CHAPTER II

ANTIMICROBIAL ACTIVITIES OF SOME
ARYL STYRYL KETONES

2.1 INTRODUCTION

Chalcones possess various multipronged and biological activities. The insect anti-feedant activities of chalcones against the larvae of Achoea Janata L and caster semi looper have been studied. In an effort to develop new antimicrobial agents, a series of chalcone derivatives, were prepared by Claisen–Schmidt condensation of appropriate acetophenones and 2-furyl methyl ketones with appropriate aromatic aldehydes, furfural, and thiophene-2-carbaldehyde in an aqueous solution of NaOH and EtOH at room temperature. All compounds were tested for their antibacterial and antifungal activities by the disc diffusion method. For the most active compounds, minimum inhibitory concentrations (MICs) were determined.

Three monoterpene-chalcone conjugates, including two novel compounds isorubraine and sumadain C, and a known compound rubraine were isolated from the seeds of Alpinia katsumadai.

Cytotoxic activities of these compounds were evaluated against cell lines HepG2, MCF-7 and MAD-MB-435, and compound 3 exhibited potent cytotoxic activity.

Anthocyanins are flavonoids and possess extensive bioactivities and pharmacological properties.
Many series of chalcones were synthesized and studied for activity against *Candida albicans*. The SAR analysis showed that the antifungal activity was highly dependent on the substitution pattern of the aryl rings and correlated to a large extent with the ability of compounds to interact with sulfhydryl groups\(^2\).4\(^1\).

The ability of 11 chalcones with 3, 4, 5-trimethoxy substitution on ring A to inhibit the transport activity of P-glycoprotein was studied\(^2\)42. The majority of the tested compounds were proved to be effective inhibitors of the outward transport of rhodamine-123.

The development of chalcones as antimitotic agents had led to the design of other analogues able to interact with tubulin and inhibit its assembly into microtubules. This activity had also been associated with their anti-vascular activity\(^2\)43.

The heterocyclic analogues of chalcones were synthesized by Claisen Schmidt reaction of (a) benzaldehyde with 2-acetylfuran, 2-acetylpyrrole and 2-acetylthiophene and (b) acetophenone with furfural, thiophene-2-carbaldehyde and pyrrole-2-carbaldehyde. The antibacterial and antifungal activity of the precursor chalcones and the dimeric products showed antimicrobial activities of different extents with respect to individual compounds. In general, photolysis of heteroaryl chalcones causes the depletion of antimicrobial activity\(^2\)44.

A new series of 2, 4-disubstituted-2, 3-dihydro substituted-1, 5-benzodiazepine derivatives were synthesized by the condensation of o-phenylene diamine and various 1-(4'-substituted phenyl)-3-(3 mono-, or
4 mono-, or 3, 4 di-, or 3, 4, 5 tri-substituted phenyl)-2-propene-1-one under microwave irradiation conditions\textsuperscript{231}. All the compounds were screened for their in vitro activities against Gram-positive, Gram-negative bacteria and fungal strains.

Chalcones are absorbed in the daily diet and appear to be promising cancer chemopreventive agents. Moreover, numerous compounds from the family of dietary chalcones appear to show activity against cancer cells, suggesting that these molecules or their derivatives may be considered as potential anticancer drugs\textsuperscript{33}.

Chalcones constitute an important group of natural compounds that are especially abundant in fruits, vegetables and various plants and spices, many of which have been used for centuries in traditional herbal medicine\textsuperscript{33}.

Chalcones exhibit anti-inflammatory properties generally due to the presence of $\alpha$, $\beta$ unsaturated bond. A new class of C8-linked pyrrolo[2,1-c][1,4]benzodiazepine-chalcone conjugates have been prepared by employing a solid-phase synthetic protocol\textsuperscript{231}.

Sulfonamide chalcones had more potent alpha-glucosidase inhibitory activity than aminated chalcone. 4'-(p-Toluenesulfonamide)-3, 4-dihydroxy chalcone IC(50)=0.4\textmu M) was the best inhibitor against alpha-glucosidase, and these sulfonamide chalcones showed non-competitive inhibition\textsuperscript{245}.

Dihydroartemisinin chalcones linked by ether are more cytotoxic than dihydroartemisinin chalcones linked by ester with apoptosis induction abilities\textsuperscript{233}. 

262
Twentyseven novel chalcone derivatives were synthesized using Claisen-Schmidt condensation and their antimalarial activity against asexual blood stages of *Plasmodium falciparum* was determined. 3, 4, 5-trimethoxy groups on chalcone derivative probably cause steric hindrance in binding to the active site of cysteine protease enzyme, explaining the relative lower inhibitory activity.\(^{246}\)

The stabilizing action of chalcones on the vascular wall, vasodilating and anti-aggregating effects, and a favourable effect of their antioxidative activity on the functions of the cardiovascular system had been established.\(^{247}\)

According to Rahman et.al.,\(^{248}\) chalcones, and their derivatives have attracted increasing attention due to numerous potential pharmacological applications. It is useful for the development of new medicinal agents having improved potency and lesser toxicity.

Chalcones have different biological activities including analgesic, antibacterial, anti-fungal, anticancer, anti-inflammatory, anti-hyperglycemic, anticoagulant, antidepressant, antifibrogenic, antifibrogenic activities and modulation of P-glycoprotein-mediated multi-drug resistance, antifouling, antifungal, antiHIV, antihyperglycemic, antiinvasive, antileishmanial, antimalarial, antimicrobial, antimitotic, antioxidant, antiplasmodial, immnosuppressive, cytotoxic, antitumor and antioxidant properties, antitubercular, antitumor, antitrichomonal, antiviral.
cardiovascular disease/activity\textsuperscript{295}, chemopreventive activity\textsuperscript{296}, cysteinyll leukotriene\textsuperscript{297}, cytotoxic\textsuperscript{279,298}, cytotoxic and anti-Trypanosoma cruzi\textsuperscript{299}, gastroprotective\textsuperscript{300}, immunomodulatory\textsuperscript{271,277}, inhibition of aldose reductase\textsuperscript{301,302}, inhibition of chemical mediators release, inhibition of leukotriene B\textsubscript{4}\textsuperscript{303}, inhibition of tyrosinase\textsuperscript{304,305} leishmanicidal\textsuperscript{306}, modulation of nitric oxide production\textsuperscript{307}, protein tyrosine kinase\textsuperscript{308}, receptor-1[CyLT1](LTD\textsubscript{4}) antagonist\textsuperscript{309}, trypanocidal\textsuperscript{310}, vascodialatory\textsuperscript{311}, xanthine oxidase activities\textsuperscript{312}.

According to Rahman et.al.,\textsuperscript{248} malaria is globally recognized as a serious problem of public health, mainly in the tropical and subtropical regions of the world. The increase of resistant malarial parasite strains represents the largest obstacle to antimalarial chemotherapy.

Motta et.al.,\textsuperscript{313} studied several chalcone derivatives. He performed quantitative structure-activity relationships of a series of chalcone derivatives (1, 3-Diphenyl-2-propen-1-one) as anti-Plasmodium falciparum agents (antimalarial agents).

Awasthi et.al\textsuperscript{38}, synthesized several new chalcone analogues and evaluated as inhibitors of malaria parasite. Inhibitory activity was determined \textit{in vitro} against a chloroquine-sensitive \textit{P.falciparum} strain of parasites.

In order to accelerate the development of relatively inexpensive antimalarials that are effective against chloroquine-resistant strains of \textit{P.falciparum}, Cheng et.al.,\textsuperscript{314} had developed a methodology for the solid phase synthesis of chalcone analogues in reasonably high yields.
As a part of the search for novel antimalarial agents from plants or via chemical synthesis, Lim et al.,\textsuperscript{39} prepared twenty derivatives of flavonoids and chalcones, four derivatives for each of flavones, flavanones, chalcones, dihydrochalcones, and 3'-chlorochalcones, and evaluated for in vitro antimalarial activity against \textit{P.falciparum} strain FCR-3 and cytotoxicity against FM3A cells (a mouse mammary tumor cell).

Achanta et al.,\textsuperscript{315} evaluated a series of boronic chalcones for their anticancer activity and mechanisms of action.

A series of chalcone-like agents, in which the double bond of the enone system is embedded within a thiophene ring, were synthesized and evaluated by Romagnoli et al.,\textsuperscript{316}. The synthesized compounds were found to inhibit the growth of several cancer cell lines at nanomolar to low micromolar concentrations.

Echeverria et al.,\textsuperscript{317} studied relationships between the structural characteristic of synthetic chalcones and their antitumoral activity.

Chalcones exhibit chemopreventive and antitumor effects. Szliszka et al.,\textsuperscript{318} examined the cytotoxic and apoptotic effect of five chalcones in combination with TRAIL on prostate cancer cells and evaluated the cytotoxicity by the MTT and Lactate Dehydrogenase (LDH) assays.

Ilango et al.,\textsuperscript{34} synthesized a series of chalcones and evaluated them for their in vitro cytotoxic activity by microculture Tetrazolium Test Assay method using two breast cancer cell lines MCF-7 and T47D. The IC50 value was calculated at the 0.1-100 µM concentration range.
Ten chalcones were synthesized and tested as leishmanicidal and trypanocidal agents by Lunardi et al.,\textsuperscript{306} against in vitro growth of Leishmania braziliensis and Trypanosoma cruzi. The results showed that the positions of the substituents seem to be critical for their antiprotozoal activities.

Yadav et al.,\textsuperscript{319} synthesized a series of chalcone derivatives containing \(\alpha, \beta\)-unsaturated carbonyl moiety which is responsible for anti-inflammatory activity.

In an effort to develop potent anti-inflammatory agents, a series of substituted chalcone derivatives was synthesized and evaluated for anti-inflammatory activity by Zhang et al.,\textsuperscript{320} through in vivo inhibition assay monitoring of their ability to inhibit xylene-induced ear edema in mice.

Hamdi et al.,\textsuperscript{321} synthesized a series of new coumarin derivatives containing a chalcone moiety and evaluated for possible anti-oxidant and antibacterial activities.

A series of chalcone derivatives were synthesized and evaluated for antibacterial activity by Bhatia et al.,\textsuperscript{322} All the compounds were screened for their antibacterial activities.

Chalcone derivatives were evaluated by Awasthi et al.,\textsuperscript{323} for their antifilarial activity on Setaria cervi using glutathione-S-transferase (GST) enzyme as a drug target. The methoxy-substituted chalcones can be used for further studies against filariasis.

With the aim of developing potential antifungals, Bag et al.,\textsuperscript{324} synthesized a series of chalcones incorporating sulfur either as part of a
hetero-aromatic ring (thiophene) or as a side chain (thiomethyl group) and tested for their in vitro activity.

Lahtchev et.al.,\textsuperscript{266} reported the synthesis, antifungal evaluation and study on substituent effects of several chalcones. A lot of genetically defined strains belonging to different yeast genera and species, namely \textit{Saccharomyces cerevisiae}, \textit{Hansenula polymorpha} and \textit{Kluyveromyces lactis}, were used as test organisms.

Yayli et.al.,\textsuperscript{325} synthesized N-alkyl derivatives and photochemical dimers of 3 \(\alpha\)-, \(m\)-, and \(p\)-nitro substituted 4-azachalcones. The monomeric compounds showed good antimicrobial activity against test micro-organisms \textit{E.coli}, \textit{K.pneumoniae}, \textit{Yersinia pseudotuberculosis}, \textit{P.aeruginosa}, \textit{Enterococcus faecalis}, \textit{S.aureus}, \textit{Bacillus cereus}, and \textit{Candida tropicalis}.

A series of chalcone analogues and some of their derivatives were synthesized and subjected to the mosquito larvicidal study (larvae of \textit{Culex quinquefasciatus}), SAR and QSAR by Begum et.al.,\textsuperscript{326}.

Some new phenoxy chalcones were prepared and screened for their anticonvulsant activity using Maximal Electroshock Method (MES) by Kaushik et.al.,\textsuperscript{327} Neurotoxicity study was performed using rotarod method.

Vasil’ev et.al.,\textsuperscript{328} studied six anti-oxidants from the class of chalcones (ArOH), compounds from which flavonoids are obtained in nature. The antiradical activity of chalcones and a number of related compounds was determined by a chemiluminescence method.
Sivakumar et al., synthesized 25 chalcone derivatives and evaluated their antioxidant activity through four different methods namely, superoxide radical-scavenging, hydrogen peroxide-scavenging, reducing power, and DPPH radical-scavenging assays at 50 µg/ml in vitro.

Vogel et al., established a general strategy for the synthesis of 3'-prenylated chalcones and synthesized a series of prenylated hydroxychalcones, the synthesized compounds was also investigated for their antioxidant activity evaluation and revealed the highest activity for the compounds. From the above review, it can be said that chalcones and their derivatives display a wide range of pharmacological activities, such as antimalarial, anticancer, antiprotozoal (antileishmanial and antityranosomal), anti-inflammatory, antibacterial, antifilarial, antifungal, antimicrobial, larvicidal, anticonvulsant and antioxidant activities. They also show inhibition of the enzymes, especially mammalian alpha-amylase, cyclooxygenase (COX) and monoamine oxidase (MAO) and antimitotic activity too. Because of this, chalcones and their derivatives have attracted increasing attention of the scientists for the search of new potent pharmacological activity in it.

Varun Arora et al., had synthesized a series of chalcones of 2-acetyl naphthalene and substituted aryl aldehydes and evaluated for antimicrobial activity. Synthesis of chalcones and their derivatives has significant biological activity.

Among these wide variety of heterocyclic that have been explored for developing pharmaceutical important molecules pyrimidine, pyridine, indole, flavones, and pyrдинethiones have important role in medicinal
chemistry. The presence of reactive unsaturated ketone in chalcone is responsible for antibacterial\cite{336-338}, and antifungal activities.

Senthamizh Selvi et al\cite{339}, reported that Chalcones represent an essential group of natural as well as synthetic products and some of them possess wide range of pharmacological activity.

The antifungal actions have been largely attributed to the reactive enone moiety\cite{36,340}. As a Michael reaction acceptor the enone unit binds thiol groups of certain proteins. The Michael reactions of chalcones are facilitated by electron withdrawing groups.

According to Senthamizh Selvi et al\cite{339}, due to the rapid development of bacterial resistance to antibacterial agents, it is vital to discover novel scaffold for the design and synthesis of the new antibacterial agents to help in the battle against pathogenic microorganisms. It was observed that the antibacterial efficiency depends on the length of the alkyl substituents in the polymer repeat units. As the polymer became more hydrophobic (hexyl and higher alkyl chain lengths in the repeat unit) the integrity of the membrane was more efficiently disrupted\cite{308,341}. The bactericidal effects have been related to the ability of the \(\alpha, \beta\)-unsaturated ketone to undergo a conjugated addition to a nucleophilic group.

Some substituted chalcones and their derivatives including heterocyclic analogues are reported to possess interesting biological properties, which are detrimental to the growth of microbes, tubercle bacilli, malarial parasites and intestinal worms. Some of these chalcones are found to exhibit inhibitory action on several enzymes, fungi and herbaceous plants\cite{342}. 
The synthesis and biological activities of various chalcones and their derivatives has been reviewed by Dhar\textsuperscript{1,343}. The compounds were screened for their antimicrobial activities according to tube dilution method\textsuperscript{465}.

According to Vasant et al.,\textsuperscript{344} naturally occurring and synthetic chalcones have shown promising biological activities. The presence of enone functional its in the chalcones help them to display various pharmacological activities\textsuperscript{345-347} 1, 5-Benzothiazepine nucleus has been well proved as illustrated by a large number of patents chemotherapeutic covering their utilities. A number of biological activities such as squalene synthetase inhibitor\textsuperscript{348} V2 arginine vasoperision receptor antagonist\textsuperscript{349}, HIV-1 reverse transcriptase inhibitor\textsuperscript{350}, etc. have been displayed by 1, 5-benzothiazepines.

Musa, et al.,\textsuperscript{351} had studied the analgesic effect of the chalcone compound, using acetic acid induced writhing and hot plate tests in mice. The compound isolated showed significant analgesic activity in acetic acid induced writhing test but no activity in the hot plate test, suggesting that it possess peripheral analgesic activity. To the best of our knowledge, this is the first report of the isolation of this compound.

Manisha et al.,\textsuperscript{352} have synthesized two series of novel chalcones and evaluated for their in-vitro antimalarial activity against chloroquine sensitive strain of \textit{Plasmodium falciparum}.

The four species of \textit{Plasmodium} responsible for disease in human beings are \textit{Plasmodium falciparum}, \textit{Plasmodium vivax}, \textit{Plasmodium ovale} and \textit{Plasmodium malariae}.\textsuperscript{353} Among the four species of \textit{Plasmodium parasite}, \textit{P. falciparum} is the most wide spread and dangerous as it can lead to the fatal cerebral malaria, which often results in death\textsuperscript{354}. 

270
World Health Organization (WHO) report on malaria reveals that 247 million malaria cases among 3.3 billion people are at risk in 2006, causing nearly a million deaths, mostly of children under 5 years. Out of 109 countries which were endemic for malaria in 2008, 45 were within the WHO Africa region. Among a million deaths, 95% deaths are caused in Africa.

A number of chalcone derivatives have also been found to inhibit several important enzymes in cellular systems, including xanthine oxidase, aldose reductase, epoxide hydrolase, protein tyrosine kinase, and quinone reductase. Interest in chalcones as antimalarials was initiated by the discovery of antiplasmodial activity of Licochalcone A, an oxygenated chalcone isolated from the roots of the Chinese licorice during routine screening.

Computational structural analysis also identified chalcones as potential plasmodial cysteine protease inhibitors consistent with the experimental data.

Chalcones showed a good level of inhibitory activity towards bovine lens aldose reductase (AR) and have been shown the promising compound for the prevention or treatment of diabetic complications.

Glycogen stores in the brain are small relative to the liver especially muscle. Nevertheless, brain glycogen turns over rapidly, and contributes significantly to normal brain energy metabolism. Brain glycogen is located entirely in astrocytes, which are distributed throughout the brain but are more concentrated in fiber bundle and white matter. In the mammalian liver, glycogen is present in the form of rosettes. Glycogen is present in central nervous system (CNS) although at much lower
concentrations than liver or skeletal muscle with the commonly accepted ratio of liver/ skeletal muscle/ brain: 100:1:1\(^{370}\).

The concentration of the glycogen in the liver can vary according to the nutritional state of the animal. In the liver of fasted rats or mice, this concentration is about 1-5 mg/g of wet wt and increases rapidly at the rate of about 10 mg (g wet wt)-1 h\(^{-1}\)\(^{371}\).

The accepted role of glycogen is that of a carbohydrate reserve utilized when glucose falls below need. However, there is a rapid continuous breakdown and synthesis of glycogen (17\(\mu\)mol/kg/min)\(^{372}\).

The ALR2 inhibitors (ARIs) have been developed as potential agents to prevent or delay the onset of diabetic complications\(^{373}\). There is strong evidence to show that diabetes is associated with increased oxidative stress\(^{374}\).

Flavonoids with insulin-trigerring and/or insulin like properties have been extracted from plants\(^{375}\).

Chalcones have been shown to display a diverse array of pharmacological activities\(^{31}\).

Several hydroxylated and methoxylated chalcones showed good level of inhibitory activity towards bovine lens aldose reductase (AR)\(^{376}\), and have been shown the promising compound for the prevention or treatment of diabetic complications\(^{377}\).

In recent report 3-nitro-2'-benzyloxychalcone showed potent insulin–stimulated glucose uptake in a concentration dependent manner in 3T3-L1 adipocytes in a cell based glucose uptake screening assay\(^{378}\).
ALR2 inhibitors have been shown to prevent or delay significantly diabetic complications\textsuperscript{373} and chalcones display significant inhibitory activity towards this enzyme. Thus, the aim of the present study was to determine the effects of chalcones on glycogen contents of liver, brain and spinal cord.

According to Jamal et.al.,\textsuperscript{361} chalcones, which are potent inhibitors of aldose reductase, caused an increase in glycogenolysis rate by decreasing the liver glycogen content. It is interesting to note that chalcones showed no activity against brain and spinal cord glycogen content.

Okunrobo et.al.,\textsuperscript{379} had synthesised 1,3-diaryl propen-1-ones (chalcones) by the Claisen-Schmidt condensation between acetophenones and benzaldehydes in potassium hydroxide /methanol medium at room temperature. The synthesized compounds were found to have anti-inflammatory and anti-ulcer activities at the doses employed.

Non-steroidal anti-inflammatory drugs (NSAIDs) are used as anti-inflammatory agents but their use often causes gastric erosion and ulcers, which are among the most serious clinical problems\textsuperscript{380,381} NSAID induced gastric damage has been attributed to suppression of endogenous prostaglandin synthesis resulting in the direct toxic effect on the gastric epithelial cells such as apoptosis or necrosis\textsuperscript{382}.

The inhibition of prostaglandin biosynthesis, which has cyto-protective effect on the gastric mucosa, was thought to be the major mechanism of gastrointestinal problems with NSAIDs\textsuperscript{383}.

Marrapua et.al.,\textsuperscript{384} had synthesized a series of twenty seven novel aryloxy azolyl chalcones and evaluated in vitro for the growth inhibition of Mycobacterium tuberculosis H37Rv.
Marrapua et.al.,\textsuperscript{384} have identified a new cheap chalcone molecular scaffold that can be easily prepared from commercially available reagents. The compounds were evaluated against \textit{M.tuberculosis} H37Rv in vitro with impressive MIC values.

Thanh-Dao.Tran.et.al.,\textsuperscript{385} had synthesized a series of 2'-hydroxychalcones and screened for their \textit{in vitro} inhibitory effects.

In an effort to develop antimicrobial agents, Balkrishna Tiwari et.al.,\textsuperscript{386} had synthesized a series of chalcones by Claisen-Schmidt condensation method. All the compounds were tested for their antibacterial and antifungal activities by the cupplate method.

The antimicrobial activity was performed by filter paper disc plate method\textsuperscript{387,388}, at concentration 100µg/mL and reported. Muller Hinton agar and Sabouroud Dextrose agar were employed as culture medium and DMSO was used as solvent control for antimicrobial activity. Streptomycin and Fluconazole were used as standard for antibacterial and antifungal activities respectively.

Saeed Attar et.al.,\textsuperscript{389} had synthesized a series of 30 organic chalcones and 33 ferrocenyl chalcones. The biological activity of each compound against the model nematode \textit{Caenorhabditis elegans} was examined.

One of the more recent developments in organometallic chemistry has occurred at its interface with the biological sciences, hence appropriately called bioorganometallic chemistry\textsuperscript{390}.

The ferrocene derivatives have featured prominently due to their excellent stability in aqueous, aerobic media, the easy accessibility of a large variety of derivatives, and favorable electrochemical properties\textsuperscript{391}.
The new bioorganometallic conjugate is dramatically more effective than the original organic analog, one notable example being that reported by Jaouen and co-workers on Tamoxifen (the drug used most often to treat breast cancer) and its active metabolite, hydroxytamoxifen\textsuperscript{392}.

When one of the aromatic rings was replaced with a ferrocenyl group, the resulting ‘ferrocifen’ was found to be a more effective drug, possibly due to the reversible oxidation and reduction of the iron atom, which could produce hydroxyl radicals that damage DNA. On the other hand, in a separate study\textsuperscript{393}, Jaouen et.al., reported that the use of a titanocenyl-Tamoxifen conjugate led to an increased rate of growth of estrogen-dependent breast tumors because it acted like estrogen. In another set of studies, Biot and co-workers\textsuperscript{394-396}, have shown that ferroquine and other ferrocenyl analogs of chloroquine (an established antimalarial compound) are very active, \textit{in vitro}, against both chloroquine-sensitive and chloroquine-resistant \textit{Plasmodium falciparum} across a variety of strains.

Wu.et.al.,\textsuperscript{397} had synthesized a series of ferrocenyl chalcones and evaluated for in vitro antimalarial activity against a chloroquine resistant strain of \textit{Plasmodium falciparum}. Many reports of ferrocene-based antimalarial drugs have emerged in the past 5 years. The most outstanding compound reported so far is ferrochloroquine, the ferrocenyl analogue of chloroquine\textsuperscript{394,398, 399}.

The series of ferrocenic artemisinin derivatives has activity comparable to artesiminin against \textit{P.falciparum} \textit{in vitro}\textsuperscript{400}. Ferrocenyl analogues of mefloquine and quinine are less active than the parent compounds\textsuperscript{400}.
An investigation of ellagitannins as antimalarial agents showed that derivatives with ferrocene and biphenic acid entities exhibit micromolar to submicromolar activity, but derivatives that lack either groups are inactive or have significantly less activity\textsuperscript{401}.

A novel series of benzylimidazolium compounds carrying ferrocenyl substituents have also been reported to have antimalarial activity\textsuperscript{402}.

Ferrocene is a lipophilic, electron donating entity with no hydrogen bond donor or acceptor property\textsuperscript{403}. The ferrous ion can undergo reversible oxidation–reduction and the nature of the substituents on the ferrocene ring has a marked influence on this process\textsuperscript{216}.

In order to investigate the role of ferrocene in anti-malarial activity, several ferrocenyl chalcones have been synthesized in this study. Firstly, their syntheses are readily achieved by conventional methods and a good number of members can be synthesized for evaluation. Secondly, we have investigated the antimalarial activities of alkoxylated and hydroxylated chalcones in an earlier study\textsuperscript{277} and the results of these two classes of chalcones can be compared to give useful conclusions.

Antiplasmodial activity of ferrocenyl chalcones was reported by Xiang et.al.\textsuperscript{404} Bhatt and co-workers reported cytotoxic properties of chalcones and their pyrazoles derivatives\textsuperscript{405}.

They have shown antibacterial activity against \textit{S.aureus}, \textit{E.coli}, \textit{C.albicans}, \textit{T.utilis}, \textit{S.sake}, \textit{W.anomala} and some other organisms\textsuperscript{406}. Devaux et.al.\textsuperscript{407} synthesized some nitrofuryl chalcones and tested for their antibacterial activity.
Some chalcones containing indole moiety were synthesized and tested for antibacterial and antifungal activity by Dandia et.al.,\textsuperscript{408}. Chalcones incorporated with benzopyran moiety were reported by Hismat et.al.,\textsuperscript{409}.

Salvie et.al.,\textsuperscript{410}, reported α-substituted chalcones. The α-methyl compound was found to be the most active and tested for the chemotherapy of leukemias.

Heterocyclic substituted chalcones were prepared by Bombardeli and Valenti\textsuperscript{411}, They reported that some of them were introduced for the treatment of breast cancer, menopausal disorders and osteoporosis. Uenaka et.al.,\textsuperscript{412} synthesized β-hydroxy chalcones.

Compounds having fluoro substitution showed considerable activity against Human Immuno Virus (HIV). Seele\textsuperscript{413}, reported chalcone having heterocyclic moiety and reported their insecticidal activity.

Mukherjee et.al.,\textsuperscript{290} had synthesized fourteen novel C-prenylated and 0-allylated 1, 3-diarylpropenones (chalcones) by Claisen-Schmidt condensation method.

Certain prenylated chalcones isolated from Sophora sub-prostrata have been studied in polorus-ligated, stress- induced ulcers in rat and found to possess potent inhibitory action on ulcer formation\textsuperscript{414, 415}. A di-0-prenylated chalcone, synthesized by Kyogoku et.al.,\textsuperscript{416} is a clinical candidate for the treatment of ulcers.

Flavone acetic acid, a compound of the same family, is an antitumour agent against murine adenocarcinoma cells in vivo and this compound has undergone phase I and II clinical trials\textsuperscript{417-419}.
Chalcones have found uses in the production of nematic liquid crystals\textsuperscript{420}, photosensitive polymers\textsuperscript{421}, and as antioxidants\textsuperscript{422, 423}.

Aryl styryl ketone derivatives are also known to inhibit the destruction of myelin sheath in the central nervous system of multiple sclerosis patients and are thus useful in controlling the progressive nature of the disease\textsuperscript{424}.

Chalcones and the corresponding heterocyclic analogues are valuable intermediates in organic synthesis and exhibit a wide range of biological activities\textsuperscript{31, 425}.

In countries such as China, Korea and Japan, butein (a tetrahydroxychalcone) has been traditionally used for treatment of pain, thrombotic disease, gastrics, stomach cancer and parasitic infections as well as a food additive. Liquorice has been used in China for the treatment of gastric and duodenal ulcers, bronchial asthma, Addison’s disease, food and drug poisoning and skin disease such as eczema and urticaria\textsuperscript{426}. It still finds medical application because of its wide ranging therapeutic properties including relief of rheumatic and other types of pain and healing effect on ulcers. The crude extract of liquorice has also found commercial use as food additive in Japan since it contains the sweetening agent glycyrrhin\textsuperscript{427}. Isoliquiritigenin, a liquorice chalcone, is currently in use as a phosphodiesterase-III inhibitor for the treatment of cardiovascular diseases\textsuperscript{428}.

A large number of chalcone derivatives have also been found to inhibit several important enzymes in cellular systems, including xanthine oxidase\textsuperscript{363}, aldose reductase\textsuperscript{429}, epoxide hydrolase\textsuperscript{358}, protein tyrosine kinase\textsuperscript{308} and quinine reductase\textsuperscript{359}. 

278
Many chalcones have been described for their high antimalarial activity, probably as a result of Michael addition of nucleophilic species to the double bond of the enone \(^{310}\).

Licochalcone isolated from Chinese liquorice roots, has been reported as highly effective in chloroquine resistant Plasmodium falciparum strains in a \([3H]\) hypoxanthine uptake assay \(^{430}\).

In an effort to develop antioxidant and antibacterial agents, a series of chalcones were prepared by Mohammed. Rayees Ahmad et al., \(^{234}\) by Claisen-Schmidt condensation method. All the compounds were tested for their antioxidant and antibacterial activities by the cup plate method.

Chetana et.al., \(^{431}\) aimed a review to give summary of methods for synthesis of chalcones, its chemical modifications to flavonoids, flavanone, pyrazoles, oxazoles, pyrimidines.

According to Evgenia Bila et.al., \(^{432}\) \(\alpha, \beta\)-Unsaturated ketones are important intermediates also known as chalconic pharmakophores \(^{433}\). Recent publications emphasize the anti-microbial properties of chalcones, especially of their p-nitro-substituted derivatives \(^{434}\). Traditional approach to the search of promising biologically active substances is combining several pharmacological fragments in one molecule.

According to Farzana Latif Ansari et.al., \(^{435}\) the synthesized chalcones are significantly active against Bordetella bronchiseptica (ATCC 4617), gram negative respiratory pathogen that infects wide range of animals and human using cefixime as standard antibiotic as control.

Bordetella bronchiseptica ATCC 4617 is an aerobic, gram-negative bacterium that belongs to the genus Bordetella within the family
Alcaligenaceae. It causes respiratory tract infections in a wide variety of domestic and wild animals particularly in dogs, swine, rabbits and pigs leading to a number of respiratory tract diseases such as atrophic rhinitis. Most frequently, *B. bronchiseptica* infections in humans are seen in immunocompromised individuals with increasing number of cases in AIDS patients or in elderly people. During infection, it produces adhesions which help the bacteria to adhere to ciliated cells causing mechanical blocking of the respiratory cilia, resulting in failure of the respiratory tract to clear mucus secretions. For the treatment and control of respiratory tract infections some antimicrobial agents such as trimethoprim, sulfonamides, tetracycline and β-lactams are used most frequently. However, the current vaccines and therapies are not capable of eliminating infections as relapses have been commonly observed and a long duration of antibiotic therapy is generally required. Although a number of reports have focused on the synthesis and antibacterial properties of chalcones, however, their potential as antibacterial agents against *B. bronchiseptica* has not yet been explored. We have reported earlier the design and synthesis of a 120-member library and its screening against a number of bacterial strains and the lead structure was identified through deconvolution based on positional scanning protocol.

Prompted by the findings and in continuation to our interest in the synthesis of biodynamic chalcones.

Mustafa ceylan et.al., had stated that chalcones, either natural or synthetic, are known to exhibit various biological activities.

According to Mohamed A.Hassan.et.al., chalcones are α, β-unsaturated ketones that often occur in the plant kingdom. It is well
known that most of the natural or synthetic chalcones are highly biologically active with many pharmaceutical and medicinal applications.

Oxidative damage which is implicated in various pathological events such as cancer and aging is induced by free radicals and reactive oxygen species\textsuperscript{449}. Antioxidants are the compounds that prevent such as oxidative damage due to their free radical scavenging ability\textsuperscript{449}, In chalcones, such the ability is attributable to phenolic-OH group attached to the ring structure\textsuperscript{450}, Chalcones with antioxidant activity (and compounds with such activity in general) have been demonstrated to have anticancer, anticardiovascular, anti-inflammatory, and many other activities\textsuperscript{451, 452}. As such, they have gained immense interest from bioorganic and medicinal chemistry research.

Synthesized chalcones holding allylic substitutions and pyrazolicchalones were recently reported as potent antimicrobial and antioxidant agents\textsuperscript{453-456}. In addition, to the presence of enone function in chalcones having pyrazole moiety has been found to enhance the biological activity\textsuperscript{457}. Prompted by all these observations, they report herein the synthesis, antioxidant and antimicrobial activities of novel chalcones, pyrazolicchalones and allylic chalcones.

The minimum inhibitor concentrations (MICs) of the compounds were determined using micro dilution susceptibility method\textsuperscript{458}. Sulfamethoxazole and Keto-conazole were the reference drugs for antibacterial and antifungal testing respectively.

Compounds were assessed for antioxidant activity using 1, 1-biphenyl-2-picrylhydrazyl (DPPH) radical scavenging method\textsuperscript{459}, in summary; they have synthesized a series of novel chalcones, pyrazolicchalones and
allylic chalcones. They also reported antimicrobial and antioxidant evaluations of these compounds.

According to R.K. Upadhyay et al., infectious diseases caused by micro and myco organisms, viz. bacteria, fungi, viruses and parasites are still a major threat to human health, despite tremendous inventions in drug chemistry.

According to Sarojini et al., chalcones are one of the major classes of natural products, and they are gave interesting pharmacological activities.

Mohammed Rayees Ahmada et al., reported that free radicals are constantly formed in human system either as accidental products during metabolism or deliberately during the process of phagocytosis or due to environmental pollutants, ionizing radiations, ozone, heavy metal poisoning, etc. It is found from literature survey that chalcones (α, β-unsaturated carbonyl derivatives) exhibit great antioxidant activity.

Superoxide scavenging activity of the compounds was determined by McCord and Fridovich method, which depends on light induced superoxide generation by riboflavin and corresponding reduction of NBT. DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging activity was measured by the method of Lamaison.
2.2 Characters of microorganisms

2.2.1 Bacterial species:

Gram positive Bacteria

Bacillus subtilis
Micrococcus luteus
Staphylococcus aureus

Gram negative Bacteria

Escherichia coli
Klebsiella pneumoniae
Pseudomonas aeruginosa

Fungal species:

Aspergillus niger
Mucor species
Trichoderma viride
Penicillum scup

2.2.1.1 Bacillus subtilis

Bacillus subtilis is a gram-positive commonly found in soil. B. subtilis is rod shaped and has the ability to form a tough protective endospore allowing the organism to tolerate environmental conditions. It is not a human pathogen. It may contaminate food but rarely causes food poisoning. It was popularly world-wide before the introduction of consumer antibiotics as an immunostimulatory agent to aid treatment of gastrointestinal and urinary tract diseases. It can convert (decompose) some explosives into harmless compounds of nitrogen, carbon-dioxide and water. Its surface binding properties play a role in safe radionuclide waste (eg. thorium (IV) and plutonium (IV)) disposal.
2.2.1.2 **Micrococcus luteus**

*Micrococcus luteus* gram-positive, *coccoid bacterium* is capable of dividing in more than one plane and forms clusters of bacteria. *M. luteus* can be found in soil, dust, water and air as well as on human skin. It is not usually considered a pathogen, or disease causing organism of healthy people. Only in immuno compromised individuals, it will cause problems such as septic shock, pneumonia endocarditis or sepsis. *M. luteus* is known for its growth in dairy products and can be transmitted via consumption of milk. It has an unusual ability to tolerate and to use very toxic organic molecules as carbon sources and metals. It can be used for the degradation of metals such as zinc, lead and nickel. Due to these features *M. luteus* is having potential applications in Bioremediation and Biotechnology.

2.2.1.3 **Staphylococcus aureus**

*Staphylococcus aureus* is a major nosocomial pathogen. This species is capable of causing a wide range of diseases and is often associated with high morbidity and mortality rates. The disease spectrum includes food borne illness, cutaneous infections, endocarditis, pneumonia, septic arthritis and osteomyelitis. *S. aureus* infections are difficult to control due to a combination of toxin-mediated virulence, invasiveness and antibiotic resistance. Therefore there is a continuing need to discover new and improved antimicrobial agents to treat *S. aureus* illness with potential benefits for both the food and pharmaceutical industries. *Staphylococcus aureus* is a facultatively anaerobic, gram positive coccus which appears as grape like clusters and has large, round golden yellow colonies.
2.2.1.4  *Escherichia coli*

*E.coli* is the name of a germ or bacterium that lives in the digestive tract of humans and animals. There are many types of *E.coli* and most of them are harmless. But some cause bloody diarrhea. People get infected by *E.coli*, when coming into contact with the feces or stool of humans or animals. In some people, *E.coli* may also cause severe anemia or kidney failure which can lead to death. Many *E.coli* infected people will also experience abdominal pain, loss of appetite, fever and in rare cases vomiting. *E.coli* infection will be through contaminated water from lakes, pools and water supplies. *E.coli* can spread from an infected person’s hands to other people or to objects.

2.2.1.5  *Klebsiella pneumoniae*

*Klebsiella pneumoniae* is a gram-negative, rod shaped and non-motile bacteria. Species of *Klebsiella* are ubiquitous (present everywhere) and are human pathogens (disease causing organisms) found in the respiratory, intestinal and urinogenital tracks. They cause pneumonia (inflammatory illness of the lungs), urinary tract infections (UTI), ankylosing spondylitis septicemia (whole body inflammation) and soft body infections to humans. *Klebsiella pneumoniae* is a facultative anaerobic meaning that it has both aerobic and anaerobic surviving feature depending upon the situation. It causes pneumonia in humans. It is opportunistic pathogen found in the environment and in mammalian mucosal surfaces. Clinical syndromes caused by these bacteria include pneumonia, bacteremia, thrombophlebitis, urinary tract infection, choleoystitis, diarrhea, upper respiratory tract infection, wound infection, osteomyelitis and meningitis.
2.2.1.6  \textit{Pseudomonas aeruginosa}

It is the epitome of an opportunistic pathogen of humans. It is a gram-negative, aerobic rod, belonging to the bacterial family pseudomonadaceae. It is notorious for its resistance to antibiotic and is therefore a particularly dangerous and dreaded pathogen. It is naturally resistant to many antibiotics due to the permeability barrier afforded by its outer membrane LPS (Liquid Protein Stability). \textit{Pseudomonas aeruginosa} causes urinary tract infections, respiratory system infections, dermatitis, soft tissue infections, bactermia and a variety of systemic infections, particularly in victims of severe burns and in cancer and AIDS patients who are immune-suppressed.

2.2.1.7  \textit{Aspergillus niger}

\textit{Aspergillus niger} is a fungus and one of the most common species of the genus Aspergillus. It causes a disease called black mould on certain fruits and vegetableless such as grapes, onions and peanuts and is a common contaminant of food. It is less likely to cause human disease than some other \textit{A.species}. If large amounts of spores are inhaled a serious lung disease called Aspergillosis can occur. \textit{A.niger} is one of the most common causes of otomycosis (ear infection) which can cause pain, temporary hearing loss and in severe cases, damage ear canal and tympanic membrane. Various strains of \textit{A.niger} are used in the industrial preparation of citric acid and gluconic acid.
2.2.1.8  *Mucor species*

The genus *Mucor* is a filamentous fungus with several species, few of which grow well at 37°C and thereby able to infect humans *Mucor spp.* has been implicated as an agent in zygomycosis, particularly in the debilitated patient. *Mucor* is ubiquitous in nature, found in the soil or growing on decaying vegetative matter. *Mucor* is a rapidly growing fungus which will fill a culture plate in a matter of a few days with woolly growth resembling cotton candy. New growth is white but turns a grayish-brown with ageing.

It is an opportunistic pathogen, attacking individuals with significantly compromised immune systems, metabolic acidosis, uncontrolled diabetes, starvation, severe trauma or other forms of debilitation.

2.2.1.9  *Trichoderma viride*

*Trichoderma viride* is a fungus and biofungicide. It is used for seed and soil treatment for suppression of various diseases caused by fungal pathogens. It is also a pathogen on its own right causing green mould rot of onion. *T. viride* is a mould which produces spores asexually by mitosis. The mycelium of *T. viride* can produce a variety of enzymes, including cellulases and chitivases which can degrade cellulose and chitin respectively. The mould can grow directly on wood.

It is a filamentous fungus that is widely distributed in the soil, plant material, decaying vegetation and wood. They grow rapidly and mature in five days on potato dextrose agar. The colonies are wooly. As the conidia are formed, scattered blue green or yellow-green patches become visible.
2.2.1.10 *Penicillium scup*

*Penicillium* is a genus of ascomycetous fungi of major importance in the natural environment as well as food and drug production. The genus was first described in the scientific literature by Johann Heinrich Friedrich in his 1809 work *Observationes in ordines plantarum naturales*. The three fungus such as *P. candidum*, *P. expansum*, and *P. glaucum* are produced a brush-like conidiophore (asexual fruiting structure). The common apple rot fungus *P. expansum* was selected as the type species.

*Penicillium* is classified as a genus of anamorphic fungi in the division Ascomycota (order-Eurotiales, class-Eurotiomycetes, family-Trichocomaceae). The genus name is derived from the Latin root *penicillum*, meaning "painter's brush", and refers to the chains of conidia that resemble a broom.

Some *Penicillium* species affect the fruits and bulbs of plants, including *P. expansum* which affects apples and pears, citrus fruits by *P. digitatum* and garlic by *P. allii*. Some species are known to be pathogenic to animals; *P. corylophilum*, *P. fellutanum*, *P. implicatum*, *P. janthinellum*, *P. viridicatum* and *P. waksmanii* are potential pathogens of mosquitoes. *P. marneffei* which causes mortality in the Vietnamese bamboo rats has become a common opportunistic infection of HIV-infected individuals in south-east Asia.
2.3 MATERIALS AND METHODS

The chemicals namely nutrient broth, Mueller Hinton agar, potato dextrose agar, Tween-80 solution and other materials required have been procured from Himedia, Mumbai.

2.3.1 Collection of Microorganisms

*Bacillus subtilis, Escherichia coli, Klebsila pneumonia, Micrococcus luteus, Pseudomonas aerogenosa, Staphylococcus areus, Aspergillus niger, Mucor species* and *Trichoderma viride* were procured from the Research department of Microbiology, Sengunthar Arts and Science College, Thiruchengode, Namakkal Dt., Tamilnadu. The stock cultures have been stored in the refrigerator for further studies.

2.3.2 Innoculum preparation

The nutrient broth was procured from Himedia, Mumbai. The nutrient broth was prepared by weighing 1.3 gram of the broth and dissolved it in 100 ml of sterile distilled water. The flask was swirled gently while adding the nutrient broth and the pH of the medium was adjusted to 7.0. The Erleumayer flask was plugged with non-adsorbent cotton and sterilized in an autoclave at 121°C and 15 lbs/ins² pressure for 15 minutes. After cooling inside a laminar flow, a loopful of fresh bacterial sample was inoculated and incubated in an orbital shaker at 37°C for 24 hours. Then the cultures were diluted 1:50 with sterile physiological saline and 0.5 ml of the innoculum was used for the preparation of the spread plate. The same procedure has been adopted for all test bacterial samples.
2.3.3 Preparation of agar slants

Nutrients agar medium was prepared and sterilized in an autoclave at 121°C and 15 lbs/inc² pressure for 15 minutes. After sterilization the medium was dispensed into the test tubes. The test tubes were kept in the slanting position on a support. After complete solidification of the medium, streaking of the microorganism was done in the slant area using sterile inoculation loop. After the streaking the test tubes were incubated at 37°C for 24 hours. After good growth, the slants have been stored in a deep freezer (2°C) for further studies.

2.3.4 Preparation of Mueller Hinton agar plates

The Mueller Hinton agar of weight 38 gram was dissolved in 1000 ml of sterile distilled water. The pH of the medium was adjusted to 7.0. The flask was plugged with cotton and sterilized at 121°C and 15 lbs/inc² pressure for 15 minutes. After sterilization, the medium was cooled to 45-47°C, poured 15 ml of it in each sterile Petri-plates and allowed to solidify.

2.3.5 Preparation of test compound

The newly synthesized Chalcone compounds of weight 15 mg of each was dissolved in 1ml of DMSO solvent. Using 100µml solution, the discs were impregnated and placed on the Mueller Hinton solidified Agar medium to find out the antimicrobial activity of the compounds on each organism. By adapting the above procedure, the antimicrobial activity of the five series of chalcones has been studied on six microorganisms and the results have been discussed.
2.3.6 Antibacterial sensitivity assay

Antibacterial sensitivity assay was performed using Kirby-Bauer\textsuperscript{468} disc diffusion technique. In each Petri plate about 0.5 ml of the test bacterial sample was spread uniformly over the solidified Mueller Hinton agar using sterile glass spreader. Then the discs with 5mm diameter made up of Whatman No.1 filter paper, impregnated with the solution of the compound were placed on the medium using sterile forceps. The plates were incubated for 24 hours at 37°C by keeping the plates upside down to prevent the collection of water droplets over the medium. After 24 hours, the plates were visually examined and the diameter values of the zone of inhibition were measured. Triplicate results were recorded by repeating the same procedure.

2.3.7 Preparation of the Potato dextrose agar medium

PDA agar medium was prepared in a conical flask by dissolving 3.9gram of the agar in 100ml distilled water. It was sterilized in the autoclave for 15min. at 121°C and 15 lbs/inch\textsuperscript{2} pressure. Then the medium was allowed for solidification for an hour. After that the fungal species was inoculated in the medium and kept for 5 to 7 days at room temperature.

2.3.8 Preparation of the fungal inoculam

About 20 to 25 ml of sterile water (after cooling) is mixed with the medium. The water over the medium is swirled and decanted with the fungal species. Tweeen-80(1 to 2 ml) may be added with this solution for uniform growth.
2.3.9 Antifungal sensitivity assay

Antifungal sensitivity assay was performed using Kirby-Bauer\textsuperscript{468} disc diffusion technique. PDA medium was prepared and sterilized as above. It was poured (ear bearing heating condition) in the Petri-plate which was already filled with 1 ml of the fungal species. The plate was rotated clockwise and counter clock-wise for uniform spreading of the species. The discs were impregnated with the test solution. The test solution was prepared by dissolving 15mg of the Chalcone in 1ml of DMSO solvent. The medium was allowed to solidify and kept for 24 hours. Then the plates were visually examined and the diameter values of zone of inhibition were measured. Triplicate results were recorded by repeating the same procedure.
2.4 RESULTS AND DISCUSSION

2.4.1 Antibacterial Activities

The antibacterial effect of the styryl 1-pyrenyl ketones in Series-A is shown in Fig: (84) for Plates (1)-(10). Analysis of the zone of inhibition as given in Table-(29) and the Clustered column Chart given in Fig: (85), reveals that all the aryl styryl ketones except those with 3-Br substituent have shown moderate antibacterial activity against all the bacterial species, under investigation.

The aryl styryl ketone with 3-NO$_2$ substituent has shown more antibacterial activity than standard (Ampicillin) against B.subtilis species.

The aryl styryl ketone with 2-Cl substituent has shown more antibacterial activity than standard (Ampicillin) against S.aureus species.

The aryl styryl ketone with 4-Cl substituent has shown equal antibacterial activity with standard (Ampicillin) against M.luteus species.

The parent aryl styryl ketone compound has shown equal antibacterial activities against all bacteria except P.aeruginosa.

The aryl styryl ketones with 2-Cl, 3-Cl and 4-Cl substituents have shown equal antibacterial activities against B.subtilis bacterial species. The aryl styryl ketones with 3-NO$_2$ and 4-NO$_2$ substituents have shown equal antibacterial activities against M.luteus and S.aureus bacterial species.
Antibacterial Activities of substituted Styryl 1-pyrenyl ketones in Series-A

Figure - 84
<table>
<thead>
<tr>
<th>S.NO.</th>
<th>COMPOUND</th>
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<th>S.aureus</th>
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Control DMSO - - -
Antibacterial activity of substituted styryl 1-pyrenyl ketones

Fig - 85: Antibacterial activity of substituted Styryl 1-pyrenyl ketones: Series-A
The antibacterial effect of the styryl 3-nitrophenyl ketones in Series-B is shown in Fig-(86) for Plates (11)-(20). Analysis of the zone of inhibition as given in Table-(30) and the Clustered column Chart given in Fig: (87), reveals that aryl styryl ketones with the 3-Cl and 2-OCH$_3$ substituents have shown more antibacterial activity than standard (Ampicillin) against *K.pneumoniae* species, under investigation.

The aryl styryl ketone with 3-Cl substituent has shown more antibacterial activity than standard (Ampicillin) against *E.coli* species.

All the aryl styryl ketones, in this series-B have shown satisfactory antibacterial activity against *E.coli* bacterial species.

The aryl styryl ketone with 2-OCH$_3$ substituent has shown high antibacterial activity, but remaining compounds have fair activity against *S.aureus* species.

The parent aryl styryl ketone compound (H) has shown equal activity against all bacteria except *K.pneumoniae*. The aryl styryl ketone with 3-Br substituent has shown equal antibacterial activity against all bacteria except *S.aureus*. The aryl styryl ketone with 4-Cl substituent has shown equal antibacterial activity against all bacteria except *B.subtilis*.

The aryl styryl ketones with 3-Br and 4-Br substituents have shown equal antibacterial activity against *B.subtilis, M.luteus* and *K.pneumoniae* bacterial species. The aryl styryl ketones with 2-OCH$_3$ and 4-OCH$_3$ substituents have shown equal antibacterial activity against *E.Coli* bacterial species. The aryl styryl ketones with 2-CH$_3$ and 4-OCH$_3$ substituents have shown equal antibacterial activity against *B.subtilis* bacterial species.
Antibacterial Activities of substituted Styryl 3-nitrophenyl ketones in Series-B

Figure - 86
### Table 30

<table>
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<th>S.NO.</th>
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**Standard**
- Ampicillin: 9
- DMSO: -

**Control**
- -
Fig-87: Antibacterial activity of substituted styryl 3-nitrophenyl ketones: Series-B
The antibacterial effect of the styryl 4-nitrophenyl ketones in Series-C, is shown in Fig-(88) for Plates (21)-(30). On analyzing the zone of inhibition as given in Table-(31) and the Clustered column Chart given in Fig-(89), it is established that most of the aryl styryl ketone compounds have shown moderate antibacterial activity against \textit{B.subtilis} and \textit{M.luteus} species, under invesitgation.

The aryl styryl ketone with 4-F substituent has shown more antibacterial activity than standard (Ampicillin) against \textit{Ecoli} species.

The parent aryl styryl ketone compound of this series-C has shown more antibacterial activity than standard (Ampicillin) against the \textit{P.aeruginosa} bacterial species.

The aryl styryl ketone with 3-Br substituent has shown equal antibacterial activity against all bacteria except \textit{S.aureus}. The aryl styryl ketone with 3-Cl substituent has shown equal antibacterial activity against all bacteria except \textit{M.luteus}.

The aryl styryl ketones with 3-Cl and 4-Cl substituents have shown equal antibacterial activity against \textit{B.subtilis} and \textit{P.aeruginosa} bacterial species. The aryl styryl ketones with 2-NO\textsubscript{2}, 3- NO\textsubscript{2} and 4-NO\textsubscript{2} substituents have shown equal antibacterial activity against \textit{B.subtilis} bacterial species.
Antibacterial Activities of substituted Styryl 4-nitrophenyl ketones in Series-C

Figure - 88
<table>
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<th>S.NO.</th>
<th>COMPOUND</th>
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<td>8</td>
<td>4- OCH₃</td>
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<td>4-NO₂</td>
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<td>Ampicillin</td>
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<tr>
<td></td>
<td>Control</td>
<td>DMSO</td>
<td>-</td>
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</table>
Antibacterial activity of substituted styryl 4-nitrophenyl ketones

Fig-89: Antibacterial activity of substituted Styryl 4-nitrophenyl ketones: Series-C
The antibacterial effect of the styryl 3-thienyl ketones in Series-D, is shown in Fig-(90) for Plates (31)-(40). Analysis of the zones of inhibition as given in Table-(32) and the Clustered column Chart given in Fig-(91), reveals that all the aryl styryl ketones have shown moderate antibacterial activity against the *M.luteus* and *S.aureus* bacterial species, under investigatation.

The aryl styryl ketone with 4-Br substituent has shown more antibacterial activity than standard (Ampicillin) against *B.subtilis* species and equal antibacterial activity with standard (Ampicillin) against *M.luteus* species.

The aryl styryl ketone with 4-Cl substituent has shown equal antibacterial activity with standard (Ampicillin) against *B.subtilis* species.

The aryl styryl ketones with 3-NO$_2$ and 4-NO$_2$ substituents have shown more antibacterial activity in this series-D against all the bacterial species.

The aryl styryl ketone with 3-NO$_2$ substituent has shown equal activity against all bacteria except *E.Coli*. The aryl styryl ketone with 4-F substituent has shown equal antibacterial activity against all bacteria except *S.aureus*.

The aryl styryl ketones with 3-NO$_2$ and 4-NO$_2$ substituents have shown equal antibacterial activity against *B.subtilis* and *S.aureus* bacterial species.
Antibacterial Activities of substituted Styryl 3-thienyl ketones in Series-D

Figure - 90
### Table-32
Zone of inhibition (mm) values of antibacterial activity of **substituted Styryl 3-thienyl ketones** (Series-D)

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>COMPOUND</th>
<th>B.subtilis</th>
<th>M.luteus</th>
<th>S.aureus</th>
<th>E.coli</th>
<th>P.aeruginosa</th>
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</tr>
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<td>7</td>
</tr>
<tr>
<td>3</td>
<td>4-Br</td>
<td>9</td>
<td>8</td>
<td>8</td>
<td>-</td>
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<td>4-Cl</td>
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<tr>
<td>5</td>
<td>4-F</td>
<td>7</td>
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<td>6</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>2-CH₃</td>
<td>-</td>
<td>7</td>
<td>6</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>4-CH₃</td>
<td>6</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>3-NO₂</td>
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<td>6</td>
<td>6</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>4-NO₂</td>
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<td>7</td>
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<td>Standard</td>
<td>Ampicillin</td>
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<td>12</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Control</td>
<td>DMSO</td>
<td>-</td>
<td>-</td>
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</table>
Antibacterial activity of substituted styryl 3-thienyl ketones

Fig-91: Antibacterial activity of substituted Styryl 3-thienyl ketones: Series-D
The antibacterial effect of the styryl 3, 5-dichloro-2-hydroxyphenyl ketones in Series-B, is shown in Fig-(92) for Plates (41)-(50). Analysis of the zones of inhibition as given in Table-(33) and the Clustered column Chart given in Fig-(93), reveals that all the aryl styryl ketone compounds except one with 3-Cl substituent have shown moderate antibacterial activity against all the bacterial species, under invesitigation.

The aryl styryl ketone with 3-NO\(_2\) substituent has shown improved antibacterial activity than standard (Ampicillin) against \textit{S.aureus} and \textit{B.subtilis} species. The parent aryl styryl ketone compound and aryl styryl ketones with 4-F and 4-NO\(_2\) substituents of this series-B have shown equal antibacterial activity with standard (Ampicillin) against \textit{S.aureus} bacterial species.

The aryl styryl ketone with 4-Br substituent of this series-D has shown equal antibacterial activity with standard (Ampicillin) against \textit{M.luteus} bacterial species.

The aryl styryl ketone with 3-Br substituent has shown equal antibacterial activity against all bacteria except \textit{M.luteus}. The aryl styryl ketones with 2-Cl and 3-Cl substituents have shown equal antibacterial activity against all bacteria except \textit{E.Coli}. The aryl styryl ketone with 4-NO\(_2\) substituent has shown equal antibacterial activity against all bacteria except \textit{B.subtilis}.

The aryl styryl ketones with 3-Br and 4-Br substituents have shown equal antibacterial activity against \textit{B.subtilis} and \textit{S.aureus} bacterial species. The aryl styryl ketones with 2-Cl, 3-Cl and 4-Cl substituents have shown equal antibacterial activity against \textit{M.luteus} and \textit{P.aeruginosa} bacterial species.
Antibacterial Activities of substituted Styryl 3, 5-dichloro-2-hydroxyphenyl ketones in Series-E

Figure - 92
### Table-33

Zone of inhibition (mm) values of antibacterial activity of substituted Styryl 3, 5-dichloro-2-hydroxyphenyl ketones (Series-E)

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>COMPOUND</th>
<th>Gram positive Bacteria</th>
<th>Gram negative Bacteria</th>
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</thead>
<tbody>
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<td></td>
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<td>B.subtilis</td>
<td>M.luteus</td>
</tr>
<tr>
<td>1</td>
<td>H</td>
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<td>7</td>
</tr>
<tr>
<td>2</td>
<td>3-Br</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
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</tr>
<tr>
<td>7</td>
<td>4-F</td>
<td>6</td>
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</tr>
<tr>
<td>8</td>
<td>4-CH₃</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
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<td>6</td>
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<tr>
<td>10</td>
<td>4-NO₂</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

Standard Ampicillin 8 8 7 9 9
Control DMSO - - - - -
Fig-93: Antibacterial activity of substituted styryl 3,5-dichloro-2-hydroxyphenyl ketones: Series-E
2.4.2 Antifungal Activity:

The antifungal effect of the substituted Styryl 1-pyrenyl ketones in Series-A, is shown in Fig-(94) for Plates (51)-(56). Analysis of the zone of inhibition as given in Table-(34) and the Clustered column Chart given in Fig-(95), reveals that parent compound and aryl styryl ketones with 3-Cl and 3-NO$_2$ substituents have shown moderate antifungal activity against all the fungal species namely $A.niger$, $P.scup$ and $T.viride$, under investigation.

The aryl styryl ketones with 2-Cl and 4-CH$_3$ substituents of this series-A have shown inactivity against all the above three fungal species. The parent compound and aryl styryl ketone with 3-Cl substituent have shown equal antifungal activity against all fungal species under examination.

**Table-34**

<table>
<thead>
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<th>S.NO.</th>
<th>COMPOUND</th>
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<td></td>
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<tr>
<td>8</td>
<td>3-NO$_2$</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>4-NO$_2$</td>
<td>-</td>
</tr>
<tr>
<td>Standard</td>
<td>Miconazole</td>
<td>10</td>
</tr>
<tr>
<td>Control</td>
<td>DMSO</td>
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</table>
Antifungal Activities of substituted Styryl 1-pyrenyl ketones in Series-A

Figure - 94
Antifungal activity of substituted styryl 1-pyrene ketones.

Fig-95: Antifungal activity of substituted Styryl 1-pyrenyl ketones: Series-A
The antifungal effect of the substituted Styryl 3-nitrophenyl ketones in Series-B is shown in Fig-(96) for Plates (51)-(56). Analysis of the zone of inhibition as given in Table-(35) and the Clustered column Chart given in Fig-(97), reveals that the parent compound and aryl styryl ketones with 2-OH and 4-OH substituents have shown moderate antifungal activity against all the fungal species namely *A.niger*, *P.scup* and *T.viride*, under investigation.

The aryl styryl ketone with 4-Br substituent of this series-B has shown inactivity against the above three fungal species. The parent compound (H) and aryl styryl ketone with 2-OH substituent have shown equal antifungal activity against all fungal species namely *A.niger*, *P.scup* and *T.viride*.

**Table-35**

<table>
<thead>
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<th>Zone of Inhibition (mm)</th>
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<td>4-Br</td>
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</tr>
<tr>
<td>4</td>
<td>3-Cl</td>
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<tr>
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<td>4-Cl</td>
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<tr>
<td>6</td>
<td>4-F</td>
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<td>2-OH</td>
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<td>8</td>
<td>4-OH</td>
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<tr>
<td>Control</td>
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</table>
Antifungal Activities of substituted Styryl 3-nitrophenyl ketones in Series-B

Figure - 96
Antifungal activity of substituted styryl 3-Nitrophenyl ketones

Fig-97: Antifungal activity of substituted Styryl 3-nitrophenyl ketones : Series-B
The antifungal effect of the substituted Styryl 4-nitrophenyl ketones in Series-C is shown in Fig-(98) for Plates (51)-(56). Analysis of the zone of inhibition as given in Table-36 and the Clustered column Chart given in Fig-(99), reveals that the parent compound and aryl styryl ketones with 2-OCH$_3$, 4-OCH$_3$, 2-NO$_2$ and 4-NO$_2$ substituents have shown moderate antifungal activity against all the fungal species namely *A.niger*, *P.scup* and *T.viride*, under investigation.

The aryl styryl ketones with 3-Br, 4-Br, 3-Cl, 4-F and 4-CH$_3$ substituents have shown lesser activity than other compounds for the above three fungal species. The aryl styryl ketones with 2-OCH$_3$ and 4-OCH$_3$ substituents have shown equal antifungal activity against the above three fungal species.

**Table-36**

Zone of inhibition (mm) values of antifungal activity of substituted Styryl 4-nitrophenyl ketones (Series-C)

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>COMPOUND</th>
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<td>4-Br</td>
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</tr>
<tr>
<td>4</td>
<td>3-Cl</td>
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<tr>
<td>5</td>
<td>4-Cl</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>4-F</td>
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<td>8</td>
<td>4-OCH$_3$</td>
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</tr>
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<tr>
<td>Control</td>
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Antifungal Activities of substituted Styryl 4-nitrophenyl ketones in Series-C

Figure - 98
Antifungal activity of substituted styryl 4-nitrophenyl ketones

Fig-99: Antifungal activity of substituted Styryl 4-nitrophenyl ketones: Series-C
The antifungal effect of the **substituted Styryl 3-thienyl ketones** in Series-D is shown in Fig-(100) for Plates (69)-(74). Analysis of the zone of inhibition as given in **Table-37** and the Clustered column Chart given in Fig-(101), reveals that the parent compound has shown more antifungal activity than standard (miconazole) compound against *A.niger* fungal species.

All the aryl styryl ketones of this series-D have shown satisfactory activity against the fungal species namely *A.niger* and *P.scup*. All the aryl styryl ketones except those with 3-Br, 2-OCH$_3$ and 3-NO$_2$ substituents have shown satisfactory activity for the *T.viride* fungal species. The aryl styryl ketones with 2-CH$_3$ and 4-CH$_3$ substituents have shown equal activity against *A.niger* fungal species.

<table>
<thead>
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<th>S.NO.</th>
<th>COMPOUND</th>
<th>Zone of Inhibition (mm)</th>
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</thead>
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<tr>
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<td>4-Br</td>
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<td>9</td>
<td>4-NO$_2$</td>
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<td>Miconazole</td>
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<td>DMSO</td>
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</table>

*Table-37:* Zone of inhibition (mm) values of antifungal activity of substituted **Styryl 3-thienyl ketones** (Series-D)
Antifungal Activities of substituted Styryl 3-thienyl ketones in Series-D

Figure - 100
Fig-101: Antifungal activity of substituted styryl 3-thienyl ketones: Series-D
The antifungal effect of the substituted Styryl 3,5-dichloro-2-hydroxyphenyl ketones in Series-E is shown in Fig-(102) for Plates (75)-(80). Analysis of the zone of inhibition as given in Table-38 and the Clustered column Chart given in Fig-(103), reveals that the parent compound and aryl styryl ketones with 4-Br and 4-CH$_3$ substituents have shown satisfactory antifungal activity against fungal species namely *A.niger* *P.scup* and *T.viride*, under invesitgation. All the aryl styryl ketones except those with 2-Cl and 3-Cl substituents have shown satisfactory antifungal activity against the *T.viride* fungal species. The aryl styryl ketones with 3-Cl, 4-Cl, 3-NO$_2$, and 4-NO$_2$ substituents of this series-E have shown inactivity for the above three fungal species. The aryl styryl ketone with 4-Br substituent has shown equal activity against three fungal species namely *A.niger*, *P.scup* and *T.viride*.

**Table-38**

Zone of inhibition (mm) values of antifungal activity of substituted Styryl 3, 5-dichloro-2-hydroxyphenyl ketones (Series-E)

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>COMPOUND</th>
<th>Zone of Inhibition (mm)</th>
</tr>
</thead>
<tbody>
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</tr>
<tr>
<td>2</td>
<td>3-Br</td>
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</tr>
<tr>
<td>3</td>
<td>4-Br</td>
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</tr>
<tr>
<td>4</td>
<td>2-Cl</td>
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<td>4-Cl</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>4-F</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>4-CH$_3$</td>
<td>5</td>
</tr>
<tr>
<td>9</td>
<td>3-NO$_2$</td>
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</tr>
<tr>
<td>10</td>
<td>4-NO$_2$</td>
<td>-</td>
</tr>
<tr>
<td>Standard</td>
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<td>12</td>
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<tr>
<td>Control</td>
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</table>
Antifungal Activities of substituted Styryl 3, 5-dichloro-2-hydroxyphenyl ketones in Series-E Figure - 102
Fig-103: Antifungal activity of substituted Styryl 3,5-Dichloro-2-hydroxyphenyl ketones: Series-E

Antifungal activity of substituted styryl 3,5-Dichloro-2-hydroxyphenyl ketones

Zone of Inhibition (mm)

- A.niger
- P.scup
- T.viride

Fig-103: Antifungal activity of substituted Styryl 3, 5-dichloro-2-hydroxyphenyl ketones: Series-E
SCOPE OF THE PRESENT STUDY

Aryl styryl ketones have been used as antibacterial and antifungal activity. Aryl styryl ketones have also acted as potential anti-diabetic agents. Several methoxy substituted aryl styryl ketones have been reported to inhibit completely the selected five human cancer cell lines as compared to standard flavopiridol and germicitabine. These methoxy substituted aryl styryl ketones have shown to possess the anti-inflammatory activity. Several mono and dimethoxy substituted aryl styryl ketones have shown significant anticonvulsant activity.

Aryl styryl ketones with hydroxy and chloro substituents were shown to be potent inhibitors of aldose reductase, caused an increase in glycogenolysis rate by decreasing the liver glycogen content. It is interesting to note that aryl styryl ketones show no activity against brain and spinal cord glycogen content.

Tri-hydroxy aryl styryl ketones have been synthesized by Zhao and his co-workers and evaluated for their antiplatelet activity.

Substituted quinolinyl aryl styryl ketones, have been synthesized by Sharma et. al., as a new class of anti-infective agents.

A series of substituted aryl styryl ketones have been synthesized by Montes-Avila et. al., and tested for their antiparasitary activity.

Aryl styryl ketones with electron withdrawing substituents have shown excellent anti pesticidal activity. Aryl styryl ketones with electron donating substituents have shown high mosquito larvicidal activity.
A series of aryl styryl ketones containing quinoline nucleus have been synthesised by Gupta et al., and screened for their anti-HIV activity.

Ahmed et al., synthesized a new kind of aryl styryl ketones derivative possessing anti-cytotoxic and anti-oxidant activity.

A series of new (E)-4-substituedphenyl-1-(thiophen-2-yl) but-3-en-1-ones were synthesized by Ramesh et al., and the compounds were subjected to preliminary evaluation for the anti-inflammatory activity.

Boumendjel and his co-workers synthesized some aryl styryl ketones and reported their antimitotic and antiproliferative activity. Some substituted aryl styryl ketones have been synthesized by Purnima et al., which exhibit anti hyperglycemic activity.

The o-chloro, o-bromo and o-hydroxy substituted aryl styryl ketones exhibit the highest activity with glucose medium concentration. Several ortho and para-substituted aryl styryl ketones have been shown to have potential anti-HIV activity.

Some of the synthesized substituted aryl styryl ketones in the present investigation may be studied for above such activity and these studies may be utilized for the betterment of the society.

Some of the synthesized aryl styryl ketones with methoxy, chloro and bromo substituents and those with electron withdrawing and electron donating groups may have been synthesized and above such activity may be studied in future.
CONCLUSION

All the synthesized aryl styryl ketones have been screened for antibacterial activity against certain bacteria namely *B. subtilis*, *M. luteus*, *S. aureus*, *E. coli* and *K. pneumoniae* and antifungal activity against certain fungi namely *A. Niger*, *M. species*, *P. Scup* and *T. viride*.

Antibacterial activity:

In series-A, all the aryl styryl ketones except those with 3-Br substituent have been shown moderate antibacterial activity against all the bacterial species. The aryl styryl ketones with 3-NO$_2$ substituent have shown more antibacterial activity against *B. subtilis* species. The aryl styryl ketones with 2-Cl substituent has shown more antibacterial activity against *S. aureus* species.

In series-B, the aryl styryl ketones with 3-Cl and 2-OCH$_3$ substituents have shown more antibacterial activity against *K. pneumoniae* species. The aryl styryl ketone with 3-Cl substituent has shown more antibacterial activity against *E. coli* species. All the aryl styryl ketones, in this series have shown satisfactory antibacterial activity against *E. coli* bacterial species. The aryl styryl ketone with 2-OCH$_3$ substituent has shown high antibacterial activity, but remaining aryl styryl ketones have shown fair and good activity against *S. aureus* species.

In series-C, all the aryl styryl ketones have shown moderate antibacterial activity against *B. subtilis* and *M. luteus* species. The aryl styryl ketone with 4-F substituent has shown more antibacterial activity against
$E$-coli species. The parent aryl styryl ketone compound of this series has shown more antibacterial activity against the $P.aeruginosa$ bacterial species.

In series-D, all the aryl styryl ketones have shown moderate antibacterial activity against the $M.luteus$ and $S.aureus$ bacterial species. The aryl styryl ketone with 4-Br substituent has shown more antibacterial activity against $B.subtilis$ species. The aryl styryl ketones with 3-NO$_2$ and 4-NO$_2$ substituents have shown more antibacterial activity in this series against all the bacterial species under examination.

In series-E, all the aryl styryl ketone compounds except one with 3-Cl substituent have shown moderate antibacterial activity against all the bacterial species under examination. The aryl styryl ketone with 3-NO$_2$ substituent has shown improved antibacterial activity against $S.aureus$ and $B.subtilis$ species.

Antifungal activity:

In series-A, parent compound and aryl styryl ketones with 3-Cl and 3-NO$_2$ substituents have shown moderate antifungal activity against all the fungal species namely $A.niger$, $P.scup$ and $T.viride$. The aryl styryl ketones with 2-Cl and 4-CH$_3$ substituents of this series have shown inactivity against the above three fungal species under examination.

In series-B, parent compound and aryl styryl ketones with 2-OH and 4-OH substituents have moderate antifungal activity against all the above fungal species. The aryl styryl ketone with 4-Br substituent of this series-B has shown inactivity against all the above three fungal species.
In series-C, parent compound and aryl styryl ketones with 2-OCH₃, 4-OCH₃, 2-NO₂ and 4-NO₂ substituents have shown moderate antifungal activity against all the above fungal species. The aryl styryl ketones with 3-Br, 4-Br, 3-Cl, 4-F and 4-CH₃ substituents of this series have shown lesser activity than other substituents for the above three fungal species.

In series-D, parent compound has shown more antifungal activity against *A.niger* fungal species. All the aryl styryl ketones of this series have shown satisfactory antifungal activity against the fungal species namely *A.niger* and *P.scup*. All the aryl styryl ketones except those with 3-Br, 2-OCH₃ and 3-NO₂ substituents of this series-D have shown satisfactory activity for the *T.viride* fungal species.

In series-E, parent compound and aryl styryl ketones with 4-Br and 4-CH₃ substituents have shown satisfactory antifungal activity against fungal species namely *A.niger* *P.scup* and *T.viride*. All the aryl styryl ketones except those with 2-Cl and 3-Cl substituents of this series have shown satisfactory antifungal activity against the *T.viride* fungal species. The aryl styryl ketones with 3-Cl, 4-Cl, 3-NO₂, and 4-NO₂ substituents of this series have shown inactivity for the above three fungal species.
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