PYR₁</td>
<td>2.14</td>
</tr>
<tr>
<td>04</td>
<td>PYR₂</td>
<td>8.67</td>
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<td>PYR₆</td>
<td>26.10</td>
</tr>
<tr>
<td>06</td>
<td>PYR₉</td>
<td>7.66</td>
</tr>
<tr>
<td>07</td>
<td>PYR₁₀</td>
<td>9.78</td>
</tr>
<tr>
<td>08</td>
<td>PYR₁₄</td>
<td>14.14</td>
</tr>
</tbody>
</table>

Result: The representative compounds of pyrozolines showed weak activity. The compound PYR₁₄ is inactive.
Table 54: Analgesic Activity of Pyrazolines (PYR series)

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Treatment</th>
<th>Mean ± S.E.M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0 hr</td>
</tr>
<tr>
<td>01</td>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>02</td>
<td>Pentazocin</td>
<td>6.24±0.889</td>
</tr>
<tr>
<td>03</td>
<td>PYR₁</td>
<td>4.50±0.43</td>
</tr>
<tr>
<td>04</td>
<td>PYR₂</td>
<td>5.66±0.67</td>
</tr>
<tr>
<td>05</td>
<td>PYR₆</td>
<td>4.66±0.49</td>
</tr>
<tr>
<td>06</td>
<td>PYR₉</td>
<td>5.33±0.49</td>
</tr>
<tr>
<td>07</td>
<td>PYR₁₀</td>
<td>5.33±0.49</td>
</tr>
<tr>
<td>08</td>
<td>PYR₁₄</td>
<td>3.83±0.48</td>
</tr>
</tbody>
</table>

Result: The compounds exhibited weak analgesic activity.
List of References


17. Ead HA, Hassneen HM, Abdullah MA, Mousa HAH. Arch Pharm Weinheim (Ger) 1991; 324: 35.


33. Frangly AM, Chaban 1, Khalil MA, Behkit AA. Arch Pharm Weinheim 1990; 325.
47. Gover RK and Moore JD. Phyto Pathology 1962; 52: 876.