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An Explicative Review of Thiadiazole: Medicinal Chemistry Aspects

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ABSTRACT

This review examined the biological effects of thiadiazole on humans. In recent years compounds featuring thiadiazole moiety have gained significance in pharmaceutical chemistry. Among the various structural isomers of thiadiazole, 1,3,4-thiadiazole stands out due to its extensive range of pharmacological activities, prompting numerous studies to assess its relevance. The 1,3,4-thiadiazole nucleus is integral to various classes of medications, including antioxidants, antimicrobials, anti-inflammatories, anticonvulsants, and antivirals, among others. In this study, An attempt has been made with recent research finding to review the structural modification on different derivatives for various pharmacological activities.

Keywords: Thiadiazole, Heterocyclic, 1,3,4-thiadiazole, Antioxidant, Antimicrobial, Anti-inflammatory, Anticancer, Biological activity.

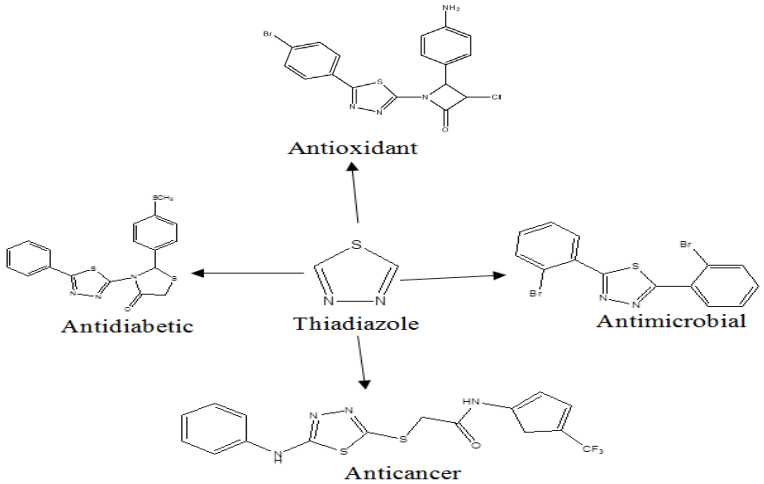

Fig. 1. Graphical abstract of Thiadiazole

INTRODUCTION

Compounds that are cyclic containing carbon atoms and another element atom, that are sulfur, oxygen, and nitrogen in the ring are known as heterocyclic compounds. These heterocyclic compounds show great interest in our life. Their nucleus is found in many biologically active compounds. Thiadiazole is an example of a heterocyclic compound.

The significant 5-membered heterocyclic ring thiadiazole has 2 nitrogen and 1 sulfur atoms as heteroatoms. The general formula of thiadiazole is $C_2H_2N_2S$. Four different structures are available depending on the relative placements of the heteroatoms; these forms are structural isomers because they do not interconvert. 1,3,4-thiadiazole is the most common and appears in several medications.

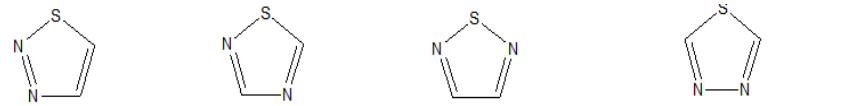

Fig. 2. Different thiadiazole isomers

In comparison to pyridine, benzene, and thiophene, the ring structure is less aromatic. The π electron delocalization is used to quantify the aromatic character. Because nitrogen atoms withdraw electrons, nucleophilic substitution reactions occur often whereas electrophilic attack at carbon is quite uncommon. There has been evidence of electrophilic bombardment at the sulfur atom. 1,3,4-thiadiazoles are easily acylated and alkylated because of the inductive effects of additional heteroatoms. In aqueous acid solutions, the ring is rather stable, but in aqueous basic solutions, it cleaves. thione-thiol or amine-imine equilibrium of tautomeric determines the electrophilic processes that give rise to the ring reactivity of nitrogen atoms. Deprotonation of the ring atom (nitrogen) can occur in the thione or imine form, making the ring atom (nitrogen) susceptible to acylation, alkylation or transformation into 1,3,4-thiadiazolium salt. Electrophiles including alkyl halides, trimethylsilylmethyl trifluoro methanesulfonate, and formaldehyde are used in the processes. 1,3,4-thiadiazole core skeletons undergo a variety of replacement processes involving sulfonyl chlorides, acid chlorides and alkyl halides to produce a range of drugs, including 2-amino substituted 1,3,4-derivatives of thiadiazole.

Structural isomers that have a different double bond and differ in proton locations are known as tautomerism. Their carbon backbone remains the same.[1-3]

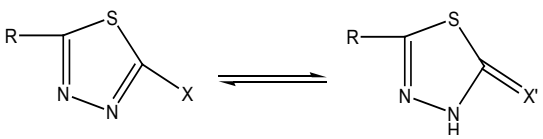

Fig. 3. Tautomerism in thiadiazole

Antioxidant properties

Malak Ajit Sajid *et al.,* (2024) Describe a fusion of 1,3,4 Thiadiazole substituted Schiff bases. The synthesised compounds were characterised by Mass spectroscopy, FTIR, ^{1}HNMR and ^{13}CNMR. These compounds were tested for antioxidant activity. Among all compounds, 3b (Fig. 4) gives excellent activity.[4]

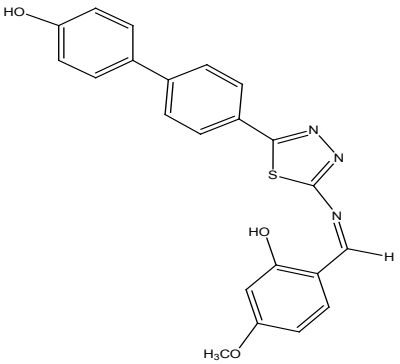

Fig. 4

Rakesh Kumar Marwaha *et al.,* (2023) reported a synthesis of thiadiazole derivatives as an antioxidant property through a DPPH assay. Among the synthesised compounds, AZ-15 (Fig. 5) shows good potential compared with standard drug (ascorbic acid). (IC_{50}: 42.88).[5]

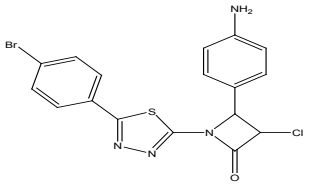

Fig. 5

Cakmak Sukriye *et al.,* (2023) describe the synthesis of thiadiazole derivatives as an antioxidant

activity. Compound II (Fig. 6) shows greater ABTS+ radical scavenging capacity. [IC_{50}:68.93][6]

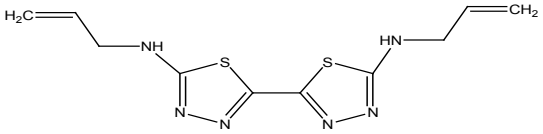

Fig. 6

Amer Zainab *et al.,* (2022) reported thiadiazole derivative compound 2d (Fig. 7) as an antioxidant whose scavenging percentage of 69.07% at 50 mg/mL.[7]

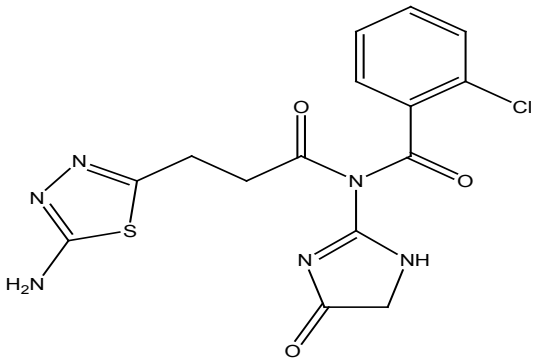

Fig. 7

Yakan Hasan (2020) provided the synthesis of thiadiazole derivatives. Synthesised molecule's in-vitro antioxidant properties were determined by the DPPH process. They observed that the II molecule (Fig. 8) shows potent antioxidant properties with IC_{50} 25.17 µg/mL.[8]

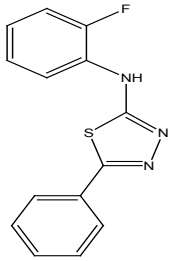

Fig. 8

Hacer Bayrak *et al.,* (2019) reported the synthesis of a novel compound of imidazole[2,1-b] [1,3,4-]thiadiazole (ITD). These compounds were tested for antioxidant activity. The compounds 2 (IC_{50}7.05), 3a (IC_{50}1.14), and 3b (IC_{50}3.37) show more prominent antioxidant activity than Trolox, a standard drug.[13]

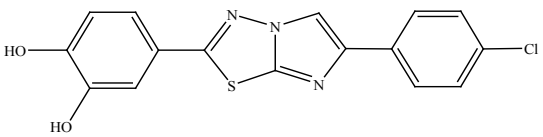

Fig. 9

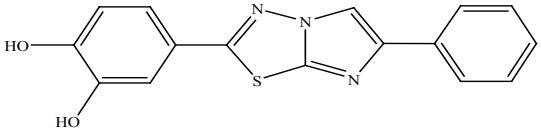

Fig. 10

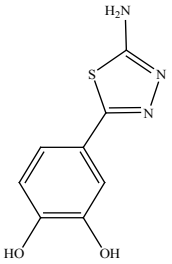

Fig. 11

Kamboj Kumar Vipan *et al.,* (2019) reported a synthesis of derivatives of [1,2,4]triazolo[3,4-b] [1,3,4]thiadiazole was performed. Compound TH-13 was found to have antioxidant activity, which is better than the standard compound. The IC_{50} value of the compound is 8.1±0.325 µg/mL.[44]

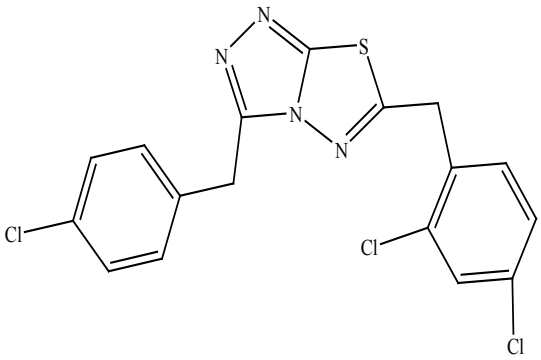

Fig. 12

Markovic Violeta *et al.,* (2019) reported a synthesis of 15 new 1,3,4-thiadiazole derivatives that have protocatechuic acid moiety present in them. The antioxidant property was determined by the DPPH and ABTS assays. Among these 15 compounds, 3c shows better antioxidant properties with an IC_{50} value of 3.53 µg/mL.[47]

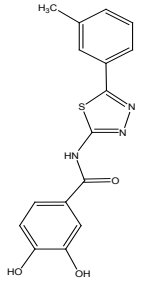

Fig. 13

Gowda Kemparaje *et al.,* (2019) reported the synthesis of a group of 2,5-disubstituted 1,3,4 compounds and tested for antioxidant properties. Among the synthesized compounds 4k shows excellent antioxidant properties. Molecular docking was performed to check the binding property of 4k with proteins.[46]

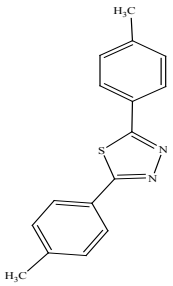

Fig. 14

Rabie M. Amgad *et al.,* (2018) reported thirteen compounds of 1,3,4-thiadiazole-2-thiols. These structures were synthesised and evaluated for antioxidant activities. The structure of these compounds was established by spectroscopy and chemical analysis. Three compounds (3b,d,h) show promising antioxidant activity.[45]

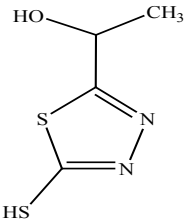

Fig. 15

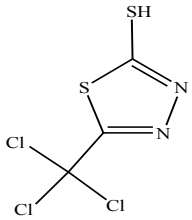

Fig. 16

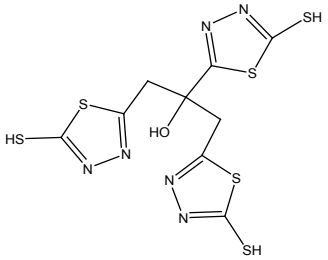

Fig. 17

Structure-Activity Relationship

The above literature survey tells that SAR of derivatives of thiadiazole for Antioxidant activity exists due to the presence of the NH_2 group at the para position in the compound AZ-15(4-(4-aminophenyl)-1-(5-(4-bromophenyl)-thiadiazole-2yl)-3-chloroazetidin-2-one). Presence of allyl group ($-CH_2CH=CH_2$) increase the activity in Compound II (N5,N5'-diallyl-[2,2'-bi(1,3,4-thiadizole)]-5,5'-diamine). This literature survey also revealed the presence of electron-donating groups such as NH_2, and OCH_3 that can act as free radicals and inhibit the oxidation process increasing antioxidant activity like in compound 2d. presence of an E.W.D such as fluorine which withdraws electrons by inductive effect, causing electron density to reduce. This helps in the easier loss of proton as shown in compound II.

Anti-inflammatory properties

Zaharia Valentin *et al.,* (2024) reported that Reverse-phase thin-layer chromatography was used to conduct the experimental lipophilicity study in a binary isopropanol-water mobile phase. The theoretical lipophilicity parameters derived using different computational techniques were compared with the observed results. They synthesise 32 heterocyclic compounds among which 1b-16b are imidazo[2,1-b][1,3,4]thiadiazoles derivatives. Compounds having excellent antioxidant activity after evaluating lipophilicity and POM analysis are 1b, 4b, 5b,9b, 12b, and 13b. these compounds show an excellent reduction in acute inflammation in vivo.[25,27]

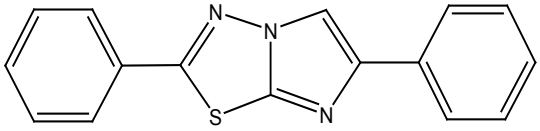

Fig. 18

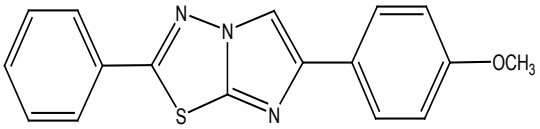

Fig.19

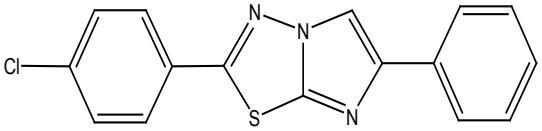

Fig.20

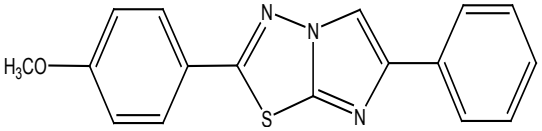

Fig.21

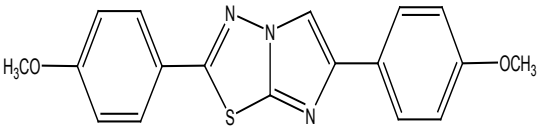

Fig.22

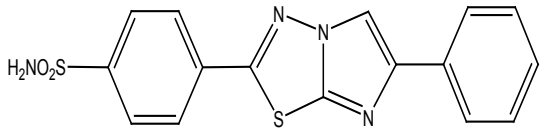

Fig.23

Dhadde Shivsharan *et al.,* (2024) reported the synthesis of new derivatives of N-{[5-(substituted)-1,3,4- thiadiazole-2-yl] carbamothioyl}. These compounds were synthesised using a green chemistry approach assisted by microwave. Compounds were tested for anti-inflammation properties. A carrageenan-induced paw edema model in rats were used to check the anti-inflammatory activity. All synthesis compound shows remarkable anti-inflammatory properties. 1b shows a greater anti-inflammatory property. At 50mg/kg dose, 1b shows 50% depletion in paw edema volume.[26]

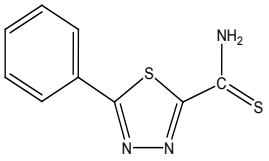

Fig. 24

El-Saghier M. Ahmed *et al.,* (2024) reported the synthesis of 1,3,4-thiadiazole derivatives having carboxamide. The newly synthesised compounds were subjected to an anti-inflammatory test (protein denaturation). Among all compounds, three compounds show excellent inhibition properties. These compounds are 4c, 3a, 8c.[28]

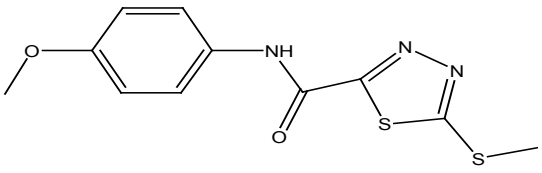

Fig. 25

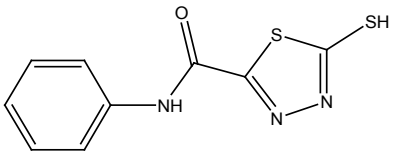

Fig. 26

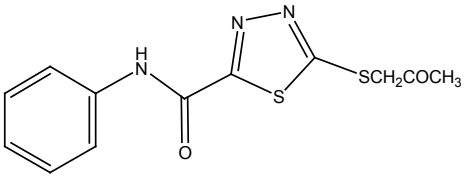

Fig. 27

Shaik B. Afzal *et al.,* (2024) reported the synthesis of thiadiazole derivatives containing a pyridine base. They were tested for anti-inflammatory properties. Among all compounds, NTD3 shows excellent results in anti-inflammatory properties.[29]

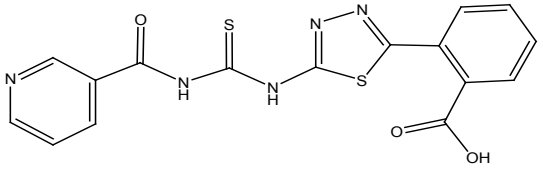

Fig. 28

Shakirzyanova S.G *et al.,*(2024) reported a synthesis of 5,5-(Disulfanediyl)bis[3-phenyl-1,3,4-thiadiazole-2(3H)-thione](1). Compound was tested for anti-inflammatory property. The anti-inflammatory test was conducted using the carrageenam footpad edema model. They concluded that the compound showed activity at doses of 10mg/kg.[30]

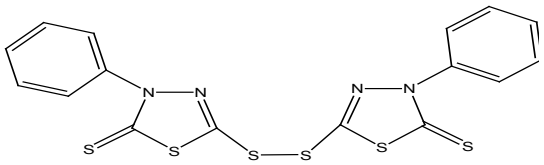

Fig. 29

Haroun Michelyne *et al.,*(2023) reported the synthesis of new 5-andamathylthiadiazole-contain thiazolidinone derivatives. These derivatives were examined for anti-inflammatory activity and have an excellent gastric profile. Four compounds show excellent antioxidant activity compared to the indomethacin(control drug). These compounds are 3,4,10, and 11.[31]

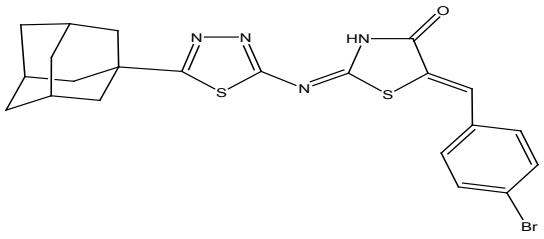

Fig. 30

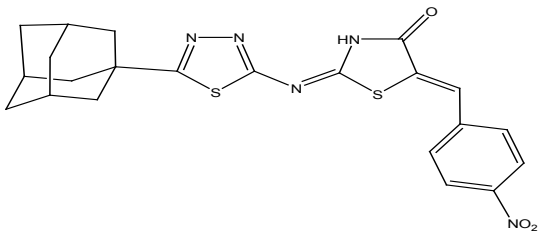

Fig. 31

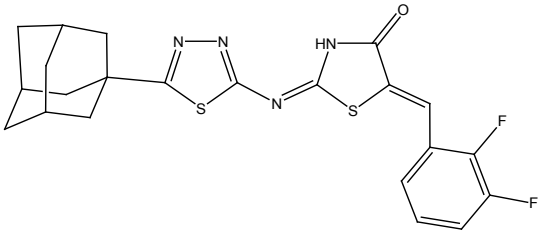

Fig. 32

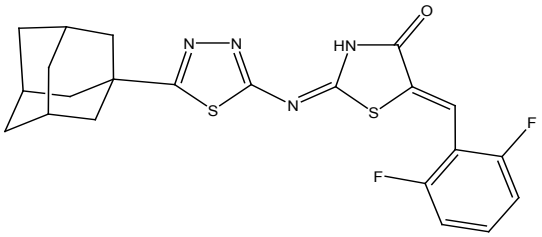

Fig. 33

Omar M. Yasser *et al.,*(2020) reported the synthesis of 1,3,4-thiadiazole and 1,3-thiazolidin-4-one derivatives among the synthesis compounds compound 3a,4r and 4q gives excellent anti-inflammatory activity in in vivo study.[32]

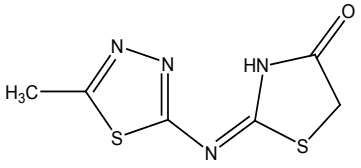

Fig. 34

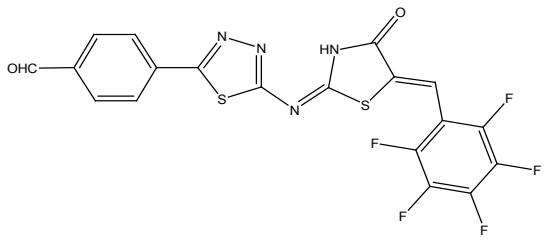

Fig. 35

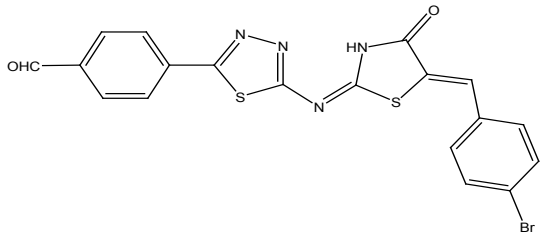

Fig. 36

Pathak Prateek *et al.,*(2019) reported a synthesis of 1,2,4-triazole-containing 1,3,4-thiadiazole hybrid compounds and tested these compounds for their anti-inflammatory activity. 13f and 13g are the most potential compounds of all.[33]

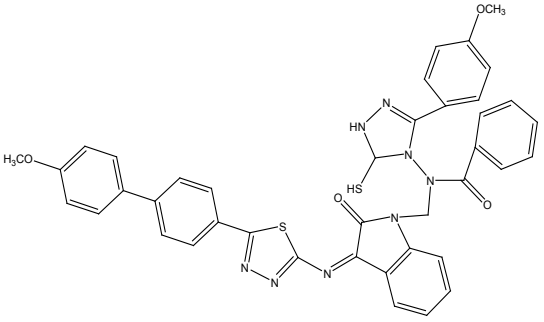

Fig. 37

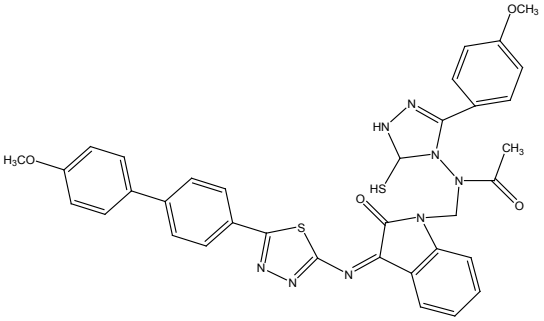

Fig. 38

Mehta K. Dinesh *et al.,*(2019) synthesis of thiadiazole derivatives and tested for anti-inflammatory activity. Compounds 6d.6i,6j and 6l show excellent antioxidant activity.[34]

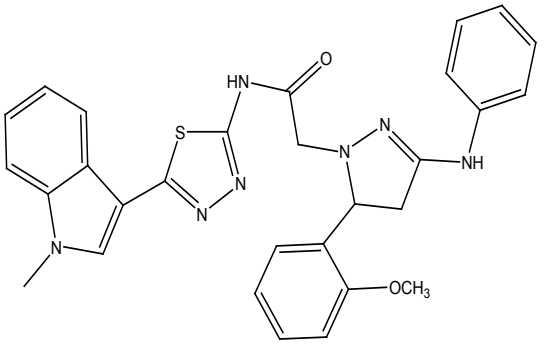

Fig. 39

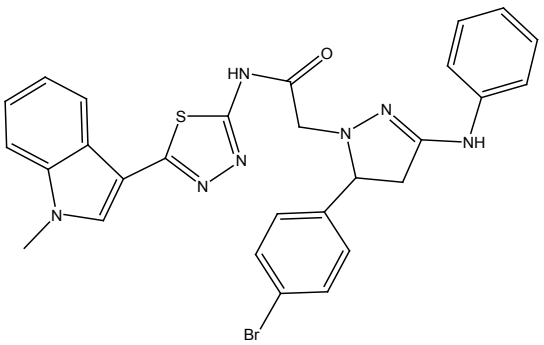

Fig. 40

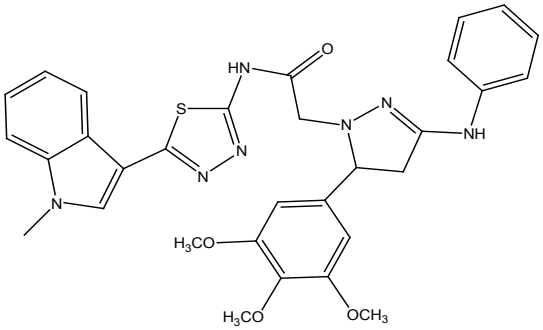

Fig. 41

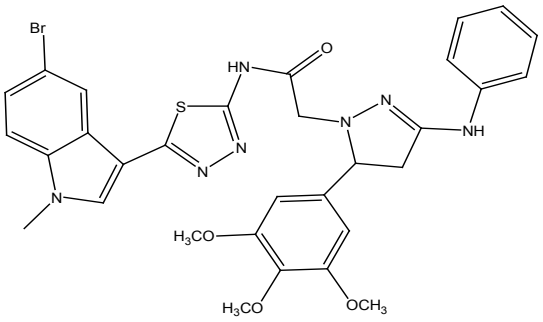

Fig. 42

Abdu-Allah M.H. Hajjaj *et al.,*(2018) reported the synthesis of Thiazolidinone-thiadiazole derivatives containing 5-alk/arylidene. Synthesised compounds were tested for anti-inflammatory activity. Three compounds show excellent anti-inflammatory activity. These compounds were 6a,6l and 9.[35]

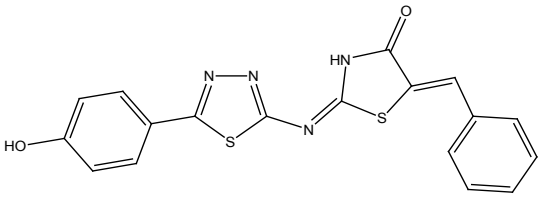

Fig. 43

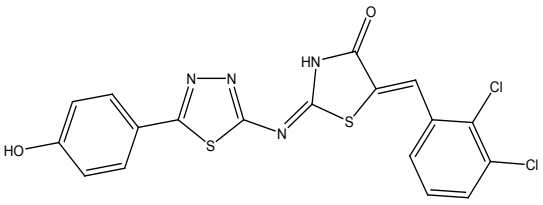

Fig. 44

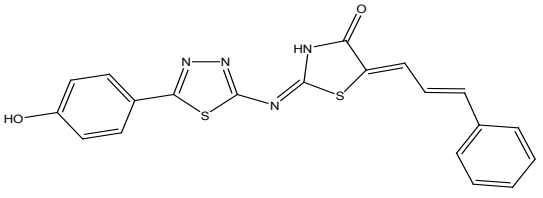

Fig. 45

Structure-activity relationship

The following literature survey shows that the presence of a 4-benzenesulfonamide compound at C-2 of imidazole[2,1-b][1,3,4]-thiadiazole is essential to linking with COX-2 inhibitors, as seen by Zaharia Valentin et al.'s report. On the thiadiazole ring, electron-donating groups such as methyl and phenyl increase the inflammatory activity. Similarly, electron-withdrawing groups decrease the inflammatory activity. N.Podila *et al.,* Reported that the presence of phenyl carboxylate at C-5 of thiadiazole having pyridine at C-2 shows greater anti-inflammatory activity than having phenyl attached to C-5.

Antimicrobial properties

Saki Neslihan *et al.,* (2022) describe 1,3,4- thiadiazole derivatives synthesis that contain the thiophene group as an antibacterial molecule. Antibacterial activity is determined using well diffusion, TLC-Dot blot, growth curve and macro dilution analytical methods. Compounds 1 (Fig. 9) and 6 (Fig. 10) show remarkable antibacterial activity, as opposed to *Gram-positive* and negative bacteria.[9]

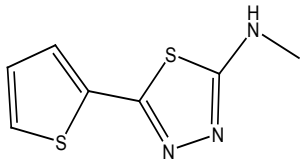

Fig. 46

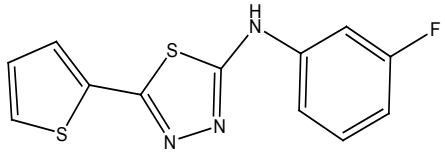

Fig. 47

Gidwani Bina *et al.,* (2021) show in their study, the synthesis of 1,3,4-thiadiazole by cyclisation. The synthesised compound has benzaldehyde groups. All compound shows promising activity but compound II shows excellent activity against *Gram+* and *Gram-* bacteria.[41]

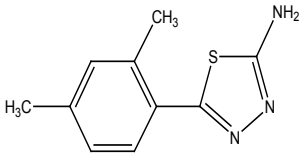

Fig. 48

Khanum ara shaukath *et al.,* (2020) Give a synthesis of substituted thiadiazole. These compounds were examined for antimicrobial activity. Compound 5b (Fig. 11) among all compounds shows excellent antimicrobial properties.[10]

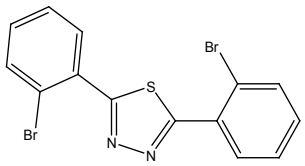

Fig. 49

Ibrahim G. Ahmed (2020) reported a synthesis of two polymers. These two polymers are 1,3,4-thiadiazole molecules linked with chitosan. They were tested for antimicrobial growth. They inhibit the growth of *P. aeruginosa, S. aureus, E. coli*, and *B. subtilis*. MIC value of Cs-EATT (Fig. 13) (polymer) is in the scale of 25–100 μg mL^{-1} and Cs-BATT (Fig. 14) (polymer) is in the scale of 25–200 μg mL^{-1}.[12]

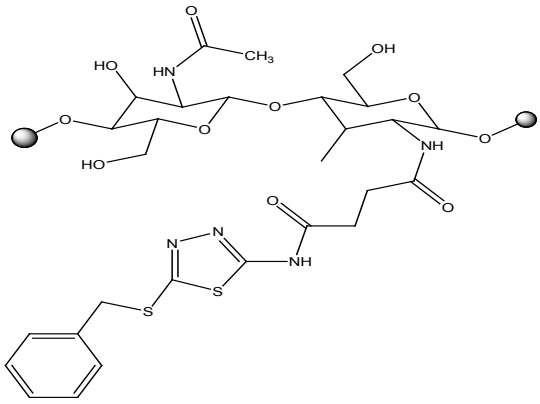

Fig. 50

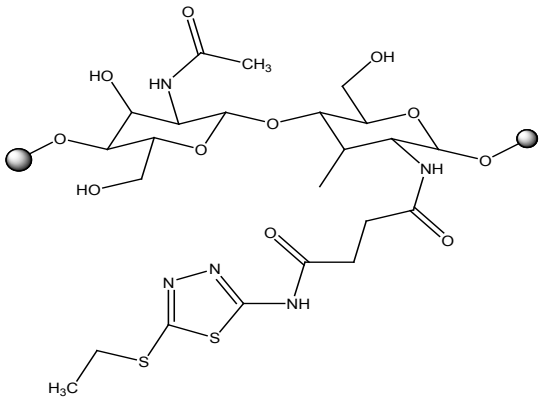

Fig. 51

Gomha M. Sobhi *et al.,* (2019) reported a group of 1,3,4-thiadiazole derivatives. These compounds were checked for antimicrobial properties. Among all the synthesized compounds 6b shows excellent properties.[11]

Bayrak Hacer *et al.,* (2019) published a synthesis of imidazole thiadiazole (ITD) derivatives that are examined for antimicrobial activity. Compound 3b (Fig.15) shows excellent antimicrobial activity. It is a chloride derivative of ITD. It shows great activity against *Gram-negative* and positive bacteria.[13]

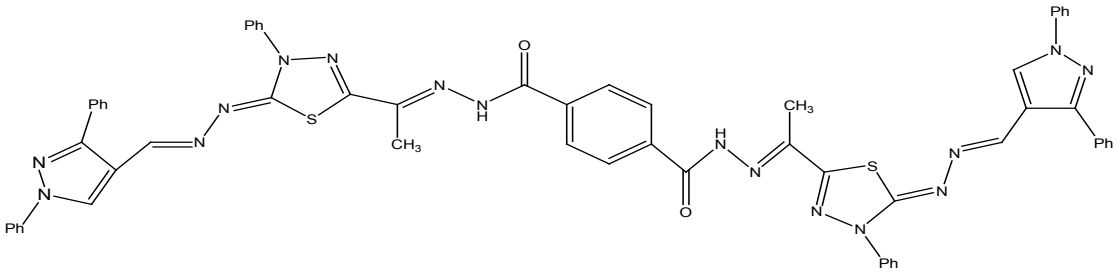

Fig. 52

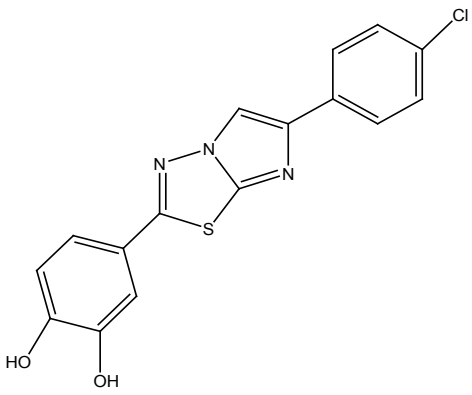

Fig. 53

Abdallah A.Magda *et al.,* (2012) reported a group of compounds having 1,3,4-thiadiazole moiety. These compounds were examined for antimicrobial activity. All compounds give excellent results. Compounds 7a,7c, and 7d give positive results against all bacteria used for the evaluation. Four different bacterial colonies are used to test antimicrobial activity, these are *Bacillus subtilis* (RCMB 000107, BS), *Staphylococcus aureus* (RCMB 000106, SA), *Escherichia coli* (RCMB 000103, EC), and *Pseudomonas aeruginosa* (RCMB 000102, PA).[42]

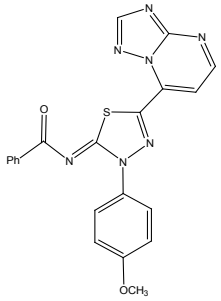

Fig. 54

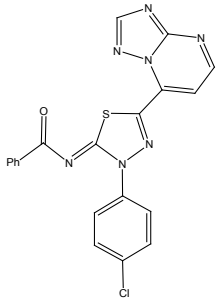

Fig. 55

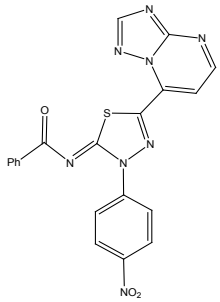

Fig. 56

Foroumadi Alireza *et al.,*(2011) reported the synthesis of 1,3,4-thiadiazole derivatives containg imidazole. These compounds were examined for antimicrobial properties. Among all, compound 6b gives promising activity against *Bacillus subtilis*, *Staphylococcus aureus*, and *Staphylococcus epidermidis*.[49]

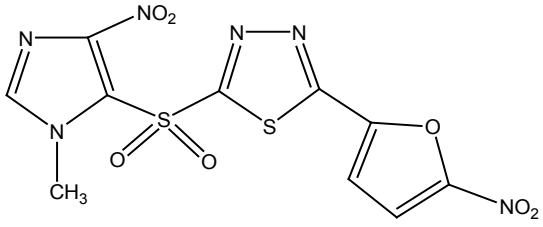

Fig. 57

Kotresh Oblennavar *et al.,* (2010) designed an effective route to synthesise 1,3,4-thiadiazole derivatives. The synthesised compound were tested for antimicrobial activity. Three compounds show excellent activity from others. These compounds are 3h(Fig. 58), 3f(Fig. 59), 3e(Fig. 60).[48]

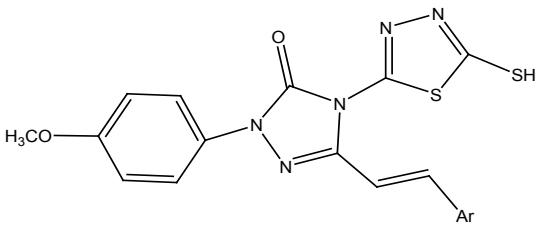

Fig. 58

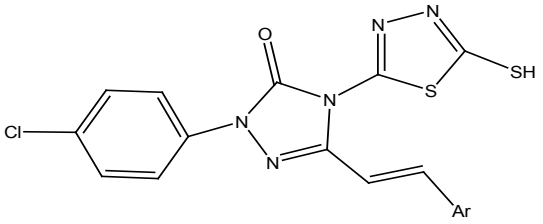

Fig. 59

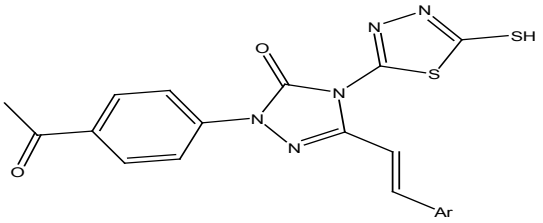

Fig. 60

Profire Lenuta *et al.,* (2007) published the synthesis of 1,3,4- thiadiazole having D, L-methionine moiety. These compounds were examined for antimicrobial effect by using *Bacillus antracis* ATCC 8705, *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Bacillus cereus* ATCC 10987, and *Sarcina lutea* ATCC 9341 strains. Amongst all 5c shows excellent antimicrobial activity against *Bacillus cereus* and *Bacillus antracis*.[43]

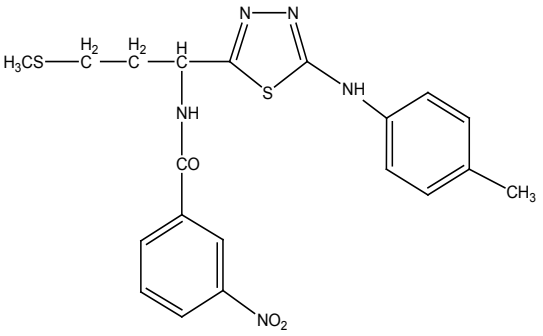

Fig. 61

Structure-Activity Relationship

The literature survey indicated that the electron-donating group decreased the antimicrobial activity. If the hydrophobic character of R increases it increases the activity except if electron density increases at the π-π interaction it decreases the activity. Less hindered group present on R gives potential activity. The electron-donating group decreases the activity. The present literature survey indicates the presence of two different aromatic rings with two Bromo at the ortho part of the aromatic ring attached to the thiadiazole structure giving excellent activity.

Anticancer properties

Osmaniye Derya *et al.,* (2020) Give the synthesis of 1,3,4-thiadiazole descendant as chemotherapeutic compounds. Compound 4i (Fig.16) demonstrates possible action against the rat brain cancer cell line C6 with IC_{50} 0.097mM.[14]

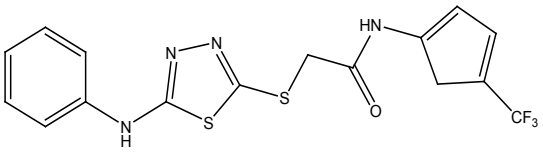

Fig. 62

Cevik Acar Ulviye *et al.,* (2020) composed the substituted thiadiazole derivative. these compounds were investigated for anticancer activity. Among all compounds, 4y (Fig. 17) shows incredible cytotoxic ability opposite to MCF7 cancer cells. [IC_{50}: 0.084±0.020.][15]

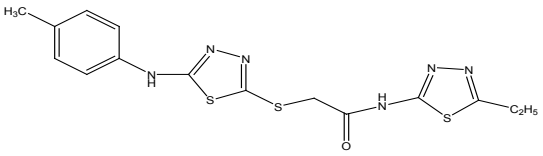

Fig. 63

Emami Saeed *et al.,* (2020) Tell a synthesis of ciprofloxacin derivative modified at C-3. The maximum compound shows remarkable properties against several cancer cells in the MTT assay. Compounds 13e (Fig. 18) and 13g (Fig. 19) show excellent anticancer activity.[16]

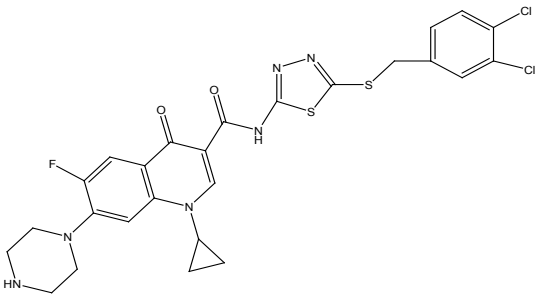

Fig. 64

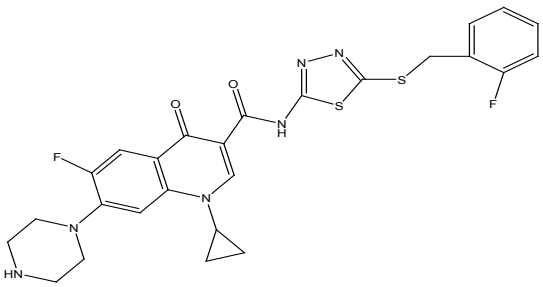

Fig. 65

Raju Ramesh Rudraraju *et al.,* (2020) reported a group of amides containing thiadiazole triazole compounds. These compounds were synthesised and tested for anticancer activity. Among all compounds, 8b (Fig. 20) shows excellent activity against A549 (0.17±0.032μM), DU-145 (0.83±0.091μM), MCF-7(0.10±0.084μM), and MDA MB-231 (0.28±0.017 μM).[17]

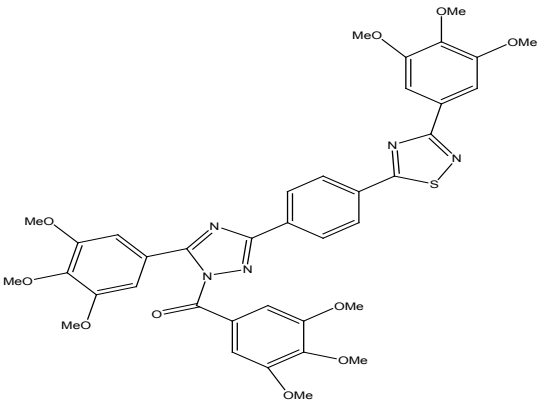

Fig. 66

Antidiabetic

Rehman Wajid *et al.,* (2022) tell of the synthesis of 25 newly two fused thiadiazole having 1,4-benzodioxine compounds. These compounds were tested for antidiabetic activity. Among all compounds, 22 (Fig. 21) show great activity.[18]

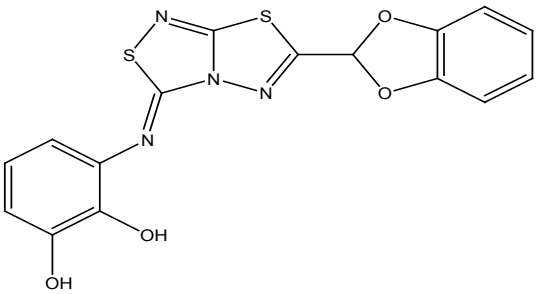

Fig. 67

Singh Parvesh *et al.,* (2021) discloses the synthesis of a thiazolidine-4-one carrying 1,3,4-thiadiazole. The compound was tested for antidiabetic. Among all compounds, 4e (Fig. 22) shows promising activity.[19]

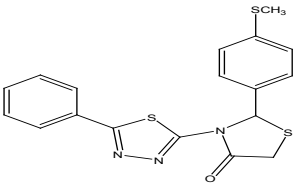

Fig. 68

Cui Zi-Ning *et al.,* (2021) put out the union of 2,5-disubstituted furan derivatives have 1,3,4-thiadiazole derivatives antidiabetic activity. Compound 9 (Fig. 23) shows excellent inhibitory properties with an IC_{50} value is 0.186μM.[20]

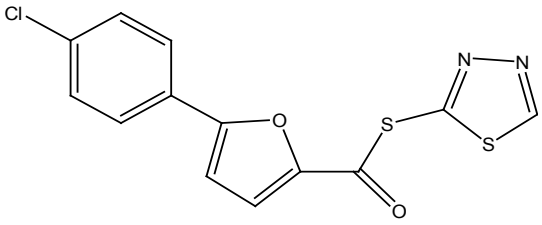

Fig. 69

Hameed A. Sherin *et al.,* (2020) reported a group of 5-furyl-1,3,4-thiadiazole-2-imine derivatives as antidiabetics. Among all compounds, SA03 (Fig. 24) and compound SA07 (Fig. 25) have high docking scores and a good percentage of inhibiting alpha-amylase.[21]

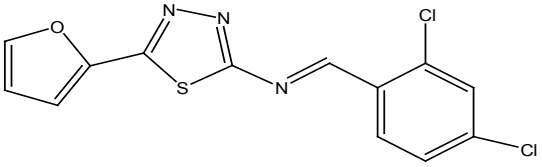

Fig. 70

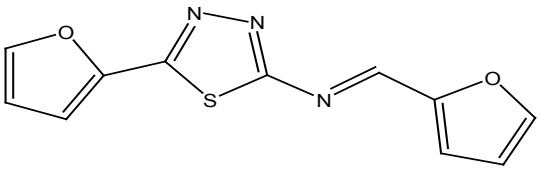

Fig. 71

Structure-activity relationship (SAR)

The above literature survey indicates that the presence of dihydroxy on the ortho, meta site of the phenyl ring gives significant α-amylase and α-glucosidase activity in compound 22 of Rehman Wajid *et al.,* electron-donating nature of thiomethyl at para position gives high binding affinity for α-glucosidase. 4e which has a thiomethyl unit at the para position shows great activity. Substituting R at phenyl is essential for activity as it was observed in compound 9 which shows greater activity. Hameed A. Sherin *et al.,* observed that compounds having electron-donating groups at the phenyl ring at 2 and 4th position (SA03) and furyl ring (SA07) attached to the imine bond give higher biological activity.[50]

CONCLUSION

This analysis has delivered comprehensive insights into thiadiazole, with a particular focus on 1,3,4-thiadiazole. In this review, we examine the antioxidant, antimicrobial, and anticancer properties of thiadiazole derivatives. Modifications to the thiadiazole structure lead to compounds with notable pharmacological effects, which may eventually serve as effective therapeutic agents. While the primary clinical applications include antibacterial, antifungal, carbonic anhydrase inhibition, and anticancer activities, there remain additional potential targets yet to be investigated. Although various positions have been explored to enhance the efficacy of 1,3,4-thiadiazole, none of the derivatives have demonstrated significant antitubercular activity. The literature has been thoroughly reviewed to offer a substantial overview of the structural prerequisites for activity, wherever applicable.

ACKNOWLEDGMENT

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Conflict of interest

The author declare that we have no conflict of interest.

REFERENCES

1. Mathews Prabha.; George Mathew.; Joseph Lincy.., *Journal of pharmaceutical, chemical and biological sciences.*, **2015**, 329-345.
2. Mishra Geeta.; Singh K. Arvind.; Jyoti Kshtiz., *International Journal of ChemTech Research.*, **2011**, *3*, 1380-1393.
3. Singh K. Arvind.; Mishra Geeta.; Jyoti Kshitiz., *Journal of Applied Pharmaceutical Science.*, **2011**, 44-49.
4. Malak Ajit Sajid.; Patil Satish Madhuri.; Mohd. Sahrif Mustakum., *Latin American Journal of Pharmacy.*, **2024**, 49-60.
5. Kumar Davinder.; Aggarwal Navidha.; Kumar Virender.; Kumar Harsh.; Deep Aakash.; Bibi Shabana.; Chopra Hitesh.; Marwaha Kumar Rakesh.; Alshammari Abdulrahman.; Alharbi Metab.; Hayee Abdul., *Pharmaceuticals.*, **2023**, 1-19.
6. Cakmak Sukriye.; Cavus Serdar Muhammet., *Cumhuriyet Science Journal.*, **2023**, 81-89.

7. Amer Zainab.; Al-Tamimi O. Entesar., *Chemical Methodologies*., **2022**, 608-611.
8. Yakan Hasan., *El-Cezeri Journal of Science and Engineering*., **2021**, *8*, 155-163.
9. Saki Neslihan.; Guzel Emre.; Yakan Hasan.; Cavus Serdar M.; Akin Mustafa.; Muglu Halit., *Computational Biology and Chemistry*., **2022**, 1-9.
10. Zabiulla.; Khadri Nagesh A Begum Bushra.; M K Sunil.; Khanum Ara Shaukath., *Results in Chemistry*., **2020**, 1-47.
11. El-Enany A. M. A Walled.; Gomha M. Sobhi.; Hussein Wesam.; Sallam A. Hanan.; Ali S. Rania.; El-Ziaty Ahmed., *Polycyclic Aromatic Compounds*., **2020**, 1-12.
12. Mohamed E.Ahmad.; Elgammal E. Walid.; Dawaba M. Aya.; Ahmed G. Ibrahim.; Fouda Amr.; Hassan M. Saber., *The Korean Society for Applied Biological Chemistry*., **2022**, 2-18.
13. Bayrak Hacer.; Taflan Ebru.; Er Mehtap.; Karaoglu Alpay Sengul Bozeveci Arif., *Bioorganic Chemistry*., **2019**, 1-10.
14. Cevil Acar Ulviye.; Osmaniye Derya.; Levent Serkan.; Saglik Nurpelin Begum.; Cavusoglu Kaya Betul Ozkay Yusuf Kaplancikl Asum Zafer., *Heterocycle. Commun*., **2020**, 6-13.
15. Cevik Acar Ulviye.; Osmaniye Derya.; Levent Serkan.; Saglik Nurpelin Begum.; Cavusoglu Kaya Betul Karaduman Burak Abdullah.; Ozkay Yusuf.; Kaplancikli Asim Zafer., *Acta Pharm*., **2020**, 499-513.
16. Ahadi Hamideh.; Shokrzadeh Mohammad.; khah-hosseini Zahra.; Barghi Ghassemi Nasirn.; Ghsemian Majid.; Emadi Elnaz Zargari Mehryar.; Razzaghi-Asl Nima.; Emami Saeed., *Bio-organic Chemistry*., **2020**, 1-28.
17. Pragathi Jyothsna Yazala.; Sreenivasulu Reddymasu.; Veronica Deekala.; Raju Ramesh Rudraraju., *Arabian journal for science and engineering*., **2021**, 225-232.
18. Hussain Rafaqat.; Shah Mazloom.; Iqbal Shahid.; Rehman Wajid, Khan Shoaib.; Rasheed Liaqat.; Naz Haseena.; Al-ghoulish A. Hanan.; Elkaeed B. Eslam.; Pashameah Adel Rami.; Alzahrani Eman.; Farouk Abd-ElAziem., *Frontiers in Chemistry*., **2022**, 1-17.
19. Gummidi Lalitha.; Kerru Nagaraju.; Ebenezer Oluwakemi.; Awolade Paul.; Sanni Olkaunle.; Islam Shahidul md. Singh Parvesh., *Bio-organic Chemistry*., **2021**, 1-12.
20. Li Sheng-Ya.; He Min.; Zhou Shun-Tao.; Wang Qin.; He Lulu.; Wang Jia-Si.; Hu Bei.; Wei Bin.; Wang.; Cui Ning-Zi., *European journal of medicinal chemistry*., **2021**, 1-9.
21. Hameed A. Sherin.; Varkey Joyamma.; Jayasekhar P., *International Journal of Pharma Sciences and Research*., **2020**, 152-159.
22. Hashem E. Heba.; E.Amr El-Galil Abd.; Nossier S. Eman.; Elsayed A. Elsayed, Azmy M., *Eman*., **2020**, 1-18.
23. Amrel Zainab.; Al-Tamimi O. Entesar., *History of Medicine*., **2023**, 2105-1210.
24. Amer., *Journal of Global Pharma Technology.,* **2019**, *11*(03), 433-438.
25. Anamaria Apan.; Dorina Casoni.; Denisa Leonte.; Cristina Pop.; Irina Iaru.; Cristina Mogos.; Valentin Zaharia., *Pharmaceuticals*., **2024**, 1-21.
26. Shivsharan Dhadde.; Dr. Swapnil Mohod.; Pratiksha Jadhav.; Anup Patil.; Swati Udugade., *International Journal of Medical Toxicology & Legal Medicine*., **2024**, 236-249.
27. Anamaria Apan.; Dorina Casoni.; Denisa Leonte.; Cristina Pop.; Irina Iaru.; Cristina Mogos.; Valentin Zaharia., *Pharmaceuticals*., **2024**, 1-21.
28. Ahmed M. El Saghier.; Asmaa Abdul Baset.; Omer M. El Hady.; Walaa M. Abd El Raheem.; Asmaa M. Kadry., *BMC Chemistry*., **2024**, *138*(1-21).
29. Naresh Podila.; Naveen Kumar Penddinti.; Mithun Rudrapal.; Gourav Rakshit.; Sathish Kumar Konidala.; Veera Shakar Pulusu.; Richie R. Bhandare.; Afzal B. Shaik., *Heliyon*., **2024**, 1-17.
30. G. S. Shakirzyanova.; L. Yu. Izotova.; O. Kh. Kholbekov.; F. Yu. Zhaloliddinov.; G. G. Rakhmonova, and B. N. Babaev., *Pharmaceutical Chemistry Journal.,* **2023**, 1898-1902.
31. Michelyne Haroun.; Maria Fesatidou.;Anthi Petrou.; Christophe Tratrat.; Panagiotis Zagaliotis.; Antonis Gavalas.; Katharigatta N. Venugopala.; Hafedh Kochkar.; Promise M. Emeka.; Nancy S. Younis.; Dalia Ahmed Elmaghraby.; Mervt M. Almostafa.; Muhammad Shahzad Chohan.; Ioannis S. Vizirianakis, Aliki Papadimitriou-Tsantarliotou.; Athina Geronikaki., *Molecules*., **2023**, 1-18.
32. Yasser M. Omara.; Samia G. Abdel-Motya.; Hajjaj H. M. Abdu-Allah., *Bio-organic Chemistry*., **2020**, 1-35.

33. Prateek Pathak.; Parjanya K. Shukla.; Vladislav Naumovich.; Maria Grishina.; Amita Verma.; Vladimir Potemkin., *Arch Pharm*., **2019**, 1-20.
34. Dinesh K. Mehta.; Poonam Taya.; Rina Das.; Kamal Dua., *Anti-inflammatory & Anti-allergy agents in medical chemistry*., **2019**, 91-109.
35. Yasser M. Omara.; Hajjaj H. M. Abdu-Allaha.; Samia G. Abdel-Moty., *Bioorganic Chemistry.,* **2018**, 1-34.
36. Ajit Kumar Pandey.; Pranita P Kashyap.; Chanchal Deep Kaur.; Hemant A Sawarkar.; Hemant J Dhongade.; Mukesh Kumar Singh.; Chiang Mai., *Journal Science*., **2018**, 917-926.
37. Anamaria Cristina.; Denisa Leonte.; Laurian Vlase.; László Csaba Bencze.; Silvia Imre.; Gabriel Marc.; Bogdan Apan.; Cristina Mogos, Valentin Zaharia., *Molecules*., **2018**, 1-19.
38. Debarshi Kar Mahapatra.; Ruchi S. Shivhare.; Animeshchandra G. M. Haldar., *Asian journal of chemical and pharmaceutical sciences*., **2017**, 27-32.
39. Anas M. H. Shkair.; Ashok K. Shakya.; Nulgumnalli M. Raghavendra.; Rajashri R. Naik., *Medical chemistry*., **2016**, 90-100.
40. S. Maddila.; S. Gorle.; Ch. Sampath.; P. Lavanya., *Journal of saudi chemical society*., **2012**, 306-312.
41. Sagar Sahu.; Tanesh Sahu.; Gunjan Kalyani.; Bina Gidwani., *Journal of pharmacopuncture*., **2021**, 32-40.
42. Thoraya A. Farghaly.; Magda A. Abdallah.; Mohamed R. Abdel Aziz., *Molecules*., **2012**, *146*, 25-14636.
43. Otilia Pintilie.; Lenuta Profire.; Valeriu Sunel.; Marcel Popa.; Aurel Pui., *Molecules*., **2007**, 103-113.
44. Vipan Kumar Kamboj.; Archana Kapoor.; Sandeep Jain., *Wiley library*., **2019**, 1-7.
45. Amgad M. Rabie.; Atif S. Tantawy, and Sahar M. I. Badr., *Researcher*., **2018**, 21-43.
46. Kemparaje Gowda.; Hassan A. Swarup.; Sandhya C. Nagarakere.; Shobith Rangappa.; Rangappa S. Kanchugarkoppal & Mantelingu Kempegowda., *Synthetic communication*., **2019**, 1-17.
47. Katarina Jakovljevic.; Milan D. Joksovic.; Bruno Botta.; Ljiljana S. Jovanovic.; Edina Avdovic.; Zoran Markovic.; Vladimir Mihailovic.; Marijana Andric.; Snezana Trifunovic.; Violeta Markovic., *Comptes rendus chimie*., **2019**, 585-598.
48. Kumar Sanjeev S. Lamani.; Oblennavar kotresh., *IISN*., **2010**, 545-550.
49. Bahram letafat.; Negar mohammadhosseini.; Ali asadipour.; Alireza foroumadi., *ISSN*., **2011**, 1120-1123.
50. Khare Ekta.; Singh Arvind Kumar.; H.S. Chauhan., Evaluation of Benzimidazole Derivatives by using aldehydes., *Research Journal of Pharmacy &Technology*., **2014**, *7*(3), 677-685.