CHAPTER I
INTRODUCTION

Antimicrobial Activities of Chalcones, Chalconedibromides, and Pyrazoles:

Modern medicine is considered since ‘Hippocrates’. Greek physician (400 B.C.), introduced for the first time, the concept of disease as a pathologic process and organised the science of medicine on the basis of observations, analysis and deduction.

The structural basis to living organism is provided by chemical agents, which also regulate their functional activities. Potent chemicals provide effective methods for diagnosis, treatment and prevention of many diseases. Chemical compounds used for treatment and/or prevention of diseases are called ‘drugs’ and their action on living system is referred as ‘drug effect’. The subject of drug is as old as disease. Sickness has been man’s heritage from the beginning of his existence and search for remedies to combat is perhaps equally old.

From early times, antibacterial agents have been used as remedies. The earliest source of medicine came from ‘Egypt’ and two kingdoms of ‘Assyria’ and ‘Babylonia’. ‘Papyri’ was the first written account of medical experiences from Egypt and date back to 1900 B.C. Papyrus was discovered by Elber in 1872 and was prepared in 1500 B.C. and mentions about 700 herbal medicines including ‘Opium’.

James Gregory (1753-1821) carried out heroic symptomatic treatment consisting of blood letting, large doses of emetics and drastic purgatives with
disastrous results. This type of treatment without any rational basis was called ‘Allopathy’.

‘Hanneman’, first introduced the concept of ‘Homeopathy’ in the beginning of 19th century and thought that ‘Like cures like’. Homeopathy outlines the therapy for various ailments with drugs in very high dilution.

The action of drug gives an insight on living organisms and isolated tissues. Knowledge of the mode of action of drug, its effect on various body systems and the probable adverse effect is important. The antibiotics which are synthesized by micro-organisms and are lethal to other micro-organisms in low concentrations. An effective antibiotic must be selectively toxic to the microbial pathogens with little toxicity for the human body.

Pasteur and Koch established that, micro-organisms were the cause of infectious diseases. Paul Ehrlich for the first time proposed that infectious disease may be cured by using chemicals that kill the infecting agent but do not harm the host at the concentration employed. He discovered ‘Salvarson’ which was active against the causative organism of ‘Syphilis’. He used the term ‘Chemotherapy’. According to him, cells possess chemical receptors to which the drug binds. He recognised the importance of quantitative measurement to determine the drug dose, which would be effective against the causative agent and would not have toxic effect on the host. He gave a number of methods for screening a large number of compounds for biological activity in relation to chemical structure. Different drugs were then synthesized and tested to see whether they have improved antibacterial activity and reduced toxicity.
The world’s oldest pharmacological writing came from India and China. The great herbal of Chinese ‘Material Medica’, ‘Pan Tsao’ was probably written in 2735 B.C. The earliest Indian records are ‘Vedas’. Although there are medical descriptions in ‘Rigveda’ (2500-3000 B.C.), it was Charak renowned ancient Indian physician and later Sushruta and Vagbhatt, who discovered various medicines, included in ‘Ayurveda’ the science of life. Initially it consisted mostly nonpoisonous vegetable drugs and minerals. Charak described about 300 vegetable drugs and classified them according to their effects, mostly on symptoms into fifty groups.

Development in modern pharmacology is fairly recent and started taking shape following the introduction of experimental procedure by Francois Magendie (1783-1855) and Claude Bernard (1813-1878). Spectacular developments in physiology, biochemistry and organic chemistry during the recent years have greatly accelerated the advances in pharmacology.

According to literature much work has been done on heterocyclic compounds for their antibacterial activities on gram positive and gram negative bacteria. Chalcones and their derivatives are reported to have antibacterial, antifungal, antiparasitic, antitubercular, antiinflammatory and insect repellent properties.

Warik, H. and Medewar, G.,
Reddy, T.K.K. and Naidu, M.S.R.,
Bhatt et al.\textsuperscript{4} synthesized quinoline derivatives of chalcones and screened the products for antibacterial activities, while Ahluwalia and coworkers\textsuperscript{5} screened dihydrochalcones and their derivatives against some microbial organisms.

Pyrazolines are known to have bactericidal, fungicidal\textsuperscript{6} and insecticidal\textsuperscript{7} properties. Some pyrazolines are also reported to have antiinflammatory, antidiabetic, anaesthetic and analgesic properties\textsuperscript{8-11}.

Van Hes and Crossurt\textsuperscript{12} have synthesized pyrazolines (a) which were found to have insecticidal properties.

\begin{center}
\textbf{(a)}
\end{center}

3-amino-1-phenyl and substitutedphenyl-2-pyrazoles\textsuperscript{13} (b) were synthesized and found to be anti-inflammatory, bactericidal and fungicidal agents.

![Diagram](b)

El-Sharif and Ammar\textsuperscript{14}, reported pyrazolines with sulphonamidophenyl group which have considerable biological interest.

![Diagram](c)

Upadhyay et al.\textsuperscript{15}, studied antimicrobial activities of pyrazolines (d).

![Diagram](d)

\[ R = \text{H or Ph} \]


\textsuperscript{15} Upadhyay Jatin, Utpal Dave and Hansa Parekh, J. Indian Chem. Soc., 68(7) (1991), 413.
Hussain and Kumar, reported N-(acetyl/phenyl)-5-aryl pyrazolin-3-yl) phenylarylsulfonamides (e) as oral hypoglycemic agents.

\[
\begin{align*}
R &= \text{H or Me} \\
R^1 &= \text{H, Cl, OMe, Me, NO}_2 \\
R^2 &= \text{Ac or Ph}
\end{align*}
\]

(e)

Patel Pankaj et al., reported antimicrobial activities of pyrazolines (f).

\[
\begin{align*}
\text{Cl-} & \text{SO}_2\text{NH-} \\
\text{H} & \text{SO}_2\text{NH-} \\
\text{N} & \text{N}
\end{align*}
\]

(f)

Koregaonkar S.S. et al., studied antimicrobial activities of 3,5-diarylpyrazolines (g).

\[
\begin{align*}
\text{Cl-} & \text{SO}_2\text{NH-} \\
\text{H} & \text{SO}_2\text{NH-} \\
\text{N} & \text{N}
\end{align*}
\]

(g)

Fernandes and Parekh\textsuperscript{19}, reported antimicrobial activities of pyrazolines (i).

\[
\text{Ph-SO}_2\text{NH} - \begin{array}{c}
\text{Ar} \\
\text{N} \\
\text{I} \\
\text{R}
\end{array}
\]

(i)

Ganguli S.S. et. al.\textsuperscript{20}, reported antimicrobial activities of pyrazolines (j).

\[
\text{Ph-SO}_2\text{NH} \\
\begin{array}{c}
\text{Ar} \\
\text{N} \\
\text{H}
\end{array}
\]

(j)

Sorathiya S.D. et. al.\textsuperscript{21}, reported antimicrobial activities of some halogenated pyrazolines (k).

\[
\begin{array}{c}
\text{Br} \\
\text{Br}
\end{array}
\text{SO}_2\text{NH} - \begin{array}{c}
\text{Ar} \\
\text{R}
\end{array}
\]

(k)

\begin{itemize}
\item 19. Fernandes, Y.J., Parekh Hansa,
\item 20. Ganguli, S.S., Vadodariya, M.S.,
\item 21. Sorathiya, S.D., Patel, V.B.,
\end{itemize}

\text{and Parikh, H.R., J. Indian Chem. Soc., 74(3) (1997), 238.}

\text{J. Inst. Chem., 68(1) (1996), 1920.}

\text{Indian J. Chem., 30B (1997), 630.}
Recently, Parikh A.R. et al.\textsuperscript{22}, reported pyrazolines (I) as a potential antimicrobial agents.

\begin{center}
\includegraphics[width=0.3\textwidth]{structure1.png}
\end{center}

(I)

Anderson and Paolella\textsuperscript{23}, reported 1-phenyl pyrazole derivatives (m) as a effective hypoglycemic agent.

\begin{center}
\includegraphics[width=0.15\textwidth]{structure2.png}
\end{center}

R = Me, CF\textsubscript{3}, NH\textsubscript{2}

n = 1, 2

(m)

Sharma et al.\textsuperscript{24}, reported antimicrobial activities of hydroxyaryl pyrazoles (n).

\begin{center}
\includegraphics[width=0.3\textwidth]{structure3.png}
\end{center}

(n)


Alkyl pyrazole derivative (o) have also been reported as hypolidermic agents\textsuperscript{25}.

\[
\begin{array}{c}
\text{R}_3 \\
\text{N} \\
\text{R}_1 \\
\text{R}_2
\end{array}
\]
(o)

Mittal and Singhal\textsuperscript{26}, reported antimicrobial activities of substituted pyrazoles (p).

\[
\begin{array}{c}
\text{R}_1 \\
\text{N} = \\
\text{N} \\
\text{R}_2 \\
\text{OCH}_3 \\
\text{R}_3
\end{array}
\]
(p)

Basu et. al.\textsuperscript{27}, reported the synthesis of pyrazoles (q) as useful intermediates for pesticides and anticonvulsants.

\[
\begin{array}{c}
\text{R}_3 \\
\text{N} \\
\text{R}_1 \\
\text{R}_2
\end{array}
\]
(q)

\textsuperscript{27} Basu, U.I.F., Reuther and Wolfgang; Chem. Abstr., \textbf{113} (1990), 172013.