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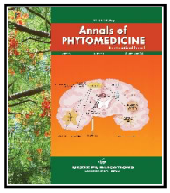

Review Article : Open Access

Thiazole chalcones: Promising agents with diverse pharmacological properties

Afroz Patan and M. Vijey Aanandhi◆

Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai-600117, Tamil Nadu, India.

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Abstract

Hybrid molecules/combination of heterocyclic rings with natural and synthetic origins are a desirable source for the creation of therapeutic agents. The chalcones are important biologically active heterocyclic compounds which contain two aryl rings joined by a three-carbon ketovinyl group. Two significant families of natural chemicals with a variety of pharmacological actions, thiazole and chalcone constitute excellent building blocks for thiazole-chalcone hybrid, scaffolds as bioactive agents. Encouraged by the promising medicinal application of such hybrids the scientific community has reported numerous thiazole-chalcone hybrids with a wide spectrum of biological properties including anticancer, antimicrobial, antidiabetic, antioxidant, antitubercular, and so on, through synthetic hybridization strategy. The present review covers the development, the mechanisms of action as well as structure-activity relationships of chalcone hybrids with potential therapeutic application for many ailments in recent one decade to assist medicinal chemists for successful and effective development of thiazole-chalcone hybrids.

1. Introduction

Heterocyclic compounds is essential class of substances for drug development. Most medications have heterocyclic rings in their structure, hence heterocyclic chemistry is crucial in the creation of new therapeutic entities. Diverse biological actions of many heterocyclic compounds are seen with five-membered rings, a significant class of five-membered heterocyclic compounds is the thiazole which is very prominent with wide variety of pharmacological effects due to the presence of numerous reaction pathways. Several pharmacologically effective compounds have thethiazole, heterocyclic nucleus including dasatinib, dabrafenib, bleomycin, epothiolone-B (anticancer agents) (Shobhit Srivastava *et al.,* 2022) sulfathiazole (antibacterial agents), ritonavir (antiviral agent), abafungin, ravuconazole (antifungal agent), nitazoxanide (antiprotozoal agent), and pramipexole (antidepressant agents), chlormethiazole/clomethiazole (sedative) and many others (Figure 1). Over the years, researchers have used molecular hybrid-based techniques to identify several intriguing chemical architectures incorporating two or more biologically active pharmacophores. These hybrid compounds often have multiple mechanisms of action, which can reduce unwanted effects, improve efficacy, overcome drug resistance, and augment pharmacodynamics with pharmacokinetic features. Hence, the study has a focus on developments in the creation of chalcone-based thiazole hybrids (Figure 3) with a variety of biological activities(Kumawat Kumar Mukesh *et al.,* 2022).

A chalcone is a simple chemical scaffold which is considered to be precursors of flavonoids and isoflavonoids and has wide distribution in the plant kingdom. Chalcones can be converted to the corresponding (2S)-flavanones in a stereospecific reaction catalyzed by the enzyme chalcone isomerase, this is reasonwhy chalcones and flavones has close structural and biogenetic relationship between them (Shaik KhadarYazdan *et al.,* 2018). “Chalcones” is derived from the greek word “chalcos”, meaning “bronze” which results from the colors of most natural chalcones. Chalcones have common chemical scaffold diarylpropenones (diaryl vinyl ketones) shown in (Figure 2) also called as chalconoid. The trans isomer is thermodynamically more stable than the cis isomer (Zhuang *et al.,* 2015). Chalcones are a type of chemical compounds with two aryl rings connected by a three-carbon bond, or ketovinyl group. The numerous pharmacological activities that have been identified in chalcones have been detailed by a number of authors (Salehi *et al.,* 2020). The nature of the aryl rings determines the level or intensity of the activity of chalcones, which is predominantly caused by the ketovinyl chain (Singh *et al.,*2014). The fundamental chalcone core’s phenyl ring was substituted by medicinal chemists with a number of aryl or heteroaryl rings. Heteroaryl rings were found to have greater bioactivity than negligible phenyl or substituted phenyl rings (Jaiswal *et al.,* 2018). This higher activity may be the result of the heteroaryl scaffolds superior biological properties, such as their high pharmacokinetics, metabolic stability, and effective interaction with the target receptors (Ammaji *et al.,* 2022). Several pure chalcones has been approved for clinical use or tested in humans. Metochalcone marketed as a cholerectic drug and sofalcone as a antiulcer, mucoprotective drug (Figure 2). Chalcone bridge is a crucial chemical synthon for creating various heterocyclic templates with a variety of beneficial biological and therapeutic effects. Chalcones

Corresponding author: Dr. M. Vijey Aanandhi
Professor and Head, Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science, Technology, and Advanced Studies (VISTAS), Pallavaram, Chennai-600117, Tamil Nadu, India.
E-mail: hodpchemistry@velsuniv.ac.in
Tel.: +91-9840959519

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not only make great synthetic manipulation scaffolds, but they also have a variety of biological functions. According to the literature, chalcones have a wide range of biological potential, including cytotoxic, anticancer, antihelmentic, antiulcer (Dandu Chaithra *et al.,* 2022), antioxidant (Sevgi Gezici *et al.,*2020) anti-inflammatory (Falguni Modi *et al.,*2019), analgesic, mono amino oxidase inhibition, antidiabetic (Yamina Bouatrous *et al.,* 2019, Amisha Sharma *et al.,* 2021) antiangiogenic, and anti-leishmanial activities (Ni *et al.,* 2014).

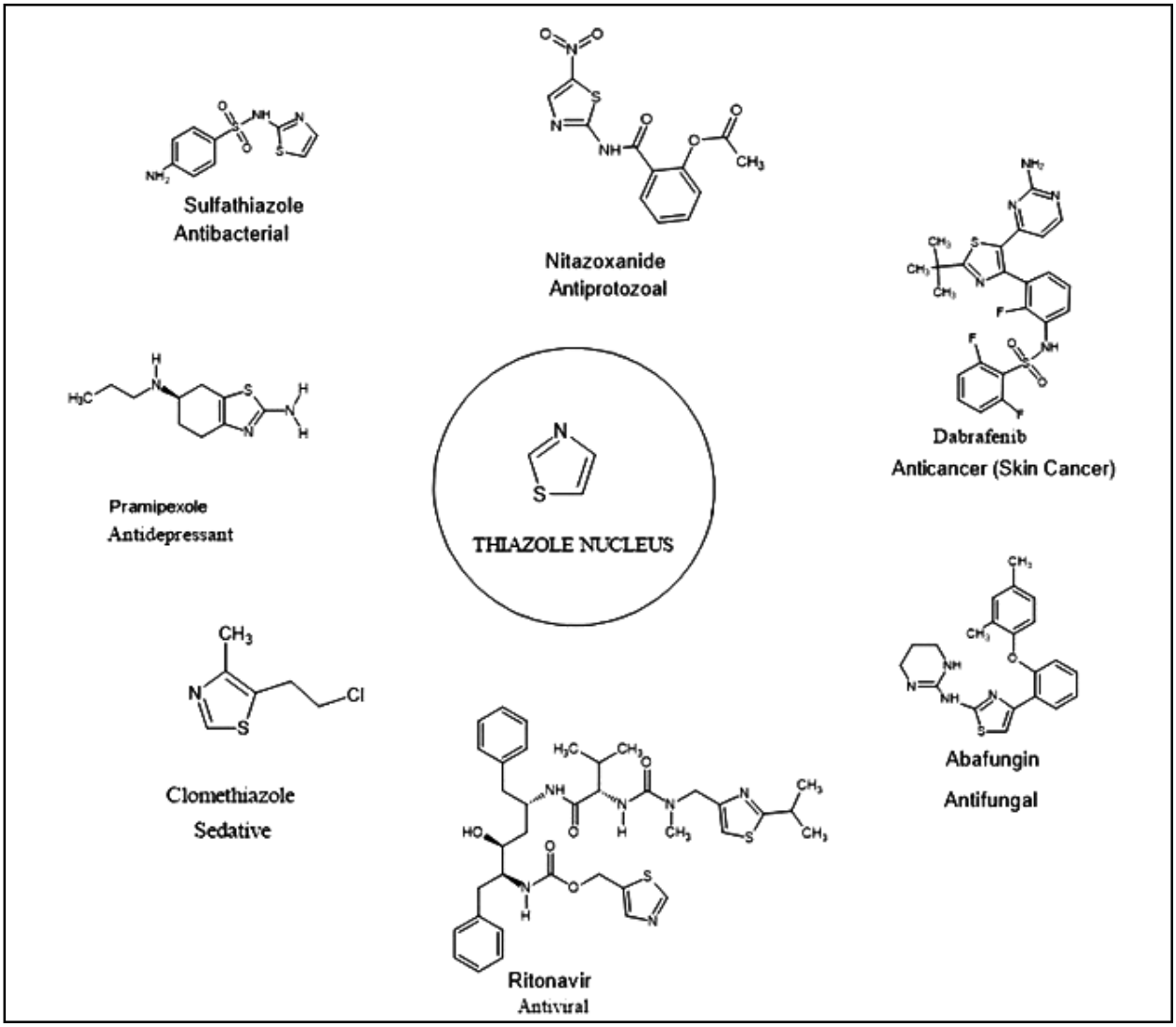


Figure 1: Clinically approved thiazole containing drugs.

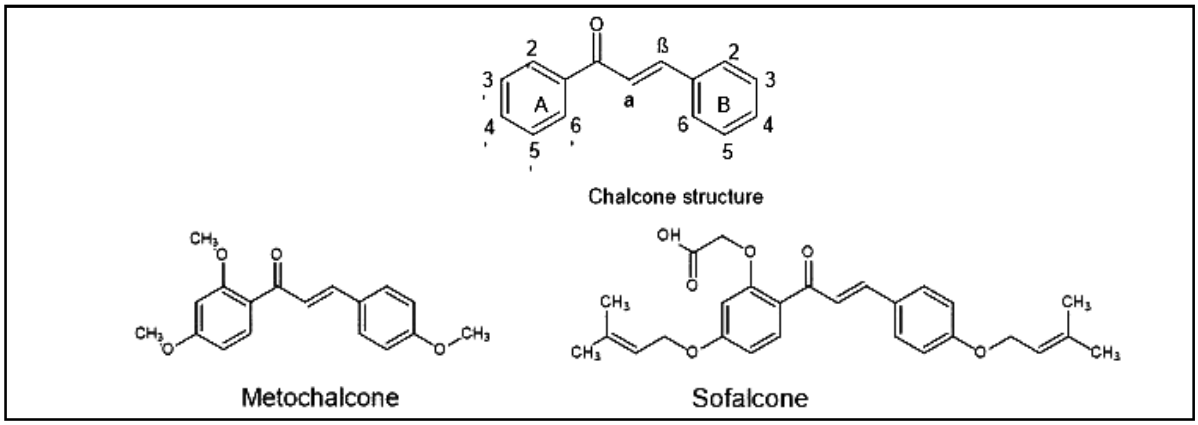


Figure 2: Chalcone structure and clinically approved chalcone containing drugs.

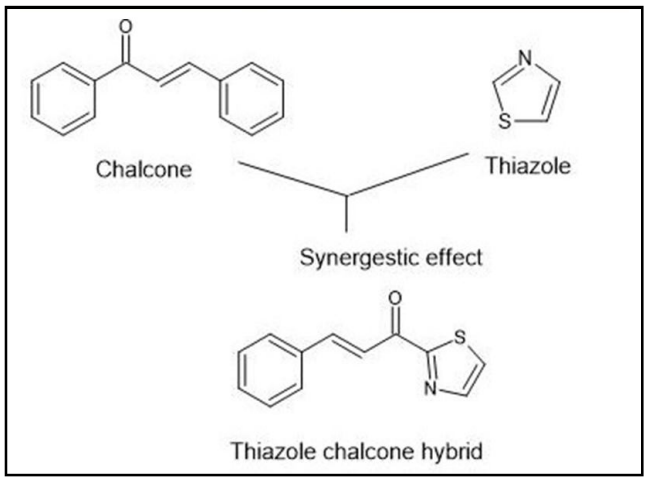


Figure 3: Thiazole chalcone containing hybrids.

2. Synthesis of chalcones

The Claisen-Schmidt condensation, one of the most traditional reactions in organic chemistry, is the most effective way to make chalcones. Strong bases or acids are indeed the catalysts. The chalcone is produced from the aldol product in base catalysis *via* dehydration in an enolate mechanism, whereas it is produced in acid catalysis *via* an enol mechanism (Nielsen *et al.,* 2011). The key drawback of this reaction is its slow rate of reaction; it often form complex combination structures are formed as byproducts. Yet, this reaction has been used in the majority of papers due to the simplicity of the experiment and the highly efficient production of the carbon-carbon double bond with little restriction to the complexity of the molecules.

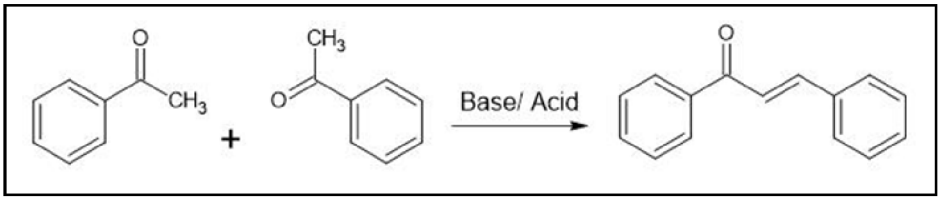


Figure 4: Claisen-Schmidt condensation reaction of chalcone.

The traditional Claisen-Schmidt condensation process has occasionally been carried out with minor catalyst or solvent system modifications. For simple water removal, alkaline earth metal hydroxides of calcium, barium, or strontium can be used to create chalcones. Lithium bis (trimethylsilyl) amide (LiHDMS), a base that has been utilised in the past to catalyse the condensation, has also been employed to produce chalcones with yields that are less than 50% (Patel *et al.,* 2012). For the Claisen-Schmidt condensation process, another incredibly effective basic catalyst is the $NaNO_3$ or $LiNO_3$/natural phosphate/methanol combination.

Other well-known reactions, such as crosscoupling (such as Suzuki, Heck, Julia-Kocienski, and Wittig reactions), Friedel-Crafts acylation, photoFries rearrangement, and one-pot synthesis from alcohols, have been investigated for the synthesis of chalcones because the Claisen-Schmidt condensation process occasionally results in a complex mixture that is challenging to purify for the desired chalcone compound.

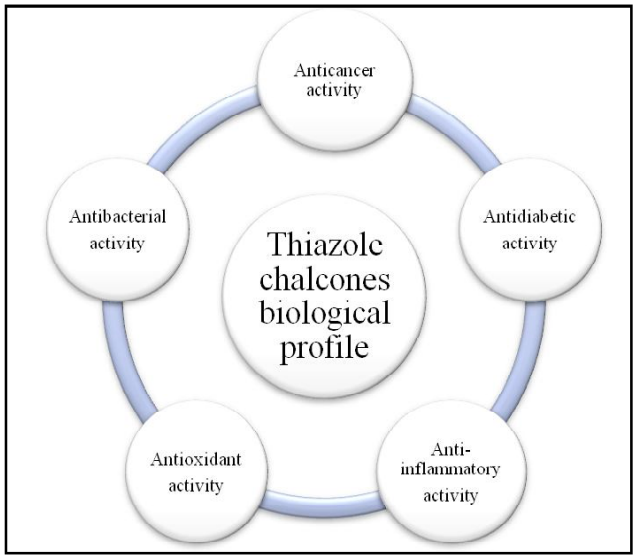
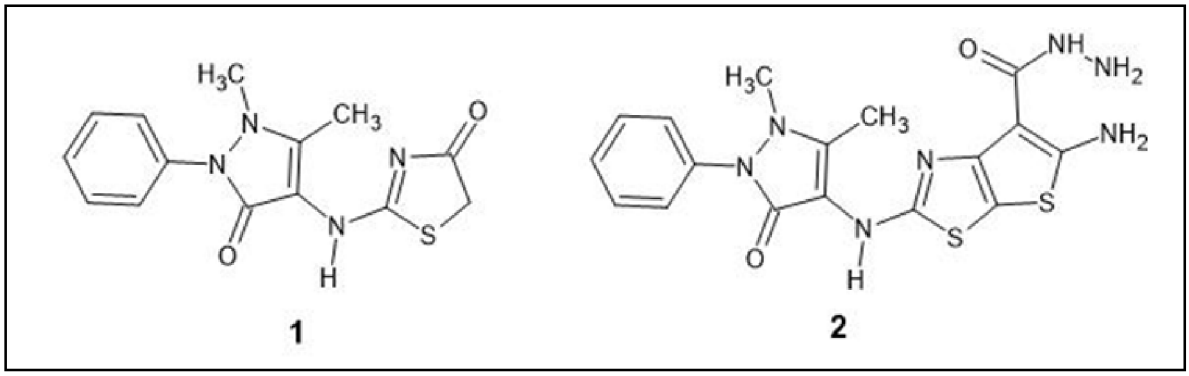


Figure 5: Biological characterization of thiazolechalcones.

3. Pharmacological properties of thiazole nucleus

3.1 Anticancer activity

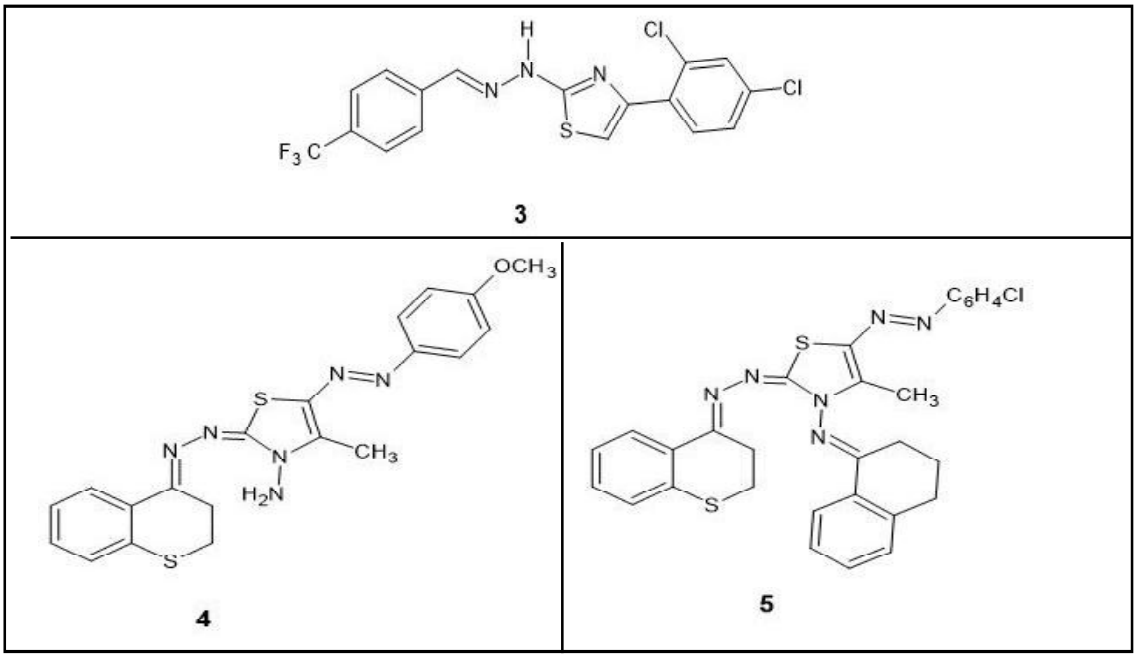
Othman *et al.* (2022) considered pyrazolinone-thiazolinone as a crucial precursor, designed and synthesised two sets of derivatives (3a-d) and (5a-d) bearing a pyrazoline-3-one ring conjugated either with a thieno [3,2-d] thiazole or with a dihydrothiazolo [4,5-d] thiazole scaffold *via* an NH linker. Two cancer cell lines (MCF-7 and HepG-2) were used to test the *in vitro* anticancer activity of all freshly produced drugs. Further testing of the most active cytotoxic candidates safety profiles was done as multitargeting kinase inhibitors on normal human cell line WI-38. Molecular docking studies were performed by selecting co-crystallized structures of EGFR, VEGFR-2 and BRAFV600E kinases with their ligands erlotinib, sorafenib and SB-590885 having (PDB codes: 1M17, 4ASD and 2FB8, respectively, and then followed by docking of the derivatives within the ATP-binding sites after elimination of the co-crystallized ligands Compound 1 and 2 shows promising results.



De Santana *et al.* (2018) synthesised 22 new substnaces containing three thiosemicarbazones and nineteen thiazoles derivatives that insert a 4- (trifluoromethyl)-benzylidene moiety. Eight compounds were shown to be promising in at least three tumor cell lines; NCI-H292, HEp-2, and HT-29 done by MTT assay.The compound **3** was considered the most promising among the samples tested and its influence on cell cycle, DNA fragmentation and mitochondrial depolarization was evaluated.

3.2 Antimicrobial activity

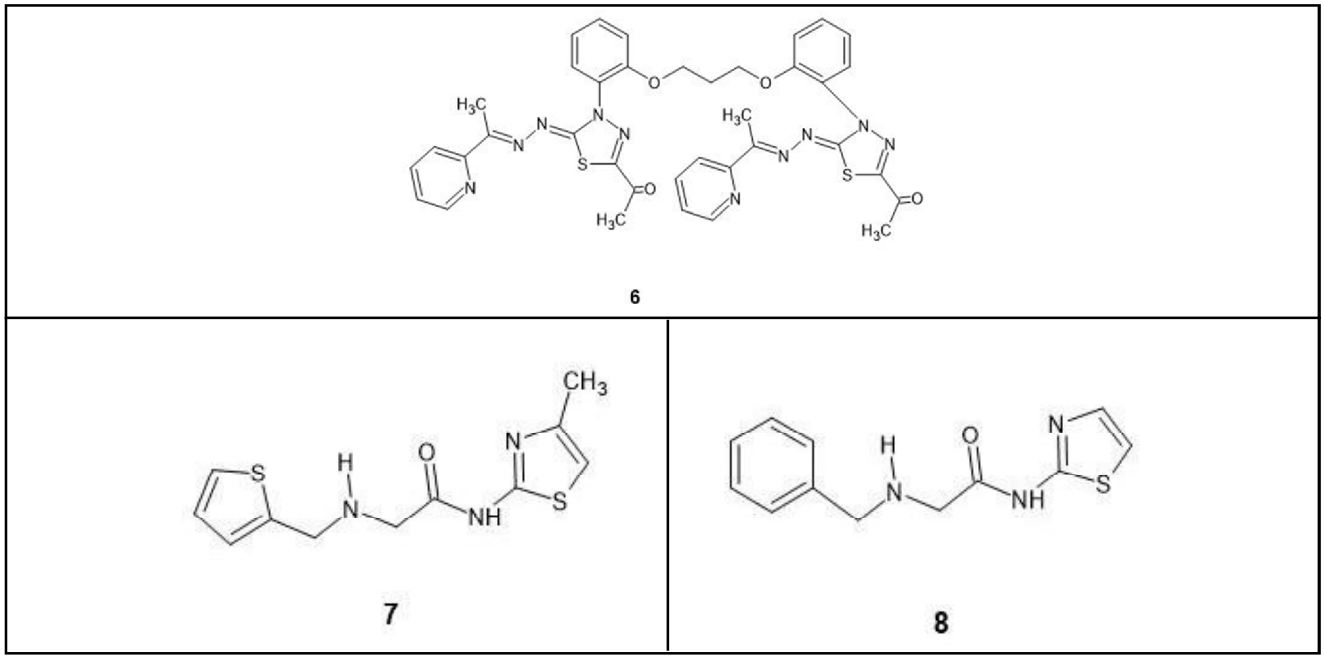
Farghaly *et al.*(2017) synthesised novel thiochromane derivatives incorporating 1,3-thiazole moiety by reacting 4-thiochromane thiocarbohydrazone with a series of hydrazonoyl halides in dioxane in the presence of triethylamine, produced 6a-e, 10a-3 , 13 a-c and 14 series. The antimicrobial activity was tested between both gram +ve and gram-vebatceria. Among all compounds, 4 and 5 are more potent toward some used microorganisms than the applied standard fungicide and bactericide. Molecular docking study confirmed that the binding affinity of these compounds with topoisomerase II (PDB id:2XCT) was found to be satisfactory with values-28.50 and – 25.93 kcal/mol.



Huda Mahmoud *et al.(*2020) has synthesised many bis-1,3,4-thiadiazoles 7, 10a,b, 13a-c and bis-thiazoles 16a-d, 19a-d were synthesized from reaction of bis (hydrazonoyl) chloride with a series of methyl carbodithioate and thiosemicarbazone derivatives. The *in vitro* antimicrobial activity of the prepared compounds were performed against bacterial and fungal strains, compound **6** revealed higher activity against (*Aspergillus flavus)* and showed equal activity against *(Candida albicans)* compared with ketoconazole. Molecular docking done by MOE 2014.010 software against secreted aspartic proteinase PDB ID (1EAG), enoyl-ACP reductase enzyme PDB ID (1LXC) has shown good binding energy values.

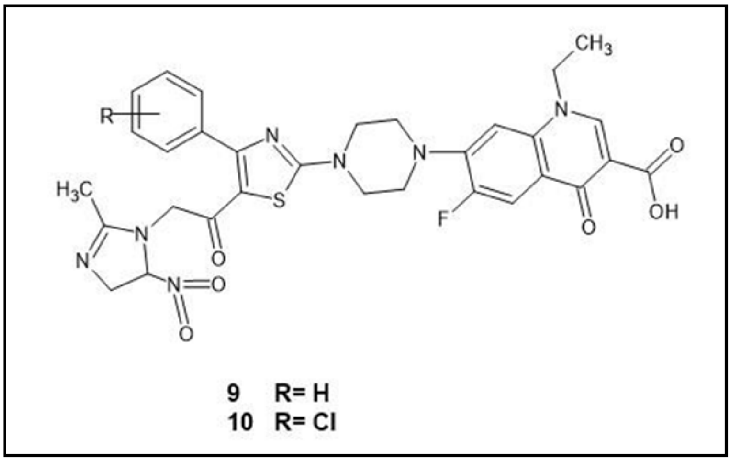
3.3 Antidiabetic activity

Abhishek Kumar *et al.* (2021) developed a series of sixteen different thiazole-containing derivatives as dipeptidyl peptidase IV (DPP-IV) inhibitors. The study of all thiazole derivatives was done for their blood glucose level decreasing activity through a rat oral glucose tolerance test (OGTT). The results of this study showed that two compounds **7** and **8** displayed good hypoglycemic activity to decrease the blood glucose level at % inhibitory rate 24.9 and 19.2 (at 100 mg/kg dose), respectively, and were equally potent to gliclazide; this signifies the importance of these derivatives as a promising lead for the treatment of type II diabetes (DM).



3.4 Anti-inflammatory activity

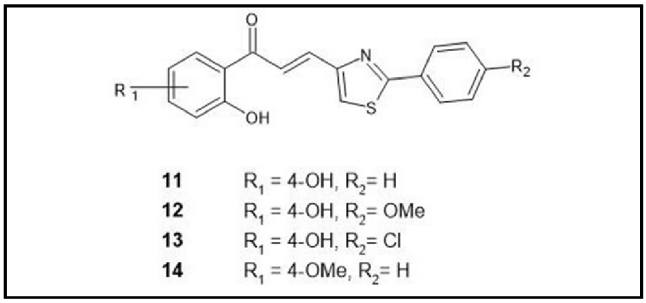
In a another study, Aejaz Ahmed *et al.* (2020) reported a series of novel 2, 3, 5-tri-substituted thiazole derivatives and diclofenac sodium and ibuprofen were used as reference standards, and all the synthesised analogues were evaluated *in vitro* and *in vivo* anti-inflammatory effects using the human red blood cell (HRBC) membrane stabilisation method and a carrageenan-induced rat paw edema. In the inflamed paw model, compounds **9** and **10** elicited the greatest anti-inflammatory activity, offering 59% and 61% protection at 20 mg/kg, respectively, demonstrating that both compounds are potential monotherapy candidates for the treatment of bacterial infections and chronicinflammatory diseases.



4. Thiazole chalcone hybrid pharmacological activites

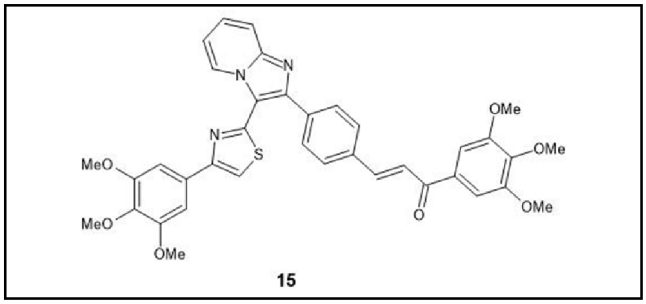
4.1. Anticancer activity

Coman *et al.* (2018) designed and developed thiazole-containing chalcone hybrid derivatives shown significant activity against a panel of nine cancer cell lines, including drug-sensitive (CCRF-CEM, MDA-MB-231, HCT116($p53^{+/+}$), U87MG, and HepG2) and drug-resistant (CEM/ADR 5000, MDA-MB-231/BCRP, and HCT116 ($p53^{-/-}$), and U87MG/EGFR) phenotypes. All compounds were possessing (IC_{50}: 0.02 2.15 µM) and more effective than doxorubicin (IC_{50}: 66.83 M) but, against CEM/ADR 5000 cells (IC_{50}: 2.72 - 41.04 M) and none of them were better than doxorubicin (IC_{50}: 0.02 - 2.15 M) against the remaining eight cancer cell lines. The SAR showed that adding hydroxyl, a hydrogen-bond donor, to the R_1 position was beneficial to the activity, but neither electron-donating nor electron-withdrawing groups could be introduced to the R_2 position enhance the endeavour. All nine of the studied cancer cell lines showed cytotoxic effects less than 75 µM for four hybrids synthesised while compound 11, 12,13,14 demonstrated IC_{50} values of less than 10 M against eight cancer cell lines.



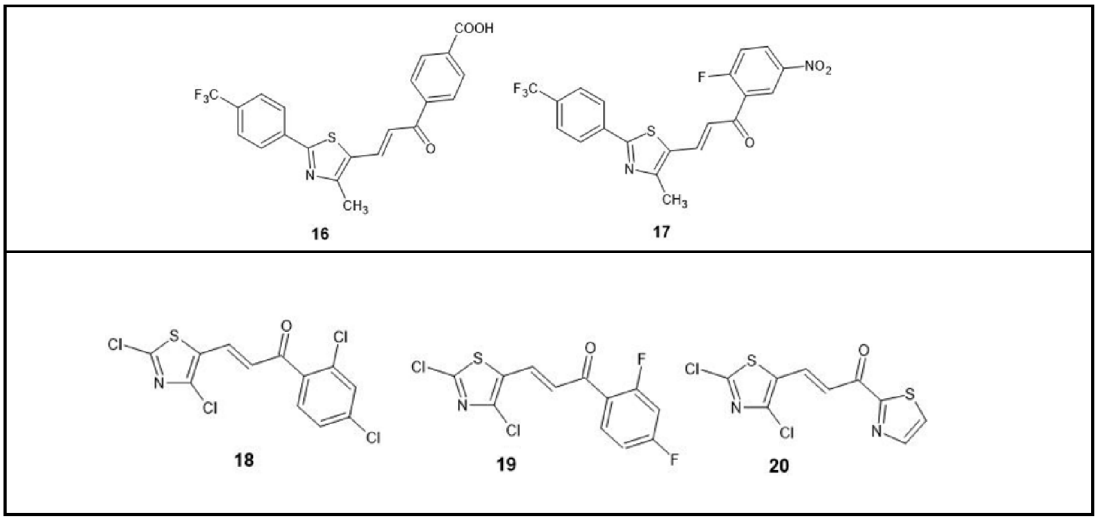
11 R_1 = 4-OH, R_2= H
12 R_1 = 4-OH, R_2= OMe
13 R_1 = 4-OH, R_2= Cl
14 R_1 = 4-OMe, R_2= H

A novel collection of chalcone-linked diazole-imidazopyridine (12a-j) derivatives were synthesized by Suma *et al.* (2020) and researchers examined the anticancer effects by using MTT assay method on four human cancer cell lines: MCF-7 (breast carcinoma), A549 (lung carcinoma), DU-145 (prostate carcinoma), and MDA MB-231 (breast carcinoma) with etoposide as the positive control, which has 3,5-dimethoxy-4-hydroxy phenyl as active scaffold. By changing the substituents on the phenyl ring, researcher created several variants for the study. The compound **15** with the electron-rich (3,4,5-trimethoxy) group on the phenyl ring had the highest anticancer activity out of all the compounds examined, with IC_{50} values for MCF-7 of 0.18 ± 0.094 M, A549 of 0.66 ± 0.071 M, DU-145 of 1.03 ± 0.45 M, and MDA MB-231 of 0.065 ± 0.0082 M. Substituents with strong withdrawing group $–NO_2$ and weak electron-with drawing groups like bromo and chloro present at positions 3, 5, and on the phenyl ring, has very little anticancer effect. As a result, the electron-donating group is replaced with electron-withdrawing groups in this sequence of derivatives, diminishes the cytotoxicity impact.



15

By employing a variety of substituted acetophenones, Chekrapani Kesari *et al.* (2021) synthesized 4-Methyl-2-(4-(trifluoromethyl) phenyl) thiazole-5-carbaldehyde as a crucial intermediate for the synthesis of the novel nine thiazole derivatives. By employing selected guanidines to mask the enone system eight pyrimidine derivatives SARs were further investigated. HT29, HCT116, and LoVo are three genetically distinct colo rectal cancer cell lines that were used to test the antiproliferative efficacy of the seventeen new thiazole derivatives. and their IC_{50} ranges between 12.5 to 50 mM. In all three cell lines, compounds **16** and **17**were shown to be more powerful than the reference chemical cisplatin, demonstrating their strong efficacy in cell lines with various genetic backgrounds. Most active compound **16** has CF_3 substituent in the A ring which is crucial for increased antiproliferative activity. In the HT-29 cell, several pyrimidine derivatives continue to have activity that is comparable to cisplatinwith IC_{50} values of 25 mM, but none of these substances showed enhanced antiproliferative action than thiazole derivatives. Hence, the enone linker was more potent than changing it intopyrimidine derivatives, as a result enonelinkeris essential for producing additional active molecules in this family.



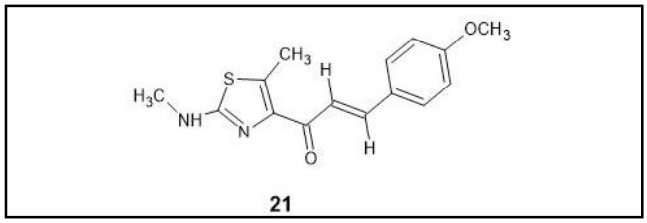
16 **17**

18 **19** **20**

4.2 Antitubercular and anticancer activity

Ashok Babu Kasetti *et al.* (2021) developed a novel series of Thiazole –chalcone hybrids (1-20) and evaluated for antitubercular and antiproliferative activities using MABA and MTT assays. Among the twenty compounds, two chalcones compound **18** and **19** bearing halogen atoms in both ortho and para positions, *i.e.,* 2,4-difluorophenyl (MIC 2.43 ± 1 µM) and 2,4- dichlorophenyl (MIC 4.41 ± 2 µM) showed antitubercular potencies 10.42 and 5.74 times more than the standard pyrazinamide (MIC 25.34 ± 2 µM). Compound **20** containing heteroaryl 2-thiazolyl moiety exhibited promising antiproliferative activity against the prostate cancer cell line (DU-145), higher than the standard methotrexate (IC_{50}11 ± 1 µM) with an IC_{50} value of 6.86 ± 1 µM. but against normal human liver cell lines (L02) comparatively less selective. Molecular docking analysis displays strong binding affinity (ranges from –5.7 to –7.3, against the potential antitubercular and anticancer targets isocitratelyase (PDB id: 1F8M) and topoisomerase IIa ATPase, respectively (PDB id: 1ZXM).

Thoraya Farghaly *et al.* (2020) synthesized a series of thiazolyl chalcone derivatives *via* aldol condensation of the 4-acetyl thiazole derivative with various types of aromatic aldehydes and evaluated the *in vitro* antitumor activity by MTT assay using reference standard as doxorubicin. All produced chalcones demonstrated strong cytotoxicity against the three tested cell lines. Among all the most active substance, **21** carrying a 4-methoxyphenyl moiety, demonstrated twice the activity of doxorubicin against HepG-2, A549, and MCF-7 (IC_{50} = 1.56, 1.39, and 1.97 M). Along with that *in silico* molecular docking studies were conducted on CDK1 enzyme with PDB ID: 4Y72, a very similar binding mode to that reported in with RMSD = 0.847 and docking score = 7.429 kcal/mol in comparison with the LZ9 a strong CDK1 enzyme ATP-competitive inhibitor.



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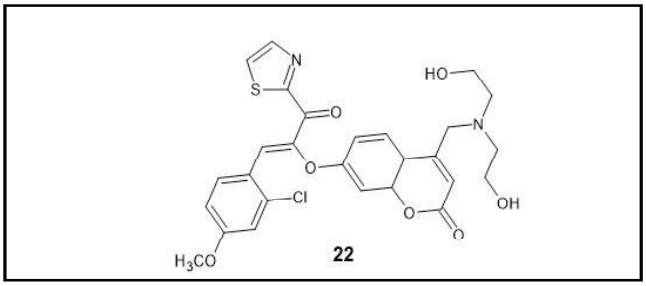
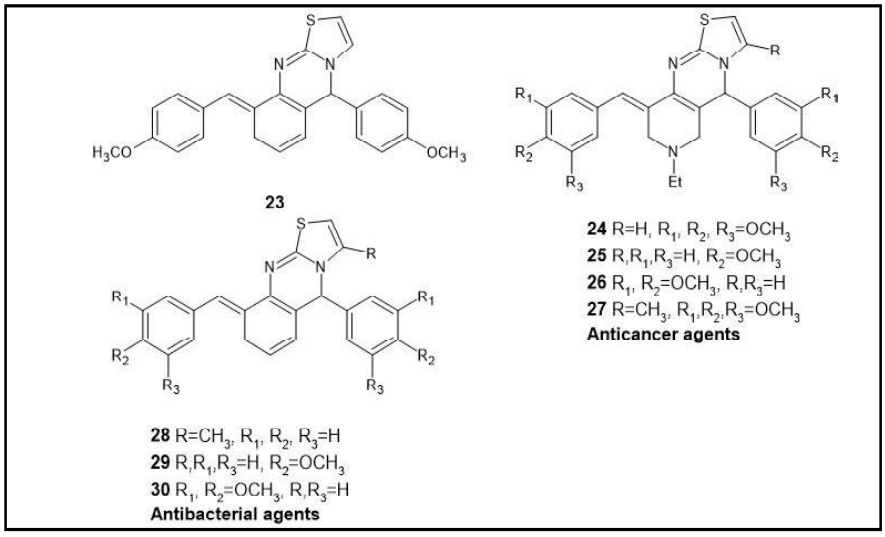
4.3 Antibacterial activity

A novel structural candidate of chalcone-conjugated, coumarinthiazole hybrids with exceptional bacteriostatic potential is designed and created by Yuanyuan Hu *et al.* (2021). The methoxybenzene-modified coumarinthiazole hybrid **22** demonstrated good selectivity and considerable inhibitory efficacy against MRSA (MIC 14 0.004 mM), which was six times better than that of norfloxacin (MIC 1/4 0.025 mM). Molecular docking also states highly active molecule **22** may attach to DNA gyrase by stable hydrogen bonds. Also, preliminary mechanistic studies revealed that hybrid **22** might damage MRSA's bacterial membrane and introduce itself into the organism's DNA to prevent replication, potentially developing into an antibacterial repressor for MRSA.

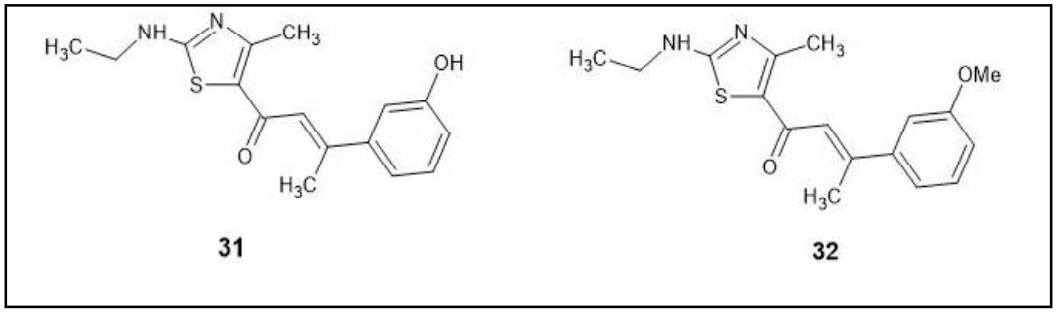


22

Antitumor derivatives of thiazole-based chalcones, such as thiazolo [2,3-b] quinazoline and pyrido [4,3-d] thiazolo [3,2-a] pyrimidine analogues, have been developed by Waad Alrohilya *et al.* (2019). Compound **23** demonstrated the strongest antibacterial action on, both against gram +ve and gram -ve microorganisms. Synthesized compounds were subjected to molecular docking tests against the DHFR enzyme (PDB id: 1DLS). The majority of active antibacterial compounds, **24, 25, and 26**, as well as active anticancer prospects **27, 28, 29, and 30**, bind to DHFR with almost identical amino acid residue similarly as seen in methotrexate. Also, ADMET studies also support our theory that these compounds might inhibit DHFR to act as anticancer or antibacterial agents, making thiazole-based chalcones effective leads for developing new antibacterial medication candidates in the future.

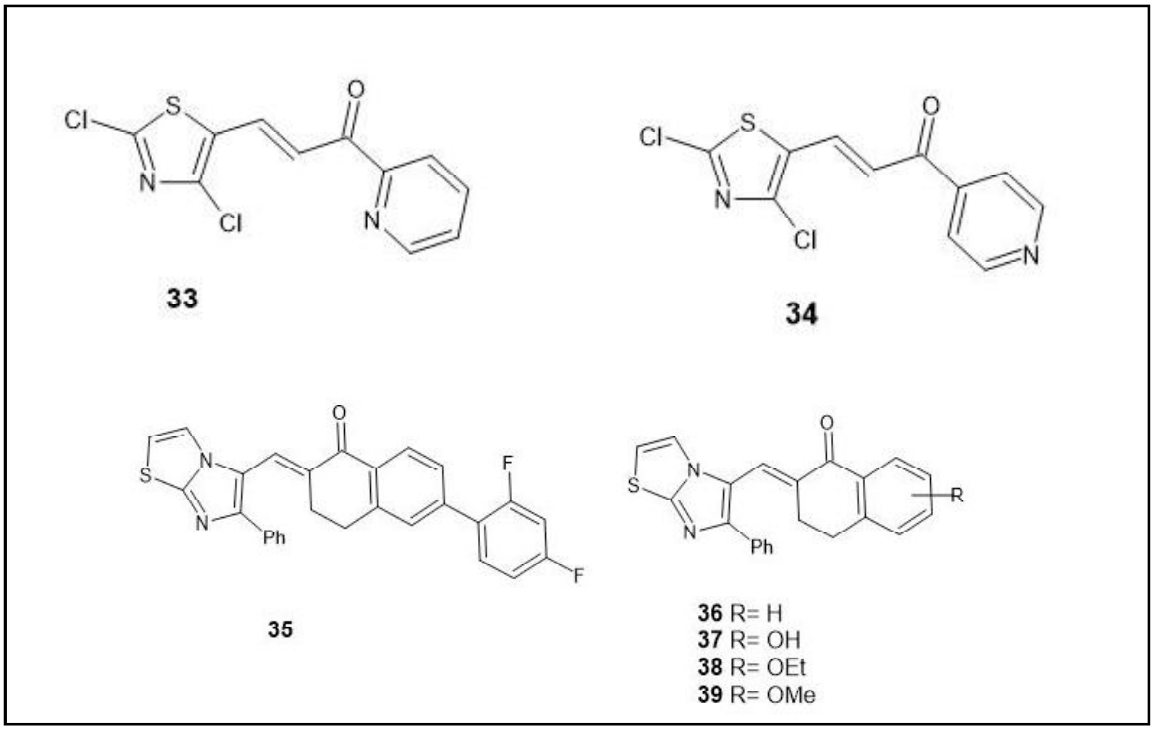


Christophe Tratrat *et al.*(2019) designed twenty eight novel thiazole-based chalcones. All the twenty eight compounds exhibited antibacterial activity against the three resistant strains, MRSA, *P. aeruginosa* and *E.coli.* with MIC and in the range of 0.65-11.00 ìmol× 10^{-2}/ml. Compounds **31, 32** appeared to be the most active against *P. aeruginosa,* being much more active (58-70 and 56 to 68 fold) than streptomycin and ampicillin. All the twenty eight compounds showed antifungal activities with MIC in the range of 0.17-53.9 µmol × 10^{-2}/ml. The best antifungal activity was shown by compound **29** (MIC of 0.69-1.94 µmol × 10^{-2}/ml. The SAR found that replacement of OH and Methoxy groups at 3rd position of benzene and ethyl substituent of the amino group is increases activity. Docking results for antibacterial activity were also promising with *E.coli* DNA GyrB (1KZN), MurA (3KR6), MurB (2Q5), PBP1a (3VMA), PBP3 (4BJP).



4.4 Antioxidant activity

Kasetti *et al.* (2021) assessed antioxidant potential of 20 thiazole-bearing chalcone derivatives containing different kinds of substituted aryl and heteroaryl rings. Heteroaryl aldehyde, *i.e.,* 2,4-dichloro-5-carboxaldehyde was dissolved in glacial acetic acid and hydrochloric acid and to this mixture aryl/heteroaryl ketone were added to produce of 20 thiazole-bearing chalcone derivatives. *In vitro* antioxidant activity is performed using DPPH method with gallic acid as reference standard, compounds **33 and 34** with heteroaryl 2 and 4-pyridinyl rings had IC_{50} values of 4 g/ml and 3 g/ml, respectively, and were more active than the standard gallic acid (IC_{50} = 5 g/ml).

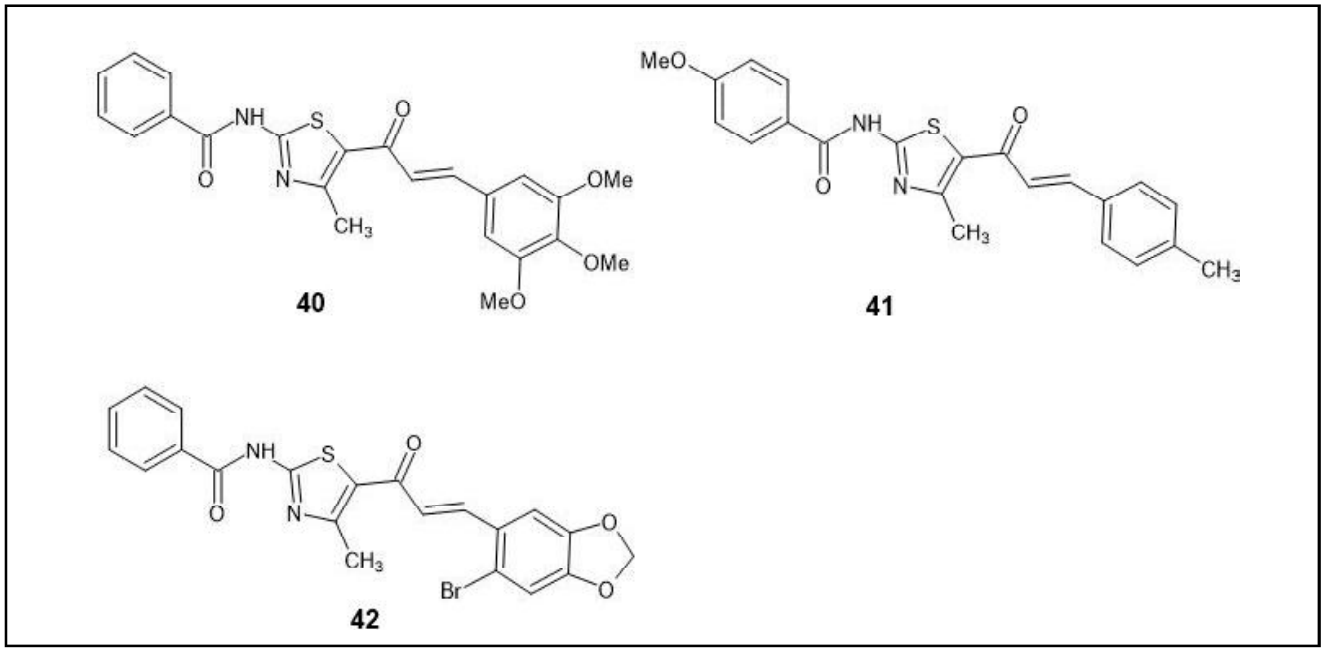


Sonawane *et al.*(2019) synthesized a series of condensed Imidazo [2, 1-b] [1,3] thiazole chalcones by Claisen-Schmidt condensation reaction. Imidazo thiazole-3-carboxaldehydes and different acetyl ketones in PEG-400, condence to produce imidazothiazole-based chalcones. *In vitro* screening for antioxidant activity was performed by DPPH and SOD technique. Researchers were able to increase antioxidant activity of compounds with hydroxyl, fluoro, methoxy, ethoxy, and fluoro substituents as well as benzimidazole and a ferrocenyl moiety in chalcone structure. Notably, compounds like **36, 37, 38** and **39** exhibit a moderate proportion of antioxidant

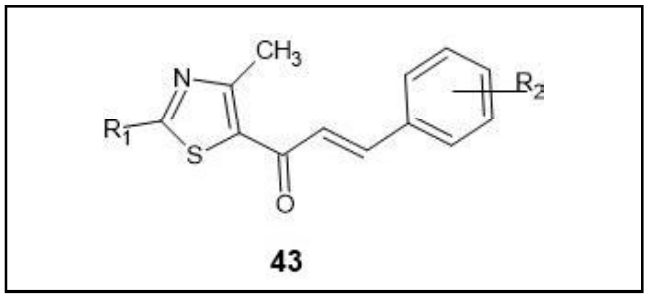
activity inhibition, while **35** exhibits the highest percentage of inhibition, with ascorbic acid as standard having values of 44.18 and 74.07 mM for DPPH and SOD, respectively. Most of the compounds found to have powerful SOD scavenging activity, and this property may be the reason for the imidazothiazole chalcones as effective anti-inflammatory properties. According to the findings, the modified chalcones have considerable biological assessment as antioxidant agents. More over research into the structural configurations on the B ring of imidazothiazole chalcones produce new entities with promising antioxidant activity.

4.5. Anti-inflammatory activity

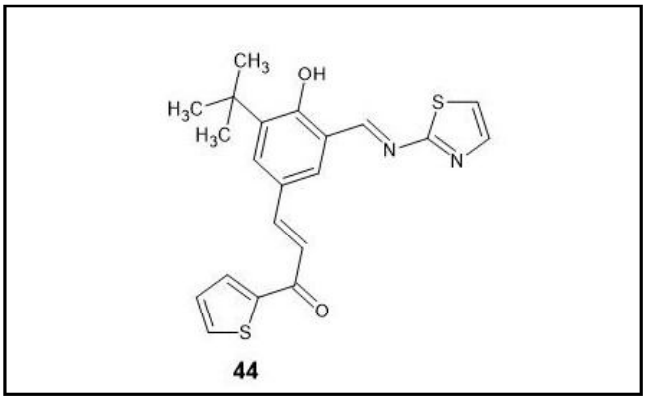
Shweta Sinha *et al.* (2019) designed and developed novel chalcone-thiazole hybrid molecules. Using hybrid pharmacophore approach to obtain a new class of 5-LOX inhibitors. *In vitro* 5-LOX Inhibition reveals that three compounds were best in the series, Compound **40** trimethoxy substituted compound, is a highly active inhibitor (IC_{50} of 0.07 ± 0.02 µM) and compound **41**electron donating substituents, -OCH_3 (R1) and –CH_3 (R_3) contributed to a synergistic effect exhibiting an IC_{50} of 0.08 ± 0.05 µM. Compound **42** methylenedioxybromophenyl group at R_2which resulted in significantly promising inhibitory activity (IC_{50} of 0.12 ± 0.04). SAR indicated that the presence of methoxy/methyl either in the vicinity of chalcone or both thiazole and chalcone contributed to the synergistic inhibitory effect.



Christophe Tratrat *et al.*(2020)synthesized a series of compounds with nucleus **43** by Claisen-Schmidt condensation of 1-(4-methyl-2-alkylamino) thiazol-5-yl) ethanone with the appropriate aromatic aldehyde. *In vivo* and *in vitro* anti-inflammatory activity evaluation was done by carrageenan mouse paw edema method and soybean lipoxygenase inhibition study. Eight out of thirteen tested chalcones showed anti-inflammatory activity in a range of 51- 55%. The molecular docking study on lipoxygenase enzyme shows satisfactory binding and proposed a scope that these compounds can be used for further modifications in order to develop more active and safe agents.



4.6 Antifilarial activity



In the presence of a catalytic quantity of conc HCl, the aromatic dicarbaldehydes and different substituted acetophenones underwent condensation to produce regioselective (3a-n) derivatives by Koneni Sashidhara *et al.* (2014). The final eight compounds were subsequently produced by condensing these chalcones with 2-aminothiazoles (4a-n). These hybrids' antifilarial abilities were tested

on adult *Brugia malayi* worms as well as Microfilariae. Only compound **44**, were found to be promising in *in vitro* studies by MTT assay out of all the produced compounds. *In vivo* testing is carried out using the jird model (jirds carrying adult *B. malayi* transplanted intraperitoneally and the chemical that is positive in this model is evaluated in the second rodent model, *M. coucha* with L3 induced *B. malayi* infection, at a dose of 50/100 mg/kg for 5 days by s.c. route. In jirds and *M. coucha* models, compound **44** had a 100% embryostatic effect and a 49% macrofilaricidal effect which creates a new structural clue for the development of novel antifilarial lead compounds by this study.

5. Conclusion

Hybrid molecules are intriguing models for medical chemists looking to create brand-new, powerful medications. Natural compounds with high bioactive potency are considered asoutstanding building blocks to create a hybrid molecular scaffold for therapeutic medicines. As a result, the impressive lead that was created by combining two distinct natural compounds with different bioactivities thiazole and chalcone is one that many medicinal chemists are interested in. The current review updates our understanding of natural and synthetic thiazole-chalcone hybrids, with a focus on their potential as anticancer, antimicrobial, anti-malarial, antidiabetic, anti-inflammatory and antioxidant agents. The most promising agentsthiazole-chalcone hybrids along with their synthesis, structure-activity relationships (SAR) and pharma-cological characteristics, presented in this brief review may help a researcher in medicinal chemistry to select the proper nucleus and functions when creating thiazole-chalcone hybrids that are effective against a variety of disorders.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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