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Heteroaryl Chalcones: Prominent Pharmacophores of Synthetic and Biological Interest

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Abstract: *Heterocyclic ring containing chalcones were regarded as useful scaffolds in organic synthesis for the construction of biologically potent molecules. Apart from their synthetic utility, these chalcones themselves possess enormous amount biological applications, and also physicochemical properties. The structural modification, introduction of different substituents in the synthesized compounds proved to be dynamic strategies for enhanced biological profiles of the drugs. In this context, we have attempted to summarize the recent developments in the field of heteroaryl chalcones in recent years together in this review article. The emphasis was given for the synthetic protocols, the exploration of these chalcones to medicinally potent molecules, and biological activity potencies were critically discussed in depth. The discussion made on the physico-chemical properties, particularly of photosensing and NLO properties would be beneficial to those who are undertaken research in this area.*

Key words*: Annulation, antimicrobial, anticancer, medicinal, photosensing, optical, synthetic.*

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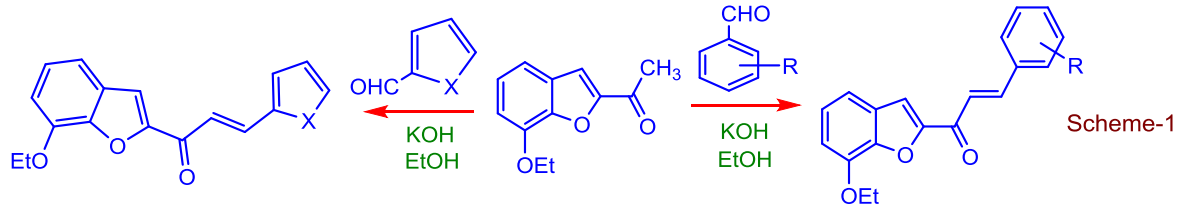
I. Introduction

Chalcones are open-chain flavonoids characterized by two aromatic rings joined by a three-carbon α,β-unsaturated carbonyl system. These classes of compounds were prepared using Claisen-Schmidt condensation of aromatic aldehydes and aromatic ketones, the aromatic group might be a substituted or unsubstituted phenyl, thiophene, furan, pyrrole, benzimidazole, indole, pyridine, quinoline, benzofuran, benzopyrrole, etc., [1-3]. In this review work, we focused on the recent drug discovery based on heteroaryl-chalcones. The work emphasizes the development in the synthetic protocols of heteroaryl chalcones, their efficacy as useful scaffolds in the construction of diverse classes of bioactive molecules, their biological potencies, and physicochemical properties of heteroaryl chalcones and their derivatives. More importantly, the strongest pharmacological molecules are identified based on the inhibitory properties, and cytotoxic values, a structure-activity relationship is established amongst the evaluated molecules, and it is helpful for the discovery of new pharmacological agents.

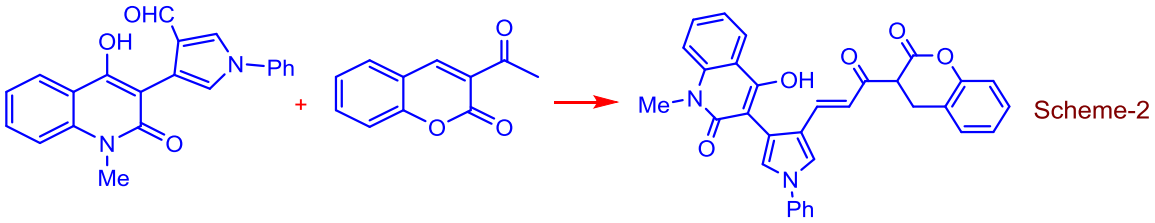
II. Synthesis And Synthetic Applications

A number of methods have been developed and reported in the literature for the synthesis of heteroaryl chalcones, amongst them, a base catalyzed Claisen-Schmidt condensation reaction between the aromatic aldehydes and aromatic ketones was most commonly employed method due to its accessible and easier to perform procedure. For instance, A series of benzofuran substituted chalcones were synthesized by the base-catalyzed Claisen-Schmidt reaction of the 1-(7-ethoxy-1-benzofuran-2-yl)ethanone with different aromatic aldehydes (Scheme-1) [4]. The anti-growth effect of chalcones tested in breast cancer (MCF-7), non-small cell lung cancer (A549) and prostate cancer (PC-3) cell lines shows that these have anticancer activity showing cytotoxic effects on cancer cells. In addition, one of the chalcone induced apoptosis through caspase dependent pathways in prostate, lung and breast cancer cells. Adopting the same reaction conditions, Lokanath and coworkers synthesized (*E*)-1-(5-chlorothiophen-2-yl)-3-(p-tolyl)prop-2-en-1-one [5], (*E*)-1-(5-chlorothiophen-2-yl)-3-(2,4-dimethylphenyl)prop-2-en-1-one[6], and (*E*)-3-(4-methoxyphenyl)-1-(thiophen-2-yl)prop-2-en-1-one[7] and characterized their structure by crystallographic studies.



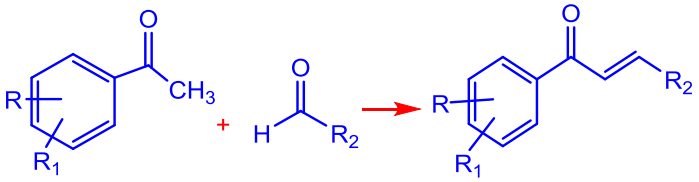
Scheme-1

A series of unexpected dihydrochalcones attached with cyanoiminopyrimidine moiety in addition to expected cyanoaminopyrimidines were synthesized by efficient and facile method via reaction of cyanoguanidine with chalcones in the presence of sodium ethoxide [8].Hassan and coworkers [9] reported the synthesis of 4-hydroxy-1-methyl-3-(4-(2-oxo-chromen-3-yl)prop-2-enoyl)-1-phenyl-1*H*-pyrazol-4-yl)quinolin-2(1*H*)-one via Claisen-Schmidt reaction of 3-(4-hydroxy-1-methyl-1,2-dihydro-2-oxoquinolin-3-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde and 3-(2-oxo-2*H*-chromen-3-yl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (Scheme-2). The synthesized compounds have showed their effect of growth on some selective crop of plants.



Scheme-2

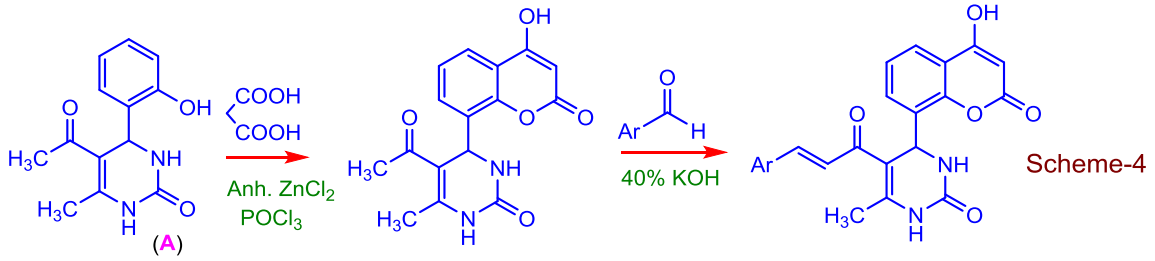
New anti-tuberculosis drugs are urgently needed to battle drug-resistant Mycobacterium tuberculosis strains and to shorten the current long treatment regime. In this line, Andrade and co-workers [10] developed chalcone-based anti-TB compounds by using an *in silico* design and QSAR-driven approach, and synthesized a series of heteroaryl chalcones (Scheme-3). Their study showed that ten compounds of the series were found to exhibit nanomolar activity against replicating mycobacteria, low micromolar activity against nonreplicating bacteria, and nanomolar and micromolar against rifampin (RMP) and isoniazid (INH) monoresistant strains (rRMP and rINH), and also showed good selectivity toward *M. tuberculosis*, with very low cytotoxicity against Vero cells.



R_2 = Substited Furan, Thiophene, Pyrrole, piperidine, Indole etc.

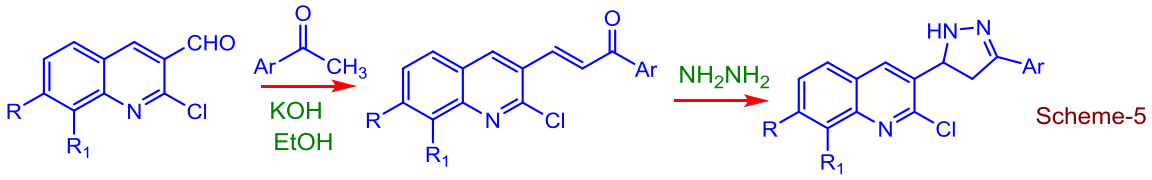
Scheme-3

A series of coumarin-yl-chalcone derivatives were synthesized through sequence of reactions. 5-Acetyl-4-(2-hydroxyphenyl)-6-methyl-3,4-dihydro pyrimidin-2(1*H*)-one (**A**) was prepared by multi-component one pot reaction of salicylaldehyde, methyl acetoacetate and urea, and was further reacted with malonic acid employing $ZnCl_2$ catalyst to get 5-acetyl-4-(4-hydroxy-2-oxo-2*H*-chromen-8-yl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one, which on Claisen-Schmidt reaction with aromatic aldehydes in the presence of KOH produced the target coumarinyl chalcones (Scheme-4) [11]. The *in vitro* cytotoxicity evaluation results indicate that two compounds of the series display significant anticancer activity against human cell-lines A549 (Lung), Jurkat (Leukemia) and MCF-7 (Breast), and were less cytotoxic compared with standard.



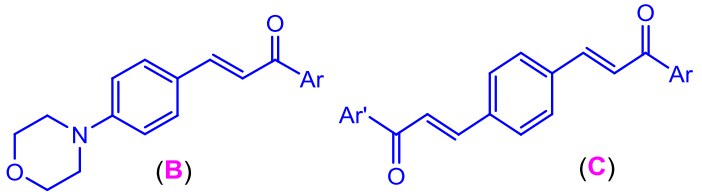
Scheme-4

Kumar and coworkers have synthesized furan containing chalcones by the reaction of furan-2-al and substituted aromatic acetophenones through Claisen-Schmidt approach, and then by 1,3-dipolar cycladdition reactions, they transformed these chalcones to furan tethered isoxazoles [12], pyrazoles [13]; and by (3+2) annulation reactions to benzothiazepines [14] and 2-pyrazolines [15]. Interestingly their synthesized compounds have showed good antimicrobial, antioxidant and anti-inflammatory activities. A series of quinoline based chalcones were prepared by the reaction of formylquinolines with acetylthiophenes, and these chalcones were transformed to pyrazoline derivatives by their reaction with hydrazine (Scheme-5) [16], which showed promising antileishmanial activities.



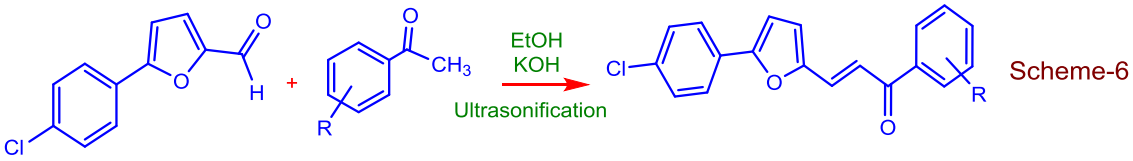
Scheme-5

Gutierreza and co-workers [17] developed a new approach for the synthesis of the chalcone (**B**) and bis-chalcone (**C**) derivatives. Their method involves Claisen-Schmidt condensation with KOH in ethanol at room temperature under sonication conditions. The study shows that, some compounds of the series antioxidant properties. Raghavendra and coworkers initially synthesized a two series of thienyl chalcones by Claisen-Schmidt approach, and efficiently transformed these chalcones in to biologically active lignan conjugates [18, 19], dyestuffs [20] and pyrazole derivatives [21, 22].



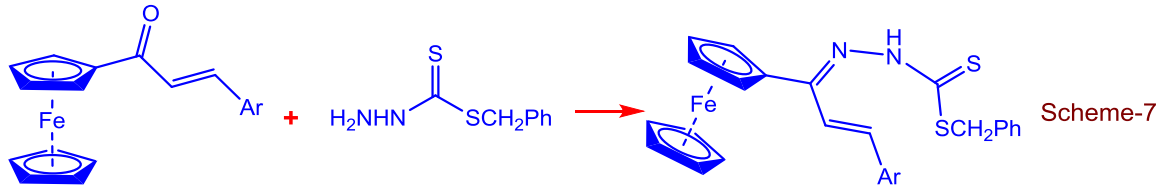
Ar, Ar' = substotutee furan, thiophene, phenyl, pyrazole, pyrimidine, quinoline, piperidine, pyridine, etc.

Gurierrez and coworkers [23] developed new approach for the synthesis of chalcones, which involves the reaction of 5-(4-chlorophenyl)furan-2-carbaldehyde and acetophenones under ultrasonic conditions to yield (*E*)-3-(5-(4-chlorophenyl)furan-2-yl)-1-arylprop-2-en-1-ones (Scheme-6). The study indicated that the chalcones show antioxidant activities against singlet oxygen species.



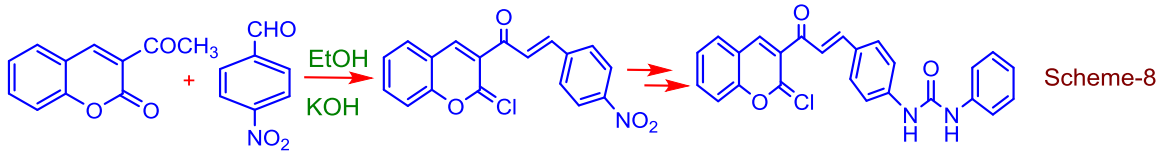
Scheme-6

Sun and coworkers [24] developed an efficient method for the synthesis of ferrocenyl chalcone Schiff bases and their Zn(II), Pb(II), Cd(II), Ni(II) complexes using *p*-TsOH as catalyst (Scheme-7). The synthesized ligands and their metal complexes have showed promising antibacterial **(***S. aureus, E. coli, P. aeruginosa*), antifungal properties (*C. albicans, A. fumigatus, A. niger, A. flavus, S. cerevisiae*), in particular Zn(II) complexes were the most active against all bacterial and fungal strains. Chalcones have been efficiently transformed in to biologically active pyrrolines [25], thiadiazoles [26], isoxazoles [27-29] and pyrazolines [30].



Scheme-7

The increasing interest on new drug discovery is constantly up to date as drugs do not increase survival adequately against increasing cancer cases worldwide. Based on the reported anticancer activity of coumarin, chalcone and urea derivatives, Kucukislamoglu and co-workers [31] synthesized coumarin conjugated chalcone-urea moieties (Scheme-8). The target compounds have showed promising antiproliferative activities against the cancer cell lines (H4IIE and HepG2), representing a promising lead for further optimization.

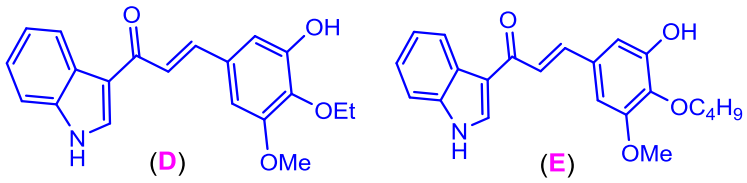


Scheme-8

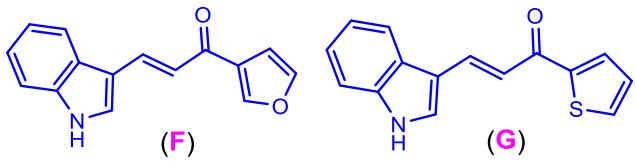
III. Biological Applications

The increase in antibiotic resistance due to various factors has encouraged the look for novel compounds which are active against multidrug-resistant pathogens. The heteroaryl chalcones and their derivatives possess a high degree of structural diversity and pharmacological properties. A series of indole-derived methoxylated chalcones were shown as anti-dermatophyte agents. The *in vitro* antifungal susceptibility

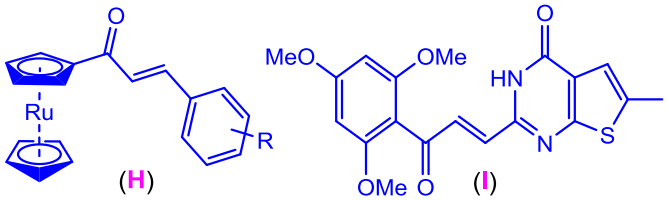
testing against different dermatophytes revealed that most of compounds had potent activity against the dermatophyte strains. In particular, the 4-ethoxy derivative (**D**) found more potent [MIC's: 0.25−2.0 µg/ml] against *T. interdigitale, T. veruccosum* and *M. fulvum*. and the 4-butoxy analogue (**E**) [MIC's: 1−16 µg/ml] had the highest inhibitory activity against *T. mentagrophytes, M. canis,* and *A. benhamiae*. The results facilitate in the design of more effective antifungals with tubulin inhibition mechanism [32].



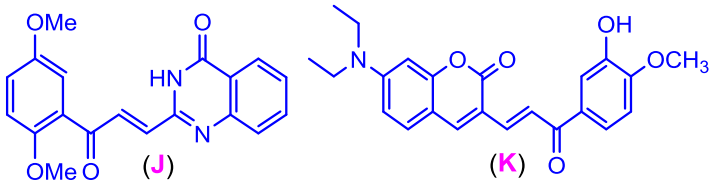
It was found that series of chalcones bearing bis(piperazine) linker indicated that most bispiperazinochalcone derivatives displayed good inhibition of NO (IC_{50} < 20 µM) and low cytotoxicity (IC_{50} > 40 µM), and selectively inhibited the production of IL-1β via inhibiting NLRP3 inflammasome activation, and were promising candidates for the treatment of NLRP3 inflammasome-driven diseases [33], the chalcone derived pyrazoles and 1,3,4-oxadiazoles showed antimicrobial and antioxidant activities [34]. Kannan and co-workers [35] designed and synthesized a library of furan-indole, thiophene-indole chalcones as a promising set of compounds against H_{37}Rv strain of Mycobacterium tuberculosis. The study showed the compounds (*E*)-1-(furan-3-yl)-3-(1*H*-indol-3-yl)prop-2-en-1-one (**F**),and **(***E*)-3-(1*H*-indol-3-yl)-1-(thiophen-2-yl)prop-2-en-1-one (**G**) displayed high anti-tubercular activity at 50 µg/ml with MIC values of 210, and 197µM respectively, and were non-cytotoxic to human megakaryocytes and murine B cells.



A series of ruthenocenyl chalcones (**H**) were synthesized by using Claisen-Schmidt reaction between acetyl rethenocene and aryl aldehydes, have displayed remarkable inhibitor cytotoxic activity against NCI lung cancer cell line with 45% inhibition and 91% inhibition against MDA-MB-4355 breast cancer cell line, comparable with 5-flurouracil [36]. The platinum(IV) complexes of heteroaryl chalcones have shown the reverse cisplatin resistance, and displayed excellent anti-tumor activities *in vitro* and *in vivo*against the tested human cancer cells and have low toxicity [37]. The chalcones with a thieno[2,3-d]pyrimidin-2-yl group were evaluated for their cytotoxic activity towards cultured human lung cancer A549 and colorectal HCT-116 cells. The results indicate that, the compound (**I**) of the series found most potent with IC_{50} values between 2.65-11.44 µM in seven cancer cell lines [38].

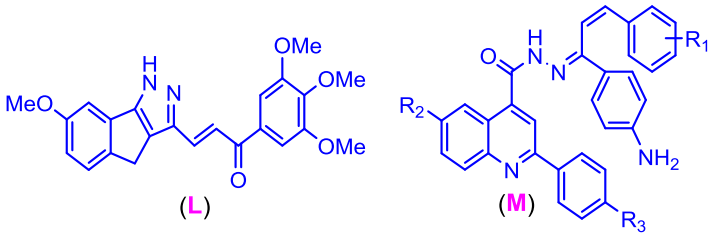


A series of chalcones with a 4-oxoquinazolin-2-yl group were screened for their cytotoxic activities. The compound (**J**) of the series is found most cytotoxic one with IC_{50}s of 3.56 and 4.08 µM in HCT-116 and MCF-7 cells. The HCT-116 cells treated with compound (**J**) resulted in a dose-dependent accumulation of cells in the sub-G1 phase, which is representative of apoptotic cells [39]. The selenoprotein thioredoxin reductases (TrxRs) have been extensively studied as a potential target for the development of anticancer drugs. A coumarin-chalcone hybrids developed as TrxR inhibitors for anticancer agents by Gao *et al*[40]. The study reveals that, the representative compound (**K**) of the series was observed as fluorescence agent, and it down-regulated the expression of TrxR, markedly induced ROS accumulation to activate mitochondrial apoptosis pathway, and inhibited cancer cell metastasis and abolished the colony formation ability of cancer cells.



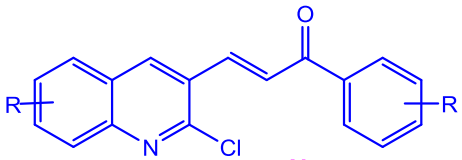
(J) (K)

In an attempt to identify potent and selective anticancer agents, Kumar and coworkers [41] evaluated 1,4-dihydroindeno[1,2-c]pyrazole chalcones (**L**) conjugates for their antiproliferative activity against MCF7, A549, MDA-MB-231, HCT116 and SKBR3 human cancer cell lines. Results indicated that some compounds of the series showed promising activities with IC_{50} values of 3.82-5.33 µM on A549 cell with respect to the positive control. Proenca and coworkers [42] demonstrated that chalcone-chromene derivatives have anticancer properties in the breast cancer cells MCF-7, Hs578T and breast non-neoplastic cells (MCF-10A). The chromene acted as a cell migration inhibitory agent and triggered regulated cell death associated with G_2/M cell-arrest and microtubule destabilization. A series of quinoline-chalcone hybrids (**M**) were designed with an anticipation to act as potential anti-cancer agents. The experimental results by different cytotoxic assays revealed that compounds found potent against all the cell lines tested with IC_{50} = 1.91–5.29 µM against A549 and K-562 cells. The findings support the antitumor potential of quinoline-chalcone derivatives for NSCLC and CML by inhibiting the PI3K/Akt/mTOR pathway [43].



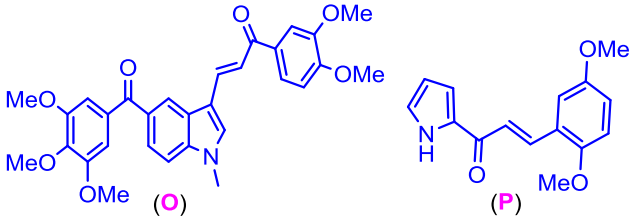
(L) (M)

Silva and coworkers [44] prepared triazole-benzimidazole-chalcone hybrids via click chemistry, between azide derivatives and substituted benzimidazole terminal alkynes bearing a chalcone moiety. The study on the anti-proliferative potential in breast and prostate cancer cell lines showed that the presence of chloro substituents at the chalcone ring of the triazole-benzimidazole-chalcone skeleton enhanced the cytotoxic effects. The benzyl group linked to the 1,2,3-triazole moiety provides more antiproliferative potential. The metal complexes of (*E*)-3-(4-(dimethyl-amino)phenyl)-1-(pyridin-2-yl)prop-2-en-1-one have shown higher antimicrobial activities than the free chalcones, also metal chelates exhibited moderate anticancer activities against MCF7 cell [45]. Ghodsi and co-workers [46] proved that quinoline-chalcone hybrids (**N**) have anticancer activities against four human cancer cell lines A2780, A2780/RCIS, MCF-7, MCF-7/MX and normal Huvec cells. The compounds having benzoyl group showed significant cytotoxic activity against both resistant cancer cells and their parents, further these demonstrated the antiproliferative activity with IC_{50} values ranging from 2.32 to 22.4 µM. The benzoyl derivatives also identified as tubulin inhibitors and induced cell cycle arrest at G2/M phase and apoptosis.



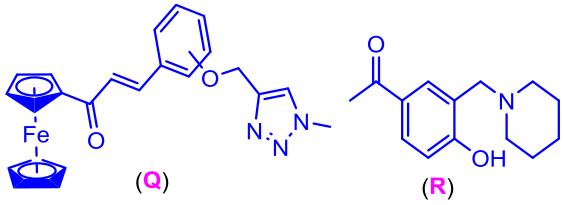
(N)

Kamal and coworkers [47] designed a library of phenstatin based indolyl chalcones as anticancer agents. The compound (*E*)-1-(3,4-dimethoxyphenyl)-3-(1-methyl-5-(3,4,5-trimethoxybenzoyl)-1*H*-indol-3-yl)prop-2-en-1-one (**O**) of the series, found efficacious against the human oral cancer cell line SCC-29B, and reduced growth of 3D spheroids. It exhibited activity through disrupting cellular integrity and affecting glucose metabolism, which is a hallmark of cancer. The cellular architecture was affected by inhibition of tubulin polymerization. It destabilized tubulin assembly in oral cancer cells leading to loss of cell integrity. A series of chalcone-pyrazole hybrids were assessed for their nitric oxide (NO) and prostaglandin E_2 (PGE_2) suppression ability on IFN-γ/LPS-induced RAW 264.7 macrophage cells. It was found that the compound 3-(2,5-dimethoxyphenyl)-1-(1*H*-pyrrol-2-yl)-prop-2-en-1-one (**P**) of the series showed remarkable inhibition towards PGE_2 and NO production with IC_{50} values of 0.5 ± 1.5 µM and 12.1 ± 1.5 µM, respectively. Therefore, the potential of compound (**P**) as a new hit anti-inflammatory agent [48].

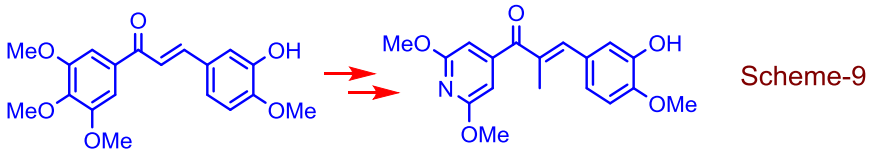


Kumar and coworkers [49] reported 1*H*-1,2,3-triazole linked 4-aminoquinoline-chalcone/-N-acetylpyrazoline conjugates acts as antiplasmodial agents. Results indicated that, the dependence of activity on the length of the alkyl chain and aromatic methoxy substituents of the chalcone. The pyrazoles derived from thienyl chalcones have found potent anti-inflammatory and antimicrobial agents [50]. Ferrocenyl chalcone-triazoles coupled organosilatranes (**Q**) [51] were designed with the aim of amalgamating the pharmacological action of the constituting moieties into a single molecular scaffold, which showed good antimicrobial activities.

The design of an acetylcholinesterase inhibitor with multifunctional properties became the perspective for the development of an effective drug against Alzheimer's disease. The compound 1-{4-hydroxy-3-[(piperidin-1-yl)methyl]phenyl}ethan-1-one (**R**) demonstrated excellent inhibitory activity against AChE (IC_{50} 1.0 nM) showing 33-fold better inhibition than donepezil, biometal chelating ability and also antioxidant activity. Therefore, these fascinating multifunctional proprieties make it a good candidate for the development of AD treatments [52].

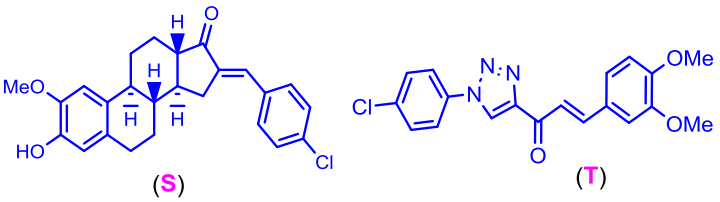


The optimization of the trimethoxyphenyl scaffold of parent chalcone compound by introducing a pyridine ring afforded a series of novel pyridine-chalcone derivatives as potential anti-tubulin agents (Scheme-9) [53] One compound of the series showed potent activity with the IC_{50} values of 0.023-0.045 µM against a panel of cancer cell lines. The cellular mechanism studies disclosed that the compound caused G2/M phase arrest, induced cell apoptosis, disrupted the intracellular microtubule network and effectively suppressed tumor growth *in vivo* without obvious toxicity.

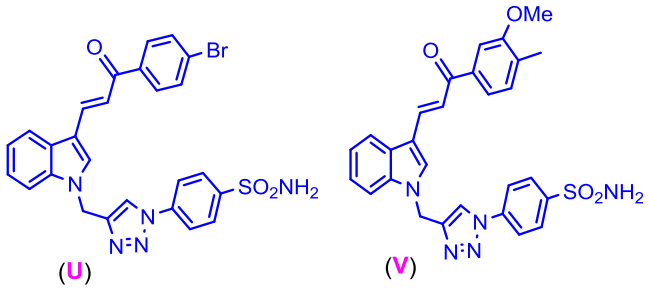


Scheme-9

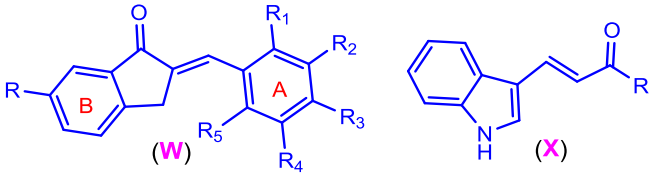
Angiogenesis plays an essential role in tumorigenesis and tumour progression, and anti-angiogenesis therapies have shown promising antitumor effects in solid tumors. 2-Methylestradiol is an endogenous metabolite of estradiol considered as a potential antitumor agent that targets angiogenesis. In this context, Shi and co-workers [54] have showed that 2-methoxyestradiol based chalcones posess antitumor activities, in which the compound (**S**) of the series displayed potent antiangiogenic activity by suppressing tumor growth in MCF-7 xenograft models without side effects, and has low toxicity. Selim and coworkers [55] demonstrated that 1,2,3-triazole-chalcone hybrids have anticancer properties, the (*E*)-1-(1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (**T**) of the series, found most potent anticancer agent with IC_{50} values less than 1 µM on six cancer cell lines. It induced cell cycle arrest in RPMI-8226 and SR leukemia cell lines by 99.73% and 94.95% at 10 µM, at G2/M phase and triggered mitochondrial apoptotic pathway.



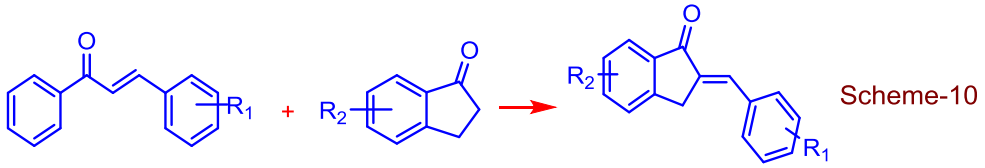
The dihydrotriazine-chalcones at non-lethal concentrations suppressed *in vitro* migration of MDA-MB-231 breast carcinoma cells, and was correlated with a dose-dependent downregulation of PMA-induced MMP-9 expression and secretion. The compounds also suppressed expression of inflammatory mediators inducible iNOS and COX-2 in LPS-stimulated murine macrophage-like RAW 264.7 cells, and TNF-α in LPS-stimulated human monocytes [56]. Thienyl chalcones reacted with urea and thiourea to form thiophene tethered substituted pyrimidin-2-one and pyrimidin-2-thiones, which showed antimicrobial activities [57,58]. Arifuddin and coworkers [59] reported that indolylchalcones - benzenesulfonamide-1,2,3-triazole hybrids acts as human carbonic anhydrases inhibitors with an interesting inhibition constants in the nanomolar range. The compounds (**U**) (18.8 nM), and (**V**) (38.3 nM) of the series have 13, and 6 times more potent than standard drug acetazolamide against hCA I isoform, respectively.



Pancreatic lipase (PL), a crucial enzyme responsible for hydrolysis of dietary lipids, has been validated as a key therapeutic target to prevent and treat obesity-associated metabolic disorders. In this pretext, Huo and coworkers [60] reported that chalcones behaves as potent and reversible PL inhibitors. The the structural modifications at both A and B rings of a chalcone, confirmed that the compound (**W**) displayed the most potent PL inhibition activity, with an IC_{50} value of 0.33 μM. Also, it displayed excellent stability in artificial gastrointestinal fluids and good metabolic stability in human liver preparations. SARS-CoV-2 is distinctly infective and there is a need to find a drug for this pandemic. Flavonoids exist in many traditional medicine, indole-chalcones are effective in fighting various diseases. Hence, flavonoids and structurally related indole chalcones were studied *in silico* for their pharmacokinetic properties like absorption, distribution, metabolism, excretion, toxicity and anti-SARS-CoV-2 against their proteins. It was seen that, indole chalcones (**X**) are capable of fighting SARS-CoV-2 [61]. The pyrazole derived from thienyl chalcones have promising antimicrobial activities [62].



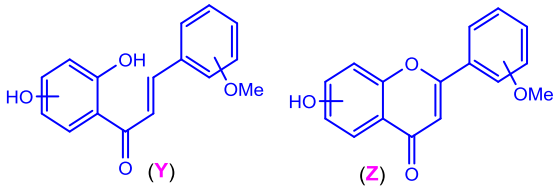
Human carboxylesterase 2 (hCES2A), one of the major serine hydrolases distributed in the small intestine, plays a crucial role in hydrolysis of ester-bearing drugs. The hCES2A inhibitor therapy can modulate the pharmacokinetic and toxicological profiles of hCES2A-substrate drugs. In this pretext, hCES2A inhibitors, Huo and coworkers synthesized a series of indanone–chalcone hybrids (Scheme-10) and studied their SAR [63]. It was found that most indanone–chalcone hybrids displayed strong hCES2A inhibition activities. Structure-hCES2A inhibition activity relationship studies showed that introduction of a hydroxyl at the C4' site and an N-alkyl group at the C6 site were beneficial for hCES2A inhibition. The compound (*E*)-2-(4-hydroxy-3-methoxybenzylidene)-6-(pyrrolidin-1-yl)-2,3-dihydro-1*H*-inden-1-one showed most potent inhibition on hCES2A with great specificity, and was capable of inhibiting intracellular hCES2A in living cells, and therefore, is a promising candidate for the development of novel anti-diarrhea agents.



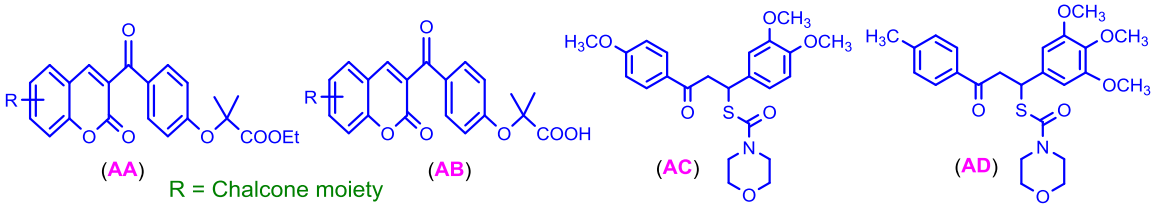
Scheme-10

Farnesoid X receptor (FXR), a nuclear receptor mainly distributed in liver and intestine, has been regarded as a potential target for the treatment of various metabolic diseases, cancer and infectious diseases

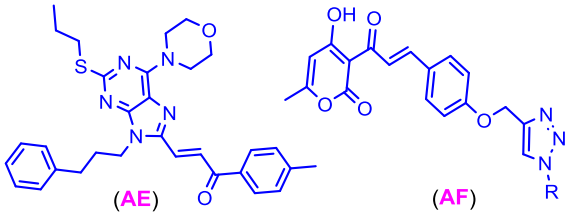
related to liver. In this context, Fang and coworkers [64] designed a library of chalcones, flavones and chromenes, based on substitution and conformation restriction strategy. They were successful in identifying chalcones (**Y**) and chalcone derived chromenes (**Z**) as microM potent FXR antagonists, among which (**Z**) significantly decreased the plasma and hepatic triglyceride level in KKay mice.



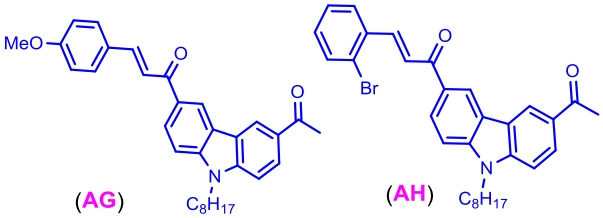
Coumarin-chalcone fibrates were evaluated for their PPARa/g agonist and antioxidant activities. Amongst them, compounds (**AA**) and (**AB**) were identified as potent PPARa and g dual agonists. Also, the compound (**AA**) exhibited greater antioxidant potency than Trolox with IC50 values of 9.40 mM [65]. Chalcone-based dithiocarbamate derivatives potent antimicrobial activities. Of the series, compound (**AC**) proved to be the most active candidate with MIC of 8 µg/ml against both Ps12 and K4 and MBC of 32 µg/ml against Ps12 and 16 µg/ml against K4; and compound (**AD**) has better DNA binding than doxurubucin with IC_{50} of 27.48 µg/ml, suggesting that it could have a role in their higher antibacterial effect [66].



To explore anti-gastric cancer agents with high efficacy and selectivity, Liu and coworkers [67] tested 3-(2,6,9-trisubstituted-9H-purine)-8-chalcone derivatives for their antiproliferative effects. The study showed the compound (**AE**) was most active against MGC803 cell line with an IC_{50} value of 0.84 µM, with high selectivity observed between cancer and normal cells (23.35 µM against GES-1). It inhibited colony formation and migration, induce the apoptosis of MGC803 cells through both the mitochondrial-mediated intrinsic and death receptor-mediated extrinsic pathways. DHA-chalcone-1,2,3-triazole hybrids Dehydroacetic acid chalcone-1,2,3-triazole hybrids (**AF**) showed markable antimicrobial activities comparable to the standard and DHA, which itself an antimicrobial agent [68].



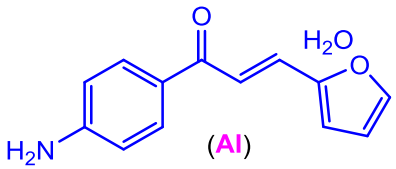
Although a diverse range of chemical entities offering striking therapeutic potential against urease enzyme has been reported, the key challenges (toxicity and safety) associated with these inhibitors create a large unmet medical need to unveil new, potent and safe inhibitors of urease enzyme. In this pursuit, Aliyalbrar and coworkers [69] demonstrated that carbazole-chalcone hybrids, particularly, compounds (**AG**) and (**AH**) acts as potent inhibitors with IC_{50} values of 8.93 ± 0.21 and 6.88 ± 0.42 Mm.



IV. Physicochemical Properties

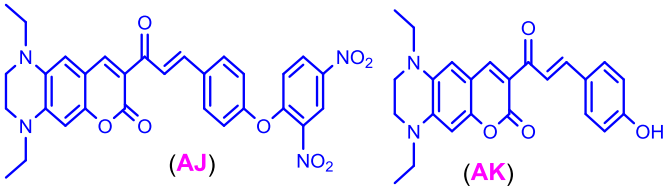
The chalcone-phthalocyanine complexes are important due to their physical properties, in particularly for photodiode properties. In this context, the heteroaryl chalcone-substituted phthalonitrile reacted with Co(II)

acetate under solid phase heating condition to form chalcone substituted metallo-phthalocyanine. The chalcone substituted metallo-phthalocyanine has a photodiode and photocapacitor characteristic, and therefore, can be applied in solar tracking systems [70]. Pyrazole derived from heteroaryl chalcones possess good NLO properties [71, 72]. Barreto and coworkers [73] demonstrated that, the compound (2*E*)-1-(4-aminophenyl)-3-(furan-2-yl)prop-2-en-1-one monohydrate (**AI**) has a strong candidate for fluorescent probes, luminescent materials and optoelectronic devices.

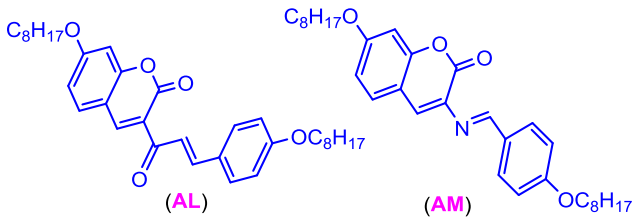


(**AI**)

Coumarin-chalcone hybrids have attracted much attention in recent years due to their important optical properties. In this view, Zhang and coworkers [74] have studied the photophysical properties of coumarinyl chalcones and the sensing mechanism for H_2S of a related fluorescent probe. The that fluorescence "off-on" effect and the fluorescent quenching mechanism of the probe revealed that the first excited state of the probe (**AJ)** is a dark state with obvious charge transfer from coumarin unit to 2,4-dinitrophenyl moiety, resulting fluorescence quenching via the nonradiative photoinduced electron transfer process. On the other hand, the excited state in the thiolysis product (**AK)** decayed directly to ground state, and thus the fluorescence is recovered.



Chalcone and cyanopyridine derivatives have emerged as attractive light sensitive materials, with potential use in cell probing and optoelectronic applications. They are highly fluorescent both in solution and solid state and thus well-suited for OLED applications. With this in view, Shetty and coworkers [75] reported that chalcone derivatised cyanopyridine has dual emission in the blue and green regions and a single band in orange emission, in which the solid-state emission in orange region inferring its suitability for the OLED application. The heteroaryl chalcone derivatised benzothiazepines [76], pyrazoles [77-79], cyclobutane [80] have been extensively studied for physicochemical properties, and these molecules possess promising NLO properties. The synthesized n-alkoxy coumarin derivatives with chalcone and imine linkages (**AL**) and (**AM**) have exhibited optical, liquid crystal properties [81].



The ferrocene containing chalcone derivative (*E*)-3-(2-methylpyrimidin-5-yl)-1-ferroceynlprop-2-en-1-one has explored as intramolecular charge transfer of a bioactive ferrocenylchalcone derivative, from a strong electron-donor (ferrocene) to an electron-acceptor (pyrimidine) through the π-conjugated bridge [82].

V. Conclusion

The organic compounds, particularly, the chalcones with heterocyclic moieties were extensively used as scaffolds in the synthesis of diverse classes of compounds of biological interest. The present review concluded and focuses on the recent developments in the area of synthetic protocols for heteroaryl chalcones, their utility as building blocks, pharmaceutical perspectives, and also describes their structure-activity relationships studies. The discussion that made on the physical properties, particularly of photosensing and NLO properties of heteroaryl chalcones explore the diverse chemical structures of potent physical properties, like their utility in photosensing and optical switching devices. The synthetic structure and structural optimization is promising for potential drug design and discovery and development.

References

[1]. Atukuri D, Vijayalaxmi S, Sanjeevamurthy R, Vidya L, Prasannakumar R and Raghavendra MM: Identification of quinoline-chalcones and heterocyclic chalcone-appended quinolines as broad-spectrum pharmacological agents. Bioorg Chem. 2020; 105: 104419.

[2]. Ajay Kumar K andRenuka N:Thienyl chalcones: Small molecules that play pivotal roles, Int. J. Curr. Res. 2021: 13(02); 16067-16074.

[3]. Basappa VC, Ramaiah S, Penubolu S, Kariyappa AK: Recent developments on the synthetic and biological applications of chalcones-A Review, Biointerface Res. App. Chem. 2022: 12(1); 180-195.

[4]. Coskun D, Erkisa M, Ulukaya E, Coskun MF and Ari F: Novel 1-(7-ethoxy-1-benzofuran-2-yl) substituted chalcone derivatives: Synthesis, characterization and anticancer activity. Eur. J. Med. Chem. 2017 136; 212-222.

[5]. Kumara K, Naveen S, Prabhudeva MG, Ajay Kumar K, Lokanath NK and Warad I: (*E*)-1-(5-chlorothiophen-2-yl)-3-(p-tolyl)prop-2-en-1-one.IUCrData, 2017: 2; x170038.

[6]. Naveen S, Prabhudeva MG, Ajay Kumar K, Lokanath NK and Abdoh M: (*E*)-1-(5-chlorothiophen-2-yl)-3-(2,4-dimethylphenyl) prop-2-en-1-one.IUCrData, 2016: 1; x161974.

[7]. Renuka N,Lokanath NK, Ajay Kumar K and Prabhuswamy M: (*E*)-3-(4-methoxyphenyl)-1-(thiophen-2-yl)prop-2-en-1-one.Acad. J. Chem. 2016: 1;32-39.

[8]. Moustafa AH and Amer AA: Unexpected products from the reaction of chalcones with cyanoguanidine. Tetrahedron, 2018: 74;324-328.

[9]. Hassan MM, Alzandi ARA and Hassan MM: Synthesis, structure elucidation and plants growth promoting effects of novel quinolinyl chalcones. Arab. J. Chem. 2020: 13; 6184–6190.

[10]. Gomes MN, Braga RC, Grzelak EM, Neves BJ, Muratov E, Ma R, Klein LL, Cho S, Oliveira GR, Franzblau SG and Andrade CH: QSAR-driven design, synthesis and discovery of potent chalcone derivatives with antitubercular activity. Eur. J. Med. Chem. 2017: 137; 126-138.

[11]. Kumar KS, Kotra V, Kola PK, Praveena Devi CHB, Anusha N, Babu BH, Adil SF, Shaik MR, Khan M, Al-Warthan A, Alduhaish O and Alam MM: $ZnCl_2$ catalyzed new coumarinyl-chalcones as cytotoxic agents. Saudi J. Biol. Sci. 2021: 28; 386–394.

[12]. Lokeshwari DM, Kameshwar VH and Kariyappa AK: Synthesis of furan tethered 2-pyrazolines via 1,3-dipolar cycloaddition reactions: *In vitro* evaluation for their antioxidant and antimicrobial activities. Biointerface Res. App. Chem. 2017: 7(5); 2158-2165.

[13]. Lokeshwari DM, and Ajay Kumar K: Synthesis of isoxazoles via 1,3-dipolar cycloaddition reactions: Pharmacological screening for their antioxidant and antimicrobial activities. Asian J. Chem. 2017: 29; 2660-2664.

[14]. Lokeshwari DM, Rekha ND, Srinivasan B, Vivek HK and Kariyappa AK: Design, synthesis of novel furan appended benzothiazepine derivatives and *in vitro* biological evaluation as potent VRV-PL-8a and H^+/K^+ ATPase inhibitors. Bioorg. Med. Chem. Lett. 2017: 27; 3048-3054.

[15]. Mahadevaswamy LD and Kariyappa AK: An environmentally benign lemon juice mediated synthesis of novel furan conjugated pyrazole derivatives and their biological evaluation. Pharm. Chem. J. 2017: 51;670-677.

[16]. Rizvi SUF, Siddiqui HL, Ahmad MN, Ahmad M and Bukhari MH: Novel quinolyl-thienyl chalcones and their 2-pyrazoline derivatives with diverse substitution pattern as antileishmanial agents against *Leishmania major*. Med. Chem. Res. 2012: 21; 1322–1333.

[17]. Poloa E, Ibarra-Arellanoa N, Prent-Penalozaa L, Morales-Bayuelob A, Henaoc J, Galdamezd A. and Gutierreza M: Ultrasound-assisted synthesis of novel chalcone, heterochalcone and bis-chalcone derivatives and the evaluation of their antioxidant properties and as acetylcholinesterase inhibitors. Bioorg. Chem. 2019: 90; 103034.

[18]. Raghavendra KR, Ajay Kumar K and Shashikanth S: An efficient synthesis of new Lignan scaffolds as antimicrobial inhibition agents. J. Chem. Pharm. Res.2015: 7(8);638-644.

[19]. Raghavendra KR, Renuka N, Kumar KA and Shashikanth S:An accessible route for the synthesis of novel lignan derivatives and their biological evaluation. Pharm. Chem. J. 2017: 51; 661-669.

[20]. Raghavendra KR and Ajay Kumar K: Synthesis of some novel azo dyes and their dyeing, redox and antifungal properties. Int. J. ChemTech Res.2013: 5(4); 1756-1760.

[21]. Raghavendra KR, Kumar KA and Shashikanth S: A convenient route to the synthesis of new trisubstituted pyrazolines and their antimicrobial activity. Res. J. Pharm. Biol. Chem. Sci.2014: 5(1); 629-637.

[22]. Kumar AD, Vivek HK, Srinivasan B, Naveen S, Kumara K, Lokanath NK, Byrappa K and Kumar KA,Design, synthesis, characterization, crystal structure, Hirshfeld surface analysis, DFT calculations,anticancer, angiogenic propertiesof new pyrazole carboxamide derivatives,J. Mol. Struct. 2021: 1235; 130271.

[23]. Diaz-Uribe C, Vallejo W, Florez J, Trilleras J, Gurierrez M, Rodriguez-Serrano A, Schott E and Zarate X: Furanyl chalcone derivatives as efficient singlet oxygen quenchers. An experimental and DFT/MRCI study. Tetrahedron, 2020: 76; 131248.

[24]. Liu Y, Yang L, Yin D, Dang Y, Yang L, Zou Q, Li J and Sun J: Solvent-free synthesis, characterization, biological activity of schiff bases and their metal (II) complexes derived from ferrocenyl chalcone. J. Organomet. Chem. 2019: 899; 120903.

[25]. Ajay Kumar K, Lokanatha Rai KM and Umesha KB: A new approach for the transformation of alkenes to pyrrolines via aziridine intermediates. Tetrahedron, 2001: 57; 6993-6996.

[26]. Ajay Kumar K, Renuka N and Vasanth Kumar G: Thiadiazoles: Molecules of diverse applications-A review. Int. J. PharmTech Res.2013: 5(1); 239-248.

[27]. Ajay Kumar K, Govindaraju M, Vasantha Kumar G: Synthesis of isoxazoles via 1,3-dipolar cycloaddition reactions and their antimicrobial activity. Ind. J. Heterocycl. Chem.2010: 20; 183-184.

[28]. Ajay Kumar K, Lokanatha Rai KM and Umesha KB: Synthesis and evaluation of antifungal and antibacterial activity of ethyl 3,5-diarylisoxazole-4-carboxylates. J. Chem. Res. (S), 2001: 436-438.

[29]. Lokeshwari DM, Prabhudeva MG, Ajay Kumar K andJayadevappa HP; Synthesis, characterization of novel isoxazoles: Biological evaluation for their antifungal and radical scavenging potencies, IOSR J. App. Chem. 2020: 13(10);8-12.

[30]. Jayaroopa P and Ajay Kumar K: Synthesis and antimicrobial activity of 4,5-dihydropyrazoline derivatives. Int. J. Pharm. Pharm. Sci. 2013: 5(4); 431-433.

[31]. Kurt BZ, Kandas NO, Dag A, Sonmez F and Kucukislamoglu M: Synthesis and biological evaluation of novel coumarin-chalcone derivatives containing urea moiety as potential anticancer agents. Arab. J. Chem. 2020: 13; 1120–1129.

[32]. Mirzaei H, Abastabar M and Emami S: Indole-derived chalcones as anti-dermatophyte agents: In vitro evaluation and in silico study. Comput. Biol. Chem. 2020: 84; 107189.

[33]. Tang Y-L, Zhang X, Qi Y, Pu X-J, Liu B, Zhang X, Li XS, Xiao W-L, Wan C-P and Mao Z-W: Synthesis and anti-inflammatory evaluation of new chalcone derivatives bearing bispiperazine linker as IL-1β inhibitors. Bioorg. Chem. 2020: 98; 103748.

[34]. Gurunanjappa P and Kariyappa AK: Design, synthesis and biological evaluation of 1,3,4-oxadiazoles/thiadiazoles bearing pyrazole scaffold as antimicrobial and antioxidant candidates. Curr. Chem. Lett.2016: 5(3);109-122.

[35]. Ramesh D, Joji A, Vijayakumar BG, Sethumadhavan A, Mani M and Kannan T:Indole chalcones: Design, synthesis, in vitro and in silico evaluation against Mycobacterium tuberculosis. Eur. J. Med. Chem. 2020: 198; 112358.

[36]. Khanapure S, Jagadale M, Bansode P, Choudhari P and Rashinkar G: Anticancer activity of ruthenocenyl chalcones and their molecular docking studies. J. Mol. Struct. 2018: 1173; 142-147.

[37]. Huang X, Liu Z, Wang M, Yin X, Wang Y, Dai L and Wang H: Platinum(IV) complexes conjugated with chalcone analogs as dual targeting anticancer agents: *In vitro* and *in vivo* studies. Bioorg Chem. 2020: 105; 104430.

[38]. Wang F-C, Peng B, Cao S-L, Li H-Y, Yuan X-L, Zhang T-T, Shi R, Li Z, Liao J, Wang H, Li J and Xu X: Synthesis and cytotoxic activity of chalcone analogues containing a thieno[2,3-*d*]pyrimidin-2-yl group as the A-ring or B-ring. Bioorg. Chem. 2020: 94; 103346.

[39]. Han X, Peng B, Xiao B-B, Cao S-L, Yang C-R, Wang W-Z, Wang F-C, Li H-Y, Yuan X-L, Shi R, Liao J, Wang H, Li J and Xu X: Synthesis and evaluation of chalcone analogues containing a 4-oxoquinazolin-2-yl group as potential anti-tumor agents. Eur. J. Med. Chem, 2019: 162; 586-601.

[40]. Wang Y, Zhang W, Dong J and Gao J: Design, synthesis and bioactivity evaluation of coumarin-chalcone hybrids as potential anticancer agents. Bioorg. Chem. 2020: 95; 103530.

[41]. Khan I, Garikapati KR, Setti A, Shaik AB, Makani VKK, Shareef MA, Rajpurohit H, Vangara N, Pal-Bhadra M, Kamal A and Kumar CG: Design, synthesis, **in silico** pharmacokinetics prediction and biological evaluation of 1,4-dihydroindeno[1,2-**c**]pyrazole chalcone as EGFR /Akt pathway inhibitors. Eur. J. Med. Chem. 2019: 163; 636-648.

[42]. Pontes O, Costa M, Santos F, Sampaio-Marques B, Dias T, Ludovico P, Baltazar F and Proenca F: Exploitation of new chalcones and 4H-chromenes as agents for cancer treatment. Eur. J. Med. Chem. 2018: 157; 101-114.

[43]. Abbas SH, Abd El-Hafeez AA, Shoman ME, Montano MM and Hassan HA: New quinoline/chalcone hybrids as anti-cancer agents: Design, synthesis, and evaluations of cytotoxicity and PI3K inhibitory activity. Bioorg. Chem. 2019: 82;360-377.

[44]. Djemoui A, Naouri A, Quahrani MR, Djemoui D, Lahcene S, Lahrech MB, Boukenna L, Albuquerque HMT, Saher L, Rocha DHA, Monteiro FL, Helguero LA, Bachari K, Talhi Q and Silva AMS: A step-by-step synthesis of triazole-benzimidazole-chalcone hybrids: Anticancer activity in human cells. J. Mol. Struct. 2020: 1204; 127487.

[45]. Fayed TA, Gaber M, El-Nahass MN, Diab HA and El-Gamil MM: Synthesis, Structural characterization, thermal, molecular modeling and biological studies of chalcone and Cr(III), Mn(II), Cu(II) Zn(II) and Cd(II) chelates. J. Mol. Struct. 2020: 1221; 128742.

[46]. Mirzaei S, Hadizadeh F, Eisvand F, Mosaffa F and Ghodsi R: Synthesis, structure-activity relationship and molecular docking studies of novel quinoline-chalcone hybrids as potential anticancer agents and tubulin inhibitor**s.** J. Mol. Struct. 2020: 1202; 127310.

[47]. Kode J, Kovvuri J, Nagaraju B, Jadhav S, Barkume M, Sen S, Kasinathan NK, Chaudhari P, Mohanty BS, Gour J, Sigalapalli DK, Kumar CG, Pradhan T, Banerjee M and Kamal A: Synthesis, biological evaluation, and molecular docking analysis of phenstatin based indole linked chalcones as anticancer agents and tubulin polymerization inhibitors. Bioorg. Chem. 2020: 105 104447.

[48]. Faudzi SMM, Abdullah MA, Manap MRA, Ismail AZ, Rullah K, Aluwi MFFM, Ramli ANM, Abas F and Lajis NH: Inhibition of nitric oxide and prostaglandin E_2 production by pyrrolylated-chalcones: Synthesis, biological activity, crystal structure analysis, and molecular docking studies. Bioorg. Chem. 2020: 94; 103376.

[49]. Kumar S, Saini A, Gut J, Rosenthal PJ, Raj R and Kumar V: 4-Aminoquinoline-chalcone/-N-acetylpyrazoline conjugates: Synthesis and antiplasmodial evaluation. Eur. J. Med. Chem. 2017: 138; 993-1001.

[50]. Kumar AD, Prabhudeva MG, Bharath S, Kumara K,Lokanath NK and Kumar KA: Design and Amberlyst-15 mediated synthesis of novel thienyl-pyrazole carboxamides that potently inhibit Phospholipase A2 by binding to an allosteric site on the enzyme. Bioorg. Chem.2018: 80; 444-452.

[51]. Singh G, Arora A, Kalra P, Maurya IK, Ruizc CE, Estebanc MA, Sinha S, Goyal K and Sehgal R: A strategic approach to the synthesis of ferrocene appended chalcone linked triazole allied organosilatranes: Antibacterial, antifungal, antiparasitic and antioxidant studies. Bioorg. Med. Chem. 2019: 27; 188-195.

[52]. Aljohani G, Al-Sheikh Ali A, Said MA, Hughes DL, Alraqa SY, Amran S, Ahmad F and Basar N: 2-Benzyloxynaphthalene aminoalkylated chalcone designed as acetylcholinesterase inhibitor: Structural characterisation, in vitro biological activity and molecular docking studies. J. Mol. Struct. 2020: 1222; 128898.

[53]. Xu F, Li W, Shuai W, Yang L, Bi Y, Ma C, Yao H, Xu S, Zhu Z and Xu J: Design, synthesis and anticancer properties of isocombretapyridines as potent colchicine binding site inhibitors. Eur. J. Med. Chem. 2019: 173; 1-14.

[54]. Wang C, Li L, Fu D, Qin T, Ran Y, Xu F, Du X, Gao H, Sun S, Yang T, Zhang X, Huo J, Zhao W, Zhang Z and Shi X: Discovery of chalcone-modified estradiol analogs as antitumour agents that Inhibit tumour angiogenesis and epithelial to mesenchymal transition. Eur. J. Med. Chem. 2019: 176; 135-148.

[55]. Ashour HF, Abou-Zeid LA, El-Sayed MA-A and Selim K.B: 1,2,3-Triazole-Chalcone hybrids: Synthesis, in vitro cytotoxic activity and mechanistic investigation of apoptosis induction in multiple myeloma RPMI-8226.Eur. J. Med. Chem. 2020: 189; 112062.

[56]. Gan F-F, Zhang R, Ng H-L, Karuppasamy M, Seah W, Yeap WH, Ong S-M, Hadadi E, Wong S-C, Chui W-K and Chew E-H: Novel dual-targeting anti-proliferative dihydrotriazine-chalcone derivatives display suppression of cancer cell invasion and inflammation by inhibiting the NF-κB signaling pathway. Food Chem. Toxicol. 2018: 116B; 238-248.

[57]. Hegde SG, Dileep Kumar A and Ajay Kumar K,Synthesis and antifungal activity of novel pyrimidin-2-one analogues.J. Chem. Pharm. Res.2015: 7(8);72-76.

[58]. Shruthi VK, Vagish CB and Ajay Kumar K: An easy route to synthesis of thiophene tagged pyrimidin-2-thiones as antibacterial agents.J. Chem. Pharm. Res.2015: 7(8);39-43.

[59]. Singh P, Swain B, Thacker PS, Sigalapalli DK, Yadav PP, Angeli A, Supuran CT and Arifuddin M: Synthesis and carbonic anhydrase inhibition studies of sulfonamide based indole-1,2,3-triazole chalcone hybrids. Bioorg. Chem. 2020: 99; 103839.

[60]. Huo P-C, Hu Q, Shu S, Zhou Q-H, He R-J, Hou J, Guan X-Q, Tu D-Z, Hou X-D, Liu P, Zhang N, Liu Z-G and Ge G-B, Design, synthesis and biological evaluation of novel chalcone-like compounds as potent and reversible pancreatic lipase inhibitors. Bioorg. Med. Chem. 2020: 29; 115853.

[61]. Vijaykumar BG, Ramesh D, Joji A, Prakasan JJ and Kannan T:In silico pharmacokinetic and molecular docking studies of natural flavonoids and synthetic indole chalcones against essential proteins of SARS-CoV-2.Eur. J. Pharmcol. 2020: 886; 173448.

[62]. Prabhudeva MG, Prabhuswamy M, Dileep Kumar A, Lokanath NK, Naveen S, and Ajay Kumar K: Synthesis, crystal and molecular structure and antimicrobial studies of 1-(3-chlorophenyl)-3-(5-chlorothiophen-2-yl)-5-phenyl-4,5-dihydro-1*H*-pyrazole.Chem. Data Coll. 2017: 9-10; 80-88.

[63]. Huo P-C, Guan X-Q, Liu P, Song Y-Q, Sun M-R, He R-J, Zou L-W, Xue L-J, Shi J-H, Zhang N, Liu Z-G and Ge G-B: Design, synthesis and biological evaluation of indanone-chalcone hybrids as potent and selective hCES2A inhibitors. Eur. J. Med. Chem. 2021: 209; 112856.
[64]. Zhang G, Liu S, Tan W, Verma R, Chen Y, Sun D, Huan Y, Jiang Q, Wang X, Wang N, Xu Y, Wong C, Shen Z, Deng R, Liu J, Zhang Y and Fang W: Synthesis and biological evaluations of chalcones, flavones and chromenes as farnesoid x receptor (FXR) antagonists. Eur. J. Med. Chem. 2017: 129; 303-309.
[65]. Niu H, Wang W, Li J, Lei Y, Zhao Y, Yang W, Zhao C, Lin B, Song S and Wang S: A novel structural class of coumarin-chalcone fibrates as PPARα/γ agonists with potent antioxidant activities: Design, synthesis, biological evaluation and molecular docking studies. Eur. J. Med. Chem. 2017: 138; 212-220.
[66]. Ayman M, El-Messery SM, Habib EE, Al-Rashood ST, Almehizia AS, Alkahani HM and Hassan GS: Targeting microbial resistance: Synthesis, antibacterial evaluation, DNA binding and modeling study of new chalcone-based dithiocarbamate derivatives. Bioorg. Chem. 2019: 85; 282-292.
[67]. Zhao T-Q, Zhao Y-D, Liu X-Y, Li Z-H, Wang B, Zhang X-H, Cao Y-Q, Ma L and Liu H-M: Novel 3-(2,6,9-trisubstituted-9H-purine)-8-chalcone derivatives as potent anti-gastric cancer agents: Design, synthesis and structural optimization. Eur. J. Med. Chem. 2019: 161; 493-505.
[68]. Lal K, Yadav P, Kumar A, Kumar A and Paul AK: Design, synthesis, characterization, antimicrobial evaluation and molecular modeling studies of some dehydroacetic acid-chalcone-1,2,3-triazole hybrids. Bioorg. Chem. 2018: 77; 236-244.
[69]. Kazmi M, Khan I, Khan A, Halim SA, Saeed A, Mehsud S and Al-Harrasi AA: Developing new hybrid scaffold for urease inhibition based on carbazole-chalcone conjugates: Synthesis, assessment of therapeutic potential and computational docking analysis. Bioorg. Med. Chem. 2019: 27; 115123.
[70]. Demirol M, Sirka L, Caliskan E, Biryan F, Koran K, Gorgulu AO and Yakuphanoglu F: Synthesis and photodiode properties of chalcone substituted metallo-phthalocyanine. J. Mol. Struct. 2020: 1219; 128571.
[71]. Barakat A, Shivalingegowda N, Renuka N, Kariyappa AK, Abdoh M, Warad I and Lokanath NK: Crystal structure of 3-(thiophene-2-yl)-5-p-tolyl-4,5-dihydro-1H-pyrazole-1-carboxamide.Zeitschrift fur Krysta. New Crystal Struct. 2016: 231; 267-269.
[72]. Kumara K, Dileep Kumar A, Ajay Kumar K and Lokanath NK: Synthesis, spectral and X-ray crystal structure of 3-(3-methoxyphenyl)-5-(3-methylthiophen-2-yl)-4,5-dihydro-1H-pyrazole-1-carboxamide: Hirshfeld surface, DFT calculations and thermo-optical studies.Chem. Data Coll. 2018: 13-14;40-59.
[73]. Nogueira CES, de Oliveira MM, Teixeira AMR, Bandeira PN, dos Santos HS, Ayala AP, Bezerra BP, Barreto ACH and Freire PTC: Crystal structure, FT-Raman and FTIR spectra and DFT calculations of chalcone (2E)-1-(4-aminophenyl)-3-(furan-2-yl)prop-2-en-1-one monohydrate. J. Mol. Struct. 2020: 1212; 128141.
[74]. Xue Y, Liu Y, Wang G, An L, Teng Y, Chen M, Xie Y and Zhang L: TDDFT study on the photophysical properties of coumarinyl chalcones and sensing mechanism of a derived fluorescent probe for hydrogen sulfide. Spectrochim. Acta A: Mol. Biomol. Spect. 2020: 234; 118263.
[75]. Hegde H, Sinha RK, Kulkarni SD and Shetty N.S: J. Photochem. Photobiol A: Chem. Synthesis, photophysical and DFT studies of naphthyl chalcone and nicotinonitrile derivatives. 2020: 389; 112222.
[76]. Manjunath BC, Manjula M, Raghavendra KR, Shashikanth S, Ajay Kumar K and Lokanath NK: 2-(3, 4-Dimethoxyphenyl)-4-(thiophen-2-yl)-2, 3-dihydro-1, 5-benzothiazepine.Acta Crysta. Sect. E, 2014: E70; o121-o121.
[77]. Prabhudeva MG, Naveen S, Raghavendra KR, Dileep Kumar A, Kumara K, Lokanath NK and Ajay Kumar K: 1-(3-Chlorophenyl)-5-(4-chlorophenyl)-3-(5-chlorothiophen-2-yl)-4,5-dihydro-1H-pyrazole.IUCrData, 2017: 2;x162048.
[78]. Naveen S, Pavithra G, Abdoh M, Ajay Kumar K, Warad I and Lokanath NK: Crystal structure of 3(thiophene-2-yl)-5-p-tolyl-4,5-dihydro-1H-pyrazole-1-carbothioamide.Acta Crysta. Sect. E, 2015: E71;763-765.
[79]. Vagish CB, Kumar AD, Kumara K,Vivek HK, Renuka N,Lokanath NK and Kumar KA; Environmentally benign synthesis of substituted pyrazoles as potent antioxidant agents, characterization anddocking studies, J. Iran. Chem. Soc. 2021: 18(2);479-493.
[80]. Renuka N, Naveen S, Raghavendra KR, Dileep Kumar A, Lokanath NK and Ajay Kumar K: (3,4-bis(2,3-dichlorophenyl)cyclobutane-1,2-diyl)bis(furan-2-ylmethanone) monohydrate.IUCrData, 2017: 2; x170318.
[81]. Durgapal SD, Soni R, Soman SS and Prajapati AK: Synthesis and mesomorphic properties of coumarin derivatives with chalcone and imine linkages. J. Mol. Liq. 2020: 297; 111920.
[82]. Twinkle AR, Leenaraj DR, Ratkovic Z, Arunsasi BS, Bright KC and Reshma R: Ferrocenyl chalcone derivative (E)-3-(2-methylpyrimidin-5-yl)-1-ferroceynlprop-2-en-1-one: Synthesis, Structural analysis, Docking study and their Antibacterial evaluation. J. Mol. Struct. 2020: 1210; 128049.

K. Ajay Kumar, et. al. "Heteroaryl Chalcones: Prominent Pharmacophores of Synthetic and Biological Interest." *IOSR Journal of Applied Chemistry (IOSR-JAC)*, 14(6), (2021): pp 41-52.