

HETEROCYCLES, Vol. 106, No. 5, 2023, pp. 819 - 839. © 2023 The Japan Institute of Heterocyclic Chemistry
Received, 24th January, 2023, Accepted, 16th March, 2023, Published online, 31st March, 2023
DOI: 10.3987/REV-23-1003

EVALUATION OF 1,3-THIAZOLE DERIVATIVES WITH PHARMACEUTICAL AND CHEMICAL ACTIVITY: A REVIEW

Sheetal Tresa Fernandes, Jyothi Damodara,* and Smitha Maria DSouza

Department of Chemistry, St Joseph Engineering College, Mangaluru, 575028, Karnataka, India.

*Email: jyothik@sjec.ac.in

Abstract – 1,3-Thiazole is one of the most adaptable scaffolds for heterocyclic compounds. In recent years, thiazole has attracted focus in organic and medicinal chemistry due to its improved effectiveness and significant biological activities. Numerous reviews have reported on the synthesis and pharmacological activities of thiazoles. However, synthesis, pharmaceutical, and chemical applications have not been completely reviewed. The present review focuses on recent work on the synthesis, pharmaceutical and chemical applications of substituted thiazoles. This review discusses the most recent advancements in thiazole-based compounds and emphasizes the importance of design, drug discovery, and the use of thiazole in chemical applications. Additionally, this article is aimed to aid researchers in identifying potential future avenues for the creation of more effective thiazoles.

CONTENTS

1. INTRODUCTION
2. RELATED WORK
 - 2.1 Synthesis of Thiazole Derivatives
 - 2.2 Therapeutic Applications of Thiazole Derivatives
 - 2.2.1 Anticancer Study
 - 2.2.2 Antioxidant Study
 - 2.2.3 Antiviral Study
 - 2.2.4 Antitubercular Study
 - 2.2.5 Antimicrobial Study
 - 2.3 Chemical Applications of Thiazole Derivatives
 - 2.3.1 Corrosion Inhibition Study

- 2.3.2 Photovoltaics
- 2.3.3 Bioimaging and Biolabeling Applications
- 2.3.4 Textile Dyes
- 2.3.5 Algicides
- 2.3.6 Supercapacitors
- 2.3.7 Fluorometric and Colorimetric Sensor for Fluoride Ions

3. CONCLUSIONS

4. REFERENCES

1. INTRODUCTION

Thiazole is a five-membered aromatic heterocycle having sulfur and nitrogen atoms at 1 and 3 positions. Thiazole with the molecular formula C_3H_3NS is a pale-yellow liquid.¹ Vitamin B1 thiamine has a thiazole ring as the significant component.² Thiazoles seek special attraction because of their medicinal and chemical applications. The delocalization of pi electrons on the sulfur atom makes the thiazole ring planar and aromatic.³ According to the electron density, electrophilic substitution is prominent at C5, while the nucleophilic substitution is prominent at C2.⁴ This has resulted in the synthesis of numerous compounds containing thiazole core structure having wide applications in the advancement of new therapeutic drugs.⁵ The degree of acidity or basicity depends on the type of substituents at different positions on the thiazole ring.⁶ When an electron-donating group, such as methyl, is positioned at the C-2, C-4, or C-5 regions, there is increase in the nucleophilicity and basicity of a molecule.⁷ C2 being close to the methyl group along with two heteroatoms on either side is observed to have the greatest substituent effect.⁸ Basicity of the molecule decreases when electron-withdrawing nitro group is attached to the thiazole ring.⁹ Thiazole derivatives show various pharmacological applications such as anti-inflammatory¹⁰ e.g.: Meloxicam,¹¹ antifungal¹² e.g.: Abafungin,¹³ anti-microbial¹⁴ e.g.: Sulphathiazole,¹⁵ anti-cancer¹⁶ e.g.: Tiazofurin,¹⁷ anti-convulsant,¹⁸ anti-viral,¹⁹ e.g.: ritonavir,²⁰ anti-aging²¹ e.g.: Alagebrium, anti-diabetic,²² anti-Parkinson's²³ e.g.: Pramipexazole, anti-hypertensive,²⁴ tyrosinase inhibitor,²⁵ antioxidant,²⁶ analgesic,²⁷ and insecticides,²⁸ anti-parasitic agent,²⁹ e.g.: Tiabendazole. The highest corrosion inhibition is exhibited by thiazole compounds with protonated nitrogen atoms in an acidic medium.³⁰ Thiazoles are widely used in the textile sector. Cotton is dyed using thiazole-based dyes, such as Vat Yellow 2. The firefly's distinctive yellow light emission is caused by a thiazole ring that contains firefly luciferin.³¹ Thiazoles are used as azo disperse dyes.³² The thiazole dyes, that are sulfur heterocyclic azo dyes, have brilliant, striking colours that span from yellow, orange, red, and blue to green.³³ The dyed cloth exhibits great sublimation fastness as well as extremely good rubbing, perspiration, and washing fastness.³⁴ Due to the diverse applications of benzothiazole and thiazole compounds these compounds are of great importance

today, hence massive research is being carried out to study their diverse applications in various fields.

Owing to the synthetic flexibility, electrochemical and optical properties of thiazole containing heterocyclic sulfur moieties, these compounds play a vibrant role in photovoltaic devices.³⁵ Corrosion of metals in the acid environment is one of the major drawbacks affecting the World's economy, this can be overcome by using cost-effective corrosion inhibitors. Organic compounds containing sulfur have greater inhibitive potency due to their increased capacity as electron donors and simple polarizability.³⁶ Studies have shown that thiazole is an effective inhibitor for C-steel dissolved in 1 M H₂SO₄.³⁷ Thiazole and benzothiazole show good corrosion inhibition in 15% HCl solution for N80 steel. Currently, cyanobacterial blooms are proving to be a major global issue for aquatic environments, contributing to climate change and water eutrophication. As a result, managing cyanobacterial blooms is the most crucial component of managing water sources. Studies show that thiazole amide analogs have an algicidal activity that is comparable to that of the herbicide Diuron³⁸ and the commercial algicide CuSO₄.

Thiazoles are therapeutically active compounds that can be used for synthesizing various derivatives having diverse pharmacological activities (**Figure 1**) and can be further utilized for their various chemical applications. Several approaches for the synthesis and diverse structure reactions of thiazoles offer massive scope in medicinal chemistry and industrial applications. Based on these applications of thiazole derivatives, an extensive review of these thiazole derivatives has been carried out and presented in the subsequent sections of this study. Many researchers are working on the wide applications of thiazole derivatives in various fields, but there is no consolidation of the knowledge. Therefore, to give a new direction to future researchers and to draw improvements and conclusions from the previous work, this review has been carried out. The present article highlights the latest literature for the synthesis, therapeutical, chemical, and computational study of thiazole compounds along with prominence on recent developments. This paper is organized as follows; the section of related work presents the various synthetic approaches used in the synthesis of thiazole, therapeutic applications of thiazole derivatives, and chemical applications of thiazole derivatives in corrosion inhibition, photovoltaics, textile dyes, algicides, supercapacitors, etc. The next section is the conclusion and analysis of the review paper where the main contribution of the research work has been summarized.

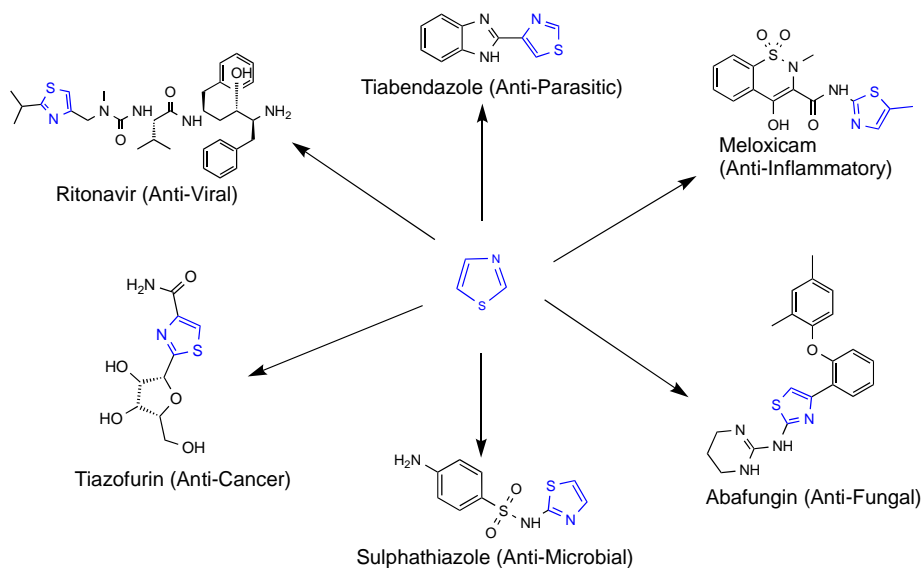
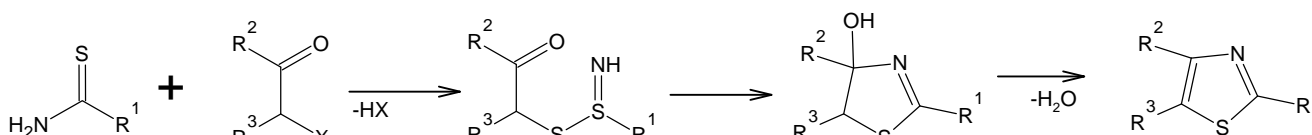


Figure 1. Pharmaceutically active derivatives of thiazole

2. RELATED WORK

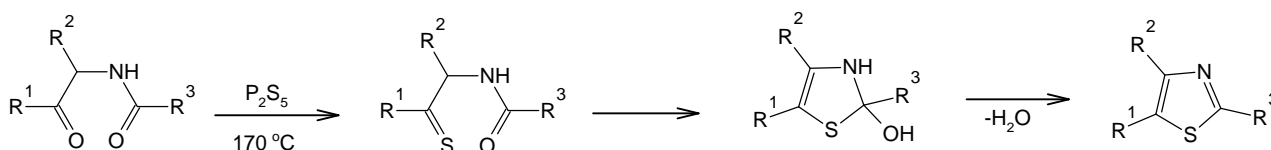
2.1 Synthesis of Thiazole Derivatives

Thiazole derivatives are synthesized by various approaches. Hantzsch synthesis is one of the oldest and most reliable routes to thiazole synthesis. According to this process, condensation of α -haloketones with thioamides, thiourea, thiosemicarbazides, and thiosemicarbazones resulted in production of disubstituted 2-aminothiazole derivatives in higher yields. A wide range of thiazoles can be synthesized through Hantzsch synthesis (**Scheme 1**) with various substituents.³⁹



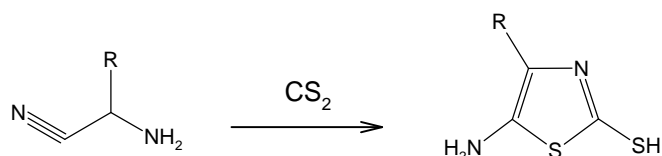
Scheme 1. Hantzsch synthesis

Thiazoles can also be prepared in high yields by another approach Gabriel synthesis (**Scheme 2**), i.e. condensation of amino acetal or α -acylamino ketones or with phosphorus pentasulfide formed 2,5-disubstituted thiazoles.⁴⁰



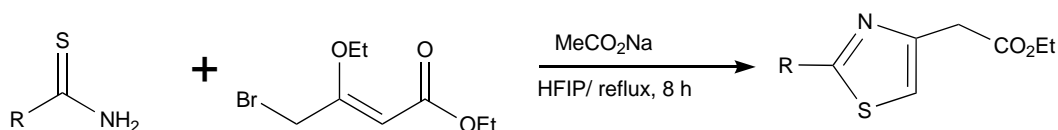
Scheme 2. Gabriel synthesis

Another approach for thiazole synthesis is Cook–Heilbron thiazole synthesis (**Scheme 3**), according to this synthesis 5-aminothiazoles are formed by the chemical reaction of α -aminonitriles with isothiocyanates, carbon disulphide and dithioacids, at room temperature and under aqueous conditions. With different starting materials substituents at the 2nd and 4th positions of the thiazole can be varied.⁴¹



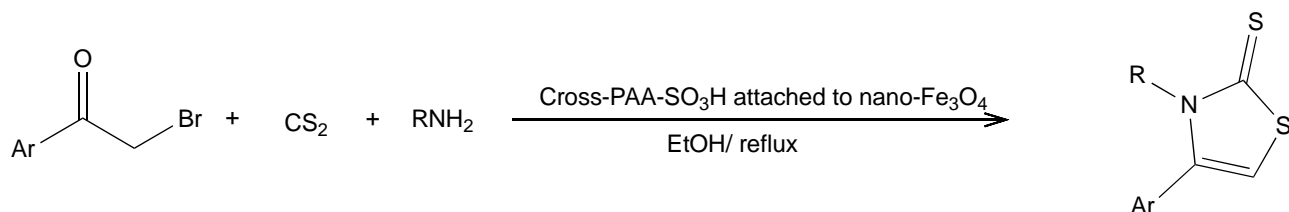
Scheme 3. Cook–Heilbron thiazole synthesis

Alsharif and co-workers⁴² synthesized thiazoles using thiourea derivatives with 4-bromo-3-ethoxycrotonate (**Scheme 4**). When HFIP (hexafluoroisopropanol) was used, the yield obtained was 90%, while the yield was 74% with 2,2,2-trifluoroethanol and 65% with isopropanol as solvents. Fluorinated solvents like HFIP is reported to be more efficient due to its high ionizing power, high hydrogen-bonding donor ability, and the ability to solvate water.



Scheme 4. Synthesis of thiazoles with thiourea and 4-bromo-3-ethoxycrotonate in hexafluoroisopropanol solvent

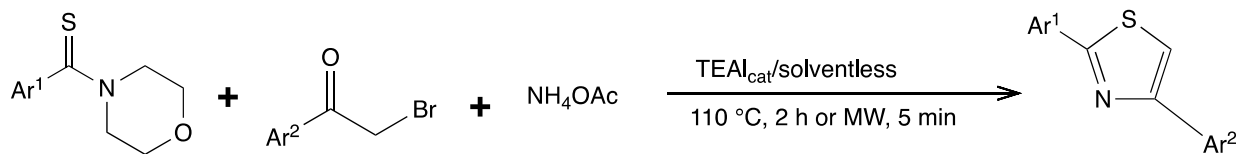
Hossein *et al.*⁴³ designed a cost-effective, one-pot multicomponent synthetic route to produce 1,3-thiazoles (**Scheme 5**). In this study 3-alkyl-4-phenyl-1,3-thiazole-2(3*H*)-thione derivatives were synthesized using primary amine, carbon disulfide, and phenacyl bromide in the presence of catalyst i.e crosslinked sulfonated polyacrylamide (Cross-PAA-SO₃H) attached to nano-Fe₃O₄, under reflux condition in ethanol.



Scheme 5. Synthesis of thiazoles using Cross-PAA-SO₃H attached to nano-Fe₃O₄ as catalyst

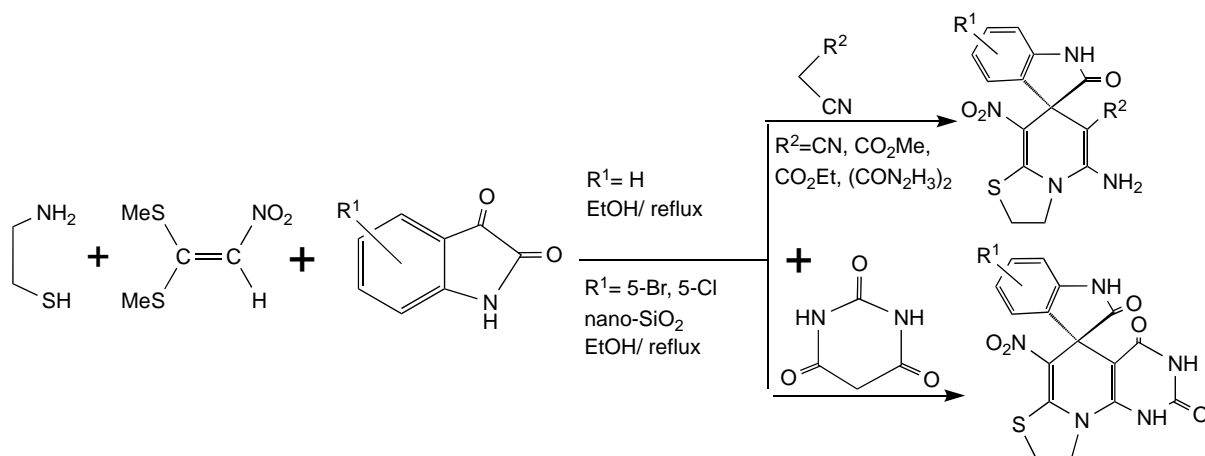
Zali-Boeini *et al.*⁴⁴ developed a one-pot three-component reaction to synthesize thiazole derivatives in the absence of solvents (**Scheme 6**). In this process, the reactants tertiary thioamides, α -haloketones, and

NH₄OAc were mixed, and the reaction was carried out at 110 °C under microwave irradiation to produce thiazole derivatives in good yields.



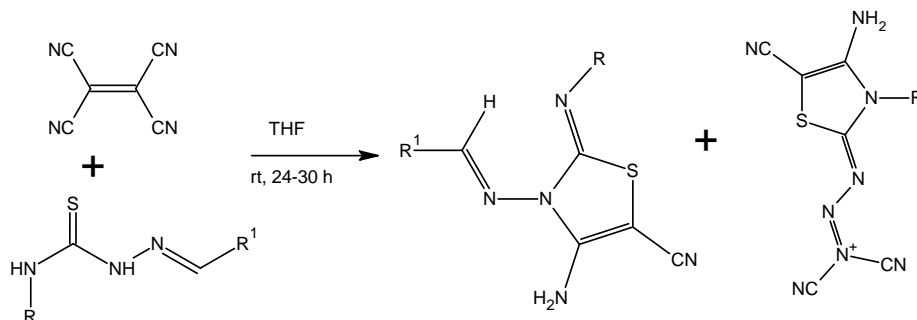
Scheme 6. Synthesis of thiazoles under solvent-free, microwave irradiation

According to Nasri *et al.*⁴⁵ a method for producing thiazolopyridine-fused spirooxindoles and thiazolopyridopyrimidine-fused spirooxindoles by reacting active methylene compounds, substituted isatin, and bifunctional 2-nitromethylenethiazolidine molecule in ethanol in the presence of nano-SiO₂ (**Scheme 7**). Instead of utilising a catalyst to extract transition metals from the reaction medium, nano-SiO₂ was used in this technique as a recyclable, reasonably priced promoter.



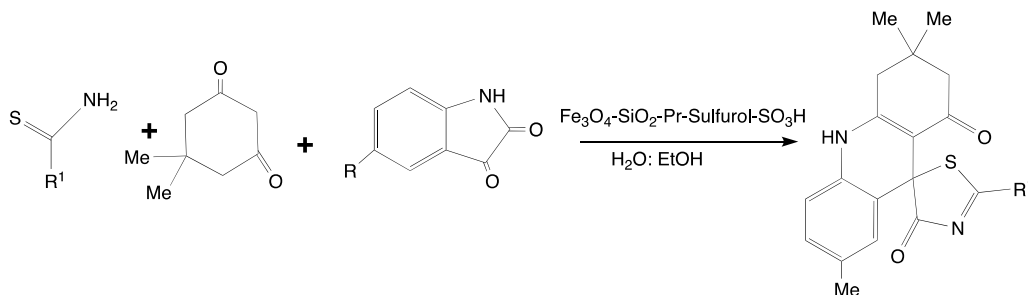
Scheme 7. Synthesis of thiazoles using nano-SiO₂ as a catalyst

Novel (Z)-(4-amino-5-cyanothiazol-2(3H)-ylidene) and (Z)-(4-amino-3-amino-2-imino-2,3-dihydrothiazole-5-carbonitrile)carbonhydrazonoyl dicyanides were produced by Hassan *et al.*⁴⁶ at room temperature without the need of a catalyst by nucleophilic addition reactions of alkenylidenehydrazinecarbothioamides on tetracyanoethylene (TCNE) (**Scheme 8**).



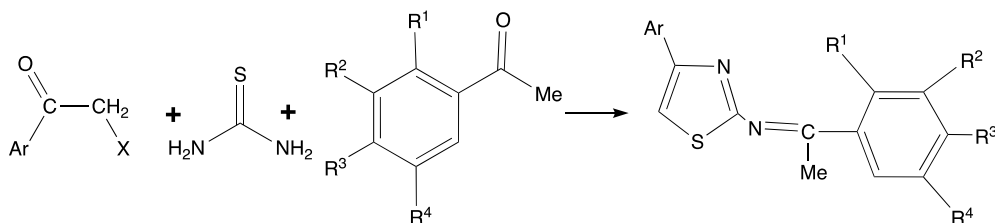
Scheme 8. Synthesis of thiazoles tetracyanoethylene (TCNE) in anhydrous THF in absence of a catalyst

Mohammadi *et al.*⁴⁷ designed a convenient, and reliable high yielding route for the synthesis of novel spiro[acridine-9,5'-thiazole]-1,4'-dione derivatives, in this method condensation of dimedone, thioamides and isatins were carried out using sulfonated magnetic nanocatalyst $\text{Fe}_3\text{O}_4\text{-SiO}_2\text{-Pr-SulfuroI-SO}_3\text{H}$ in water/ethanol as the catalyst (**Scheme 9**). In this method, the nanocatalyst was recovered, and employed a further six times with no discernible loss of catalytic activity.



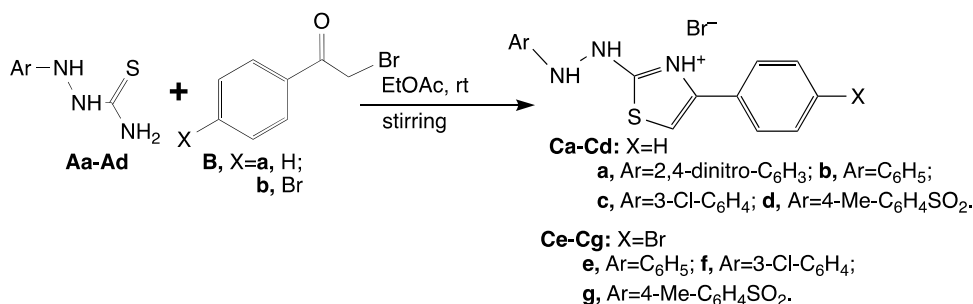
Scheme 9. Synthesis of thiazoles using sulfonated magnetic nanocatalyst

Dawane *et al.*⁴⁸ synthesized thiazole compounds with a simple and effective approach using halo ketone, thiourea, and substituted acetophenones employing polyethylene glycol-400 as a viable and reusable solvent (**Scheme 10**). The reaction speed and use of green solvents makes this one-pot condensation method more reliable and facile.



Scheme 10. Synthesis of thiazoles using polyethylene glycol-400 solvent

In another study 2-(2-arylhydrazinyl)thiazol-3-ium bromide and 4-aryl-2-(substituted amino)-3-(phenylamino)thiazol-3-ium bromide derivatives were synthesized with higher yield by Hassan *et al.*⁴⁹ from the reaction of phenacyl bromide derivatives with mono- and di-substituted thiosemicarbazides (**Scheme 11**).



Scheme 11. Synthesis of thiazoles using mono- and di-substituted thiosemicarbazides

In a study, Sayed *et al.*⁵⁰ have synthesized series of 5-(1-(2-(thiazol-2-yl)hydrazono)ethyl)thiazole derivatives that were synthesized in a one-pot three-component by the reaction of N-aryl-2-oxopropane-hydrazonoyl chlorides with 2-(2-benzylidenehydrazinyl)-4-methylthiazole and thiosemicarbazide in the presence of catalyst TEA in refluxing dioxane.

2.2 Therapeutic Applications of Thiazole Derivatives

2.2.1 Anticancer Study

Thiazole is found in the structure of many anticancer agents. This study provides a summary of current developments in thiazole-bearing compounds as anticancer agents.

Abu-Melha *et al.*⁵¹ have produced thiazole derivatives by 1,3-dipolar cycloaddition processes with chitosan-grafted poly (vinylpyridine) as a biopolymeric basic catalyst, human hepatocellular carcinoma (HepG-2), colorectal carcinoma (HCT-116), and breast cancer (MCF-7) cell lines were screened to determine the cytotoxic effects of thiazole derivatives. According to the results, two thiazole compounds **1** and **2** exhibited the highest cytotoxic potential against the cancer cell lines (**Figure 2**).

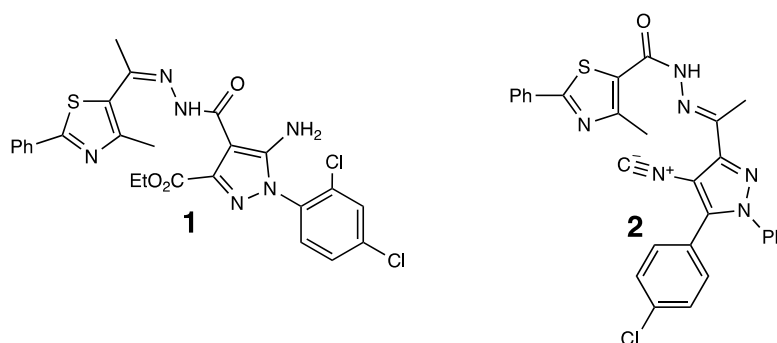


Figure 2. Thiazole compounds **1** and **2** showed anticancer activity against the HepG-2, MCF-7, and HCT-116 cell lines

In a study, Evren *et al.*⁵² synthesized a N-(5-methyl-4-phenylthiazol-2-yl)-2-(substituted thio)acetamides and studied their anticancer activity (**Figure 3**). The thiazole derivatives were obtained from the reaction between 2-chloro-N-(5-methyl-4-phenylthiazol-2-yl)acetamide and mercapto derivatives. Cytotoxicity against NIH/3T3 mouse embryoblast cell line and A549 human lung adenocarcinoma cells was studied for the synthesized compounds. High activity $IC_{50} = 23.30 \pm 0.35$ mM and >1000 mM was observed for the compound **3** against A549 and NIH/3T3 cell lines, respectively.

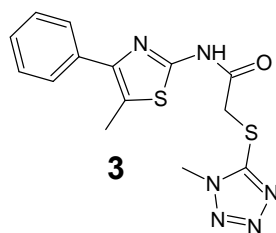
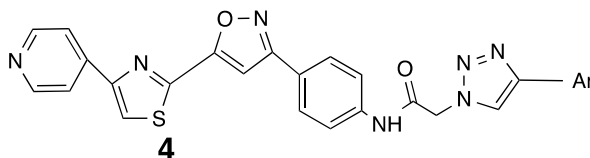


Figure 3. Thiazole compounds **3** showing anticancer activity against A549 and NIH/3T3 cell lines

1,2,3-Triazole linked thiazole-1,2-isoxazole derivatives were synthesized by Yakantham *et al.*⁵³ and the derivatives were studied for their antitumor activity for MCF-7 (breast cancer), A549 (lung cancer), Colo-205 (colon cancer), and A2780 (ovarian cancer) by the MTT method (**Figure 4**). The compounds **4a-4d** showed stronger inhibitory activity than etoposide, which was used as a reference against four cell lines.



4a; Ar =3,4,5-trimethoxyphenyl
4b; Ar =4-chlorophenyl
4c; Ar =4-nitrophenyl

Figure 4. Thiazole compounds **4** showed antitumor activity against MCF-7, A549, Colo-205, and A2780 cell lines

Series of novel phenylthiazole products were synthesized by Farani *et al.*⁵⁴ and their anticancer activity was estimated against human cancerous cell lines of SKNMC (neuroblastoma), Hep-G2 (human hepatocarcinoma), and MCF 7. Compound **5a** executed high anticancer activity ($IC_{50} = 10.8 \pm 0.08$) against SKNMC cell line (**Figure 5**). In HepG2 cell line, compound **5b** showed significant activity with $IC_{50} = 11.6 \pm 0.12 \mu M$.

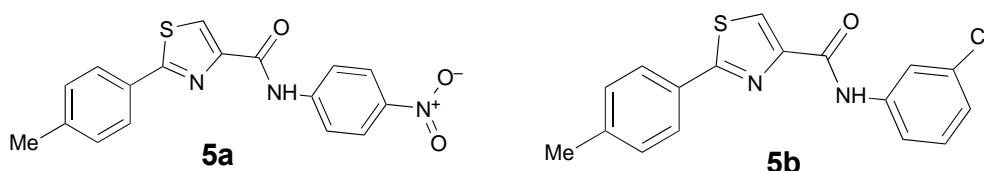


Figure 5. Thiazole compounds **5a** and **5b** showed anticancer activity against cancerous cell lines of SKNMC, Hep-G2, and MCF 7

Grozav *et al.*⁵⁵ synthesized arylidenehydrazinyl-thiazole derivatives and studied their anticancer activity against carcinoma cell lines, MDA-MB231 and HELA. Compound **6a** exhibited a remarkable antiproliferative activity on both MDA-MB-231 (IC_{50} : 3.92 $\mu g/mL$) and HELA (IC_{50} : 11.4 $\mu g/mL$) cell

lines, whereas compound **6b** exhibited cytotoxic activity (IC_{50} value 11.1 $\mu\text{g/mL}$) on the HELA cell line (**Figure 6**).

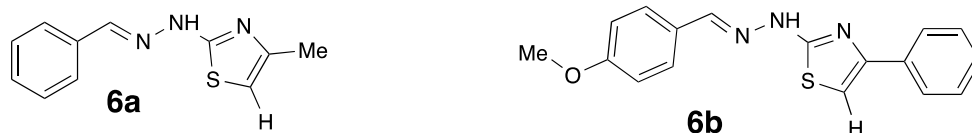


Figure 6. Thiazole compounds **6a** and **6b** showed anticancer activity against cancerous cell lines of MDA-MB231 and HELA

2.2.2 Antioxidant Study

A similar study was done by Grozav *et al.*⁵⁶ 2-(2-((1*H*-indol-5-yl)methylene)hydrazinyl)thiazole derivatives were synthesized and the antioxidant activities of the thiazole derivatives were assessed by spectrophotometric method, using DPPH radical. Compound **7a** showed scavenging potential $IC_{50} = 5.377 \mu\text{g/mL}$ and compound **7b** showed scavenging potential $IC_{50} = 9.131 \mu\text{g/mL}$ better than standard $IC_{50} = 9.74 \mu\text{g/mL}$ (**Figure 7**).

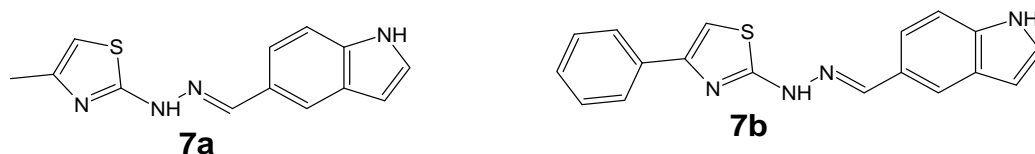


Figure 7. Thiazole compounds **7a** and **7b** showing antioxidant activity

In another work, Nastasa and coworkers⁵⁷ synthesized a series of hydrazones by the reaction of 4-methyl-2-(4-(trifluoromethyl)phenyl)thiazole-5-carbohydrazide with substituted benzaldehyde (**Figure 8**). Antioxidant properties of the compounds were studied by 2,2-diphenyl-1-picrylhydrazide assay. Thiazole derivative **8** showed high antioxidant properties than ascorbic acid.

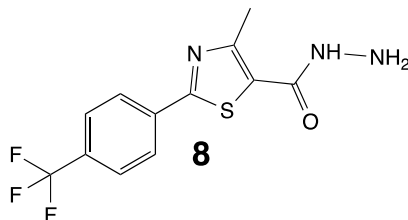


Figure 8. Thiazole compound **8** showed antioxidant activity

2.2.3 Antiviral Study

In a study reported by Stankova *et al.*,⁵⁸ rimantadine compounds with thiazole ring Gly-Thz-rimantadine executed best antiviral activity with $IC_{50} = 0.11 \mu\text{g/mL}$ and $CC_{50} = 50 \mu\text{g/mL}$ against influenza virus A/Hong Kong strain H1N1.

2.2.4 Antitubercular Study

Several poly-functionalized 3-[2-(pyrrolidin-1-yl)thiazole-5-carbonyl]-2*H*-chromen-2-one derivatives, were synthesized by Nural.⁵⁹ The compounds have been tested against *M. tuberculosis* H37Rv strain, the test was performed by resazurin microtitre assay (REMA) plate method. The thiazole compounds showed antimycobacterial activity of MIC = 31.25–125 lg/cm³ values in the range. The highest antimycobacterial activity of MIC value - 31.25 lg/cm³ was showed by compound **9**, among others. Chloro substituents showed good activity than methoxy substituents (**Figure 9**).

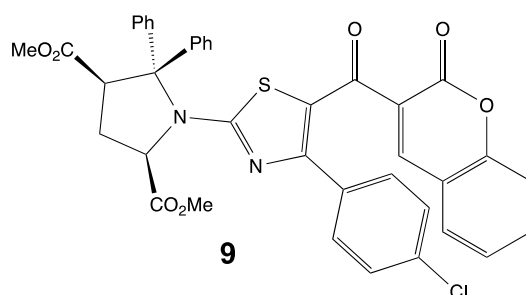


Figure 9. Thiazole compound **9** showing antitubercular activity

2.2.5 Antimicrobial Study

In the most recent study, 1,3-thiazole derivatives were synthesized with lipophilic C4-substitution by Pricopie *et al.*⁶⁰ and antifungal activities of pathogenic *C. albicans* strains were investigated. The anti-*Candida* activity was investigated by broth microdilution method. 2-Hydrazinyl-thiazole derivatives like **10a**, **10b** and **10c** have shown MIC values 3.9 µg/mL, much lower than the fluconazole reference drug i.e MIC value 15.62 µg/mL (**Figure 10**).

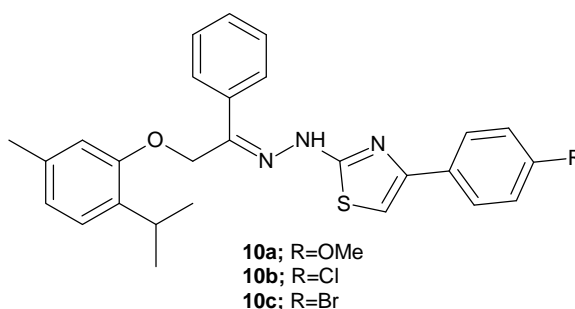


Figure 10. Thiazole compounds **10a**, **10b**, and **10c** showing antifungal activity

A series of 5-(benzo[1,3]dioxol-5-ylmethyl)-*N*-benzylidene-4-(butyl)thiazol-2-amine derivatives were synthesized by Zhilin *et al.*⁶¹ and antifungal activity of the novel derivatives was tested. Compound **11** displayed excellent inhibition for *P. infestans* and *P. oryzae* with ED₅₀ values much lower than the commercial fungicide Metalaxyl and Edifenphos, amongst other derivatives due to the presence of

dihalide phenol in compound **11**, the OH group results in easy dissolution of compounds in water (**Figure 11**).

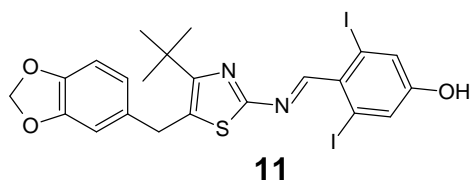


Figure 11. Thiazole compound **11** showed antifungal activity

In a recent study by Wazalwar *et al.*⁶² derivatives of thiazolyl carboxamide were synthesized using ethyl 2-amino-4-methylthiazole-5-carboxylate. Antibacterial activity of these derivatives has been studied. Thiazole derivative **12** displayed higher antibacterial activity than chloramphenicol on *E. coli*. Thiazole compounds **13** and **14** showed higher activity higher than griseofulvin towards *C. albicans* (**Figure 12**).

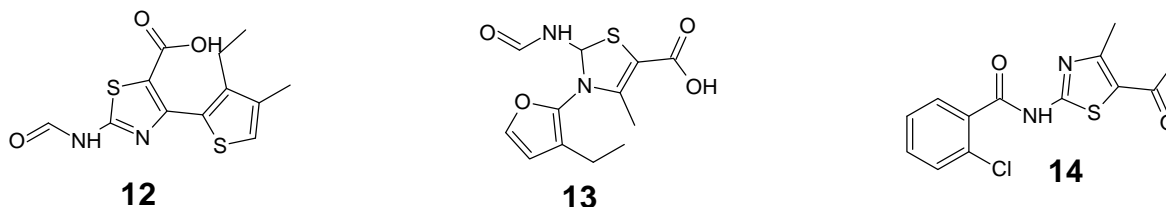


Figure 12. Thiazole compounds **12-14** displaying antimicrobial activity against *E. coli* and *C. albicans*

In another work, Biernasiuk and co-workers⁶³ synthesized thiazole derivatives containing a cyclohexene moiety, and these derivatives were evaluated for their antimicrobial activity against *Candida* spp. Compounds **15a**, **15b**, **15c**, and **16**, have shown better activity over the reference nystatin with MIC = 0.015–3.91 $\mu\text{g/mL}$ (**Figure 13**).

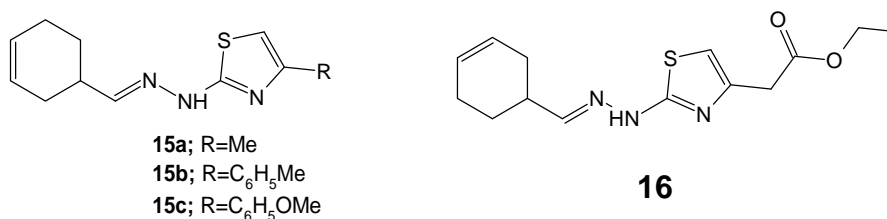


Figure 13. Thiazole compounds **15a**, **15b**, **15c**, and **16**, displaying antimicrobial activity against *Candida* spp.

Althagafi *et al.*⁶⁴ synthesized novel thiazole derivatives with di-, tri- and tetra-substituents by reacting 2-bromo-1-(4-methyl-2-(methylamino)thiazol-5-yl)ethan-1-one with heterocyclic amines, *o*-aminothiophenol, and thiosemicarbazone derivatives. Antimicrobial activity of the synthesized thiazole derivatives was studied. Compound **17**, showed activity better than ampicillin for *S. aureus*, *S. epidermidis*, *B. subtilis*, and *S. pyogenes* (**Figure 14**).

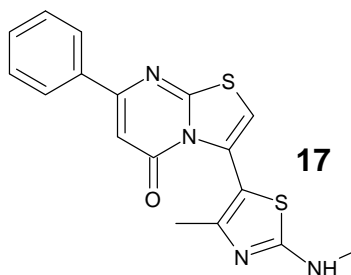


Figure 14. Thiazole compound **17** displayed antimicrobial activity against Gram-positive bacteria

Abbas *et al.*⁶⁵ have reported the synthesis and antimicrobial activity of a novel derivative **18**. Compound **18** displayed antifungal and mild antibacterial activity against *B. pumilus* and *B. subtilis*, and one fungal species *C. albicans* (**Figure 15**).

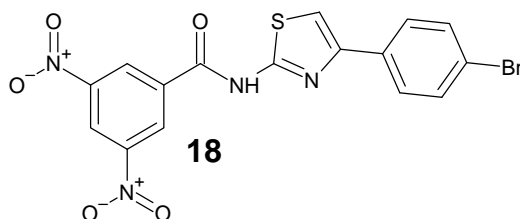


Figure 15. Thiazole compound **18** displayed antimicrobial activity against Gram-positive bacteria

2.3 Chemical Applications of Thiazole Derivatives

2.3.1 Corrosion Inhibition Study

In a recent study, Ally *et al.*⁶⁶ synthesized a novel thiazole polyamide and examined their corrosion inhibition at 40 °C on carbon steel in 0.5 mol/L H₂SO₄. Compound **19** showed inhibition efficiency (IE%) 98.24% at 1 mg/L (**Figure 16**).

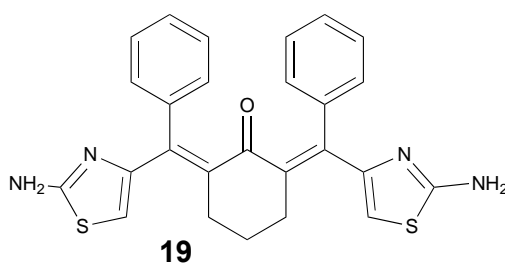


Figure 16. Thiazole compound **19** exhibited corrosion inhibition

In another study, Yadav *et al.*⁶⁷ made a study on corrosion inhibition of thiazole derivatives by potentiodynamic polarization and electrochemical impedance spectroscopy (EIS) techniques on steel (N80 steel) in 15% hydrochloric acid solution. Thiazole compounds **20a** and **20b** have shown good corrosion inhibition with high inhibitor concentration (**Figure 17**).

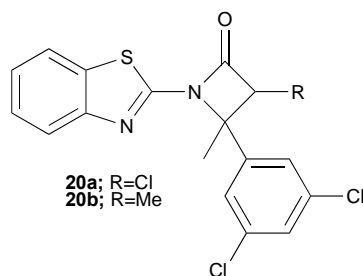


Figure 17. Thiazole compounds **20a** and **20b** exhibiting corrosion inhibition

2.3.2 Photovoltaics

In a study Allard *et al.*⁶⁸ reported the synthesis of novel poly(thienothiazole) derivatives by polycondensation of distannyl-BDT derivatives with 4,6-dibromo-2-octylthieno[3,4-*d*]thiazole. Bulk heterojunction solar cells were fabricated using PBDTTTz-1 and PBDTTTz-2 PCBM blends as active layer. The bandgaps of these thienothiazole-based copolymers PBDTTTz-1 and PBDTTTz-2 were found to be 1.8 and 1.7 eV, respectively. The current density values were calculated from the EQE measurements, both the thienothiazole-based copolymers PBDTTTz-1 and PBDTTTz-2 showed short-circuit current (J_{sc}) values higher than solar illumination AM 1.5G.

2.3.3 Bioimaging and Biolabelling Applications

Bahadur *et al.*⁶⁹ synthesized new thiazolylcoumarin derivatives in high yield through a multistep route from naphthaldehyde, thiosemicarbazide, and ethyl acetoacetate (**Figure 18**). Thiazolylcoumarin derivatives **21** with methoxy groups showed the highest HOMO energy levels and the narrowest bandgap. The fluorescence spectra of the synthesized thiazolylcoumarin derivatives exhibited a strong emission in the 430–510 nm region and UV absorption in the 330–400 nm range. Due to their strong fluorescence characteristics, the synthesized thiazolylcoumarin derivatives have been reported to be used in bioimaging and biolabeling applications.

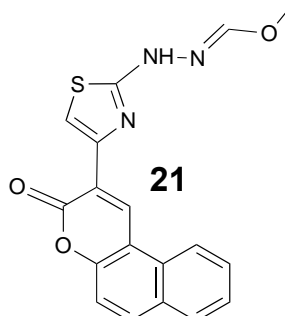


Figure 18. Thiazole compound **21** with bioimaging and biolabeling applications

2.3.4 Textile Dyes

Gaffer *et al.*⁷⁰ have synthesized a new 2-amino-5-arylazothiazole dispersed dye. These colours were used as disperse dyes on polyester fabrics, and their perspiration, resistance to washing, rubbing, sublimation,

and light were investigated. Good dyeability and fastness qualities were displayed by the thiazole dispersion dyes.

In a similar study, Yen *et al.*⁷¹ synthesized heteroaryl thiazole azo dyes by the sol-gel method. These synthetic azo dyes were applied to polyester fabrics, and the dyed polyester fabric's colour, water resistance, tensile strength, and air permeability were examined. The treated polyester fabric had three to four washing fastness grades, five to seven dry rubbing grades, and three to four wet rubbing grades. The grade 3–4 water repellence of the polyester fabric coloured with thiazole azo dye was greatly improved.

El-Borai *et al.*⁷² synthesized mono and disazo disperse dyes using 2-amino-4-(pyridin-3-yl)thiazole. The novel compounds were evaluated for their light fastness, wash, and perspiration. On treatment of these dyes on polyester fabric displayed moderate to good wash and perspiration, fastness grade, and fair to moderate light fastness.

In a study by Maradiya *et al.*⁷³ using various N-alkyl derivatives of aniline, the authors created novel monoazo dispersion colours produced from 5-acetyl-2-amino-4-methylthiazole. On cellulose triacetate cloth, the dispersed dyes dyeing abilities were evaluated. The azo dye demonstrated outstanding dispensability, and a high degree of levelness upon dyeing suggests that these dyes have a good affinity for the fabric and good penetration.

2.3.5 Algicides

Wang *et al.*⁷⁴ have synthesized thiazole alkaloid using L-alanine and their algicidal activity against three harmful algae *C. pyrenoidosa*, *M. aeruginosa*, and *S. obliquus* at different concentrations was evaluated, the study has shown **22** exhibited the best algicidal activity against *S. obliquus* with an IC_{50} - 0.08 $\mu\text{g/mL}$, much higher than the naturally occurring algicide with IC_{50} - 14.33 $\mu\text{g/mL}$ (**Figure 19**).

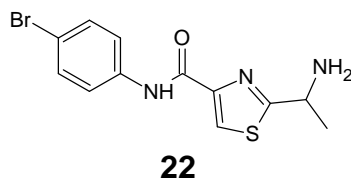


Figure 19. Thiazole compound **22** with algicidal activity

2.3.6 Supercapacitors

Shahrivari *et al.*⁷⁵ have developed a new composite to produce an electrode material. Perylene-3,4,9,10-tetracarboxylic dianhydride (PTCDA) and diamines with thiazole rings were combined to create the composite. In situ electropolymerizations were used to develop the conductive polymer poly(*ortho*-aminophenol) POAP on the surface of the produced polyimides. Using cyclic voltammetry, galvanostatic

charge/discharge, and electrochemical impedance spectroscopy, the polyimides' electrochemical capabilities were assessed. The results showed that the specific capacitances of POAP/PIa **23** and POAP/PIb were 207.2 and 322.4 F/g, respectively. This copolyimide with a thiazole ring can be employed as an electrode for supercapacitor applications because of its high specific capacitance (**Figure 20**).

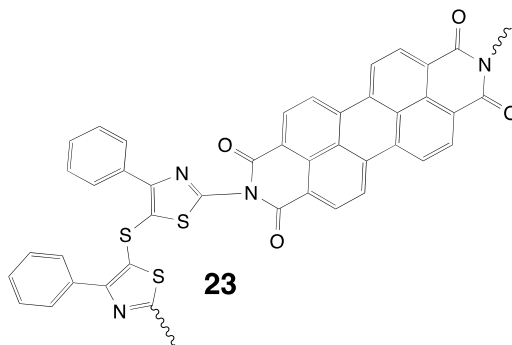


Figure 20. Thiazole copolymer **23** showing specific capacitance of 322.4 F/g

2.3.7 Fluorometric and Colorimetric Sensor for Fluoride Ions

Subrata and co-workers⁷⁶ synthesized a thiazole-based compound **24**, for detection of fluoride ion by colorimetry and fluorometry. It has been reported that the receptor selectively responds to fluoride ions over other ions and results shift in absorption spectra, and the colour change is visible. Fluoride ion binds to salicylaldehyde moiety of receptor thus being used as fluorimetric sensor for detection of fluoride ions in micro and nanomolar range. The low limit of detection reported is 8.6 nM (**Figure 21**).

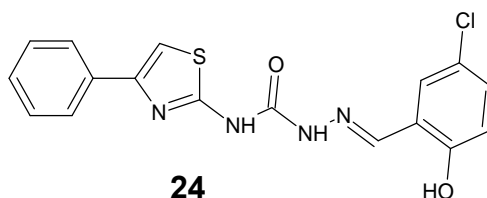


Figure 21. Thiazole compound **24** used as fluorimetric sensor

3. CONCLUSIONS

In the present review paper study has shown that thiazole heterocyclic compounds are one of the most important biologically active compounds used in many commercially available drugs. This article gives the several synthetic routes for the synthesis of thiazole-based derivatives. Furthermore, in this review, we have surveyed different series of thiazole derivatives which are far superior to the commercially available drugs. Based on the literature survey, the derivatives were investigated for biological activities like anticancer, antibacterial, antifungal, antioxidant, and antiviral properties. In conclusion, heterocyclic compounds like thiazole derivatives are potent bioactive compounds and the development of these

compounds is an alluring field of medicinal chemistry. Thiazole derivatives can be produced by designing a new practical process. The exceptional properties and potential of thiazole derivatives, makes them as the focus of future investigation. This survey will help to develop new thiazole derivatives with some modifications to examine the most potent thiazole moieties with less toxicity and better efficiency in the future. This survey will also help researchers to further use these derivatives in wide chemical applications such as corrosion inhibition, photovoltaics, supercapacitors, algicides, dyes in the textile industry, bioimaging, biolabeling and supercapacitors.

4. REFERENCES

1. A. Qureshi and A. Pradhan, *J. Drug Deliv. Ther.*, 2019, **9**, 842.
2. M. T. Chhabria, S. Patel, P. Modi, and P. S. Brahmksatriya, *Curr. Top. Med. Chem.*, 2016, **16**, 2841.
3. W. Zoubi, *J. Org. Chem.*, 2013, **3**, 73.
4. J. Seed and P. Sampson, *Liq. Cryst.*, 2017, **44**, 1894.
5. S. Nayak and S. L. Gaonkar, *Mini-Rev. Med. Chem.*, 2018, **19**, 215.
6. L. R. Abdu-Rahem, A. K. Ahmad, and F. T. Abachi, *Syst. Rev. Pharm.*, 2021, **12**, 290.
7. T. Chaban, O. Klenina, I. Chaban, V. Ogurtsov, S. Harkov, and M. Lelyukh, *Pharmacia*, 2018, **65**, 54.
8. I. H. A. Ripain and N. Ngah, *Malays. J. Anal. Sci.*, 2021, **25**, 257.
9. P. K. Shinde and K. T. Waghmode, *Int. J. Sci. Res.*, 2017, **7**, 365; R. E. Khidre, I. Ali, and M. Radini, *Sci. Rep.*, 2021, **11**, 13654; S. Sinha, M. Doble, and S. Manju, *Eur. J. Med. Chem.*, 2018, **158**, 34; R. Kamblea, R. Meshramb, S. Hesea, R. Moreb, S. Kambleb, R. Gaccheb, and B. Dawane, *Comput. Biol. Chem.*, 2016, **61**, 86.
10. S. J. Kashyap, V. K. Garg, P. K. Sharma, N. Kumar, R. Dudhe, and J. K. Gupta, *Med. Chem. Res.*, 2012, **21**, 2123.
11. W. Hussein and G. Turan-Zitouni, *MOJ Bioorg. Org. Chem.*, 2018, **2**, 53.
12. P. S. Kumar and P. Umadevi, *Russ. J. Gen. Chem.*, 2018, **88**, 2611.
13. W. Cai, A. Liu, Z. Li, W. Dong, X. Liu, and N. Sun, *Appl. Sci.*, 2016, **6**, 1.
14. G. Sridhar, S. Palle, J. Vantikommu, and K. Gangarapu, *Synth. Commun.*, 2020, **50**, 3221.
15. M. H. Sherif, I. M. Eldeen, and E. O. Helal, *Res. Chem. Intermed.*, 2013, **39**, 3949.
16. Y. N. Mabkhot, M. M. Alharbi, S. S. AlShowiman, H. A. Ghabbour, N. A. Kheder, S. M. Soliman, and W. Frey, *Chem. Cent. J.*, 2018, **12**, 1.
17. Y. H. Zaki, M. S. Al-Gendey, and A. O. Abdelhamid, *Chem. Cent. J.*, 2018, **12**, 70; M. S. Al-Saleem, A. I. El-Shenawy, M. A. El-Moneim, and E. H. El-Sayed, *Russ. J. Gen. Chem.*, 2018, **8**, 2675; N. Y. Guerrero-Pepinosa, M. C. Cardona-Trujillo, S. C. Garzón-Castaño, L. A. Veloza, and J. C.

- Sepúlveda-Arias, *Pharmacother.*, 2021, **138**, 111495; N. Siddiqui and W. Ahsan, *Eur. J. Med. Chem.*, 2010, **45**, 1536; S. M. Gomha, H. A. Abdelhady, D. Hassain, A. H. Abdelmonse, M. El-Naggar, M. M. Elaasser, and H. K. Mahmoud, *Drug Des. Devel. Ther.*, 2021, **15**, 659.
18. Y. Samuel, A. Garg, and E. Mulugeta, *Biochem. Res. Int.*, 2021, **2021**, 14; A. Grozav, L. I. Găină, V. Pileczki, O. Crisan, L. S. Dumitrescu, B. Therrien, V. Zaharia, and I. B. Neagoe, *Int. J. Mol. Sci.*, 2014, **15**, 22059.
19. A. Grozav, I. D. Porumb, L. I. Găină, L. Filip, and D. Hanganu, *Molecules*, 2017, **22**, 12; J. S. Barradas, M. I. Errea, N. B. D'Accorso, C. S. Sepúlveda, and E. B. Damonte, *Eur. J. Med. Chem.*, 2010, **46**, 259; M. D. Altıntop, H. I. Ciftci, M. O. Radwan, B. Sever, Z. A. Kaplancıklı, T. F. S. Ali, R. Koga, M. Fujita, M. Otsuka, and A. Özdemir, *Molecules*, 2018, **23**, 17.
20. A. Chowdhury, S. Patel, A. Sharma, A. Das, P. Meshram, and A. Shard, *Chem. Heterocycl. Compd.*, 2020, **56**, 455; O. Bozdağ-Dündar, M. Ceylan-Ünlüsoy, V. J. Eugen, and R. Ertan, *Arzneim.-Forsch.*, 2006, **56**, 621.
21. C. A. Hofmann and J. R. Colca, *Diabetes Care*, 1992, **15**, 1075; O. Bozdağ-Dündar, M. Ceylan-Ünlüsoy, E. J. Verspohl, and R. Ertan, *J. Enzyme Inhib. Med. Chem.*, 2010, **25**, 784.
22. N. Etivand, M. A. Sabegh, and J. Khalafy, *Monatsh. Chem.*, 2019, **150**, 32; A. Petrou, M. Fesatidou, and A. Geronikaki, *Molecules*, 2021, **26**, 3166; B. Rosada, A. Bekier, J. Cytarska, W. Płaziński, O. Zavyalova, A. Sikora, K. Dzitko, and K. Z. Łączkowski, *Eur. J. Med. Chem.*, 2019, **184**, 111765; M. Mic, A. Pîrnău, C. G. Floare, G. Marc, A. H. Franchini, O. Oniga, L. Vlase, and M. Bogdan, *J. Mol. Struct.*, 2021, **1244**, 131278.
23. I. Parašotas, K. Anusevičius, R. Vaickelionienė, I. Jonuškienė, M. Stasevych, V. Zvarych, O. Komarovska-Porokhnyavets, V. Novikav, S. Belyakov, and V. Mickevicius, *ARKIVOC*, 2018, **iii**, 240.
24. Y. Kaddouri, F. Abrigach, E. B. Yousfi, M. el Kodadi, and R. Touzani, *Heliyon*, 2020, **6**, 3185.
25. V. Jaishree, N. Ramdas, J. Sachin, and B. Ramesh, *J. Saudi Chem. Soc.*, 2011, **16**, 371.
26. Z. Muhammad, G. S. Masaret, M. M. Amin, M. A. Abdallah, and T. A. Farghaly, *Curr. Med. Chem.*, 2017, **13**, 226; K. Liaras, M. Fesatidou, and A. Geronikaki, *Molecules*, 2018, **23**, 685.
27. M. M. Alsharekh, I. I. Althagafi, M. R. Shaaban, and T. A. Farghaly, *Res. Chem. Intermed.*, 2019, **45**, 127; H. B. Ouici, O. Benali, and A. Guendouzi, *AIP Conference Proceedings*, 2015, **1653**, 020086.
28. P. K. Paul and M. Yadav, *J. Electroanal. Chem.*, 2020, **877**, 114599.
29. A. M. Borcea, I. Ionuț, O. Crișan, and O. Oniga, *Molecules*, 2021, **26**, 624.
30. A. I. Vogel, A. R. Tatchell, B. S. Furnis, A. J. Hannaford, and P. W. G. Smith, 'Vogel's Textbook of Practical Organic Chemistry', 5th ed, Harlow Longman: London, UK, 1989, 1151.

31. S. H. Ali and A. R. Sayed, *Synth. Commun.*, 2021, **51**, 670; G. Meng, M. Wang, A. Zheng, J. Dou, and Z. Guo, *Green Chem. Lett. Rev.*, 2014, **7**, 46.
32. H. Beyzaei, R. Aryan, H. Molashahi, M. M. Zahedi, A. Samzedeh-Kermani, B. Ghasemi, and M. M. Manesh, *J. Iran. Chem. Soc.*, 2017, **14**, 1023.
33. F. A. Saad, H. A. El-Ghamry, and M. A. Kassem, *Appl. Organometal. Chem.*, 2019, **33**, 4965.
34. E. Abdel-Latif, F. A. Amer, M. A. Metwally, and M. E. Khalifa, *Pigment Resin Technol.*, 2009, **38**, 105.
35. T. Tao, F. Xu, X. C. Chen, Q. Q. Liu, W. Huang, and X. Z. You, *Dyes Pigm.*, 2012, **3**, 916.
36. K. I. Aly and M. A. Hussein, *Chin. J. Polym. Sci.*, 2015, **33**, 1.
37. A. M. Fekry and M. A. Ameer, *Int. J. Hydrog. Energy*, 2010, **35**, 7641.
38. D. Jančula and B. Maršálek, *Chemosphere*, 2011, **85**, 1415.
39. A. Hantzsch and J. H. Weber, *Eur. J. Inorg. Chem.*, 1887, **20**, 3118; S. H. Ali and A. R. Sayed, *Synth. Commun.*, 2020, **51**, 670; W. Wang, L. Wang, M. Mao, X. Zhang, X. Zheng, X. Huang, C. Xue and B. Ning, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2018, **193**, 164; H. Beyzaei, R. Aryan, and H. Molashahi, *J. Iran. Chem. Soc.*, 2017, **14**, 1023.
40. B. Pop, I. Ionuț, G. Marc, D.A.N.C. Vodnar, L. Vlase, and O. Oniga, *Farmacia*, 2021, **69**, 724; A. R. Katritzky, 'Handbook of Heterocyclic Chemistry', 1st Edition, Pergamon Press, New York, 1985.
41. A. H. Cook, I. Heilbron, S. F. MacDonald, and A. P. Mahadevan, *J. Chem. Soc.*, 1949, 1064.
42. Z. A. Alsharif and M. A. Alam, *RSC Adv.*, 2017, **7**, 32647.
43. H. Shahbazi-Alavi, S. Khojasteh-Khosro, J. Safaei-Ghomi, and M. Tavazo, *BMC Chemistry*, 2019, **13**, 1.
44. H. Zali-Boeini and S. G. Mansouri, *J. Iran. Chem. Soc.*, 2016, **13**, 1571.
45. S. Nasri, M. Bayat, H. V. Farahani, and S. Karami, *Heliyon*, 2020, **6**, 03687.
46. A. Hassan, A. Aly, and N. Mohamed, *Res. Chem. Intermed.*, 2020, **46**, 1571.
47. H. Mohammadi and H. R. Shaterian, *Res. Chem. Intermed.*, 2019, **46**, 1109.
48. B. S. Dawane, B. M. Shaikh, N. T. Khandare, V. T. Kamble, S. S. Chobe, and S. G. Konda, *Green Chem. Lett. Rev.*, 2010, **3**, 205.
49. A. A. Hassan, N. K. Mohamed, A. A. Aly, H. N. Tawfeek, S. Bräse, and M. Nieger, *Monatsh. Chem.*, 2020, **151**, 1143.
50. A. R. Sayed, S. M. Gomha, E. A. Taher, Z. A. Muhammad, H. R. El-Seedi, H. M. Gaber, and M. M. Ahmed, *Drug Des. Devel. Ther.*, 2020, **14**, 1363.
51. S. Abu-Melha, M. M. Edrees, H. H. Salem, N. A. Kheder, S. M. Gomha, and M. R. Abdelaziz, *Molecules*, 2019, **24**, 539.

52. A. E. Evren, L. Yurttas, B. Ekselli, and G. Akalin-Ciftci, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2019, **194**, 820.
53. T. Yakantham, R. Sreenivasulu, G. Alluraiah, M. B. Tej, and R. R. Raju, *Russ. J. Gen. Chem.*, 2019, **89**, 2522.
54. A. Mohammadi-Farani, A. Foroumadi, and M. R. Kashani, *Iran J. Basic Med. Sci.*, 2014, **17**, 502.
55. A. Grozav, L. Găină, V. Pileczki, O. Crisan, L. Silaghi-Dumitrescu, B. Therrien, V. Zaharia, and I. Berindan-Neagoe, *Int. J. Mol. Sci.*, 2014, **15**, 22059.
56. A. Grozav, I. D. Porumb, L. G. Ioana, L. Filip, and D. Hanganu, *Molecules*, 2017, **22**, 260.
57. C. Nastasa, B. Tipericiuc, M. Duma, D. Benedec, and O. Oniga, *Molecules*, 2015, **20**, 17325.
58. I. Stankova, K. Chuchkov, R. Chayrov, L. Mukova, A. Galabov, J. Bu, and D. Danalev, *Int. J. Pept. Res. Ther.*, 2020, **26**, 1781.
59. Y. Nural, *Monatsh. Chem.*, 2018, **149**, 1905.
60. A. I. Pricopie, M. Focsan, I. Ionut, G. Marc, L. Vlase, L. I. Găină, D. C. Vodnar, E. Simon, G. Barta, A. Pîrnău, and O. Oniga, *Molecules*, 2020, **25**, 1079.
61. Z. Wu, N. Ding, D. Lin, A. Hu, J. Ye, and G. Li, *Chem. Res. Chin. Univ.*, 2016, **32**, 49.
62. S. S. Wazalwar, A. R. Banpurkar, and F. Perdih, *J. Chem. Crystallogr.*, 2020, **50**, 319.
63. A. Biernasiuk, M. Kawczyńska, A. Berecka-Rycerz, B. Rosada, A. Gumieniczek, A. Malm, K. Dzitko, and K. Z. Łączkowski, *Med. Chem. Res.*, 2019, **28**, 2023.
64. I. I. Althagafi, N. M. El-Metwaly, and T. A. Farghaly, *Molecules*, 2019, **24**, 1741.
65. S. S. Abbas and A. Kubba, *Iraqi J. Pharm. Sci.*, 2018, **27**, 69.
66. K. I. Aly and M. A. Hussein, *Chinese J. Polym. Sci.*, 2015, **33**, 1.
67. M. Yadav, D. Sharma, and S. Kumar, *Korean J. Chem. Eng.*, 2015, **32**, 993.
68. N. Allard, S. Beaupré, B. R. Aïch, A. Najari, Y. Tao, and M. Leclerc, *Macromolecules*, 2011, **44**, 7184.
69. A. Bahadur, S. Iqbal, R. Ujan, P. A. Channar, M. Mana AL-Anazy, A. Saeed, Q. Mahmood, M. Shoaib, M. Shah, I. Arshad, G. Shabir, M. Saifullah, G. Liu, and M. A. Qayyum, *Luminescence*, 2021, **36**, 1189.
70. H. E. Gaffer, M. M. G. Fouda, and M. E. Khalifa, *Molecules*, 2016, **21**, 122.
71. M. S. Yen, M. C. Kuo, C. W. Chen, and J. H. Wu, *Fibers Polym.*, 2015, **16**, 1106.
72. M. A. El-Borai, H. F. Rizk, G. B. El-Hefnawy, H. F. El-Sayed, and S. A. Ibrahim, *Fibers Polym.*, 2013, **14**, 2061.
73. H. R. Maradiya, *J. Saudi Chem. Soc.*, 2013, **14**, 2010.
74. Y. Wang, Q. Liu, Z. Wei, N. Liu, Y. Li, D. Li, and Z. Jin, *Sci. Rep.*, 2018, **8**, 8555.
75. S. Shahrivari, E. Kowsari, A. Shockravi, and A. Ehsani, *Res. Chem. Intermed.*, 2020, **46**, 871.

76. S. Mondal, P. Gupta, F. Rahaman, P. Gautam, and I. C. Lekshmi, *Spectrochim. Acta A. Mol. Biomol. Spectrosc.*, 2022, **264**, 120301.
-



Sheetal Tresa Fernandes is an academician with 10 years of teaching experience, having specialization in Analytical Chemistry. As well, a researcher in the field of organic synthesis. She is currently working as Assistant Professor in the department of Chemistry, St Joseph Engineering College, Mangaluru, India. She is also pursuing her Ph. D under the guidance of Dr K Jyothi, she is engaged in the synthesis of biologically active organic compounds.



Dr K Jyothi is an Academician with 24 years of teaching experience and active researcher in the field of synthetic, structural, electrochemical and medicinal chemistry. She is currently working as Professor and head in the department of Chemistry, St Joseph Engineering College, Mangaluru, India.



Smitha Maria DSouza is an academician with 10 years of teaching experience, Specialized in Applied Chemistry. She is also a researcher in the field of organic chemistry. She is currently working as Assistant Professor in the department of Chemistry, St Joseph Engineering College, Mangaluru, India. She is also pursuing her Ph. D under the guidance of Dr K Jyothi, she is engaged in the synthesis of biologically active organic compounds.